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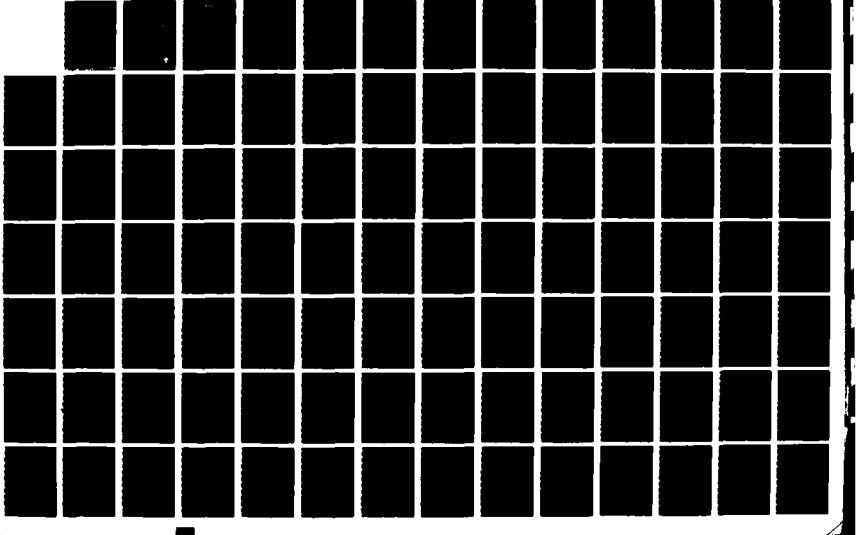

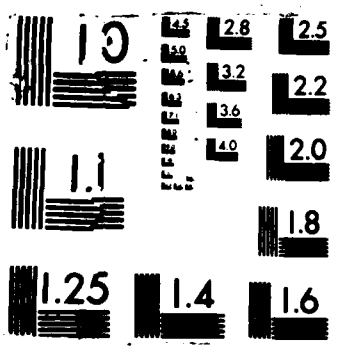
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CRITIQUE OF THE LITERATURE ON BIOEFFECTS OF RADIOFREQUENCY RADIATION: A COMPREHENSIVE REVIEW PERTINENT TO AIR FORCE OPERATIONS

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This report presents the analyses of research results and other pertinent information on the biological effects of radiofrequency radiation (RFR). The frequency range of primary interest is 10 kHz to 300 GHz. The main purpose of this report is to serve as a basic reference for other documents dealing with the environmental impact of proposed or currently operating USAF emitter systems with regards to health and safety aspects of exposure to RFR. The report is divided into 7 sections with various aspects of the present knowledge regarding biological effects of RFR. More than 600 references from the world's literature are cited.

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CRITIQUE OF THE LITERATURE ON BIOEFFECTS OF RADIOFREQUENCY RADIATION: A COMPREHENSIVE REVIEW PERTINENT TO AIR FORCE OPERATIONS

1 INTRODUCTION

1.1 DEFINITION OF "RFR"

The generic term "RFR" (radiofrequency radiation) will be used in this document to include other designations commonly found in the literature, such as microwave radiation, microwave fields, electromagnetic radiation (EMR), nonionizing electromagnetic radiation (NIEMR), electromagnetic fields (EMF), radiofrequency electromagnetic (RFEM) fields, and others. The frequency range of primary interest to the Air Force is from 10 kHz to 300 GHz. Where appropriate, however, frequencies lower than 10 kHz will also be included under the RFR rubric.

1.2 PURPOSE OF THIS REVIEW

This document is an updated and expanded version of an earlier review by Heynick and Polson (1983). Its primary purpose is to present analyses of research results and other pertinent information on the biological effects of RFR. It is to serve as a basic reference for other documents dealing with the environmental impact of proposed or currently operating Air Force radar and communication systems with regard to whether the health of people exposed briefly or chronically to the RFR transmitted by such systems is likely to be affected adversely. The various reports on bioeffects at power-line frequencies (50 and 60 Hz) or the uses of RF fields or currents for medical purposes (e.g., diathermy, hyperthermia, magnetic resonance imaging, repair, growth) are outside the purview of this document.

To foster use of this review by many individuals and organizations, and to facilitate retrieval of specific items by computer-automated search techniques, the information in this document is stored as a set of computer files in ASCII format, with special efforts to ensure maximum compatibility with personal and desktop computers. Toward that end, superscripts, subscripts, Greek letters, underlining, and any other embedded formatting commands (except for "hard" carriage returns, with a maximum of 72 characters per line) are not used. (As examples, "sq cm" is used to avoid the corresponding exponent superscript, and letters of the Greek alphabet are spelled out.) In addition, to eliminate the need for computergraphics capabilities, no graphs are presented; instead, the contents of graphs deemed important are described briefly in the text.

About a third of the papers on RFR bioeffects discussed herein had been analyzed previously; those analyses were published in a series of five reports: Heynick and Krebs (1981), Heynick (1982), Heynick and Polson (1984a,b; 1985).

The references cited in each major section or subsection are listed at the end thereof. Section 7 of this document is a master list of all the

reference citations in alphabetical order by first author (or organization acronym in appropriate cases). In square brackets after each citation in the printed version are the page numbers in which the citation appears; in the computer-stored version, the file designations for the sections or subsections are shown instead of page numbers.

1.3 LITERATURE SELECTION

Almost all of the papers selected for discussion in this document were published in scientific journals presumably after having been given peer review; the papers were organized by bioeffects topics. Presentations at recent scientific symposia or abstracts thereof were excluded from consideration (with few exceptions) under the assumption that either more complete and peer-reviewed accounts of such studies will appear subsequently or accounts will not be published at all (perhaps because the study was flawed or the investigators were not able to reproduce their results). Adequate numbers of papers were selected to provide a comprehensive coverage of each topic; those selected included accounts of early important studies as well as those embodying results of recent investigations.

Presentation of all of the currently available published information on RFR bioeffects, to comprise a virtually complete data base that includes discussion, analysis, and comparisons of findings, was not considered an appropriate goal in this project; the utility of such a complete data base in a review is questionable because the findings in many papers have been superseded by those obtained in later studies by researchers in the same laboratory by use of significant improvements in biological methodology, exposure systems, and techniques and instrumentation for measuring incident and absorption dose rates.

Note that sections on exposure systems and instrumentation, which were included in the earlier review, are not presented herein because such engineering aspects have become greatly diversified; instead, the novel features of the systems and instruments used in specific studies are described in the discussions of such studies if appropriate. It is also noteworthy that many uncertainties regarding the engineering aspects in the early studies of RFR bioeffects have been largely removed in recent studies and perhaps supplanted by questions about the correct usage of more recently developed, very sophisticated life-sciences methodology.

1.4 ASSESSMENT OF SCIENTIFIC INFORMATION AND RISK

In assessing potential biological effects of the RFR emitted from any specific system, consideration must be given to appropriate quantitative relationships among the following: (1) the physical parameters of the RFR (e.g., frequency, power density, polarization), (2) the distribution of the energy absorbed within the organism, and (3) the occurrence and magnitudes of effects that can be linked with exposure to the RFR, as determined by observations of functional or anatomic alterations. The body of experimental evidence for such effects can be used to formulate biophysical theories, and as is done in other scientific disciplines,

such theories are refined, revised, or discarded as valid new evidence accumulates.

The knowledge in any discipline can never be completed or closed, and it is scientifically impossible to prove with absolute certainty that any postulated phenomenon will not or cannot occur. Instead, scientists recognize that their findings are probabilistic in nature, in that the data for such findings or predictions therefrom contain various degrees of uncertainty, ascribable to the level of accuracy or precision of the instrumentation used and/or to uncontrolled variations in the subjects or population studied. Thus, results are usually reported to within some explicitly stated level of probability for a given population, and the applicability of the findings to a particular individual may be open to question. For example, the term "median effective dose" for a certain agent refers to the dose that will elicit the response characteristic of that agent in half of the exposed individuals. However, before the dose is administered, whether any specific individual will respond cannot be predicted, but the prediction that an individual will have a 50% chance of exhibiting the response is valid.

In effect, the probabilistic nature of scientific evidence means that no amount of scientific data, however large, can be used to guarantee the absolute safety of any agent for any individual or group of individuals. Analysts disagree over whether the conventional scientific approach, in which an investigator finds or fails to find a statistically significant difference (a predefined very low probability of chance occurrence) in the results between experimental and control groups, is appropriate to considering potential hazards to humans. The scientist's statement that the differences between the groups are not statistically significant is not equivalent to the absolute statement that there is no difference between the groups.

Experimental evidence regarding RFR bioeffects is derived from studies of laboratory animals and, sometimes, of humans who have been exposed to RFR. The characteristics of the RFR, the interaction mechanisms, and the biological responses are known at least qualitatively in some cases. To obtain the most directly applicable evidence about possible effects of any specific RFR-emitting system on humans would require experiments in which humans were exposed to its specific frequency range and likely power density values, and quantitative evaluation of such exposure on the many biological endpoints that may be suspect. Such data, however, do not exist, and for pragmatic reasons cannot be obtained. Instead, recourse is usually had to use of laboratory animals as surrogates for humans, a practice widely used for assessing possible effects of other agents. Thus, almost all of the information available on the effects of RFR on humans is indirect since it was derived primarily by projection of the findings with other species that have much different anatomies and functional characteristics than humans and that are usually studied with different RFR parameters and exposure durations.

Some investigations of human exposure to RFR have been done, either with volunteers or as epidemiologic studies. For obvious reasons, very

few of the former have been conducted. On the other hand, epidemiologic studies, also relatively few in number, elucidate the distribution of a physiological condition or disease in human populations and describe the factors influencing this distribution (Lilienfeld and Lilienfeld, 1980). Although such studies do deal with human subjects and thus might furnish direct evidence from a species standpoint, such epidemiologic evidence is also indirect: First, numerical values of the exposure parameters (particularly exposure levels and durations) vary widely with time for each individual and are highly variable from person to person; thus, they cannot be determined in detail. Instead, for example, the exposed group is often selected by occupation. Second, the extent to which the unexposed control group of people selected for comparison differs from the exposed population (other than in exposure to RFR) is critical in assessing the validity of the conclusions.

Regardless of the kind of evidence being considered, certain concepts and constraints affect the interpretation. In particular, scientists disagree over whether an effect, especially one that is reversible or can be compensated, constitutes a hazard. Furthermore, only rarely is any specific investigation subjected to confirmation by the performance of an identical experiment by another investigator. More often instead, an analogous--but not identical--experiment is conducted for the purpose of clarifying or expanding the results of the initial experiment. The later experiment ideally provides a better means of incorporating the findings into the theory underlying the knowledge in a particular field of investigation, but it does not necessarily confirm the results of the first investigation.

Conceivably, agents may have effects that are biologically real but so small in magnitude that the difference in mean response between the experimental and control populations may not be discernible within the scattering of values for both populations if the sample sizes are small. Biological studies to detect such small differences and to show that they are statistically significant (to a prespecified probability that they are not due to chance) would require the use of large numbers of animals and, in some cases, long exposure times. The expenditures in time and money necessary to perform such studies may be so large that sponsoring institutions with limited budgets often decide that such studies are not cost-effective with regard to the sponsor's overall objectives. A frequent alternative is to predict effects at very low levels by extrapolation from findings at higher levels, on the basis of assumptions about the mathematical relationship between the level (or dose) of the agent and the degree of the effect. Such assumptions are open to challenge, however, and this approach may lead to disagreement over the possible existence of a threshold dose or dose rate below which the agent has no effects.

Scientific experiments are often restricted to the evaluation of only one factor. In the real world, however, interactions are far more complex. The effect of combinations of factors is illustrated in the incidence of lung cancer in uranium miners, which is higher than in the general population, presumably because of the inhalation of radioactive

material. The increased incidence in nonsmoking miners is marginal, but miners who smoke cigarettes have a much higher incidence of lung cancer than either nonsmoking miners or the general population.

It must be remembered also that scientists have personal values, goals, and attitudes. It has been said frequently that unbiased experts do not exist, because to become an accepted authority requires a long personal commitment to the chosen field that automatically leads to emphasis of certain viewpoints. Thus, objectivity, like probabilistic scientific findings, may well be characteristic of scientists as a group but not necessarily of any individual scientist. The personal biases among the researchers in any study can consciously or subconsciously affect how an experiment is designed and how the data are interpreted. Particularly important is how the findings are applied to decision making, a process not necessarily involving the specific investigators, but others outside the field of expertise.

Assessment of risk to human health of environmental agents, including RFR, and setting of protection standards to reduce potential risk are extremely complex problems. In addition to technical and scientific questions, there are those of law, socioeconomics, and administration, often leading to risk-versus-benefit analyses. It is clearly beyond the scope of this document to deal with those subjects in detail, but it is important that they be mentioned.

The subject of the existence or nonexistence of thresholds for noxious or deleterious effects of various agents has been debated at length. As a practical scientific matter, thresholds do exist at least for some substances, because many naturally occurring substances are essential to life at specific concentrations and are toxic at higher concentrations (Horne, 1972). In this document, the possible existence of threshold levels is considered for various specific RFR effects where possible, with due regard for the physiological mechanisms of effect.

1.5 RFR SAFETY STANDARDS

Terms such as "safety standards" and "exposure standards" are generally applied to, and frequently used interchangeably with, specifications or guidelines for permissible occupational and/or nonoccupational exposure of humans to electromagnetic fields. Such standards are expressed as permissible exposure limits (PELs), threshold limit values (TLVs), or allowable maximum power densities or field intensities, in indicated frequency ranges and for stated exposure durations.

In 1982, the American National Standards Institute (ANSI) Subcommittee C95.IV adopted a frequency-dependent standard (ANSI, 1982) for both occupational and general-public exposure to RFR, to replace the ANSI Radiation Protection Guide, published in 1974, which was 10 mW/sq cm or the equivalent electric and magnetic field strengths over the entire frequency range from 10 MHz to 100 GHz (ANSI, 1974). The newer limits, like the older ones, are not to be exceeded for exposures averaged over any 0.1-hr period.

The 10-mW/sq-cm value in the older ANSI (1974) standard originated from the physiological consideration that whole-body exposure of a human to a level of about 100 mW/sq cm or more would cause mild-to-severe increase in thermal load (depending on the level), and by application of a safety factor of 10 to this lower power-density limit. Underlying this guide was the belief, based on the then-available scientific evidence, that nearly all workers could be exposed to RFR at 10 mW/sq cm or lower levels during the normal series of working days without adverse effects. Adoption of the guide also recognized that electromagnetic fields at or below the maximum allowable level might cause biological effects that have no medical consequences, or that workers could readily accommodate to such effects. The 1974 ANSI standard was promulgated by the Federal Occupational Safety and Health Administration (OSHA) for occupational exposure and was also adopted by other organizations, including the U.S. Department of Defense.

The 1982 ANSI standard, shown in Table 1, was derived from analyses of a large number of experimental and theoretical results selected by a subcommittee of ANSI C95.IV as representative of the state of knowledge at that time. The standard covers the frequency range from 300 kHz to 100 GHz and is based on a mean whole-body specific-absorption-rate (SAR) limit of 0.4 W/kg, which renders the incident power density frequency-dependent. The term "SAR," discussed in more detail in Section 2.1, is defined as the rate at which RF electromagnetic energy is imparted to an element of mass of a biological body. In the 1982 ANSI standard, the lowest power-density limit, 1 mW/sq cm, is for the range from 30 to 300 MHz, within which absorption of RFR by the human body as a resonant entity (Section 2.1) is highest. As with the 1974 ANSI standard, the value 0.4 W/kg contains a safety factor of 10, and the specified limits are not to be exceeded for exposures averaged over any 0.1-hr period.

TABLE 1: ANSI (1982) RADIOFREQUENCY RADIATION PROTECTION GUIDES

(1) Frequency Range (MHz)	(2) E-Squared (V-sq/sq-m)	(3) H -Squared (A-sq/sq-m)	(4) Power Density (mW/sq-cm)
0.3 - 3	400,000	2.5	100
3 - 30	4,000x(900/f-sq)	0.025x(900/f-sq)	900/f-sq
30 - 300	4,000	0.025	1.0
300 - 1,500	4,000x(f/300)	0.025x(f/300)	f/300
1,500 - 100,000	20,000	0.125	5.0

Note: f is the frequency in MHz.

In the far field of an RFR source, the governing maximum values are the power densities shown in column 4 of Table 1, and the corresponding

squares of the electric- and magnetic-field amplitudes (E-squared and H-squared) in columns 2 and 3 are approximate "free-space" equivalents, defined as follows for 1 mW/sq cm (10 W/sq m):

$$E\text{-sq} = (Z0) \times 10 \text{ W/sq m} \quad (1)$$

$$H\text{-sq} = (1/Z0) \times 10 \text{ W/sq m}, \quad (2)$$

where Z0 represents the impedance or value of E/H for free space, but rounded up from 377 to 400 ohms to yield limit values to one significant figure only.

In the near field of an RFR source, the governing maxima are the values of E-sq and H-sq. In such exposure situations, the values of E-sq and H-sq can be expressed in terms of their corresponding power densities by using equations 1 and 2, but primarily for convenience in expressing the entire standard in terms of one parameter (power density).

The 1982 ANSI standard has the following exclusions:

(1) At frequencies between 300 kHz and 100 GHz, the protection guides may be exceeded if the exposure conditions can be shown to produce SARs below 0.4 W/kg as averaged over the whole body, and spatial peak values below 8 W/kg as averaged over any one gram of tissue.

(2) At frequencies between 300 kHz and 1 GHz, the protection guides may be exceeded if the radiofrequency input power of the radiating device is 7 W or less. [This exclusion was provided in recognition that many low-power devices in common use by the general population may produce fields that appear to exceed the exposure guides in local regions of the body close to the devices but which would yield whole-body SARs much lower than those in the exposure guides.]

In consonance with an ANSI nominal five-year review cycle, Subcommittee C95.IV is undertaking examination of selected recent studies (as well as relevant earlier ones) in the literature on RFR bioeffects, with a view toward issuance of a revised standard in 1987. Small (if any) changes are expected in the 1987 standard for frequencies of 30 MHz and higher; the lower frequency limit will be extended downward to 3 kHz; based on experimental studies in the near field at frequencies below 30 MHz, the specifications for exposure to an electric field alone or magnetic field alone may be relaxed, leading to an upward shift of the 100-mW/sq-cm free-space-equivalent power-density limit; the new standard, however, probably will contain a specification of the maximum body current for contact by persons with large metallic objects immersed in RF (near) fields below 30 MHz, to avoid RF shocks or burns.

The American Conference of Governmental Industrial Hygienists published threshold limit values (ACGIH, 1984) also based on 0.4 W/kg but intended for occupational exposures only. These TLVs, to be averaged over any six-minute period, are shown in Table 2. Later ACGIH publications on this subject contained no revisions to these TLVs.

TABLE 2: ACGIH (1984) RADIOFREQUENCY/MICROWAVE THRESHOLD LIMIT VALUES

Frequency Range (MHz)	Power Density (mW/sq-cm)	E-Squared (V-sq/sq-m)	H-Squared (A-sq/sq-m)
0.01-3	100	377000	2.65
3-30	900/f-sq	3770x(900/f-sq)	900/(37.7xf-sq)
30-100	1	3770	0.027
100-1000	f/100	3770xf/100	f/(37.7x100)
1000-300,000	10	37700	0.265

TABLE 3: AFOSH (1984) MAXIMUM PERMISSIBLE LIMITS FOR EXPOSURE TO RFR (AVERAGED OVER ANY SIX-MINUTE PERIOD)

Frequency Range (MHz)	PEL for Average-Size Adult (mW/sq cm)	PEL for Small-Size Human (mW/sq cm)
0.01-3	100	100
3-30	900/f-sq	900/f-sq
30-100	1	1
100-300	f/100	1
300-1000	f/100	f/300
1000-1500	10	f/300
1500-300,000	10	5

Notes:
1) All exposures must be limited to a maximum (peak) electric field intensity of 100 kV/m.
2) f is the frequency in MHz.
3) Use the PELs under the heading "Average Size Adult" for Air Force workers and workplaces. Use the more restrictive PELs under the heading "Small Size Human" when assessing potential hazards in areas where the public has unrestricted access.
4) A small size human is an individual less than 55 inches (140 cm) tall.
5) When exposure is to multiple-frequency radiation, the sum of the fractions of the PELs at the separate frequencies must not exceed unity.
6) When an RF emitter operates over a band of frequencies in which the PEL varies, such as between 3 and 30 MHz, the lowest PEL shall apply.

One major difference between the 1982 ANSI and 1984 ACGIH standards is that the 1-mW/sq-cm value in the latter extends only from 30 to 100 MHz and rises with a slope f/100 at 100 MHz to 10 mW/sq cm at 1 GHz. This difference is based on the premise that children, who have higher whole-body resonant frequencies than adults (see Section 2.1), are not likely to be occupationally exposed to RFR. Also different in the 1984 ACGIH standard is that the equivalent free-space field intensities for 1 mW/sq cm are given by equations 1 and 2 but with Z0 = 377 ohms instead of the rounded up value 400 ohms. Last, the lower frequency limit for the 100-mW/sq-cm TLV of the ACGIH standard is at 10 kHz instead of 300 kHz. On

the basis of whole-body SAR, this TLV appears to be safe, but does not exclude possible occurrence of RF shocks or burns under some conditions. The 1984 ACGIH standard provides procedures for minimizing such possible hazards. The TLVs are intended for use in the practice of industrial hygiene only by persons trained in that discipline.

The currently applicable permissible exposure limits (PELs) for the Air Force are given in the Air Force Occupational Safety and Health Standard 161-9 (AFOSH, 1984). These PELs are shown in Table 3 above:

The AFOSH (1984) standard also provides guidance and procedures for the management of reported overexposures of Air Force personnel to RFR, a subject discussed in Section 3.1.3.

A system denoted as the Ground Wave Emergency Network (GWEN) is being implemented by the U.S. Air Force (GWEN, 1985). This system is designed to operate within the range 150-175 kHz, in the very-low-frequency (VLF) region. The U.S. Air Force has suggested a limit of 50 V/m for exposure of the general population to RFR from that system, with a view toward avoiding possible hazards of RFR shock or burn (see Section 3.1.4.4).

Scientific Committee 53 of the National Council on Radiation Protection and Measurements has issued its report (NCRP, 1986), in which a power-density exposure limit of 0.2 mW/sq cm for the frequency range 300 kHz to 100 GHz is recommended for the general population and the 1982 ANSI limits for occupational exposure. The fivefold lower value recommended for the general population (relative to 1 mW sq cm, the lowest value in the 1982 ANSI guide) is based on the assumption that the general public is exposed continuously (168 hours per week) and that the ratio of 40 hours in the work week to 168 hours is about 0.2.

The U.S. Occupational Safety and Health Administration (OSHA), which had promulgated the 10-mW/sq cm level of the 1974 ANSI guide as a voluntary occupational standard, subsequently found that the standard was legally unenforceable. In June 1985, the National Institute for Occupational Safety and Health issued a draft (NIOSH, 1985), for external review, of an occupational standard based on a maximum whole-body SAR of 2 W/kg instead of 4 W/kg, with a safety factor of 10 (0.2 W/kg), based on a review of the RFR-bioeffects literature, which included some reported findings of adverse effects in animals at SARs between 1.8 and 4.5 W/kg.

There is common agreement that non-occupational exposure standards for the general public should be more stringent than those for occupational exposure, based on the points that the general public is chronically exposed to RFR and that such standards should be sufficient to protect those who are potentially most vulnerable, such as children, pregnant women, the ill, and the elderly. The Environmental Protection Agency (EPA), which has been considering an exposure standard for the general population over a number of years, has not yet issued such a standard. The most recent EPA action on the subject at this writing was a "Notice of Proposed Recommendations" published on 30 July 1986 (EPA, 1986), in which 1 W/kg was given as the basis for a proposed standard for the

general public, with indicated reasons for the lower SAR. EPA had performed a comprehensive review of the literature (Elder and Cahill, 1984) to provide the rationale for the proposed standard.

Also presented in EPA (1986) were summaries of the population exposure levels estimated by EPA in 15 U.S. cities, field intensities measured in the vicinity of transmitting antennas atop several tall buildings and at other sites (see Section 1.6), and the three options under consideration for setting such standards based on risk/benefit/cost analyses (plus the fourth option of no action on issuing a general-population standard at this time). In essence, the three options are to base the standard on whole-body SARs of 0.04, 0.08, or 0.4 W/kg, respectively representing tenfold, fivefold, and no reductions from the 1982 ANSI basis.

In the absence of a governing Federal standard (but not necessarily for that reason), various state, county, and municipal governmental bodies have issued ordinances regarding exposure of the general population to RFR that in some cases are more considerably stringent than those of ANSI (1982). Petitions by the National Association of Broadcasters and other groups for a Federal standard to preempt state and local exposure standards are being considered by the Federal Communications Commission. However, preemption could become a legal issue between Federal and state bodies when EPA does promulgate its standard.

In the realm of standards in other countries, the Non-Ionizing Radiation Committee of the International Radiation Protection Association (IRPA), with participants from Australia, Denmark, France, Germany, Netherlands, Poland, the U.K., and the U.S., has published interim guidelines (IRPA, 1984) applicable to the general public as well as occupationally; the environmental health criteria issued by the World Health Organization (WHO, 1981) provided the rationale for this standard. For occupational exposure, the standard is based on 0.4 W/kg over the whole body or 4 W/kg in any 1 gram of tissue, and for general-public exposure, 0.08 W/kg and 0.8 W/kg respectively over the whole body and 1 gram of tissue (all averaged over any six minutes). Countries participating in IRPA, as well as others, have also issued separate national standards, some that are comparable to the 1982 ANSI standard and others more stringent.

Of particular interest are the current standards in the Eastern European countries, recently reviewed by Czerski (1985), who also provided some of the background that led to the adoption of the previous and current standards. In the USSR, the exposure limits (ELs) for occupational and general-public exposure are distinct. For frequencies below 300 MHz, the ELs are given separately for the E-field and H-field; for the range from 300 MHz to 300 GHz, the concept of "permissible energy load" or allowable product of incident power density and exposure duration (PT) is used in the occupational standard, subject to a maximum power density of 1 mW/sq cm. The current (1984) occupational ELs and PTs are shown in Table 4.

TABLE 4: USSR 1984 RFR OCCUPATIONAL STANDARD

Frequency (MHz)	E-Field EL (V/m)	H-Field EL (A/m)
0.06-1.5	50	5
1.5-3	50	*
3-30	20	*
30-50	10	0.3
50-300	5	*
300-300000	**	*

*No EL specification for H-field in this frequency range.
**PT = 2 W.hr/sq m for stationary fields; PT = 20 W.hr/sq m for rotating or scanning antennas (beams).

As noted by Czerski (1985), Savin et al. (1983) arrived at the lower PT value by analyzing data on animals indicating that exposure to 0.2 mW/sq cm [2 W/m] for 1 hr [PT = 20 W.hr/sq-m] does not yield untoward effects, and by applying a safety factor of 10.

The current (1984) USSR ELs for the general population in the frequency range 30 kHz to 300 MHz are presented in Table 5. No H-field ELs are specified. For the frequency range 300 MHz to 300 GHz, the limit is on power density, 0.1 W/sq m (0.01 mW/sq cm).

TABLE 5: USSR 1984 STANDARD FOR PUBLIC EXPOSURE TO RFR (0.03-300 MHZ)

Frequency (MHz)	E-Field EL (V/m)
0.03-0.3	25
0.3-3	15
3-30	10
30-300	3

Czerski (1985) also described the Czechoslovakian and Polish standards. These too are more stringent than the 1982 ANSI standard but less so than the 1984 USSR standards.

With the advent of frequency-dependent standards (e.g., ANSI, 1982), the differences in standards of Eastern-European and Western countries have diminished to some extent. It is especially noteworthy that standards for occupational exposure of these countries are in closer agreement among one another than are their respective standards for general-public exposure. Regarding the latter, differences in philosophy and the standard-setting processes are still extant. Only harmful effects are normally considered in the U.S., but the U.S. standards include safety factors to ensure that exposure to the specified maximum levels will not cause medically significant effects. By contrast, Trakhtenberg (quoted in Goldmann, 1982) in the USSR, for example, defined significant changes as "characterized by the deviation of the factors studied beyond the limits of annual or seasonal fluctuations by more than two standard

deviations away from the norm," but in many cases such deviations may not have medically important implications.

1.6 MEASUREMENTS OF ENVIRONMENTAL LEVELS OF RFR IN SELECTED U.S. CITIES AND AT SPECIAL LOCATIONS

Several years ago, the EPA measured the environmental field intensities at selected locations in 15 U.S. cities. The sites in each city were selected to permit analyses and estimations of cumulative fractions of the total population in each city exposed at or below various average power densities, based on the population figures derived from the 1970 census-enumeration districts. Tell and Mantiply (1980) and Janes (1979) presented the results for these cities (a total of 486 sites). These results were also summarized in Hankin (1985) and in EPA (1986).

Measurements of field intensity were made at 6.4 m (20 ft) above ground at each site in the following frequency ranges (Janes et al., 1977): 0.5-1.6 MHz (the standard AM-radio broadcast band), 54-88 MHz and 174-216 MHz (the VHF-TV bands), 88-108 MHz (the standard FM-radio broadcast band), about 150 and 450 MHz (land-mobile bands), and 470-890 MHz (the UHF-TV bands). The signals in each band were received with separate antennas designed specifically for each band. However, measurements in the standard AM-radio broadcast band were not included in the analyses because this band was below the then prevailing 10-MHz lower frequency limit of the 1974 ANSI standard.

The measured field strengths at each site were integrated over the frequency bands (54 to 890 MHz) included in the analyses and converted into equivalent average power densities. The site values in each city were then used, with the population figures for the census enumeration districts, in a statistical model designed to estimate the population-weighted median exposure value for that city, and for calculating other statistics of interest.

The population-weighted median value for each city was defined as the average power density at or below which half the population of the city was being exposed. The estimates were based on the assumption that the people were under continuous exposure at their place of residence; the estimates did not endeavor to account for population changes since the 1970 census, population mobility, exposure at heights greater than 6.4 m (20 ft), attenuation of signals by buildings, or periods of time when any of the contributing RFR sources were not transmitting. The fifteen cities and their median values are shown in Table 6:

TABLE 6: ESTIMATED POPULATION EXPOSURES FOR 15 U.S. CITIES IN MICROWATTS PER SQUARE CENTIMETER

City	Median exposure	Percent exposed to less than 1 microwatt per sq cm
Boston	0.015	98.50
Atlanta	0.016	99.20
Miami	0.0070	98.20
Philadelphia	0.0070	99.87
New York	0.0022	99.60
Chicago	0.0020	99.60
Washington	0.009	97.20
Las Vegas	0.012	99.10
San Diego	0.010	99.85
Portland (Oregon)	0.020	99.70
Houston	0.011	99.99
Los Angeles	0.0048	99.90
Denver	0.0074	99.85
Seattle	0.0071	99.81
San Francisco	0.002	97.66
All cities	0.0048	99.44

It is seen that the median exposures ranged from 0.000002 mW/sq cm (for Chicago and San Francisco) to 0.000020 mW/sq cm (for Portland, Oregon) and that the population-weighted median for all 15 cities was 0.0000048 mW/sq cm. Also, the percentages of the population exposed to less than 0.001 mW/sq cm in each city ranged from 97.2% (for Washington, D.C.) to 99.99% (for Houston, Texas), with a mean for all cities of 99.44%. The major contributions to these exposure values were from FM-radio and TV broadcast stations.

The EPA also measured RFR levels at sites close to single or multiple RFR emitters, e.g., at the bases of transmitter towers and at the upper stories (including the roof) of tall buildings or hospital complexes in the vicinity of transmitter towers. At the base of an FM tower on Mt. Wilson, CA, the fields were found to range from the equivalent of about 1 to 7 mW/sq cm (Tell and O'Brien, 1977). Most measurements in tall buildings near FM and TV transmitters yielded values well below 0.01 mW/sq cm, but a few values were close to or slightly exceeded 0.2 mW/sq cm (e.g., 0.23 mW/sq cm on the ro ` of the Sears Building, Chicago).

In Hawaii, however, considerably higher levels were recently found by EPA and FCC personnel in a few sites very close to AM (550 kHz to 1.5 MHz) broadcast towers and FM (88-108 MHz) broadcast towers (MICROWAVE NEWS, January/February 1985). Highest levels found were in the vicinity of several AM-broadcast stations. Next to a tower in Kaimuki having one FM station and three AM stations, for example, the maximum AM magnetic field was 9 A/m, the square of which is about 32 times higher than the 1982 ANSI standard for the frequency range 0.3-3 MHz. Whether transient or intermittent exposure to such AM-RFR levels would be harmful is the

subject of debate. In most areas accessible by the general public, the levels were within the 1982 ANSI standard.

REFERENCES:

ACGIH
THRESHOLD LIMIT VALUES (TLV) FOR CHEMICAL SUBSTANCES AND PHYSICAL AGENTS IN THE WORK ENVIRONMENT WITH INTENDED CHANGES FOR 1983-84
Ann. American Conference of Governmental Industrial Hygienists, Vol. 8, pp. 190-191 (1984)

AFOSH STANDARD 161-9
EXPOSURE TO RADIOFREQUENCY RADIATION
Headquarters, U.S. Air Force, Washington, DC 20330-5000 (1984)

ANSI C95.1-1974
SAFETY LEVEL OF ELECTROMAGNETIC RADIATION WITH RESPECT TO PERSONNEL
Published by the Institute of Electrical and Electronics Engineers, New York (1974)

ANSI C95.1-1982
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
Published by the Institute of Electrical and Electronics Engineers, New York (1982)

Czerski, P.
RADIOFREQUENCY RADIATION EXPOSURE LIMITS IN EASTERN EUROPE
J. Microwave Power, Vol. 20, No. 4, pp. 233-239 (1985)

Elder, J.A. and D.F. Cahill (eds.)
BIOLOGICAL EFFECTS OF RADIOFREQUENCY RADIATION
Final Report EPA-600/8-83-026F, Environmental Protection Agency, NC 27711 (September 1984)

EPA
FEDERAL RADIATION PROTECTION GUIDANCE; PROPOSED ALTERNATIVES FOR CONTROLLING PUBLIC EXPOSURE TO RADIOFREQUENCY RADIATION; NOTICE OF PROPOSED RECOMMENDATIONS
Federal Register (Part II), Vol. 51, No. 146, pp. 27318-27339 (30 July 1986)

Goldmann, N.
THE ROLE OF "OCCUPATIONAL HAZARD" DEFINITIONS IN THE ESTABLISHMENT OF MICROWAVE STANDARDS
Abstracts of Bioelectromagnetics Symposium, Los Angeles, CA, p. 2 (June-July 1982)

GWEN
GENERIC ENVIRONMENTAL ASSESSMENT FOR THE GROUND WAVE EMERGENCY NETWORK
Office of Public Affairs, Electronic Systems Division, Hanscom AFB, MA 01731 (April 1985)

Hankin, N.N.
THE RADIOFREQUENCY RADIATION ENVIRONMENT: ENVIRONMENTAL EXPOSURE LEVELS AND RF RADIATION EMITTING SOURCES
U.S. EPA Technical Report EPA 520/1-85-014 (1985)

Heynick, L.N. and J.S. Krebs
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-81-2ca 1-1
4 (November 1981)

Heynick, L.N.
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: SECOND REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-82-16 (May 1982)

Heynick, L.N. and P. Polson
BIOEFFECTS OF RADIOFREQUENCY RADIATION: A REVIEW PERTINENT TO AIR FORCE OPERATIONS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-1 (March 1983)

Heynick, L.N. and P. Polson
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: THIRD REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-84-6 (March 1984a)

Heynick, L.N. and P. Polson
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: FOURTH REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-84-17 (May 1984b)

Heynick, L.N. and P. Polson
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: FIFTH REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-85-7 (March 1985)

Horne, R.A.
BIOLOGICAL EFFECTS OF CHEMICAL AGENTS
Science, Vol. 177, pp. 1152-1153 (1972)

IRPA
INTERIM GUIDELINES ON LIMITS OF EXPOSURE TO RADIOFREQUENCY ELECTROMAGNETIC FIELDS IN THE FREQUENCY RANGE FROM 100 KHZ TO 300 GHZ
Health Phys. J., Vol. 46, No. 4, pp. 975-984 (1984)

Janes, D.E., R.A. Tell, T.W. Athey, and N.N. Hankin
RADIOFREQUENCY RADIATION LEVELS IN URBAN AREAS
Radio Sci., Vol. 12, No. 6S, pp. 49-56 (1977)

Janes, D.E.
RADIATION SURVEYS--MEASUREMENT OF LEAKAGE EMISSIONS AND POTENTIAL EXPOSURE FIELDS
Bull. N.Y. Acad. Med., Vol. 55, No. 11, pp. 1021-1041 (1979)

Lilienfeld, A.M. and D.E. Lilienfeld
FOUNDATIONS OF EPIDEMIOLOGY
2nd edition, Oxford University Press, New York and Oxford (1980)

NCRP
BIOLOGICAL EFFECTS AND EXPOSURE CRITERIA FOR RADIOFREQUENCY ELECTROMAGNETIC FIELDS
Report No. 86, NCRP Publications, Bethesda, MD 20814 (1986)

NIOSH
RADIOFREQUENCY/MICROWAVE OCCUPATIONAL EXPOSURE STANDARD AND RATIONALE, EXTERNAL REVIEW DRAFT
National Institute for Occupational Safety and Health, U.S. Department of Health and Human Services (1985)

Savin, V.M., K.V. Nikonova, and E.A. Lobanowa
NEW TENDENCIES IN STANDARDIZATION OF MICROWAVE ELECTROMAGNETIC RADIATION
Gigiena Truda i Prof. Zabolevaniya (in Russian), No. 3, pp. 1-3 (1983)

Tell, R.A. and P.J. O'Brien
AN INVESTIGATION OF BROADCAST RADIATION INTENSITIES AT MT. WILSON, CALIFORNIA
Tech. Note ORP/EAD 77-2, U.S. Environmental Protection Agency (1977)

Tell, R.A. and E.D. Mantiply
POPULATION EXPOSURE TO VHF AND UHF BROADCAST RADIATION IN THE UNITED STATES
Proc. IEEE, Vol. 68, No. 1, pp. 6-12 (1980)

WHO
ENVIRONMENTAL HEALTH CRITERIA 16, RADIOFREQUENCY AND MICROWAVES
World Health Organization, Geneva, Switzerland (1981)

2 INTERACTIONS OF RFR WITH BIOLOGICAL ENTITIES

Interactions of electromagnetic fields with biological entities often have been loosely characterized in the RFR-bioeffects literature as "thermal" or "nonthermal," usage that led to considerable confusion and controversy. It is therefore appropriate to provide working definitions of these terms at this point, with the understanding that the boundary between these types of interaction may not be sharp in some cases.

The interaction of an agent (e.g., RFR) with an entity (biological or nonbiological) can be characterized as thermal if the energy absorbed by the entity is transformed at the absorption site into heat. Absorption of heat, in turn, is defined in classical thermodynamics as either an increase in the mean random speed (or kinetic energy) of the molecules at the site (a local increase in temperature), or as an increase in the disorder or randomness of the molecular motion (entropy) unaccompanied by an increase in mean kinetic energy (a first-order phase change, such as the process involved in ice melting at 0 deg C), or a combination of the two processes.

An entity can also absorb energy at specific discrete frequencies in the form of energy packets or quanta, with each quantum yielding up energy to the entity in proportion to the discrete frequency of that quantum. Although large numbers of molecules can be involved, quantum absorption is essentially a microscopic phenomenon in that the constituents and configurations of the various molecular species comprising the entity determine the specific frequencies or characteristic spectra at which such absorption can occur. The kinds of interactions involved in such absorption are of varying degrees of complexity and the quantum energies involved cover a very wide range.

Interactions that require relatively large quantum energies include bond disruption within or between molecules and excitation of molecules or atoms to states of higher electron energy (including ionization). The activation energies for such interactions range from about 0.08 electron volts (eV) for hydrogen-bond disruption to about 10 eV for ionization. The corresponding quantum frequencies extend from about 19,000 GHz to 2.4 million GHz (Cleary, 1973). However, an electromagnetic quantum, at, say, 100 MHz, has an energy of 0.42-millionths of an eV or about 5-millionths of the energy required for hydrogen-bond disruption, so RFR quanta, even in great numbers, are most unlikely to be involved in such interactions.

On the other hand, changes of molecular orientations and configurations that do not alter the basic identities of the molecules require much lower quantum energies. Indeed, cooperative interactions occur among subunits of molecules within biological cells, in membranes and other cellular structures, and in extracellular fluids; in such interactions, the energy absorbed at one specific site in a structure (in a membrane or in a biological macromolecule, for example) may not be sufficient to disrupt a bond but could alter a process at the site or elsewhere in the structure, or trigger a function of the structure as a

whole by release of the energy stored in the structure, thereby producing biological amplification of the incident quantum of energy. Therefore, it has been postulated that such interactions could occur at frequencies that extend down into the RFR range as defined herein.

All quantum interactions such as those mentioned above are nonthermal, particularly if essentially all of the energy absorbed by the entity is used for such processes. If most of the absorbed energy is subsequently transformed locally into heat (as defined above), however, the thermal-vs-nonthermal distinction becomes blurred. Pragmatically, therefore, to characterize an RFR interaction with a biological entity as nonthermal requires that the interaction produce an effect sharply dependent on the specific RFR frequency and experimentally distinguishable from heating effects due to thermalization of the RFR energy absorbed.

It has been widely believed that since interactions of an incident field on a complex macromolecular structure such as a membrane are nonlinear, thermal equilibrium would be quickly attained by distribution of the incoming energy among the many macromolecular resonant normal modes of the structure. However, some current theories suggest that the incoming energy can be periodically exchanged among a few resonant modes for a relatively long time before being thermalized in the sense above, and thereby give rise to effects not ascribable to heat per se.

On the other hand, the mean thermal energy that corresponds to the physiological temperature 37 deg C is about 0.027 eV, with a relative maximum at about 6,500 GHz and a classical spectral distribution that encompasses the frequency range for cooperative processes. Therefore, as a counterargument to the manifestation of such nonthermal effects in vivo, it has been suggested that such effects would be swamped by those spontaneously induced thermally in vivo. Alternatively, separation of such RFR interactions from those thermally induced may require that the rates of occurrence of the former exceed the rates for the latter. This requirement implies that for manifestation of such effects of RFR, the intensity of the incident field must exceed minimum values or thresholds related to the specific processes.

2.1 THERMAL INTERACTIONS AND SPECIFIC ABSORPTION RATES (SARs)

The relative magnetic permeability of most organic constituents is about unity. Therefore, thermal interactions (as defined previously) of RFR with a biological entity are dependent on the complex-dielectric and thermal properties of its constituents and their distribution within the entity, as well as on the characteristics of the RFR.

Measurements of such properties were made some years ago for various mammalian tissues, blood, cellular suspensions, protein molecules, and bacteria over the spectral region from about 10 Hz to 20 GHz by Cook (1951, 1952) and by Schwan and coworkers (Schwan and Li, 1953; Schwan and Piersol, 1955; Schwan, 1957; 1963). In general, the dielectric constants were found to vary inversely with frequency, with distinct dispersion regions ascribed to three different predominant relaxation mech-

anisms. In the low and intermediate frequency ranges (from about 10 Hz to 100 MHz), the properties of cell membranes predominate because of their large specific capacitances (about 1 microfarad/sq cm). In the range above about 10 GHz, membrane impedances are negligible, and the behavior of the water and electrolyte content are most predominant.

In the frequency range from 3 to 30 MHz, the dielectric constant of muscle varies from about 360 to about 110. The values for skin, blood, and other tissues with high water contents are comparable. The values for fat, bone, and other tissues with low water content are about an order of magnitude smaller and are sensitive to the amount of water the tissues contain. From about 300 MHz to about 10 GHz, the dielectric constants of skin, muscle, and blood vary little with frequency. The mean dielectric constants of these three constituents are about 40, 50, and 60, respectively; the differences in values are largely ascribable to the proportion of water in each constituent, since the dielectric constant of water is about 80.

Subsequent in-vitro measurements were done with more advanced techniques and instrumentation as they became available. Among such studies were those of Lin (1975), Bianco et al. (1979), Schwan and Foster (1980), Foster and Schepps (1981), and Foster et al. (1982). Burdette et al. (1980) and Stuchly et al. (1981) measured the dielectric properties of various animal tissues in vivo at frequencies up to 10 GHz. Differences in dielectric constant and electrical conductivity found between in-vivo and in-vitro measurements of similar tissues were ascribed primarily to differences in water content. Stuchly and Stuchly (1980) tabulated data for the range from 10 kHz to 10 GHz.

Because the refractive index of a material is related to its dielectric constant, electromagnetic fields are reflected and refracted at the air-surface interface and at internal boundaries between constituents of widely different dielectric properties (for example, at the interfaces between connective and fatty tissues or between a body cavity and the adjacent tissues), thereby affecting the internal field distributions. At an air-muscle interface, for example, only about 22% of the incident power density of 100-MHz RFR is transmitted (the rest being reflected), and similarly, about 41% and 46% are transmitted for 1-GHz and 10-GHz RFR, respectively. The corresponding values for the air-skin interface are approximately the same.

At an air-surface interface, the fraction of incident energy that is not reflected enters the body and undergoes partial or complete absorption. The attenuation constant of any material (rate of energy absorption per unit distance along the propagation direction) is proportional to the square-root of the electrical conductivity of the material. For muscle, skin, blood, and other constituents of the body, conductivities increase slowly with frequency up to about 1 GHz, and rapidly from that frequency upward. The concept of "penetration depth" (the inverse of attenuation constant) is often used. For homogeneous isotropic planar specimens, the penetration depth is defined as the distance at which the electric-field amplitude is 1/e (37%) of its value or the power density

is 1/(e-squared) of its value just within the surface. At 1 GHz, for example, the penetration depth for muscle is about 2.4 cm, whereas at about 10 GHz and higher, field penetration is confined to the skin. Thus, in the latter frequency range, RFR penetration is much like that of sunlight.

In the RFR-bioeffects literature, absorption of energy from an incident electromagnetic field by a biological entity is generally quantified by the "specific absorption rate" (SAR). The SAR of a small volume at any locale within an entity is defined as the rate of energy absorption per unit volume divided by the mean mass density of the constituents in that volume, and is usually expressed in units of W/kg or mW/g (1 mW/g = 1 W/kg). The local value of SAR thus defined at any site within an entity depends on: the characteristics of the incident RFR (carrier frequency, modulation, amplitudes and directions of its components); the spatial distribution of complex-dielectric and thermal properties of the entity (including those of the site and its location within the entity); and the configuration of the entity and its orientation relative to the RFR.

For entities that have complex shapes and large spatial variations of constituents, distributions of local SAR are difficult to determine by experiment or by calculation. Thus, the concept of "whole-body SAR," which represents the spatial mean value for the body (in any specified configuration and orientation) is useful because it is a quantity that can be measured experimentally--e.g., by calorimetry--without the need for information on the internal SAR distribution.

Although SAR (local or whole-body) by this definition appears to be a measure of RFR-absorption as heat (true in most cases), it is also used as a measure of internal field intensities in studies characterized as nonthermal, in which the heat generated by the RFR is negligible.

After the SAR concept gained acceptance, many investigators calculated whole-body SARs for relatively simple geometric models (homogeneous and multilayered spheroids, ellipsoids, and cylinders) having masses and dimensions representative of various species (including humans), which were assumed to be exposed (in free space) to linearly polarized plane waves in various orientations. In some studies, such calculations were verified experimentally.

Many important results of such theoretical and experimental studies were embodied in a series of handbooks (Johnson et al., 1976; Durney et al., 1978, 1980), in which plots are presented of whole-body SARs (normalized to an incident power density of 1 mW/sq cm) vs frequency for three major orientations. Such plots have proved useful for approximate frequency-scaling and interspecies comparisons of whole-body SARs. A significant finding of such studies is that the largest value of whole-body SAR is obtained when the longest dimension of each model is parallel to the electric-field component (polarization direction) of the RFR and when the wavelength of the RFR is about 2.5 times the longest dimension. The frequency corresponding to this wavelength is often referred

to as the "resonant frequency" for that species. The whole-body SAR for each such model at its resonant frequency also varies inversely with the dimension of the model that is perpendicular to the polarization and propagation directions of the field. Thus, the model has absorption characteristics somewhat similar to those of a lossy dipole antenna in free space.

Resonances would also occur for circularly polarized RFR. Such RFR can be resolved into two mutually perpendicular components, each having half the total power density. Therefore, an entity exposed to circularly polarized RFR would have lower resonant SAR values than it would have if exposed to linearly polarized RFR of the same total power density.

Plots of whole-body SAR versus RFR frequency for the prolate-spheroidal homogeneous model of an "average" or "standard" man, about 5 ft 9 inches (1.75 m) tall and weighing about 154 lb (70 kg), are given in Durney et al. (1978), p. 78, for three orientations defined as follows: the "E-orientation," in which the long axis of the spheroid is parallel to the electric vector and perpendicular to the magnetic vector and propagation direction; the "H-orientation," in which that axis is parallel to the magnetic vector and perpendicular to the electric vector and propagation direction; and the "K-orientation," in which that axis is parallel to the propagation direction. The resonant frequency (E-orientation) for this model of a man is about 70 MHz; at this frequency, the SAR is about 0.2 W/kg for an incident power density of 1 mW/sq cm, or about 1/6 of his resting metabolic rate, or 1/21 to 1/90 of his metabolic rate for exercises ranging from walking to sprinting (Ruch and Patton, 1973).

Similar whole-body-SAR plots were presented in Durney et al. (1978), pp. 81 and 84 respectively for prolate-spheroidal models of the "average" woman and 10-year-old child exposed to 1 mW/sq cm of plane-polarized RFR. The average woman is assumed to be about 5 ft 3 inches (1.61 m) tall and to weigh about 135 lb (61.14 kg). Her resonant frequency is about 80 MHz and her whole-body maximum SAR is about the same as for the man. The child is assumed to be about 4 ft 6 inches (1.38 m) tall and 71 lb (32.2 kg). Its resonant frequency is still higher, about 95 MHz; its whole-body maximum SAR is about 0.3 W/kg, somewhat larger than for the adults. It is noteworthy that all three maximum SARs are smaller than the 0.4-W/kg value used as the basis for the current ANSI standard (ANSI, 1982).

To illustrate how the concept of whole-body SAR could be interpreted, consider the standard model man. Absorption of RFR energy as heat by exposure of such a model man at his resonant frequency (70 MHz) in the E-orientation to an average power density of 1 mW/sq cm (SAR 0.2 W/kg) for 1 hr would produce a mean body temperature rise of only about 0.2 deg C if no heat removal mechanisms were present and if no first-order phase changes were involved.

In general, the whole-body SAR at frequencies (f) below resonance in the E-orientation is approximately proportional to f-squared; at fre-

quencies above resonance, the whole-body SAR is approximately proportional to 1/f for about one decade of frequency and exhibits smaller relative maxima (secondary resonances) at higher frequencies. The data from which such plots were derived can be used to calculate, by simple proportion, the incident power densities necessary to produce an SAR of 0.4 W/kg. Plots of power density versus frequency derived in this manner are higher than the limits of the current ANSI standard, indicating that the ANSI limits are somewhat more stringent than such data.

Similar data for a prolate-spheroidal model of a "small" rat (0.14 m long and weighing 0.11 kg) are presented in Durney et al. (1978), p. 92. Not only is the resonant frequency in the E-orientation (about 900 MHz) higher than any of the values for humans, but the resonant SAR is also larger (about 1.1 W/kg for the rat, compared with about 0.2 W/kg for the adult human, per mW/sq cm). Therefore, in scaling experimental results from animals to humans, such differences of whole-body SAR as well as frequency must be considered.

The presence of a ground plane or other reflecting surfaces shifts the resonant frequencies downward and can produce higher values of whole-body SAR at the lower resonant frequencies (Gandhi, 1975; Gandhi et al., 1977; Hagmann and Gandhi, 1979). Hagmann and Gandhi (1979) showed that for a homogeneous block model (see below) of "standard" man standing in electrical contact with a perfectly conducting infinite ground plane, the whole-body resonant frequency (in the E-orientation) is shifted from the free-space value of 77 MHz to 47 MHz. Moreover, the whole-body SAR at 47 MHz is 32.5% higher than at 77 MHz. However, they also noted that such ground-plane effects are largely eliminated if conductive contact with the ground is removed.

The foregoing discussion of whole-body SARs is also largely applicable to modulated RFR (including pulsed RFR) at the corresponding carrier frequencies and time-averaged incident power densities.

Numerical calculations of internal spatial distributions of SAR have been done for "block" models. In such models, the shape of the body is approximated by an appropriate arrangement of many rectangular cells of various sizes, and each cell is assumed to be biologically homogeneous and to have constant internal field over its volume when the model is exposed to RFR. In addition, the biological properties ascribed to each cell are selected to approximate those of the tissues in corresponding locations of the body (Chen and Guru, 1977; Hagmann et al., 1979a, 1981; Chatterjee et al., 1980). More accurate values of whole-body SAR have been obtained with such models than from simpler ones.

Block models, as well as homogeneous and multilayered spheroidal and cylindrical models that have appropriate electromagnetic and thermal characteristics have been used also to represent various parts of the body, such as the head and limbs (Joines and Spiegel, 1974; Weil, 1975; Lin, 1975; Kritikos and Schwan, 1975, 1976; Neuder et al., 1976; Wu and Lin, 1977; Rukspollmuang and Chen, 1979; Massoudi et al., 1979; Hagmann et al., 1979a, 1979b, 1981; Janna et al., 1980; Spiegel et al., 1980;

Kritikos et al., 1981).

An early, very significant finding for spherical models of the isolated head assumed to be exposed to plane-wave RFR was the discovery of local regions of relative maximum SAR values. The locations of such regions depend on the size of the head, the electromagnetic characteristics of its layers, and the wavelength of the incident field. These regions have been dubbed "hot spots," even for combinations of incident power density and exposure duration that would produce temperature increases at such spots that are biologically insignificant. An analysis of a homogeneous lossy spherical-head model (Kritikos and Schwan, 1975) showed that in the frequency range from about 300 MHz to 12 GHz, there are hot spots inside spheres having radii between 0.1 and 8 cm; there are also internal hot spots for larger radii and other frequencies, but the hottest spots are at the front surface (facing the RFR source).

Similar results were obtained for multilayered spherical models (Weil, 1975; Kritikos and Schwan, 1976). Specifically, Kritikos and Schwan (1976) analyzed two such models, one with a radius of 5 cm and the other, 10 cm. For the 5-cm head, the hot spots are internal over the approximate frequency range from 400 MHz to 3 GHz. The highest relative maximum SAR occurs near the center of the head at about 1 GHz, and has a value of about 9 W/kg for an incident power density of 1 mW/sq cm. (Of course, the whole-head SARs are considerably lower.) By contrast, for the head of 10-cm radius (about that for an adult human head), no deep internal hot spots are produced at any frequency; the hot spots are always at or just beneath the front surface.

Rukspollmuang and Chen (1979) obtained qualitatively similar results for a block model of an isolated multilayered spherical head. They then studied, at 918 MHz and 2.45 GHz, a block model with shape and internal structure more closely approximating that of the human head (including eyes, nose, skull bone, and brain), and found that much of the energy within the head would be absorbed by the skull. In particular, frontal exposure of the more accurate model at 918 MHz would yield a maximum SAR for the brain region about one-third that for the brain region of a 7-cm-radius multilayered spherical model. Also, for frontal exposure of the model to 2.45 GHz, the induced field is concentrated primarily near the proximal surface, and therefore energy dissipation within the brain would be relatively low.

Hagmann et al. (1979b) calculated SAR distributions in the attached head of a block model of the human, and derived the whole-head and whole-body SARs for three orientations of the model relative to the source of RFR. For front-to-back propagation with the long axis of the body parallel to the electric vector, they found a broad head resonance at about 350 MHz, with a whole-head SAR of about 0.12 W/kg per mW/sq cm; the corresponding whole-body SAR is about 0.05 W/kg per mW/sq cm. For propagation in the head-to-toe direction, a sharper head resonance at 375 MHz was obtained, with whole-head and whole-body SARs respectively approximately 0.22 and 0.07 W/kg per mW/sq cm.

Results of theoretical analyses of whole-body SARs and SAR distributions have been verified experimentally. Physical models of simple geometry or of human- or animal-figurine shape were constructed from synthetic biological materials of electromagnetic characteristics about equivalent to their corresponding biological constituents. The models were exposed to RFR at power densities sufficient to produce accurately measurable temperature increases, which were measured immediately after exposure.

To use available sources of RFR that provide only specific frequencies and to avoid problems of exposing large full-scale models, smaller models are often chosen by use of scaling relationships so that results of exposing such smaller models at the available frequencies can be extrapolated to obtain results on full-size models at other frequencies of interest. Using this approach, Guy et al. (1976) exposed homogeneous human figurines having lengths of 37.6 and 26.5 cm (as well as spheres and ellipsoids) at approximately 143 MHz to simulate exposures of full-size figurines (1.74 m in length) at 31.0 and 24.1 MHz. In their study of head resonances, Hagmann et al. (1979b) exposed human figurines with lengths of 20.3, 25.4, 33.0, and 40.6 cm at 2.45 GHz, to correspond with full-size figurines exposed respectively at scaled frequencies of 284.5, 355.6, 462.3, and 569.0 MHz.

A technique widely used to determine the SAR distributions in physical models or animal carcasses is to embed such an object within Styrofoam, section the object along the parting planes of interest, reassemble the object, and expose it to RFR. Immediately after exposure, the spatial distribution over each parting plane is measured with scanning infrared thermography. However, such spatial temperature distributions should not be regarded as in direct correspondence with the in-vivo internal temperature distributions, because such carcasses and physical models have heat transfer characteristics much different from those of live animals and do not possess thermoregulatory mechanisms. Instead, such measured temperature distributions represent reasonable approximations to the distributions of internal field or SAR.

Guy et al. (1976, 1977) discovered that exposure of a full-size human figurine to an electric field parallel to its length at frequencies in the HF band yields relatively high SARs in regions of the body where the cross section perpendicular to current flow is relatively small, such as in the neck, knees, and ankles. In addition, exposure of the figurine to a magnetic field perpendicular to the frontal plane at frequencies in the same range produces eddy currents that yield relatively high SARs where such currents are forced through relatively small cross-sectional areas or are diverted by sharp angular changes, such as in the groin and along the sides of the body near the ribs. These results are especially pertinent to near-field exposure situations, for which it is necessary to measure the spatial variations of the electric and magnetic fields separately because their amplitude ratio may vary from point to point, and the field components may not be perpendicular to one another and to the propagation direction.

Whole-body (and detached whole-head) SARs, as well as (attached) part-body SARs, were measured by calorimetry alone or in conjunction with scanning infrared thermography by Hunt and Phillips (1972); Kinn (1977); Allen and Hurt (1979); Hagmann et al. (1979b); Olsen et al. (1980). Whole-body SARs were also determined in waveguide exposure systems by measuring the input, output, and reflected values of RFR power without and with the object present and performing the requisite arithmetic (Ho et al., 1973). The experimental results are in qualitative agreement with those derived from the theoretical models.

Burr and Krupp (1980) measured real-time temperature increases induced by 1.2-GHz RFR at 70 mW/sq cm in homogeneous spheres (3.3-cm radius); in Macaca mulatta cadaver heads (attached to the body and detached); and in living, anesthetized (attached) heads of the same species. They used a sensitive, accurate temperature probe (Bowman, 1976) that essentially does not perturb, or is not perturbed by, the RFR. The bodies of the animals were exposed with their longest axes parallel to the electric or magnetic component of the incident RFR (respectively the E-orientation or H-orientation). The results indicated that temperature distributions in attached cadaver heads vary strongly with body orientation. They also found that the temperature distribution in the head of the live animal is affected by blood flow in a complex manner not adequately predicted by current theoretical models.

Olsen (1984) measured SARs in a full-size model of a human exposed to far-field 2.0-GHz RFR, using a nonperturbing temperature probe and a gradient-layer calorimeter. Local SARs were much higher in the limbs than in the trunk, and the whole-body SAR was about threefold larger than the value estimated from a prolate-spheroidal model. The author suggested that resonant interactions involving the limbs may account for the disparity.

Hill (1984a) measured the whole-body SARs of five male volunteers at frequencies in the range 3-41 MHz. The subjects were exposed at about 0.01 mW/sq cm in a very large transverse electromagnetic (TEM) cell, with the long body axis parallel to the electric vector, and either in profile (EKH-polarization) or frontally (EHK-polarization) relative to the propagation direction. The exposures were done with the subjects ungrounded or grounded.

With the humans ungrounded, the SARs were found to be about 40% higher for the EKH-polarization than the EHK-polarization, but only about 6% higher with the humans grounded. Results were also presented, showing that the method used in making electrical contact between the feet and the ground plane is unimportant, that even use of a sheet of paper to eliminate direct conductive contact did not affect those SARs. Also reported was that for a grounded average human exposed to 3-41 MHz in the EKH-polarization to the power densities specified in ANSI (1982), i.e., 100 to 1 mW/sq cm in the range 3 to 30 MHz and 1 mW/sq cm for 30-41 MHz, the SAR over most of the frequency range is 0.58 +/- 0.14 W/kg, a value slightly higher than the 0.4 W/kg underlying ANSI (1982). Hill (1984b), however, found that for people with ordinary footwear, the SARs

are about half those for grounded humans at frequencies below resonance and about 20% lower near resonance, and thus do not exceed 0.4 W/kg.

Much of the dosimetry work discussed thus far was done for actual or assumed exposures to far-field (planar) RFR. Because of concern with possible hazards from the use of RFR in broadcast, industrial, and biomedical applications in which personnel are occupationally in the near field of the RFR, research has also been done to determine SAR distributions induced in such exposure situations (Chatterjee et al., 1980, 1981, 1982; Iskander et al., 1980; Karimullah et al., 1980; Spiegel, 1982; Stuchly et al., 1985a,b). As expected, the results are sensitive to the type, location, and orientation of the RFR source, as well as to the characteristics of the RFR and the properties of the biological entity exposed.

2.2 QUANTUM INTERACTIONS AND NONTHERMAL EFFECTS

The literature on theories of direct interactions of RFR with biological entities at the microscopic level (such as neurons and other cells) is extensive. Mechanisms of interaction have been proposed to account for various reported effects on cellular membranes, microtubules, DNA, and other intracellular structures and constituents, and on the transport of various ions and/or biomolecules across cell membranes. Topics such as these have been addressed in various symposia and review articles. The proceedings of several symposia have been published, e.g., Taylor and Cheung (1978, 1979), Illinger (1981), and Adey and Lawrence (1984).

A recent symposium for which the proceedings were not yet available at this writing is "Radiation Field Effects as Signal Transducing Mechanisms in Biological Systems," held at the University of Texas Health Science Center at San Antonio, TX, under the sponsorship of its Department of Pharmacology and of the Air Force Office of Scientific Research during 11-12 December 1985. Review articles by Cleary (1973, 1977, 1979), Adey (1981), Lawrence and Adey (1982), Froehlich (1980, 1982), and Taylor (1981) are representative.

Theories of direct RFR interaction have been proposed and/or used to account for various experimental results deemed by the investigators in many cases as nonthermal. Such studies will be discussed later herein under several appropriate topic headings (Auditory Effects, Blood-Brain-Barrier Effects, Calcium Efflux, Erythrocyte Studies, Cellular and Subcellular Effects, and possibly others).

2.3 INTERACTIONS OF MODULATED RFR

2.3.1 SINUSOIDAL AMPLITUDE MODULATION

The effects of sinusoidally-amplitude-modulated RFR that are ascribable to average power density per se (i.e., to the RFR-induced heat) do not differ from those for CW RFR or for frequency-modulated-CW (FMCW) RFR at the same carrier frequency and power density. However, studies

have been conducted with sinusoidally-amplitude-modulated RFR of specified characteristics, in which effects were described that were attributed to the frequency of the amplitude modulation per se, as well as the average power density, notably the calcium-efflux phenomenon. This phenonemon will be discussed in Section 3.4.4.

2.3.2 RFR PULSES AT LOW DUTY CYCLES

The temperature increase of any given region within a biological entity due to the arrival of a single RFR pulse would be small because of the relatively large thermal time constants of biological materials and the operation of heat-exchange mechanisms, unless the total energy within the pulse is extremely large (high enough peak power density and pulse duration). However, if the region contains a boundary between layers of widely different dielectric properties, the temperature gradient (rate of change of temperature with distance) can be large at such a boundary even if the mean temperature increase in the region is small.

A well known phenomenon that occurs in vivo is perception of single pulses, or of repetitive pulses of RFR that are short relative to the duration between pulses (low duty cycle), as apparently audible clicks, usually called the "microwave-hearing" or "RFR-auditory" effect. The interaction mechanisms involved are not yet fully understood. However, most of the experimental results tend to support the theory that pulse perception occurs because of transduction of the electromagnetic energy into sound pressure waves in the head at an interface between layers of widely different dielectric properties (e.g., at the boundary between the skull and the skin or cerebrospinal fluid). The energy in a pulse arriving at such a boundary is believed to be converted into an abrupt increase in momentum that is locally thermalized, producing a negligible volumetric temperature increase but a large temperature gradient across the boundary. Under such conditions, rapid local differential expansion would occur and create a pressure (sound) wave that is detected by the auditory apparatus.

The RFR-auditory effect has been characterized as nonthermal because the average power density can be minuscule. Specifically, the time-averaged power density for any two successive pulses is inversely proportional to the time interval between the arrival of the pulses at the perceiver and this interval can be indefinitely long without affecting the perception of each pulse. For this reason, the time-averaged power density has no relevance to perception. This effect and postulated mechanisms for its occurrence will be discussed more fully in Section 3.1.4.2.

Pulsed RFR has also been reported to produce other effects, such as alterations of the blood-brain barrier and behavioral changes. Such effects will be discussed in Sections 3.4.1 and 3.7.1, respectively.

REFERENCES:

Adey, W.R.
TISSUE INTERACTIONS WITH NONIONIZING ELECTROMAGNETIC FIELDS
Physiol. Rev., Vol. 61, pp.435-514 (1981)

Adey, W.R. and A.F. Lawrence (eds.)
NONLINEAR ELECTRODYNAMICS IN BIOLOGICAL SYSTEMS
(Proceedings of the International Conference on Nonlinear Electrodynamics in Biological Systems, held at Pettis Memorial Veterans Hospital under sponsorship of the Veterans Administration, Loma Linda, CA, during 5-9 June 1983), Plenum Press, New York (1984)
[2.1]

Allen, S.J. and W.D. Hurt
CALORIMETRIC MEASUREMENTS OF MICROWAVE ENERGY ABSORPTION BY MICE AFTER SIMULTANEOUS EXPOSURE OF 18 ANIMALS
Radio Sci., Vol. 14, No. 6S, pp. 1-4 (1979)

ANSI, C95.1-1982
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
Published by the Institute of Electrical and Electronics Engineers, New York (1982)

Bianco, B., G.P. Drago, M. Marchesi, C. Martini, G.S. Mela, and S. Ridell
MEASUREMENTS OF COMPLEX DIELECTRIC CONSTANT OF HUMAN SERA AND ERYTHROCYTES
IEEE Trans. Instr. & Meas., Vol. 28, No. 4, pp. 290-295 (1979)

Bowman, R.R.
A PROBE FOR MEASURING TEMPERATURE IN RADIO-FREQUENCY-HEATED MATERIAL
IEEE Trans. Microwave Theory Tech., Vol. 24, No. 1, pp. 43-45 (1976)

Burdette, E.C., F.L. Cain, and J. Seals
IN VIVO PROBE MEASUREMENT TECHNIQUE FOR DETERMINING DIELECTRIC PROPERTIES OF VHF THROUGH MICROWAVE FREQUENCIES
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 4, pp. 414-427 (1980)

Burr, J.G. and J.H. Krupp
REAL-TIME MEASUREMENT OF RFR ENERGY DISTRIBUTION IN THE MACACA MULATTA HEAD
Bioelectromagnetics, Vol. 1, No. 1, pp. 21-34 (1980)

Chatterjee, I., M.J. Hagmann, and O.P. Gandhi
ELECTROMAGNETIC-ENERGY DEPOSITION IN AN INHOMOGENEOUS BLOCK MODEL OF MAN FOR NEAR-FIELD IRRADIATION CONDITIONS
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 12, pp. 1452-1459 (1980)

Chatterjee, I., M.J. Hagmann, and O.P. Gandhi
AN EMPIRICAL RELATIONSHIP FOR ELECTROMAGNETIC ENERGY ABSORPTION IN MAN FOR NEAR-FIELD EXPOSURE CONDITIONS
IEEE Trans. Microwave Theory Tech., Vol. 29, No. 11, pp. 1235-1238 (1981)

Chatterjee, I., O.P. Gandhi, and M.J. Hagmann
NUMERICAL AND EXPERIMENTAL RESULTS FOR NEAR-FIELD ELECTROMAGNETIC ABSORPTION IN MAN
IEEE Trans. Microwave Theory Tech., Vol. 30, No. 11, pp. 2000-2005 (1982)

Chen, K.-M. and B.S. Guru
INTERNAL EM FIELD AND ABSORBED POWER DENSITY IN HUMAN TORSOS INDUCED BY 1-500-MHZ EM WAVES
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 9, pp. 746-756 (1977)

Cleary, S.F.
UNCERTAINTIES IN THE EVALUATION OF THE BIOLOGICAL EFFECTS OF MICROWAVE AND RADIOFREQUENCY RADIATION
Health Phys., Vol. 25, pp. 387-404 (1973)

Cleary, S.F.
BIOLOGICAL EFFECTS OF MICROWAVE AND RADIOFREQUENCY RADIATION
CRC Critical Reviews in Environmental Control, Vol. 8, pp. 121-156 (1977)

Cleary, S.F.
RECAPITULATION: BIOMEDICAL EFFECTS
Bull. N.Y. Acad. Med., Vol. 55, No. 11, pp. 1119-1125 (1979)

Cook, H.F.
DIELECTRIC BEHAVIOR OF SOME TYPES OF HUMAN TISSUES AT MICROWAVE FREQUENCIES
Brit. J. Appl. Phys., Vol. 2, pp. 295-300 (1951)

Cook, H.F.
A COMPARISON OF DIELECTRIC BEHAVIOR OF PURE WATER AND HUMAN BLOOD AT MICROWAVE FREQUENCIES
Brit. J. Appl. Phys., Vol. 3, pp. 249-255 (1952)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Durney, C.H., M.F. Iskander, H. Massoudi, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [THIRD EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-80-32 (1980)

Foster, K.R. and J.L. Schepps
DIELECTRIC PROPERTIES OF TUMOR AND NORMAL TISSUES AT RADIO THROUGH MICROWAVE FREQUENCIES
J. Microwave Power, Vol. 16, No. 2, pp. 107-119 (1981)

Foster, K.R., J.L. Schepps, and B.R. Epstein
MICROWAVE DIELECTRIC STUDIES ON PROTEINS, TISSUES, AND HETEROGENEOUS SUSPENSIONS
Bioelectromagnetics, Vol. 3, No. 1, pp. 29-43 (1982)

Froehlich, H.
THE BIOLOGICAL EFFECTS OF MICROWAVES AND RELATED QUESTIONS
In L. and C. Marton (eds.), ADVANCES IN ELECTRONICS AND ELECTRON PHYSICS, Vol. 53, Academic Press, pp. 85-152 (1980)

Froehlich, H.
WHAT ARE NON-THERMAL ELECTRIC BIOLOGICAL EFFECTS?
Bioelectromagnetics, Vol. 3, No. 1, pp. 45-46 (1982)

Gandhi, O.P.
CONDITIONS OF STRONGEST ELECTROMAGNETIC POWER DEPOSITION IN MAN AND ANIMALS
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 12, pp. 1021-1029 (1975)

Gandhi, O.P., E.L. Hunt, and J.A. D'Andrea
DEPOSITION OF ELECTROMAGNETIC ENERGY IN ANIMALS AND IN MODELS OF MAN WITH AND WITHOUT GROUNDING AND REFLECTOR EFFECTS
Radio Sci., Vol. 12, No. 6S, pp. 39-47 (1977)

Guy, A.W., M.D. Webb, and C.C. Sorensen
DETERMINATION OF POWER ABSORPTION IN MAN EXPOSED TO HIGH FREQUENCY ELECTROMAGNETIC FIELDS BY THERMOGRAPHIC MEASUREMENTS ON SCALE MODELS
IEEE Trans. Biomed. Eng., Vol. 23, pp. 361-371 (1976)

Guy, A.W., M.D. Webb, and J.A. McDougall
RF RADIATION ABSORPTION PATTERNS: HUMAN AND ANIMAL MODELING DATA
U.S. Dept. of Health, Education, and Welfare, National Institute for Occupational Safety and Health (NIOSH), Cincinnati, Ohio, Publication PB-274 749 (1977)

Hagmann, M.J. and O.P. Gandhi
NUMERICAL CALCULATIONS OF ELECTROMAGNETIC ENERGY DEPOSITION IN MODELS OF MAN WITH GROUNDING AND REFLECTOR EFFECTS
Radio Sci., Vol. 14, No. 6S, pp. 23-29 (1979)

Hagmann, M.J., O.P. Gandhi, and C.H. Durney
NUMERICAL CALCULATIONS OF ELECTROMAGNETIC ENERGY DEPOSITION FOR A REALISTIC MODEL OF MAN
IEEE Trans. Microwave Theory Tech., Vol. 27, No. 9, pp. 804-809 (1979a)

Hagmann, M.J., O.P. Gandhi, J.A. D'Andrea, and I. Chatterjee
HEAD RESONANCE: NUMERICAL SOLUTION AND EXPERIMENTAL RESULTS
IEEE Trans. Microwave Theory Tech., Vol. 27, No. 9, pp. 809-813 (1979b)

Hagmann, M.J., I. Chatterjee, and O.P. Gandhi
DEPENDENCE OF ELECTROMAGNETIC ENERGY DEPOSITION UPON ANGLE OF INCIDENCE FOR AN INHOMOGENEOUS BLOCK MODEL OF MAN UNDER PLANE-WAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 29, No. 3, pp. 252-255 (1981)

Hill, D.A.
THE EFFECT OF FREQUENCY AND GROUNDING ON WHOLE-BODY ABSORPTION OF HUMANS IN E-POLARIZED RADIOFREQUENCY FIELDS
Bioelectromagnetics, Vol. 5, No. 2, pp. 131-146 (1984a)

Hill, D.A.
EFFECT OF SEPARATION FROM GROUND ON HUMAN WHOLE-BODY RF ABSORPTION RATES
IEEE Trans. Microwave Theory Tech., Vol. 32, No. 3, pp. 772-778 (1984b)

Ho, H.S., E.I. Ginns, and C.L. Christman
ENVIRONMENTALLY CONTROLLED WAVEGUIDE IRRADIATION FACILITY
IEEE Trans. Microwave Theory Tech., Vol. 21, No. 12, pp. 837-840 (1973)

Hunt, E.L. and R.D. Phillips
ABSOLUTE PHYSICAL DOSIMETRY FOR WHOLE ANIMAL EXPERIMENTS
Digest of Papers of the Microwave Density Workshop, Atlanta, Georgia, Department of Microwave Research, Walter Reed Army Institute of Research (1972)

Illinger, K.H. (ed.)
EFFECTS OF NONIONIZING RADIATION
American Chem. Soc. Series ACS 157 (1981)

Iskander, M.F., P.W. Barber, C.H. Durney, and H. Massoudi
IRRADIATION OF PROLATE SPHEROIDAL MODELS OF HUMANS IN THE NEAR FIELD OF A SHORT ELECTRIC DIPOLE
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 7, pp. 801-807 (1980)

Janna, W.S., E.P. Russo, R. McAfee, and R.M. Davoudi
A COMPUTER MODEL OF TEMPERATURE DISTRIBUTION INSIDE A LOSSY SPHERE AFTER MICROWAVE RADIATION
Bioelectromagnetics, Vol. 1, No. 3, pp. 337-343 (1980)

Johnson, C.C., C.H. Durney, P.W. Barber, H. Massoudi, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-76-35, pp. 100-101, (1976)

Joines, W.T. and R.J. Spiegel
RESONANCE ABSORPTION OF MICROWAVES BY HUMAN SKULL
IEEE Trans. Biomed. Eng., Vol. 21, pp.46-48 (1974)

Karimullah, K., K.-M. Chen, and D.P. Nyquist
ELECTROMAGNETIC COUPLING BETWEEN A THIN-WIRE ANTENNA AND A NEIGHBORING BIOLOGICAL BODY: THEORY AND EXPERIMENT
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 11, pp. 1218-1225 (1980)

Kinn, J.B.
WHOLE BODY DOSIMETRY OF MICROWAVE RADIATION IN SMALL ANIMALS: THE EFFECT OF BODY MASS AND EXPOSURE GEOMETRY
Radio Sci., Vol. 12, No. 6S, pp. 61-64 (1977)

Kritikos, H.N. and H.P. Schwan
THE DISTRIBUTION OF HEATING POTENTIAL INSIDE LOSSY SPHERES
IEEE Trans. Biomed. Eng., Vol. 22, No. 6, pp. 457-463 (1975)

Kritikos, H.N. and H.P. Schwan
FORMATION OF HOT SPOTS IN MULTILAYER SPHERES
IEEE Trans. Biomed. Eng., Vol. 23, pp. 168-172 (1976)

Kritikos, H.N., K.R. Foster, and H.P. Schwan
TEMPERATURE PROFILES IN SPHERES DUE TO ELECTROMAGNETIC HEATING
J. Microwave Power, Vol. 16, Nos. 3 and 4, pp. 327-344 (1981)

Lawrence, A.F. and W.R. Adey
NONLINEAR WAVE MECHANISMS IN INTERACTIONS BETWEEN EXCITABLE TISSUE AND ELECTROMAGNETIC FIELDS
Neurolog. Res., Vol. 4, No. 1/2, pp. 115-153 (1982)

Lin, J.C.
MICROWAVE PROPERTIES OF FRESH MAMMALIAN BRAIN TISSUES AT BODY TEMPERATURE
IEEE Trans. Biomed. Eng., Vol. 22, pp. 74-76 (1975)

Massoudi, H., C.H. Durney, and C.C. Johnson
A GEOMETRIC-OPTICS AND AN EXACT SOLUTION FOR INTERNAL FIELDS IN AND ENERGY ABSORPTION BY A CYLINDRICAL MODEL OF MAN IRRADIATED BY AN ELECTROMAGNETIC PLANE WAVE
Radio Sci., Vol. 14, No. 6S, pp. 35-42 (1979)

Neuder, S.M., R.B. Kellogg, and D.H. Hill
MICROWAVE POWER DENSITY ABSORPTION IN A SPHERICAL MULTILAYERED MODEL OF THE HEAD
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. II, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8011, pp. 199-210 (1976)

Olsen, R.G., T.A. Griner, and G.D. Prettyman
FAR-FIELD MICROWAVE DOSIMETRY IN A RHESUS MONKEY MODEL
Bicelectromagnetics, Vol. 1, No. 2, pp. 149-160 (1980)

Olsen, R.G.
FAR-FIELD DOSIMETRIC MEASUREMENTS IN A FULL-SIZED MAN MODEL AT 2.0 GHZ
Bioelectromagnetics, Vol. 3, No. 4, pp. 433-441 (1984)

Ruch, T.C. and H.D. Patton
PHYSIOLOGY AND BIOPHYSICS
Vol. III, W.B. Saunders Co., Philadelphia, Pennsylvania (1973)

Rukspollmuang, S. and K.-M. Chen
HEATING OF SPHERICAL VERSUS REALISTIC MODELS OF HUMAN AND INFRAHUMAN HEADS BY ELECTROMAGNETIC WAVES
Radio Sci., Vol. 14, No. 6S, pp. 51-62 (1979)

Schwan, H.P. and K. Li
CAPACITY AND CONDUCTIVITY OF BODY TISSUES AT ULTRAHIGH FREQUENCIES
Proc. IRE, Vol. 41, pp. 1,735-1,740 (1953)

Schwan, H.P. and G.M. Piersol
THE ABSORPTION OF ELECTROMAGNETIC ENERGY IN BODY TISSUE, PART II
Amer. J. Phys. Med., Vol. 34, pp. 425-448 (1955)

Schwan, H.P.
ELECTRICAL PROPERTIES OF TISSUE AND CELL SUSPENSION
In ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS, Vol. 5, Academic Press, New York, pp. 147-209 (1957)

Schwan, H.P.
ELECTRICAL CHARACTERISTICS OF TISSUES: A SURVEY
Biophysik, Vol. 1, pp. 198-208 (1963)

Schwan, H.P. and K.R. Foster
RF-FIELD INTERACTIONS WITH BIOLOGICAL SYSTEMS: ELECTRICAL PROPERTIES AND BIOPHYSICAL MECHANISMS
Proc. IEEE, Vol. 68, No. 1, pp. 104-113 (1980)

Spiegel, R.J., D.M. Deffenbaugh, and J.E. Mann
A THERMAL MODEL OF THE HUMAN BODY EXPOSED TO AN ELECTROMAGNETIC FIELD
Bioelectromagnetics, Vol. 1, No. 3, pp. 253-270 (1980)

Spiegel, R.J.
THE THERMAL RESPONSE OF A HUMAN IN THE NEAR-ZONE OF A RESONANT THIN-WIRE ANTENNA
IEEE Trans. Microwave Theory Tech., Vol. 30, No. 2, pp. 177-185 (1982)

Stuchly, M.A. and S.S. Stuchly
DIELECTRIC PROPETTIES OF BIOLOGICAL SUBSTANCES--TABULATED
J. Microwave Power, Vol. 15, No. 1, pp. 19-26 (1980)

Stuchly, M.A., T.W. Athey, S.S. Stuchly, G.M. Samaras, and G. Taylor
DIELECTRIC PROPERTIES OF ANIMAL TISSUES IN VIVO AT FREQUENCIES 10 MHZ-1 GHZ
Bioelectromagnetics, Vol. 2, No. 2, pp. 93-103 (1981)

Stuchly, S.S., A. Kraszewski, M.A. Stuchly, G. Hartsgrove, and D. Adamski
ENERGY DEPOSITION IN A MODEL OF MAN IN THE NEAR FIELD
Bioelectromagnetics, Vol. 6, No. 2, pp. 115-129 (1985a)

Stuchly, M.A., A. Kraszewski, and S.S. Stuchly
EXPOSURE OF HUMAN MODELS IN THE NEAR AND FAR FIELD--A COMPARISON
IEEE Trans. Biomed. Eng., Vol. 32, nO. 8, pp. 609-616 (1985b)

Taylor, L.S. and A.Y. Cheung (eds.)
THE PHYSICAL BASIS OF ELECTROMAGNETIC INTERACTIONS WITH BIOLOGICAL SYSTEMS
U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 78-8055 (1978)

Taylor, L.S. and A.Y. Cheung (eds.)
THE MECHANISMS OF MICROWAVE BIOLOGICAL EFFECTS
Report of Workshop Held at University of Maryland, College Park, Maryland (May 14-16, 1979)

Taylor, L.S.
THE MECHANISMS OF ATHERMAL MICROWAVE BIOLOGICAL EFFECTS
Bioelectromagnetics, Vol. 2, No. 3, pp. 259-267 (1981)

Weil, C.M.
ABSORPTION CHARACTERISTICS OF MULTILAYERED SPHERE MODELS EXPOSED TO VHF/MICROWAVE RADIATION
IEEE Trans. Biomed. Eng., Vol. 22, pp. 468-476 (1975)

Wu, C.L. and J.C. Lin
ABSORPTION AND SCATTERING OF ELECTROMAGNETIC WAVES BY PROLATE SPHEROIDAL MODELS OF BIOLOGICAL STRUCTURES
IEEE Antenna & Propagation Society Int. Symp. Digest, pp. 142-145 (1977)

3 PRESENT STATE OF KNOWLEDGE REGARDING BIOLOGICAL EFFECTS OF RFR

3.1 STUDIES OF HUMANS

3.1.1 EPIDEMIOLOGIC/OCCUPATIONAL STUDIES

Epidemiology as used in this document refers to studies of whether one or more health-related conditions can be associated statistically with purported or actual RFR exposure of human populations (as distinguished from assessments based on extrapolation to humans of experimental data on animals). Epidemiologic results are frequently based on unknown or imprecise estimates of exposure characteristics (RFR frequency, power density, and duration). The extent to which the control group matches the exposed group in other than exposure characteristics is sometimes open to question. Because adequate matching of all relevant factors except exposure is the basis for concluding that observed differences between groups are related to the RFR exposure, the selection of an appropriate control group is critical. Despite possible limitations such as these, epidemiologic studies do provide most of the information available on possible effects of actual RFR exposure in humans.

Pazderova (1971), in one of the early epidemiologic studies on possible effects of RFR conducted in Eastern Europe, reported results of medical tests carried out in 1969-1970 on 49 male employees (mean age, 31.8 years) and 9 female employees (mean age, 33.9 years) of TV transmitter stations throughout Czechoslovakia. The males and females were employed for averages of 7.3 and 6.9 years, respectively, and represented two-thirds of all persons in that country thus employed. The exposure frequencies ranged from 48.5 to 230 MHz, and field intensities (with transmitter operating at maximum power and doors open) were up to 9.2 V/m (0.022 mW/sq cm free-space equivalent power density) with a mean of 2.9 V/m (0.002 mW/sq cm). The 58 subjects monitored the operation of the transmitters during most of their working shifts; in the remaining periods, they recorded and adjusted instrument readings and performed routine maintenance on the transmitters. The shifts varied in length but averaged 40 hours per week.

During a 5-day confinement at the Clinic of Occupational Diseases in Prague, the medical history of the subjects were recorded, with some attention also to their social histories and current non-shift-related activities. Each subject was given a complete medical examination that included chest x-rays and EKGs, and the female subjects were given gynecologic examinations. The data collected included pulse rate, blood pressure, and blood-sugar curves (by the Hagedorn-Jensen method), which were compared with data for corresponding age groups in the Czechoslovak population. Electrophoresis was used to determine blood-protein spectra (percentages of total protein; alpha-1, alpha-2, beta, and gamma globulins; and albumin-globulin ratio) of 54 of the subjects, and samples of venous blood were used for complete assays (erythrocyte, platelet, total and differential leukocyte counts; hemoglobin and hematocrit). The results of both sets of tests were compared by t-test with data for a control group of 55 healthy persons of mean age higher by 6 years.

The medical histories of the subjects showed no preponderance of any specific prior disease among the subjects, which "in itself excluded the possibility of any correlation between these diseases and exposure, and therefore we did not evaluate them statistically." Four males exhibited hypertension. In two of them, the hypertension was of the juvenile type. The third male, 60 years old, had pronounced signs of coronary insufficiency and not readily curable hypertension, and the fourth male exhibited an anginal syndrome as well as coronary insufficiency; both of these subjects also had pathologic EKGs; in all four subjects, hypertension had been diagnosed prior to their employment with TV transmitters. For the remaining subjects, the difference in their mean blood pressure and that of the control group was nonsignificant ($p>0.05$) and no pathologic EKGs were found. The blood-sugar level was pathologic only in the 60-year-old subject noted above, who also showed signs of general arteriosclerosis. The gynecologic examinations were pathologic for four of the female subjects, but the onset of the ailments preceded their employment and apparently did not impair their fertility.

The blood-protein spectra were tabulated. There were no significant differences between exposed and control groups except for mean total protein, which was significantly higher ($p<0.01$) in the exposed group, and mean alpha-1 level, which was also significantly higher ($p<0.05$). Regarding the blood assays, mean hemoglobin was barely significantly higher ($p=0.05$) for the males than for the control group, but the difference in hematocrit was nonsignificant ($p>0.05$). The mean total leukocyte and lymphocyte counts were significantly higher in the exposed than the control group, but the leukocytosis was a concomitant symptom of inflammation of the upper-respiratory or urinary tract in five of the subjects; the differences between the remainder of the exposed group and the controls were nonsignificant.

Also performed were liver tests (total and direct bilirubin, glucose tolerance, SGOT, and SGPT), the ESR test, urinalysis and microscopic examination of the sediment. The results were pathologic for one female who had and was under treatment for chronic liver damage and pronounced hypercholesterolemia.

Neurologic examinations were given to 56 of the subjects, including EEGs, with close attention to neurovegetative [autonomic-nervous-system] symptoms (erythema, Maranyon's syndrome [scoliosis and flatfoot, with ovarian insufficiency], dermographism, changes in acral temperature and sweating, tremor of the extended fingers, and changes of pulse rate during examination, due to emotional causes or respiratory arrhythmia). Entirely normal neurologic findings were obtained for 29 (52%) of the subjects. Abnormalities of various types characterized by the author as unquestionably unrelated to RFR exposure were seen in 13 (23%) of the subjects. The remaining 14 subjects (25%) showed abnormalities of a vegetative type, 3 subjects (5%) with histories preceding exposure and 11 (20%) without apparent exogenous or endogenous cause. By comparison, 16 of 57 members (28%) of a control group of the same age exhibited vegetative-type abnormalities. In the EEGs of the exposed group, there were no statistically significant differences in the distribution of the

normal, abnormal, and pathologic rhythms as compared with the controls.

Forty-six of the exposed subjects were randomly selected and underwent psychiatric examination. Of these, 19 (41%) had no psychic disorder. On the basis of their symptoms, the remaining 27 persons (58.7%) were classified into four subgroups: 18 subjects (39.1%) with minor neurotic disturbances that did not affect their ability to work or life style; 2 subjects (4.4%) with aberrant and psychopathic personalities tolerated by themselves or their environment; 5 persons (10.8%) with aberrant and psychopathic personalities with neurotic disturbances; and 2 (4.4%) who had records of institutional psychiatric treatment or showed psychotic traits during examination. By chi-square test, comparison of findings for the 46 subjects with those for a 21-member control group of the same age and educational background showed no significant difference between the groups and no correlation of findings with age or length of service.

All 67 subjects also completed psychological questionnaires directed toward the detection of neurasthenic symptoms. Neurotic complaints were reported less frequently in the exposed than the control group.

An ophthalmologist examined the eyes of the subjects, including the anterior segment of the eye in focal light, the lens under artificially induced mydriasis, and the lens refractive power. Intraocular tension was measured in the subjects older than 40 years and the field of vision was checked when indicated. The ophthalmologic results were compared by t-test with those for a control group of 106 healthy persons of mean age 33.1 years. Refractive disorders, including presbyopia, were found in 15 subjects. One subject had chronic conjunctivitis and another small cataracts. In general, the results were more favorable than in the control group, but the difference was not significant.

The author stated: "In the examined subjects we found no sign of damage due to electromagnetic radiation. Among the laboratory test results, the mean plasma protein levels were significantly increased. Even though we do not regard this as pathological, the possibility of its correlation with exposure to electromagnetic radiation cannot be ruled out. The other test results did not differ from those of the control groups."

In a later study, Pazderova et al. (1974) reexamined the effects on blood-protein levels of occupational exposure to RFR from transmitters operating in the TV range (60-300 MHz), "SW" range (3-30 MHz), and "MW" range (640-1500 kHz). In the TV range, 51 people were exposed to fields from about 0.5 to 9 V/m (0.0001 to 0.02 mW/sq cm). The mean age of the group was 35.2 years and their average exposure duration was 10.4 years. In the SW range, 19 people with a mean age of 39.3 years were exposed for an average of 16.8 years to about 66 V/m (1.2 mW/sq cm), and in the MW range, 39 people with a mean age of 41.3 years were exposed for 16.8 years to about 55 V/m (0.8 mW/sq cm). A group of 59 workers (35.4 years mean age) served as controls.

The authors, noting that the exposed persons in the previous study

came from all parts of the country whereas the control group lived in Prague and differed in their living standards, habits, and nutrition, stated: "The control group was chosen from the same regions as the exposed persons, and from the same social standard and living conditions. The only difference is that the exposed technicians worked in irregular shifts, while more than half of the people in the control group only worked morning shifts, but we have not found any data in the literature describing any influence of irregular shifts on the blood proteins."

The people in the exposed group were examined, primarily to detect and exclude persons with diseases known to influence blood chemistry, and blood was taken during their work shifts in the transmitting stations. The blood sample of each subject was examined twice in the laboratory (presumably at the Clinic of Occupational Diseases in Prague); the differences in results for any subject did not exceed 1%.

The results showed that the levels of blood proteins and their fractions were within physiologic limits, both mean values and individual ones, but statistically significant differences were found between the mean values for the control and exposed groups. Total blood proteins were significantly higher ($p<0.05$) for the MW group than the control; the alpha-one globulin values for the MW and SW groups were significantly higher ($p<0.01$) for all three exposed groups relative to controls, with the greatest elevation for the SW group. The alpha-two globulins were nonsignificantly ($p>0.05$) different, but gamma-globulin was depressed for the TV group and elevated for the MW group.

The authors stated: "Our previous findings confirmed the data from the literature on the existence of blood protein changes in persons and experimental animals exposed to electromagnetic radiation. To our great surprise, the character of the changes diverged from those so far described, as we did not find any elevation of gamma-globulin, which is considered to be typical. We are unable to explain this difference, unless we attribute it to the fact that, contrary to our previous investigation, blood was taken directly at the transmitting stations immediately after exposure to electromagnetic fields. This explanation still remains open to discussion. The more pronounced changes in radio technicians might be ascribed to the higher and longer exposures in comparison with TV technicians."

Klimkova-Deutschova (1974) surveyed 530 persons occupationally exposed to RFR in various industries in Czechoslovakia. From these, a sample of 352 workers was selected and analyzed by computer on the basis of 119 parameters, and divided into the groups quoted below:

"1. Workers engaged in metal welding, exposed to frequencies ranging from 0.5 MHz up to 3.5-32 MHz [levels not indicated].

2. Workers from two steel factories engaged in tempering steel and exposed to frequencies of 0.45-150 MHz, with a daily exposure of 50-112 V/m (0.66-3.3 mW/sq cm free-space equivalent power density), and occasionally 400 V/m (42 mW/sq cm).

3. Welders of plastics: frequency range 12-150 MHz, daily exposure 20-57.7 V/m (0.11-0.88 mW/sq cm).

4. Technicians operating television transmitters [frequencies and levels not indicated].

5. Workers at a radio transmitting station operating at a wide range of frequencies, from 6 MHz up to 30 MHz, and using a pulsed field system [pulse characteristics and levels not indicated].

6. Persons exposed to radiation in the 3-13 cm waveband working in industry and at research institutes with frequencies ranging from 3 GHz to 30 GHz. Intensity measurements showed permissible levels in some places, but in others values exceeding the permissible level ten or more times were found.

7. Persons working on a linear particle accelerator [frequencies and levels not indicated].

8. A mixed group which included the administrative staffs of two factories, who were not directly exposed to nonionizing radiation, some workers with exposures of less than 300 MHz and others with exposures of 300-800 MHz [levels not indicated]."

The general conclusions of the author are quoted below:

"(1) Confirmation that disturbances of the nervous system may be divided into three main stages: (a) the neurasthenic syndrome with autonomic disorders; (b) pseudoneurasthenia with similar subjective complaints, but with microsymptoms of an organic nature, especially in motor systems; and (c) very rare cases of encephalopathy.

(2) The occurrence of contralateral responses to cerebellar [pyramidal] and extrapyramidal disturbances facilitates the detection of early signs of extrapyramidal syndromes, which are identical with those caused by cerebellar irritation.

(3) The predominance of fatigue in certain of the exposed groups was paralleled by a reduction in vigilance, as noted in the EEG recordings and in earlier studies of higher nervous functions.

(4) The occurrence of synchronized EEG activity, with slow rhythms of high amplitude similar to those seen in epileptic seizures, taken in conjunction with the clinical and biochemical findings, permits the conclusion that the involvement of the nervous system is localized in the mesodiencephalic region. Such activity is seen in persons subjected to high levels of exposure, particularly in the form of a pulsed field.

(5) Possible explanations of the pathophysiology include direct penetration of the radiation into the midline structures and the thermal effect in the cisterna magna, which would explain the rare cases of arachnitis of the posterior fossae and the cerebellar phenomena. The

rectangular branching of the blood vessels of the temporal and basal ganglia explains the slowing of the blood stream in these parts of the brain, accompanied by reduced oxygenation. It may be assumed that the subclinical paroxysmal activity is induced by alkalosis resulting from these disturbances.

(6) The nonthermal effects and reversible neurotic manifestations may be attributed to the interruption of synaptic transmission and to changes in reflex activity under enzymatic influences."

Specific findings included EEG disorders (consisting of synchronized waves of high amplitude and slow rhythm) and biochemical changes (such as elevation of fasting blood glucose, serum beta-lipoprotein, and cholesterol). The changes in brain-wave patterns and in blood sugar, protein, and cholesterol levels were described as more pronounced in the people exposed in the 3-30 GHz range.

The author noted that "By making an exact evaluation of the extent of the disturbances, we were able to estimate that most of our patients had suffered less serious injury than had some other groups working with chemical noxious agents...A special feature of our results lies in the fact that when the investigations were started preventive measures were not strictly observed and less attention was paid to the hazards than is the case today. Nowadays, strict hygienic supervision of working places prevents the development of serious organic injury."

In presenting the results of this study, the author noted whether the differences among groups for specific manifestations were statistically significant at the 5% or 1% level, or not significant. Numerical data and statistical treatment thereof were not given, however, rendering it difficult to evaluate the findings or accept them at face value.

Kalyada et al. (1974) reviewed the results of prior studies (mostly their own), in which they clinically examined a group of specialists (number not given) under 40 years old in the USSR exposed to "non-thermal intensity within the range 40-200 MHz" by working with RFR generators for 1 to 9 years. They found no organic lesions, but noted the frequent occurrence of functional changes in the central nervous system (52%), the principal form of which was described as vegetative dysfunction accompanied by neurasthenic symptoms. They stated that the relationship between the frequency of neurodynamic disturbances and duration of work was clear-cut.

Several of the manifestations were biphasic. Specifically, for those employed for up to 1 year, the level of thermal-receptor activity was higher (about 160% of control level), and the temperature-sensitivity threshold and threshold excitability of the visual analyzer were both lower (80% and 50% of respective control levels). By contrast, for those employed for 3 to 9 years, the level of thermal-receptor activity was lower (about 60% of control level) and the temperature-sensitivity threshold and threshold excitability of the visual analyzer were both somewhat higher (about 110% and 120% of respective control levels.)

Among the specific changes reported were deviations in physicochemical and functional properties of erythrocytes and leukocytes, including lower osmotic resistance of leukocytes and lower phagocytic reaction that led to weakened immunobiological reactivity.

The authors also stated: "Experimental data obtained in volunteers under laboratory conditions of irradiation mimicking industrial variants revealed certain principles concerning general physiologic responses of the human body towards electromagnetic fields. The thermoregulatory system, some systems of hemodynamics and thermal, optical and auditory analysers proved most functionally reactive and sensitive to the influence of experimental irradiation. The dynamics of functional deviations were compared with those accompanying the presumed action of the factor. The irradiation was systematic with daily 15 min exposures and the 30 days' duration of each series of treatments. The ambient temperature ranged from 22.6 to 23.4 deg C with relative humidity of 40-46%. The results showed that some functional deviations took place during irradiation, while others followed it. The skin temperature of distal parts of the body (hands, feet) was elevated during the whole period of actual irradiation with simultaneous intensification of heat loss through emission and demobilization of heat receptors. The number of active cold receptors sharply increased."

No RFR intensity values were given for either the specialists or the volunteers. Most of the findings were presented in narrative form, with no actual data cited. Bar graphs showing changes, relative to controls, of a few specific parameters with exposure duration were given, such as the biphasic manifestations mentioned above, but the control group used for comparison was not described and no statistical treatment of the results was presented. Consequently, this paper per se yielded little basis for affirming or denying the occurrence of adverse effects of occupational or laboratory exposure of humans to RFR. (Translations of papers on prior studies cited by the authors were not available.)

Sadchikova (1974) presented clinical observations on the health status of two groups of USSR workers engaged in the regulation, tuning, and testing of diverse equipments emitting RFR at unspecified "microwave" frequencies. Both groups were comparable with respect to sex and age, but differed in intensity of exposure and duration of work. Those in the first group (1000) were exposed at levels up to a few mW/sq cm, whereas those in the second group (180) were exposed to values rarely exceeding several hundredths of a mW/sq cm; exposures to higher levels could have occurred during extremely short periods. Young men with long histories of employment (5-15 years) with microwave sources predominated in both groups. Some nervous tension during work could not be excluded. A group of 200 people matched with respect to sex, age, and character of work processes that did not involve RFR exposure served as controls.

Reported on as bar-graphs with standard-error bars for each group were percentage changes in 16 symptoms: five "neurologic" (head heaviness, tiredness, irritability, sleepiness, and partial loss of memory); six "autonomic-vascular" (inhibited dermographism, expressed dermographism,

hyperhidrosis, bradycardia based on pulse rate, arterial hypotension, and arterial hypertension); and five "cardiac" symptoms (cardiac pain, dullness of the heart sounds, systolic murmur, bradycardia by EKG, and lowering of deflections T-I and T-II).

For the higher-RFR group, the percentage changes were larger than for the control group for all symptoms except arterial hypertension, which was about the same. All of the percentages for the lower-RFR group were also higher than for the control group, except for arterial hypotension, which again was about the same. For 11 of the 16 symptoms, however, the percentage changes were larger for the lower-RFR group than the higher-RFR group. The authors did not provide statistical analyses of these results, but from the standard-error bars shown, some of the differences between each RFR group and the control group and between the two RFR groups appeared to be significant.

Eye examinations with the slit lamp revealed some lens opacities, mainly in the cortical layer and in superficial layers of the mature nucleus along its equator; only single opacities were found in the center. The numbers of opacities for the RFR groups did not exceed control values. However, the opacities progressed with increasing duration of exposure. A few subjects of the higher-RFR group who were said to have worked under unspecified "unfavorable" conditions developed cataracts. It seems likely that these persons had been exposed to power densities in excess of the cataractogenesis threshold (see Section 3.1.4.1).

The authors described the "asthenic syndrome" in detail, based on prior work as well as the results discussed in the paper. The progression of "microwave sickness" in 100 cases was described in a table in the paper; the text predicted little chance for recovery without patient removal from the work environment. However, symptomatology similar to asthenic syndrome or microwave sickness has not been reported in Western studies, so it is difficult to accept these USSR findings at face value.

Siekierzynski (1974) examined the health status and fitness for work of 841 men in Poland of ages 20 to 45 years who were occupationally exposed to pulsed RFR "of various frequencies within the whole range used in radar operations" (other characteristics not specified) during working hours for 2 to 16 years, depending on age. (By regression analysis, a high degree of correlation between age and duration of employment was found). Of these, 507 were exposed at average power densities exceeding 0.2 mW/sq cm (group I). The men "worked both in closed rooms and in the open, observing typical individual protective measures according to the regulations of work safety and hygiene existing in this country." The remaining 334 men (group II) were exposed at the same installations to less than 0.2 mW/sq cm. The author noted that exposure group II was selected for comparison because it was difficult to find an unexposed group who worked under otherwise similar specialized conditions. The hygienic factors, however, i.e., type and intensity of various stress factors, changes in circadian cycle, noise intensity, temperature and humidity of the rooms, etc., were comparable in the two groups.

All examinations were performed in the same clinic; the tests included ophthalmoscopy by slit-lamp and neurologic checkups supplemented with psychological tests and EEG recordings. After completion of clinical observation and possible treatment, a decision was made on each person regarding his fitness for further work in RFR environments. The author noted that only data for the most frequent problems were presented in this paper. The numbers of persons in each group were tabulated with regard to: (1) fitness for work in four categories (able to work or unfit because of ophthalmic, functional, or "other" disorders); (2) incidence of functional disorders in four categories (none, neurosis, gastrointestinal disorder, abnormal EKG); and (3) lens translucency (graded as 1, 2, or 3 degrees).

The mean percentages of occurrence and standard deviations of each fitness-, functional-disorder-, and lens-translucency characteristic in each group were determined, and their correlations with duration of employment and age were analyzed statistically by Student's t-test and Fisher's F-test, with significance taken at the 5% level. The results of those analyses were presented in a set of tables. For both groups, there was no statistically significant correlation between the causes of unfitness for work and duration of employment. Found within each group, however, was a significant correlation between lens translucency and age. Also significant was a correlation between lens translucency and duration of employment but only for group I, the group with the greatest pulsed-RFR exposure.

In summary, the findings of this study were negative with regard to the the effects of occupational exposure to RFR on the health status of either group. Additional details regarding specific aspects of this study were presented in three other papers: Czerski et al. (1974) and Siekierzynski et al. (1974a,b). Indicated therein was that the maximum exposure level of group I was 6 mW/sq cm "...during short periods of time, according to Polish rules about safe exposure" (Siekierzynski et al. 1974a).

Robinette and Silverman (1977), in a study of males (mostly white) who had served in the Navy during the Korean War, selected 19,965 equipment-repairmen as having had occupational exposure to RFR on the basis of their titles of Electronics Technician, Fire Control Technician, or Aircraft Electronics Technician. For comparison, the authors selected, and denoted for brevity as the "control group," 20,726 Naval equipment-operation men who, by virtue of their titles of Radioman, Radarman, or Aircraft Electrician's Mate, presumably had little occupational exposure to RFR. The mean age of the control group was about 1.5 years lower than of the exposed group. Used in the study were extant records of mortality for 1955-1974, in-service morbidity for 1950-1959, morbidity for 1963-1976 in Veterans Administration hospitals, and records of both granted and disallowed requests in 1976 for disability compensation.

Only mortality results were presented in this paper. There were 619 deaths (3.1%) from all causes in the exposed group versus 579 deaths (2.8%) in the control group; the difference was not statistically signi-

ficant. The authors noted that the death rates of both groups were lower than for the comparable age-specific white males (937 and 916) in the U.S. population at large.

These decedent data showed no significant difference between exposed and control groups in deaths from all disease, respectively 311 (1.6%) and 321 (1.5%), both significantly lower than for corresponding groups in the age-specific white male population, but the death rate from trauma was significantly higher ($p<0.01$) in the exposed than the control group, 295 (1.5%) vs 247 (1.2%). When the trauma deaths were divided into accident (motor-vehicle and "other"), suicide, and homicide categories, the only significant difference ($p<0.01$) between exposed and control groups was in the "other-accident" category, 130 (0.65%) vs 70 (0.34%). Examination of the death certificates and other mortality information about the men in the exposed group, however, showed that many had died in military-aircraft accidents after the Korean War, presumably because more of them later became flying officers (5.3% vs 2.3%).

The deaths from disease were divided into the following categories: all malignant neoplasms; cardiovascular (including vascular lesions of the central nervous system [strokes], and arteriosclerotic heart); chronic nephritis, other renal; influenza and pneumonia; and cirrhosis of the liver. In all these categories, the total numbers were less than those in the U.S. age-specific white male population. Also, none of the differences in total numbers between the exposed and control groups was significant, but the numbers of deaths associated specifically with arteriosclerotic heart disease were 8 (0.04%) vs 26 (0.13%), i.e., significantly lower ($p<0.05$) in the exposed group. The mortalities from cancer were also divided into various categories, but there were no significant differences between exposed and control groups.

Silverman (1979), in a review of RFR-epidemiologic studies, included this one of Naval personnel (with the two groups called "high-exposure" and "low-exposure" and with 144 and 55 additional men, respectively). The author noted: "There have been enough accidental exposures at estimated levels exceeding 100 mW/sq cm to indicate that there are occupations in which some men at some times on certain classes of ships have been exposed well in excess of the [then] 10 mW/sq-cm limit [citing Glaser and Heimer, 1971]." Also noted: "Shipboard monitoring programs in the Navy since 1957 show that men in other occupations rarely, if ever, were exposed to doses in excess of this limit. Radiomen and radar operators (our low-exposure group), whose duties keep them far from radar pulse generators and antennae, were generally exposed to levels well below 1 mW/sq cm, whereas gunfire control technicians and electronics technicians (our high-exposure group) were exposed to higher levels in the course of their duties."

Individual personnel records were used (in addition to assessing occupation) to determine length of time in occupation, class of ship, and power of equipment on the ship at the time of exposure, but because of cost and time considerations, these were done only for the men in the high-exposure occupations who had died from nonaccidental causes and for

a randomly selected 5% sample of living men in the same occupations. From this information, an index of potential RFR exposure called the Hazard Number was constructed for each man, defined as the product of the number of months of assignment to a ship or aircraft with the sum of the power ratings of all the gunfire-control radars aboard that ship or of all the search radars aboard that aircraft.

The percentages of men with high values of Hazard Number were much larger for the occcupations Fire Control Technician and Aircraft Electronics Technician than for Electronics Technician. However, the author did not present comparisons of mortality data among them.

Silverman (1979) concluded: "Differential health risks associated with potential occupational exposure to radar in the Navy more than 20 years ago are not apparent with respect to long-term mortality patterns or hospitalized illness around the period of exposure, two endpoints for which there is virtually complete information for the total study group. Later hospitalization (in Veterans Administration facilities only) and awards for service-connected disability, the two other endpoints examined, provide incomplete information. While some significant differences among the occupational groups classified by level of potential exposure have been found with respect to all endpoints studied, the differences could not be interpreted as a direct result of microwave exposure."

Morbidity data and other health-related aspects were not presented in either paper, but Silverman (1979) noted the possibility that effects involving the cardiovascular, endocrine, and central nervous systems may be transient and may disappear shortly after termination of exposure or not produce symptoms that warrant hospitalization.

The information above was also presented in Robinette et al. (1980). In addition, the numbers of admissions to Naval hospitals during 1952-1959 (except for 1955, for which the files were not available) and admission rates (per 1000 per year) for men in the low-exposure and high-exposure groups were tabulated by diagnosis (per International Classification of Diseases). Of 18 comparisons between groups, only two were significant: the low-exposure group had larger admission rates for mental disease ($p<0.001$) and for accidents, poisonings, and violence ($p<0.01$) than the high-exposure group. For no disease class was the admission rate of the high-exposure group significantly larger than of the low-exposure group.

Data were also obtained for admissions and admission rates to Veterans Administration (VA) hospitals during 1963-1976, but it was evident that admissions to VA hospitals comprised only small fractions of hospital care of these veterans, which precluded drawing any firm conclusions. Also examined were the numbers and rates (per thousand) of men who received VA compensation in December 1976 by diagnosis and exposure class. The only statistically significant difference was for mental conditions, 7.1 per thousand for the low-exposure group vs 4.8 per thousand for the high-exposure group ($p<0.01$).

In a letter, Morton (1981) questioned the basis used for selecting the high-exposure and low-exposure groups, stating: "Is it possible that no suitable controls existed among personnel assigned to shipboard duty?" In response, Robinette (1981) noted that: "A search for men of similar educational attainment, aptitude for technical work, and training by the Navy in their occupation, led to the selection of the equipment operators as members of the potential low-exposure cohort. The duties of these men required, for the most part, that they be below decks in areas where equipment was not being repaired and which were not traversed by operating radars."

The U.S. Embassy in Moscow was subjected to RFR from 1953, the year after the United States moved its chancery to Chekovsky Street, until February 1977 (Pollack, 1979). The presence of RFR had been detected intermittently before 1962, during routine surveillance of the building; continuous monitoring of the signals was instituted during that year.

Details regarding signal frequencies, characteristics, irradiation durations, and average power densities (or equivalent field intensities) at various locations within and on the roof of the chancery were given in a report issued by the National Telecommunications and Information Administration of the U.S. Department of Commerce, (NTIA, 1981). The signals consisted of up to 7 noise bands, each a few MHz wide, in the frequency range from 0.5 to 10 GHz, with maximum amplitudes in the 2-3 GHz range. The incident average power densities and exposure durations varied with the period: 5 microwatts/sq cm for 9 hr/day at inception in 1953, 15 microwatts/sq cm for 18 hr/day from June 1975 to 7 February 1976, and less than 1 microwatt/sq cm for 18 hr/day thereafter. Within rooms with windows or doors in outside walls toward the RFR sources, the levels were typically about 4 microwatts/sq cm within 2 ft of a door or window and 2.5 microwatts/sq cm elsewhere therein. The highest level cited was 24 microwatts/sq cm, which occurred in one room during a 2-hr period of unusual signal strength on 24 January 1976.

It is noteworthy that the maximum level cited was applicable only to one part of the embassy, so the exposure levels of most of the personnel for most of the time were probably well below the maximum permissible level (5 microwatts/sq cm) specified in the (then) USSR standard for exposure of the general population.

Lilienfeld et al. (1978) conducted a study of the health of the U.S. personnel assigned to the Moscow embassy during the period from 1953 to 1976, and for comparison, the health of those assigned to other U.S. Eastern European embassies. The authors, after expending considerable effort in tracing employees and dependents, identified 1,827 employees and 1,228 dependents as having been at the Moscow embassy during the 1953-1976 period. The control population consisted of 2,561 employees and 2,072 dependents assigned to embassies and consulates in Budapest, Leningrad, Prague, Warsaw, Belgrade, Bucharest, Sofia, and Zagreb during the same time period. Periodic tests for RFR at these control sites showed only background levels.

Medical records were reviewed for 1,209 of the Moscow employees and 834 of their dependents. The corresponding numbers for the control group were 1,882 and 1,507. Health questionnaires were returned by 969 Moscow employees and 1,129 control employees. The number of questionnaires completed by the dependents was not clearly indicated in the report.

The authors recognized and commented on the limitations of this study due to their inability to acquire complete sets of medical records, death certificates, and returned health questionnaires, and to the imprecision in classifying individual employees with regard to probable extent of RFR exposure. They also noted that the size of the study population was insufficient to detect excess risks that were less than twofold for many of the medical conditions studied. In addition, they indicated that highest RFR levels were recorded late in the period of irradiation and therefore, for the subgroup with the highest potential exposure, the period of time during which health effects might have become apparent was the shortest. However, despite these acknowledged limitations, the authors were able to draw the following conclusions.

No discernible differences were found between the Moscow and control groups in total mortality or mortality from specific causes, nor were there differences in mortality between the Moscow and control groups of dependent children or adults. The mortality rates for the Moscow and control groups were lower than for the U.S. population at large, with the exception of cancer-related deaths, which were fractionally higher among Moscow-female (8 of 11 deaths) than control-female employees (14 of 31 deaths). The authors stated: "It is difficult to attach any significance to the relatively proportion of cancer deaths in females because of the small numbers of deaths involved."

Although the study groups were subject to a large variety of health problems, the medical records indicated that these problems were shared nearly equally by both Moscow and control groups with two exceptions: The Moscow male employees had a threefold higher risk of acquiring protozoal infections, and both men and women of the Moscow group were found to have slightly higher frequencies of most of the common kinds of health conditions reported. However, the authors could not relate these two exceptions to RFR exposure.

The health-questionnaire information indicated higher incidences of some health problems in the Moscow employee groups than in controls: more correctable refractive eye problems; more cases of psoriasis in men; more cases of anemia in women; and more frequent cases of depression, irritability, difficulty in concentrating, and memory loss. The authors noted: "In view of the possibilities which had been publicized of the increased danger to their health and that of their children, it is not at all surprising that the Moscow group might have had an increase in symptoms such as those reported. However, no relationship was found between the occurrence of these symptoms and exposure to microwaves; in fact, the four symptoms mentioned earlier, which showed the strongest differences between the Moscow and Comparison groups, were all

found to have occurred most frequently in the group with the least exposure to microwaves."

For dependents, the authors found no differences between adult Moscow and control groups. The incidence of mumps in Moscow-based dependent children was twice as great as in the control children. The incidences of congenital anomalies in children born after arrival of the parents at their duty stations were comparable for the Moscow and control groups.

Lilienfeld et al. (1978) concluded: "With very few exceptions, an exhaustive comparison of the health status of the State and non-State Department employees who had served in Moscow with those who had served in other Eastern European posts during the same period of time revealed no differences in health status as indicated by their mortality experience and a variety of morbidity measures. No convincing evidence was discovered that would directly implicate the exposure to microwave radiation experienced by the employees at the Moscow embassy in the causation of any adverse health effects as of the time of this analysis."

Lester and Moore (1982a) postulated that prolonged, repeated exposure to weak RFR might be associated with increased cancer incidence. Because radars have been in operation at military air bases since World War II, the authors hypothesized that detectable increases in cancer mortality might be found in areas surrounding air bases. To test this hypothesis, they searched "Guide to Air Force Bases" (Air Force Magazine, 1969) to determine Air Force Bases (AFBs) in the continental United States that were operational in the period 1950-1969, and found 92 counties that had at least one AFB. They then determined the population of each of these counties from 1960-census data (CENSUS, 1967), and selected a control county for each AFB county, defined as the one in the same state that was closest in population (sometimes larger, sometimes smaller) but without an AFB. The mean population and standard deviation for the AFB counties were 237,684 and 254,683, respectively; the corresponding values for the non-AFB counties were 209,893 and 242,128. Statistically, these distributions did not significantly differ.

The authors indicated that data on civilian air bases for that period were not available. They also stated: "It should be noted that many counties in both groups had other air bases. Also, the counties varied considerably in geographic and economic characteristics. These factors would tend to bias the data against the hypothesis. Despite this confounding, the design demands that the presence of an AFB produce sufficient electromagnetic effect that it would be relatable to a higher cancer mortality in that county. No attempt was made to assess the possible role of other carcinogens."

Cancer mortality ratings (deaths from all types of cancer) for AFB and control counties were obtained from the "Atlas of Cancer Mortality for U.S. Counties: 1950-1969" (HEW, 1975). These mortality data were age-adjusted and presented in the following five categories with respect to cancer mortality in the general U.S. population (with index numbers

assigned by the authors):

MORTALITY RANKING	LESTER AND MOORE INDEX
Significantly high, in highest decile	4
Significantly high, not in highest decile	3
In highest decile, not significant	2
Not significantly different from U.S.	1
Significantly lower than U.S.	0

Data were available separately for males (M) and females (F). Lester and Moore (1982a) presented the results shown in Table 7 (their Table 1):

TABLE 7: CATEGORIES OF CANCER MORTALITY

	MALES		FEMALES		INDEX
	Counties		Counties		
	AFB	nonAFB	AFB	nonAFB	
	21	12	13	7	4
	2	1	4	2	3
	5	6	0	3	2
	16	21	33	34	1
	48	52	42	46	0
Totals	92	92	92	92	

From these results, the authors made the following assumptions:

"a. Categories 4 and 3 can be combined as significant incidence (+); categories 1 and 0 as nonsignificant incidence (-).

b. Category 2 can be deleted.

c. Since there was an effort to match counties by population, the proper statistical analysis is a test for correlated proportions comparing AFB with nonAFB counties."

The authors then reclassified their data in pairs as shown in Table 8 (their Table 2):

TABLE 8: RECLASSIFIED CANCER MORTALITY DATA

INCIDENCE	M	F
AFB (+) and nonAFB (+)	9	7
AFB (-) and nonAFB (-)	57	70
AFB (+) and nonAFB (-)	12	10
AFB (-) and nonAFB (+)	4	2
Totals	82	89

Their analysis of the data in Table 8 ("test for correlated proportions, corrected for continuity, one-tailed test") yielded p=0.04 for males, p=0.02 for females, from which they concluded that AFB counties, when compared with population-matched nonAFB counties, had significantly higher incidence of cancer mortality for the period 1950-1969.

This paper is one of only a few in the scientific literature to suggest that exposure to RFR is linked with increased cancer incidence and mortality. However, the results as presented do not confirm that increased cancer mortality is associated with RFR exposure, but only that such mortality appears to be correlated with the presence of an operational AFB.

The test for a statistically significant difference between AFB and control counties depends heavily on how well the control counties were matched with the AFB counties in all factors except presence of an AFB. The identities of the AFBs were not given in the paper, so on inquiry, Dr. J. Lester kindly made available the raw data. Review of these data revealed several apparent inconsistencies, so an independent analysis was conducted using the list of AFBs provided by Dr. Lester and the methodology described in the paper.

For the analysis, the Rand-McNally "1982 Commercial Atlas and Marketing Guide" (Rand-McNally, 1982) was used to ascertain the counties in which the specific AFBs were located. The populations of these counties were determined from CENSUS (1967), the reference used by Lester and Moore, and the control counties closest in population in the same state were identified. The categories of male and female cancer mortality for the control and AFB counties were obtained from HEW (1975), also used by Lester and Moore.

On reassembly of the raw data, the following emerged:

1. The total number of AFB counties is reduced to 91 because one county was counted twice (Luke AFB and Williams AFB are in the same county).

2. Of these 91, Lester and Moore located 13 AFBs in incorrect counties.

3. In 43 of the remaining 78 cases, Lester and Moore either used the incorrect control county (as defined above) or incorrectly assigned the M or F category to the control county.

4. Of the remaining 35 cases where Lester and Moore had selected the AFB and control counties correctly, there were 22 cases (16 counties) for which they had incorrectly assigned the M or F categories.

Thus, of the original 92 AFB/control county pairs of data used by Lester and Moore, only 19 and their M and F categories appeared to be correct.

Use of the corrected data for the 91 AFB counties yielded Table 9:

TABLE 9: REVISION OF TABLE 7

	MALES		FEMALES		INDEX
	Counties		Counties		
	AFB	nonAFB	AFB	nonAFB	
	16	10	9	7	4
	0	1	3	3	3
	6	8	0	2	2
	17	24	33	36	1
	52	48	46	43	0
Totals	91	91	91	91	

Reclassification of these data based on the assumptions of Lester and Moore yielded Table 10:

TABLE 10: REVISION OF TABLE 8

INCIDENCE	M	F
AFB (+) and nonAFB (+)	6	6
AFB (-) and nonAFB (-)	58	73
AFB (+) and nonAFB (-)	10	6
AFB (-) and nonAFB (+)	6	5
Totals	80	90

A statistician was consulted about the "test for correlated proportions" used by Lester and Moore. A test by this name does not appear in any of the references familiar to the statistician. However, McNemar's Test (Fleiss, 1981) is suitable and is similar to the test by Lester and Moore because use of this test yielded the same z and p values cited by Lester and Moore for Table 8 (their Table 2). McNemar's Test of the data in Table 10 yielded $z=0.7$, $p=0.23$ for males and $z=0$, $p=0.50$ for females, both nonsignificant.

In summary, a complete reanalysis of data for 91 AFB counties found by Lester and Moore (1982a) and the population-matched control counties not having an AFB did not confirm their finding. Instead, counties with an AFB had incidences of cancer mortality for either males or females, for

the period 1950-1969, that did not significantly differ statistically from those in counties without an AFB that were most closely matched in population. The original finding of significance by Lester and Moore (1982a) apparently was the result of an incorrectly assembled data base. This reevaluation was published by Polson and Merritt (1985) in the same journal, together with a response by Lester (1985), who took issue with some aspects of the reanalysis and did not accept the revised finding.

In another study, Lester and Moore (1982b) sought to determine whether there was a geographic pattern of cancer incidence within the city of Wichita, Kansas, and whether specific sources of RFR could be identified and related to any such pattern. They reported finding a neighborhood pattern of cancer incidence in that city, with the suggestion of a time element in its appearance, and noted that cancer tended to occur on leading terrain crests relative to radar transmissions and was less frequent in the valleys. They presented a formula relating cancer incidence to the terrain and the presence of RFR, leading to the overall finding that cancer incidence in Wichita appears to be related to the probability of exposure to radar.

Wichita is the largest city, population 262,766 (from a 1973 census) in Kansas. With the exception of two industrial areas, it is divided into 94 census tracts of approximately equal population. However, Lester and Moore (1982b) included only 76 tracts in their analysis. The Department of Community Health stratified the tracts into three health and economic classes (good, fair, poor), based on determinants such as education, income, crowding, unskilled workers, infant mortality, venereal disease, tuberculosis, and housing. Wichita is virtually free of air pollution (ranked second out of 52 major cities of over 80,000 population in the U.S.), presumably removing that agent as a possibly confounding factor.

The city lies on essentially a flat plain bisected by the Arkansas River, with two low ridges (100-ft and 20-ft elevation changes) to the west and northwest of the city limits. Wichita Mid-Continent Airport lies 9.7 km southwest and 35 ft higher than the city center. McConnell AFB lies 7.2 km southeast and 130 ft higher than the city center.

Morbidity data were obtained on all first diagnosed cancer cases of Wichita residents for 1975, 1976, and 1977 from five city hospitals, 3004 cases total for the three years. The ratio of number of diagnosed cases to tract population for each year yielded the incidence rates for 76 census tracts. The information on incidence rates, age, economic stratification (of the tract of residence of each person), male/female ratio, and race were analyzed, and a correlation matrix was obtained for the 76 tracts. Also obtained were mortality data for all cancer deaths of Wichita residents for 1975, 1976, and 1977. Again, incidence rates, age, economic stratification, male/female ratio, and race were analyzed, and a correlation matrix obtained for the 76 census tracts.

The formula derived by the authors for treating the data was based on the following hypotheses: First, the major contributors to RFR exposure

were radar transmitters at the airports. Second, radar exposure is a line-of-sight phenomenon. Third, RFR exposure correlates directly with elevation. Fourth, shielding by intervening terrain confounds the elevation criterion of exposure.

This paper is replete with flaws, the most serious of which is that the authors, "to find a possible connection between cancer incidence and external electromagnetic fields," assumed that the population is exposed only to the RFR from radars at the two airports adjacent to the city. They cited no measurements to support this assumption and gave no indication that the scan sectors of such radars were considered. It is noteworthy, however, that the Environmental Protection Agency (EPA) measured ambient RFR levels in 15 major cities around the U.S.A. (Tell and Mantiply, 1980), which showed that by far the major contributors to environmental levels of RFR are FM and TV broadcast transmitters, not radar systems (Janes, 1979). Even though EPA did not include Wichita as one of the cities it surveyed, it would be reasonable to assume that the RFR environmental situation there differs little from those of the 15 cities surveyed.

If the radar assumption above is to be considered correctly, a model of RFR exposure should be used that is based on the physical laws of RFR propagation, particularly the inverse-square-law of attenuation with distance and the RFR shielding effects of artificial structures and buildings, as well as of terrain. Other flaws in the paper were the arbitrary assumptions for the heights of the radars and the false sense of precision imparted by citing the city and airport elevations to five significant figures ("average" elevations accurate to within 5 mm).

Unfortunately, the model used by the authors bore no relationship to such factors, and any conclusions drawn therefrom are unrelated to actual exposure levels. Instead, the results of this paper appear to be a good example of spurious correlation. Any relationship between radar exposure and cancer incidence, if such exists, is not demonstrated by the data and analysis presented in this paper.

Milham (1983) used an age and year-of-death standardized proportionate mortality ratio (PMR) program to analyze the information on 429,926 male decedents for 1950-1979 and 25,066 female decedents for 1974-1979 in Washington State, and published detailed cause-of-death analyses (160 causes) for each of 219 male and 51 female occupational categories. The author stated:

"The Washington State mortality pattern is, in general, consistent with both the Registrar General's results and with the published literature. Some of the new occupational mortality findings published in the 1950-1971 report and in this updated version have been confirmed. Others warrant follow-up. These include a lung cancer excess in workers at the ASARCO Tacoma copper smelter, increased mortality due to multiple myeloma and pancreatic cancer in workers at the Hanford atomic energy facility, and excess mortality due to cancer of the pancreas, lymphoma, leukemia, and emphysema in aluminum workers.

"New findings in this report are a leukemia increase in workers exposed to electric and magnetic fields and a deficit of multiple sclerosis deaths among outdoor workers."

In this report, 20 microfiche negatives were provided in addition to 167 pages of text; these microfiches contain the detailed raw mortality data and calculated PMRs for males and females by gender occupations. (The "occupation" of each decedent was obtained from the statement on the Washington-State death certificate.) Also contained in the microfiches is additional information on occupations ranked by PMR within each cause of death and causes of death with significantly ($p<0.05$) elevated or reduced PMRs by occupation, both for males only. Eighty pages of the printed report described the occupation codes (common for both men and women) used in filling out the death certificates, occupation groupings for men, occupation groupings for women, an index of occupations for men, and an index of occupations for women.

The analysis by Milham (1983) progressed from raw mortality information through successive clusterings of data in like occupational groupings, presumably in order to obtain sufficient numbers in each cluster for meaningful statistical analysis. The statistical method used was the PMR, and a detailed example of one such calculation was given in the report (p. 96). However, the statistical method used by the Registrar General is the more common and widely accepted standardized mortality ratio (SMR) (Lilienfield and Lilienfield, 1980).

In the printed report, 63 pages contain one-paragraph commentaries describing the mortality pattern as seen by the author in each of the occupation groupings. There are 219 such commentaries for males and 51 for females. Some of these commentaries appear to be highly subjective and to reflect the personal biases of the author. For example, the commentary below on female mortality in one occupation appears on p. 63:

"Waitresses
Occupation code 875
Total deaths 862

Cancers of the esophagus, stomach, larynx, lung, cervix and uterus unspecified have increased PMRs. Psychoses, pulmonary emphysema, cirrhosis of the liver, motor vehicle accidents, and homicide have mortality increases. Much of this mortality pattern may be due to life-style patterns, i.e., smoking, drinking, and promiscuity."

Other commentaries seem to include some nonsignificant but elevated PMRs because the author apparently believes that they contribute to the over-all mortality pattern considered appropriate by him for that occupation. For example (p. 54):

"Dietitians and Nutritionists
Occupation code 073
Total deaths 104

These women show a significant excess of malignant neoplasms of the digestive organs (PMR=254 based on 7 deaths) in the 20-64 age class. This is due to 4 deaths observed due to cancer of the pancreas to less than 2 expected. Malignant neoplasms of lymphatic and hematopoietic tissues (age 20-64) show a PMR of 476 based on 5 deaths, 3 of which were in the other lymphoma category. Diabetes mellitus had a PMR of 225 based on 5 deaths."

It is seen that of 104 total deaths in this occupation for women, the author selected 17 deaths and presented them as though dietitians and nutritionists might be expected to die more often of malignant neoplasms of the digestive organs and diabetes mellitus. The other 87 deaths were ignored. This clearly demonstrates a subjective and selective bias in the author's application of the PMR analytical technique.

The author carried the analysis one step further by examining mortality by cause of death and showing occupational groupings with statistically significant elevations or reductions in PMR. There are several problems with some of the patterns that emerged in this treatment. For example, in the commentary on male mortality by occupation within cause-of-death groups is the following (p. 67):

"Malignant Melanoma of Skin (ICD 190)

Three of the four occupations with high PMRs (clergymen, school teachers, hotel managers) have no obvious relationship to outdoor work or exposure to sunlight. Navy and Coast Guard personnel, however, probably are exposed to sunlight."

This presumption that Navy and Coast Guard personnel have elevated PMRs for malignant melanoma of the skin because they are exposed to sunlight would seem to indicate a considerable bias on the part of the author. He did not indicate why these personnel would spend more time in the sun than school teachers, for instance, other than his personal belief that they do so.

In the next step in the analysis, the author examined the mortality patterns of groups of selected occupations that appeared to have similar environmental exposures. It is here, in one page of the entire report (p. 75), that categories of workers presumed to be occupationally exposed to magnetic and/or electrical fields are juxtaposed, and PMRs for two categories of leukemia (acute leukemia, and all leukemia) are presented. There are 11 occupations: electrical engineers, electronic technicians, radio and telegraph operators, electricians, power and telephone linesmen, television and radio repairmen, motion picture projectionists, aluminum workers, streetcar and subway motormen, power station operators, and welders and flame cutters. Of the 22 categories for the two leukemia categories by 11 occupations, there are 3 cases where the PMR is significant at the 1% level, plus 2 at the 5% level. The other PMRs, though elevated in 13 cases and depressed in 3 (with 1 the same), are not statistically significant. The significant cases, electricians (both categories of leukemia), aluminum workers (both cate-

gories of leukemia), and power station operators (all leukemia only), comprised 79 of the total of 136 leukemia deaths actually observed in these occupations. The excess number of deaths (observed minus expected) for these three occupations was 28. At this point, the author is quoted on the PMR technique (p. 5):

"The major flaw of the proportionate mortality ratio (PMR) is that it says nothing about total force of mortality for a given occupation... All occupations have a total PMR of 100. Also, since the cause-of-death specific PMRs must sum to 100, a very high or low PMR in a common cause-of-death group will affect the other PMRs for that occupation."

In other words, by virtue of the technique itself, the 5 significantly high PMRs mentioned above might have arisen because other PMRs in three of the 11 occupations were abnormally low. In view of this point, great credence cannot be given to the author's claim that the increased PMRs for all leukemia and for acute leukemia are associated with exposure to electric and magnetic fields. The other point to be made is that there must be a dose-response relationship to conclude that cause-and-effect applies in this or other epidemiologic studies. Such a relationship is at best unproven here. Without exposure data for the individuals or even for the occupations, it is solely an assumption that persons in these occupations actually do experience greater exposure to electrical and magnetic fields than do those in other occupations. For example, electricians, the occupation with the largest number of leukemia deaths (51), actually spend a large part of their time working on circuits that are not energized.

Perhaps the strongest criticism of this study as a whole is that it demonstrates an approach that statisticians commonly refer to as "data mining." A very large data base is "picked over" for "nuggets" of (locally) statistically significant items, which are then assembled to show purported relationships. Unfortunately, there is no a priori hypothesis being tested. Normal statistical methodology is reversed--statistical significance is found first and then the hypotheses are formulated. Results from such an approach generally are considered to not carry much weight.

In summary, when viewed in the context of the complete report of occupational mortality in Washington State, the claim that workers who had been exposed occupationally to electric and magnetic fields showed increased incidence of all leukemia and acute leukemia is seen to be weak at best. The methodological approach used did not meet the normal criteria for the statistical testing of hypotheses--no hypotheses were assumed a priori. The commentaries on patterns of mortality underlying different occupations from which the groups, such as the electrical and magnetic field workers were selected, seemed to show personal bias by the author, and the PMR technique has analytical problems that could have yielded an apparent increase in the PMR in one cause-of-death category from an abnormally low PMR in one or another category. The relationship between leukemia and exposure to electric and magnetic fields therefore should be treated cautiously until better analytical

techniques are used and better exposure information is obtained. (These criticisms apply equally to the cause-and-effect relationships claimed in the report for other agents and occupations.)

Milham (1982) presented a brief initial report on this study as a correspondence item, which gave few details on the statistical treatment of the data. Liburdy (1982) commented unfavorably on this item.

Hamburger et al. (1983) noted that physical therapists are known to use various diathermy modalities (characterized by the authors as microwave, shortwave, infrared, and ultrasound equipment) in the course of treating patients. They therefore endeavored to determine whether therapists might be suffering adverse health effects from exposure to the emissions from such units on a dose-related basis by statistically analyzing the responses from male members of the American Physical Therapy Association (APTA) to a mail questionnaire. The only consistently significant finding was an apparent association between heart disease and exposure to shortwave radiation.

Although other factors were considered in the questionnaire, emphasis was placed on those health experiences reported in the literature as being associated with exposure to low levels of RFR. The responses requested from each subject included occupational history of diathermy utilization by length of employment in each position held since entering the clinical affiliation and the number of treatments of each modality administered per typical work week. Ascertained from the responses was that for the operators under 35 years of age, the mean time spent within 3 ft of the equipment was 2.4 min per treatment with microwave diathermy and 2.7 min per treatment with shortwave diathermy. (The therapist usually initiates a treatment, then leaves to attend other matters for the remainder of the treatment.) Other factors considered were the frequency of treatments, the years of work experience, and the use of infrared and ultrasound diathermy.

The authors also cited a survey, conducted by Ruggera (1980), of three microwave (2.45-GHz) and six shortwave (27-MHz) diathermy units at sites in 6 health facilities. The results of the survey were expressed as means and ranges of free-space-equivalent power densities 1 meter from the units at eye and waist levels of an operator. The measurements for the 2.45-GHz units yielded a mean and range of 0.65 and 0.08-1.30 mW/sq cm at eye level, and 0.71 and 0.08-1.20 mW/sq cm at the waist. For the 27-MHz units, the mean and range for the magnetic component were 1.06 and 0.09-4.11 mW/sq cm at eye level, and 2.49 and 0.09-8.32 mW/sq cm at waist level; the corresponding values for the electric component were 1.21 and 0.06-5.19 mW/sq cm at eye level, and 4.05 and 0.04-16.58 mW/sq cm at the waist.

Three mailings of questionnaires were made, to reduce the number of nonresponses. The final population sample consisted of 3004 respondents from a total of 5187 therapists solicited; the respondents were divided into subgroups according to exposure across and within the energies of the four modalities above emitted from diathermy equipment. The authors

coded the four diathermy modalities as U (ultrasound), I (infrared), M (microwave), and S (shortwave), and initially distributed the population among the 15 exposure subgroups comprised of those exposed solely to each modality and those exposed to all possible combinations thereof, plus 1 nonexposure group. However, the small sizes of several groups necessitated merging them into other groups to ensure more meaningful statistical results, which yielded the following nine subgroups and the numbers of therapists in each: U=208, MU=116, SU=512, IU=64, MSU=390, ISU=429, IMSU=1097, other=67, and none=121.

Since age is usually closely related to cumulative exposure and to certain pathologic, psychologic, and physiologic processes, the authors divided each subgroup into those under 35 and those 35+, and further stratified the 35+ group into the three subgroups 35-44, 45-54, and 55+. Subgroups were also dichotomized into high- and low-exposure categories by using mean duration of employment (<14 years and 14+ years), mean frequency of treatments administered (<17 and 17+ per week), and jointly by employment duration and treatment frequency.

Before analyzing for potential effects of microwave and/or shortwave RFR, the hypothesis that ultrasound alone does not contribute to potential effects was tested for those in the high-exposure, 35+ age group by comparing those of this age category in the U subgroup with those in the "none" subgroup, on the assumption that a negative finding would apply to the younger, less-exposed groups as well. There were no statistically significant differences between subgroups for any of the health effects considered. This hypothesis also was tested for infrared only by comparing the SU and ISU groups (the I group being too small for this purpose). Again, no significant differences were found.

Tabulated for the nine coded exposure subgroups above were selected characteristics of respondents (age, race, marital status, present work setting, personal therapy with any modality, x-ray exposures) and the prevalence among them of the following reported conditions: blood disorder, cataracts, diabetes, endocrine disorder, hearing disorder, heart disease, high and low blood pressure, nervous breakdown, and "other." The authors stated that: "For the entire cohort, the reported prevalence rates are below population rates in all instances. Although the rates vary by subgroups for each condition, no one subgroup appears to exhibit markedly higher rates relative to total rates.

"The prevalence of conditions are higher for the respondents in the 35+ age group relative to the total of all respondents...Despite the fact that the heart disease rate appears higher among the microwave exposed than the shortwave exposed, a test of the microwave subgroup against the remainder of the cohort showed no statistically significant difference. In fact, the only subgroup where heart disease rates were significantly higher than the remaining total was the IMSU subgroup. Most rates for specific subgroups which exceed the total rates are based on small sample size and therefore are thought not to be real increases."

The authors then tried a different approach. New subgroups were formed for microwave, shortwave, and joint microwave/shortwave exposure, and further divided into high- and low-exposure groups. A respondent with any exposure to microwave was included in the microwave group, and similar definitions were used for shortwave and for joint exposure. Thus, the subgroups were not mutually exclusive, and the resulting tables clearly showed considerable double-counting of subjects. (This point was recognized by the authors: "The analysis of the microwave and shortwave modalities for both subgroups and total cohorts is compromised since the internal contrasts were never completely independent. Sample size considerations prohibited contrasts involving independent groups.")

Contingency tables were constructed for internal comparisons across subgroups. That is, for the three types of exposure (microwave only, shortwave only, and joint microwave/shortwave) and for the three high- vs low-exposure situations (by frequency of treatments/wk, length of employment, and combination thereof), 3x3 or nine separate contingency tables of condition vs modality were constructed. This was done for each of the 10 medical conditions, for a total of 90 contingency tables. The values in each table were tested with the Mantel-Haenszel chi-square test for homogeneity. Some significant results were obtained. Most of those results, however, became nonsignificant when age groups were combined by the Mantel-Haenszel method (stratification by age group), which permits correction for age-related effects.

Odds ratios for high vs low exposure for the three exposure categories were also calculated for each contingency table, and the confidence intervals were determined for those odds ratios that were statistically significant after age adjustment. Heart disease was the only condition that remained statistically significant in this new approach. It is interesting that for the nine types of exposure-vs-high/low situations (described above), only four were significant: microwave x frequency of treatments/week, shortwave x combined frequency of treatments/week and duration of employment, and joint microwave/shortwave x frequency of treatments/week. The other five situations were not significant at the 5% level, i.e., all three of the cases where duration of employment alone was a criterion of high vs low exposure, the case for joint microwave/shortwave exposure x combined treatment frequency and employment duration, and the case for microwave exposure x combined treatment frequency and employment duration.

It should be noted that of the 90 contingency tables, only four showed significance at the 5% level, a finding that is no better than chance. None of the other nine medical conditions was statistically significant, nor was the incidence of neoplasms. Also assessed were the possible confounding effects of diagnostic X-ray and diathermy treatments on individual respondents. After age adjustment, no conditions related to such treatments were found to be statistically significant.

This study most likely will be widely cited as "proof" that exposure to microwave/shortwave RFR causes heart disease. However, careful study of the paper did not provide convincing evidence that this is so.

First, the paper illustrated well the problems associated with attempts to uncover causal relationships between a purported health-effects agent (RFR in this case) and medical conditions in an identified population by using the results of a mailed, self-administered questionnaire. The response rate to the mailings was 58%, so 42% (2183 persons) did not respond. No mention was made of any attempt to contact a sample of nonrespondents by telephone or in person, to endeavor to characterize them as a group. (Statistical techniques exist to correct for bias in a large nonrespondent group.) Therefore, the 58% that did respond were self-selected in the sense that many of them may have responded because they had medical conditions and were curious about how such conditions may have arisen.

The difficulty in extrapolating from a pilot study of 3 microwave plus 6 shortwave RFR exposure situations to a cohort of 3004 respondents who had used diathermy equipment for up to 20 or more years is also not strong evidence of actual RFR exposure conditions.

As discussed above, a straightforward analysis of prevalence rates by subgroup for all reported medical conditions yielded nonsignificant differences between subgroups and the prevalence rates for the entire cohort. Furthermore, the reported prevalence rates for the entire cohort were below population rates in all instances (the "healthy worker" effect, plus the higher socioeconomic group effect--therapists are better off as a group than the general population). It was only after a regrouping of subjects into non-mutually-exclusive categories (i.e., double-counting of subjects in more than one category) that the analysis showed statistical significance, and then for only one medical condition out of 10 tested. For blood disorder, cataracts, diabetes, endocrine disorder, hearing disorder, high blood pressure, nervous breakdown, and "other" (including cancer), neither of the two analytical approaches showed any statistically significant relationship between the condition and diathermy usage.

The major finding, that there is a statistical link between heart disease and self-reported recollection of one aspect of occupational exposure (frequency or number of treatments/week, but not employment duration) to shortwave and microwave radiation (the latter downplayed), but not to joint shortwave/microwave exposure, is weak at best. If shortwave exposure is a causal agent but joint shortwave/microwave exposure is not, it could be inferred that microwave exposure protects against the possible adverse effects of shortwave exposure with respect to heart disease, a most unlikely conclusion. Furthermore, duration of employment, which normally would be considered a factor in "cumulative exposure," showed no statistically significant role.

On the basis of the RFR-bioeffects literature, the authors classified into: (1) disorders of conduction/rhythm and ischemia and (2) "other," and found statistical significance only for the first category. Heart disease, however, is a combination of many symptoms that have various etiologies. Cigarette smoking is identified as a major risk factor and is widely known to be a strong predictor of heart disease in an aging

population such as the 35+ group, for which the relationship with shortwave exposure was claimed in the present study. Inexplicably (but acknowledged by the authors), smoking history was not included in the questionnaire. Failure to consider this major biasing factor does not inspire great confidence in the sole positive result of this study.

Last, the authors stated: "To our knowledge, no epidemiologic studies of cardiovascular effects associated with shortwave exposure have been reported." Overall, their study does not provide strong evidence of such an association either.

Several epidemiologic studies were done expressly on possible ocular effects of chronic exposure to RFR. These studies are discussed in Section 3.1.4.1.2.

In summary, the epidemiologic/occupational studies examined provide no clear evidence of detrimental health effects in humans from chronic exposure to RFR at levels within prior or current U.S. standards.

REFERENCES:

Air Force Magazine
GUIDE TO AIR FORCE BASES
Air Force/Space Digest, pp. 221-239 (September 1969)

CENSUS
U.S. Bureau of the Census
COUNTY AND CITY DATA BOOK, 1967 (A STATISTICAL ABSTRACT SUPPLEMENT)
U.S. Government Printing Office, Washington, D.C. (1967)

Czerski, P., M. Siekierzynski, and A. Gidynski
HEALTH SURVEILLANCE OF PERSONNEL OCCUPATIONALLY EXPOSED TO MICROWAVES. I. THEORETICAL CONSIDERATIONS AND PRACTICAL ASPECTS
Aerospace Med., pp. 1137-1142 (October 1974)

Fleiss, J.L.
STATISTICAL METHODS FOR RATES AND PROPORTIONS
2nd Edition, John Wiley and Sons, New York (1981)

Glaser, Z.R. and G.M. Heimer
DETERMINATION AND ELIMINATION OF HAZARDOUS MICROWAVE FIELDS ABOARD NAVAL SHIPS
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 232-238 (1971)

Hamburger, S., J.N. Logue, and P.M. Silverman
OCCUPATIONAL EXPOSURE TO NON-IONIZING RADIATION AND AN ASSOCIATION WITH HEART DISEASE: AN EXPLORATORY STUDY
J. Chron. Dis., Vol. 36, No. 11, pp. 791-802 (1983)

HEW
U.S. Department of Health, Education, and Welfare
ATLAS OF CANCER MORTALITY FOR U.S. COUNTIES: 1950-1969
DHEW Publication (NIH) 75-780, National Cancer Institute, Washington, D.C. (1975)

Janes, D.E., Jr.
RADIATION SURVEYS--MEASUREMENTS OF LEAKAGE EMISSIONS AND POTENTIAL EXPOSURE FIELDS
Bull. N.Y. Acad. Med., Vol. 55, No. 11, p. 1021 (1979)

Kalyada, T.V., P.P. Fukalova, and N.N. Goncharova
BIOLOGIC EFFECTS OF RADIATION IN THE 30-300 MHZ RANGE
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 52-57 (1974)

Klimkova-Deutschova, E.
NEUROLOGIC FINDINGS IN PERSONS EXPOSED TO MICROWAVES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 268-272 (1974)

Lester, J.R. and D.F. Moore
CANCER MORTALITY AND AIR FORCE BASES
J. Bioelectricity, Vol. 1, No. 1, pp. 77-82 (1982a)

Lester, J.R. and D.F. Moore
CANCER INCIDENCE AND ELECTROMAGNETIC RADIATION
J. Bioelectricity, Vol. 1, No. 1, pp. 59-76 (1982b)

Lester, J.R.
REPLY TO "CANCER MORTALITY AND AIR FORCE BASES: A REEVALUATION"
J. Bioelectricity, Vol. 4, No. 1, pp. 129-131 (1985)

Liburdy, R.P.
CARCINOGENESIS AND EXPOSURE TO ELECTRICAL AND MAGNETIC FIELDS
New England J. Med., Vol. 307, No. 22, p. 1402 (1982)

Lilienfeld, A.M., J. Tonascia, S. Tonascia, C.H. Libauer, G.M. Cauthen, J.A. Markowitz, and S. Weida
FOREIGN SERVICE HEALTH STATUS STUDY: EVALUATION OF STATUS OF FOREIGN SERVICE AND OTHER EMPLOYEES FROM SELECTED EASTERN EUROPEAN POSTS
Final Report, July 31, 1978, Contract No. 6025-619073, Dept. of Epidemiology, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD (1978)

Lilienfield, A.M. and D.E. Lilienfield
FOUNDATIONS OF EPIDEMIOLOGY
2nd Edition, Oxford University Press, New York, Oxford (1980)

Milham, S., Jr.
MORTALITY FROM LEUKEMIA IN WORKERS EXPOSED TO ELECTRICAL AND MAGNETIC FIELDS (Correspondence)
New England J. Med., Vol. 307, No. 4, p. 249 (1982)

Milham, S., Jr.
OCCUPATIONAL MORTALITY IN WASHINGTON STATE: 1950-1979
DHHS (NIOSH) Publication No. 83-116, Contract No. 210-80-0088, U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health, Cincinnati, Ohio (October 1983)

Morton, W.E.
RE: "EFFECTS UPON HEALTH OF OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR)"
Am. J. Epidemiol., Vol. 113, p. 201 (1981)

NTIA
MICROWAVE RADIATION OF THE U.S. EMBASSY IN MOSCOW AND ITS BIOLOGICAL IMPLICATIONS: AN ASSESSMENT
Report NTIA-SP-81-12, National Telecommunications and Information Administration, Department of Commerce (March 1981)

Pazderova, J.
WORKERS' STATE OF HEALTH UNDER LONG-TERM EXPOSURE TO ELECTROMAGNETIC RADIATION IN THE VHF BAND (30-300 MHz)
Pracovni Lekarstvi (in Czech), Vol. 23, No. 8, pp. 265-271 (1971)
English translation: JPRS No. UDC 616-001.228.1-057-07 (1971)

Pazderova, J., J. Pickova, and V. Bryndova
BLOOD PROTEINS IN PERSONNEL OF TELEVISION AND RADIO TRANSMITTING STATIONS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 281-288 (1974)

Pollack, H.
EPIDEMIOLOGIC DATA ON AMERICAN PERSONNEL IN THE MOSCOW EMBASSY
Bull. N.Y. Acad. Med., Vol. 55, No. 11, pp. 1182-1186 (1979)

Polson, P. and J.H. Merritt
CANCER MORTALITY AND AIR FORCE BASES: A REEVALUATION
J. Bioelectricity, Vol. 4, No. 1, pp. 121-127 (1985)

Rand McNally and Company
1982 COMMERCIAL ATLAS AND MARKETING GUIDE
113th Edition (No. 113 07949), Chicago, New York, San Francisco (1982)

Robinette, C.D. and C. Silverman
CAUSES OF DEATH FOLLOWING OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR) 1950-1974
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIOFREQUENCY/MICROWAVES, Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication No. (FDA) 77-8026 (1977)

Robinette, C.D., C. Silverman, and S. Jablon
EFFECTS UPON HEALTH OF OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR)
Am. J. Epidemiol., Vol. 112, No. 1, pp. 39-53 (1980)

Robinette, C.D.
Response to Morton, W.E.
RE: "EFFECTS UPON HEALTH OF OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR)"
Am. J. Epidemiol., Vol. 113, pp. 201-202 (1981)

Ruggera, P.S.
MEASUREMENTS OF EMISSION LEVELS DURING MICROWAVE AND SHORTWAVE DIATHERMY TREATMENTS
Dept. of Health and Human Services, Bureau of Radiological Health, Rockville, MD, Publication No. (FDA) 90-8119 (1980)

Sadchikova, M.N.
CLINICAL MANIFESTATIONS OF REACTIONS TO MICROWAVE IRRADIATION IN VARIOUS OCCUPATIONAL GROUPS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 261-267 (1974)

Siekierzynski, M.
A STUDY OF THE HEALTH STATUS OF MICROWAVE WORKERS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 273-280 (1974)

Siekierzynski, M., P. Czerski, H. Milczarek, A. Gidynski, C. Czarnecki, E. Dziuk, and W. Jedrzejczak
HEALTH SURVEILLANCE OF PERSONNEL OCCUPATIONALLY EXPOSED TO MICROWAVES. II. FUNCTIONAL DISTURBANCES
Aerospace Med., pp. 1143-1145 (October 1974a)

Siekierzynski, M., P. Czerski, A. Gidynski, S. Zydecki, C. Czarnecki, E. Dziuk, and W. Jedrzejczak
HEALTH SURVEILLANCE OF PERSONNEL OCCUPATIONALLY EXPOSED TO MICROWAVES. III. LENS TRANSLUCENCY
Aerospace Med., pp. 1146-11485 (October 1974b)

Silverman, C.
EPIDEMIOLOGIC APPROACH TO THE STUDY OF MICROWAVE EFFECTS
Bull. N.Y. Acad. Sci., Vol. 55, No. 11, pp. 1166-1181 (1979)

Tell, R.A. and E.D. Mantiply
POPULATION EXPOSURE TO VHF AND UHF BROADCAST RADIATION IN THE UNITED STATES
Proc. IEEE, Vol. 68, No. 1, p. 6 (1980)

3.1.2 CONGENITAL ANOMALIES

Two studies were conducted on the possible relationship between the occurrence of Down's syndrome (Mongolism) in Baltimore, MD, and presumed exposure of the fathers to RFR from radars during military service. In the first study, Sigler et al. (1965) examined the data, derived from Baltimore hospital records and interviews with parents, on 216 Caucasian children with Down's syndrome. A case child was included only if, by personal inspection, the child appeared to be mentally retarded and exhibited at least six primary physical criteria for Down's Syndrome or if at least seven such criteria were listed by a qualified observer on the child's medical record. The 216 case children included were matched with 216 control children for hospital of birth (or at home), sex, and birthdate (within 6 months) and nearly all were matched for maternal age (within 1 year) at time of birth. All the case and control children were born between January 1946 and October 1962. Their parents were also well matched for birthplace, residence, and treatment in Baltimore hospitals.

Histories of irradiation of the mothers were obtained and categorized as: diagnostic radiation excluding fluoroscopy, fluoroscopic exposure, radiation for therapy, and occupational contact. Among the significant findings was that 17.7% of the case mothers had one or more fluoroscopic examinations *prior* to the birth of the case child as compared with only 8.1% of the control mothers ($p<0.01$). The fluoroscopic histories of the case and control fathers did not differ significantly. The other significant findings were that 14.5% of the case mothers reported having had therapeutic radiation exposures (mostly for skin ailments) compared with 5.1% of the control mothers ($p<0.01$), and that 7.9% of the case mothers had worked in a professional or technical capacity in medical fields vs 3.3% of the control mothers ($p<0.05$).

About the case and control fathers, 63.1% and 56.6% respectively had been in the military service (a nonsignificant difference), but 8.7% vs 3.3% had reported close association with radars as technicians or operators, both within and outside of military service ($p=0.02$).

Sigler et al. (1965) thus ascribed the higher incidence of Mongolism primarily to greater exposure of the case mothers to ionizing radiation, but concluded that "the only truly puzzling association is the suggested relationship between Mongolism and paternal radar exposure," and "one can only speculate concerning possible mechanisms, but the association between Mongolism and radar exposure deserves further investigation."

Cohen et al. (1977) reexamined the data used in the first study, denoted as the "Original Series," together with data on 128 additional matched pairs, denoted as the "Current Series." These authors requested more detailed information about RFR exposure and military service in the questionnaires used for the Current Series, and acquired service-record information on the fathers (using Army and Navy consultants to classify military job titles as an aid toward assessing the extent of exposure). They also tried to obtain similarly detailed data on the fathers of the

Original Series, and to determine whether there was any residual damage in the peripheral-blood chromosomes of case fathers.

From interviews of the fathers, Cohen et al. (1977) classified exposure as follows: (a) no evidence of exposure prior to conception of the index child, (b) probably no exposure (not in excess of that of the general population), (c) probably some exposure in service and industry (in excess of that of the general population), and (d) exposed (occupation or service definitely involving radar). Categories (a) and (b) were combined and called "definitely no exposure," and categories (c) and (d) respectively called "questionable exposure" and "definite exposure."

As noted above, Sigler et al. (1965) found that 8.7% of the case fathers vs only 3.3% of the control fathers in the Original Series had reported close association with radars ($p=0.02$). Reevaluation of this series by Cohen et al. (1977) yielded 13.8% vs 11.5%, still a positive, but no longer significant difference ($p>0.05$). In the Current Series, the total of case fathers in the "definitely-no-exposure" and "questionable-exposure" categories comprised only 8.3%, whereas 12.6% of the control fathers were in the "definite-exposure" category. Even though the difference was not significant ($p=0.84$), the trend was opposite to that of the Original Series. The opposite trend was also found when the "questionable-exposure" and "definite-exposure" categories were summed (21.7% vs 23.5%). When the numbers in the Original and Current Series were combined, the respective numbers of case and control fathers in the "definite-exposure" category comprised 11.5% and 12.0%, indicating that the opposite trends in the two series were counterbalanced. Summing those with "questionable exposure" and "definite exposure" yielded 19.9% vs 17.8% ($p=0.62$).

Cohen et al. (1977) concluded that the Current Series did not confirm the suggestions of the Original Series that the fathers of the children with Down's syndrome had either an excess of radar exposure or a larger proportion of military experience. The authors noted: "In view of the suggestive findings of the Original Series with regard to a possible radar association, it was certainly necessary to investigate this question further. The initial steps were taken. A replication study was the simplest and least expensive immediate approach. Supplementing it with the independent search of service records added an objective approach eliminating any possible differential in parental responses. These methods have been attempted with inconclusive findings; it is now necessary to look to the prospective, longitudinal, surveillance studies to resolve the issue."

The authors also remarked that the statistically significant differences in medical (ionizing) radiation history between case and control mothers found in the Original Series were absent in the Current Series, and they speculated that this negative finding may be due to increased awareness by medical practitioners of the potential health hazards of ionizing radiation to women in the childbearing years, leading to more restricted exposure.

In view of the absence of statistically significant differences between the incidence of Down's syndrome and "radar" exposure of the fathers in the Current Series and in the combination of the Current and the Original Series, the positive finding of such an association in the Original Series appears to have been a statistical anomaly. Results of the search for chromosome damage in case fathers were not reported.

A major problem with this and other retrospective epidemiologic studies for possible RFR-induced bioeffects is the difficulty in determining, with any degree of confidence, differences in levels and durations of exposure between so-called exposed groups and unexposed groups. Records and interviews regarding military service, even at stations where the use of radar and communications systems is prevalent, rarely provide insight into actual exposure histories for either group.

Peacock et al. (1971) had examined an Alabama-statewide file by counties (stored in a computer at the School of Public Health, University of Alabama School of Medicine) of birth certificates filed during the 17 months from July 1969 to November 1970. There were 31,700 white males, 29,400 white females, 14,900 black males, and 14,900 black females comprising a total of 90,900 infants. The records showed 932 infants with 968 birth defects of various types (by I.S.C. number) corresponding to an overall rate of 10.3 newborns with anomalies per thousand births, a rate comparable with those in similar registries elsewhere.

Among the findings was that "except for congenital anomalies of the genital organs (I.S.C. 752) where there is the expected male excess, differences by sex are not very striking." However, the authors noted: "Within the State there are concentrations of certain defects in defined geographical areas (Counties)," and they presented a table for the six counties (Butler, Calhoun, Coffee, Dale, Henry, and Jefferson), in which the totals of male and female incidence for specific anomalies departed significantly ($p<0.05$) from random. For the white infants, anencephalus (I.S.C. 740), found in excess only in Calhoun, had the highest level of significance of all anomalies irrespective of race. Excess incidences among the white infants at successively lower levels of significance were for: clubfoot (I.S.C. 754) in Dale, spina bifida (I.S.C. 741) in Henry, anomalies of the genital organs (I.S.C. 752) in Jefferson, spina bifida (I.S.C. 741) in Butler, clubfoot (I.S.C. 754) in Coffee, and anomalies of the heart (I.S.C. 746) in Dale. For the black infants, the only anomaly with a significant excess was cleft palate and lip (I.S.C. 749), which was found only in Calhoun and which had the lowest level of significance of all of the anomalies.

It is noteworthy that in this paper, the authors did not mention Fort Rucker, which is located in Dale and Coffee Counties, or offer possible causal factors for the excess incidences cited. They also discussed overall rates found by other investigators for other regions within and outside of the U.S., citing rates ranging from 7.4 to 75.4 per thousand, depending on the population studied, the types of anomalies included, whether the investigators personally examined all births or relied on a notification system, and on whether the children concerned were followed

prospectively for some years.

In a subsequent report, Peacock et al. (1973) indicated that: "Fort Rucker is a pilot training base for fixed- and rotary-wing aircraft with a military population in recent years of approximately 20,000 persons and a civilian complement of about 9,000 persons. There are 46 radar installations located within 30 miles of the base, which comprise one of its particularly unique characteristics." The authors then stated that an unpublished, more detailed study by Peacock of birth certificates showed that during the same period considered by Peacock et al. (1971), there were 59 reported congenital anomalies of 3,505 births to military personnel in the six-county area surrounding Fort Rucker; clubfoot comprised 14 of these anomalies for a rate of 4.0 per thousand. By contrast, there were 75 anomalies in 10,996 civilian births, of which 1 was clubfoot, for a rate of 0.1 per thousand, which was slightly lower than for the state.

Peacock et al. (1973) then stated: "An exhaustive investigation of the accuracy of data and the validity of tests used in the previous study uncovered a number of data processing errors and revealed that certain assumptions on which the hypothesis tests were based are of questionable validity. As a result, a complete evaluation of the earlier study results was conducted. The data used in this evaluation, however, span a four-year time period rather than the 17-month period covered in the previous study. In addition, the data were corrected and are considered more accurate than those originally used. Also, a more precise test of the reliability of inferences was performed that does not rely on the questionable use, in this particular test, of a normal approximation."

To adjust the reported anomalies for "non-radar" factors, the authors also considered the numbers of fetal deaths vs race, age, income of parents, and selected characteristics of hospitals and hospital staffs that might influence how anomalies are diagnosed and recorded. The authors stated: "This comparison revealed that the reported anomaly rates differ substantially among hospitals and that the state average rate does not, in general, constitute a valid norm to compare against the number of anomalies observed at individual hospitals."

After accounting for the non-radar factors, the authors repeated the tests for the Fort Rucker area and specifically for Lyster Hospital (at Fort Rucker). In addition, as a "control" test, they compared the fetal death anomaly rates in military hospitals at "radar bases" Fort Rucker and Eglin Air Force Base with those of three military hospitals in bases with minimal radar networks. The results of the retests confirmed that the total anomaly rate and the rates for anomalies of the heart, genital organs, and musculoskeletal categories were abnormally high at Lyster Hospital. Also, fetal deaths for Lyster and for the hospital at Eglin Air Force Base were almost the same, and "constitute evidence that the problem may be associated with radar."

Interestingly, the authors attributed the apparently high clubfoot rate to reporting differences. They stated: "While the clubfoot rate at

Lyster is still higher than expected, the probability is only about 0.74 that the difference is statistically significant. The factor that most influences this difference in the level for clubfoot is the fact that the Lyster Hospital is a military hospital, rather than because of the proximity of major radar installations," noting that social stigma is less likely to influence reporting this anomaly for births at military than civilian hospitals.

Burdeshaw and Schaffer (1977) reexamined the Alabama birth record data studied previously by Peacock et al. (1971) for possible RFR-related anomalies. Instead of using statewide averages, however, Burdeshaw and Schaffer (1977) compared the data for Coffee and Dale Counties with those of each of the other 65 counties in Alabama on a score and rank basis. They also sent questionnaires to 46 Alabama hospitals to acquire more detailed information on hospital characteristics and reporting procedures, to permit prediction of expectation values for Lyster Army Hospital in Fort Rucker. They found the following evidence against the conclusion that there is an unusually high incidence rate of congenital anomalies in the Fort Rucker area:

1. During the study period July 1968-December 1972, the overall rates for Coffee and Dale Counties ranked only sixth and eighth among the 67 counties in Alabama.

2. Although the two highest rates in a sample of 47 hospitals were 18.0 at the Air Force Regional Hospital in Maxwell Air Force Base (Montgomery County) and 17.7 at Lyster Army Hospital, there were five nonmilitary hospitals in Alabama that had lower, but not statistically different, rates from those for Maxwell and Lyster: 14.5 at Stabler-Memorial (Butler County), a private nonprofit hospital; 14.3 at Henry-County; 13.4 at North-Jackson (Jackson County); 12.5 at Hale-County; and 12.2 at Burdick-West-Memorial (Winston County), the last four of which were Government (nonmilitary) hospitals.

3. Prediction intervals showed that Lyster's overall rate was well within what would be expected from a hospital with characteristics similar to those of Lyster.

4. When the addresses of the mothers of anomalous infants were plotted on county road maps, no significant clustering, especially in the vicinity of presumed radar sites, was apparent.

5. The rates, by International Classification of Diseases catego y, from Lyster appeared to be consistent with rates obtained from carefully controlled studies, such as one reported for Mayo Clinic (Harris et al., 1975). Because there was no reason to believe that the rates at Mayo were unusually high, they were taken as reasonable comparison data for the Rucker study.

6. When the occurrences of anomalies within categories with the highest rates at Lyster were plotted on a time axis, significant clustering was apparent. There is evidence that, in most cases, the reporting of ano-

malies within a cluster may be attributable mainly to one or two physicians, rather than the several physicians on the staff at any one time.

Burdeshaw and Schaffer (1977), however, cited two observations that prevented the dismissal of the anomaly question:

(a) The two highest rates from the hospital survey, at Fort Rucker and Maxwell AFB, were both from military installations and aviation centers. These rates cannot be explained easily by the fact that military hospitals are more alert to the presence of anomalies, because the rates at Redstone Arsenal and Fort McClellan in Alabama were respectively 7.1 and 0.7.

(b) Thirteen of 17 counties with overall rates in the upper quartile lie within a contiguous band that has one terminus in Houston County, the southeasternmost county in Alabama, and that extends west-northwesterly to Marengo, one county removed from the Mississippi state line. Ten of the 20 counties in the southeast quadrant of Alabama had rates in the upper quartile, more than can be explained by chance. This phenomenon, however, may involve more than a "military base" explanation.

Their overall conclusion was that on the basis of the birth-record data, it could not be concluded that an unusually large number of infants with congenital anomalies were born to military personnel at Fort Rucker or to other residents in the immediate area.

Kallen et al. (1982), hypothesizing that physiotherapists were more likely to have been occupationally exposed to various agents (chemicals, drugs, X-rays, RFR) than the general population, conducted a cohort study on 2,043 infants (including 25 pairs of twins) born during 1973 to 1978 in Sweden to 2,018 females registered as physiotherapists at the time of pregnancy. The authors noted that certified physiotherapists in that country are registered and given unique identification numbers in a computer file at the National Board of Health and Welfare. In addition, the Medical Birth Register contains computerized information on all deliveries in Sweden since 1 January 1973, including newborn survival, the presence of possible malformations, and the identification number of the mother. Cross-linking of files in these registers made it possible to identify infants of mothers registered as physiotherapists at the time of delivery.

This cohort was then analyzed, with respect to perinatal mortality and the presence of malformations, by comparison with information on all deliveries in the Medical Birth Register. Identifications of newborns diagnosed as malformed were verified further in the Swedish Register of Congenital Malformations, which contains much more detailed data on malformed infants. Expected values were calculated for each parameter studied, with corrections for age and parity distribution (pregnancy number) of the mothers, and hospital of delivery (which influences the reported diagnosis of malformations, notably minor ones).

Shown in Table 11 are the results for the total cohort, with the

expectation values for the entire population in parentheses:

TABLE 11: RESULTS FOR TOTAL COHORT

Number of infants born before 38th week: 170 (200)
Number of infants weighing less than 2.5 kg: 64 (92)
Sex ratio: 1.08 (1.06)
Number of stillbirths: 7 (12)
Number of deaths before 7th day: 9 (11)
Total perinatal deaths: 16 (23)
Number of infants with malformation diagnosis: 101 (102)
Number of infants with major malformation: 27 (32)

The authors suggested that the excellent outcome of this cohort study could have been the result of a "healthy worker" effect. However, they considered the possibility that the total outcome is "loaded" by a small subgroup with an occupationally higher risk for fetal damage, stating: "Theoretically, if a hazardous exposure exists, it should be more common among the few females who had dead or malformed infants than among the females who had normal babies." Accordingly, the authors performed a case-control study within the cohort, in which each of 37 selected infants with major malformations or without malformations who died perinatally were compared with two normal infants matched for maternal age, parity, and time of delivery during the year (to compensate for seasonality of work), for a total of 74 controls. Exposures for the case and control mothers were estimated from answers to a questionnaire that asked (in part):

"Did you, during the pregnancy, work with or in close proximity to the following:

Shortwave equipment: daily/often/seldom/never
Microwave equipment: daily/often/seldom/never
Ultrasonic equipment: daily/often/seldom/never
X-Ray equipment: daily/often/seldom/never
Electrostimulator: daily/often/seldom/never

Did you use hexachlorophene-containing soap (e.g., Phisehex):
daily/often/seldom/never"

The final response rate to the questionnaire (after a reminder) was 93%, comprising 36 case mothers and 67 control mothers, plus one reply from a mother indicating that she did not wish to participate. Among the 104 who responded, 96 had worked as physiotherapists during the relevant pregnancy; of the remaining eight, one had become a doctor, one was a veterinary student, and the other six were not working outside their homes. Of the 96 physiotherapists, 33 were case mothers and 63 were control mothers, distributed among the four exposure modalities. Of particular interest is the authors' table of shortwave equipment usage (based on the responses to the questionnaire), shown below as Table 12:

TABLE 12: CATEGORIES OF SHORTWAVE EQUIPMENT USAGE (2X4)

	Case Mothers	Control Mothers
never	15	25
seldom	7	29
often	2	5
daily	9	4

The authors chose to combine the categories "never" and "seldom" and the categories "often" and "daily," thus obtaining 2x2 Table 13:

TABLE 13: CATEGORIES OF SHORTWAVE EQUIPMENT USAGE (2X2)

	Case Mothers	Control Mothers	Total
never/seldom	22	54	76
often/daily	11	9	20
		Total	96

They tested the latter table with Fisher's 1-tailed Exact Test (Meddis, 1975), and found a statistically significant difference ($p=0.03$) between case and control mothers in the "often/daily" category. Examination of the diagnoses of the infants of those 11 case mothers, however, showed no obvious pattern of malformations.

The authors also noted that there were no significant differences in exposure to the other modalities (or for the usage of hexachlorophene-containing soap), but that the trend found for shortwaves, though not significant, was present for the use of ultrasound equipment. They stressed that these two modalities were heavily associated: of the 96 mothers, 17 reported using only ultrasonics and 6 only shortwaves, but 14 reported using both (vs only 6.5 expected by random association).

In their discussion, the authors carefully reviewed and interpreted the results of their study. They concluded that the physiotherapists as a group had a slightly better-than-expected outcome for perinatal deaths and major malformations than did the general Swedish population for the same period. Regarding the statistically significant higher use of shortwave equipment among those physiotherapists who gave birth to a malformed or perinatally dead infant, the authors were aware that the results could have arisen at random because the significance level was borderline, but found it difficult to dismiss the finding on that basis.

This paper is an example of a well conceived and conducted epidemiologic investigation into whether occupational exposure to RFR is potentially hazardous. Especially noteworthy was the availability of computerized comprehensive and complete data files on many aspects of the

economy and population in Sweden, in direct contrast to the relative inaccessibility and/or lack of completeness of data in many similar studies. The authors also reported on their methodology and intermediate results in sufficient detail to permit independent checking of their statistical calculations. (These were correct.)

Their overall findings appear to be valid. As they noted, however, the results of the case-control study did indicate a possible relationship between higher use of shortwave equipment and increased incidence of perinatal mortality and malformations, a finding of possible importance. In view of the relatively small numbers of subjects in the case-control study, a sensitivity analysis, discussed below, was performed on the reported case-control data in addition to checking the correctness of the authors' statistical calculations.

The Fisher 1-tailed exact test on 2x2 Table 13 above does yield $z=1.91$, $p=0.028$. Suppose, however, that one of the case mothers had responded "often" rather than "seldom". Table 13 would become Table 14:

TABLE 14: ASSUMED ALTERATION OF TABLE 13

	Case Mothers	Control Mothers	Total
never/seldom	23	54	77
often/daily	10	9	19
		Total	96

For this new table, $z=1.59$, $p=0.056$. That is, shifting one response from "often" to "seldom" would result in a statistically nonsignificant result (at the 5% level). A similar exercise wherein one response in the control group is moved from "seldom" to "often," with no change in case responses, would result in $z=1.70$, $p=0.045$, which is close to the 5% arbitrarily defined level dividing significance from nonsignificance. Shifting two responses would yield the nonsignificant $z=1.49$, $p=0.068$. Thus, it is seen that although the results presented by the authors are technically correct and the study was performed with great care, their finding regarding exposure to shortwaves was critically dependent on the recollection accuracy of the respondents with regard to the frequency of use of the shortwave equipment, and should serve only to indicate a need for a case-control study with larger populations (if available) for greater statistical robustness.

In overall conclusion, none of these epidemiologic studies provide conclusive evidence that congenital anomalies or perinatal infant deaths are caused by chronic exposure of females during pregnancy, or of males prior to becoming fathers, to RFR at levels within prior or current U.S. standards, a finding consonant with those for the occupational studies discussed in Section 3.1.1.

REFERENCES:

Burdeshaw, J.A. and S. Schaffer
FACTORS ASSOCIATED WITH THE INCIDENCE OF CONGENITAL ANOMALIES: A LOCALIZED INVESTIGATION
Final Report, Report No. XXIII, 24 May 1973-31 March 1976, Contract No. 68-02-0791, EPA 600/1-77-016 (March 1977)

Cohen, B.H., A.M. Lilienfeld, S. Kramer, and L.C. Hyman
PARENTAL FACTORS IN DOWN'S SYNDROME-RESULTS OF THE SECOND BALTIMORE CASE-CONTROL STUDY
In E.G. Hook and I.H. Porter (eds.), POPULATION GENETICS-STUDIES IN HUMANS, Academic Press, New York, pp. 301-352 (1977)

Harris, L.E., L.A. Stayura, P.F. Ramirez-Talavera, and J.F. Annegers
CONGENITAL AND ACQUIRED ABNORMALITIES OBSERVED IN LIVE-BORN AND STILLBORN NEONATES
Mayo Clinic Proc., Vol. 50, (1975)

Kallen, B., G. Malmquist, and U. Moritz
DELIVERY OUTCOME AMONG PHYSIOTHERAPISTS IN SWEDEN: IS NON-IONIZING RADIATION A FETAL HAZARD?
Arch. Environ. Health, Vol. 37, No. 2, pp. 81-85 (1982)

Meddis, R.
STATISTICAL HANDBOOK FOR NON-STATISTICIANS
McGraw-Hill, Berkshire, England (1975)

Peacock, P.B., J.W. Simpson, C.A. Alford, Jr., and F. Saunders
CONGENITAL ANOMALIES IN ALABAMA
J. Med. Assoc. Ala., Vol. 41, No. 1, pp. 42-50 (1971)

Peacock, P.B., S.R. Williams, and E. Nash
RELATIONSHIP BETWEEN THE INCIDENCE OF CONGENITAL ANOMALIES AND THE USE OF RADAR IN MILITARY BASES
Final Report, Report No. III, Project No. 3118, Contract No. 68-02-0791 submitted by Southern Research Institute to EPA (Nov. 1973) (unpublished)

Sigler, A.T., A.M. Lilienfeld, B.H. Cohen, and J.E. Westlake
RADIATION EXPOSURE IN PARENTS OF CHILDREN WITH MONGOLISM (DOWN'S SYNDROME)
Bull. Johns Hopkins Hosp., Vol. 117, pp. 374-395 (1965)

3.1.3 CLINICAL STUDIES OF ACCIDENTAL OVEREXPOSURE

There have been various cases of occupational exposure to high levels of RFR, especially for some years after World War II, in which the subjects were reported to have suffered physiological harm. In a presentation by Graham (1985), the history of the Air Force's activities and its program for protection of personnel against possible hazards of RFR and of its investigations of incidents of possible accidental overexposure to RFR were reviewed. That presentation is summarized below.

In recounting the program's history, Graham indicated that before 1970, programs within the Air Force community for protection against RFR were largely managed separately by each Air Force base. In mid-1970 however, the U.S. Air Force Radiological Health Laboratory (RHL), a predecessor of the USAF Occupational and Environmental Health Laboratory (OEHL) was tasked by the Air Force Surgeon General to develop an RFR protection program for Air-Force-wide implementation. Also about 1970, allegations were widely made that radar operators had been exposed to hazardous RFR levels while in certain aircraft, which caused cataracts. To respond, the RHL and the Air Force Communications Service (AFCS) conducted one of several studies (Penikas et al., 1970, 1973) to determine whether there existed a basis for such allegations. Graham stated: "That first study lacked sophistication, but the investigators were unable to distinguish any difference in the eyes of career RF workers when compared to a matched group of non-RF workers."

In 1972, USAF performed a more comprehensive study (Odland, 1972; Odland et al., 1972) involving nearly 1000 subjects. About half the subjects had worked in RFR occupations from 2 to more than 45 years. The others comprised a control group carefully selected for having no occupational exposure to RFR and who were carefully age-matched with the exposure group. Graham stated: "The results of that so called 'Five-Base Study' demonstrated that microwave cataractogenesis was a non-entity within the Air Force work force. Primarily as a result of that study, microwave radiation was largely dismissed as a possible/probable cause of cataract activity among Air Force workers who are/were occupationally exposed at levels within the PEL [permissible exposure limit, then 10 mW/sq cm]. That fact remains essentially true today." [Other studies of possible RFR cataractogenesis are discussed in Section 3.1.4.1.2.]

Graham (1985) discussed the successive Air Force exposure standards that culminated in the current revision of Air Force Occupational Safety and Health Standard 161-9 (AFOSH, 1984), which, in addition to specifying frequency-dependent PELs, includes the guidance and procedures for the management of overexposures to RFR. He noted that since 1972, it has been Air Force policy that every suspected or alleged exposure to RFR in excess of the PELs be investigated thoroughly:

- To determine whether or not an overexposure actually did occur.
- If an overexposure did occur, to definitively determine both the power density encountered and the duration of exposure.

3) To recommend and coordinate appropriate medical evaluations if such be indicated.

Standard AFOSH (1984) requires that whenever a suspected overexposure occurs or is alleged, the individuals involved must promptly report the matter to their supervisor. The supervisor must then ensure that the individuals report promptly to an appropriate medical facility, usually the base hospital. The standard also requires that Directors of Base Medical Services (DBMS) ensure that their physician staffs know and understand the principles of RFR injury and the appropriate tests and treatments that may be needed.

Of primary importance during the initial post-accident visit of the individual to the medical facility are to try to quantitate the exposure history in relation to any manifest symptoms and to document in detail certain medical baselines against which changes can be measured later, should they occur. It is therefore imperative to establish a complete and comprehensive case record to facilitate future decisions about the need for follow-up medical examinations and evaluation of findings.

The incident must be meticulously reconstructed, using the same emitter operating at identical parameters and at the direction of the personnel involved. On completing the reconstruction, the data must be evaluated and a definitive determination must be made regarding whether or not an overexposure had occurred. If it should be determined conclusively that an overexposure had not occurred, all medical activity connected with the incident is to be halted and detailed documentation supporting that conclusion is to be prepared. For conclusively determined incidents of overexposure, the standard requires:

a) An accurate as possible quantification of the exposure.
b) A determination as to what part of the body was primarily exposed or whether the whole body was exposed.
c) Detailed review of any clinical symptoms manifested by the victims.
d) Prompt consultation with Board Certified Occupational Medicine Physicians at USAF OEHL to determine what, if any, further medical evaluations are needed and where they will be obtained.

For incidents where the investigation is inconclusive, the individuals involved are to be treated as if they had been overexposed.

The standard specifies what kinds of medical consultations/evaluations should be necessary relative to the kinds of overexposure situations and which medical offices/agencies are responsible for the professional and administrative management of the individuals. These persons are also to be tracked throughout their Air Force careers, including the scheduling of periodic medical reevaluations as appropriate.

To illustrate the operation of the program, Graham presented in detail six cases of actual or possible overexposure that occurred during the period 1974-1983. He stated: "All six of the exposees have undergone extensive medical evaluations at the USAFSAM and four have also been

evaluated at one or more civilian institutions. The preliminary results obtained from the medical files at USAFSAM are inconclusive in that no findings were noted that could be directly attributed to the exposures, with the exception of acute situational anxiety reactions. All other manifestations were viewed as being transitory in nature with no permanent effects expected. Reevaluations of these individuals are expected to continue on a regular basis for some years to come."

Last, Graham summarized the medical evaluations of possible accidental overexposure to RFR involving more than 330 persons during the period from the spring of 1972 to 1 August 1984. He noted that not all of the personnel involved had been Air Force employees; incidents had occurred on Air Force bases involving civilian contractors, foreign nationals, and U.S. Army and Marine Corps personnel. He also stated: "In many cases the medical data obtained from the evaluations of the accidental RFR overexposures are incomplete in several respects, primarily due to a lack of standardization of the clinical examinations. Nevertheless, these case files can and do provide important anecdotal information concerning human exposure to RFR fields. This repository of case files is the only one of its kind known to exist."

Only 58 individuals with files in the repository were positively confirmed to have had exposures exceeding the PEL. Of those 58 persons, 26 reported that they had clearly felt a warming sensation at the time of overexposure, 20 had felt no warmth, and 12 had not been sure. It was therefore concluded that about 45% of those overexposed had probably terminated the exposure because they felt the energy. Of approximately 240 persons presumed to have been overexposed but who were subsequently confirmed to have had exposures not exceeding the PEL, 26 had felt a warming sensation and had terminated the exposure before the PEL could be exceeded, 173 had felt no sensation, and 39 had not been sure.

Graham indicated that medical review of the results revealed few if any consistent clinical patterns. Even in the cases where intense localized exposures had occurred, erythema and/or edema were rarely seen at the time of physical examination. Lenticular imperfections such as small punctuate opacities and vacuoles were noted frequently in individuals whose overexposure was primarily to the head. However, none of these ocular observations were considered to be clinically significant because no concomitant visual impairment was noted. Moreover, it was impossible to determine whether any of these imperfections were present in these persons before the RFR incident; the same types of ocular imperfections are very prevalent in the general population and are often encountered during routine ophthalmological examinations.

In the entire group of overexposed persons, serum enzyme levels, blood counts, blood pressures, sedimentation rates, and electrocardiograms were all judged unremarkable after clinical review by several physicians well experienced in evaluating RFR exposees, strongly suggestive that no clearly defined tissue damage had occurred. Some of the overexposees were given detailed psychological testing. On occasion, the evaluators attempted to draw some conclusions, but such efforts were hampered se-

verely by the lack of preexposure baseline data for comparison and interpretation. During neurological examinations conducted in concert with the psychological studies, however, no abnormalities were noted.

Persons accidentally exposed to levels of RFR exceeding the PEL often manifest clinical symptoms such as headache, nausea, fatigue, malaise, and palpitations, which can be attributed to anxiety reactions to the situations, but it is impossible to completely rule out an organic etiology. Some high-level overexposures, e.g., at levels exceeding 500 mW/sq cm, resulted in anxiety reactions so severe that hospitalization and sedation were necessary. The reactions were severe enough in some cases to warrant psychiatric referral and evaluation.

REFERENCES:

AFOSH STANDARD 161-9, EXPOSURE TO RADIOFREQUENCY RADIATION
Headquarters, U.S. Air Force, Washington, DC 20330-5000 (1984)

Graham, R.B.
THE MEDICAL RESULTS OF HUMAN EXPOSURES TO RADIO FREQUENCY RADIATION
Advisory Group for Aerospace Research and Development (AGARD) Lecture Series No. 138, THE IMPACT OF PROPOSED RADIO FREQUENCY RADIATION STANDARDS ON MILITARY OPERATIONS, pp. 6-1 to 6-8 (1985)

Odland, L.T.
OBSERVATIONS, OPINIONS AND RECOMMENDATION; U.S. MEDICAL SERVICE PROGRAM FOR CONTROL OF RADIOFREQUENCY HAZARDS
USAF Radiological Health Laboratory, Report 72W-25 (1972)

Odland, L., V. Penikas, and R. Graham
RESULTS OF OPHTHALMOLOGICAL STUDIES ON SELECTED GROUPS OF USAF PERSONNEL WHOSE OCCUPATIONS PRESENTED A POTENTIAL FOR EXPOSURE TO MICROWAVES
USAF Radiological Health Laboratory, Report 72W-124 (1972)

Penikas, V., R. Graham, H. Piltingsrud, and J. Stencel
SURVEY OF RADIATION LEVELS GENERATED BY EQUIPMENT USED ON EC-121 AIRCRAFT, AND CLINICAL EVALUATION OF SELECTED CREW MEMBERS
USAF Radiological Health Laboratory, Reports 70W-109 (1970) and 73W-26 (1973)

3.1.4 SPECIAL SENSES

This section is devoted to studies of RFR-induced ocular effects, the RFR-hearing effect, and cutaneous perception of RFR. Although these topics are presented under "Studies of Humans," it is more convenient to include here appropriate studies with animals than in separate sections.

3.1.4.1 OCULAR EFFECTS

The fear that RFR can cause cataracts is a recurring theme in newspapers and other popular media. The eye lens is most vulnerable to heating by RFR because other regions have more effective means of heat removal, such as greater blood circulation, and from some of the experimental results described below with animals, it is undoubtedly true that if a person's eyes were exposed to intensities high enough to elevate the temperature of the lens by about 5 deg C or more, the lens would quickly suffer damage.

3.1.4.1.1 ANIMALS

One of the earlier studies of effects of RFR exposure on the eyes of live experimental animals was by Cogan et al. (1958), who endeavored to compare cataractogenic levels of whole-body exposure of rabbits to CW RFR with levels that caused death. These authors exposed groups of rabbits to either 468-MHz RFR within a rectangular-waveguide system or to free-space 385-MHz RFR from a horn. Rectal temperatures were taken before and after each exposure. Ophthalmoscopic examinations were made before, and at variable intervals after, exposures. Also conducted in selected cases were slit-lamp biomicroscopic examinations.

The results of initial exposures in the waveguide system indicated that rabbits could tolerate 10 mW/sq cm, at which the absorption rate was about 3 W, for many hours without significant rectal-temperature rise or other apparent effect. At 30 mW/sq cm (absorption rate about 10 W), however, several rabbits died within about 2 hr, and at 60 mW/sq cm (absorption rate about 20 W), some deaths occurred after about 30 min. Accordingly, most later exposures (discussed below) were done at levels and durations that were sublethal but caused rectal-temperature rises of 1.5-2 deg C. Noted by the authors was that for 184 exposures of 23 rabbits at 60 mW/sq cm, the mean whole-body SAR was 8.1 W/kg with a standard deviation of 1.25 W/kg.

Ten rabbits were exposed individually to 468-MHz RFR at 60 mW/sq cm (about 8 W/kg) for 20 min weekly and 12 rabbits for 20 min daily, with 15 rabbits for each group serving as controls. Eight other rabbits were exposed twice weekly to 385-MHz RFR, four at 60 mW/sq cm (about 8 W/kg) for 15 min and four at 30 mW/sq cm (about 4 W/kg) for 90 min (nearly lethal levels), with 10 rabbits as controls.

Examinations of the eyes of the RFR-exposed rabbits showed no cataracts. Punctate opacities were seen occasionally in the posterior subcapsular cortex, but were also seen prior to exposure and were as

frequent in the controls as in the exposed rabbits.

Carpenter et al. (1960) exposed 136 rabbits to 2.45-GHz CW RFR once each at a power density in the range from 120 to 400 mW/sq cm and a duration in the range from 60 to 10 min. The exposures were done in an anechoic chamber at about 2 inches from the plastic housing of a corner-reflector antenna, with the corneal surface of the right eye positioned opposite the dipole crossover of the antenna. Power densities were determined at the position of the right eye by calorimetry with a plastic sphere about the size of the rabbit eye and filled with saline solution of dielectric constant similar to that of the eye. However, the authors regarded the measurements as nothing more than "reproducible equivalents of absorbed power at the position of the eye." Following exposure, the eyes were examined regularly with an ophthalmoscope and slit-lamp microscope.

The left eye of each rabbit remained clear after exposure. Level- and duration-dependent degrees of opacity were observed in the right eye for some exposure conditions. These opacities were uniformly located in the posterior subcapsular cortex and first appeared within 1 to 6 days after exposure, with a mean latency of 3.5 days. The outcome of each exposure condition was shown as a circle on a power-density vs exposure-duration graph, with solid circles for those that yielded lens opacities and open circles for those that had no effect. The curve connecting the circles corresponding to the minimum duration at each power density that caused a recognizable opacity to develop was taken as the curve of time and power-density threshold for opacity induction by single exposure. This curve was a rectangular hyperbola indicative of reciprocity, with a non-zero power-density offset (asymptote). The threshold durations at 400 and 120 mW/sq cm were about 3 and 35 min, respectively; the durations were intermediate for power densities between these two values. By extrapolation beyond 60 min, the asymptotic threshold power density (for indefinitely long exposure) was roughly 80 mW/sq cm.

Temperatures within the eyes of 34 anesthetized rabbits during exposure at nine RFR levels were measured with a 22-gauge shielded hypodermic-needle thermistor with its tip inserted in the vitreous at a location directly behind the posterior pole of the lens but not in contact with the lens capsule, an operation said to not damage the eye. The curves of temperature vs exposure time all showed rises, within the first 10 min, from about 38 deg C to plateau temperatures ranging from about 41 deg C for 40 mW/sq cm to about 55 deg C for 400 mW/sq cm.

The thresholds determined from the single-exposure experiments served as the basis for investigating whether repeated exposures at sub-threshold levels would be cumulative and yield opacities. In particular, 5 min had been found to be the minimal duration for causing opacities at 280 mW/sq cm. In one set of experiments, therefore, 4-min exposures at this level were done once per day on four successive days. Opacities were seen in 4 of 7 eyes so treated. Opacities were also evident in 3 of 7 eyes exposed at 280 mW/sq cm twice or thrice for 4 min each at 7-day intervals and in 3 of 8 eyes exposed at this level for 4

min three times at 14-day intervals.

In a similar set of experiments at 280 mW/sq cm, the duration used was only 3 min, and opacities were seen in 5 of 5 eyes given five daily exposures and in 5 of 5 eyes given three exposures at 4-day intervals. However, no opacities were evident in 5 of 5 eyes given five exposures at 7-day intervals. The authors also similarly found that at 120 mW/sq cm, five daily 25-min exposures yielded opacities in 5 of 5 eyes and three 30-min exposures at 2-day intervals yielded opacities in 4 of 4 eyes; at 80 mW/sq cm, 15 daily 60-min exposures yielded opacities in 3 of 3 eyes, whereas at 40 mW/sq cm, none were seen in 2 of 2 eyes given 15 daily 60-min exposures.

The authors concluded: "If either the power density or the duration of the irradiation are below a certain threshold value, then the damage done to the lens is not irreparable and recovery can occur, provided sufficient time elapses before a subsequent similar episode. In the experiments described above, it appears that the interval necessary for recovery after damage done by a 3-minute exposure must be greater than 4 days but need not be longer than a week."

Carpenter et al. (1960) also exposed the right eyes of 18 rabbits for 20 min to pulsed 2.45-GHz RFR at an average power density of 140 mW/sq cm and 0.5 duty cycle, for a peak power density of 280 mW/sq cm. They noted that in terms of thermal flux, 20 min of exposure at this average level was 5 min less than the threshold duration for CW RFR at 140 mW/sq cm. The results were not clear-cut. Opacities were seen in 10 eyes; four of them were classified as minimal cataracts and six as extensive. With a 0.25 duty cycle (560 mW/sq cm peak), cataracts were seen in 2 of 4 eyes. Exposures for 45 min at 80 mW/sq cm average and 0.2 duty cycle (400 mW/sq cm peak) were ineffective; however, exposures for 60 min at this level yielded cataracts in 4 of 4 eyes. In general, the authors noted that opacities occurred in more than half of 37 eyes from exposure to pulsed RFR for significantly shorter periods than from exposure at the same level of CW RFR, which led them to question whether RFR-induced cataracts are caused solely by the heat generated.

In a subsequent paper, Carpenter and Van Ummersen (1968) elaborated on the basis for the question above. Among the 2.45-GHz data cited were: For the threshold opacity-yielding single 5-min exposure at 280 mW/sq cm, the intraocular temperature rose to 49.3 deg C; a 3-min exposure raised the temperature to 47.2 deg C and caused no opacity. However, three 3-min exposures at 4-day intervals (yielding 47.2 deg C each time) yielded cataracts, but five such exposures at weekly intervals did not. Similarly, a single 35-min exposure at 120 mW/sq cm increased the eye temperature to 44.2 deg C and invariably yielded cataracts, but 25- or 30-min exposures at this level, which raised the eye temperature to 44 deg C, did not. Thus, cataract formation was not solely dependent on the final eye temperature.

Carpenter and Van Ummersen (1968) also exposed single eyes of rabbits to 8.2-GHz or 10-GHz RFR in a "closed" waveguide system. In this sys-

tem, the source was fed to a waveguide through appropriate power-measurement instrumentation and the output end of the waveguide was terminated with an iris against which one eye of the anesthetized animal was placed. An E-H tuner was used for impedance matching with the eye in position, to achieve minimal reflection (VSWR of 1.01), thereby readily permitting measurement of the power entering the eye. (The authors expressed the results in terms of the latter rather than power density, presumably because of the shorter penetration depths at these frequencies.)

At 10 GHz, delivered power levels of 1090, 980, 870, 760, and 650 mW for various durations were used; the corresponding threshold durations were about 3, 5, 7, 12, and 40 min, with 650 mW being the asymptotic power level. The threshold curve for 8.2 GHz was essentially the same, and both were similar to the curve for 2.45 GHz. However, for 8.2 and 10 GHz, the cataracts always developed in the anterior cortex region of the lens as localized granular opacities just under the epithelium ("like those produced by infrared radiation"), whereas those resulting from exposure to 2.45 GHz were typically located in the posterior cortex ("resembling, in location, form, and growth, cataracts produced by ionizing radiation").

Van Ummersen and Cogan (1976) exposed 82 anesthetized rabbits to 2.45-GHz CW RFR at an incident power density of 585 mW/sq cm for 7 min in an anechoic chamber at 2 inches from the housing of a corner-reflector antenna, with the corneal surface of the right eye positioned opposite the dipole crossover of the antenna, as described in Carpenter et al. (1960). By calculation from calorimetric measurements in a phantom eye, the rate of energy absorption was 280 mW/sq cm.

The rabbits were euthanized at intervals varying from 6 hr to 1 month after exposure. One hour before death, the rabbits were anesthetized, both eyes were treated topically with tetracaine, and physiologic saline containing tritiated thymidine was injected into the anterior chamber of each eye for subsequent assay of DNA synthesis. On death, each eye was enucleated and the anterior hemisphere was fixed. The lens was removed and the epithelium and anterior capsule were peeled from the cortex. Each epithelial "peel" was processed to lie flat and was mounted and dipped in photographic emulsion. Following one month in darkness in an oxygen-free atmosphere of low humidity, the emulsion was developed, and the epithelium was stained with Ehrlich hematoxylin and mounted for microscopic study. The mitotic figures and tritium-labeled cells in the epithelia of each pair of preparations from the same rabbit, one from the exposed eye and the other from the control eye, were counted. Both eyes of 27 control rabbits with normal lenses were similarly processed.

The control group had no visible lens abnormalities under examination with the slit lamp and ophthalmoscope. The counts for this group showed no constant proportion of labeled (DNA-synthesizing) cells to mitotic figures even within a pair; e.g., one control rabbit had 49 labeled cells and 10 mitotic figures for the right eye, but 2 labeled cells and 59 mitotic figures for the left eye. Therefore, the authors summed the

counts of labeled cells and mitotic figures for each eye. Also, based on further analysis of the data, the percentage differences between the total counts for right and left epithelia were treated statistically. For the control group, the mean difference was 5.6% (+/- 3% SD).

The slit lamp and ophthalmoscope showed no lens changes in the eyes of the groups euthanized 6, 12, 18, and 24 hr after exposure, but both mitotic activity and DNA synthesis were inhibited in the exposed eyes; these eyes had a mean count that was 87.3% (5% SD) lower than for the control eyes. For the groups euthanized 2-28 days after exposure, the percentage differences in mitotic activity and DNA synthesis diminished successively, but with a few exceptions; as an example of the latter, the count for the exposed eye of one rabbit euthanized 14 days after exposure was 20.7% higher than for its other eye.

The group euthanized 2 days after exposure (20 cases) showed moderate lens changes in the exposed eyes, including small, circumscribed, crescent-shaped opacities; postequatorial granules; and posterior cortical banding. Changes in the exposed eyes of those euthanized 3-4 days postexposure (16 cases) covered a wide range of responses, with maximal response consisting of a diffuse opacity involving either the entire posterior region of the cortex or a large part thereof.

Vesicle strings were seen in 4 cases and not in the other 12 cases of those euthanized 3-4 days postexposure. Because of this difference in response, the counts for these subgroups were treated separately. For the cases without vesicle strings, the counts were 63.2% lower than for controls; for the cases with vesicle strings, the counts averaged 820% higher than for controls in 2 of the exposed eyes and were only 3.2% lower in the other 2 cases. Qualitatively similar effects but usually of diminishing magnitudes were observed in the groups euthanized at later postexposure times. For those euthanized 4 weeks postexposure, no concentrations of labeled cells in any one area were found whether or not vesicle strings were present.

In their summary, the authors suggested that for the lenses that did not develop equatorial vesicles from exposure to the RFR, the epithelium followed a course similar to that observed after exposure to ionizing radiation; for the lenses that developed equatorial vesicles, the higher activity in the epithelium closely paralleled that observed in rats after galactose feeding and may have been the result of lens hydration.

Birenbaum et al. (1969a,b) also used a closed-waveguide system to expose one eye each of anesthetized rabbits to RFR but at discrete frequencies in the range 0.8-6.3 GHz. In the system for exposures to 5.5-GHz RFR, the rectangular waveguide had inner dimensions of 1.872-inch by 0.872-inch and in lieu of an iris, a special transition section was inserted between the output of the waveguide and a half-inch-diameter circular waveguide, the exit aperture of which was shaped to receive the eye. As in the system of Carpenter and Van Ummersen (1968), impedance matching was done with the eye in place. This system was also used for exposures to 5.4-, 5.2-, and 4.2-GHz RFR. The eyes of each

rabbit were examined immediately before and after exposure, on day 4 after exposure, and subsequently at weekly intervals for about 1 month.

Exposures to CW or pulsed 5.5-GHz RFR (5-microsecond pulses, 0.001 duty cycle) were done at average powers ranging from about 650 to 1000 mW for durations in the range 1.5 to 50 min at each level. (With a half-inch exit aperture, the average power densities were roughly numerically the same as the powers.) The results for 100 exposures to the pulsed RFR and 62 exposures to the CW RFR were shown on graphs of log-power vs log-duration. A straight line was drawn on each graph (analogous to the rectangular hyperbola on linear coordinates) to represent acute exposure levels and durations that had 50% probability of yielding lens damage, the latter defined as irreversible loss of transparency in at least part of the lens.

The threshold lines for pulsed and CW RFR did not differ significantly; both had values ranging from about 1000 mW for exposures of 2-3 min to about 650 mW for exposures of 20-30 min. However, comparison of the thresholds at 5.5. 5.4, 5.2, and 4.2 GHz at 1000 mW indicated that longer exposures were necessary as the frequency was decreased, e.g., about 17 min for 4.2 GHz vs 2-3 min for 5.5 GHz.

To extend the frequency range upward and downward, the transition above was replaced with a broadband coaxial adapter, and was used to expose rabbit eyes at 0.8 and 6.3 GHz, as well as at 4.2, 4.6, and 5.2 GHz. The threshold duration at 0.8 GHz was about 25 min; at 4.2 and 4.6 GHz it was 17 and 14 min, respectively; and at 5.2 and 6.3 GHz it was about 5 min.

In a preliminary experiment, Birenbaum et al. (1969b) used a rectangular horn (aperture 1.0 x 0.7 cm) to expose one eye each of rabbits to 70-GHz CW RFR at a spacing of 1/32 inch. A severe injury resulted from a 30-min exposure at 610 mW. Initially, a constricted pupil heralded the onset of iritis, and by the second day, diffuse corneal opacification was visible. Four other exposures at levels close to 600 mW resulted in corneal injury also, but no gross lens injuries could be seen through the corneal haze. A 30-min exposure at 570 mW had no effect, but the authors indicated that the exposure may have been faulty. They noted that these and their results at the lower frequencies are consistent with penetration-depth considerations.

Seth and Michaelson (1965) exposed the left eyes of rabbits to 2.8-GHz CW RFR from a magnetron connected to a waveguide, the open end of which was fitted with an attachment to produce a uniform Fresnel-zone field. The rabbits were not anesthetized or tranquilized during exposure. The eyes were examined with an ophthalmoscope and a hand slit lamp before, and at frequent intervals for up to 6 months after, exposure.

A single exposure at 220-240 mW/sq cm (1 rabbit) for 30 min produced conjunctival congestion and miosis, which subsided the next day, but no lenticular changes were noticed over a period of 5 months. Exposure for 45 min at this level (1 rabbit) caused a marked conjunctival reaction

and purulent discharge from the eye. The rabbit was very restless and salivated considerably during exposure. The development of a cataract started 10 days after exposure and the lens was completely opaque at 20 days. At 2.5 months postexposure, the opacity started to regress and the retinal light reflex could be seen at the periphery. The regression continued for the next 2 months.

Three rabbits were very agitated and salivated profusely during a single exposure for 60 min at 220-240 mW/sq cm. After exposure, the left eyes showed marked conjunctival reactions and edema, which subsided after 3-4 days. Also, suborbital skin burns developed. The lenticular changes differed among the rabbits. In 1 rabbit, the lens became pearly and remained so for 1.5 months, at which time the animal died. Lens changes in another rabbit progressed during the 45 days after exposure, at which time regression started; the lens became completely clear by day 56. A week later, the lens showed a small black spot, which developed into a well defined opacity by day 75, after which the opacity regressed slowly and disappeared by day 165 postexposure. In the third rabbit, a small opacity was seen 2 days after exposure, which developed until day 15 and remained stable until the animal died on day 45.

Three successive daily 10-min exposures at 220-240 mW/sq cm (1 rabbit) yielded marked agitation and salivation. Severe uveitis developed 2 days after the last exposure, which led to the formation of a completely pearly opacity. The eyeball shriveled up and the lenticular changes remained unaffected during 6 months of observation.

Single exposure at 160-170 mW/sq cm for 30 or 45 min (1 rabbit each) produced mild conjunctival reactions but yielded no substantive lens changes. Single 60-min exposures at this level (6 rabbits) caused moderate conjunctival reactions. Four of the rabbits showed lenticular changes. In three of these, diffuse opacities found in the posterior cortex 1-2 days after exposure cleared completely by day 4. However, small well-defined opacities appeared 5-7 days after exposure, which regressed in one rabbit, remained stable in the second, and waxed and waned in the third over a 4-month observational period. A small opacity appeared in the fourth rabbit on day 20 and remained stable over a 3-month observational period.

Of 4 rabbits given five successive daily 30-min exposures at 160-170 mW/sq cm, 1 rabbit exhibited a transient diffuse opacity but the other 3 rabbits showed no lens changes over a 3-month observational period.

The authors indicated that their results showed two types of lenticular lesions. One type, from exposure to "high-intensity" RFR, consisted of rapid and complete opacifications, with associated gross damage to other ocular structures; the other, in response to "low-level" RFR, consisted of small lenticular opacities that appeared several days to weeks after exposure, with minimal damage to or reaction of other ocular structures, and with a tendency to regress, disappear completely, and reappear. No results were presented for control eyes of the rabbits.

Guy et al. (1975a) investigated the cataractogenic effects of near-field 2.45-GHz CW RFR in rabbits. Exposures of anesthetized rabbits were done at a distance of 5 cm between the crossing point of the dipole feed of a corner reflector and the corneal surface of the right eye, with the left eye serving as control. Just before and after 20-second exposures at 540 mW/sq cm, measurements of intraocular temperature vs depth from the corneal surface (in 2-mm increments) were made with a thermocouple inserted through a surgically implanted thin glass tube, from which SAR variation with depth was calculated. Temperatures at a fixed depth in the vitreous body (just behind the posterior pole of the lens) were also measured immediately after 5-min intervals of exposure at: 100 mW/sq cm for 60 min, 200 mW/sq cm for 35-40 min, and 300 mW/sq cm for 30-35 min. Rectal temperatures and pulse rates were recorded before and after each exposure. Temperature measurements in the rabbit head at depths beyond the eye were made immediately after euthanizing the animal.

Maximum absorption was found to occur within the vitreous at a depth of about 1.5 cm behind the cornea, with a normalized mean SAR of 0.92 W/kg per mW/sq cm. Also, rectal temperature and pulse rate rose respectively by 0.97 deg C and about 30% during exposure. For the 5-min exposures at 100 mW/sq cm (90 W/kg), vitreous temperature just behind the posterior pole of the lens reached a plateau of 41 deg C. As indicated below, the exposure of intact rabbits at this level for at least 100 min (maximum duration used) did not produce cataracts. For the exposures at 200 and 300 mW/sq cm (180 and 270 W/kg), the plateaus were about 42 and 45 deg C and were cataractogenic. The vitreous-temperature plateaus at all three levels were reached in 15-20 min due to the gradual increase in body-core temperature. Orbital temperatures, however, never rose as high as those of the vitreous, presumably because of greater orbital blood flow.

To determine cataractogenic thresholds (at 2.45 GHz), Guy et al. (1975a) exposed the right eyes of 81 sedated rabbits at various RFR levels for various durations, with the left eyes as controls. Both eyes of each rabbit were examined with slit lamp and ophthalmoscope before exposure, immediately following exposure, and periodically afterward.

Depending on RFR level, varying degrees of transient tearing, pupillary constriction, and anterior-chamber turbidity were seen after exposure, which disappeared by the second day after exposure. Lens changes were usually detectable on the first or second day after exposure. At the lower RFR levels, mild and often reversible changes, such as a milky band (single, double, or triple) in the posterior cortex, close to the posterior capsule and extending to the equator, were observed. Also, a chain of vacuoles or small vesicles formed in the area of the posterior suture.

At higher RFR levels, more advanced and permanent cataractous changes were observed, consisting of pronounced banding, higher numbers of vacuoles, and a well-circumscribed opacity in the posterior cortex. Large vesicles were seen occasionally in the lens equator, and in a few

cases, the posterior cortical opacity was found to extend from the equator to the anterior subcapsular cortex; however, most cataracts were confined to the posterior cortical area. No abnormalities were found in the fundi. Control eyes remained normal.

The power-density vs exposure-duration data were plotted in the same manner as those in Carpenter and Van Ummersen (1968), and the resulting cataractogenesis-threshold curve was displayed together with the curve from Carpenter and Van Ummersen (1968). The two curves matched closely, except that the asymptotic power density found by Guy et al. (1975a) was slightly lower, about 150 mW/sq cm (138 W/kg) for 100 min.

Guy et al. (1975a) also presented plots of numerical calculations of intraocular temperature distributions in the intact rabbit eye from a computer model that incorporated conduction, evaporation, and radiation cooling, and based on a spatially constant specific heat (for a saline solution), the vitreous-humor thermal conductivity of beef eye, and a calculated lens thermal conductivity. Also assumed were appropriate values of other parameters, including blood-supply rate, temperature in the orbit, and heat-transfer rate at the corneal surface. The predicted values of vitreous and orbit temperatures vs time during and subsequent to exposure at 200 mW/sq cm (183 W/kg) were in good agreement with the experimental values, indicating that RFR cataractogenesis is thermal.

Kramar et al. (1975) similarly exposed the right eyes of rabbits to suprathreshold levels of near-field 2.45-GHz RFR, but using general hypothermia to ensure that retrolental temperature did not exceed 41 deg C. In the first part of the experiment, three groups of three rabbits each were surgically prepared for intraocular-temperature measurements as in Guy et al. (1975a) and were rendered hypothermic by immersing their bodies in ice water until the desired rectal temperature was reached, at which time they were immersed in water at a temperature sufficient to maintain that rectal temperature. Then, one group each was exposed at 200 mW/sq cm (184 W/kg) for 30 min, 300 mW/sq cm (276 W/kg) for 20 min, and 400 mW/sq cm (368 W/kg) for 15 min, exposure conditions previously found to produce cataracts.

For the group exposed at 200 mW/sq cm (186 W/kg), a plateau retrolental temperature of about 36 deg C was obtained by holding rectal temperature slightly above 30 deg C. Holding rectal temperature at 30 deg C for the group exposed at 300 mW/sq cm (276 W/kg) yielded a plateau retrolental temperature of about 39 deg C. To maintain the retrolental temperature of the group exposed at 400 mW/sq cm (368 W/kg) at about the same level required a hypothermic level of about 25 deg C.

In the second part of the experiment, three groups of three surgically intact rabbits each were similarly rendered hypothermic, and one group each was exposed at the three levels of RFR above as soon as the rectal temperatures had stabilized. At exposure end, the rabbits were removed from the water bath, dried, and allowed to recover, and their eyes were examined periodically with a slit lamp. Slight tearing and pupillary constriction was observed on the right side immediately after exposure,

effects that disappeared on the second day. The lenses of all rabbits remained clear throughout the 2-3 months of observation. The periods of hypothermia had no apparent ill effects on the rabbits.

Using the model mentioned above, numerical calculations of intraocular temperature distributions in rabbits under general hypothermia were made and the agreement was found to be very good with respect to both time characteristics and maximum temperature. The isotherms were similar to the normothermic ones except for the lower temperature levels.

Appleton et al. (1975a) exposed 8 groups of anesthetized rabbits to 3-GHz CW RFR from an ellipsoidal dish antenna 6 ft in diameter within an anechoic chamber, with the left eye on the axis and 1 ft beyond the second focal point of the dish or about 87 inches from its vertex (a site well within the near field). Before exposure, the rabbits were examined with slit lamp and ophthalmoscope and only those with eyes free of lenticular opacities, vacuoles, and subcapsular iridescence were included. Groups I and II were exposed at 100 mW/sq cm for 15 and 30 min, respectively. Groups III and IV were also exposed for 15 and 30 min, but at 200 mW/sq cm, as were groups V and VI at 300 mW/sq cm. Groups VII and VIII were given 15-min exposures at 400 and 500 mW/sq cm, respectively, and Group IX served as controls. The groups consisted of 3 rabbits each except VIII, which had 6 rabbits. The authors noted that unanesthetized rabbits exposed for 15 min at 100 mW/sq cm became heat-stressed and struggled out of the field, hence the need for anesthesia.

Groups I-IV (100 or 200 mW/sq cm for 15 or 30 min) underwent no ocular changes during or immediately after exposure, or in daily examinations for 14 days or weekly examinations for one month followed by monthly examinations for one year. Groups V, VII, and VIII (15-min exposures at 300, 400, or 500 mW/sq cm), however, showed acute ocular changes during exposure, consisting of hyperemia of the lids and conjunctiva, miosis, anterior chamber flare, engorgement of iris vessels, and periorbital cutaneous burns. The miosis and flare persisted for about 24 hr. Most of the severe changes occurred for the higher RFR levels. Subsequent examinations showed no morphologic lenticular abnormalities. These results indicated the existence of a threshold between 200 and 300 mW/sq cm for exposure durations between 10 and 20 min, roughly consistent with the threshold curve of Guy et al. (1975a), a point noted by Appleton et al. (1975a).

The 3 rabbits of group VI (300 mW/sq cm for 30 min) and 3 of the [illegible] group VIII (500 mW/sq cm for 15 min) died immediately after exposure; the 3 group-VIII survivors were greatly stressed. No ocular effects were seen in control rabbits at a one-year followup examination.

Kramar et al. (1978) exposed rabbits and rhesus monkeys [illegible] field of a cavity-backed 2.45-GHz resonant slot [illegible] ground plane (Lin, 1974), said to simulate a [illegible]. The right corneas of the animals were exposed [illegible] in consonance with the U.S. emission standard [illegible] the electric-field (E) levels in V/m were [illegible]

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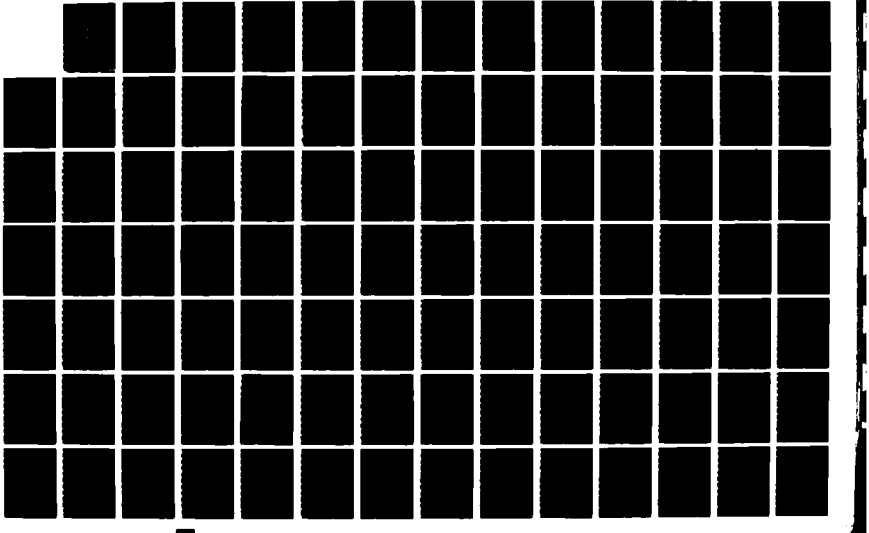

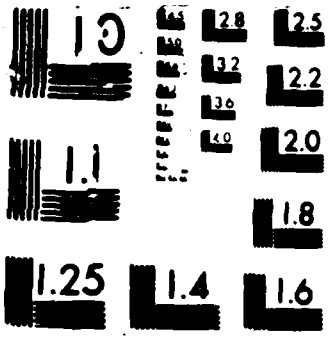
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densities (APDs) in mW/sq cm by dividing the values of E-squared by ten times the impedance of free space (i.e., 3770 ohms).

With a thermocouple-insertion technique similar to that used by Guy et al. (1975a), temperatures were measured along the anterior-posterior axis of the rabbit eye in 2-mm increments immediately before and after exposures at 540 mW/sq cm (APD) for 15-20 seconds, from which the SAR distribution with depth was determined. The normalized peak SAR, about 0.55 W/kg per mW/sq cm, was at a depth of 4 mm.

The cataractogenesis threshold was determined by exposing 22 rabbits at APDs of 500 to 150 mW/sq cm (peak SARs of 275 to 82.5 W/kg) for various durations. Immediate and delayed effects were seen in the exposed eyes. The former included tearing, constricted pupil, dilated conjunctival and iris vessels, a turbid anterior chamber, and a milky band in the lens posterior cortex. Delayed effects were confined to the lens and were seen 5-7 days after exposure. These were vacuole formation along the posterior suture line followed by progressive opacification of the posterior cortex, the latter only occurring for the higher levels. The mildest, often reversible change was posterior cortical banding, taken to be the threshold effect. The lowest APD-duration combination to show any lens change was 180 mW/sq cm (99 W/kg) for 140 min.

SAR variation with depth in the eye of the rhesus monkey was similarly determined in two animals by centering the slot radiator 5 cm over the bridge of the nose. Excessive heating of the nasal bridge, however, led to centering the radiator over one eye at 5 cm between slot and cornea in a third monkey. With the slot centered over the nose, the peak SAR within both eyes was in the vicinity of the lens, 0.29 W/kg per mW/sq cm. With the slot over the right eye, the peak SAR was not in the lens but in the anterior chamber; the maximum SAR in the right lens was 0.35 W/kg per mW/sq cm, much higher than for the slot centered over the nose, but was much lower than 0.29 W/kg per mW/sq cm in the left lens.

In the cataractogenesis-threshold determinations, exposure of 1 monkey with the slot centered over the nose for 22 min at an APD of 300 mW/sq cm (87 W/kg) caused second- to third-degree burns on the bridge, but the eyes remained unaffected; varying degrees of nasal burns were caused by exposure with the slot over the right eye, 1 monkey each at 400 mW/sq cm (140 W/kg) for 30 and 60 min and 1 at 500 mW/sq cm (175 W/kg) for 60 min. In the last case, lid edema, contracted pupil, and a moderately severe reaction in the anterior chamber also occurred, with the reaction in the anterior chamber persisting for 10 days. However, the lenses of all 3 monkeys remained clear during a 13-month examination period.

Computer prediction of intraocular temperature-vs-time profiles in the rabbit and monkey eye for various exposure levels yielded numerical results consistent with experimental values. Because of the facial-bone configuration in the monkey, its SAR distribution differs considerably from that of the rabbit. For exposure at 300 mW/sq cm, the highest retrolental temperature in the monkey was only 40.2 deg C as compared with 45.1 deg C in the rabbit. Even for 500 mW/sq cm, the maximum

retrolental temperature in the monkey would be about 42 deg C. Since the latter is the minimum temperature at which lens damage would occur, severe facial burns would be produced in primates (including humans) at RFR levels much below their cataractogenesis thresholds.

McAfee et al. (1979b) trained rhesus monkeys, by operant-lever pressing for apple-juice reward, to face a source of 9.3-GHz pulsed RFR (half-microsecond pulses at 1050 pps). The monkeys were then exposed without restraint to the RFR with the head 15 cm from a vertically polarized standard-gain horn, at an average power density of 150 mW/sq cm (peak power density 286 W/sq cm). The SAR, determined in saline phantoms, exceeded 15 W/kg. Each of 12 monkeys was exposed for up to 20 min/day for 30 to 40 sessions over several months. Seventy-five monkeys neither exposed nor sham-exposed served as controls.

No cataracts or corneal lesions were found in any of the exposed monkeys up to 12 months after exposure. The authors cited a 3-deg-C rise in 150 ml of saline for 15 min of exposure. Even though the locus of maximum temperature in the eye would be closer to the surface of the eye for 9.3-GHz than for 2.45-GHz RFR, the absence of cataracts was consistent with the finding of Guy and coworkers that an intraocular temperature rise of at least 5 deg C is necessary for cataractogenesis.

Weiter et al. (1975) studied the effects of exposing rabbit lenses in vitro to 2.45-GHz CW RFR or 2.86-GHz pulsed RFR on the ascorbic-acid concentration in the lenses. Prior to exposure, paired lenses were aseptically excised, placed in petri dishes containing culture medium consisting of 20% rabbit serum and 80% medium 199 (Earle's modified salt base) with penicillin and streptomycin, and incubated for 48 hr at 37 deg C in air containing 5% CO2.

One of each pair was exposed by removing the petri-dish cover, lowering the fluid level to leave the upper third of the lens in air, and placing the dish 1 m below a horn in an anechoic chamber. Before and during exposure, the culture-fluid temperature was monitored with a thermistor about 2.5 cm from the lens and oriented perpendicular to the electric vector. The other (control) lens of each pair was heated by indirect forced hot air to match the culture-fluid temperature produced by the RFR. After exposure or heat treatment, the lenses were incubated for 24 hr, removed from the medium, rolled on filter paper to remove adherent media and vitreous, and weighed. Then the lenses were homogenized, deproteinized in trichloroacetic acid, and assayed for total ascorbic acid (including dehydroascorbic acid).

Exposure of one lens each to 2.45-GHz CW RFR for 10 min at 0, 50, 100, 150, 200, and 250 mW/sq cm yielded an approximately linear decrease in total ascorbic-acid concentration (expressed in micrograms per gram of lens tissue) from about 85 at 0 mW/sq cm (sham-exposure) to about 30 at 250 mW/sq cm, with no apparent threshold power density for this effect. For 15 min of exposure of lenses to the CW RFR at 0, 50, 100, 150, and 200 mW/sq cm, the corresponding temperatures of the culture fluid were about 26, 34, 36, 41, and 47 deg C and the ascorbic-acid concentrations

decreased linearly from about 105 to 30. Corresponding concentrations for the control lenses heated (in the medium) for 15 min to the same temperatures were similar, indicating that the changes induced by the RFR were thermally caused. Lenses exposed to 2.45-GHz CW RFR and 2.86-GHz pulsed RFR (1-microsecond pulses at 500 pps) at 50, 100, and 150 mW/sq cm (average) for an unstated duration showed equivalent decreases in concentrations.

Examination of the lenses with both the slit-lamp biomicroscope and the inverted microscope showed that in all cases where the ascorbic-acid concentration was 60 or higher, the lens was clear, and that at lower concentrations, the lens epithelium became progressively cloudier (edematous), especially toward the equator.

Guy et al. (1980b), in a multi-endpoint study, concurrently exposed 4 rabbits dorsally in acrylic cages within individual anechoic chambers to 2.45-GHz CW RFR 23 hr/day at 10 mW/sq cm for 180 days in the far field of a horn in each chamber. The electric vector was parallel to the long axis of the rabbit. For controls, 4 other rabbits were sham-exposed in similar chambers concurrently with the RFR-exposed rabbits. The eight chambers were maintained at 24 deg C by a common air conditioner.

Dorsal exposure, selected for compactness in multiple-chamber design, was rather uncommon in prior investigations. Therefore, in preliminary dosimetric experiments, rabbits were exposed laterally and dorsally to determine the respective power densities needed to produce the same mean SAR in the eye. The exposures were for 15 seconds at 525 mW/sq cm measured at eye location, and a thermocouple was used to measure SAR as a function of depth in the eye. Greater variation of SAR was obtained for dorsal than lateral exposure, but the spatial-average SARs for the eye were comparable: 0.679 and 0.481 W/kg per mW/sq cm, respectively.

Lines of constant SARs were obtained by use of thermography on rabbit carcasses. The results indicated that 10 mW/sq cm would produce a peak SAR of 17 W/kg in the head when the animal is in the normal resting position in the cage. By calculation (Durney et al., 1978, p. 92), the whole-body SAR for a prolate-spheroidal model of a rabbit exposed to 2.45-GHz RFR at 10 mW/sq cm laterally or dorsally is about 1.5 W/kg.

Periodic eye examinations with a slit-lamp microscope showed normal aging changes in the lenses, but the differences between exposed and control groups were not significant. The other endpoints studied are discussed in Section 3.5.2.

Kues et al. (1985) exposed both eyes of 7 cynomolgus monkeys from above to 2.45-GHz CW RFR and 8 monkeys to 2.45-GHz pulsed RFR (10-microsecond pulses at 100 pps) in 4-hr sessions at 5-30 mW/sq cm (average), with one week between sessions in most cases. For exposure, each monkey was anesthetized and placed supine with its eyelids closed on a Styrofoam slab within a 1.2-m cubical anechoic chamber. The antenna was an HP-S281A coaxial-cable-to-waveguide transition with an aperture of 7.2 x 3.4 cm centered over the nasal bridge 10 cm from the ocular surfaces (at

about the start of the conventional far-field distance) and with larger dimension transverse to the monkey's long body axis. The forward and reflected powers were measured with a bidirectional coupler in the line feeding the antenna, and the power densities at the monkey site in the absence of the monkey and Styrofoam slab were measured with a Narda 8201 electromagnetic monitor and a 8221 near-field probe; these measurements showed that a forward power of 2.9 W was required to obtain 10 mW/sq cm.

The authors stated: "The use of the HP-S281A coaxial cable to waveguide transition as an antenna may be questionable. Its use was necessitated by the required power densities and available equipment limitations. It was also found to be inappropriate to change the source to something more conventional halfway through our study... A multiple reflection between the test animal and the antenna, primarily its waveguide flange, could alter the intensity of the incident field. This alteration in intensity could go in either direction. Measured specific absorption rate (SAR) indicates that this is probably not occurring...These facts and the realization that the presence of the animal may have introduced some change in field symmetry were accepted for the present experiment."

SARs were based on in-vivo temperature measurements made, during a 4-hr exposure at 20 mW/sq cm, with a fluoroptic probe surgically implanted in the anterior chamber of the eye and butted up against the endothelial layer of the cornea. During exposure, the temperature was recorded at 4-second intervals for the first hour and at 1-min intervals for the other three hours. The authors did not present the temperature data, but indicated that the temperature had risen by 0.77 (from 34.5) deg C during the 4-hr exposure and that a 1-min temperature rise of 0.09 deg C was selected from the steepest part of the temperature curve and used in the calorimetric equation, which yielded 0.26 W/kg per mW/sq cm.

Rectal temperatures measured during several 4-hr sham- and RFR-exposures at 10 mW/sq cm (2.6 W/kg) showed respective mean decreases of 2.5 and 2.4 deg C, attributed to the anesthesia.

Before and at stated intervals after exposure, an eyelid speculum was inserted and a wide-field contact specular microscope (Keeler-Konan Model SP-1) was used to scan and photograph the central 6 mm of cornea, with each photographic field at 120x covering about 1 sq mm of cornea. (The specular microscope is reputed to have a resolution far exceeding that of the slit-lamp microscope.) During examination, the cornea was kept moistened with balanced salt solution. The number of lesions in each field was counted and the degree of endothelial damage in each eye was taken to be the number in the field that had the most lesions. The numbers were classified as: no change, 0-2 lesions; minor change, 3-10 lesions; moderate change, 11-50 lesions; major change, >50 lesions.

Monkeys 1-7 were given the CW RFR. Monkey 1 was exposed at 5 mW/sq cm (1.3 W/kg) for 44 weekly 4-hr sessions and examined with the specular microscope every 4 weeks (10 examinations); monkeys 2 and 3 were exposed at 10 mW/sq cm (2.6 W/kg) for 56 and 10 weekly sessions and given 12 and

3 examinations, respectively; monkey 4 was exposed at 20 mW/sq cm (5.2 W/kg) for 18 weekly sessions and given 6 examinations. Monkeys 1, 3, and 4 exhibited no changes (as defined above) and monkey 2 minor change in only one eye during one examination.

Monkey 5 was exposed at 30 mW/sq cm (7.8 W/kg) for one 4-hr session and examined once; it exhibited major change in one eye and moderate change in the other eye. Monkey 6 was exposed for one session at 20 mW/sq cm (5.2 W/kg) and showed no change in one examination; it was then exposed at 30 mW/sq cm (7.8 W/kg) for 5 weekly sessions; moderate change was reported for 3 of 5 examinations. Monkey 7, given 22 weekly sessions at 20 mW/sq cm (5.2 W/kg), showed minor change in 1 of 14 examinations; on exposure at 30 mW/sq cm (7.8 W/kg) for 8 sessions, it showed "minor-to-moderate" change in 2 of 6 examinations; when then given 2 series of 4 consecutive daily 4-hr sessions at 20 mW/sq cm (5.2 W/kg) and examined after each series, it exhibited major change in both examinations.

Monkeys 8-15 were given the pulsed RFR. Monkey 8, exposed at 10 mW/sq cm (2.6 W/kg) for 5 weekly 4-hr sessions and examined 5 times, showed no change; when given 4 series of 4 consecutive daily 4-hr sessions at the same RFR level and examined after each series, it exhibited minor change in each examination. Monkey 9, exposed for one session at 15 mW/sq cm (3.9 W/kg) and examined once, showed major change. Monkey 10 showed "minor-to-major" change after each of 5 weekly sessions at 10 mW/sq cm (2.6 W/kg) and major change after one session at 15 mW/sq cm (3.9 W/kg).

Monkey 11, given 5 weekly sessions at 10 mW/sq cm (2.6 W/kg), exhibited "very minor change" in 2 of 5 examinations, but showed major change for each of 4 series of 4 consecutive daily 4-hr exposures at this level. Monkey 12, given 11 weekly sessions at 10 mW/sq cm (2.6 W/kg), exhibited "minor-to-moderate" change in 6 of 11 examinations. Monkey 13 showed no change after exposure for 2 weekly sessions at 5 mW/sq cm (1.3 W/kg); it showed "minor-to-major" change after each of 4 weekly sessions and major change for 1 series of 4 consecutive daily sessions at 10 mW/sq cm (2.6 W/kg). Monkeys 14 and 15 were given 4 and 2 weekly sessions at 10 mW/sq cm (2.6 W/kg), respectively; minor change was found in monkey 14 in 1 of 4 examinations and no change in monkey 15. Based on the results, the authors noted that at corresponding average power densities, the pulsed RFR was more effective than the CW RFR.

Five monkeys were sham-exposed for a total of 10 sessions (presumably in 4-hr sessions): three for two sessions each, one for three sessions, and one for a single session; they were otherwise treated similarly. Four of these monkeys were subsequently used in the RFR-exposure protocols. No endothelial abnormalities were detected.

Several representative photographs were presented. Among these was a wide-field specular micrograph (x120) of central corneal endothelium from monkey 6 before exposure, which clearly delineated the hexagonal cell boundaries and the nuclei of most cells, and showed no lesions. However, a micrograph from monkey 9, taken 48 hr after the single 4-hr

exposure at 15 mW/sq cm (3.9 W/kg) and classified as exhibiting major change, showed numerous lesions distributed over areas of normal mosaic (about 50 lesions per sq mm), each lesion involving one cell or several contiguous cells. A specular micrograph for monkey 10 taken 48 hr after a 4-hr exposure at 10 mW/sq cm (2.6 W/kg) showed a similar distribution.

Four of the RFR-exposed monkeys were euthanized after confirmation of an effect by specular microscopy. The eyes were enucleated, and one eye of each pair was prepared for vital staining with alizarin red and trypan blue and the other for transmission electron microscopy. Representative micrographs were presented only for monkey 10, classified as exhibiting minor-to-major change after 5 exposures at 10 mW/sq cm (2.6 W/kg) and major change after 1 exposure at 15 mW/sq cm (3.9 W/kg). In the normal areas of corneal endothelium treated with alizarin red and trypan blue, the photomicrograph (x400) displayed well-defined hexagonal cell walls and faintly stained nuclei; also seen were two lesions characterized by the absence of cells and uptake of trypan blue. A transmission electron micrograph (x4000) of the corneal endothelium 48 hr after exposure at 10 mW/sq cm (2.6 W/kg) showed prominent intracellular vacuolization and a space between basal endothelial surface and Descemet's membrane. It is unclear why this monkey was subsequently exposed at 15 mW/sq cm, as noted in the protocol, if its eyes had been removed.

Open to question is the adequacy of the relatively small number of sham-exposure sessions (10 total) as compared, for example, with 56 sessions for monkey 2 at 10 mW/sq cm (2.6 W/kg) of CW RFR, with anesthesia used for each sham or RFR session. However, no major ocular effects were seen in this monkey or in monkey 1, exposed at 5 mW/sq cm (1.3 W/kg) of CW RFR for 44 weekly sessions.

The authors noted: "During our study, changes observed with the specular microscope were not visible by slit-lamp examination. As for histologic examinations, our study has revealed that a time `window' may exist during which time the reported change is observable. Before and after this period, the endothelium probably would appear relatively normal. It was by use of the in vivo examination, that we were able to find this window of effect and then study the corneas histologically." The point is obscure; it seems to imply that the effect is reversible. If so, by what mechanism (since the authors noted that the primate corneal endothelium is not known to repair itself through cell division)?

Several investigators (most recently Kues et al., 1985) looked for differences in levels of pulsed and CW RFR for ocular damage. Most of these investigators found no significant differences between the effects of pulsed and CW RFR at equivalent average power densities. However, as noted above, Kues et al. (1985) found that pulsed RFR was more effective in altering the corneal endothelium than CW RFR.

In summary of the animal studies, many of the results indicated that an inverse relationship (reciprocity) exists between average power density and exposure duration for cataract formation. The mean threshold

values probably vary to some extent from species to species, but are of the order of 100 mW/sq cm. Increases in intraocular temperature of about 5 deg C or more appear to be necessary for eye damage. Moreover, lens opacifications caused solely by exposure to suprathreshold RFR levels were not produced at the same average power densities when the eye was adequately cooled during exposure, indicating that RFR cataractogenesis is essentially a gross thermal effect. (The RFR threshold power density corresponds to a heat-generation rate that can be just compensated for by the heat-removal rate to maintain the eye at below the temperature for damage.)

3.1.4.1.2 HUMANS

Cases of ocular damage in humans ascribed to occupational exposure to RFR have been reported (e.g., Hirsh and Parker, 1952; Shimkovich and Shilyaev, 1959; Kurz and Einaugler 1968; Zaret, 1969; and Issel and Emmerlich, 1981). Although the exposure histories of these individuals could not be ascertained with any degree of certitude, it is likely that their actual or incipient vision impairment resulted from exposure to average power densities substantially greater than the threshold found in animal studies (about 150 mW/sq cm).

Cleary et al. (1965) performed a retrospective study of the incidence of cataracts in Army and Air Force veterans of World War II and the Korean War to determine whether such incidence could have been related to occupational exposure to RFR. A preliminary study had indicated that a sample of about 2,500 cataract cases and a control group of the same size would be sufficient to permit detection of a twofold increase in relative risk with a probability of 80% at the 5% level of significance. Examination of Veterans Administration hospital records yielded 2,946 veterans born after 1910 who had been treated for cataracts during the period 1950-1962. A random sample of 2,164 veterans hospitalized during the same period for other ailments was selected for control. On the basis of military occupational specialties (MOSs), each individual was classified by the authors as a radar worker, a nonradar worker, or one whose specialty could not be discerned.

In the radar group, they found 19 individuals with cataracts and 2,625 individuals without cataracts; in the nonradar group, 21 individuals had cataracts and 1,935 did not. (Of the other 510 subjects, 202 of those with cataracts and 125 of those without cataracts had no indicated MOSs and the remaining 100 of those with cataracts and 125 of those without cataracts had MOSs that did not permit determination of occupational category.) These numbers yielded an overall relative risk factor of 0.67, with unity representing no increase in relative risk and values larger than unity representing the degree of severity of the effect.

The authors noted that examination of the Air Force data separately yielded a risk factor of 2.18, but at a significance level greater than 10%, and indicated that the number of cases was too small to draw any inferences. They also stated that an analysis of all the data by age grouping suggested no alteration in age-specific incidence of cataracts

due to RFR exposure.

Cleary and Pasternack (1966) obtained responses to a questionnaire on occupational histories from personnel then currently employed at 16 microwave installations and used the histories to differentiate controls from exposure cases. By this method, the authors selected 736 workers as occupationally exposed to RFR and 559 workers from the same locations and occupational environments (other than RFR) as controls. Exposure cases were classified in occupational specializations and relative RFR-exposure severity by considering: types and functions of equipments used; average generated powers, frequencies, and modes of power termination; and duration of work with each type of equipment, working distance from equipment during normal operation, and specific type of work performed. Relative exposure scores were determined by assigning appropriate weights to these factors (e.g., proportionality to average power and inverse proportionality to equipment distance).

Histograms representing the age distribution (for the 5-year intervals from 16 to 65 years) were presented for each group. The mean ages for the exposed and control groups were 32.76 and 33.20 years, respectively; however, the exposed group had a relative maximum of 25% in the subgroup 26-30 years of age, whereas the control group had a relative maximum of 19% in the 21-25-year subgroup and a larger proportion of older workers than the exposed group. The authors indicated that chi-square analysis confirmed the significant difference in age composition between the two groups and noted that "man-for-man age matching of exposed and controls would have eliminated age differences but, due to sampling restrictions, this was not possible."

Also presented for the exposed group were histograms representing the age distribution of exposure scores (from 1 to 85 in 5-point intervals) and the age distribution of exposure durations (from 0 to 299 months in 20-month intervals). The first histogram showed that the largest number of workers, 36%, had exposure scores in the 6-10 interval, with a sharp falloff to about 2% for exposure scores in the 31-35 interval; the other histogram showed that the largest number of workers, 20%, were exposed for 0-19 months, with an approximately linear decrease to about 2% for exposures of 140-159 months.

Exposed and control groups were given slit-lamp examinations and each person was graded (on a double-blind basis) for subcataractous lens changes, classified as minute defects, opacification, relucency, sutural defects, and posterior polar defects. A grade of 0 for "insignificant" to 3 for "large numbers or major degree of change (short of clinically recognized cataract)" was assigned in each category for each lens. An "eye score" consisting of the unweighted sum of scores for each type of defect was calculated.

A linear regression model was used for each group to relate mean eye score to age on the basis that the major increase in eye score with time was due to physiological aging of the lens. The slope for the exposed group was significantly higher than for the control group; the lines

crossed over at 20 years of age with a mean score of about 4.2. The authors stated: "At this time, no detrimental effects such as loss of visual acuity or increased propensity for cataract formation have been associated with these changes. These subclinical changes induced with greater frequency in the lenses of microwave workers than controls may in fact indicate an acceleration of aging of lens tissue." The authors subsequently added terms corresponding to exposure score, duration, and duration-exposure interaction to the linear regression equations and found that the differences in regression coefficients were significant ($p<0.05$), with age providing the highest contributions to eye score and successively smaller contributions from the other terms.

The authors then used a 2x4 contingency chi-square table to determine which of the lens-defect categories contributed substantially to the scores. The highest mean scores were for minute defects, 1.66 and 1.61 for the exposed and control groups, respectively, but the difference was nonsignificant ($p>0.05$). Respective mean scores of 1.58 and 1.47 were obtained for opacification, a significant difference ($p<0.025$). The mean scores for relucency were 1.56 and 1.53; those for sutural defects were 1.19 and 1.21; both differences were nonsignificant. The lowest mean scores were for posterior polar defects, 0.62 and 0.41 for the exposed and control groups, respectively, but the difference between them had the highest significance ($p<0.0005$).

Open to question in this study, in addition to the usual uncertainties regarding actual exposure frequencies, levels, and durations, were the grading of each worker for lens changes on an arbitrary 0-3 scale and the use of composite eye scores, measures that were subjective and not associated with actual reduction in visual acuity in the individuals examined; statistical analyses based on such measures can be misleading. Other problems were the previously noted age-distribution difference between the exposed and control groups and the age-related lens changes in both. Regarding the latter, the authors stated: "Since the number of defects increased significantly with age in the control group as well as in the group of microwave workers, this process may be interpreted as indicating lens aging. Occupational exposure to microwave radiation may be implicated as a stress which increases the rate of lens aging although it is impossible at present to relate this effect to functional impairment such as loss of visual acuity or cataracts."

Aurell and Tengroth (1973) investigated 98 personnel involved in the industrial development of radar equipment (presumably in Sweden). Of these, 68 had been exposed to microwaves for a "certain" period (not specified) or had been still working in this field, and included persons testing radar equipment and measuring microwave radiations from various klystrons and persons from the experimental laboratories. The control group consisted of 30 people from the same industry who had never been exposed as far as was known. Two eye specialists independently examined these 128 people without knowledge of their occupation or exposure. The examination included refraction and determination of visual acuity, a study of the optical media with a corneal microscope and slit lamp under complete pupil dilation, and an ophthalmoscopic study of the retina.

The numbers of persons who had opacities larger than 0.5 mm in diameter or a large concentration of smaller opacities in the subcortical region were displayed as bar graphs for those less than 26 years of age and for the 5-year age subgroups 26-30 to 56-60 years. None of the 6 persons in the exposed group and the 7 persons in the control group younger than 26 years had opacities. Those in the 26-30, 31-35, and 36-40 comprised the three largest exposure subgroups. In the 26-30 subgroup, 6 of 20 had opacities, as compared with 2 of 15 in the control subgroup; the results for the 31-35-year exposed and control subgroups were 5 of 14 and 0 of 4, respectively; and in the 36-40 subgroups, there were 6 of 15 and 1 of 2, respectively. Of 6 persons in the 41-45 exposed subgroup, 2 had opacities, but neither of the 2 persons in the control subgroup did. The three older exposed subgroups each had at least one person with opacities, but there were no persons older than 41 years in the control group for comparison. The retinal-lesion results were qualitatively similar to those for opacities; 19 (of 68) exposed people exhibited such lesions, as compared with only 1 (of 30) in the control group.

In their discussion, the authors stated: "It is of great interest that eye lesions, both lenticular and retinal, found in this material are significantly higher in the group of persons belonging to the test group than the persons working in the laboratories. It is difficult to draw conclusions as to which kind of work entails the most risk, but one knows that the personnel testing the equipment for measuring radiation are more liable to exposure from higher power levels than others, i.e. laboratory personnel...Another explanation is that the eye lesions observed are due to leakages from the equipment, or carelessness on the part of the personnel."

Appleton and coworkers initiated a survey consisting of examinations of the eyes of personnel at Army posts where various types of electronic communication, detection, guidance, and weather equipment were under development, test, and use. In Appleton and McCrossan (1972), results of semiannual examinations conducted between November 1968 and May 1971 of 226 persons employed at Fort Monmouth, NJ, were presented. The selection of personnel was based on the Occupational Vision Program of the post, and all personnel with histories of working with microwave equipment, lasers, xenon arcs, ultraviolet, and welding were asked to participate. Examinations were conducted by ophthalmologists without prior knowledge of the histories of the individuals. The visual acuity of each person was determined. Then the pupil of each eye was dilated and the fundus examined by direct ophthalmoscopy, with special attention on the details of the posterior pole. This was followed by examination of the anterior segment with a slit lamp having a beam-splitter and observation tube attached. Recorded were:

1. Presence or absence of opacities visible as shadows against the red reflex seen in the coaxial view (lighting and viewing lines coincident). If present, the number, location, and shape of the opacities were noted.

2. Presence or absence of vacuoles. If present, their number and

location were noted.

3. Presence or absence of posterior subcapsular iridescence (PSCI), a polychromatic luster caused by interference patterns at the level of the posterior lens shagreen when the angles of illumination and viewing are equal with respect to the normal line for the region where the sutures meet and in the same horizontal plane as this line.

4. Absence of all of the foregoing, termed "negative results."

Following the examinations, the population was divided on the basis of microwave history. The individuals who provided histories of working directly with microwaves, either as test-development personnel or as operators of such equipment were called "experimental" (91 persons). Those employed at the post but who denied ever having worked with or being near such equipment were called "controls" (135 persons). Each group was divided into five subgroups comprising the 10-year age spans 20-29 through 60-69 years; the size of each subgroup and the number of persons therein in each of the four categories above are tabulated in Table 15. (Note that some persons were counted in more than one category.)

TABLE 15: RESULTS OF APPLETON AND McCROSSAN (1972)

Age	Size	Opacities	Vacuoles	PSCI	Negative
EXPERIMENTAL GROUP					
20-29	15	0 (0%)	2 (13%)	3 (20%)	11 (73%)
30-39	21	5 (24%)	7 (33%)	5 (24%)	11 (52%)
40-49	31	10 (32%)	8 (26%)	17 (55%)	9 (29%)
50-59	18	7 (39%)	4 (22%)	13 (72%)	3 (17%)
60-69	6	4 (67%)	3 (50%)	4 (67%)	0 (0%)
CONTROL GROUP					
20-29	37	0 (0%)	4 (11%)	9 (24%)	25 (68%)
30-39	32	6 (19%)	6 (19%)	10 (31%)	15 (47%)
40-49	38	10 (26%)	10 (26%)	21 (55%)	9 (24%)
50-59	20	6 (30%)	7 (35%)	17 (85%)	6 (30%)
60-69	8	1 (13%)	2 (25%)	4 (50%)	3 (38%)

The authors concluded: "It appears from this study that available clinical evidence does not support the assumption that cataracts which develop in personnel performing duties in the vicinity of microwave generating equipment are a result of microwave exposure, unless a specific instance of severe exposure can be documented and correlated with subsequent cataract development." They presented no statistical treatment of the data. Noteworthy in the tables above, however, are the larger percentages of negative results for the three younger subgroups (20 to 49 years old) of the experimental group than in the corresponding

subgroups of the control group and the converse for the two older subgroups (50 to 69 years old).

In a later paper, Appleton (1973) elaborated on the selection and use by ophthalmologists of opacities, vacuoles, and PSCI as easily recognizable measures or diagnostic criteria of possible subclinical eye damage, and noted that one or more of these signs are seen more often in people as they age and in younger persons who are developing cataracts. The same Fort Monmouth data (with a few minor discrepancies) were presented. In addition, results were presented for examinations of personnel at White Sands Missile Range, NM, and Fort Bliss, TX, and subsequently obtained results for personnel at Tobyhanna Depot, PA, and Fort Huachuca, AZ, yielding totals of 605 experimental and 493 control personnel.

The abstract for this paper stated: "Preliminary results indicate no statistically significant differences in ocular findings between study groups." Again, *no* statistical treatment of the data was presented.

Final results of the survey were presented in Appleton et al. (1975b), which encompassed 1542 experimental and 801 control subjects at the posts noted above, who were examined semiannually over the period from November 1968 to September 1973 and included individuals less than 20 years old. These results are reproduced in Table 16. (The authors did not present the negative results.)

TABLE 16: RESULTS OF APPLETON ET AL. (1975b)

EXPERIMENTAL GROUP

Age	Size	Opacities	Vacuoles	PSCI
<20	43	1 (2%)	4 (9%)	8 (19%)
20-29	506	17 (3%)	94 (19%)	163 (32%)
30-39	433	44 (10%)	102 (24%)	180 (42%)
40-49	316	37 (12%)	108 (35%)	188 (60%)
50-59	196	45 (23%)	66 (34%)	132 (68%)
60-69	48	15 (31%)	16 (33%)	16 (33%)

CONTROL GROUP

<20	13	0 (0%)	1 (8%)	1 (8%)
20-29	188	10 (5%)	33 (18%)	53 (28%)
30-39	196	21 (10%)	55 (28%)	99 (51%)
40-49	247	37 (15%)	71 (29%)	138 (56%)
50-59	128	25 (20%)	53 (41%)	95 (74%)
60-69	29	8 (28%)	14 (48%)	20 (69%)

Stated by the authors: "The conclusions that can be drawn from such a survey are necessarily limited: if any population has been partitioned on the basis of some possible occupational exposure and the health of the `target' group is the same as the `control' group (a negative

result), then it is reasonable to conclude that the occupational exposure (if any) has been insufficient to affect health. On the other hand, if there is a difference between the two groups with respect to health, this difference may be due to the exposure, or it may be due to some other variable, known or unknown; so the only conclusion that could be drawn in that second case would be that harmful effects of occupational exposure have not been ruled out."

Hollows and Douglas (1984) examined, with slit lamp, the lenses of 53 radiolinemen from the same communication organization throughout Australia who were occupationally exposed to RFR by erecting and maintaining radio, television, and repeater towers. The group included workers who had maximal cumulative RFR exposure but excluded persons known to have cataracts or who had cataracts removed. The frequencies ranged from 558 kHz to 527 MHz. Measurements of power density in and around work areas yielded values varying from 0.08 to 3956 mW/sq cm.

The results of these examinations were statistically compared with those for 39 age-matched controls from the same Australian states who had never been radiolinemen. The authors noted: "For most of the working lives of the radiolinemen in this study there was no national standard for permitted exposure limit...The radio and television towers appear to be the only occupational source of microwaves to which these men were exposed...It was not possible completely to exclude from the control group persons with ocular symptoms that could have related to cataract." All of the subjects were under 60 years old. Each examination was done without prior knowledge of whether the subject was a radiolineman.

The primary ocular finding was of "posterior subcapsular cataract (PSC)" in 21% (11/53) of the radiolinemen as compared with 8% (3/39) of the controls, or in 18% (19/106) of the eyes of the radiolinemen as compared with 8% (6/78) of the control eyes. The significance levels by use of the Freeman-Tukey transformation were p=0.086 and p=0.043, respectively. The mean ages were 46 +/- 10 (SD) and 42 +/- 9 for the radiolinemen with and without PSC, respectively; for the controls with and without PSC, the values were respectively 37 +/- 6 and 44 +/- 9.

The authors also reported: "Nuclear sclerosis, a type of lens opacity possibly attributable to exposure to solar irradiation, was present in 50 (47%) of the eyes of radiolinemen (grade 1 in 42, grade 2 in 8) and in 34 (44%) of the eyes of controls (grade 1 in 32, grade 2 in 2) (chi-squared= 2.18; not significant.) Pseudoexfoliation of the lens capsule was not found in either group. Pterygium occurred four times in the radiolinemen, and once in the non-radiolinemen." The authors concluded: "The results of this controlled examination suggest an increase in PSC in radiolinemen that may be work related."

Not indicated in this paper is the degree of vision degradation due to the presence of postcapsular cataract (and/or of nuclear sclerosis). In this context, it is not clear whether postcapsular cataract (not defined by the authors) is more severe than, or qualitatively differs from,

posterior subcapsular iridescence (PSCI), one of the three precursors to cataract development described in Appleton and McCrossan (1972).

Frey (1985) recently took issue with the findings of Appleton and McCrossan (1972) and cited "three major flaws:" "First, the exposed group likely included persons with little or no exposure. This mixing in the sample they selected as the exposed group would tend to minimize the possibility of finding microwave effects. Secondly, their control group consisted of people working with equipment known to cause eye damage, a factor that would also tend to minimize the possibility of finding microwave effects. Thirdly, and most important, they did not do a statistical analysis on their data. When the writer [Frey] did one, it showed that Appleton and McCrossan had a statistically significant difference between groups, with the microwave exposed group showing more lens opacities than would be expected by chance."

Regarding the first two points, Frey reproduced the percentages of opacities by age subgroup in the exposure and control groups found by Appleton and McCrossan [see column 3 of Table 15], and for comparison, presented the percentages of cataracts in males published by the National Center for Health Statistics. These percentages are shown in columns 2-4 of Table 17, with the Appleton and McCrossan control and experimental percentages denoted "A&M-Controls" and "A&M-Exposed," respectively, and those for the National Center for Health Statistics survey as "NCHS."

TABLE 17: PERCENTAGES OF OPACITIES

Age	A&M-Controls	NCHS	A&M-Exposed	A-Controls
20-29	0	2	0	5
30-39	19	2	24	10
40-49	26	6	32	15
50-59	30	16	39	20
60-69	13	34	67	28

Frey commented that the differences in percentages in the Appleton and McCrossan control group relative to those for the NCHS survey were indicative of the bias in the control group, because some of the persons in the latter group had worked with equipment known to damage the eye. Not clear, however, was why Frey (1985) chose to analyze that earlier study rather than the final results in Appleton et al. (1975b), of which he evidently was aware, and which encompassed much larger experimental and control groups; instead, he merely dismissed the later study as "also flawed." The percentages of opacities in the control group of that study (from Table 16) are shown under "A-Controls" in column 5 of Table 17; these percentages are closer to those for the NCHS survey than are the corresponding values for the A&M-Controls.

Regarding the statistical significance of the Appleton and McCrossan (1972) data, Frey (1985) indicated that he had performed a Kilmogorov-Smirnov test and found that the differences in opacity percentages were

not related to a difference in age distribution between groups. He then counted all (without regard to age subgroup) reported by Appleton and McCrossan as having opacities: 26 and 23 individuals in the experimental and control groups, respectively, and all who did not have opacities (including those reported to have vacuoles and/or exhibiting PSCI), 65 and 112 individuals, respectively. To test the hypothesis that exposure to microwaves increases opacities, he performed a chi-square test on these four numbers and obtained 4.2, $p<0.05$.

In a response to Frey (1985), Wike and Martin (1985) noted that Frey's comparison of percentages of opacities with the NCHS percentages of cataracts was inappropriate because opacities and cataracts are not identical and that Appleton and coworkers "deliberately used three reliable physical signs (opacities, vacuoles, and posterior subcapsular iridescence) of developing cataracts rather than the diagnosis of cataract because ophthalmologists cannot agree on the diagnosis of cataract except in fully matured cases."

Wike and Martin (1985) noted that Appleton and coworkers did not provide any information regarding the characteristics of their subjects except for their age ranges and that their conclusions rest on the validity of the assumption that the two groups are equivalent in other subject characteristics, such as diet, exercise, general health, etc., an assumption challenged by Frey. Wike and Martin stated: "Frey's logic is puzzling. If he deemed the design [of the Appleton survey] to be inadequate, then why should the data be analyzed?"

Regarding Frey's statistical analysis, Wike and Martin (1985) stated four major reservations. First, they cited Chapter 10 of Fleiss (1973), who included the method [used by Frey] of doing a chi-square on a table of totals under "Methods to be Avoided" and who presented an example in which two nonsignificant chi-square tables produced a significant chi-square table when combined. Second, they also noted Frey's dismissal of the Appleton et al. (1975b) study and noted that had Frey analyzed the latter (which included the results of Appleton and McCrossan, 1972), he would have obtained 2.82, $p=0.09$ (nonsignificant).

Third, Frey did not analyze the data on vacuoles or PSCI. Wike and Martin indicated that if Frey had applied his chi-square method to the vacuole and PSCI data in Appleton and McCrossan (1972), he would have found that the differences between experimental and control groups were nonsignificant for either response; for the data in Appleton et al. (1975b), the chi-square test would have shown that the proportion of vacuoles were nonsignificantly lower, and the proportion of PSCIs were significantly lower, in the experimental than the control group.

Fourth, Wike and Martin indicated that Frey's analysis of groups was not optimal for the factorial design of the Appleton studies, in which the factors were age (five levels), group (two levels, experimental and control), and opacity response (two levels, presence or absence), and that therefore Frey learned nothing about the other main effect of age and the interaction of age and group on opacities. Instead, Wike and

Martin noted that log-linear analyses for models of various levels of complexity are appropriate and provided the results of such analyses of the data in Appleton and McCrossan (1972) and Appleton et al. (1975b). The analyses of both sets of data yielded the same conclusions: that the occurrence of opacities was significantly associated with age and not with groups, and that Frey's conclusion was erroneous.

In summary, most of the data above on possible cataractogenesis from human exposure to RFR yielded negative findings (subject to the usual uncertainties regarding exposure parameters and durations common to epidemiologic studies); possible exceptions were individual cases of occupational exposure to RFR levels and durations that might have been sufficient to heat the eye to temperatures well in excess of those found to be damaging in animal experiments.

REFERENCES:

Appleton, B. and G.C. McCrossan
MICROWAVE LENS EFFECTS IN HUMANS
Arch. Ophthal., Vol. 88, pp. 259-262 (1972)

Appleton, B.
RESULTS OF CLINICAL SURVEYS FOR MICROWAVE OCULAR EFFECTS
U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 73-8031 (1973)

Appleton, B., S.E. Hirsh, and P.V.K. Brown
INVESTIGATION OF SINGLE-EXPOSURE MICROWAVE OCULAR EFFECTS AT 3000 MHZ
Ann. N.Y. Acad. Sci., Vol. 247, pp. 125-134 (1975a)

Appleton, B., S.E. Hirsh, and P.V.K. Brown
MICROWAVE LENS EFFECTS: II. RESULTS OF FIVE-YEAR SURVEY
Acta Ophthal., Vol. 93, pp. 257-258 (1975b)

Aurell, E. and B. Tengroth
LENTICULAR AND RETINAL CHANGES SECONDARY TO MICROWAVE EXPOSURE
Acta Ophthal., Vol. 51, No. 6, pp. 764-771 (1973)

Birenbaum, L., G.M. Grosof, S.W. Rosenthal, and M.M. Zaret
EFFECT OF MICROWAVES ON THE EYE
IEEE Trans. Biomed. Eng., Vol.16, pp. 7-14 (1969a)

Birenbaum, L., I.T. Kaplan, W. Metlay, S.W. Rosenthal, H. Schmidt, and M.M. Zaret
EFFECT OF MICROWAVES ON THE RABBIT EYE
J. Microwave Power, Vol. 4, No. 4, pp. 232-243 (1969b)

Carpenter, R.L., D.K. Biddle, and C.A. Van Ummersen
OPACITIES IN THE LENS OF THE EYE EXPERIMENTALLY INDUCED BY EXPOSURE TO MICROWAVE RADIATION
IRE Trans. Med. Electronics, Vol. 7, pp. 152-157 (1960)

Carpenter, R.L. and C.A. Van Ummersen
THE ACTION OF MICROWAVE RADIATION ON THE EYE
J. Microwave Power, Vol. 3, No. 1, pp. 3-19 (1968)

Cleary, S.F., B.S. Pasternack, and G.W. Beebe
CATARACT INCIDENCE IN RADAR WORKERS
Arch. Environ. Health, Vol. 11, pp. 179-182 (1965)

Cleary, S.F. and B.S. Pasternack
LENTICULAR CHANGES IN MICROWAVE WORKERS
Arch. Environ. Health, Vol. 12, pp. 23-29 (1966)

Cogan, D.G., S.J. Fricker, M. Lubin, D.D. Donaldson, and H. Hardy
CATARACTS AND ULTRA-HIGH-FREQUENCY RADIATION
A.M.A. Arch. Ind. Health, Vol. 18, pp. 299-302 (1958)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander,
J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22
(1978)

Fleiss, J.L.
STATISTICAL METHODS FOR RATES AND PROPORTIONS
Wiley, NY (1973)

Frey. A.H.
DATA ANALYSIS REVEALS SIGNIFICANT MICROWAVE-INDUCED EYE DAMAGE IN HUMANS
J. Microwave Power, Vol. 20., No. 1, pp. 53-55 (1985)

Guy, A.W., J.C. Lin, P.O. Kramar, and A.F. Emery
EFFECT OF 2450-MHz RADIATION ON THE RABBIT EYE
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 6, pp. 492-498 (1975a)

Guy, A.W., P.O. Kramar, C.A. Harris, and C.-K. Chou
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: METHODOLOGY AND
EVALUATION OF OCULAR AND PHYSIOLOGIC EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 37-44 (1980b)

Hirsh, F.G. and J.T. Parker
BILATERAL LENTICULAR OPACITIES OCCURRING IN A TECHNICIAN OPERATING A
MICROWAVE GENERATOR
AMA Arch. Ind. Hyg. Occup. Med., Vol. 6, pp. 512-517 (1952)

Hollows, F.C. and J.B. Douglas
MICROWAVE CATARACT IN RADIOLINEMEN AND CONTROLS
Lancet, No. 8399, pp. 406-407, Vol. 2 (18 August 1984)

Issel, I. and P. Emmerlich
LENS CLOUDING AS A RESULT OF THE EFFECTS OF MICROWAVES
(Engl. Trans. of LINSENTRUEBUNG INFOLGE MIKROWELLENEINWIRKUNG)
Deutsche Gesundheitswesen, Vol. 36, No. 18, pp. 17-19 (1981)

Kramar, P.O., A.F. Emery, A.W. Guy, and J.C. Lin
THE OCULAR EFFECTS OF MICROWAVES ON HYPERTHERMIC RABBITS: A STUDY OF MICROWAVE CATARACTOGENIC MECHANISMS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 155-163 (1975)

Kramar, P.O., C. Harris, A.F. Emery, and A.W. Guy
ACUTE MICROWAVE IRRADIATION AND CATARACT FORMATION IN RABBITS AND MONKEYS
J. Microwave Power, Vol. 13, No. 3, pp. 239-249 (1978)

Kues, H.A., L.W. Hirst, G.A. Lutty, S.A. D'Anna, and G.R. Dunkelberger
EFFECTS OF 2.45-GHZ MICROWAVES ON PRIMATE CORNEAL ENDOTHELIUM
Bioelectromagnetics, Vol. 6, No. 2, pp. 177-188 (1985)

Kurz, G.H. and R.B. Einaugler
CATARACT SECONDARY TO MICROWAVE RADIATION
Am. J. Ophthal., Vol. 66, No. 5, pp. 866-869 (1968)

Lin, J.C.
A CAVITY-BACKED SLOT RADIATOR FOR MICROWAVE BIOLOGICAL EFFECT RESEARCH
J. Microwave Power, Vol. 9, No. 2, pp. 63-67 (1974)

McAfee, R.D., A. Longacre, Jr., R.R. Bishop., S.T. Elder, J.G. May, M.G. Holland, and R. Gordon
ABSENCE OF OCULAR PATHOLOGY AFTER REPEATED EXPOSURE OF UNANESTHETIZED MONKEYS TO 9.3-GHZ MICROWAVES
J. Microwave Power, Vol. 14, No. 1, pp. 41-44 (1979b)

Seth, H.S. and S.M. Michaelson
MICROWAVE CATARACTOGENESIS
J. Occup. Med., Vol. 7, No. 9 (1965)

Shimkovich, I.S. and V.G. Shilyaev
CATARACT OF BOTH EYES WHICH DEVELOPED AS A RESULT OF REPEATED SHORT EXPOSURES TO AN ELECTROMAGNETIC FIELD OF HIGH DENSITY
Vestn. Oftal., Vol. 72, pp. 12-16 (1959)

Van Ummersen, C.A. and F.C. Cogan
EFFECTS OF MICROWAVE RADIATION ON THE LENS EPITHELIUM IN THE RABBIT EYE
Arch. Ophthal., Vol. 94, pp. 828-834 (1976)

Weiter, J.J., E.D. Finch, W. Schultz, and V. Frattali
ASCORBIC ACID CHANGES IN CULTURED RABBIT LENSES AFTER MICROWAVE IRRADIATION
Ann. N.Y. Acad. Sci., Vol. 247, pp. 175-181 (1975)

Wike, E.L. and E.J. Martin
COMMENTS ON FREY'S "DATA ANALYSIS REVEALS SIGNIFICANT MICROWAVE-INDUCED EYE DAMAGE IN HUMANS"
J. Microwave Power, Vol. 20, No. 3, pp. 181-184 (1985)

Zaret, M.
OPHTHALMIC HAZARD OF MICROWAVE AND LASER ENVIRONMENTS
39th Ann. Sci. Meeting Aerospace Med. Assoc., San Francisco, CA (1969)

3.1.4.2 AUDITORY EFFECTS

Humans near some types of pulsed radar systems have perceived individual pulses of RFR as audible clicks (without use of electronic receptors). This phenomenon, first investigated by Frey (1961), attracted much interest because it has been cited often as evidence that nonthermal effects can occur and because an initial hypothesis was that a possible mechanism for perception is direct stimulation of the central nervous system by RFR.

Many of the results support the hypothesis that a pulse of RFR having the requisite pulse power density and duration can produce a transient thermal gradient large enough to generate an elastic shock wave at some boundary between regions of dissimilar dielectric properties within the head, and that this shock wave is transmitted to the middle ear, where it is perceived as a click. Persons with impaired hearing are unable to hear such clicks, and experimental animals in which the cochlea (inner ear) has been destroyed do not exhibit brainstem-evoked responses.

Although this topic is presented here under "Studies of Humans," the results of experiments with animal subjects and nonbiological targets are also discussed, to avoid fragmenting the descriptions of several studies that involved both human and animal subjects.

Frey (1961) exposed human subjects to either 6-microsecond pulses of 1.3-GHz RFR at 244 pps (0.0015 duty cycle) or 1-microsecond pulses of 3.0-GHz RFR at 400 pps (0.0004 duty cycle). The ambient noise levels were respectively about 70 and 80 dB, but earplugs decreased the noise by about 25-30 dB. The mean threshold of average power density for RFR perception was about 0.4 mW/sq cm at 1.3 GHz for eight subjects and 2 mW/sq cm at 3.0 GHz for seven subjects. The corresponding peak power densities were about 270 and 5000 mW/sq cm. (No variances or other statistical data were given.)

The subjects were unable to match the RFR sounds to audio sine waves. With white noise controlled by a variable band-pass-filter, best match was obtained by removing all frequencies below about 5 kHz.

Four subjects with various degrees of hearing loss (for air-conducted and bone-conducted sound) were tested for perception of the 1.3-GHz RFR. Subject 1 with significant hearing loss of both kinds above about 2 kHz was unable to perceive the RFR sound at intensities 30 times above the threshold. Subject 2, who had bilateral severe air-conduction loss (about 50 dB) but moderate bone-conduction loss (about 20 dB), was able to perceive the RFR sound at about threshold level. Subject 3, with tinnitus and bilateral hearing loss ranging from about 10 dB at 250 Hz to about 70 dB at 8 kHz for air conduction, more severe loss for bone conduction, and who had been diagnosed as having neomycin-induced nerve deafness, was unable to perceive the RFR. Subject 4, who had normal bilateral air-conduction hearing to about 4 kHz but severe bilateral bone-conduction loss was also unable to perceive the RFR.

The author had concluded that a necessary condition for perception of RFR as sound was the ability to hear sound above about 5 kHz, but not necessarily by air conduction. Frey (1962), however, stated that some subjects with an audiogram notch around 5 kHz (i.e., with adequate hearing for frequencies above 5 kHz) did not perceive RFR sound. In this later study, the RFRs used were 425-MHz pulses of 125, 250, 500, 1000, and 2000 microseconds at 27 pps (respective duty cycles of 0.0034, 0.0068, 0.0135, 0.027, and 0.054) and 2.5-microsecond pulses of 8.9-GHz RFR at 400 pps (duty cycle 0.001). The ambient noise levels were 70-90 dB and the subjects wore Flent antinoise ear stopples, which diminished the ambient levels by about 20 dB from 100 Hz to 2 kHz and by about 35 dB at 10 kHz.

The average-power-density thresholds for perception of 125-, 250-, 500-, and 1000-microsecond pulses of 425-MHz RFR were 1.0, 1.9, 3.2, and 7.1 mW/sq cm, respectively; the corresponding peak power densities were 300, 280, 240, and 260 mW/sq cm (again given without statistical data). (The threshold for 2000-microsecond pulses of 425-MHz RFR was not determined because of inadequate instrumentation.) Thus, all four 425-MHz peak-power values were comparable to the 1.3-GHz threshold previously found (Frey, 1961), implying insensitivity to frequency in this range. The 3-GHz peak-power threshold was much higher, however, about 5 W/sq cm, and the 8.9-GHz RFR was not perceived for peak-power densities as high as 25 W/sq cm. The author suggested that the perception-threshold rise from 1.3 GHz upward was related to the dependence of penetration depth on frequency. The author, noting the high ambient noise levels, also suggested that the thresholds would be lower in quieter environments.

Frey (1962) also speculated about the possible sites and mechanisms of detection of pulsed-RFR, including RFR-induced changes of the electrical capacitance between the tympanic membrane and the oval window, detection in the cochlea, and interaction of RFR with neuron fields in the brain. The first possibility was discounted because of insensitivity of the RFR-hearing effect to head orientation relative to the RFR source. He indicated that the then-current experimental results were inconclusive relative to the other two possibilities.

Frey (1967) endeavored to resolve this point by studying the potentials evoked in the cat brain by exposure to 10-microsecond pulses within the range 1.2-1.5 GHz. One electrode was implanted in the brain stem of each cat, with tip in the nucleus subthalamicus, formatio reticularis, nucleus olivaris, or nucleus reticularis paramedianus. The electrode was of coaxial design to avoid RFR energy pickup. (The author stated that during extensive testing, the electrode showed no indication of energy pickup.)

The procedure after recovery from surgery (4-6 weeks) was to anesthetize the cat with Fluothane in oxygen, place it in an exposure chamber lined with RFR-absorbent materials, adjust the anesthesia to a depth that just prevented voluntary movement, and evaluate the status of the electrode by monitoring the pattern of brain electrical activity for a

short time. The head of the cat was then exposed to the RFR from a horn 50 cm above, and the first 30-ms of brain-stem output after each pulse was recorded and averaged over successive pulses with a computer. Synchronization pulses at appropriate repetition frequencies were used to trigger the RFR generator and (with a 1-ms time delay) the oscilloscope, recorder, and computer used for assessing the evoked responses.

During experimental sessions, exposures of each cat to the RFR were alternated with 5-min rest periods. Interspersed with the RFR-exposures were runs with CW or pulsed acoustic stimuli at the repetition frequency of the RFR, but no details were given regarding how such stimuli were presented. The electrical activity in each brain region was recorded just before, and a few minutes after, euthanizing the cat.

The author indicated, without giving data, that the threshold average and peak power densities necessary to evoke brain-stem potentials were about 0.03 and 60 mW/sq cm. These values correspond to a duty cycle of 0.0005 and (for 10-microsecond pulses) to a pulse repetition frequency of 50. The results presented were representative averaged waveforms evoked in the four brain-stem regions by the RFR and pulsed acoustic stimuli. These showed that responses were evoked by both stimuli before but not after euthanization, indicating that the responses were not artifactual. The author also stated that no cochlear microphonic was apparent in response to the RFR, but this point could not be discerned from the waveforms shown.

A set of four waveforms from the nucleus subthalamicus evoked by RFR at frequencies of 1.2, 1.3, 1.425, and 1.525 GHz showed the amplitudes for the two lower frequencies to be about the same, but that the amplitude was lower at 1.425 GHz and almost negligible at 1.525 GHz, results taken by the author to indicate that there is a broad range of optimal carrier frequencies consonant with calculations of RFR penetration in the head.

Frey and Messenger (1973) exposed humans to pulsed 1.245-GHz RFR at 50 pps in an RFR anechoic chamber. In one set of experiments, the average power density was held constant at 0.32 mW/sq cm and the pulse width was varied from 10 to 70 microseconds in 10-microsecond increments, yielding peak power densities from 640 to 91 mW/sq cm. In another set, the peak power density was held constant at 370 mW/sq cm and the pulse width was varied over the same range, yielding average power densities from 0.19 to 1.3 mW/sq cm. Four subjects with clinically normal hearing were each given 3 trials. The start of each trial was signaled optically. After a variable interval of up to 5 seconds, each subject was first given a pulsed RFR signal for 2 seconds, the perceived loudness of which was to be taken as reference level 100. About 5 seconds later, the test RFR signal was presented for 2 seconds and the subject was to signal its numerical loudness relative to the reference.

The results were presented as plots of perceived loudness vs peak power density and vs average power density (all on logarithmic scales). The point plotted for each test condition was the median value, without

deviations, for all subjects and repetitions; no individual data were given. In the peak-power-density plot, the loudness rose sharply from about 3 at 91 mW/sq cm (70-microsecond pulses) to 60 at 125 mW/sq cm (50-microsecond pulses); at higher power densities, the sound level rose more slowly to a slightly rising plateau, i.e., to about 100 at 210 mW/sq cm (30-microsecond pulses), 120 at 315 mW/sq cm (20-microsecond pulses), and a slightly lower value at 630 mW/sq cm (10-microsecond pulses). The plateau indicated that there is an optimal band of pulse widths, within which the perceived loudness depends on the peak power density. The author ascribed the loudness diminution at 630 mW/sq cm to 10-microsecond pulses being shorter than optimal duration. The plot of median loudness vs average power density showed more scatter, with the points ranging from about 60 at 0.19 mW/sq cm (10-microsecond pulses) to a relatively flat maximum of 100 at 0.55 mW/sq cm (30-microsecond pulses) and diminishing to about 40 at 1.29 mW/sq cm (70-microsecond pulses). The author ascribed the dip for 70-microsecond pulses to this duration being longer than optimum.

From their data, Frey and Messenger (1973) calculated that the peak-power-density threshold for perception of RFR pulses is about 80 mW/sq cm, a value lower than those reported subsequently by Cain and Rissman (1978), discussed later. In the absence of information on scatter of the responses by each subject and because subjective judgments of relative loudness may be imprecise, the accuracy of the results of Frey and Messenger (1973) could not be evaluated.

White (1963) reported that when the surface of a body is transiently heated by RFR-absorption (or electron bombardment), elastic waves are produced by surface motion due to thermal expansion. This process was analyzed theoretically, with emphasis on the case of an input heat flux varying harmonically with time, to relate the amplitude of the elastic waves to the characteristics of the input flux and thermal and elastic properties of the body. Experiments with both electron impact and RFR-absorption verified the proportionality of the stress wave amplitude and the absorbed power density, and correlated well with the thermal and elastic properties of the heated medium.

Elastic waves were detected in all metals tested, in several carbon-loaded plastics, in water, and in a silver-coated barium titanate piezoelectric crystal. Mixing (production of beat frequencies) was observed when two pulses of different RFR frequencies were absorbed simultaneously. Comparison of the elastic-wave stress amplitude with radiation pressure showed that the former may be much greater than the latter, as demonstrated experimentally. When a barium titanate crystal was used to detect the elastic waves produced, heating by a single 2-microsecond pulse of electrons or RFR produced easily detectible signals at pulse power densities down to 2 W/sq cm, which corresponded to a computed peak surface-temperature rise of about 0.001 deg C and which produced piezoelectric-crystal voltages ranging from about 1 to more than 60 mV per kW/sq cm of absorbed power density.

Foster and Finch (1974) confirmed White's findings that RFR pulses can

produce acoustic transients in water, and showed by calculation that for short pulses, the peak sound pressure is proportional to the energy per pulse, whereas for long pulses, it is proportional to the incident power density. Using 2.45-GHz RFR in several pulse-power-density and pulse-duration combinations and a hydrophone in saline (0.15-N KCl), they found that the transition between the two regimes occurs for pulse durations between 20 and 25 microseconds. The authors noted that the dependence of sound pressure on pulse duration and incident peak power density is consistent with the results of Frey and Messenger (1973) at 1.245 GHz. They also found that acoustic signals were not obtained in water at 4 deg C (where its thermal expansion coefficient is essentially zero) and that the polarity of the transient acoustic signal between 0 and 4 deg C was reversed from that for temperatures above 4 deg C. These results support the thermoelastic expansion hypothesis.

Sharp et al. (1974), in an experiment involving shielding regions of a subject's head from 1.5-GHz RFR pulses with RFR absorber, noticed that the apparent locus of the perceived sound moved from the head to the absorber. They then confirmed transduction of the RFR by the absorber into acoustic signals by using a sound-level meter to measure the delay times for acoustic propagation for distances of 0.3 to 0.6 m between the absorber and microphone. The pulses were 14-microseconds long and were randomly triggered at about 3 pps. By calculation, the power per pulse was 4.5 kW and that the pulse power densities were 7.5-15 kW/sq m (750-1500 mW/sq cm) for the range of separations above.

Subsequent tests by Sharp et al. (1974) showed that varying the carrier frequency from 1.2 to 1.6 GHz or using 2.45 GHz made little difference in the level or quality of the sound. In addition, detectable sounds could be produced with various sizes and shapes of absorber, including pieces as small as 4 mm square by 2 mm thick, and in various types of absorber and in crumpled aluminum foil. The threshold pulse power for audibility was about 275 W, yielding estimated pulse power densities in the range 0.46-0.92 kW/sq m (46-92 mW/sq cm). Tests were also done with constant pulse repetition rates up to 500 pps, with the finding: "The sound produced from the absorber seemed to track the repetition rate of the microwave pulses."

Taylor and Ashleman (1974) surgically prepared three groups of three cats, for recording potentials evoked by acoustic and RFR stimuli in three brain regions and determining the effect of cochlear disablement. Each cat was fitted on the dorsal surface of the frontal bone with a piezoelectric transducer for presentation of acoustic stimuli; it was removed for RFR-exposure. In the cats of group 1, the eighth cranial (vestibulocochlear) nerve was exposed, a glass pipette microelectrode filled with Ringer's solution was inserted into the nerve, and the round window on the same side was exposed. In those of group 2, a similar electrode was advanced into the medial geniculate to a location in the nucleus that yielded acoustically evoked potentials of appropriate characteristics, and both round windows were exposed. In the cats of group 3, a Teflon-covered carbon electrode was placed on the anterior ectosylvian gyrus of the primary auditory cortex and both round windows were

exposed. Connections to the electrodes were made with carbon leads of high resistance.

The acoustic stimuli were produced by feeding 10-microsecond electric pulses to the piezoelectric transducer at 1 pps. The RFR stimuli were 32-microsecond, 2.45-GHz pulses at 1 pps fed via a directional coupler to a horn placed 10 cm posterolaterally from the cat's head at 30 deg relative to the sagittal plane. Incident power densities were measured with a bolometer.

Following post-surgical stabilization, the lowest piezoelectric voltage that yielded a response was determined and the voltage was increased to a level that was maximal in evoking activity. The transducer was then removed, the head of the cat was exposed to the RFR, and the minimum and maximal levels for evoking responses were determined. When responses to both acoustic and RFR pulses were clearcut, the cochlea was disabled by perforating the round window and aspirating the perilymph, and again the response to each stimulus was determined. The responses of the medial geniculate nucleus and auditory cortex were assessed after disabling each cochlea. When no evoked response occurred after disabling the cochlea, the stimulus was raised to the maximum available in each case.

The results indicated that cochlea destruction led to total loss of evoked potentials to both acoustic and RFR stimuli. Specifically, the eighth-nerve potentials were lost after unilateral cochlea destruction, the evoked-potential amplitudes from the medial geniculate and auditory cortex were markedly attenuated by aspiration of the contralateral cochlea, and disablement of the remaining cochlea resulted in total loss of the potentials.

From their results, the authors concluded: "We believe that the data strongly support the contention that the microwave auditory effect is exerted on the animal in a manner similar to that of conventional acoustic stimuli. Clearly, the elimination of the first stage of transduction affects the central nervous system response to both of these forms of stimulus energy in the same way."

Guy et al. (1975b) determined the power density threshold and modulation characteristics for the RFR-hearing effect in human volunteers, compared the potentials evoked in four successive levels of the cat auditory nervous system by RFR and acoustic pulses, used optical interferometry to quantitate the transduction of RFR pulses to acoustic energy in RFR-absorbing materials, and provided evidence that the RFR-hearing effect is due to direct conversion of RFR energy to acoustic energy in the tissues.

The back of the head of each of two human subjects was exposed to RFR at 15-30 cm from the aperture of a horn (in the near field) in an anechoic chamber at an ambient noise level of 45 dB, with RFR-absorbent material around the vicinity of the subject to eliminate reflections. The RFR consisted of 2.45-GHz pulses of duration that was varied from 1

to 32 microseconds. For each pulse duration, the RFR was presented in trains of three pulses per second, with the pulses in each train spaced 100 ms apart. The subject used a switch to signal perception of an auditory sensation. Standard audiograms taken prior to exposure showed that the hearing threshold of subject 1 was normal and that subject 2 had a deep notch at 3.5 kHz for both ears, with similar results for air and bone conduction.

The results for subject 1 showed that irrespective of pulse duration, the threshold for perception of the RFR was a constant peak energy density per pulse (product of peak power density and pulse duration) of 40 microjoules/sq cm. The corresponding incident average power density (for 3 pps) was 0.12 mW/sq cm. When subject 1 wore ear plugs, the threshold peak was only 28 microjoules/sq cm per pulse. Based on a spherical model of the head (Johnson and Guy, 1972), the threshold peak specific absorbed energy (SAE) corresponding to 40 microjoules/sq cm per pulse was 16 mJ/kg. The threshold for a pair of pulses within several hundred microseconds apart was the same as for one pulse with the same total energy as the pair. Similar results were obtained for subject 2 except that the threshold peak energy density was 135 microjoules/sq cm per pulse or about threefold (5 db) higher than for subject 1.

The authors noted that each pulse was perceived individually as a click and that short pulse trains were heard as chirps of tones corresponding to the pulse recurrence rate. Also, when the pulse generator was keyed manually, digital (Morse) code transmitted thereby could be interpreted accurately by the subject.

For the study of cats, each was fitted with a removable piezoelectric transducer to provide bone-conducted acoustic stimuli. A nonperturbing electrode consisting of a glass pipette filled with Ringer's solution was inserted surgically into the medial geniculate nucleus to a location that yielded acoustically evoked responses of the proper latency period. To minimize RFR pickup by the instrumentation, the electrode and ground connection were coupled with high-resistance carbon-loaded plastic leads through a low-pass filter to a high-impedance amplifier, oscilloscope, computer of average transients, and x-y plotter.

The acoustical stimuli consisted of pulses 1-30 microseconds in duration that were air-conducted from a speaker 17 cm to the right of the cat's head or were transducer-induced. The RFR stimuli were pulses, 0.5-32 microseconds in duration, of 918-MHz or 2.45-GHz RFR from a horn or aperture 8 cm from the occipital pole of the cat. Pulses of 8.5-10 GHz RFR were also used, as noted below. Each stimulus was presented at 1 pps. A noise generator provided background noise of up to 90 dB in the range 50-15000 Hz.

Representative response curves evoked by 20-microsecond air-conducted and bone-conducted acoustic pulses and by 20-microsecond pulses of 2.45-GHz RFR were displayed and were similar. The threshold peak energy-density per pulse for perception of 2.45-GHz RFR varied only from 17.8 microjoules/sq cm for 0.5-microsecond pulses to 21.6 microjoules/sq cm

for 10-microsecond pulses, values about half the human threshold, but it increased more steeply with pulse duration, to 47.0 microjoules/sq cm for 32-microsecond pulses (except for 25-microsecond pulses, for which the threshold was only 15.2). The peak SAEs were determined by scanning infrared thermography. The values corresponding to 21.6 and 47.0 microjoules/sq cm per pulse respectively were 12.3 and 26.7 mJ/kg.

The threshold energy-density values for 918-MHz pulses were 22.6 and 28.3 microjoules/sq cm per pulse respectively for 10- and 32-microsecond pulses (with no dip for 25-microsecond pulses), and the corresponding peak SAEs per pulse were 16.0 and 20.0 mJ/kg.

The RFR thresholds above were obtained with 64 dB of background noise. Increases of the noise level to 80 dB (for pulses up to 10 microseconds) yielded insignificant changes in thresholds. However, the energy-density threshold for bone-conducted acoustic stimulation was about tenfold higher at 80 than 64 dB; for air-conducted acoustic stimulation, the threshold was a hundredfold higher for 70 dB of noise and was still higher for 80 dB, but by a factor of less than ten.

With 8.5-10 GHz, responses could be evoked only by exposing the brain through a large hole in the skull, with the RFR horn within a few cm from the hole. The threshold values were a peak incident power density of 14.8-38.8 W/sq cm per pulse, which corresponded to an average power density of 0.472-1.240 mW/sq cm (for 32-microsecond pulses, 1 pps) and an energy density of 472-1240 microjoules/sq cm per pulse.

In another series of experiments, Guy et al. (1975b) fitted cats with a piezoelectric transducer and inserted a nonperturbing electrode in the medial geniculate nucleus as before, and also surgically exposed the round window of the cochlea and attached thereto an electrode and leads, both of high-resistance material, for recording the cochlear responses evoked by acoustic and RFR pulses. The responses of one cat to an acoustic pulse from a loudspeaker and a 2.45-GHz pulse were displayed. The curve obtained for stimulation with the loudspeaker pulse showed the N1 and N2 auditory-nerve response and a cochlear microphonic similar to the pulse-induced decaying vibratory movement of the loudspeaker cone, which was determined with an optical interferometer. By contrast, the curve evoked by the RFR pulse showed the N1 and N2 response only, and no evidence of a cochlear microphonic. However, the cochlear microphonic for another cat stimulated by speaker pulse was of much lower amplitude (relative to the N1 and N2 response) and was absent in the response of another cat stimulated acoustically with the piezoelectric transducer. Thus, the absence of an RFR-induced cochlear microphonic does not rule out theories of the RFR-hearing effect based on transduction of RFR to acoustic energy.

In experiments similar to those of Taylor and Ashleman (1974), Guy et al. (1975b) also studied the effect of cochlea disablement. Cats were prepared surgically for recording evoked potentials in the eighth cranial nerve, medial geniculate nucleus, and primary auditory cortex. After establishing that appropriate responses were obtained with RFR and

acoustic pulses, the cochlea was disabled, which resulted in total loss of all evoked potentials, even with the highest available peak acoustic and RFR powers and with computer averaging of larger numbers of signals.

Guy et al. (1975b) used an interferometer and a laser source to detect surface movements of several lossy materials induced by absorption of RFR pulses. (This device was also used to observe the speaker-cone movements noted above.) The results showed that surface displacement amplitude is dependent on the dielectric constant and loss factor of the material and on its density and elastic properties. An interesting result noted by the authors was the high amplitude obtained in a widely used RFR-absorbent material, a finding ascribed to its relatively low density and high compressibility.

Chou et al. (1975) studied the induction of cochlear microphonics (CM) in the guinea pig by pulses of 918-MHz RFR. For this purpose, they placed a fine RFR-transparent carbon lead against the round window and cemented it onto the bulla. An indifferent electrode was fastened to nearby tissue. Only preparations that yielded CM amplitudes exceeding 0.5 mV in response to 70-dB speaker clicks were used. The head of the guinea pig was placed within a section of cylindrical waveguide through a hole. The section was terminated with a sliding short, adjusted to yield maximum RFR absorption in the head. With this arrangement, the average SAE per pulse at 10 kW peak input power was 1.33 J/kg, or about an order of magnitude larger than the levels used in previous studies. The sound level near the animal's head was about 65 dB, mostly due to the noise from the pulse generator.

Each guinea pig was exposed intermittently for 1.5-min durations to 1-10 microsecond pulses of 918-MHz RFR, 100 pps, at various levels of peak power. The responses were amplified and recorded on a magnetic tape system that had a frequency response up to 80 kHz. After 3-5 hr, the animal was euthanized and recording of its response was continued until the physiological potentials disappeared completely. Recorded responses were processed off-line with a Computer of Averaged Transients.

The electrical responses at the round window of a guinea pig stimulated with single acoustic clicks showed that the CM preceded in time the N1 and N2 action potentials, and that when the polarity of the electrical pulses delivered to the speaker was inverted, only the polarity of the CM was reversed. Stimulation of the same animal with single RFR pulses yielded N1 and N2 potentials of about the same amplitude. In addition, barely discernible was an "electrical event" during the 200-microsecond interval immediately following the recording artifact caused by the RFR pulse. Time-expansion of this interval showed this event to be a 50-kHz oscillation of amplitude about 50 microvolts, which decayed within the 200-microsecond interval. This event, which was observed in five guinea pigs, was denoted as the RFR-induced CM response.

Comparison of the CM responses to 10-, 5-, and 1-microsecond, 10-kW RFR pulses, which corresponded to SAEs of 1.33, 0.67, and 0.133 J/kg per

pulse, showed that the CM frequency remained the same but the amplitude dropped with decreasing pulse duration and SAE. Also evident was that the stimulus artifact masked the onset of the CM in each case, but that the latency for successive oscillations was about the same for the three pulse widths. These results support the conclusions that the CMs are physiological responses time-locked to the onset of the RFR pulses and are generated within the cochlea, specifically by hair-cell activation.

With death of an animal, the N1 and N2 responses to acoustic and RFR pulses disappeared, but the RFR-induced CM persisted for many minutes after the N1 and N2 responses had gone. The stimulus artifact remained after the CM had disappeared, indicating that the 50-kHz signal is a genuine physiological response.

The threshold SAE for producing the RFR-hearing effect in the guinea-pig head was 20 mJ/kg, about the same order of magnitude as for the cat head (10-16 mJ/kg) and the human head (16 mJ/kg). The authors surmised that previous failures to observe RFR-induced CMs in animals may have been due to use of SAEs below the threshold, masking by stimulus artifact, or use of amplifiers with pass bands that did not include 50 kHz.

The authors noted that guinea pigs can respond to tones up to 100 kHz, and suggested that the 50-kHz CM may be related to the size of the animal's skull. Based on this premise, the CM frequency would be within the range 15-50 kHz for cats and 5-18 kHz for humans.

Guy et al. (1975b) and Lin (1976a,b; 1977a,b,c) analyzed the postulated mechanisms for the conversion of RFR energy to acoustic energy in lossy dielectric materials. They concluded that pulsed-RFR-induced thermal expansion forces, which are proportional to the square of the peak electric field, are much larger than the radiation pressure or the electrostriction produced by the same RFR pulses and can generate in the head acoustic waves of the requisite magnitude for the hearing effect.

In Lin (1977c), equations developed for a spherical model of the head consisting of brain-equivalent material were used to obtain the acoustic resonant frequencies generated in the heads of guinea pigs, cats, and human adults and infants by exposure to RFR pulses. The results showed that the (fundamental and higher-harmonic) frequencies produced by RFR pulses are independent of the carrier frequency, but are dependent on head size, and specifically that the fundamental frequency is inversely proportional to the radius of the head.

Predicted from the equations was a fundamental frequency of 45 kHz for a 2-cm (guinea-pig) head, which was close to the 50-kHz experimental value found by Chou et al. (1975). For a 3-cm head, the predicted fundamental was 30 kHz, as compared with 38 kHz found experimentally for a typical cat. For humans, the predicted fundamental frequencies were 13 kHz for an adult and 18 kHz for an infant.

Chou et al. (1977), using the method described in Chou et al. (1975), recorded CMs from the round windows of guinea pigs and cats of various

sizes induced by exposure to 10-microsecond pulses of 918-MHz and 2.45-GHz RFR. Exposures were done with horn applicators and the cylindrical waveguide system described above. In the guinea pigs, the CM frequency varied inversely with body mass; in the cats, however, there was no consistent variation of CM frequency with body mass. The authors noted that although head mass, skull mass, skull dimensions, skull thickness, and cerebellar-cavity dimensions all increase with body mass, the brain cavity and bulla dimensions increase only slightly. They found that CM frequency correlates well with the length of the brain cavity but not with the other dimensions of the head or skull. The average threshold energies per pulse for CM responses were 10 mJ/kg for adult cats, 2.5 for kittens, and 7.5 for adult guinea pigs.

Cain and Rissman (1978) used 3.0-GHz RFR pulses to study the auditory effect in two cats, two chinchillas, one beagle, and eight human volunteers. For the animals, surface or brainstem-implanted electrodes were used to measure the responses evoked by audio clicks from a speaker and the responses to 5-, 10-, and 15-microsecond pulses.

The threshold peak power densities were 2.2 W/sq cm for 5-microsecond pulses, 1.3 W/sq cm for 10-microsecond pulses, and 0.58 W/sq cm for 15-microsecond pulses for one cat, and respectively 2.8, 1.3, and 0.58 W/kg for the other cat. The corresponding threshold peak power densities for the beagle were 1.8, 0.30, and 0.20 W/sq cm. The values were 2.8, 2.0, and 0.58 W/sq cm for one chinchilla and 2.2, 1.0, and 0.50 W/sq cm for the other. Thus, for corresponding pulse durations, the beagle had the lowest thresholds and the lowest absolute threshold (irrespective of pulse duration).

The authors found that depending on pulse width, the range of threshold energy density for RFR perception was 8.7-14 microjoules/sq cm per pulse for the cats and 7.5-20 microjoules/sq cm for the chinchillas, and that the threshold averaged 5.0 microjoules/sq cm for the beagle. For 10-microsecond pulses, the threshold pulse power densities were 1.3 W/sq cm for both cats, 1 and 2 W/sq cm for the two chinchillas, and 300 mW/sq cm for the beagle.

The eight humans were given standard audiograms for both air-conducted and bone-conducted sound. In addition, because audiograms do not test hearing above 8 kHz, binaural hearing thresholds were determined for seven of the subjects for tone frequencies in the range 1-20 kHz. The RFR pulses were presented at 0.5 pps. Each subject wore foam ear muffs during exposure, to reduce the ambient noise level, which was 45 dB.

Subjects 1-5 could hear 15-microsecond pulses as clicks; their peak power density thresholds were respectively 300, 300, 300, 600, and 1000 mW/sq cm, and their energy density thresholds were 4.5, 4.5, 4.5, 9.0, and 15.0 microjoules/sq cm. Subjects 1-5 could also hear 10-microsecond pulses, with peak power density thresholds of 1800, 225, 600, 2000, and 2000 mW/sq cm, respectively, and energy density thresholds of 18.0, 2.3, 6.0, 20.0, and 20.0 microjoules/sq cm. Subject 1 was the only one able to perceive 5-microsecond pulses, with a threshold peak power density

and energy density of 2500 mW/sq cm and 12.5 microjoules/sq cm. The other three subjects, 6-8, could not hear these pulses at the highest available peak power density but could perceive 20-microsecond pulses.

The authors found no correlation between the results and the standard audiograms. However, they did note that a strong correlation existed between RFR perception and hearing ability above 8 kHz as determined from the binaural thresholds. They also stated that their results are consistent with the hypothesis that an induced pressure wave in the human head in response to short RFR pulses (less than 20 microseconds) contains a significant portion of its energy at frequencies above 8 kHz.

In summary of these results with humans, only subjects 1-3 were able to perceive 15-microsecond pulses at a pulse-power-density threshold as low as 300 mW/sq cm (energy-density-threshold of 4.5 microjoules/sq cm); of this group, only subject 2 could hear 10-microsecond pulses, with 225 mW/sq cm (2.3 microjoules/sq cm) as the threshold; the thresholds for the other subjects were much higher than 300 mW/sq cm. The latter value of pulse power density can be taken as the nominal human threshold for the RFR hearing effect (e.g., for environmental assessments). It should be noted that the thresholds cited were for an ambient noise level of 45 dB and could be higher in noisier environments. It is also noteworthy that these investigators exposed the human volunteers to pulse power densities as high as 2,000 mW/sq cm without apparent ill effects.

Lebovitz and Seaman (1977) studied the responses in single auditory units of cats to acoustic clicks and pulses of 915-MHz RFR. For this purpose, the posterolateral aspect of the cerebellum was removed and a recording micropipette was inserted into the proximal portion of the eighth nerve. Acoustic clicks ranging from 25 to 200 microseconds in duration, but typically 70 microseconds, were presented to one ear at 10 clicks per second, with the contralateral ear stoppled. The durations of the RFR pulses were in the same range, the repetition rates were 10 pps or less, and the pulses were delivered at forward peak powers of up to 70 W with an applicator, yielding average power densities that never exceeded 1 mW/sq cm.

Medullary SARs were determined by euthanizing the cats after completing several experiments, letting the medullary temperature fall to about 30 deg C, exposing the heads of the cats to an appropriate level of CW RFR for periods of up to 80 seconds, inserting a thermistor into the medulla immediately before and after exposure, deriving the cooling curves, and using them to determine the linear relationship of temperature rise to exposure duration. From the slope of this line, 0.011 deg per second, and the effective forward power, 48.6 W, the normalized SAR was 0.94 W/kg per mW/sq cm. The energy absorbed per pulse was then calculated from the SAR and the peak power and duration.

Of 133 auditory units studied, 63 were responsive to both stimuli, and additional dose responses were obtained for the latter units as long as each showed stable responses. The apparent absence of response of 70 units to RFR was ascribed to the limited range of intensities available,

about 10 dB as compared with 50-80 dB for the acoustic clicks. For a typical single auditory unit that did respond to RFR, the response was very similar to its response to acoustic clicks, differing primarily only in amplitude. The lowest RFR-energy-absorption threshold for a single unit was 4 mJ/kg. The latency interval between stimulation and response increased with decreasing acoustic or RFR stimulus intensity. The smallest latencies observed were 1.5-2 ms, with values up to 5 ms for near-threshold intensities.

The authors noted that the characteristic frequency (CF) of a unit is the frequency at which its response threshold is lowest and that the CF is determined by the mechanical properties of that part of the basilar membrane to which the cell is most directly related. Therefore, for responses to a click that show multiple peaks, the interpeak interval (i.e., the period between the first and second peaks) is about the same as the oscillation period of the basilar membrane and the former is a measure of the latter. The results showed high correlation between unit CFs for acoustic and RFR stimuli, an indication that the same mechanical factors within the cochlea are involved.

Chou and Galambos (1979) investigated the effects in 10 guinea pigs of external-ear blocking, middle-ear damping, and middle-ear destruction on brainstem-evoked responses (BERs) to both acoustic and RFR stimuli. The basic measurement technique was to record the amplitudes and latencies of the BERs to acoustic stimuli and RFR with a pair of carbon-loaded Teflon electrodes (Chou and Guy, 1979a), one of which was attached to the left mastoid process and the other to the skin.

The head of each guinea pig was exposed to 10-microsecond pulses of 918-MHz RFR at 30 pps in a cylindrical waveguide system (Chou et al., 1975) at energies ranging from 0.027 to 11.05 J/kg per pulse. All 10 animals were exposed to 0.1-ms acoustical pulses at 30 pps from a piezoelectric tweeter placed 15 cm from the nose (air conduction). For three animals, comparisons were also made between BERs to airborne and bone-conducted acoustic stimuli, using a piezoelectric transducer in contact with the frontal bone for the latter.

BERs were recorded after each of the following successive treatments: (1) blocking of the left external meatus with mineral-oil-soaked cotton balls, (2) alteration of the mechanical damping of the ossicular chain by filling the bulla with mineral oil, (3) destruction of the middle ear by cutting the ossicular chain and piercing the tympanic membrane, and (4) destruction of the cochlea by piercing the round window.

Treatments 1 and 2 reduced the airborne acoustically-stimulated BERs but not the RFR-induced BERs. Treatment 3 further reduced the airborne acoustic BERs, and also reduced the bone-conducted acoustic BERs and the RFR BERS to a lesser extent than the airborne acoustic BERs. After treatment 4 (cochlea destruction), no BERs were obtained from either acoustic or RFR stimuli.

These results constitute strong evidence that activation of the coch-

lea is necessary for auditory perception of pulsed RFR. The similar BERs obtained from bone-conducted-acoustic and RFR stimuli after destruction of the middle ear and the much lower BERs obtained for airborne-acoustic stimuli support the hypothesis that perception is due to transduction of RFR into acoustic waves that travel via bone conduction to the cochlea or are generated directly in the cochlea itself.

Chou and Guy (1979b) performed similar experiments with BERs induced in guinea pigs, to determine the RFR thresholds for BERs. The input-power thresholds for BERs induced by 918-MHz RFR were determined for pulse widths of 10 to 500 microseconds, and the values were divided by the cross-sectional area of the cylindrical waveguide (about 320 sq cm) to obtain the corresponding threshold peak incident power densities. Also derived was the incident energy density per pulse for each pulse width, and the pulse repetition frequency (30 pps) was used to calculate the incident average power density. Lastly, the threshold SAE per pulse was obtained from the incident energy density per pulse by dividing the latter by the mass of the animal's head.

The authors found that the threshold energy density for evoking BERs was essentially constant (1.56-1.87 microjoules/sq cm per pulse) for pulse durations of 10, 20, and 30 microseconds. The threshold SAE was 5 mJ/kg per pulse and the corresponding incident peak power densities were 156, 78, and 62.4 mW/sq cm, respectively. For pulse durations longer than 30 microseconds, however, the threshold SAE increased with pulse duration, and for pulses longer than 70 microseconds, the threshold peak power density for evoking BERs was essentially constant (90 mW/sq cm), with corresponding pulse-width related increases of energy density per pulse.

The waveforms of the RFR and acoustic BERs were found to be similar except for the longer latency of the latter (due to the longer sound-propagation path). Despite the large differences in pulse width, the latencies of the RFR-induced BERs were about the same, indicating that the evoked response is time-locked to the onset of the RFR pulse. Chou and Guy indicated that their experimental results agreed well with the predictions of the thermal expansion theory.

In a subsequent study, Chou et al. (1985a) exposed anesthetized rats to 2.45-GHz RFR pulses within a circularly polarized waveguide (Guy et al., 1979) in three orientations: (1) body along the waveguide axis and head toward the source, (2) body across the waveguide, and (3) body along the waveguide axis and head away from the source. The BERs were recorded with carbon-loaded Teflon electrodes, one at the vertex of the rat's head and another at either the left or right mastoid process (behind the pinna).

In one experiment, exposures were to pulses 10, 5, 2, and 1 microseconds in duration at 10 pps and a fixed peak power of 4 kW (spatially averaged peak power density of 12.3 W/sq cm) in the first orientation. The corresponding energy densities were 123.4, 61.7, 24.7, and 12.3 microjoules/sq cm. Representative BERs from one rat showed amplitudes

that decreased with decreasing pulse duration or energy density. The responses were similar to those obtained from guinea pigs by Chou and Galambos (1979), but the latency of the peak BER was shorter in rats.

In another experiment, rats were exposed to RFR in each orientation, and the largest responses were obtained in the first orientation. In this experiment, exposures were to pulses of 1, 2, 5, and 10 microseconds at 10 pps and different peak powers, to yield various energy densities. The BER amplitudes at the four pulse durations and constant energy density were about the same, indicating that the response is dependent on energy per pulse and not on pulse duration. The threshold energy density (in the first orientation) was 1.5 to 3 microjoules/sq cm per pulse. Based on calorimetric data, the whole-body SAE was in the range 0.9-1.8 mJ/kg. The corresponding peak power densities for the four pulse durations were in the ranges 1.5-3, 0.75-1.5, 0.3-0.6, and 0.15-0.30 W/sq cm. respectively. The authors noted that these peak power densities were for exposure in the circularly polarized waveguide and that free-space exposure would require about threefold higher values.

Lin et al. (1979b) studied BERs induced in cats by acoustic and RFR pulses and the alterations of the BERs by the successive coagulative formation of lesions in several brainstem regions. Under anesthesia, the dorsal aspect of the skull of each cat was surgically exposed and several stainless-steel electrodes (100-250 microns in diameter) were advanced stereotaxically into the selected brainstem nuclei to locations that yielded maximal evoked potentials. In addition, a stainless-steel screw electrode was fastened to the skull at the vertex and a reference gold-pin electrode was placed near the lowest part of the right pinna.

Acoustic pulses about 70 dB above threshold sound level, generated by feeding currents 0.1 ms in duration into a pair of commercial earphones, were presented binaurally at 10 to 100 pps. Pulses of 2.45-GHz RFR, 0.5 to 25 microseconds wide and up to 10 kW peak, were delivered at 10-100 pps to the dorsal or frontal surface of the head with a small-diameter (15-mm), dielectrically loaded, direct-contact, diathermy applicator. The bioelectric activities at the vertex and at each brainstem location were fed through amplifiers having a passband of 80 Hz to 10 kHz and were summed with a signal-averaging computer. The first 10 ms of averaged responses were displayed on a video monitor and photographed.

Brainstem lesions were produced in succession at the tips of electrodes inserted in the inferior colliculus nucleus, lateral lemniscus, and superior olivary nucleus. The BERs were recorded after each lesion and compared with the pre-lesion BERs, as were microwave-evoked potentials (MEPs) and acoustically-evoked potentials (AEPs) recorded by the vertex electrode. At the end of each experiment, each cat was euthanized and its brain was fixed, removed, embedded in paraffin, and sectioned to ascertain the exact locations of the lesions and electrode tracks.

For each brainstem region, the pre-lesion RFR-induced BER was similar

to the acoustic BER, but with no significant propagation delay for the RFR-induced BER relative to the stimulus pulses. The vertex MEPs showed four successive cycles, designated sequentially as Waves I, II, III, and IV. Of these, Wave III was often the largest and Wave IV the smallest. The sources of the waves (as well as for the AEPs) were thought by the authors to be the volume-conducted action potentials generated in the cochlea and auditory brainstem nuclei.

To determine the effects on the MEPs of changing the pulse repetition rate (PRR), 10-microsecond RFR pulses at 5 kW were applied sequentially at PRRs of 10, 25, 50, and 100 pps and then in reverse order. Minimal or no changes in latency were evident, but the amplitudes of the MEP waves were found to decrease with increasing PRR, a reversible effect.

Next, 10-microsecond pulses with peak powers of 10 to 2 kW were applied at 10 pps. Again, any changes in latency of the MEPs were minimal. The amplitudes of the MEPs decreased with decreasing peak power, but not in the same proportion for each wave. In the example presented (for one cat), the amplitude of Wave I at 10 kW was larger than of Wave II, but decreased faster with decreasing power than for Wave II, so the Wave-II amplitude at 4 kW was larger than that of Wave I, also a reversible effect.

The effects of pulse-duration changes on the MEPs were determined with 5-kW pulses of widths 2.5 to 25 microseconds at 10 pps. Once more, the latency changes were minimal. However, wave amplitudes increased with increasing pulse durations to a plateau for about 10-microsecond and longer pulses, and the temporal relationships among all of the waves were not altered.

Using 25-microsecond, 10-kW pulses at 10 pps, the effects of the lesions formed successively in the inferior colliculus, lateral lemniscus, and superior olive on the BER recorded by the electrode in each region were compared with the pre-lesion BER from that electrode. Also compared were the pre- and post-lesion MEPs recorded by the vertex electrode. The results for one cat were presented.

Each successive lesion yielded decreases in the BER amplitudes from all regions. The most pronounced effect was on the BER from the inferior colliculus nucleus following lesion formation in that region; the BERs from the other two brainstem regions and the MEP remained practically unchanged after producing a lesion in the inferior colliculus nucleus. Similarly, the lesion in the lateral lemniscus yielded the largest effect on the BER recorded by the electrode in that region, with minor changes in the BERs from the other auditory structures except for the inferior colliculus. The BER amplitudes from the superior olive were less affected by the lesions in the inferior colliculus and the lateral lemniscus, reflecting the distal location of the superior olive in the auditory pathway, but its BER amplitude was drastically reduced by the lesion in its nucleus. The amplitudes of the vertex MEPs were altered after each successive lesion, indicating that they were a function of the integrity of brainstem nuclei along the auditory pathway.

Tyazhelov et al. (1979) studied the qualities of the apparent sounds perceived by humans from exposure to 800-MHz pulsed RFR. The parietal area of the head was exposed to the open end of a waveguide fed from a 500-W source. The ambient noise level did not exceed 40 dB and was reduced by plugging the subjects' ears with stoppels or sound-conducting tubes. The pulse durations used ranged from 5 to 150 microseconds. The pulses were presented either continuously at 50 to 2000 pps (the latter for short pulse durations, to limit the average power density) or in trains of duration 0.1 to 0.5 seconds at rates of 0.2 to 2.0 trains per second. Each subject could be presented with sinusoidal audiofrequency (AF) sound waves independently of, or concurrently with, the pulsed RFR and could adjust the amplitude, frequency, and phase of the AF signal to match the timbre and loudness of the perceived RFR. Acoustic signals were presented to the subject by means of a pair of small hollow tubes extending from a speaker to the ears.

The high-frequency auditory limit (HFAL) of each subject for sinusoidal tones from 1 kHz upward was tested first. Three of the subjects had HFALs below 10 kHz and could not perceive 10-30 microsecond RFR pulses, results consonant with those of Cain and Rissman (1978). Of 15 subjects with HFALs above 10 kHz, only one could not perceive the RFR pulses.

All of the perceptive subjects reported that 10-30 microsecond pulses delivered at 1000 to 12,000 pps at peak power densities exceeding 500 mW/sq cm produced sound of polytonal character that seemed to originate in the head, and that the quality of the sound changed with increasing pulse repetition rate (PRR) in a complex manner. Loudness diminished sharply and became more monotonal as the PRR was increased from 6000 to 8000 pps. However, no more than three distinguishable tonal transitions occurred. Subjects with HFALs below 15 kHz were unable to distinguish between the sounds perceived from a 5000-pps and a 10,000-pps signal, and subjects with more extended HFALs reported that the pitch for a 5000-pps signal was higher than for a 10,000-pps signal.

The subjects were able to detect small (5%) shifts of PRR only in the 8000-pps region; at lower PRRs, the subjects erred on 100% of tests to detect the direction of PRR change, indicating that increases of PRR were often perceived as decreases in frequency. For pulses of constant peak amplitude, loudness was perceived to increase with duration from 5 to 50 microseconds, decrease from 70 to 100 microseconds, and increase again for 100 microseconds and upward. Such perceptual patterns were exemplified by plots of threshold pulse power (normalized to the 10-kHz PRR threshold) vs PRR for a subject with a 14-kHz HFAL and for another subject with a 17-kHz HFAL. These curves were roughly W-shaped, with central relative maxima at about 8 kHz. A plot of mean threshold pulse power (normalized to the threshold at 50-microsecond pulse duration) was also presented for subjects unable to perceive sounds for pulses longer than 50 microseconds. This curve was also W-shaped, with a central relative maximum within the pulse range 100-120 microseconds.

After subjects matched the pitch and timbre of a 2-kHz acoustic tone to the perceived sound of a train of RFR pulses at 2000 pps, they were

asked to match the loudness of the acoustic tone with the loudness of the perceived pulses as the pulse duration was varied between 5 and 150 microseconds while the peak power was held constant. No actual data were given. Instead, the relationship between the ratio of acoustic signal amplitude to the pulse power for the subjects (both quantities normalized to their respective thresholds) were merged into a shaded area bounded by two straight lines through the origin on a graph that also displayed a straight line through the origin stated by the authors to represent the theoretical relationship between these quantities as predicted from the thermoelastic model. The entire shaded area was above the theoretical line, i.e., the ratios of acoustic amplitude to pulse power for all of these subjects were reported to be larger than predicted.

When acoustic tones above 8 kHz were presented concurrently with 10- to 30-microsecond pulses at PRRs slightly above or below 8 kHz, the subjects reported hearing beat-frequency notes. Also, for a PRR of 800 pps, similar beat frequencies were perceived when the acoustic frequency was set slightly above or below harmonics of the PRR. Moreover, when the tone and PRR frequencies were matched and the subjects were allowed to vary the phase of the acoustic tone, cancellation of perception of the two stimuli could be achieved. By proper phasing, subjects with HFALs below 15 kHz could also obtain cancellation between a 10-kHz acoustic signal and a 5-kHz train of pulses.

The authors also reported that the sensory characteristics (pitch and timbre) evoked by RFR pulses less than 50 microseconds in duration persisted when subjects' heads were lowered into seawater, with loudness diminishing roughly in proportion to immersion depth and vanishing entirely with total immersion. For pulses longer than 50 microseconds, even partial immersion resulted in loss of perception.

In their discussion, the authors suggested that many of their results are consistent with the thermoelastic hypothesis, but that others, such as the suppression of the perception of a 5000-pps train of RFR pulses by a 10-kHz acoustic tone, are at variance with that model.

Frey and Coren (1979) endeavored to detect surface movements purportedly induced in heads of animals by RFR pulses, using dynamic time-averaged interferometric holography. In this technique, a hologram of an object in vibratory motion is recorded for a long interval relative to one period of the vibration. Such a hologram will contain data on the spatial distribution of the time-averaged amplitude of motion of the object. Thus, nodal regions will appear brightest and antinodal regions appear darkest, with regions of intermediate intensity inversely related to their surface displacement.

Each animal studied was euthanized, placed with its abdomen on the surface of a vibrationally-isolated block of commercial RFR-absorbent material (or concrete in some tests), and exposed to RFR from above with a horn as soon as there was no detectable heartbeat or respiration. A set of 30 holograms was made for each animal, 15 each during alternating

RFR- and sham-exposures. First, holograms during three RFR- and three sham-exposures were made after removing the hair from the dorsal surface of the head and the vicinity of the left pinna. Next, the skin over those areas was removed and six holograms of the musculature revealed thereby were made. Then, the muscle tissue was removed from the dorsal surface and mastoid area and six holograms were made of the skull. Six more holograms were made of the brain after removing the dorsal surface of the skull. The last six holograms were made of the base of the skull cavity (dorsal surface of a bulla) after removing the brain.

In the first of two experiments, 10 Sprague-Dawley rats were exposed to 25-microsecond pulses of 1.275-GHz RFR at a peak power density of 1.7 W/sq cm and a PRR of 50 pps. An additional set of holograms was made at 100 pps for five of the rats. In the second experiment, 16 adult guinea pigs were used. Of these, eight were exposed to 1.1-GHz pulses in a 2x2x2 factorial design with peak power densities 1.25 and 8.5 W/sq cm, pulse durations 10 and 20 microseconds, and PRRs 25 and 50 pps. The other eight were exposed to 1.2-GHz pulses in the same design. The holograms for three of the guinea pigs exposed at 8.5 W/sq cm showed that movement was engendered in the RFR absorber supporting the animals by the RFR pulses, so the support was replaced with a cement block.

The authors indicated that they could not detect any differences between the holograms obtained from each animal during RFR exposure and the holograms from the same surfaces of the same animal taken during sham exposure. (The comparisons were made on a coded and blind basis.) They concluded therefrom that the hypothesis of RFR transduction into elastic waves in the head and propagation of the sound to the cochlea by bone conduction, predicted by other investigators, is untenable. Instead, they suggested that the transduction site is more likely to be in the cochlea itself rather than elsewhere in the head.

The authors did not provide specific information about the appearances of the holograms or the differences sought between holograms of RFR- and sham-exposed surfaces, rendering it difficult to assess the validity of these negative findings. Also, the adequacy of the sensitivity of this holographic technique for detecting such movements was disputed by Chou et al. (1980a), with a response by Frey and Coren (1980). Based on the description of the holographic technique, one would expect that the brightness of a surface having non-uniform optical reflectance would appear non-uniform even if the surface were stationary. Also, a surface having uniform reflectance and moving as a unit, i.e., without motion of any area relative to another, would appear uniformly illuminated (but of lower brightness than if the same surface were stationary).

A more fundamental question is whether or not the successive removal of skin, musculature, etc., would alter the characteristics of possible RFR-to-elastic-wave transduction wherever it occurred in the head. For example, suppose transduction takes place at the inner or outer surface of the skull with the skin and musculature intact (which may render the motion undetectable with this holographic technique). Would baring the skull by the removal of skin and musculature alter the characteristics

of the transduction process significantly?

Olsen and Hammer (1980) used a hydrophone transducer implanted in a rectangular muscle-equivalent model to detect acoustical responses to exposure of the model to pulsed RFR. The model consisted of about 15 kg of polyethylene powder, water, sodium chloride, and gelling agent in proportions given by Guy (1971) and contained within an open rectangular polystyrene box. It was exposed to 0.5-microsecond 5.7-GHz pulses at 7-ms intervals (143 pps) at 5.5 cm from a standard-gain horn (about 0.07 of the conventional far-field distance) at an average power density of 120 mW/sq cm. The corresponding pulse power density exceeded 1.5 kW/sq cm. The authors noted that in the near field, the on-axis power density is a strongly oscillating function of the distance from the horn, and they found that the amplitude of the thermoelastic waves exhibited such behavior when the distance between the horn and hydrophone was slightly increased or decreased.

The SAR was determined calorimetrically at several depths within the model. The results were about 95 W/kg at 1 mm, 50 W/kg at 1 cm, and 5 W/kg at 2 cm, showing that most of the RFR energy was absorbed within the first 2 cm. The hydrophone used was directional and sensitive in the frequency range 50-700 kHz, and was inserted into the model on the axis of the horn at 15.24 cm from the exposed surface. The hydrophone output was fed to a broad-band filter, amplified, and monitored with an oscilloscope. For comparison with prior studies, measurements with the hydrophone were also made in 1% saline (12 kg) in the polystyrene box.

The response of the muscle-equivalent model to the RFR pulses was a rapidly decaying thermoelastic wave lasting about 10 microseconds and a narrower RFR artifact, the latter serving as a convenient marker for measuring the time delay corresponding to the acoustic propagation speed of the thermoelastic wave. The delay between the thermoelastic response and the artifact was 85 microseconds. Using the depth of the hydrophone to calculate the propagation (group) speed yielded about 1800 m/s.

A second wave delayed from the first by about 380 microseconds was also evident. The authors ascribed this wave to two successive reflections, from the back and front surfaces of the model, for a total distance traveled (one round trip from the hydrophone) of twice the dimension of box parallel to the propagation direction, or 60.96 cm, a distance that yielded a propagation speed of 1600 m/s. They noted that transduction of the pulses into thermoelastic waves at the surface was tacitly assumed in the calculation of the higher speed, but that transduction actually occurs 1-2 cm from the surface. Taking 1.5 cm as the locus of transduction yields a speed of 1616 m/s for the 85-microsecond delay (with no change for the twice-reflected wave).

The amplitude of the twice-reflected wave was about 20% of the initial hydrophone response amplitude, which permitted the authors to estimate the acoustic attenuation within the model. Excluding reflection losses, estimated to be less than 10%, yielded an upper-bound loss of 14 dB for a 61-cm slab of muscle-equivalent material.

For studying transduced waves in saline, the hydrophone was placed 7.62 cm from the exposed surface. Unlike the rapidly decaying wave in the muscle-equivalent material, the RFR pulses yielded a ringing response by the hydrophone. The 61-cm-round-trip delay time between the initial and twice-reflected waves was 400 microseconds, which yielded a propagation speed of 1525 m/s, consonant with values found by others (Lin, 1978). Also prominent was a wave delayed by only 90 microseconds from the initial wave, apparently due to reflections from the hydrophone itself and from the front surface of the saline back to the hydrophone. (An analogous wave of intermediate delay time was barely discernible in the oscilloscope trace for the muscle-equivalent material.)

The authors suggested that the presence of ringing in the saline model indicated the induction of higher-frequency acoustic components and that the absence of ringing in the muscle-equivalent model may be because of a thinner RFR-absorption profile and/or greater high-frequency damping for the simulated muscle tissue.

Olsen and Hammer (1981) performed similar measurements in a rectangular muscle-equivalent model. However, the 0.5-microsecond, 5.7-GHz pulses were triggered at 760-microsecond intervals or twice the round trip time observed previously, to reinforce the thermoelectric waves. (Interpulse intervals of 380 microseconds could not be used because of equipment limitations.) An amplitude enhancement factor of about 3 was obtained at the end of a burst of four pulses.

Also studied by Olsen and Hammer (1981) was a spherical brain-equivalent model 10 cm in diameter. The model was exposed to 1.10-GHz RFR from an open section of waveguide, either as single pulses of 4-kW peak power and duration that was varied or as bursts of three such pulses with an adjustable interpulse interval. For a nominal 10-microsecond pulse, the SAR was 824 W/kg at the center of the sphere and 653 W/kg at the surface facing the source. A hydrophone was placed at the center of the model to detect thermoelastic waves.

Exposure of the model to single 14-microsecond pulses yielded ringing for each pulse, with a fundamental frequency of about 16 kHz and a time constant of about 500 microseconds, the latter said to be consistent with the attenuation obtained in the rectangular model. A plot of hydrophone response vs pulse duration over the range 10-60 microseconds showed maximum response for 20-microsecond pulses. Three-pulse bursts at burst frequencies ranging from 10 to 30 kHz yielded higher amplitudes than single pulses, with maximum enhancement at 16 kHz, as expected.

Olsen and Lin (1981) performed similar studies of spherical brain-equivalent models 6, 10, and 14 cm in diameter exposed to 10-kW, 1.10-GHz single pulses and bursts of three pulses from an open section of waveguide. To increase the amplitude of the thermoelastic waves in the 6-cm sphere, it was placed directly against the waveguide opening.

A plot of peak hydrophone responses of the 6-cm sphere to bursts of 10-microsecond pulses vs burst frequency showed maximum response at 25.5

kHz. The corresponding data for the 10-cm sphere were the same as in Olsen and Hammer (1981). The response of the 14-cm sphere to single pulses was ringing at a fundamental frequency slightly above 10 kHz, and was maximum for 35-microsecond pulses. The responses of that sphere to bursts of 35-microsecond pulses had a peak at 11.5 kHz. Plots of the experimentally determined fundamental resonant frequencies for the three models were on the curve of resonant frequency vs head radius derived from the thermoelastic theory for a homogeneous brain sphere with stress-free boundaries, thereby supporting that theory.

In a subsequent study, Olsen and Lin (1983) surgically implanted disk hydrophone transducers 3.2 mm in diameter and 0.5 mm thick in the brains of rats, guinea pigs, and cats to measure the stress waves induced by RFR pulses. Connections to the transducers were made with coaxial cable 2.5 mm in diameter.

In the experiments with cats and guinea pigs, the hydrophone transducer was implanted about 1.5 cm deep in the brain of the anesthetized animal through a hole in the skull on the left side of the head near the top of the parietal bone. Next, the animal was taken to an anechoic chamber and exposed to 0.5-microsecond, 2 kW-peak pulses of 5.7-GHz RFR at 2 pps from a standard-gain horn, and to acoustic clicks. The output cable of the hydrophone was not connected during these stimuli; instead, metallic and nonmetallic electrodes (at unspecified head locations) were used to detect and compare brainstem potentials in response to each stimulus.

After the brainstem potentials were measured, the hydrophone output cable was connected to an oscilloscope and the animal was exposed to several series of 5.7-GHz RFR pulses at 14 pps. The animal was then removed from the chamber and placed next to a 3-kW-peak 2.45-GHz source, where its head was exposed to 2.5-microsecond pulses with a surface applicator. The output of the hydrophone was recorded during each exposure.

In the experiments with rats, brainstem potentials in response to 5.7-GHz pulses and acoustic clicks were measured before the hydrophone was implanted. After implantation, hydrophone signals were recorded during exposure to 0.5-microsecond, 5.7-GHz pulses in the anechoic chamber and to 5-6-microsecond, 2.45-GHz pulses with the applicator.

Representative hydrophone output waveforms for one cat and one guinea pig for the two RFR frequencies were presented, which showed that the shorter 5.7-GHz pulses stimulated vibrations having more of the higher-frequency components than the 2.45-GHz pulses. In addition, varying the 2.45-GHz burst frequency for the cat yielded maximum response near 40 kHz. Hydrophone output waveforms for six rats were also presented and were characterized similarly. In addition, a distinct vibration near 60 kHz, the computed fundamental mode of the rat brain, was discernible.

From their results, the authors concluded that RFR pulses do induce acoustic pressure waves in the brain, confirming previous predictions,

particularly regarding the fundamental radial oscillation of the rat brain near 60 kHz. They also noted that the theoretically predicted frequencies are independent of heating patterns, but are functions only of the propagation speed of pressure waves and the size of the head. Open to question, however, is whether the use of coaxial cable and other metal leads introduced significant artifact.

Wilson et al. (1980) used C-14-labeled 2-deoxy-D-glucose (C-14-DG) to prepare autoradiographic maps of brain activity in 11 rats, to study the effects of exposure to RFR, acoustic clicks, and infrared radiation (IR) on the auditory system. In nine of the rats, the left bulla was opened, the ossicles were removed, and the bulla was packed with gelfoam. In the other two rats, one cochlea was destroyed by inserting a blunt probe through the round window. These operations, done prior to exposure, were to abolish or attenuate the response of one side of the auditory system to airborne sound.

Each rat was exposed to only one stimulus in a sound-isolation chamber for 45 min, while the rat was restrained within a cylindrical cage of RFR-transparent mesh. Just before exposure, each rat was injected with C-14-DG. On completion of exposure, the rat was euthanized and its brain was quickly removed, frozen, and sectioned in the frontal plane (30-micron slices). Autoradiographs of C-14-DG uptake throughout the brain were prepared and examined for differences in optical densities resulting from exposure to the various stimuli. Also, autoradiographs of representative sections through the auditory and vestibular nuclei were identified and enlarged, and the identified sections were stained with cresyl violet.

Two of four rats were stimulated with acoustic clicks at 87 dB SPL from a loudspeaker driven by 100-microsecond pulses at 10 pps. One of the remaining rats was exposed to IR from two heat lamps at a level stated to mimic the total thermal load induced by RFR exposure. Specifically, the voltage applied to the lamps was adjusted to yield a temperature-increase rate of a saline-filled beaker that matched the rate obtained from exposure to 918-GHz RFR at 10 mW/sq cm. (The authors did note that the spatial heating profiles for the IR and RFR were dissimilar.) The fourth rat was held in the sound-isolation chamber without stimulation.

Autoradiographs of these four rats (denoted as controls, i.e., not exposed to RFR) were qualitatively similar; all showed bilateral asymmetry in C-14-DG uptake by the inferior colliculus and medial geniculate body, with higher uptake on the side contralateral to the intact middle ear. As noted by the authors, this form of asymmetry was expected because most ascending pathways from one cochlea lead to the central nucleus of the contralateral inferior colliculus. Not clear was why the autoradiographs for two such different stimuli (acoustic clicks and IR) and those taken in their absence were so similar to one another.

In an initial experiment, one of the rats with left ossicles removed was exposed to 20-microsecond pulses, 10 pps, of 2.45-GHz RFR at an

average power density of 2.5 mW/sq cm, for a peak power density of 12.5 W/sq cm. The autoradiographs of this rat from the inferior colliculus, unlike those for the control rats, showed bilateral symmetry in C-14-DG uptake, taken as indicating the utility of the C-14-DG method for demonstrating a known effect of RFR exposure on brain activity. The four remaining rats with left ossicles removed were then exposed to 918-MHz CW RFR, two each at 2.5 and 10 mW/sq cm, to identify possible effects of the CW RFR. The corresponding SARs in the midbrain were 1.1 and 4.4 W/kg, determined thermometrically with rat carcasses. For both CW RFR levels, C-14-DG uptake in the inferior colliculus was also bilaterally symmetric and the autoradiographs were "surprisingly similar" to those for the pulsed RFR.

The authors stated: "To exclude the possibility that CW microwave radiation produced this result by direct action on brain tissue, additional data were obtained from two animals in which one cochlea was destroyed. In both animals, the uptake of C-14-DG was greatest at the inferior colliculus contralateral to the intact cochlea. The degree of asymmetry at the inferior colliculus was, in fact, at least as great as that found in any of the control animals. This finding, coupled with the finding of a bilateral symmetry of C-14-DG uptake in the auditory pathways of animals with one middle ear ablated, demonstrated that CW microwave radiation acts at some site within the cochlea in eliciting auditory responses."

C-14-DG uptake in other structures of the auditory system, such as the lateral superior olive, medial superior olive, or cochlear nucleus, showed no bilateral differences except in the two rats with one cochlea destroyed. Autoradiographs from regions outside of the auditory system were bilaterally symmetric and showed no stimulus-related qualitative differences.

In their discussion, the authors suggested that the activity of the rat's auditory system in response to CW RFR, determined by integrated C-14-DG uptake during a 45-min period, is an effect distinct from the thermoelastic responses to RFR pulses, and that the CW interaction appears to occur somewhere within the cochlea. They estimated that a steady-state increase in intracochlear temperature of between 0.1 and 0.5 deg C would be induced in live rats exposed to 918-MHz CW RFR at 2.5 mW/sq cm, suggesting that such increases in temperature may be effective in altering auditory activity. In this context, it is reiterated that the average power density of the 2.45-GHz pulsed RFR used in this study was also 2.5 mW/sq cm and that the midbrain SAR was 1.1 W/kg.

In conclusion, the preponderance of experimental results indicates that auditory perception of RFR pulses is due to induction of thermoelastic waves in the head, rather than to direct brain stimulation by the RFR. Also, because individual pulses can be perceived, it is not meaningful to calculate average power densities for two or more widely spaced pulses and cite such values as evidence that the effect is nonthermal in nature. The response to CW RFR reported by Wilson et al. (1980) is an effect distinct from the thermoelastic responses to pulses

and possibly is related to an intracochlear temperature rise of 0.1 to 0.5 deg C.

REFERENCES:

Cain, C.A. and W.J. Rissman
MAMMALIAN AUDITORY RESPONSES TO 3.0 GHz MICROWAVE PULSES
IEEE Trans. Biomed. Eng., Vol. 25, No. 3, pp. 288-293 (1978)

Chou, C.-K., R. Galambos, A.W. Guy, and R.H. Lovely
COCHLEAR MICROPHONICS GENERATED BY MICROWAVE PULSES
J. Microwave Power, Vol. 10, No. 4, pp. 361-367 (1975)

Chou, C.-K., A.W. Guy, and R. Galambos
CHARACTERISTICS OF MICROWAVE-INDUCED COCHLEAR MICROPHONICS
Radio Sci., Vol. 12, No. 6S, pp. 221-227 (1977)

Chou, C.-K. and R. Galambos
MIDDLE-EAR STRUCTURES CONTRIBUTE LITTLE TO AUDITORY PERCEPTION OF MICROWAVES
J. Microwave Power, Vol. 14, No. 4, pp. 321-326 (1979)

Chou, C.-K. and A.W. Guy
CARBON-LOADED TEFLON ELECTRODES FOR CHRONIC EEG RECORDINGS IN MICROWAVE RESEARCH
J. Microwave Power, Vol. 14, No. 4, pp. 399-404 (1979a)

Chou, C.-K., and A.W. Guy
MICROWAVE-INDUCED AUDITORY RESPONSES IN GUINEA PIGS: RELATIONSHIP OF THRESHOLD AND MICROWAVE-PULSE DURATION
Radio Sci., Vol. 14, No. 6S, pp. 193-197 (1979b)

Chou, C.-K., A.W. Guy, K.R. Foster, R. Galambos, and D.R. Justesen
HOLOGRAPHIC ASSESSMENT OF MICROWAVE HEARING
Science, Vol. 209, pp. 1143-1144 (5 Sept 1980a)

Chou, C.-K., K.-C. Yee, and A.W. Guy
AUDITORY RESPONSE IN RATS EXPOSED TO 2,450 MHZ ELECTROMAGNETIC WAVES IN A CIRCULARLY POLARIZED WAVEGUIDE
Bioelectromagnetics, Vol. 6, No. 3, pp. 323-326 (1985a)

Foster, K.R. and E.D. Finch
MICROWAVE HEARING: EVIDENCE FOR THERMOACOUSTIC AUDITORY STIMULATION BY PULSED MICROWAVES
Science, Vol. 185, pp. 256-258 (19 July 1974)

Frey, A.H.
AUDITORY SYSTEM RESPONSE TO RADIO-FREQUENCY ENERGY
Aerospace Med., Vol. 32, pp. 1140-1142 (1961)

Frey, A.H.
HUMAN AUDITORY SYSTEM RESPONSE TO MODULATED ELECTROMAGNETIC ENERGY
J. Appl. Physiol., Vol. 17, No. 4, pp. 689-692 (1962)

Frey, A.H.
MAIN STEM EVOKED RESPONSES ASSOCIATED WITH LOW-INTENSITY PULSED UHF ENERGY
J. Appl. Physiol., Vol. 23, No. 6, pp. 984-988 (1967)

Frey, A.H. and R. Messenger, Jr.
HUMAN PERCEPTION OF ILLUMINATION WITH PULSED ULTRAHIGH-FREQUENCY ELECTROMAGNETIC ENERGY
Science, Vol. 181, pp. 356-358 (27 July 1973)

Frey, A.H. and E. Coren
HOLOGRAPHIC ASSESSMENT OF A HYPOTHESIZED MICROWAVE HEARING MECHANISM
Science, Vol. 206, pp. 232-234 (12 Oct 1979)

Frey, A.H. and E. Coren
HOLOGRAPHIC ASSESSMENT OF MICROWAVE HEARING [A response]
Science, Vol. 209, pp. 1144-1145 (5 Sept 1980)

Guy, A.W.
ANALYSIS OF ELECTROMAGNETIC FIELDS INDUCED IN BIOLOGICAL TISSUES BY THERMOGRAPHIC STUDIES ON EQUIVALENT PHANTOM MODELS
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 205-214 (1971)

Guy, A.W., C.-K. Chou, J.C. Lin, and D. Christensen
MICROWAVE-INDUCED ACOUSTIC EFFECTS IN MAMMALIAN AUDITORY SYSTEMS AND PHYSICAL MATERIALS
Ann. N.Y. Acad. Sci., Vol 247, pp. 194-218 (1975b)

Guy, A.W., J. Wallace, and J. McDougall
CIRCULARLY POLARIZED 2450 MHZ WAVEGUIDE SYSTEM FOR CHRONIC EXPOSURE OF SMALL ANIMALS TO MICROWAVES
Radio Sci., Vol. 14, No. 6S, pp. 63-74 (1979)

Johnson, C.C. and A.W. Guy
NONIONIZING ELECTROMAGNETIC WAVE EFFECTS IN BIOLOGICAL MATERIALS AND SYSTEMS
Proc. IEEE, Vol. 60, No. 6, pp. 692-718 (1972)

Lebovitz, R.M. and R.L. Seaman
MICROWAVE HEARING: THE RESPONSE OF SINGLE AUDITORY NEURONS IN THE CAT TO PULSED MICROWAVE RADIATION
Radio Sci., Vol. 12, No. 6S, pp. 229-236 (1977)

Lin, J.C.
MICROWAVE AUDITORY EFFECT--A COMPARISON OF SOME POSSIBLE TRANSDUCTION MECHANISMS
J. Microwave Power, Vol. 11, No. 1, pp. 77-81 (1976a)

Lin, J.C.
MICROWAVE-INDUCED HEARING: SOME PRELIMINARY THEORETICAL OBSERVATIONS
J. Microwave Power, Vol. 11, No. 3, pp. 295-298 (1976b)

Lin, J.C.
ON MICROWAVE-INDUCED HEARING SENSATION
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 7, pp. 605-613 (1977a)

Lin, J.C.
FURTHER STUDIES ON THE MICROWAVE AUDITORY EFFECT
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 7, pp. 938-943 (1977b)

Lin, J.C.
THEORETICAL CALCULATION OF FREQUENCIES AND THRESHOLDS OF MICROWAVE-INDUCED AUDITORY SIGNALS
Radio Sci., Vol. 12, No. 6S, pp. 237-242 (1977c)

Lin, J.C.
MICROWAVE AUDITORY EFFECTS AND APPLICATIONS
Charles C. Thomas, Springfield, IL, p. 108 (1978)

Lin, J.C., R.J. Meltzer, and F.K. Redding
MICROWAVE-EVOKED BRAINSTEM POTENTIALS IN CATS
J. Microwave Power, Vol. 14, No. 3, pp. 291-296 (1979b)

Olsen, R.G. and W.C. Hammer
MICROWAVE-INDUCED PRESSURE WAVES IN A MODEL OF MUSCLE TISSUE
Bioelectromagnetics, Vol. 1, No. 1, pp. 45-54 (1980)

Olsen, R.G. and W.C. Hammer
EVIDENCE FOR MICROWAVE-INDUCED ACOUSTICAL RESONANCES IN BIOLOGICAL MATERIAL
J. Microwave Power, Vol. 16, Nos. 3 & 4, pp. 263-269 (1981)

Olsen, R.G. and J.C. Lin
MICROWAVE PULSE-INDUCED ACOUSTIC RESONANCES IN SPHERICAL HEAD MODELS
IEEE Trans. Microwave Theory Tech., Vol. 29, No. 10, pp. 1114-1117 (1981)

Olsen, R.G. and J.C. Lin
MICROWAVE-INDUCED PRESSURE WAVES IN MAMMALIAN BRAINS
IEEE Trans. Biomed. Eng., Vol. 30, No. 5, pp. 289-294 (1983)

Sharp, J.C., H.M. Grove, and O.P. Gandhi
GENERATION OF ACOUSTIC SIGNALS BY PULSED MICROWAVE ENERGY
IEEE Trans. Microwave Theory Tech., Vol. 22, No. 5, pp. 583-584 (1974)

Taylor, E.M. and B.T. Ashleman
ANALYSIS OF CENTRAL NERVOUS SYSTEM INVOLVEMENT IN THE MICROWAVE AUDITORY EFFECT
Brain Res., Vol. 74, pp. 201-208 (1974)

Tyazhelov, V.V., R.E. Tigranian, E.O. Khizhniak, and I.G. Akoev
SOME PECULIARITIES OF AUDITORY SENSATIONS EVOKED BY PULSED MICROWAVE FIELDS
Radio Sci., Vol. 14, No. 6S, pp. 259-263 (1979)

White, R.M.
GENERATION OF ELASTIC WAVES BY TRANSIENT SURFACE HEATING
J. Appl. Phys., Vol. 34, No. 12, pp. 3559-3567 (1963)

Wilson, B.S., J.M. Zook, W.T. Joines, and J.H. Casseday
ALTERATIONS IN ACTIVITY AT AUDITORY NUCLEI OF THE RAT INDUCED BY EXPOSURE TO MICROWAVE RADIATION: AUTORADIOGRAPHIC EVIDENCE USING [C-14] 2-DEOXY-D-GLUCOSE
Brain Res., Vol. 187, pp. 291-306 (1980)

3.1.4.3 CUTANEOUS PERCEPTION

Among the few studies on human perception of RFR in the skin were those of Hendler and Hardy (1960), Hendler et al. (1963), and Hendler (1968), who compared the sensitivity of the forehead area to infrared radiation (IR) and RFR. Hendler (1968) will be discussed, with references to the two earlier papers as appropriate, because it includes most of the information in those papers plus some additional data.

As described in Hendler and Hardy (1960), to overcome previous inadequacies in measuring cutaneous temperature, the authors developed a radiometic apparatus having the following capabilities: (1) applying temperature stimuli to the skin and simultaneously measuring the resulting changes in temperature with a sensitivity better than 0.001 deg C per second and an absolute accuracy of +/- 0.01 deg C, (2) freedom from stimulation of cutaneous sensations other than temperature (e.g., touch, pain, itch, etc.), (3) avoidance of mechanical deformation of tissues with resulting alteration in local cutaneous blood flow, (4) maintenance of regulated and controlled intensity and distribution of the stimulus over the stimulated area, and (5) convenient application of stimuli of varying duration and tissue penetrability.

An insulating face shield was used to block all but a central 37-sq-cm circular area of the subject's forehead. A chopper rotating at 13 Hz (77 milliseconds per period) was positioned between the face shield and a heat source and between the face shield and a detector. The aperture areas of the chopper were designed so that the source or detector was open to the face shield during successive equal time intervals (about 30 milliseconds) of each rotation, but not both simultaneously. The latter condition prevented reflection of source energy from the forehead to the detector and thereby permitted detection of only the radiant emission from the forehead. Thus, forehead cooling curves could be determined virtually immediately after heating.

The chopper also amplitude-modulated the signals from the forehead at 13 Hz, thereby permitting use of conventional detector-output amplification at that frequency. The amplified signals were rectified, filtered, and fed through a potentiometer to an ink-writing strip-chart recorder. The potentiometer was used as a bucking-voltage source, to permit recording very small skin-temperature changes. Full-scale (10-inch) deflection of the pen required 1.5 seconds and represented a temperature change of 2 deg C with typical amplifier settings.

Detection was based on the black body characteristics of skin in the IR region. Examination of the reflectance spectra of black and white skin showed large differences between them in the visible and near-IR regions from about 0.4 to 2 microns (with maxima respectively at about 1 and 0.7 microns), but that the two curves were virtually coincident in the far-IR region from about 2 to 20 microns. In addition, the black body emission curve for 35 deg C, approximately normal forehead temperature, covered the latter range, with a peak at about 8 microns.

The detector, housed in an evacuated chamber having a far-IR-transparent window, consisted of a blackened target with a thermocouple attached. Black body emission for a source at 245 deg C covers the range from about 3 to 40 microns, with a peak at about 5 microns. Therefore, the IR source used was a hot plate maintained electrically at a temperature between 200 and 300 deg C. Radiation reaching the subject's skin from this source was controlled by a thermally insulated shutter, which could be rotated silently to regulate the duration of exposure. Calibration of the intensity within the face shield (to within about 3%) was done with a portable radiometer.

The RFR source described in the two earlier papers was a magnetron-powered 3-cm (10-GHz) pulse generator set to produce 0.4-microsecond pulses at 2500 pps. Magnetron output was fed through a waveguide to a horn placed, when used, in the same relative position as the hot plate. The peak and average output powers were 60 kW and 60 W. The RFR was controlled either manually by on-off switching or automatically with a microswitch operated by a revolving cam programmed for appropriate on-off sequences.

Data obtained with a 10-cm (3-GHz) pulsed source (2-microsecond pulses at 300 pps) terminated with a horn were presented only in Hendler (1968). However, because of the larger size of the apparatus, direct measurement of skin temperature by radiometry was not feasible. The subject was placed in the far field of the horn within an anechoic chamber, behind a shield that again limited the RFR to the forehead area.

Absorption of RFR energy of each frequency by the skin was determined with a skin "simulant" consisting of a hollow acrylic disc 0.55 cm thick for 10 GHz and 1.5 cm thick for 3 GHz, with faces of polyethylene sheet about 0.02 mm thick, filled with water and placed in the aperture of the face shield. Each disc was provided with internal thermocouples and an electric heater wire. Calibration was done by measuring the electric power required to raise the water temperature by known values in given time intervals, permitting calculation of the power required raise the water temperature by the same amount as by RFR during corresponding time intervals.

The absorption coefficient, calculated from equation 2-2-1 in Hendler (1968), p. 154 (and in the other two papers) and from the electrical properties of skin, was 4.9 per cm for 10 GHz and 1.2 per cm for 3 GHz. The corresponding reciprocals (penetration depths) were about 0.2 and 0.8 cm. The penetration depths given in Durney et al. (1978), p. 38 are respectively about 0.4 and 1.8 cm or twice those in Hendler (1968). The reasons for the discrepancies are obscure except that the equation cited appears to be in error. Moreover, with the stated values of dielectric constant and specific resistance of skin at 10 GHz, the equation yields a small and therefore probably inaccurate difference between two nearly equal numbers. However, Hendler (1968) also did note that individual values of absorption coefficient deviated as much as 50% from the mean.

Each experimental session lasted about 10 min. The subjects were given auditory warning signals before each stimulus. Successive stimuli were separated by at least 40 seconds, to allow the skin to return to initial temperature. When IR was used to change skin temperature, each subject verbally reported temperature sensation (warm, cool) or no sensation (neutral) every 10 seconds, which was noted immediately on the skin-temperature record. Because of sound changes associated with use of the RFR generators, each subject was provided with sound-attenuating ear muffs, and a low-frequency masking noise was used. Subjects exposed to RFR were also provided with two manual switches, one for each hand, to continuously record warm or cool sensation by closing the appropriate switch or no sensation by closing neither switch. The IR results are discussed first.

From curves of temperature increase for IR heating (with the hot plate) vs time, the thermal inertia (product of thermal conductivity, density, and specific heat) was determined for skin. The values were found to remain stable over heating periods lasting 140 seconds, and the mean for three subjects was 108 cgs units, findings of importance relative to heating with pulsatile IR, discussed later.

Detailed examination of the forehead-skin temperature records of seven subjects exposed to the IR showed that the best correlate of temperature sensation was the time rate of change of skin temperature when the skin remained within a few degrees of its normal level; neither the time derivative of this correlate, nor skin temperature per se, nor increment of skin temperature showed any consistent relationship to temperature-sensation reports.

Representative IR results were presented, based on 788 reports of warm, cool, and neutral sensations by one experienced subject during eight experimental periods, in which skin temperature was varied from slightly higher than 32 to about 36 deg C but not by more than 0.6 deg C during any one experimental period. These results were plotted as percentages of reports of each sensation vs the measured time rate of change of skin temperature (over the range from -0.01 to +0.01 deg C per second). Even though the authors drew the curve for each sensation visually rather than by statistical curve fitting (a straight line each of positive and negative slope for warm and cool, respectively, and an inverted U for neutral), the correlations were evident. Taking the 50% probability level for each sensation as indicating the threshold for that sensation yielded a threshold skin-temperature rate of change between +0.001 and +0.002 deg C per second for warm and between -0.005 and -0.006 deg C per second for cool.

The authors noted some exceptions to the relationship between sensation and skin-temperature rate of change. First, during periods when skin temperature was not changed, only 48.6% of the reports were neutral; of the remaining reports, 19.5% were cool and 31.9% were warm. Second, rapid spontaneous fluctuations of skin temperature due to irregularly occurring convective heat losses were not accompanied by sensation reports consistent with the skin-temperature changes actually

measured. Third, when the skin was heated or cooled appreciably and allowed to return spontaneously to normal level, initial reports of cool were made irrespective of the direction of the change.

High levels of pulsatile IR were applied for short durations to the forehead skin, without and with blackening (with india ink), of an experienced subject. The radiometric apparatus was not used, because its frequency response was limited; instead, the source was a Variac-controlled 150-W incandescent lamp covered with a near-IR (1-3 microns) filter. A leaf-type camera shutter having a wide-open aperture area of 25.65 sq cm was placed over the face shield. Shutter opening times were varied to provide pulses (basically square waves) of thermal energy of duration from 39 to 570 milliseconds.

At each shutter setting (pulse duration), various intensities were tried until a level was found for which half the stimuli yielded reports of sensation. That level was taken to be the warmth threshold for that pulse duration. A plot of threshold level vs pulse duration (over the domain 39-570 milliseconds) yielded a reciprocal (constant-product) relationship, a result taken as indicating some common change within the skin under the assumption that the warmth sensation was the same for each pair of values.

IR-induced intracutaneous temperature changes were analyzed by the authors with the one-dimensional heat-conduction equation; the solution for each threshold level and pulse duration was plotted as temperature increment vs depth into skin. The shapes of the curves were similar, each showing diminution of temperature increment with depth, with the curve for the highest threshold intensity and shortest pulse yielding the highest surface temperature rise and the largest (negative) slope. Especially noteworthy was that the curves crossed one another within the depth range 150-200 microns, in which region the temperature rise was about 0.02 deg C. Thus, taking 50 microns as the approximate thickness of the epidermis, the authors associated the threshold warmth sensation with thermal stimulation of the subcutaneous region. They suggested that rapid surface-temperature fluctuations would not be very effective in stimulating this region (because of the thermal inertia of skin), which would account for the absence of responses to the spontaneous convective heat losses noted above.

Responses to heating with 10-GHz RFR yielded sensation reports that were more variable than those with IR. Among the results were those showing a different functional dependence on exposure time of threshold surface-temperature increase for 10-GHz RFR than IR. This surface-temperature increase diminished with exposure time (reciprocity) for IR, whereas it rose linearly with exposure time for 10-GHz RFR. The curves crossed at about 1.4 seconds, for which the threshold surface-temperature increase was about 0.033 deg C. The corresponding curve for 3 GHz was not shown because no direct measurements of skin temperature at this frequency were made. However, the authors noted that a curve calculated from the known absorption coefficient of skin at 3 GHz would be below and roughly parallel to the 10-GHz curve.

The only 3-GHz data presented (in Hendler, 1968) was a plot of threshold stimulus intensity vs exposure time, with similar plots for 10 GHz and far IR. Both RFR curves extended to exposure durations of 5 seconds, but the IR curve to only 3 seconds. Reciprocity was evident for all three curves, with the 3-GHz curve above that for 10-GHz and the latter above the IR curve, consonant with penetration-depth considerations. As representative quantitative results, the threshold stimulus intensities for 1-second exposures to 3 GHz, 10 GHz, and IR were respectively about 14.3, 4.5, and 1.2 mcal per second per sq cm (60, 19, and 5 mW/sq cm). For 5-second exposures, the 3- and 10-GHz thresholds were respectively about 7.6 and 3.0 mcal per second per sq cm (32 and 13 mW/sq cm); by extrapolation, the 5-second threshold for IR was about 0.05 mcal per second per sq cm (0.2 mW/sq cm).

Among the other notable results with 10-GHz RFR were delays in responses between stimulus initiation and first report of warmth sensation (onset delay) and between stimulus termination and end of warmth sensation (offset delay). In a typical experiment, the average onset and offset delays were respectively 2.4 and 6.6 seconds. The authors indicated that casually placing the hand directly in front of the RFR horn for greater intensity yielded warmth that persisted for several minutes after the hand was removed and that the subjects did not respond to suprathreshold rates of skin-temperature change in a manner that could be accounted for by the hypothesis that this measure is the effective stimulus for sensation as for IR.

More recently, Justesen et al. (1982) determined warmth thresholds by exposing the forearm of each of six subjects to vertically polarized far-field 2.45-GHz CW RFR within an anechoic chamber for 10 seconds at aperiodic intervals of about 30 seconds. For exposure, each subject was located behind an RFR-absorbing partition within the chamber, with the ventral surface of the forearm vertically placed against an aperture 15 cm in diameter in the partition. Subjects were similarly exposed to IR from focused quartz lamps through an aperture of the same size in a Styrofoam partition. During threshold measurements, the fans used for driving air through the chamber were inactivated, and the ambient temperature and relative humidity averaged 25 +/- 2.0 deg C and 50 +/- 5%, respectively. Calibrations of RFR and IR power densities were done at aperture center (in the absence of the subject) with a Narda Model 8316B E-field probe and a Hardy radiometer, respectively.

IR SARs were determined for a cylindrical red-latex-balloon model filled with 0.9% NaCl in distilled water and secured against the aperture. The length and diameter of the model were 15.5 and 2.25 cm, and the mass was 62 g. A Vitek temperature probe suspended at the geometric center of the model was used to measure the temperature rise. IR exposures for 10 min at 10.71 mW/sq cm yielded a temperature rise of 0.9 deg C, which corresponded to an SAR of 6.3 W/kg or 0.59 W/kg per mW/sq cm.

RFR SARs were similarly determined, but with a saline-filled cylindrical model of length 15.9 cm, diameter 5.8 cm, and mass 420 g, values which corresponded more closely to the mass and profile of the part of

the human forearm exposed through the aperture. The model was exposed at 70 mW/sq cm until a rise of exactly 0.5 deg C was attained, which required 394 seconds. From these values, the calculated SAR was 5.31 W/kg or 0.076 W/kg per mW/sq cm (not 0.74 microwatt/g per mW/sq cm as stated in the text). The power incident on the model, obtained by multiplying 70 mW/sq cm by the profile area exposed through the 15-cm aperture (about 88 sq cm), was 6.16 W. The rate of energy absorption in the model was 2.23 W or only about 36% of the incident power, i.e., about 64% of the incident power was scattered.

The ranges of power densities used were 0-70 mW/sq cm in 5-mW/sq-cm steps for RFR, and 0-5.5 mW/sq cm in 0.5 mW/sq-cm steps for IR. On-off switching of the RFR was done at the source. However, IR switching was done with a manually operated shutter because of the long rise time of the source lamps.

Three men and three women were the subjects for the RFR experiment and two of each gender participated in the IR experiment. The profile of each subject's forearm within a 15-cm aperture was drawn, and the area within the profile was measured with a planimeter. The trials were conducted with the subject in the dark, and lighting of a bulb before each trial signaled the subject to place the arm in the appropriate position. The 10-second exposure was done within 5-15 seconds of the signal, after which the experimenter elicited, via an intercom system, a yes or no from the subject regarding perception of the stimulus.

Thresholds for perception of RFR and IR were ascertained by the random double-staircase method (Cornsweet, 1962), in which the stimulus level to be presented during a given trial was determined as follows: If the subject reported perception of the stimulus in the preceding trial, the stimulus level was lowered by a randomly determined multiple of steps ("stairs"); if the subject responded negatively, the level was raised similarly. The randomness of the size of the multiples precluded discovery by the subject of any pattern of successive stimuli. This procedure was continued until 13 transitions (reversals of intensity direction) occurred, and the threshold was defined as the mean of stimulus intensities over the final 10 transitions.

The RFR and IR threshold data and forearm profile area for each subject were tabulated, and the means were calculated separately for the men and women. The mean thresholds for RFR perception by the men and women were respectively 25.27 and 28.88 mW/sq cm, a nonsignificant difference. Their IR thresholds were 1.48 and 2.00 mW/sq cm, also a nonsignificant difference. However, the Pearson product-moment correlation, r, between the RFR and IR thresholds for all 6 subjects (without regard to gender) was high ($r=0.97$) and reliable ($p<0.02$). The mean profile areas for the men and women were 122.67 and 91.33 sq cm, respectively, a significant difference, but the correlation between threshold power density and profile area was only 0.26 ($p<0.1$) for RFR and 0.62 ($p>0.1$) for IR.

The range of RFR thresholds over all 6 subjects was 28.85 (from 15.40

to 44.25) mW/sq cm, with a grand mean of 26.74 mW/sq cm. The deviance, defined as the ratio of range to grand mean and used as an index of instability, was 108%. The range of IR thresholds for the four subjects was 1.10 (from 1.45 to 2.55) mW/sq cm, with a grand mean of 1.74 mW/sq cm for a deviance of 63%. Thus, the grand mean RFR power-density threshold was about 15 times higher than the IR threshold. None of the four subjects exposed to both RFR and IR reported any difference in sensory quality between the two stimuli.

The threshold RFR energy absorbed by each subject during a 10-second exposure was calculated from the threshold incident power density, the exposed forearm area, and the dosimetric data from the saline models (with an absorption efficiency of 0.36 as noted above). The resulting range of threshold energies was 9.15 (6.43 to 15.58) J, with a grand mean of 10.16 J, for a deviance of 90%. The threshold IR energy was similarly calculated (with an absorption efficiency of 1.0); the range was 0.86 (1.38-2.24) J, with a grand mean of 1.83 J and a deviance of 47%. Thus, the amount of RFR energy for threshold stimulation was about fivefold higher than for IR. Also, the threshold-energy deviance for each stimulus was smaller than its threshold-power-density deviance. Therefore, the authors suggested that threshold energy absorption is a more stable predictor of just-noticeable warming by either RFR or IR than threshold power density.

Because of the high correlation between the RFR and IR thresholds, the warmth sensed is believed by the authors to be due to stimulation of the same superficially located thermoreceptors of the skin. The fifteenfold power-density difference and the fivefold absorbed-energy difference between RFR and IR thresholds for stimulation were ascribed in part to the large scatter (about 64%) of the incident RFR (vs virtually no IR scatter) and in part to the much larger penetration depth of the RFR.

The authors noted that Hendler (1968) had found that exposure of 37 sq cm of the human forehead to 3-GHz RFR (shown as 3000 GHz, a typographic error) for 4 seconds required a mean warmth threshold of 33.5 mW/sq cm. By extrapolation of Hendler's data, they obtained a threshold of about 27 mW/sq cm for 10-second exposures, a value very close to the grand mean, 26.7 mW/sq cm, found in this study. In addition, the mean IR threshold (1.7 mW/sq cm obtained in this study) was comparable to the human-forehead IR threshold (extrapolated to 10 seconds) reported by Hendler et al. (1963).

The adequacy of the RFR-SAR determinations as described in this paper may be questioned because use of a thermal probe at the geometric center of the saline model to monitor the RFR-induced temperature rise of the water during a 394-second (6.6-min) exposure appears to have ignored the variation of energy-absorption rate with depth or surface cooling. In particular, no mention was made of any measures taken to minimize heat loss from the saline model or of whether the temperature of the saline was equilibrated by stirring or other method during exposure. If such precautions were not taken, then the thresholds of energy-absorption could be inaccurate to a significant degree. Another point open to

question is how valid were the extrapolations of the threshold curves to exposures of 10 seconds. However, these comments do not gainsay the qualitative findings of this study.

Justesen et al. (1982) also performed a pilot study on whether the onset and offset delays in perceiving 10-GHz RFR reported by Hendler et al. (1963) would also occur with 2.45-GHz RFR. The forearm of one subject was exposed at 70 mW/sq cm for periods varied randomly from 10 to 60 seconds, with the subject required to signal as soon as warming was perceived and when it was no longer perceived. The onset delay ranged between 3.5 and 6.0 seconds. The offset delay usually ranged from 3 to 5 seconds, but during the longer exposures (30 and 60 seconds), the warmth sensation sometimes faded before end of exposure, an effect attributed to sensory adaptation. The authors suggested that if this sensory adaptation is a general property of RFR-heating, it may help account for the difficulty of rodents in learning to escape or avoid high levels of RFR, a subject discussed in Section 3.7.1.1.

REFERENCES:

Cornsweet, T.N.
THE STAIRCASE METHOD IN PSYCHOPHYSICS
Amer. J. Psych., Vol. 75, pp. 485-491 (1962)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Hendler, E. and J.D. Hardy
INFRARED AND MICROWAVE EFFECTS ON SKIN HEATING AND TEMPERATURE SENSATION
IRE Trans. Med. Electronics, Vol. 7, pp. 143-152 (1960)

Hendler, E., J.D. Hardy, and D. Murgatroyd
SKIN HEATING AND TEMPERATURE SENSATION PRODUCED BY INFRARED AND MICROWAVE IRRADIATION
In C.M. Herzfeld (ed.), TEMPERATURE. ITS MEASUREMENT AND CONTROL IN SCIENCE AND INDUSTRY, Vol. 3, Part 3, J.D. Hardy (ed.), BIOLOGY AND MEDICINE, Reinhold Pub. Corp., New York, pp. 211-230 (1963)

Hendler, E.
CUTANEOUS RECEPTOR RESPONSE TO MICROWAVE IRRADIATION
In J.D. Hardy (ed.), THERMAL PROBLEMS IN AEROSPACE MEDICINE, Unwin Bros. Ltd., Surrey, U.K., pp. 149-161 (1968)

Justesen, D.R., E.R. Adair, J.C. Stevens, and V. Bruce-Wolfe
A COMPARATIVE STUDY OF HUMAN SENSORY THRESHOLDS: 2450-MHZ MICROWAVES VS FAR-INFRARED RADIATION
Bioelectromagnetics, Vol. 3, No. 1, pp. 117-125 (1982)

3.1.4.4 RFR SHOCK AND BURN

Although it was known that RFR can cause electric shock in the body or burns in tissue under specific circumstances, specific exposure limits were not included in previous standards for human exposure to RFR. Guy (1985), however, noted that such effects were considered in choosing the 300-kHz lower frequency limit of the present ANSI (1982) standard.

Several studies were conducted recently to determine the RFR levels and conditions that could cause electric shock or tissue burns, and it is now likely that the findings of such studies will serve as the basis for specifying, in future RFR-exposure standards, the appropriate electrical parameters and their maximum permissible levels under stated exposure conditions to avoid such effects.

Rogers (1981) stated the problem as follows: "When a person touches an electrically energised [sic] object, he may experience an adverse effect. If the object is energised by a radio-frequency (rf) source, the predominant contact hazard is burning of tissue at the point of contact and arises when the current drawn from the object exceeds a certain value. This rf burn hazard exists on various transmitting aerials and simple precautions can be taken to avoid it. However, such a hazard can also arise on metallic objects excited by radiation from transmitting aerials in their vicinity and this paper is devoted to this aspect."

In that paper, a simple apparatus ("RF Burn Hazard Meter") was described to measure the RF currents passing through a human in shoes standing on a ground plane. Part of the apparatus consisted of a brass tube excited by an RF source, with the source connected to the ground plane. When the subject touched the tube with a finger, a loop consisting of the source, tube, body of the subject, and ground plane was closed to form the primary of a current transformer (single turn). The rest of the apparatus was the transformer secondary winding and its connections via diode detectors, resistors, and capacitors to a dc current meter. Using this apparatus, the current levels that yielded a barely perceptible sensation ("perception" current) and that caused discomfort ("let-go" or "hazard" current) were measured for frequencies in the MF (0.3-3 MHz) and HF (3-30 MHz) bands.

The author indicated that the perception current and let-go current for contact with the tip of the forefinger were both about twice those for contact with the back of the forefinger, and were even higher for large-area contact with the palm. The results for 50 persons tested (with the back of the forefinger) showed a mean hazard threshold current of about 200 mA for the band 2-20 MHz.

The paper was devoted primarily to possible shipboard hazards to humans from metallic structures in the vicinity of onboard radiating antennas. Included were measured and calculated data for various structures and distances. The author concluded: "The measurements described indicate an rf burn hazard threshold of about 200 mA for the HF

band and show that many shipboard structures can be excited sufficiently by own ship transmissions in this band to present rf burn hazards to personnel. They show also that cranes can be potent sources of rf burn hazards...It is to be noted that rf burn hazards are present on structures when irradiated at field strengths much lower than the maximum permissible for human exposure. For example the measurements on the crane reported above show that the electric field for rf burn hazard threshold is about 10 V/m compared, for example, to the American National Standards Institute for the band 3-30 MHz." [The author was referring to the ANSI (1974) standard, which specified a maximum electric field of 200 V/m for the frequency range 10 MHz to 100 GHz].

Gandhi and Chatterjee (1982) used the quasi-static approximation (Deno, 1974; Bracken, 1976) to calculate the short-circuit currents induced in metallic objects (a 2.44-m x 1.22-m metal roof, a 50-ft metal fence, a compact car, and a fork-lift truck) and in a human (height 1.75 m, mass 68 kg), when each object is in a vertically polarized electric field at frequencies in the range 10 kHz to 10 MHz, and with each object assumed to be isolated from ground by 5 cm of insulation. They then calculated the incident electric fields necessary to produce threshold-perception and let-go currents for a human in conductive finger contact with each object. The threshold-perception current was defined as the smallest current that produces a tingling or pricking sensation due to nerve stimulation. The authors noted that the sensation changes from tingling to internal heat at frequencies above about 100-200 kHz. Let-go current was defined as the maximum value at which a human can still release an energized conductor with muscles directly stimulated by that current.

The authors used the experimental data on human perception-threshold and let-go currents of Dalziel and Mansfield (1950), Dalziel and Lee (1969), and Rogers (1981) for their calculations. These data were reproduced as log-log plots of perception-threshold and let-go currents vs frequency. The perception-threshold current showed a linear rise from about 0.4 mA at 10 kHz to about 1[illegible] mA at 150 kHz, with a slower rise to about 100 mA at 20 MHz. The let-go current also showed a linear rise, from 6.4 mA at 10 kHz to about 85 mA at 150 kHz, and a slower linear rise to about 200 mA at 20 MHz.

By using the value of capacitance-to-ground for each object and ratio of its electrostatically coupled short-circuit current to the unperturbed vertical field measured at 60 Hz (Deno, 1974; Bracken, 1976), Gandhi and Chatterjee (1982) obtained the effective area (S) and height (h) of the object. They assumed that these values of S and h are also reasonably valid for frequencies in the range 10 kHz to 3 MHz because the fields are quasi-static for objects of largest dimension much smaller than the free-space wavelength.

Log-log plots of the calculated values of unperturbed electric field (E) necessary to create threshold-perception and let-go currents in a human in finger contact with each object were presented. For each object, E for threshold perception was constant in the range approxi-

mately 10-100 kHz: about 250, 160, 80, and 20 V/m for the roof, fence, car, and truck, respectively; in the range 10 kHz to 10 MHz, E for the car and truck did not change substantially but those for the roof and fence decreased to about 35 and 20 V/m at 10 MHz, respectively. The plots of E for let-go current vs frequency were similar: the plateaus for the roof, fence, car, and truck in the range 10-100 kHz were about 1040, 850, 440, and 110 V/m, respectively, with diminution for the roof and fence to less than 100 V/m at 10 MHz and smaller decreases for the car and truck.

The authors stated: "A simple analysis based on the equivalent circuit representation of a human in conductive contact with an ungrounded, metallic object in a quasi-static HF field points out that there may be situations where the thresholds of perception and let-go can be exceeded for fields considerably lower than the ANSI recommended guideline of 615 [sic] V/m, the far-field equivalent E-field associated with a power density of 100 mW/sq cm in the frequency band 0.3 to 3.0 MHz [ANSI, 1982]...The above effects will not occur if the conducting objects are grounded or insulated at the points of possible contact."

Chatterjee et al. (1986) measured the complex body impedance (magnitude and phase) and the threshold currents for perception and pain for 197 men and 170 women of ages between 18 and 70 years for the frequency range 10 kHz to 3 MHz. They defined the threshold-perception current for pain as the smallest current for which the subject reported "very uncomfortable sensations (similar to but more intense than that for perception) for which he/she will definitely not continue to touch the electrode any more."

Mean body-impedance data (and SDs) vs frequency for barefoot subjects standing on a ground plane and grasping a brass-rod electrode that was insulated from the ground plane were shown separately for men and women. Both the magnitude and the phase decreased monotonically with frequency, but at corresponding frequencies, the impedance magnitude for women was significantly higher than for men. At 10 kHz, for example, the mean values for women and men were respectively about 630 and 520 ohms. The difference in mean phase at each frequency was not significant. The results for the subjects when they used an index finger moistened with 0.9% saline to touch a metal-plate electrode insulated from the ground plane were qualitatively similar, but of much higher magnitudes, about 1900 and 1700 ohms at 10 kHz, respectively.

For men, the mean threshold-perception currents for finger contact rose linearly with frequency from about 4 mA at 10 kHz to about 40 mA at 100 kHz and remained at the latter value from 100 kHz to 3 MHz. The curve for women was parallel to that for men, but about 25% lower; by analysis of variance, the difference was highly significant. The results for grasping contact were similar. The curves of finger-contact threshold currents for pain vs frequency also rose roughly linearly to maxima at about 100 kHz, but diminished slightly with frequency in the range 100 kHz to 3 MHz. At 10 kHz, the mean pain-threshold currents for men and women were respectively about 10 and 6.5 mA, but their maxima at

100 kHz were nearly the same, about 14.5 mA. The authors noted that the values of threshold current for 10-year-old children can be obtained from those for male adults by using a scaling factor of about 60%.

The sensation reported by the 367 men and women for frequencies below 100 kHz was tingling or pricking, localized in the area adjacent to the region of contact on the finger or hand; for frequencies above 100 kHz and finger contact with the plate electrode, the sensation was warmth or heat in the area below and around the plate electrode; with grasping contact, warmth or heat was felt in the hand and wrist. To determine more accurately the frequency for transition from tingling to warmth, data were obtained for some subjects at 50 and 70 kHz. At 50 kHz, the sensation reported was always tingling, but at 70 kHz, some subjects reported tingling and others warmth. Moreover, when the current was raised slightly for those who reported tingling, the sensation changed to warmth. In addition, for frequencies above 100 kHz at which warmth was felt, when the current was adjusted to be equal to the perception threshold, pain was reported typically within 10-20 seconds, an effect that was not observed for frequencies below 100 kHz.

Also determined in this study were the short-circuit currents, at local AM broadcast stations (operating at 630, 700, and 1500 kHz) and at Coast Guard and Navy communication antenna sites in Hawaii (operating at 13.6. 23.4, 146, and 3105 kHz), induced in humans while barefoot or wearing safety, leather-soled, or rubber-soled street shoes; the short-circuit currents induced in various vehicles; and the currents induced in humans in contact with these vehicles. Among the findings were that electrical safety shoes and gloves respectively provide protection that is adequate only at frequencies less than about 1 and 3 MHz. The measurements of induced short-circuit current showed reductions to 55% of the barefoot values with rubber-soled shoes, 63% with safety shoes, and 85% with leather-soled shoes.

The mean body impedances and threshold-perception currents were used to calculate the E-fields for threshold perception by grounded humans in finger contact with a compact car, van, and school bus, and the results for adult males and 10-year-old children were plotted vs frequency in one set of graphs, and for adult females in another set. Similar sets of curves were obtained for threshold-perception E-fields with grasping contact. Also presented were similar sets of curves of the threshold E-fields for pain vs frequency for finger contact with such vehicles.

The threshold-perception curves for finger contact by men, women, and children were all entirely below 632 V/m, the value recommended in ANSI (1982) for the range 0.3-3.0 MHz, with peaks at approximately 100 kHz in ascending order respectively for the school bus, van, and compact car. (The curves for the bus and van crossed at frequencies above 100 kHz.) Thus, currents from all three vehicles could be sensed at fields smaller than those recommended by ANSI for the range 0.3-3.0 MHz. For grasping contact, the school-bus threshold-perception curves for all three groups were also below the ANSI value over the entire frequency range; those for the other vehicles were below that level except within frequency

ranges of various sizes encompassing their respective peaks at 100 kHz.

The curves of pain-threshold E-field for finger contact with each type of vehicle were entirely below 632 V/m except for the curve for men in contact with the compact car. That curve exceeded 632 V/m in the range approximately 10-80 kHz, with a maximum of about 850 V/m at 30 kHz. All the other curves also had broader maxima at frequencies less than 100 kHz than those at 100 kHz for threshold perception.

The authors had measured the capacitance-to-ground of a GMC van that was well insulated from ground at a local AM broadcasting station operating at 700 kHz. The result was 1045 pf, which they used in a calculation of the current through the hand of a grounded human in conductive contact with the handle of such a van within a 3-MHz, 632-V/m field and obtained 879 mA. Based on this result and on an effective cross-sectional area of 11.1 sq cm for the wrist, they estimated that the corresponding local SAR in the wrist would be about 1045 W/kg.

The results of this study were presented in considerably more detail in a final report by Gandhi et al. (1985a). The very high SAR value above for the wrist was not mentioned. However, given in Appendix B of that report (although not directly related to possible shock and burn hazards from contact with metallic objects) were formulas for calculating local SARs in cross sections of the human leg (ankles, just below and above the knee, and two other thigh locations) for a human (barefoot and with safety shoes) immersed in a vertical field at the levels specified in ANSI (1982) for the range 0.3-30 MHz. (These levels are 632 V/m for the frequencies f less than 0.3 MHz and 1897/f for f in the range 3-30 MHz.)

The formulas include the currents induced in the bodies, derived by the quasi-static approximation, and the effective cross-sectional areas of interest, derived from the geometric areas and specific conductivities of the tissues involved. Also presented were experimentally determined human values of normalized current (in mA per V/m) that demonstrated the validity of the quasi-static approximation to frequencies up to about 40 MHz. With these formulas, calculations based on assuming that half the body current flows through each leg indicated that SARs as high as 182 W/kg could occur in the ankle region. These results were also published (Gandhi et al., 1985b).

Guy and Chou (1985) performed an extensive study on possible hazards to humans from exposure to fields in the VLF-MF (10 kHz to 3 MHz) range, directed principally toward quantitation of thresholds and establishment of safety standards against such hazards. They noted that though SAR is generally used to quantify internal energy absorption, other quantities may be more important in the VLF-MF band for this purpose, because the amounts of energy absorbed by humans exposed to fields in that frequency range are relatively low but can cause direct neuromuscular effects from electric shock, and local tissue damage may result from electric contact between the subject and metallic objects in the field. In addition to SAR, the important quantities include total electric current, I, in the

body resulting from exposure while in contact with objects or surfaces in free space and current density, J, through various cross sections of the body.

The authors also noted that maximum energy coupling occurs when the longest dimension of the body is parallel to the electric vector, and that for exposure in this orientation to plane waves and most VLF-MF antenna sources, absorption from the magnetic component is more than an order of magnitude smaller than absorption from the electric component, so any restrictions on electric-field exposure will ensure restrictions on the corresponding magnetic fields that are more conservative by at least a factor of ten.

In this report, the prior work on possible shock and burn hazards was reviewed, and vast quantities of experimental and calculated data were presented, including:

1) Impedances for humans and various vehicles, and for humans in contact with such vehicles under various ground conditions.

2) Measurements of open-circuit voltage and short-circuit current for humans and vehicles in high-strength electric fields, with the humans barefoot or wearing standard leather-soled shoes, standard rubber-soled shoes, sandals, or stockings.

3) Impedance distributions along the axis of the body and limbs vs frequency for 275 adult men and women of various ages, shapes, and sizes.

4) Weights and heights of the populations above, and circumference and diameter of middle finger, legs, arms, torso, shoulders, neck, and head at 5-cm intervals along their body and limb axes.

5) Thresholds for electrical-stimulation perception vs frequency for the finger, arm, and ankle.

6) Threshold currents and current densities for perception of electric shock by the average-sensitive, 0.5-percentile least-sensitive, and 0.5-percentile most-sensitive subpopulations.

7) Induced body currents, current densities, SAR distributions, and average SARs in all parts of the bodies of some subjects in the low-, medium-, and high-weight ranges for exposure to fields under various conditions, including: free space, feet grounded, hand grounded, and hand in contact with an object drawing 1 mA of current.

8) Current flow in the bodies of subjects when in contact with various vehicles in VLF and MF fields at field strengths measured from ground level to a height of 7 ft.

9) Human exposures at the following sites to the frequencies indicated:

10.2 kHz	Haiku, HI
23.4 kHz	Lualualei, HI
24.8 kHz	Jim Creek, WA
146 kHz	Lualualei, HI
1 MHz	KOMO Radio, Vashon Island, WA

An important finding was that highest local SARs occur in the ankles of the subjects, a result also found by Gandhi et al. (1985a). In the rationale of the ANSI (1982) guidelines, exposures at maximum local spatial SARs as high as 8 W/kg (averaged over any gram of tissue and over any 0.1-hr period) would be permitted, provided that the whole-body-averaged SAR does not exceed 0.4 W/kg. In this context, Guy and Chou (1985) noted that exposure to fields in the VLF-MF range would have to be restricted to 97 V/m to avoid exceeding the 8-W/kg limit.

In their conclusions, Guy and Chou (1985) stated: "At the present time this study is far from complete and will require additional work before any final conclusions can be made concerning safety guidelines for the VLF-MF frequency range." They also noted: "Based on the measurements carried out under this contract, it appears that not enough attention has been placed on spark discharge hazards. This type of insult can produce a very unpleasant stimulus and an involuntary startle reaction which can occur at exposure fields much less than that required to produce a perceived steady state current."

In a presentation, Guy (1985) summarized the work described in Guy and Chou (1985) as well as that of other investigators on this topic.

As suggested at the beginning of this section, exposure standards under development, and specifically the 1987 ANSI standard, will undoubtedly include maximum permissible levels in the VLF-MF range for avoidance of shock and burn hazards.

REFERENCES:

ANSI (American National Standards Institute), C95.1-1974
SAFETY LEVEL OF ELECTROMAGNETIC RADIATION WITH RESPECT TO PERSONNEL
Published by the Institute of Electrical and Electronics Engineers, New York (1974)

ANSI, C95.1-1982
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
Published by the Institute of Electrical and Electronics Engineers, New York (1982)

Bracken, T.D.
FIELD MEASUREMENTS AND CALCULATIONS OF ELECTROSTATIC EFFECTS OF OVERHEAD TRANSMISSION LINES
IEEE Trans. Power App. Syst., Vol. 95, pp. 494-504 (1976)

Chatterjee I., D. Wu, and O.P. Gandhi
HUMAN BODY IMPEDANCE AND THRESHOLD CURRENTS FOR PERCEPTION AND PAIN FOR CONTACT HAZARD ANALYSIS IN THE VLF-MF BAND
IEEE Trans. Biomed. Eng., Vol. 33, No. 5, pp. 486-494 (1986)

Dalziel, C.F. and T.H. Mansfield
EFFECT OF FREQUENCY ON PERCEPTION CURRENTS
Trans. AIEE, Vol. 69, Pt. II, pp. 1162-1168 (1950)

Dalziel, C.F. and W.R. Lee
LETHAL ELECTRIC CURRENTS
IEEE Spectrum, Vol. 6, pp. 44-50 (1969)

Deno, D.W.
CALCULATING ELECTROSTATIC EFFECTS OF OVERHEAD TRANSMISSION LINES
IEEE Trans. Power App. Syst., Vol. 93, pp. 1458-1471 (1974)

Gandhi, O.P. and I. Chatterjee
RADIO-FREQUENCY HAZARDS IN THE VLF TO MF BAND
Proc. IEEE, Vol. 70, No. 12, pp. 1462-1464 (1982)

Gandhi, O.P., I. Chatterjee, D. Wu, J.A. D'Andrea, and K. Sakamoto
VERY LOW FREQUENCY (VLF) HAZARD STUDY
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report on Contract F33615-83-R-0613, submitted by University of Utah, Salt Lake City, UT (31 January 1985a)

Gandhi, O.P., I. Chatterjee, D. Wu, and Y.-G. Gu
LIKELIHOOD OF HIGH RATES ENERGY DEPOSITION IN THE HUMAN LEGS AT THE ANSI RECOMMENDED 3-30-MHZ RF SAFETY LEVELS
Proc. IEEE, Vol. 73, No. 6, pp. 1145-1147 (1985b)

Guy, A.W.
HAZARDS OF VLF ELECTROMAGNETIC FIELDS
Advisory Group for Aerospace Research and Development (AGARD) Lecture Series No. 138, THE IMPACT OF PROPOSED RADIO FREQUENCY RADIATION STANDARDS ON MILITARY OPERATIONS, pp. 9-1 to 9-20 (1985)

Guy, A.W. and C.-K. Chou
VERY LOW FREQUENCY HAZARD STUDY
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report on Contract F33615-83-C-0625, submitted by University of Washington, Seattle WA (May 1985)

Rogers, S.J.
RADIOFREQUENCY BURN HAZARDS IN THE MF/HF BAND
In J.C. Mitchell (ed.), USAFSAM AEROMEDICAL REVIEW 3-81, PROCEEDINGS OF A WORKSHOP ON THE PROTECTION OF PERSONNEL AGAINST RFEM, pp. 76-89 (1981)

3.2 MUTAGENESIS, CYTOGENETIC EFFECTS, AND CARCINOGENESIS

Various studies have been carried out on a variety of plants and animals to determine whether RFR induces mutagenic or cytogenetic effects. The fruit fly (Drosophila melanogaster) and several types of microorganisms have been used in tests for such RFR effects because of short life spans that permit the study of many generations, the availability of well-characterized mutation-prone strains in large numbers, and the existence of baseline data on such strains for various non-RFR mutagenic agents. Studies of possible mutagenic effects of RFR in mammals and selected mammalian tissues have been conducted as well.

Also discussed in this section are investigations for possible cancer induction in animals by RFR because carcinogenesis and mutagenesis are statistically correlated, i.e., agents found to be mutagenic for the bacterium Salmonella typhimurium are also likely to be carcinogenic (Ames et al., 1975; Ames, 1979).

3.2.1 MICROORGANISMS AND FRUIT FLIES

Blackman et al. (1976) grew cultures of bacterium Escherichia coli WWU strain for 90 min at 37 deg C to attain the logarithmic growth phase. The WWU strain was used because it needs thymidine, uridine, proline, arginine, methionine, and tryptophan in the nutrient medium for growth. WWU-strain cells that are able to grow in the absence of any of these constituents are mutants.

In this study, standardized concentrations of cultures in log phase were deposited for further growth on plates that had either of two media, one containing arginine and the other lacking it. Such plates were placed on a stand in the temperature-controlled anechoic chamber of the larger of two systems described in Elder and Ali (1975) and exposed from above at 35 deg C to 1.70-GHz or 2.45-GHz CW RFR for durations ranging from 3 to 4 hours. The durations encompassed at least one full DNA replication cycle, to ensure that each part of the genome was replicated, and the total survival rate and concentrations of mutant cells were assayed before and after RFR exposure. Thus, RFR-induced mutation of WWU cells to arginine independence was the only variable tested.

Because of limitations in 1.70-GHz source power, the exposures to that frequency were done in the near field, at 88 V/m. The equivalent free-space power density was 2.05 mW/sq cm and the SAR, estimated from probe measurements, was 3 W/kg. The exposures to 2.45-GHz RFR were at far-field power densities of 10 and 50 mW/sq cm. By calorimetry, the SARs were 15 and 70 W/kg. Controls were cultures wrapped in aluminum foil for shielding and placed on the stand with the cultures to be exposed.

Cultures of E. coli WWU were exposed to ultraviolet (254-nm) light (UV), a known mutagen, at doses up to 110 J/sq m and were assayed for survival and arginine-mutation induction as a positive control. The background mutation rate was determined in separate experiments in which

cultures were maintained at 35 deg C in an incubator, to simulate the temperature conditions during RFR exposure. A semilog plot of the concentration of mutations vs UV dose showed an increase from 100 (per 100 million cells) at 0 J/sq m to about 500 at 20 J/sq m, but only a slight decrease in survival percentage over that dose range. (Both endpoints decreased exponentially with dose at higher doses.)

The growth in total cell populations in the arginine-containing and arginine-lacking media during RFR- and sham-exposure were expressed as mean numbers of cell doublings relative to the initial populations, and were compared by Student's 2-tailed t-test. Also compared were the concentrations of arginine-independent mutants in these populations. The differences in both endpoints between cultures exposed to 1.7-GHz RFR at 88 V/m (3 W/kg) and sham-exposed were nonsignificant ($p>0.05$). This was also true for cultures exposed to 2.45-GHz RFR at 10 mW/sq cm (15 W/kg) for 3.5 hr or at 50 mW/sq cm (70 W/kg) for 3.2 hr. However, exposure of cultures to 2.45-GHz RFR at 50 mW/sq cm (70 W/kg) for 4.0 hr yielded 3.5 +/- 0.2 (SD) cell doublings vs 2.7 +/- 0.2 for the sham-exposed cultures (3 samples each), a significant increase ($p<0.01$); the respective concentrations of mutant cells (per 100 million cells) were 19 +/- 5 and 29 +/- 0.5, a significant decrease ($p<0.05$).

The authors noted that cultures grown at 35 deg C for 3.5 hr exhibited increases in total populations but decreases in relative numbers of mutant cells and that cultures exposed to RFR under the same temperature conditions in a previous study (Blackman et al., 1975, discussed in Section 3.8.3) showed a slight increase in temperature that brought them closer to their optimal growth temperature. Therefore, they regarded the significant growth increase and reduction in relative numbers of mutants above as a solely thermal effect.

Dutta et al. (1979) sought possible mutagenic effects of RFR exposure in strains TA1535, TA100, and TA98 of bacterium Salmonella typhimurium, prokaryotes (not possessing true nuclei) frequently used for testing of base-pair substitutions (TA1535 and TA100) and frame-shift alterations (TA98), and in the diploid strain D4 of yeast Saccharomyces cerevisiae, a primitive eukaryote (possessing a true nucleus) having intermediate genome complexity between prokaryotic and mammalian eukaryotic cells and often used to test for genetic conversion and mitotic recombination.

Cultures of Salmonella in log phase were exposed for 90 min to 2.45-GHz CW RFR at 20 mW/sq cm (40 W/kg) in the Elder and Ali (1975) anechoic chamber at 37.0 +/- 0.5 deg C or to several frequencies of pulsed RFR (1-microsecond pulses at 1000 pps) in the range 8.5-9.6 GHz at average power densities in the range 1-45 mW/sq cm within a similar chamber at 35.0 +/- 0.5 deg C. The SARs for 2.45 GHz were determined as described by Allis et al. (1977), but whether SAR determinations were made for 8.5-9.6 GHz was not discussed. Also exposed to the same levels of CW or pulsed RFR were cultures of the yeast in log phase, but for 120 min at 30 or 29 deg C, respectively.

Results were expressed in terms of the genetic-activity index (GAI),

defined as the ratio of the frequency of genetic events in the treated population to the frequency in the control population, an index derived from published positive-control experiments with the chemical mutagen ethyl methanesulfonate. Based on previous observations, the authors noted that: values of GAI not exceeding unity signify no RFR-induced mutagenesis, values between 1.0 and 2.0 are in the normal fluctuation range, values between 2.0 and 3.0 are "suspect," and values exceeding 3.0 definitely indicate RFR-induced mutagenesis.

The exposure of the yeast to 2.45-GHz RFR at 20 mW/sq cm (40 W/kg) for 120 min yielded mean frequencies of genetic events that differed little from those for the control cultures (1.1 vs 1.0 conversions to adenine independence per 100 thousand survivors for a GAI of 1.1, and 2.4 vs 1.6 conversions to tryptophan independence per 100 thousand survivors for a GAI of 1.5, both within the normal fluctuation range.) Exposure of Salmonella at this RFR level for 90 min also yielded essentially the same frequencies as control cultures (10 vs 11 conversions to histidine independence per 100 million survivors).

In Table 2 of the paper, results for exposure of the yeast to 9.0-GHz pulsed RFR at 1-45 mW/sq cm were presented, which showed GAIs for conversion to adenine independence that varied nonmonotonically with power density, with a range from 0.61 at 30 mW/sq cm to 1.17 at 45 mW/sq cm. Similarly, variation of conversion to tryptophan independence was nonmonotonic, with GAIs that ranged from 0.49 at 35 mW/sq cm to 1.77 at 45 mW/sq cm. The survival rates also varied nonmonotonically, with a range from 78% at 8.9 mW/sq cm to 100% at 5.0 and 15 mW/sq cm. However, there was a decreasing trend with increasing power density, related to large rises in culture temperature (at least 12 deg C at 45 mW/sq cm).

Results for exposure of the yeast to pulsed RFR of frequencies from 8.5 to 9.6 GHz at 1, 5, and 45 mW/sq cm were presented in Table 3. All GAIs were less than 2.0 except for 9.4 GHz at 45 mW/sq cm, for which the GAI was 2.17 for conversion to adenine independence, but only 0.97 for conversion to tryptophan independence. (Noteworthy, however, were the minor differences between the 9.0-GHz GAIs in Table 3 and the GAIs in Table 2 at the three corresponding power densities.)

Table 4 of the paper showed results for exposure of strain TA100 of Salmonella to pulsed 8.5-9.6 GHz RFR at 10 and 45 mW/sq cm. At both levels, the GAIs for base-pair substitutions varied nonmonotonically with frequency, ranging from 0.61 for 9.6 GHz to 1.38 for 8.8 GHz at 10 mW/sq cm, and from 0.43 for 9.0 GHz to 1.91 for 8.8 GHz at 45 mW/sq cm, but survival rate at each frequency was lower at 45 than 10 mW/sq cm.

In Table 5, the GAI-vs-frequency results for strain TA1535 (another base-pair-substitution mutant) were shown for 10 mW/sq cm; they ranged from 0.87 for 9.6 GHz to 2.57 for 9.0 GHz. Table 6 showed the GAI-vs-frequency results for strain TA98 (the frame-shift mutant) at 10 mW/sq cm; these ranged from 0.42 for 9.4 GHz to 1.91 for 9.0 GHz. (No results for either of these two strains at 45 mW/sq cm were presented.)

The authors concluded that exposure of cultures of S. cerevisiae and S. typhimurium to CW or pulsed RFR at power densities of 30 mW/sq cm or higher diminished their viability but did not reliably induce genetic changes. However, they did not present any statistical treatment of the results. Also, it was not clear whether the few "suspect" results (GAI between 2.0 and 3.0) were considered positive or negative.

Dardalhon et al. (1979) used two haploid strains (N123 and 211-1aM) and a diploid strain (D5 of Zimmermann) of yeast S. cerevisiae to determine the effects of temperature and RFR on survival and on the induction of mitotic recombination or cytoplasmic "petite" mutations. The haploid strains were genetically deficient in synthesizing certain amino acids and were of opposite mating types that form stable heterozygotic diploid cells. These strains were used to test for the effects of RFR on zygote formation. The D5 diploid strain is heteroallelic for the locus ade 2, and the two alleles can be distinguished by color, i.e., treatment by a mutagen causes a color change that permits detection of genetic effects, including induction of mitotic recombination. Detection of cytoplasmic "petite" mutations was done by the tetrazolium overlay technique (Ogur et al., 1957).

For exposure, 80 million cells in saline suspension were collected with a 0.45-micron millipore-filter disc 2.6 cm in diameter, which was placed on the surface of agar about 1 cm thick within an open petri dish 5.5 cm in diameter. The petri dish in turn was mounted on a foamed-polystyrene block. Exposures were done from above the petri dish for 180 or 330 min at 20 deg C to 70.5- or 73-GHz CW RFR at 2 or 10 mm from the face of a horn terminating a waveguide, both distances within the near field of the horn. The authors noted that the agar layer strongly absorbed the RFR transmitted through the filter, thus ensuring absence of standing waves within the sample.

The power densities were 6, 15, and 60 mW/sq cm. Not clear, however, was the following statement: "Power density was measured either with a Narda powermeter, or was calculated from power levels measured at the waveguide outlet with a matched load." Since the frequency coverage of Narda radiation monitors does not extend to the 70-GHz region, the power densities presumably were not actually measured but were calculated from values of forward and reflected powers measured with Narda power meters connected to a bidirectional coupler in the waveguide. In addition, the values cited above were those at the interface between the waveguide and the horn (or load), and the levels at the 2-mm and 10-mm sites were not given. For controls, cultures were sham-exposed. Other cultures were placed in a thermostatically controlled chamber at 30, 37, 42, 47, or 52 deg C for 330 min.

To estimate RFR-induced temperature increases, water evaporation from solidified agar (2%) was measured for exposures to 70.5-GHz RFR at 60 mW/sq cm and a baseline temperature of 20 deg C for several durations up to 180 min, and the results were compared with those from conventional heating at 20, 30, and 37 deg C for the same durations. For the latter treatments, the graphs of agar mass vs time were linear, with slopes

that were successively more negative (higher water-loss rates) with increasing temperature. The corresponding graph for RFR exposure was also linear, with a negative slope between those for heating at 30 and 20 deg C but closer to the slope for the latter. From these results, the authors concluded that exposure to RFR at a baseline temperature of 20 deg C increased sample temperature by no more than 2-3 deg C. It should be noted, however, that the RFR exposures of the agar were done at the 10-mm site, and therefore the specimen-temperature increases from exposure at the 2-mm site were most likely larger.

The ratio of cell survival of treated samples to that of controls was plotted vs duration for exposure of the D5 diploid strain at the 10-mm site to 70.5-GHz or 73-GHz RFR at 15 or 60 mW/sq cm for up to 180 min. For all four exposure conditions, these relative survival curves showed ratios that changed little from unity with time.

As noted previously, the responses of the D5 strain to a mutagenic agent can be detected by a color change. With this technique, the percentages of altered colonies were found to be "practically nil" after exposures under the four conditions above, indicating that the RFR had no effect on nuclear DNA. (The graphs showed 0.5% or less for exposed and control samples.) The results were also negative for induction of cytoplasmic "petite" mutations, an indication that the RFR had no adverse effects on mitochondrial DNA. (Results for exposures at the 2-mm site were not presented.) Conventional heating at 30, 42, and 47 deg C for the same durations also had no effect on relative survival ratios, percentages of altered colonies, or "petite" mutations. However, marked decreases in percentages of survival and increases in percentages of altered colonies and "petite" mutations were obtained at 52 deg C.

The two genetically deficient haploid strains of S. cerevisiae were tested for zygote formation by mixing suspensions containing 100 million cells/ml of each in equal volumes, depositing 0.05-ml samples of the mixture on millipore filters, setting each filter on a solid complete-growth medium in an open petri dish, placing the sample at the 2-mm or 10-mm site, and exposing the sample to 70.5-GHz RFR for 330 min at 6, 15, or 60 mW/sq cm (values at the waveguide-horn interface, as noted above). Controls were sham-exposed. Following treatment, the samples were grown in a medium containing no amino acids, thus allowing only growth of zygotes and heterozygotic diploid cells in which the genetic deficiencies of one strain were complemented by normal alleles of the other strain.

The results at each power density for both exposure sites were graphed as ratios of zygote formation for the sample treated to zygote formation for the control sample. For the 2-mm site, these ratios were 1, 1.75, and 3.1 respectively for 6, 15, and 60 mW/sq cm. For the 10-mm site, the corresponding ratios were about 1.2, 1.2, and 1.4. The ratios were much larger for samples conventionally heated for 330 min at 20, 30, and 37 deg C, about 1, 20, and 57, respectively. From these results and those on culture-temperature increases discussed above, the authors surmised that RFR exposure at 60 mW/sq cm would be equivalent to heat

treatment that increases culture temperature by no more than 3 deg C, and that culture temperature would increase by less than 0.5 deg C from exposure at 10 mW/sq cm.

Dardalhon et al. (1979) concluded that exposure to millimeter waves under the stated conditions does not induce lesions or genetic effects in cellular DNA of S. cerevisiae, whereas intense conventional heating does. However, statistical treatment of the results would have provided more confidence in the quantitative aspects of their findings.

Regarding the power densities at the 2-mm and 10-mm sites, values could not be estimated with accuracy because the dimensions of the horn used were not given. However, although both sites were within the near field, the nearer site was at a distance of only about a half-wavelength at 70 GHz, so the power densities at that site were probably comparable to the values at the waveguide-horn interface. Uncertainties of this kind would be more important if positive findings had been obtained.

Dardalhon et al. (1981) performed a similar study on various strains of E. coli and S. cerevisiae, but at 9.4 and 17 GHz (wavelengths 3.19 and 1.76 cm) as well as 70-75 GHz. For exposures to 70-75 GHz, the samples were placed at the 2-mm site. A horn was also used for exposures to 9.4 GHz, but the exposure sites were 5 mm or 3 cm from the horn; these two exposure sites were also used for 17 GHz, but the antenna was the open end of a waveguide.

Precision variable attenuators were used to obtain any power density in the range 1-60 mW/sq cm for 70-75 GHz, or 1-50 mW/sq cm for the other two frequencies. Not clear is whether the power densities cited were the values at the respective exposure planes or at the waveguide output in each case as in Dardalhon et al. (1979). However, the authors did determine the SARs in samples at the exposure sites by using a property noted in the latter study that zygote formation in S. cerevisiae is very sensitive to changes in temperature. For 17 GHz, they exposed samples at the 5-mm site to 50 mW/sq cm (measured at the waveguide outlet) and derived an SAR of 28 W/kg from the resulting cooling curves (Allis et al., 1977). For 9.4 GHz, the SAR at the 5-mm site for exposure to 60 mW/sq cm (presumably at the waveguide-horn interface) was 23 W/kg. (The SAR at the 3-cm site was not given for either frequency.) For 70-75 GHz at 60 mW/sq cm, the SAR at the 2-mm site was 9 W/kg. Most of the exposures were for 30 min. Control samples were sham-exposed.

Six E. coli strains were used. Four were deficient in DNA repair (two rec-negative strains, one uvr-negative strain, one double-mutant rec-negative/uvr-negative strain). The fifth was a DNA-repair-proficient strain (a wild-type rec-positive/uvr-positive strain that corresponded to the deficient double-mutant). The sixth was a mutant strain (trp-negative) that requires tryptophan for growth, to ascertain whether RFR can induce reversions to tryptophan independence.

The fractional survival rates of the four DNA-repair-deficient strains and the DNA-repair-proficient wild strain of E. coli after exposure to

the various frequencies and SARs indicated above were tabulated. Most values were between 0.90 and 1.0, with a few larger than 1.0 (maximum 1.10 for 9.4 GHz at 23 W/kg) and a few others less than 0.90 (minimum 0.80 for 74 GHz at 9 W/kg). The authors gave no statistical treatment, but stated: "Taking into account a mean standard error of 15%, including variations from experiment to experiment, millimeter and centimeter waves in this frequency range do not have any appreciable effects on survival even in the repair deficient mutants." They also noted that survival fractions of wild-type and mutant cells decreased strikingly after conventional heating for 30 or 60 min at temperatures above 50 deg C, with the mutants more sensitive than the wild-type cells.

For trp-negative E. coli, the ratio of number of mutations to tryptophan independence induced by 30-min exposures to 70, 71, 72, 73, 74, and 75 GHz (9 W/kg) to the number of spontaneous mutations was plotted vs RFR frequency (without error bars). The values varied nonmonotonically between 0.5 and 1.0. For exposures to 17 GHz at the 3-cm site (no SAR given), the mutation ratio varied with exposure duration from about unity for 30 min, to a minimum of 0.2 for 1 hr, to unity for 2 hr, and to 1.5 for 20 hr. Again, no error bars were given, but the authors stated: "The experimental values fluctuate with a standard error of +/- 1.25, and thus do not differ statistically significant from the spontaneous background. Thus, it can be concluded that under these conditions microwaves do not induce mutagenic effects in bacteria."

The [illegible] cerevisiae used were the haploid wild-type strain N123 and the DNA repair deficient mutant strain S 205' Ni 49 for DNA effects, the diploid strain D5 for detection of genetic alterations, and diploid D5 and N1 strains for sporulation effects. After sham-exposure, the survival fraction of wild type N123 was 0.81. For exposure (30 min) to 9 GHz (2' W/kg), the survival fraction was 0.96. For exposures to 17 GHz at the 5 mm site (28 W/kg) and the 3 cm site (SAR not given), the fractions were respectively [illegible] and 0.89. For exposures to millimeter waves (9 W/kg), the survival fraction varied nonmonotonically with frequency from 0.8[illegible] at 17 GHz to [illegible] for 75 GHz. The differences among the values were stated to be nonsignificant. As the percentages of cytoplasmic petite mutations in N123 after RFR exposure did not differ significantly from the percentage of spontaneous mutations

Results of RFR and sham exposure of the diploid strains [illegible] cerevisiae were presented as mean numbers per [illegible] and SEs of reversions to the wild type. Rejection of exposure data [illegible] and sham exposure [illegible] were treated [illegible] RFR exposures were treated [illegible] treatments are [illegible]

Exposure [illegible] with a [illegible] site [illegible] W/kg [illegible] site [illegible]

or of genetically altered colonies (including mitotic crossovers), but conventional heat treatments at 47 deg C for 24 hr or at 52 deg C for 2 hr markedly decreased the relative survival and increased the numbers of petite mutations and altered colonies.

To determine the effects of RFR on sporulation, samples of diploid strain D5 were sham-exposed or exposed for 48 hr during sporulation to 9.4 GHz (23 W/kg) or 17 GHz (28 W/kg). The sporulation efficiencies for the three treatments did not differ significantly. The diploid strain ND was similarly treated but for 72 hr during meiosis, to ascertain the effects of the RFR on segregation of "ade" and "his" genes. Again, the differences among treatments were not significant. (The means and SEs were tabulated, but statistical analysis of the data was not given.)

As for the previous study, the lack of statistical treatment of the results diminishes confidence in the findings.

Anderstam et al. (1983) also investigated whether RFR is mutagenic for E. coli and S. typhimurium (in a total of 11 strains). The exposure systems used were described in Hamnerius (1983). The RFR frequencies selected were 27.12 MHz and 2.45 GHz because of their wide occupational use. The 27.12 MHz source was CW, but as noted by Hamnerius, the 2.45-GHz source was a magnetron, so the RFR was amplitude-modulated at twice the power-line frequency (100 Hz) rather than true CW. Two types of 3.1-GHz pulsed magnetrons were used to compare the possible effects of pulsed RFR and 2.45-GHz "CW" RFR; one type produced 2-microsecond pulses (3.07 GHz) and the other, 1-microsecond pulses (3.10 GHz), both at 500 pps and 200 W mean power.

To obtain adequate biological sensitivity, most sample volumes were 10 ml each. Since most media contain substances that can be autooxidized in the presence of metal ions, possibly forming toxic components, sample containers were made of polytetrafluoroethylene (PTFE) because tests showed that the metal ion content of PTFE is very low and because the containers could be sterilized readily in an autoclave.

For exposure to a 27.12-MHz electric field, the PFTE container used was rectangular with walls 1 mm thick, dimensions 5.4 x 3.2 cm, and internal sample thickness 5 mm. It was placed inside a larger container made of polymethylmethacrylate (PMMA) through which flowed thermostatically controlled water. By this means, sample temperature during exposure was held to within +/- 0.1 deg C of that of an unexposed sample. The larger container was inserted between 20-cm square vertical aluminum plates, providing a horizontal field spaced 6 cm apart, with a 2-cm air gap between each side of the container. With this geometry the electric field was calculated and the SAR of the sample was determined from measured dielectric properties of the sample at that frequency. With 1-kW rms applied to the plates, the field between them in air was [illegible] the field in the sample was 1.4 kV/m, and the SARs of [illegible] were [illegible] W/kg, respectively.

The 2.45-GHz magnetron [illegible] was [illegible] with the [illegible]

in diameter and spaced 11 cm apart. Exposures were done either with the sample in a glass tube 6.5 cm in length and inner radius of 7 mm (using an outer cylindrical PMMA jacket for water cooling) and axis of the tube parallel to the magnetic field, or with 10 ml of sample within a groove cut in a PFTE disk at radius 7.2 cm and disk plane perpendicular to the magnetic field. The SARs for both species of bacterium at 20 A/m for the disk and tubular containers were respectively 20 W/kg and less than 0.15 W/kg.

The rectangular PFTE container (with PMMA outer container) described above was also used for exposures to 2.45-GHz (CW) and 3.1-GHz (pulsed) RFR. However, the container was placed 40 cm from a horn (far field). Thermocouple measurements of temperature were made at 15 locations on the container immediately before and after exposure to 2.45 GHz at 900 mW/sq cm for 30 seconds or 3.1-GHz at 290 mW/sq cm (average) for 60 seconds. The cooling curves were used to determine the corresponding SAR at each location, from which the local value of electric field was calculated and normalized to the mean for all locations. These normalized electric-field values ranged from 0.70 to 1.26 for 2.45 GHz and 0.88 to 1.08 for 3.1 GHz. Thus, the variation of power density over the sample area was less than +/- 3 dB for either frequency. At each frequency, the mean SAR for 200 mW/sq cm was about 100 W/kg.

For the study of forward mutations, three strains of S. typhimurium that were sensitive to arabinose, and two strains of E. coli, one dependent on streptomycin and the other sensitive to rifampicin, were used. Back mutations were investigated in two histidine-dependent strains of S. typhimurium, two tryptophan-dependent strains of E. coli, and one strain of E. coli dependent on tyrosine. Prophage induction was investigated in two strains of E. coli; a streptomycin-resistant strain was used as an indicator. Exposures to each type of RFR at the SARs above were for various durations in the range 1-7 hr. In most experiments, air was bubbled through the cell suspensions during exposure for stirring. Also investigated were the combined effects of RFR and ultraviolet light (UV) at a dose rate of 0.033 W/sq m given before or after RFR exposure.

The various treatments of each strain of the two species of bacterium were tabulated, as were the results of statistical treatment of the data by the methods described in Ehrenberg et al. (1983), in which criteria for elimination of outliers and for significance of negative as well as positive results were given. The large numbers of specific results for the 11 strains of bacteria, four types of RFR treatment, and combined UV and RFR treatment preclude their presentation here in detail; instead, the significant findings are summarized qualitatively.

For some RFR treatments, some strains exhibited higher growth and others lower growth than their respective controls; many of these changes were statistically nonsignificant ($p>0.05$), but the overall trend was toward RFR induced increase in growth. The authors stated: "The possibility that the observed growth stimulation could be due to temperature change was investigated in special studies. Temperature

variations within the sample during exposure were estimated to be +/- 0.3 deg C when the cell suspension was not stirred. The variations were considerably reduced in stirred suspensions...Stirring, brought about by air bubbling, did not change the degree of stimulation observed after exposure of unstirred specimens. Changes of temperature in unexposed samples by 0.5 deg C certainly provoked changes of the growth rate, but these changes were smaller than observed after microwave exposure."

The RFR-induced differences (both increases and decreases) in mutant counts were mostly nonsignificant. The authors stated: "The mutant counts were much less affected than bacterium growth, by electromagnetic fields. Different variance estimates of data for 2.45 GHz and 3.07 GHz fields indicate the absence of variations, except for a slightly significant difference between the two frequencies, in agreement with the difference between the pooled mean values. Since these strains were not represented in the same way in studies of the two radiation qualities, this effect is most probably fortuitous, however, and it is questionable whether mutant counts were affected at all in the regular mutation tests.

"It is possible that microwave exposure provoked, in some experiments, an increase of the mutant counts induced by UV light and, especially, that a certain prophage induction may have occurred. [Experiment 6 yielded the most significant ($p<0.001$) change.] It has been impossible, however, to identify the conditions under which the strong prophage induction of experiment 6 was obtained. Although no experimental errors are indicated we are therefore inclined to consider this positive value an 'outlier'."

Pay et al. (1972) exposed three groups of five Oregon-R, wild-type male Drosophila for 45 min to 2.45-GHz RFR, each group within an acrylic capsule at a distance of 18 cm from a standard-gain horn (in the near field) in an anechoic chamber. One group each was exposed at 2.1, 2.75, and 3.0 kW forward power. The mean power densities, calculated from measurements at 200 cm (far-field), did not exceed 4.6, 5.9, and 6.5 W/sq cm, respectively. The exposures were done within 24 hr after eclosion. A capsule of flies was sham-exposed as controls for each RFR level. To exercise control over generation times, two different growth temperatures were used prior to exposure; the flies for the 2.75- and 3.0-kW groups were grown at 22.5 deg C and those for the 2.1-kW group at 21.0 deg C. Subsequent generations derived from these exposure groups were grown at the same respective temperatures.

Within 30 min after exposure, each male was placed in a vial with two virgin females of the Muller-5 type. After this initial mating, each male was placed in a new vial with two new virgin Muller-5 females every 24 hr for 15 days after exposure, thereby obtaining 15 "Standard-Muller 5-Cross (Basc)" broods from each wild-type male fly. On day 8 after each mating, the Muller-5 females were removed and the number of days to emergence of the first adult flies in each brood was recorded as the generation time. All F1 (first generation) broods were counted and sexed on day 17 of growth (before second generation eclosion), if no

adult F1 flies were present on that day, the growth stage was noted.

Forty-five F1 pairs (male-female) from exposed males and 15 pairs from sham-exposed males were selected at random each day from the 2.75- and 3.0-kW groups, and each pair was placed in a new vial to produce an F2 generation. The F2 generations were examined on day 17 for wild-type males, since their presence in F2 would rule out the possibility of sex-linked lethal recessive mutagenesis on the X-chromosome of parent (P1) males exposed to RFR, and since such a recessive mutation would cause lethality in F2 hemizygous (having only one of a pair of genes for a specific trait) wild-type males.

All the P1 males in the control, 2.1-, and 3.0-kW groups survived for use in the brood studies, but 2 of the 5 P1 males of the 2.75-kW group died. The F1 flies from the 2.75- and 3.0-kW groups (both grown at 22.5 deg C) had mean generation times of 13.71 and 13.58 days, respectively; the means for the F1 flies from the 2.1-kW group and its control group (both grown at 21.0 deg C) were respectively 14.61 and 14.64 days. The authors ascribed the 1-day-longer generation time for the latter two groups to the difference in growth temperature, not to RFR exposure.

Brood-size variations were observed among the daily broods from each exposure and control group, so the daily results from each exposure level were pooled, divided by the number of successful cultures, and normalized to the day-1 means for the corresponding control groups. The resulting normalized average F1 brood size on each day of serial mating was presented graphically for each exposure group and its control group. On corresponding mating days, the differences in mean brood size were not significant. Relative infertility was observed between days 5 and 7, but in control as well as RFR groups.

The authors noted that since only the heterozygous F1 females would carry an exposed X-chromosome from the male parent, the nonsignificant differences in brood size above may not be an adequate assessment for detrimental effects. However, comparisons of ratios of F1 females to total F1 flies, which should reveal whether RFR had damaged the genome of the male parents, yielded no significant differences. In addition, the results for the F2 generations yielded mutations not exceeding 1%.

Hamnerius et al. (1979) exposed embryos of D. melanogaster to 2.45 GHz amplitude-modulated RFR. The embryos studied were 1-2 days old and of a sex-linked, genetically unstable stock in which eye color is light yellow (zeste). The mutation sought was somatic, in which a shift in eye pigmentation results in eye sectors with normal red pigmentation clearly visible against the yellow background, a mutation that occurs at an early stage of eye development.

For exposure, embryos were immersed in 10 ml of water within a Teflon container, which was placed inside a larger Plexiglas container through which thermostatically controlled water at 24.5 +/- 0.2 deg C flowed. The larger container was placed 40 cm from a horn (about the start of the far field region) used to terminate a waveguide. The RFR level at

this location was measured with a power-density meter. SAR calibration was done by measuring the temperature rise in a biological sample due to a 30-second exposure at 900 mW/sq cm with no water flowing through the larger container; the result was 0.5 W/kg per mW/sq cm.

Embryo exposures were at 100 W/kg (about 200 mW/sq cm) for 6 hr. For controls, embryos were similarly treated except for exposure. Following treatment, the embryos were transferred to vials that contained standard medium and were maintained at 25 deg C and 75% relative humidity. The survival rate of the flies was determined from the number of male flies hatching from treated embryos, and the percentage of flies having red sectors constituted the mutation frequency. Mean survival rates for the exposed and control flies were 83% and 91%, respectively, a difference that was nonsignificant ($p>0.05$). There were 4 mutations in 7512 RFR-exposed male flies (0.05%) and 2 mutations in 3344 control male flies (0.06%), a nonsignificant difference.

Hamnerius et al. (1979) also exposed embryos to X-rays as a positive control, and found that 1000 rad yielded 29 mutations in 1053 males (2.75%). This result led them to conclude that with a sample size of 7512 males, it would be possible to detect this mutagenic effect at 50 rad ($p=0.05$). The authors also indicated that EMS, a chemical mutagen of the alkylating type, yielded 444 mutations in 4859 males (9.14%) at 9.75 mM, but they made no further comparison.

Confounding parameters, especially temperature rise, appear to have been controlled adequately in this study, so the finding of no RFR-induced mutagenic effect is highly credible.

Hamnerius et al (1985), in a study supplementary to Anderstam et al (1983) and Hamnerius et al (1979), exposed Salmonella and Drosophila to 2.45 GHz amplitude modulated RFR, 3.10 GHz pulsed RFR, or 27.12 MHz CW magnetic field in the systems described by Hamnerius (1983). Drosophila were also exposed to these types of RFR and to the 27.12 MHz CW electric field as well. The exposure parameters were given in Table 1 of the paper, adapted and shown below as Table 18. The levels for Salmonella were slightly different than those cited in Anderstam et al (1983).

TABLE 18: EXPOSURE PARAMETERS

EXPOSURE	SAR (W/kg)	INTENSITY	DUR. (hr)	TEMP. (deg C)
Salmonella				
27.12-MHz magnetic	<0.15	21 A/m	6	37.0
27.12-MHz magnetic	22	21 A/m	2.5	25.0
2.45-GHz modulated	130	--	5.7	37.0
3.10-GHz pulsed	90	--	6	37.0
Drosophila				
27.12-MHz magnetic	<0.05	12 A/m	6	25.0
27.12-MHz electric	0.3	137 V/m	6	25.0
2.45-GHz modulated	110	--	6	25.0
3.10-GHz pulsed	60	--	6	25.0

In the Ames test (Ames et al., 1975), chemical mutagens are tested on petri plates with specially constructed mutant strains of Salmonella typhimurium selected for sensitivity and specificity to reversion from dependence on histidine to independence. Hamnerius et al. (1985) used a slight modification of this test.

Strains TA98, TA100, TA1535, and TA1537, derived from the LT2 parent strain, were grown in AM3 nutrient broth. (The first three were also studied by Dutta et al., 1979.) Exponentially growing cultures were diluted appropriately and each was divided into two parts; one part was exposed (10-ml samples) as noted above and the other served as an unexposed control. After treatment, 0.1-ml samples were spread on minimal glucose agar plates and incubated at 37 deg C for 48 hr in darkness before scoring for mutation frequency. (Since the bacteria were growing during RFR exposure, their growth on the plates was not necessary to determine mutation induction, so the trace of histidine in minimal medium was omitted.)

To test for RFR induced cell division rate or toxicity, culture samples were diluted by a factor of one million with 0.9% saline, spread on rich agar plates, and incubated at 37 deg C for 24 hr before scoring for concentrations of viable cells. Usually 10 plates (a minimum and some times 30) were used in each experiment. At least three tests per strain and treatment were performed (except for 27.12 MHz magnetic exposure of TA100 at 22 W/kg, tested in e

To establish that this modified Ames test is valid for mutagen testing, cultures were tested with methyl methanesulfate (MMS), a direct mutagen that primarily produces base substitutions during replication of the DNA chain. Exponentially growing cultures of all four strains were treated with either 0.1% or 0.2% MMS for 6 hr, after which the MMS was removed by centrifugation, the cells were resuspended in 0.9% saline to stop further mutagenic action, and were spread on minimal salt agar

plates. This positive-control experiment showed that TA100, a strain sensitive to base substitutions, exhibited fivefold to sixfold higher reversions than untreated controls, but that TA1535, a strain less sensitive to base substitutions, had only 30% higher reversions with 0.02% MMS. In addition, MMS induced no mutation-frequency increases in frameshift strains TA98 and TA1537.

The results for each strain of Salmonella after each treatment were presented in Table 19 (Table 3 of the paper) in terms of total number of reversions counted, mean percentage of mutations relative to controls and its 95% confidence interval (+/- CI), total number of colonies counted, and mean survival percentage relative to controls and its confidence interval, with *, **, and *** respectively representing significance at $p<0.05$, $p<0.01$, and $p<0.001$:

TABLE 19: RESULTS FOR SALMONELLA

TREATMENT & STRAINS	TOTAL REVERSIONS	% MUTATIONS (+/- CI)	TOTAL COLONIES	% SURVIVAL (+/- CI)
27.12-MHz magnetic:				
TA100 (<0.15 W/kg)	3,166	97.0 (3.4)	4,190	116.6 (3.9)***
TA100 (22 W/kg)	4,267	99.6 (3.0)	475	108.0 (9.7)
TA1535 (<0.15 W/kg)	249	101.3 (15.2)	2,966	97.1 (3.6)
TA1537 (<0.15 W/kg)	175	80.6 (13.3)	5,020	119.1 (3.5)***
TA98 (<0.15 W/kg)	714	110.9 (9.1)	4,648	101.8 (3.0)
Pooled (excluding TA100 at 22 W/kg)				109.7 (1.8)***
2.45-GHz modulated:				
TA100	4,516	93.8 (2.8)**	13,345	103.2 (1.8)*
TA1535	382	108.0 (11.6)	5,605	103.6 (2.9)
TA1537	101	90.2 (20.5)	462	106.9 (9.8)
TA98	1,436	103.8 (5.7)	8,266	106.6 (2.3)***
Pooled				104.3 (1.5)***
3.10-GHz pulsed:				
TA100	6,423	102.3 (2.8)	8,149	99.9 (2.2)
TA1535	85	100.2 (21.8)	4,541	121.4 (3.6)***
TA1537	117	95.2 (17.4)	3,165	138.8 (4.8)***
TA98	388	111.4 (12.1)	3,915	101.5 (3.2)
Pooled				110.4 (1.5)***

The results above show that none of the RFR exposures significantly increased the numbers of reversions in Salmonella relative to controls; in fact, the number of reversions for TA100 after exposure to 2.45 GHz was lower than for controls ($p<0.01$). However, significant increases in percentage survival were observed for various exposure conditions. The authors justified pooling the values by noting that the same tendency

grow into a more dense culture during treatment was seen in all strains. They also noticed a tendency for RFR-exposed cells to divide at a higher rate than control cells. A curious point not discussed by the authors was the lower survival rate for TA100 after exposure to the magnetic field at 22 W/kg (108.0%) than at SAR<0.15 W/kg (116.6%).

To determine whether the survival-rate increases were thermally induced by the RFR, the effect of cultivation temperature on growth and survival was ascertained. Each strain of Salmonella was cultivated at 37.0 deg C until the culture density attained was the same as that at the start of RFR exposure. Parts of each culture were then transferred to baths at 36.5 or 37.5 +/- 0.1 deg C and the percentages of survival relative to those for 37.0 deg C were measured after growth for at least six generations. Results were given in Table 20 (Table 4 of the paper):

TABLE 20: SALMONELLA SURVIVAL VERSUS CULTIVATION TEMPERATURE

STRAIN	CULTIVATION TEMPERATURE	TOTAL COLONIES	% SURVIVAL (+/- CI)
TA100	36.5	1,896	86.5 (3.9)***
	37.0	2,194	100.0 (4.2)
	37.5	1,864	96.4 (4.4)
TA1535	36.5	5,512	89.9 (2.4)***
	37.0	6,822	100.0 (2.4)
	37.5	4,653	73.3 (2.1)***
TA1537	36.5	5,027	104.8 (2.9)*
	37.0	5,738	100.0 (2.6)
	37.5	5,082	89.3 (2.5)***
TA98	36.5	1,538	90.2 (4.6)*
	37.0	1,701	100.0 (4.8)
	37.5	1,536	90.5 (4.6)*
Pooled	36.5		96.4 (1.6)**
	37.0		100.0 (1.6)
	37.5		87.1 (1.4)***

The results indicated that the cell concentration during the stationary phase was highest for cells grown at 37.0 deg C, except for TA153[illegible], for which 36.5 deg C yielded highest growth. At this stage, the cultures were no longer in the log phase of growth, but had reached a plateau in number of cells, the stationary phase, which lasted from about [illegible] hr to at least [illegible] hr after the temperature shift.

The authors stated: "The pooled data show that the optimal temperature for growing Salmonella is 37.0 deg C and that the further increases in cell concentration obtained after electromagnetic field exposure was not due to a change in temperature, since this should have lowered the [illegible]

concentration. Consequently, the consistent results obtained after electromagnetic field exposure imply that the increased growth in the exposed cultures is an effect of the electromagnetic fields per se and not secondary to an increase in temperature."

The validity of the point above is unclear because the cultures were supposedly maintained at 37.0 +/- 0.3 deg C during RFR exposure. In addition, the authors stated: "However, thermal effects should not be completely ruled out because, according to Blackman et al. (1975), even slight temperature differences (0.2-0.3 deg C) can affect the growth of Escherichia coli."

For the experiments with Drosophila, an unstable strain believed to be rendered unstable by insertion of a piece of foreign DNA to the right of the white locus was used. This insertion alters gene expression either spontaneously or to a higher degree by mutagen induction, resulting in eye-pigmentation change in males that are observed by the presence of red sectors in the light-yellow eyes.

Embryos were collected on a heavily yeasted surface of an agar plate. At age 12 +/- 4 hr, they were washed, and a 0.025-ml batch containing about 4000 eggs was transferred to 10 ml of water within the exposure container. Samples were then exposed to RFR for 6 hr at 25 deg C with air bubbled through the water to keep the embryos in motion. After exposure, the eggs were transferred to vials that contained standard cornmeal-yeast-syrup-agar medium and were kept at 25 deg C and 75% relative humidity until hatching. Males were screened for the presence of red sectors. Survival was measured by transferring a fixed number of embryos (100 or 200) to vials and counting the number of males hatched in each vial. The results, presented in Table 2 of the paper, adapted and shown as Table 21, were analyzed for homogeneity of survival by the chi-square test and for homogeneity of mutation frequencies by Fisher's exact test.

TABLE 21: RESULTS FOR DROSOPHILA

TREATMENT	MUTATIONS/TOTAL	% MUTATIONS	% SURVIVAL
27.12-MHz magnetic	3/4,989	0.06	101.8
27.12-MHz electric	5/10,817	0.05	94.4
Control	6/6,814	0.09	100.0
3.10-GHz pulsed	2/4,503	0.04	102.3
Control	2/5,025	0.04	100.0
2.45-GHz modulated*	4/7,512	0.05	105.2
Control	2/3,344	0.06	100.0
0.05% MMS	2[illegible]	[illegible]	

*Data from Hamnerius et al. [illegible]

Thus, none of the RFR exposure conditions significantly altered the mutation frequency or the survival rate of Drosophila embryos. The authors noted that the pooled mutation frequency of the controls was 0.07% (16 among 22,288 males), in good agreement with the expected spontaneous rate. The mutation frequency for MMS was 3.5%, a highly significant ($p<0.001$) increase.

3.2.2 MAMMALS AND MAMMALIAN TISSUES

Heller (1970) cultured human peripheral lymphocytes with the mitogen phytohemagglutinin for two days, after which the cultures were exposed for 30 min to 21-MHz pulsed RFR (10-microsecond pulses, 100 pps) at 500 V/cm (50 kV/m) peak-to-peak between electrodes spaced 2 cm apart. (The free-space equivalent average power density was 83 mW/sq cm.) Culture temperature was maintained at 27 deg C during exposure. The cultures were fixed immediately after exposure or after recovery periods of 24 or 36 hr. Standard air-dry films were stained and scored for six types of chromosomal abnormalities (chromosomal breaks, dicentric chromosomes, chromatid breaks, endoreduplication figures, acentric fragments, and polyploid number chromosomes).

The control culture (600 cells scored) had a mean of 0.016 abnormalities per cell. For the culture fixed immediately after exposure (500 cells scored), the mean was 0.036; by chi-square test, the difference was significant ($p=0.02$). The means for the cultures fixed 24 and 36 hr after exposure (respectively 2000 and 850 cells) were 0.056 and 0.077, both significant ($p<0.01$) relative to the control. These results are open to question because no comparisons were made between RFR- and sham-exposed cultures fixed at corresponding times.

Stodolnik-Baranska (1974), as discussed in Section 3.5.1.1, exposed human lymphocyte cultures to 2.95-GHz pulsed RFR at 20 or 7 mW/sq cm average power density for periods ranging from 10 min to 4 hr. Exposure at 20 mW/sq cm for 10 min or longer was reported to produce chromosome aberrations, but not from exposure to 7 mW/sq cm for 4 hr. The author reported a "slight" temperature increase in cultures exposed to 20 mW/sq cm but none in cultures exposed to 7 mW/sq cm. The results suggested that if RFR does cause an increase in chromosome abnormalities, there may be a power-density threshold for the effect.

Chen et al. (1974) grew cultures of Chinese-hamster cells in liquid medium within plastic containers, each of which was placed in a matched open-ended waveguide for exposure to 2.45-GHz CW RFR. The forward and reflected powers were determined with directional couplers. Waveguide ambient temperature was controlled with an electric heater and the temperature was monitored continuously during exposure to RFR. After exposure at specified RFR levels and durations, the cells were allowed to grow for 24 hr, after which they were removed, placed in medium and again allowed to grow for 24 hr. At this point, growth was stopped at the metaphase stage and the cells were fixed, placed on slides, and stained. [illegible] were sham exposed but otherwise treated [illegible]

for each treatment consisted of determining the percentages of seven types of chromosomal aberrations and the percentage of mitotic cells

In one set of experiments, the cultures were initially at 22 deg C (room temperature) and their temperatures at the end of exposure were noted. (Presumably, the temperature of the waveguide was not [illegible] with the heater.) Cultures were exposed at 50 mW/sq cm for [illegible] at the end of which the culture temperature was 37 deg C. Other cultures were then exposed at 85 mW/sq cm for 4, 8, or 12 min, which yielded final temperatures of 37, 40, and 41 deg C. Regarding the results which were presented in Table 2 of the paper, the authors stated "The differences in aberrations observed between the [illegible] and the irradiated samples were not significant at the 5% level." However, some aberrations as marked in Table 2 in the irradiated cells were [illegible] observed to be considerably higher than that in the [illegible] cause concern. Some types of aberrations were not observed at all in the control cells but appeared in the irradiated cells.

To exemplify those remarks, Table 2 shows that 5% of the cells in culture exposed at 85 mW/sq cm for 8 min showed chromatid breaks as compared to 1.8% of the control cells, polyploidy absent in the control was present in 2% of the cells exposed at 85 mW/sq cm for [illegible] and the percentages of chromatid breaks in cultures exposed at [illegible] min or at 85 mW/sq cm for 12 min were both significantly higher and polyploidy was found in 1.2% of the cells exposed at [illegible] min, but was absent in the cells exposed at 85 mW/sq cm for [illegible] Thus, no real dose-dependent effect was evident [illegible]

In a similar set of experiments the cultures were [illegible] at 37 deg C in an incubator. The waveguide temperature was [illegible] during exposure at the exposure levels of [illegible] mW/sq cm for [illegible] min. The final culture temperatures were [illegible] results were [illegible] the cells was [illegible]

large variabilities in the results, little if any credence can be given to the authors' suggestion that exposure to RFR induces chromosomal abnormalities to a significant degree.

Sterling et al. (1971) exposed 24 mature female mice concurrently in [illegible] to 2.2 to 8000 MHz RFR 2 hr/day, 5 days/week, for 35 weeks. The exposure chamber was a section of waveguide 10 ft long and 9.75x4.875 inches in cross section and shorted at both ends, with electric probes placed a quarter wavelength from both ends for input and output. The average input power was 1.2 W, division of this power level by the cross-sectional area yielded 49 mW/sq cm, the level indicated by the authors. An aluminum cage, divided into an array of 4x3 compartments, was inserted transversely at the center of the waveguide to restrain the mice during exposure; the mice were placed in the compartments on a random basis. Noted by the authors was that the mice in the centermost compartments were exposed at higher levels than those nearer the walls, but they stated that with random insertion and the large number of exposures "the dose for any one mouse should integrate out to the average exposure level." If the latter statement were taken at face value, the SAR at 915 MHz was roughly 4 W/kg (Durney et al., 1978, p. [illegible]). The 24 mice were sham-exposed.

[illegible] of the RFR group died from thermal effects during the 33rd week of exposure. The authors inserted mice unrelated to the study into the two center compartments (longitudinal location of maximum temperature rise [illegible] lethal level within 30-40 min. For subsequent exposures therefore, they moved the array of compartments 1 inch toward the short end, i.e., away from that longitudinal maximum, in order to allow these to fit comfortably in an exposure [illegible] during exposure.

The mice were observed throughout their lives, and mortality data were [illegible] the mean life span for the remaining 19 mice in the RFR group was [illegible] that for the 24 mice in the sham group; by analysis of [illegible] was not significant.

[illegible] blood characteristics (RBC, WBC, hemoglobin) were determined before the exposure sequence and at [illegible] the first month of the sequence, with longer intervals [illegible] Urinary activities were determined for 48-hr test periods [illegible] the mice had free access to either an activity cage [illegible] with food and water. For the sham group, downtimes [illegible] RBC, hemoglobin, and hematocrit (but not WBC) with [illegible] the authors used a t-test of paired differences between [illegible] corresponding times throughout the test [illegible] weeks of age. The test showed nonsignificant differences between [illegible] mean RBC, WBC, hemoglobin, hematocrit [illegible].

[illegible] differences between groups were statistically [illegible] by separate analysis of variance, the differences

were significant only at ages 121, 596, and 708 days. At 121 days, the RFR group weighed 1.1 g more than the control group, but also initially weighed 0.7 g more, so the change was only 0.4 g. At ages 596 and 708 days, the numbers of mice in both groups were far smaller and the weight ranges were much larger than at 121 days. Therefore, the authors did not ascribe any biological significance to these later-age findings.

Skidmore and Baum (1974) endeavored to determine whether rapid changes in electric and magnetic fields would induce injuries in biological systems with high cell turnover rates. They exposed male and female Sprague-Dawley rats and male AKR/J mice to electromagnetic pulses (EMP) continuously for 38 weeks (except for 2 hr/day on weekdays) for a total of 100 million pulses in an EMP simulator consisting of a parallel-plate transmission line fed by a pulse generator, with provision for placing 200 nonmetallic cages between the plates. Each pulse had a rise time of 5 nanoseconds, a 1/e fall time of 550 nanoseconds, and a peak electric field of 447 kV/m, and the pulses were delivered at 5 pulses per second. Because of the shape and short duration of the EMP, the broad RFR-frequency spectrum, and the low pulse-repetition rate, endeavors to calculate and use the equivalent free-space average power density and/or SAR for comparison with levels in other studies are not appropriate.)

One part of the study was directed toward ascertaining whether exposure to the EMP altered the concentration or proliferative capacity of bone-marrow cells (the latter assessed from concentrations of mitotic cells). The dependence of these effects on exposure duration were determined by assaying them in six each exposed and unexposed male rats after every two weeks of exposure. The results for both groups showed variations with time in numbers of nucleated bone-marrow cells and of [illegible] rubricytes and myelocytes, but the differences between mean values for exposed and unexposed rats at corresponding times were non-significant ($p>0.05$, t-test). Also in this part, bone-marrow cells were arrested in metaphase and examined for chromosomal aberrations. In 2000 cells from 40 rats exposed for 38 weeks, there were only 2 aberrations; the results were the same for 2000 cells from 40 control rats. Blood samples were taken from five each of the exposed and unexposed rats used in the bone-marrow assays were given standard blood-chemistry assays. The rats were also given postmortem and histological examinations. The differences between groups in any of the blood-chemistry parameters were not significant, and there was no RFR-associated pathology.

In another part of the study, blood samples (0.2 ml) were obtained on [illegible] weeks from two groups of 10 male rats and from unexposed [illegible] the concentrations of RBC, WBC, neutrophils, lymphocytes, [illegible] and platelets were determined. Incorporation of the [illegible] Fe-59 into newly formed erythrocytes was assayed in 30 each [illegible] exposed rats; Fe-59 was injected into the tail vein of 6 [illegible] 1, 7, 14, and 21 days from the start of EMP exposure [illegible] numbers of unexposed rats.

[illegible] reticulocyte concentration vs time for the exposed and [illegible] showed that the counts for the exposed groups were

[illegible] ... circulating WBCs, neutrophils, or lymphocytes.

Regarding the positive findings above, [illegible] the mean reticulocyte count for the exposed group [illegible] the start [illegible] was higher than for the controls and that the shapes of the [illegible] graphs for the two groups were similar for about the [illegible] of the 38-week exposure duration, possibly indicating that [illegible] factors were present.

Skidmore and Baum (1974) also exposed five pregnant rats [illegible] pulses during 17 days of gestation, with five unexposed pregnant rats as controls. On completion of exposure, the fetuses were removed, fixed, and examined for gross abnormalities. None were found. Twenty female rats were continuously exposed and, with 20 controls, were observed for possible development of mammary tumors. At age 1 year (after exposure to 10 million pulses), no mammary tumors were found in either group.

Last, 50 male AKR/J mice, a strain known to be prone to the spontaneous development of leukemia between 6 and 12 months of age, were exposed to the EMP, with 50 mice as controls. At the end of 33 weeks (86 million pulses), the 42 surviving exposed mice and the 24 surviving control mice were euthanized and examined histopathologically for the presence of leukemia. Nine of the exposed mice (21%) and 11 of the control mice (46%) were leukemic. There were no significant differences between groups in mean thymic or splenic weight or WBC count.

Baum et al. (1976), noting that the study above encompassed only about half the normal life span of the rats, performed a similar study (same EMP characteristics) with male and female Sprague-Dawley rats but for 94 weeks (except for 1 hr/day on weekdays) starting at age 4 months, for a total of 250 million pulses. During the early part of the exposure, the reticulocyte count was higher in the exposed than in the control group, as in the previous study, but the differences between groups were nonsignificant for the last 25 weeks of the period. This was also true for the platelet count. There were also no significant differences between groups in the other biological endpoints previously studied.

In addition to those endpoints, Baum et al. (1976) searched for possible effects of the EMP on fertility by exposing five male-female pairs of rats 4 months of age for about 13 weeks (34 million pulses);

[illegible] first [illegible] days of [illegible] males for the [illegible] rats were not exposed but were [illegible]. At term, the numbers of progeny were re[illegible] was examined for gross anatomical abnormal[illegible] were the effects of long-term exposure [illegible] two years and by mating them [illegible] females [illegible] with five in [illegible]. No anatomical abnormalities [illegible] differences in numbers of [illegible].

[illegible] Raum et al. [illegible] noted that the peak electric field strength used in these studies was considerably in excess of that [illegible] typically by operators of EMP facilities and [illegible] of extrapolation to humans, their negative [illegible] safety standards.

[illegible] and Traboulay [illegible], using a dominant lethal test (DLT), sought to determine whether RFR is mutagenic for mice, or by DNA analysis, whether RFR yields genetic effects. For the mutagenesis aspect, they exposed the testes of [illegible] anesthetized 56 day old Swiss mice to vertically polarized [illegible] GHz CW RFR at 50 mW/sq cm for 30 min and the testes of [illegible] other mice at [illegible] mW/sq cm for 80 min. The exposures were done in the near field of a standard gain horn within an anechoic chamber, with the rest of each mouse's body shielded with RFR-absorbing material. Ten mice were sham exposed concurrently with each RFR group.

After 24 hours for recovery, each RFR-exposed and control male was caged separately for one week with three 56-day-old unexposed virgin females. Then, the females were replaced with fresh ones each week for the next seven weeks, for a total of eight weeks of mating. The females were examined each morning for vaginal plugs. On gestation day 13, the mice were euthanized and scored for normal living implants, late fetal deaths, and resorption sites (the latter being the dominant lethals).

Three of the 10 males exposed at 50 mW/sq cm for 30 min died (one each during weeks 2, 4, and 6 postexposure) and two of the 10 sham-exposed males died. The authors stated: "The deaths in the control group cannot be attributed to treatment during sham-irradiation; these deaths did not interfere with the statistical analysis." For corresponding weeks, the number of mice mated to the exposed males each week that were pregnant was less than for those mated to the sham-exposed males. For the RFR and sham groups, the overall pregnancy rates were respectively 63.8% and 86%, indicating decreased male fertility and higher preimplantation loss for the RFR group.

The Mutagenicity Index (MI) was defined as the ratio (in percent) of the number of early deaths to the total number of implants. There were two late fetal deaths in the RFR group and five in the sham group. The authors noted that whether or not late fetal deaths should be included in a mutagenicity index was subject to debate, but decided to exclude

them from their MIs. The MIs were shown in Table 1 of the paper. For the RFR group, they ranged from a low of 1.61% for the first week to a maximum of 5.98% for the fourth week, with an overall value of 3.38%; the MIs for the sham group ranged from 0.34% for the third week to 2.28% for the eighth week, with an overall value of 1.17%. The authors noted that by chi-square test, the differences between the RFR and sham groups were significant at $p<0.01$ for the third and fourth weeks, significant at $p<0.05$ for the fifth and sixth weeks and overall, and nonsignificant ($p>0.05$) for weeks 1, 2, 7, and 8.

There were no deaths in the 10 males exposed at 10 mW/sq cm for 80 min. The overall pregnancy rates for the RFR and sham groups were 69.9% and 81.4%, respectively. There were 6 late fetal deaths in the RFR group vs 3 in the sham group, a 2:1 ratio (not "2 order of magnitude"). The MIs were shown in Table 2 of the paper. For the RFR group, they ranged from 1.54% for the seventh week to 4.72% for the sixth week, with an overall value of 3.09%; the MI range for the sham group was from 0.31% for the first week to 1.53% for the sixth week, with an overall value of 1.0%. By the authors' chi-square test, the differences between the groups were significant at $p<0.05$ for the first, second, third, and sixth weeks and overall, significant at $p<0.01$ for the fifth week, and nonsignificant ($p>0.05$) for the fourth and seventh weeks. (For unstated reasons, the results for the eighth week were not presented.)

Tables 1 and 2 of the paper contained some tabulation errors, the chi-square values for differences between RFR and sham values were calculated incorrectly, and the chi-square limit values for 5% probability were stated incorrectly. With correctly calculated chi-square values, the differences in overall values between RFR and sham groups study were significant for both exposure conditions, but nonsignificant for most of the individual weeks postexposure. Exposure at 50 mW/sq cm for 30 min caused a marked reduction in fertility of the mice, but exposure at 10 mW/sq cm for 80 min caused only a marginal reduction.

For the cytogenetic aspects of the study, Varma and Traboulay (1976) exposed the testes of groups 10 mice each to the 1.7-GHz RFR at 50 mW/sq cm for 30 min and at 10 mW/sq cm for 80 min as above, and to 0.985-GHz CW RFR at 10 mW/sq cm for 80 min. Following exposure, the testes were ground, the cells were lysed in urea, and the double-stranded DNA was extracted. Samples of the DNA from each group were pooled and assayed for their nucleotide composition, and were heated to determine their hyperchromicity (defined as the percentage difference between final and initial optical density) and their melting temperature (Tm). The authors stated that groups of 10 sham-exposed males each were similarly treated. However, the numerical results for the RFR groups (shown in Tables 3, 4, and 5 of the paper) apparently were compared with those for "normal" DNA, since the latter data were identical in all three tables.

The value of Tm for the group exposed to 1.7-GHz RFR at 50 mW/sq cm for 30 min was about 2 deg C lower than for normal DNA (85 vs 87 deg C). The asymmetry ratio (defined as the nucleotide composition ratio of A+T to G+C) was 1.6 for the RFR group and 1.32 for normal DNA, a significant

difference. The hyperchromicity for the RFR group was 24% vs 30% for normal DNA. The corresponding differences between the group exposed to 1.7 GHz RFR at 10 mW/sq cm for 80 min and normal DNA were smaller: 1 deg C in Tm (86 vs 87 deg C), asymmetry ratio of 1.455 vs 1.32, and 28.6% vs 30% for hyperchromicity. For the group exposed to 0.985 GHz RFR at 10 mW/sq cm for 80 min, however, the differences were comparable to those for the group exposed at the higher level of 1.7-GHz RFR: a Tm of 85.5, an asymmetry ratio of 1.53, and a hyperchromicity of 25.84%. The RFR induced changes in hyperchromicity reflect decreases in hydrogen bonding in the DNA molecule and thus support the possibility that RFR causes strand separation.

The authors concluded that exposure to nonionizing radiation does cause genetic damage in Swiss male mice. They discussed the significance of dominant lethal mutations, indicating that such effects are thought to represent the results of damage or fragmentation of chromosomes, rather than point mutations therein; however, not all agents that produce chromosomal damage cause dominant lethal effects, and the significance of the dominant lethal effect is still uncertain. The relationship of DNA changes to mutagenic effects is also uncertain. Moreover, the DNA assays included the entire testis, of which about 40% is structural and supportive tissue, rather than seminal epithelium.

Lastly, the mice were anesthetized during exposure and the bodies were shielded from the RFR, exposing only the testes, as noted previously. However, anesthesia markedly reduces the ability of small rodents to control body temperature. Hence, the reported experiments may have involved substantial rises in testicular temperature, so the results may not be representative for unanesthetized animals exposed at the same power densities for the same durations.

Varma et al. (1976) conducted similar DLTs (but not DNA assays), in which only the testes of Swiss male mice were exposed to 2.45-GHz RFR. In Experiment I, the testes of 15 mice were exposed once for 10 min at 100 mW/sq cm. Five of these died. The authors did not discuss the cause of death. The remaining mice were mated with fresh females each week (as in the other study) for six or seven weeks. The controls were sham-exposed and similarly mated. There was no mention of deaths in controls. On gestation days 13-15, the females were euthanized and scored for living implants, late fetal deaths, and resorption sites.

For the RFR and sham groups respectively, the overall pregnancy rates were 55.2% and 46.7% and the overall numbers of implants were 11.3 and 11.4, so the RFR-induced decrease in male fertility and the higher preimplantation loss suggested from the results of exposure to 1.7-GHz RFR at 50 mW/sq cm in the other study, were absent here. Moreover, the almost 2:1 difference in pregnancy rates of the two sham groups (86% vs 46.7%) may indicate that uncontrolled non-RFR factors were present. The MIs for the RFR group ranged from 3.9% for weeks 4 and 6 to 17.3% for week 1, with an overall value of 6.3%. For the sham group, the MIs ranged from 0.9% for week 6 to 9.5% for week 1, with an overall value of 4.7%. By the authors' chi-square test, the differences between groups

for weeks 1 and 6 and overall were significant at the $p<0.05$ level.

In Experiment II, the testes of 24 mice were exposed four times at [illegible] mW/sq cm for 10 min each at three day intervals over a period of two weeks. Three mice died after exposure, and 15 of the remaining mice were randomly selected and mated with females. For the RFR and sham groups respectively, the overall pregnancy rates were 50.0% and 41.8% and the overall numbers of implants per pregnancy were 9.0 and 9.8. There were no significant differences between the groups in weekly or overall MIs, so the authors did not ascribe any significance to the difference in the number of implants.

In Experiment III, the testes of 16 mice were exposed three times at 50 mW/sq cm for 10 min each at 2 hr intervals on the same day. Five died during exposure. For the RFR and sham groups respectively, the overall pregnancy rates were 48.5% and 33.9% and the overall numbers of implants per pregnancy were 8.9 and 9.1. The MIs for the RFR group ranged from 3.8% for week 5 to 11.1% for week 6, with an overall value of 4.6%. For the sham group, the MIs ranged from 0.8% for week 4 to 6.7% for week 2, with an overall value of 3.4%. By the authors' chi-square test, the differences between groups for weeks 4 and 6 were significant at the $p<0.05$ level and the difference in overall values was nonsignificant.

Varma et al. (1976) concluded that single exposures of mice to 2.45-GHz RFR at 100 mW/sq cm are mutagenic, but that single or multiple exposures distributed over time at 50 mW/sq cm are not. However, as in Varma and Traboulay (1976), systematic errors were made in the computation of the chi-square statistic used to evaluate significance. Correct computation of chi-square showed no significant differences between RFR and sham groups (even at 100 mW/sq cm). Moreover, consolidation and use of the results for the control groups in both studies (suggested by the large non-RFR differences among them, exemplified above), yielded no mutagenic effects for any of the frequencies (at the levels and durations used).

Not discussed by the authors were the deaths of five of 15 mice after exposure in experiment 1, three of 24 mice after exposure in experiment 2, and five of 16 mice during exposure in experiment 3. Clearly, the RFR levels used were only somewhat below that for LD50.

Berman et al. (1980), in one of three experiments, used 12 Sprague-Dawley male rats exposed to 2.45-GHz CW RFR at 5 mW/sq cm for 4 hr/day from gestation day 6 to age 90 days and 12 rats similarly sham-exposed. The rats were the 90-day-old survivors of the study by Smialowicz et al. (1979a); see Section 3.3.2.1. The mean SARs (determined by twin-well calorimetry) ranged from 4.7 W/kg for ages 1-5 days to 0.9 W/kg for ages 31-40 days and were less than 0.9 W/kg for rats older than 40 days. In the second experiment, 14 young adult rats were exposed 5 hr/day for 5 days at 10 mW/sq cm and 16 were sham-exposed. In the third experiment, 6 rats each were sham-exposed and exposed 4 hr/day, 5 days/week, for 4 weeks at 28 mW/sq cm. The exposure facility described in Blackman et

[illegible] was used. ABs were determined [illegible] experiments 2 and 3 were estimated by the authors from Turner et al. (1968) as [illegible] W/kg respectively. The latter estimates that temperatures were not affected in anesthetized mature rats during 2 hr of exposure at 10 mW/cm² and sham exposure.

The development of mature sperm in rats takes about 64 days, starting with the first day after completion of treatment. Each male of experiment 1 was housed with a pair of 90-day-old virgin females for three separate weeks of breeding spaced about a week apart, a total period encompassing the early stages of spermatogenesis. The rats of experiments 2 and 3 were similarly bred for weekly periods, but extending respectively to 70, and 80 days after treatment cessation, encompassing essentially all the stages of spermatogenesis. The males of experiments 2 and 3 were bred to one week prior to exposure, to assess their reproductive abilities. Results for those that had not sired at least one normal pregnancy with at least one fetus during the pretreatment or the first post treatment breeding were excluded. (Two RFR exposed males in experiment 2 were thereby excluded.)

On day 10 after each weekly breeding, the females were euthanized and examined for pregnancy, number of live and dead conceptuses, and number of corpora lutea. Preimplantation loss was calculated by subtracting the total number of conceptuses (live + dead + resorbed) in each litter from the number of corpora lutea. The authors noted that if the loss for an RFR group is significantly larger than for the corresponding sham group, it may indicate embryonic death due to mutagenic alteration of sperm.

During the week after the last breeding, the males in experiments 2 and 3 were euthanized. Body and organ weights were determined. Both caudal epididymes were removed from the rats of experiment 2, placed in 2 ml of warmed saline, and cut into small pieces to free the sperm from the lumena. After each suspension was diluted and fixed with 10% neutral formalin, the relative sperm concentration was determined by particle counting. Smears were taken prior to fixation, and the sperm were fixed and stained with eosin-nigrosin; two hundred cells were examined and the number of live cells was determined.

Only data from RFR and sham groups for the same breeding period and experiment were compared. The pregnancy ratios for each breeding were analyzed by the chi-square test. Litter values were used in analyzing the numbers of live and dead conceptuses and postimplantation losses. Fetal data of experiment 2 were given the Freeman-Tukey transformation, with the number of corpora lutea as the denominator, then a multivariate analysis of variance was used to test differences in means between sham and RFR groups. Body weights, organ weights, sperm concentrations, and temperature measurements were examined by analysis of variance.

In experiment 1, the only significant difference was in the mean number of dead fetuses per litter, which was higher in the females mated with sham-exposed males than in those mated with RFR-exposed males, and

...y for one of the breeding weeks. Specifically, for the matings 3-9 days after treatment, there were 2.2 +/- 3.2 (SD) dead per litter for 11 of the 24 females found to be pregnant after mating with the sham exposed males vs only 0.6 +/- 0.7 dead per litter for 22 of the 24 females found pregnant after mating with the males exposed to the RFR. Clearly this difference was not RFR induced. Moreover, in experiment 2, none of the differences in mean numbers of pregnancies or live, dead, and total fetuses per litter or preimplantation loss per litter were significant.

In experiment 3, which involved breedings during the periods 3-9, 17-23, 31-37, 45-51, 59-65, and 72-78 days after sham or RFR exposure of the males, there were only two significant differences. Eleven of the 12 females bred with sham exposed males 3-9 days after treatment were found to be pregnant vs only 6 of the 12 females bred with RFR exposed males. For the breeding period 17-23 days, the mean number of live fetuses per litter was 15.2 +/- 2.5 for 11 females of the sham group vs 11.3 +/- 3.9 for 12 females of the RFR group; the corresponding mean numbers of dead fetuses per litter were 1.0 +/- 1.3 vs 0.3 +/- 1.7, a nonsignificant difference, but the difference in total numbers of fetuses for that breeding period, 16.2 +/- 2.4 vs 11.7 +/- 3.9, was significant.

For corresponding groups of RFR- and sham-exposed males in experiments 2 and 3, there were no significant differences in mean body weights or weights of testes, liver, or adrenals. Also not significant were the differences in relative concentration of epididymal sperm or percentage of live sperm between groups in experiment 2.

During 90 min of sham-exposure of anesthetized rats, both mean rectal temperature and mean intratesticular temperature decreased, from 38.8 to 36.5 deg C and from 34.6 to 32.1 deg C, respectively. For the rats exposed at 28 mW/sq cm, mean rectal temperature increased from 38.4 to 40.9 deg C and mean intratesticular temperature from 33.9 to 37.5 deg C.

In summary, no evidence was found in this study for increase of dominant lethal mutations induced by RFR at power densities up to 28 mW/sq cm (SARs up to 5.6 W/kg). Regarding male fertility, the authors stated: "Only in the most severe regimen (experiment 3) was there any hint of a deleterious effect. In the breedings that took place from three to nine days after treatment, only 50% of the dams bred to irradiated males showed pregnancies. This effect was temporary, lasting only until the next breeding period, 17 days after treatment." Presumably, this temporary sterility was associated with the significant increases in rectal and intratesticular temperatures.

McRee et al. (1981), noting that analysis of sister chromatid exchange (SCE) induction is a sensitive technique for assaying genetic damage of mutagens and carcinogens, used this technique to determine whether RFR is mutagenic in mice. A horizontal circular array of 12 ten-week-old CD1 mice in individual Styrofoam cages was exposed from above to far-field 2.45-GHz CW RFR at 20 mW/sq cm in an anechoic chamber at 22 deg C and 55% relative humidity. The exposures were for 8 hr/day (4 hr each

in the morning and afternoon) for 28 days.

SARs were determined for several mouse configurations and orientations relative to the RFR by measuring deep colonic temperatures in dead mice during exposure at 20 mW/sq cm and using the heating and cooling curves, as described in McRee (1974). The values ranged from 15.6 to 26.8 W/kg, but the live mice were curled up during most of each exposure period and were essentially parallel to the electric vector, for which the SARs were near the upper value.

Two other groups of 12 mice each were used as controls. One group was sham-exposed within the anechoic chamber in identical Styrofoam cages under conditions otherwise similar to those for the RFR group; the other group was kept and not handled in home cages that were placed within a second environmental chamber identical to the one used for RFR exposure.

Analysis of SCEs in bone marrow of the femurs of the mice was performed by the method of Allen and Latt (1976) immediately after termination of 28 days of exposure. At least 15 cells per mouse were examined. The mitotic index was determined by scoring the proportion of metaphase cells in a sample of more than 1000 bone marrow cells from each mouse. Results for only three mice of each group were presented; the remaining mice were eliminated primarily because the numbers of cells per sample were inadequate, a feature inherent in the specific type of assay. The results, presented in Table 22 (Table II of the paper), were:

TABLE 22: FREQUENCY OF SISTER CHROMATID EXCHANGE IN MOUSE BONE MARROW CELLS

GROUP	MOUSE NO.	MITOTIC INDEX (%)	NO. OF CELLS	SCE RANGE	MEAN SCE PER CELL +/- SEM
Control	C-26	9.8	61	1-8	3.56 +/- 0.22
Control	C-27	11.0	19	0-4	2.26 +/- 0.24
Control	C-28	8.6	15	1-5	3.13 +/- 0.29
				Mean of means:	2.98
Sham	SC-14	9.7	90	0-10	3.09 +/- 0.21
Sham	SC-15	9.3	55	0-6	2.76 +/- 0.13
Sham	SC-16	10.5	24	1-6	2.83 +/- 0.29
				Mean of means:	2.89
RFR	M-2	8.2	60	0-8	2.97 +/- 0.19
RFR	M-3	8.7	54	0-11	3.28 +/- 0.29
RFR	M-4	9.8	40	1-6	2.70 +/- 0.28
				Mean of means:	2.98

As noted by the authors, the mean of means for each group, shown above, were comparable, about 3 SCEs per metaphase cell, indicating that RFR-exposure did not significantly affect sister chromatid exchanges.

In addition, analysis of the mitotic index values showed that the RFR had no significant effect on the rate of proliferation of bone marrow cells.

Saunders and Kowalczuk (1981), as discussed in Section 3.6.2, had found that exposure of the rear halves of anesthetized mature male mice to 2.45-GHz RFR at half-body SARs of 43 W/kg or higher for 30 min severely reduced sperm production during the heat-sensitive stages. Saunders et al. (1983) therefore endeavored to determine whether such exposure was mutagenic for male germ cells. Four groups of six sexually mature male C3H mice each were anesthetized i.p. with sodium pentobarbital, and the rear halves of their bodies were exposed to 2.45-GHz RFR for 30 min at 43.4 W/kg (half-body SAR) in the same waveguide system used previously. For each RFR group, a group of six mice was similarly sham-exposed. For a positive control, 11 mice (groups of 5 and 6) were exposed to 170-keV X-rays at a dose to the testes of about 1.5 Gy, with appropriate sham-exposure groups.

Rectal temperatures were measured immediately before and after exposure. The mean values at the end of RFR- and sham-exposure were 41.5 +/- 0.1 (SE) and 34.1 +/- 0.3 deg C, respectively.

Following treatment, each male was caged with two sexually mature virgin CBAxC3H F1 female mice for seven days, after which the males were placed in fresh cages and mated with a second batch of females. This process was repeated until the males had been mated for 8-10 weeks. The females were euthanized 14 days after mating if a vaginal plug was present or 18 days after caging if not. When uterine implants were present, large and small deciduomata, indicative of development halted by early embryo death, were counted. Also counted were the corpora lutea, live embryos, and late fetal deaths.

The percentage of females rendered pregnant by mating with RFR-exposed males was comparable to the percentage for mating with sham-exposed males during the first two mating weeks, but diminished significantly for weeks 3 through 8 and rose to comparable values again by week 10. For each mating week, the numbers of corpora lutea per pregnant female of the weekly RFR and sham groups were comparable. However, the number of total implants for the RFR groups diminished by week 5 to a minimum of about half that for the corresponding sham group and then recovered by week 10, but on the other hand, the percentages of live implants to total implants for the RFR and sham groups were comparable each week. Analyses of these results by a sequence of five successive hierarchical models to assess the separate contributions of various possible factors to the overall responses confirmed the statistical significance of the differences above.

Thus, the results of Saunders et al. (1983) showed no evidence of RFR-induced dominant lethal mutagenic effect. The diminution of total implants was ascribed to decreased male fertility, in consonance with the previous findings (Saunders and Kowalczuk, 1981).

3.2.3 CANCER INDUCTION AND PROMOTION IN ANIMALS

As discussed in Section 3.1.1, possible associations between chronic RFR exposure and cancer incidence have been reported in some epidemiologic studies. However, few studies specifically directed toward determining whether RFR induces or promotes cancer in animals have been performed.

Prausnitz and Susskind (1962) were among the first to study the effects of exposing animals to RFR over a long time period. They exposed 200 mice in groups of 10 for 4.5 min/day, 5 days/week, for 59 weeks to 9.3-GHz pulsed RFR (2-microsecond pulses, 500 pps) at 100 mW/sq cm average power density, which caused a mean body temperature rise of 3.3 deg C. Based on a prolate-spheroidal model of a mouse (Durney et al., 1978, pp. 97-99), the SAR was about 45 W/kg. A body temperature rise of 6.7 deg C, found sufficient to cause death in half the animals (LD50), was attained in 12 min at 100 mW/sq cm, so exposure for 4.5 min at this power density was close to but not lethal. A group of 100 mice were sham-exposed for controls.

The results of this study are discussed in detail in Section 3.5.3. As noted therein, an unexpected finding was that leukosis had developed in some of the mice, with incidence greater in the RFR-exposed than the sham-exposed mice. The authors had mistakenly described leukosis as a "cancer of the white blood cells," thereby implying a link between RFR exposure and cancer incidence. Leukosis, however, is defined basically as elevation of circulating leukocytes, which in this study may have due to infection or other functional disturbance. Moreover, Roberts and Michaelson (1983), in a reanalysis of the primary data of Prausnitz and Susskind (1962), concluded that this study provided no evidence that chronic RFR exposure does or does not induce any form of cancer.

In the study by Skidmore and Baum (1974), discussed in Section 3.2.2 above, it was found that continuous exposure of 20 females to EMP did not lead to the development of any mammary tumors, and that exposure of a strain of mice prone to spontaneous leukemia did not promote leukemia; 21% of the exposed mice vs 46% of the control mice developed leukemia.

3.2.4 CONCLUSIONS

Based on the foregoing studies, there is no evidence that exposure to RFR induces mutations in bacteria, yeasts, or fruit flies except under conditions that cause significant temperature rises in the specimens. Several studies showed that exposure of male rodents to RFR levels that produce frank heating of the testes tend to reduce fertility, but such RFR levels were not found to be mutagenic. There is also no evidence that chronic exposure to RFR induces or promotes any form of cancer in mammals.

REFERENCES

Allen, J. W., and S. A. [illegible]
IN VIVO BRIEF [illegible] HEMATOPOIETIC AND [illegible]
SISTER CHROMATID EXCHANGE, CHROMATID AND CHROMOSOME [illegible]
Chromosoma, Vol. 58, [illegible]

Allis, J. W., E. Blackmar, M. [illegible], and [illegible]
MEASUREMENT OF MICROWAVE RADIATION ABSORBED [illegible]
ANALYSIS OF HEATING AND [illegible] DATA
Bull. [illegible], Vol. [illegible], No. [illegible]

Ames, B. N., J. McCann, and E. Yamasaki
METHODS FOR DETECTING CARCINOGENS AND MUTAGENS WITH THE
SALMONELLA/MAMMALIAN-MICROSOME MUTAGENICITY TEST
Mutation Res., Vol. [illegible], No. [illegible], pp. [illegible]

Ames, B. N.
IDENTIFYING ENVIRONMENTAL CHEMICALS CAUSING MUTATIONS AND CANCER
Science, Vol. 204, pp. 587-593, 11 May 1979

Anderstam, B., Y. Hamnerius, S. Hussain, and I. Ehrenberg
STUDIES OF POSSIBLE GENETIC EFFECTS IN BACTERIA OF HIGH FREQUENCY
ELECTROMAGNETIC FIELDS
Hereditas, Vol. 98, pp. 11-32 (1983)

Baum, S.J., M.E. Ekstrom, W.D. Skidmore, D.E. Wyant, and J.L. Atkinson
BIOLOGICAL MEASUREMENTS IN RODENTS EXPOSED CONTINUOUSLY THROUGHOUT THEIR
ADULT LIFE TO PULSED ELECTROMAGNETIC RADIATION
Health Phys., Vol. 30, No. 2, pp. 161-166 (1976)

Berman, E., H.B. Carter, and D. House
TESTS OF MUTAGENESIS AND REPRODUCTION IN MALE RATS EXPOSED TO 2450-MHZ
(CW) MICROWAVES
Bioelectromagnetics, Vol. 1, No. 2, pp. 65-76 (1980)

Blackman, C.F., S.G. Benane, C.M. Weil, and J.S. Ali
EFFECTS OF NONIONIZING ELECTROMAGNETIC RADIATION ON SINGLE-CELL BIOLOGIC
SYSTEMS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 352-366 (1975)

Blackman, C.F., M.C. Surles, and S.G. Benane
THE EFFECT OF MICROWAVE EXPOSURE ON BACTERIA: MUTATION INDUCTION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF
ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare,
Washington, D.C., HEW Publication (FDA) 77-8010, pp. 406-413 (1976)

Dardalhon, M., D. Averbeck, and A.J. Bertaud
DETERMINATION OF A THERMAL EQUIVALENT OF MILLIMETER MICROWAVES IN LIVING
CELLS
J. Microwave Power, Vol. 14, No. 4, pp. 307-312 (1979)

Hamnerius, Y
EXPOSURE SYSTEMS FOR STUDIES OF THE EFFECTS OF ELECTROMAGNETIC FIELDS ON BIOLOGICAL SYSTEMS
Hereditas, Vol. 98, pp. 43-52 (1983)

Hamnerius, Y., A. Rasmuson, and B. Rasmuson
BIOLOGICAL EFFECTS OF HIGH-FREQUENCY ELECTROMAGNETIC FIELDS ON SALMONELLA TYPHIMURIUM AND DROSOPHILA MELANOGASTER
Bioelectromagnetics, Vol. 6, No. 4, pp. 405- 414 (1985)

Heller, J.H.
CELLULAR EFFECTS OF MICROWAVE RADIATION
In S.F. Cleary (ed.), BIOLOGICAL EFFECTS AND HEALTH IMPLICATIONS OF MICROWAVE RADIATION, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication BRH/DBE 70-2, pp. 116-121 (1970)

McRee, D.I.
DETERMINATION OF ENERGY ABSORPTION OF MICROWAVE RADIATION USING THE COOLING CURVE TECHNIQUE
J. Microwave Power, Vol. 9, No. 3, pp. 263-270 (1974)

M[illegible] Ma N. [illegible]s, and G.K. Livingston
[illegible] SISTER CHROMATID EXCHANGE IN BONE MARROW CELLS OF THE MOUSE
[illegible] MICROWAVE EXPOSURE
[illegible] Res. Vol. 85, pp. 340-348 (1981)

[illegible] S. [illegible], and S. Nagai
[illegible] VERLAY TECHNIQUE FOR POPULATION STUDIES OF RESPIRATION
[illegible] IN YEAST
[illegible] Vol. 25, pp. 928-929 (1957)

[illegible] Beyer, and C.F. Reichelderfer
MICROWAVE EFFECTS ON REPRODUCTIVE CAPACITY AND GENETIC TRANSMISSION IN DROSOPHILA MELANOGASTER
IEEE Microwave Power, Vol. 7, No. 2, pp. 75-82 (1972)

Brodsmitz, S. and C. Susskind
EFFECTS OF CHRONIC MICROWAVE IRRADIATION ON MICE
IRE Trans. Bio-Med. Electron., pp. 104-108 (1962)

Roberts, N.J.,Jr. and S.M. Michaelson
MICROWAVES AND NEOPLASIA IN MICE: ANALYSIS OF A REPORTED RISK
Health Phys., Vol. 44, No. 4, pp. 430-433 (1983)

Saunders, R.D. and C.I. Kowalczuk
EFFECTS OF 2.45 GHZ MICROWAVE RADIATION AND HEAT ON MOUSE SPERMATOGENIC EPITHELIUM
Int. J. Radiat. Biol., Vol. 40, No. 6, pp. 623-632 (1981)

Saunders, R.D., S.C. Darby, and C.I. Kowakczuk
DOMINANT LETHAL STUDIES IN MALE MICE AFTER EXPOSURE TO 2.45 GHZ MICROWAVE RADIATION
Mutation Research, Vol. 117, pp. 345-356 (1983)

Skidmore, W.D. and S.J. Baum
BIOLOGICAL EFFECTS IN RODENTS EXPOSED TO 10 MILLION PULSES OF ELECTROMAGNETIC RADIATION
Health Phys., Vol. 26, No. 5, pp. 391-398 (1974)

Smialowicz, R.J., J.B. Kinn, and J.A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

Spalding, J.F., R.W. Freyman, and L.M. Holland
EFFECTS OF 800 MHZ ELECTROMAGNETIC RADIATION ON BODY WEIGHT, ACTIVITY, HEMATOPOIESIS, AND LIFE SPAN IN MICE
Health Phys., Vol. 20, No. 4, pp. 421-424 (1971)

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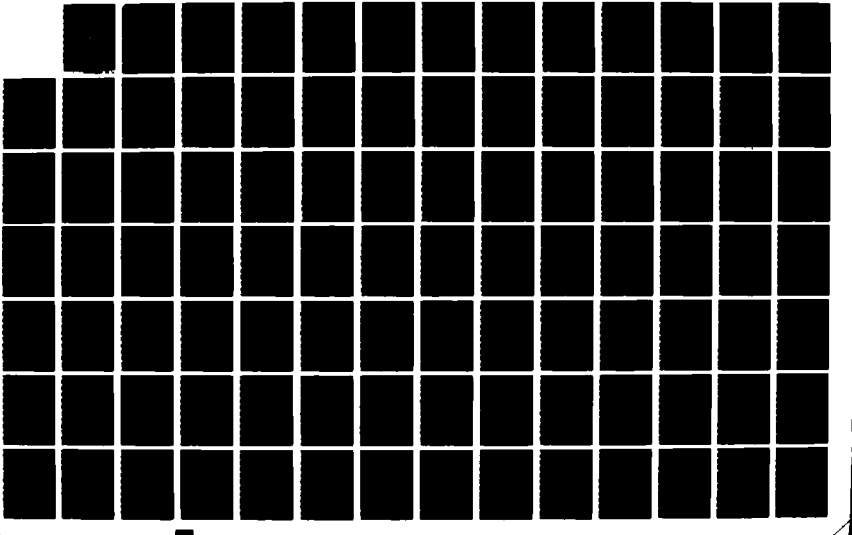

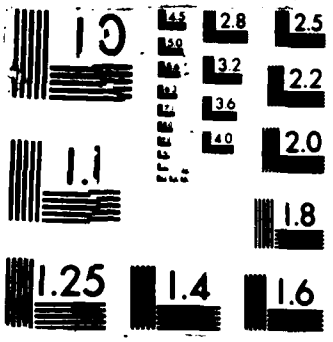
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1.8
2.0
2.2
2.5
2.8
3.2
3.6
4.0
4.5
5.0

Stodolnik-Baranska, W.
THE EFFECTS OF MICROWAVES ON HUMAN LYMPHOCYTE CULTURES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 189-195 (1974)

Varma, M.M. and E.A. Traboulay, Jr.
EVALUATION OF DOMINANT LETHAL TEST AND DNA STUDIES IN MEASURING MUTAGENICITY CAUSED BY NON-IONIZING RADIATION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW publication (FDA) 77-8010, pp. 386-396 (1976)

Varma, M.M., E.L. Dage, and S.R. Joshi
MUTAGENICITY INDUCED BY NON-IONIZING RADIATION IN SWISS MALE MICE
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 397-405 (1976)

3.3 STUDIES ON TERATOGENESIS AND DEVELOPMENTAL ABNORMALITIES

In the narrowest sense of the word, teratogenesis refers to production of anatomical aberrations in a developing fetus, but more generally includes fetal death and/or resorption, and physiological and cellular abnormalities in offspring observed postpartum. The term is most often applied to the development of mammalian fetuses. However, teratogenic and developmental effects of RFR on nonmammalian subjects, e.g., birds and insects, have also been studied.

Two general remarks are pertinent to various studies of RFR-induced teratogenesis. First, the mechanism by which terata are usually produced involves alteration (often temporary) in the rate of growth of a particular tissue under development. Development of the entire fetus is a complex process requiring that individual tissues develop within preset time frames, and interruption of this timing can result in abnormalities because a particular tissue or organ fails to complete development on schedule. Because of this, production of abnormalities is highly dependent on the time in the gestation sequence when the agent is applied and on the species of animal under study.

Second, the experimental circumstances in studies of the development of birds' eggs or insect pupae differ from those in studies of mammalian teratogenesis. In nonmammalian studies, the experimental material is exposed to the whole environment without any maternal protection; hence the studies must include rigorous control of all external conditions, including ambient temperature. In mammalian studies, the developing fetus is isolated from the environment to a considerable extent by the dam; however, the effects of noxious agents on the dam may constitute potential indirect sources of fetal abnormalities.

3.3.1 EFFECTS ON NONMAMMALIAN SPECIES

Several studies have been conducted on RFR induction of teratogenesis in pupae of the darkling beetle (Tenebrio molitor). Carpenter and Livstone (1971) exposed individual pupae to 10-GHz RFR in a waveguide at the equivalent of about 17 mW/sq cm (40 W/kg) for 2 hr or at 68 mW/sq cm (160 W/kg) for 20 or 30 min. As representative results, only 20% of the pupae exposed at 17 mW/sq cm (40 W/kg) developed into normal beetles; 4% died and 76% displayed gross abnormalities. Of the pupae exposed at 68 mW/sq cm (160 W/kg) for 20 min, 24% developed into normal beetles, 25% died, and 51% displayed gross abnormalities. About 90% of the sham-exposed pupae developed normally. Pupae were also radiantly heated to temperatures obtained with RFR, and about 75% emerged as normal beetles. The investigators therefore concluded that the abnormal development of RFR-exposed pupae cannot be explained as a thermal effect.

Lindauer et al. (1974), using CW or pulsed (0.25-microsecond pulses at 1600 pps or 16 pps) 9-GHz RFR at equivalent average power densities, also obtained statistically significant numbers of anomalies in Tenebrio exposed at 17.1 and 8.6 mW/sq cm (41 and 21 W/kg). The results showed no significant differences for pulsed and CW RFR at the same average

power density. Also, no clear dependence of the effect on dose rate or total dose was found.

Liu et al. (1975) extended this work at 9 GHz and found significant teratogenesis for 2-hr exposures at a power density as low as about 0.17 mW/sq cm (0.41 W/kg). In addition, exposures at various levels and durations corresponding to a constant incident energy dosage of 4 mW-hr (of which about a third was absorbed by each pupa) yielded evidence of an inverse (reciprocal) relationship between power density and duration.

Green et al. (1979) found that Tenebrio pupae cultured and exposed to 9-GHz RFR in ambient relative humidities of less than 35% appeared to be more susceptible to RFR teratogenesis than pupae similarly treated at higher humidities. At the lower humidities, they observed a slight rise in the incidence of terata with increasing applied RFR power (2-hr constant exposure) up to 34 mW/sq cm (80 W/kg). At 272 mW/sq cm (640 W/kg), they observed a further increase in teratogenic frequency, accompanied by an increase in pupa death before completion of development. The authors attributed the apparent "power window" at 34 mW/sq cm (80 W/kg) to an antagonism between nonthermal teratogenic effects and protective effects ascribable to the rise in temperature.

Pickard and Olsen (1979) used Tenebrio pupae from two sources. "Colony-pupae" were those derived initially as larvae from one supplier and raised on Purina dairy meal; "K-pupae" were purchased as larvae in three batches from another supplier and raised on Kellogg's Special K. Groups of K-pupae from the first batch and colony-pupae were sham-exposed or exposed at 6 GHz to: a standing-wave electric (E) field of 91 V/m (equivalent free-space power density of 2.2 mW/sq cm) for 2 hr, with the long axes of the pupae parallel to the E vector; a standing-wave magnetic (H) field of 1.53 A/m (88.3 mW/sq cm) for 2 hr, with the long axes parallel to the H vector; or a traveling-wave electromagnetic (far) field of 11 mW/sq cm for 13 hr, with the long axes either parallel to the E vector or to the direction of propagation. The standing-wave fields were produced by use of a reflecting plane in the far field of a horn, and the pupae were placed in the resulting planes of maximum E and H; absence of the reflecting plane yielded the traveling-wave field. The corresponding SARs were 130, 54, and 130 W/kg. Pupae were also exposed for 4 hr to traveling-wave 10-GHz RFR at 5 mW/sq cm (45 W/kg).

The differences in the frequencies of abnormalities between the groups exposed to the E field and the corresponding control groups of pupae of either type were not significant. However, the proportion of nonnormal beetles from the control K-pupae was significantly larger than from the control colony-pupae. Moreover, H-field exposure produced significant effects on the K-pupae but not on the colony-pupae. Repetition of the H-field experiment with K-pupae from the other two batches yielded RFR effects that ranged from "doubtfully deleterious" to "significantly beneficial." Ambiguous results were also obtained from exposures for 13 hr to the 6-GHz traveling-wave RFR (130 W/kg) and for 4 hr to the 10-GHz RFR at 5 mW/sq cm (45 W/kg). These variations appear to have been due to uncontrolled differences in such non-RFR factors as the source of

larvae, pupae maintenance regimes and handling protocols, the pupae containers used for pupation, and ambient temperature, an explanation that could account for the variabilities among the results of the other investigators cited.

Pickard and Olsen (1979) nevertheless concluded that their results indicated that RFR can be teratogenic in Tenebrio but left unproved the nonthermal hypothesis of Carpenter and Livstone (1971). Specifically, Olsen and Hammer (1982) measured spatial distributions of absorbed RFR in pupae by thermographic imaging during irradiation to 1.3, 6, and 10 GHz RFR; they found large local variations of SAR, which would not be obtained with the radiant heating used by Carpenter and Livstone.

In another study, Olsen (1982) exposed groups of Tenebrio pupae to a standing-wave, 6-GHz field in an anechoic chamber for 1.5, 3.0, 6.0, 12, or 24 hr at intensities inversely proportional to duration, to yield a constant total dosage of 1123 J/g in each pupa. Half the insects were exposed in the maximum-E-field plane with their long axes perpendicular to the E vector and the other half in the maximum-H-field plane with their long axes parallel to the H vector. With these orientations, the SARs were both 208 W/kg at the highest intensity used, i.e., for 1.5-hr exposures. The exposures were done without or with use of a ventilating fan. With the fan operating, the temperature rise in the chamber was less than 4.5 deg C as contrasted with about 11 deg C with the fan off. Control experiments consisted of sham-exposures for 6, 12, and 24 hr.

The results of the control experiments showed no morphological defects, in sharp contrast to the relatively large incidence of anomalies in control pupae observed by Liu et al. (1975). For the 1.5-hr exposures at 208 W/kg in the absence of chamber ventilation, Olsen (1982) reported that 11 of 12 pupae exposed in each plane died during pupation and that the twelfth pupa was abnormal; however, there were no deaths in the groups exposed for 3, 6, 12, or 24 hr at successively halved SARs and there were only 2 abnormal pupae in total (both in the group exposed in the E plane for 6 hr at 52 W/kg). Moreover, in the 120 pupae comprising the 10 groups exposed with the fan operating (1 group in each plane for 1.5 hr at 208 W/kg, 3 hr at 104 W/kg, 6 hr at 52 W/kg, 12 hr at 26 W/kg, and 24 hr at 13 W/kg), there were no deaths and only 1 anomaly (in the group exposed for 24 hr in the E-field plane). Olsen noted the absence of reciprocity or a graded response in his results, and suggested the existence of a hyperthermia threshold of about 40 deg C for deleterious effects on Tenebrio pupae.

McRee and coworkers have carried out a variety of studies on Japanese quail. In an early investigation, McRee et al. (1975) exposed 4x5 arrays of Japanese-quail eggs to far-field 2.45-GHz CW RFR, with the long axes of the eggs parallel to the E vector (vertical). Five arrays were exposed for 4 hr, one each at the end of the first five successive days of incubation. A sixth array was exposed for 4 hr at the end of all five incubation days. The ambient temperature and relative humidity were 24 deg C and 40%. The power density was 30 mW/sq cm, selected to yield egg temperatures (at this ambient temperature) of about 37 deg C,

the incubator temperature.

Egg temperatures at the surfaces facing the source, measured by infrared microscopy during exposure of a test array, ranged over the array from 30.6 to 34.7 deg C. Thermistor measurements of internal temperature yielded values at the centers of the eggs about 2 deg C hotter than at the surfaces. Thus, center temperatures ranged from about 33 to 37 deg C, with a spatial average of about 35 deg C. From cooling curves taken on cessation of exposure, the SAR corresponding to 35 deg C was found to be 14 W/kg. Control arrays were sham-exposed at an ambient temperature of 35 deg C and 40% relative humidity. Before treatment and afterward for the remainder of the incubation period (16-17 days), the eggs were incubated at 37 deg C and 60% relative humidity. Two days after the onset of hatching, the quail were weighed, euthanized, and examined for gross deformities. Blood samples were taken and assayed for hematocrit, hemoglobin level, red-blood-cell (RBC) count, white-blood-cell (WBC) count, and differential WBC percentages, and the mean of each endpoint was plotted (with error bars) vs day of treatment.

By paired t-test, the differences between RFR-exposed arrays and their corresponding sham-exposed arrays were nonsignificant ($p>0.05$) in hatch results, which included average body weights, numbers and percentages of eggs hatched, and numbers and percentages of hatched and unhatched live and dead birds. In addition, no deformities were found in the hatched quail. By paired t-test of all arrays, there were also no significant differences in any of the blood parameters assayed. By Mann-Whitney U-test, however, some differences in blood parameters were significant ($p<0.05$), notably an 11% decrease in hemoglobin for RFR-exposure on day 2, but there was no consistent pattern to the differences. The authors ascribed such differences in part to blood values that change more rapidly during the first day after hatching than subsequently.

In a subsequent study, Hamrick and McRee (1975) similarly exposed eight 4x5 arrays of quail eggs to 2.45-GHz RFR (30 mW/sq cm, 14 W/kg) and sham-exposed eight arrays, but for 24 instead of 4 hr, at the start of day 2 of incubation. RFR- and sham-exposed eggs were not turned during the 24-hr treatment period. The quail were kept for 24 to 36 hr after hatching. The birds were then weighed, examined for gross deformities, and euthanized. After the quail were euthanized, they were examined externally and internally for abnormalities; blood assays were performed; and the heart, liver, gizzard, adrenals, and pancreas of each bird were weighed. The results for the RFR-exposed arrays were pooled, as were those for the sham arrays, and the differences were analyzed with the two-sided Mann-Whitney U-test. The differences between the RFR and sham groups were all nonsignificant ($p>0.1$) except for hemoglobin, which was about 4% lower for the RFR group than the sham group at the $p=0.06$ level.

In another similar study, McRee and Hamrick (1977) exposed three 6x5 arrays of Japanese-quail eggs to 2.45-GHz CW RFR at 5 mW/sq cm (4 W/kg) daily for 24 hr/day during the first 12 days of development. In this study, the eggs were turned 90 deg automatically every 2 hr during

exposure to avoid sticking of embryos to their shells. On completion of exposure, the eggs were incubated normally for the remaining 5 days.

One of the arrays was exposed to the RFR with the chamber at 37 deg C (the optimum incubation temperature). The temperatures of the eggs stabilized at between 39.5 and 40 deg C, so the corresponding control array was sham-exposed in a chamber held at 40 deg C, the highest egg temperature attained during RFR-exposure. At the end of the incubation period, only two of the RFR-exposed eggs and none of the control eggs hatched, and 22 of the RFR-exposed and only one of the control embryos had developed past the eleventh day, results clearly ascribable to hyperthermia.

The other two 6x5 arrays were exposed to RFR at an ambient temperature of 35.5 deg C, which resulted in egg temperatures ranging from 37.5 to 38.0 deg C. Therefore, the sham-exposures were done at 38.0 deg C. Fifty-two of the RFR-exposed eggs hatched vs 35 of the control eggs, a result ascribed to the lower temperatures (less than 38.0 deg C) reached by some of the RFR-exposed eggs. No gross deformities were found in the quail when they were euthanized and examined 24-36 hr after hatching. By the Mann-Whitney U-test, there were no significant differences in total body weight or the weights of the heart, liver, gizzard, adrenals, and pancreas between RFR- and sham-exposed groups. The hematological assays showed 4% higher hemoglobin ($p<0.034$) and 31% lower monocyte counts ($p<0.004$) in the RFR-exposed birds, but the differences in the other blood parameters were not significant. The variations in temperature from egg to egg in the RFR-exposed arrays were as much as 0.5 deg C, rendering it difficult to associate these positive findings with the RFR per se.

In yet another study, Hamrick et al. (1977) similarly exposed groups of eggs and reared the birds for 5 weeks after hatching. No significant differences in mortality or mean body weights at 4 and 5 weeks were found between RFR and sham groups. The immunological findings of this study are discussed in Section 3.5.2.

Two subsequent studies (Galvin et al., 1980a; Hamrick and McRee, 1980) were directed toward ascertaining whether exposure of Japanese-quail eggs to 2.45-GHz pulsed or CW RFR would affect the development or beat rate of the embryonic heart. The results of those cardiovascular studies are discussed in Section 3.6.3.

Fisher et al. (1979) studied the development of chicken embryos in eggs exposed to 2.45-GHz CW RFR 24 hr/day for either 4 or 5 days. The eggs were exposed within an incubator in 6x6 arrays at power densities that ranged over the array from 1.4 to 6.2 mW/sq cm, with a mean of 3.46 mW/sq cm (SARs not determined). The long axes of the eggs were in a plane parallel to the propagation and electric vectors and were tilted 30 deg relative to the electric vector. All axes were shifted to the symmetric 30-deg orientation every 24 hr. The optimal incubation temperature for chicken embryos is about 38 deg C, so lower incubator temperatures, ranging from 32 to 36 deg C over the egg sites, were used

to compensate for the additional heat from RFR absorption. However, the incubator temperature at each site was constant. Embryo temperatures were measured for 6 sample eggs of a 6x6 array with a thermocouple inserted through an opening in each shell. The results, together with the spatial temperature variations among the 36 egg sites within the incubator, were used to estimate the temperatures of the other 30 embryos. Sham-exposed arrays served as controls. After completion of exposure, the embryos were excised, the extraembryonic membranes were removed, the wet masses were measured, and each embryo was photographed.

The stage of development of the eggs RFR-exposed for 4 days at an embryo temperature of 32 deg C was significantly later (smaller cranial lengths and wet masses) than for the sham-exposed controls. The converse was true at 36 deg C, with crossover (no difference) at embryo temperatures of about 34 deg C. Similar results, but with larger differences, were obtained for the eggs exposed for 5 days. The authors also stated that the frequency of premature deaths and of sterility did not differ significantly among groups.

These results are difficult to analyze because the authors did not include the temperature measurements of the 6 sample embryos, the locations of those eggs in the array, and the calculated temperatures of the other embryos. For the range of power densities in the array, it seems likely that the distribution of embryo temperatures over an RFR-exposed array should be significantly different from the distribution for a sham-exposed array. Moreover, the findings are open to question because the nonuniform SAR distributions within the RFR-exposed eggs undoubtedly yielded internal temperature gradients that were much larger (Clarke and Justesen, 1983) than those within the sham-exposed eggs.

Hall et al. (1983) sham-exposed and exposed suspensions of turkey sperm maintained at either 25 or 40.5 deg C to 2.45-GHz CW RFR for 30 min at an SAR of 10 or 50 W/kg in a waveguide system (Galvin et al., 1981b). The pH of each sperm suspension (an indicator of metabolic activity of the suspended cells) was measured before and after treatment. Within 2 hr after treatment, suspensions each containing 200 million sperm were used to perform single artificial inseminations of 6 groups of 16 virgin turkey hens in a 2x3 design for 25 and 40.5 deg C, and sham, 10-W/kg, and 50-W/kg exposure. Starting on the day after the inseminations, eggs were collected daily and incubated. On days 28 and 29 of incubation, the numbers and weights of the hatched birds were recorded. The remaining eggs were broken open and classified as fertile or infertile. Embryonic deaths were classified as early (days 1-5), middle (days 6-23), or late (days 24-28).

Post-treatment mean pH values were significantly lower ($p=0.015$) than pretreatment values for all 6 treatments, but RFR-related differences among the treatments were nonsignificant ($p>0.05$). The differences among groups in mean total number of eggs laid by each hen and mean number of eggs laid per week were nonsignificant (analysis of variance with week as the repeat measure). The percentage of fertile eggs, in terms of a moving 7-day time average, diminished with time for all

groups, but the differences among groups in mean number of fertile eggs per group, total and per week, were also nonsignificant, as were the differences in percentage hatchability similarly expressed.

The authors, noting that there were few middle deaths, presented data on early and late deaths only, each class tabulated in terms of numbers and percentages of deaths by week and treatment. They stated: "There were approximately 15% early and late deaths over the 10-week experimental period, and there was no difference among the groups for any treatment or temperature." However, they provided no statistical analyses of these data. Cursory examination of the data showed no consistent RFR-related pattern.

REFERENCES:

Carpenter, R.L. and E.M. Livstone
EVIDENCE FOR NONTHERMAL EFFECTS OF MICROWAVE RADIATION: ABNORMAL DEVELOPMENT OF IRRADIATED INSECT PUPAE
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 173-178 (1971)

Clarke, R.L. and D.R. Justesen
TEMPERATURE GRADIENTS IN THE MICROWAVE-IRRADIATED EGG: IMPLICATIONS FOR AVIAN TERATOGENESIS
J. Microwave Power, Vol. 18, No. 2, pp. 169-180 (1983)

Fisher, P.D., J.K. Lauber, and W.A.G. Voss
THE EFFECT OF LOW-LEVEL 2450 MHZ CW MICROWAVE IRRADIATION AND BODY TEMPERATURE ON EARLY EMBRYONAL DEVELOPMENT IN CHICKENS
Radio Sci., Vol. 14, No. 6S, pp. 159-163 (1979)

Galvin, M.J., D.I. McRee, and M. Lieberman
EFFECTS OF 2.45-GHZ MICROWAVE RADIATION ON EMBRYONIC QUAIL HEARTS
Bioelectromagnetics, Vol. 1, No. 4, pp. 389-396 (1980a)

Galvin, M.J., C.A. Hall, and D.I. McRee
MICROWAVE RADIATION EFFECTS ON CARDIAC MUSCLE CELLS IN VITRO
Radiat. Res., Vol. 86, pp. 358-367 (1981b)

Green, D.R., F.J. Rosenbaum, and W.F. Pickard
INTENSITY OF MICROWAVE IRRADIATION AND THE TERATOGENIC RESPONSE OF TENEBRIO MOLITOR
Radio Sci., Vol. 14, No. 6S, pp. 165-171 (1979)

Hall, C.A., D.I. McRee, M.J. Galvin, N.B. White, J.P. Thaxton, and V.L. Christensen
INFLUENCE OF IN VITRO MICROWAVE RADIATION ON THE FERTILIZING CAPACITY OF TURKEY SPERM
Bioelectromagnetics, Vol. 4, No. 1, pp. 43-54 (1983)

Hamrick, P.E. and D.I. McRee
EXPOSURE OF THE JAPANESE QUAIL EMBRYO TO 2.45 GHZ MICROWAVE RADIATION DURING THE SECOND DAY OF DEVELOPMENT
J. Microwave Power, Vol. 10, No. 2, pp. 211-220 (1975)

Hamrick, P.E., D.I. McRee, P. Thaxton, and C.R. Parkhurst
HUMORAL IMMUNITY OF JAPANESE QUAIL SUBJECTED TO MICROWAVE RADIATION DURING EMBRYOGENY
Health Phys., Vol. 33, pp. 23-33 (1977)

Hamrick, P.E. and D.I. McRee
THE EFFECT OF 2450 MHZ MICROWAVE IRRADIATION ON THE HEART RATE OF EMBRYONIC QUAIL
Health Phys., Vol. 38, pp. 261-268 (1980)

Lindauer, G.A., L.M. Liu, G.W. Skewes, and F.J. Rosenbaum
FURTHER EXPERIMENTS SEEKING EVIDENCE OF NONTHERMAL BIOLOGICAL EFFECTS OF MICROWAVE RADIATION
IEEE Trans. Microwave Theory Tech., Vol. 22, No. 8, pp. 790-793 (1974)

Liu, L.M., F.J. Rosenbaum, and W.F. Pickard
THE RELATION OF TERATOGENESIS IN TENEBRIO MOLITOR TO THE INCIDENCE OF LOW-LEVEL MICROWAVES
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 11, pp. 929-931 (1975)

McRee, D.I., P.E. Hamrick, and J. Zinkl
SOME EFFECTS OF EXPOSURE OF THE JAPANESE QUAIL EMBRYO TO 2.45-GHZ MICROWAVE RADIATION
Ann. N.Y. Acad. Sci., Vol. 247, pp. 377-390 (1975)

McRee, D.I. and P.E. Hamrick
EXPOSURE OF JAPANESE QUAIL EMBRYOS TO 2.45-GHZ MICROWAVE RADIATION DURING DEVELOPMENT
Radiat. Res., Vol. 71, No. 2, pp. 355-366 (1977)

Olsen, R.G.
CONSTANT-DOSE MICROWAVE IRRADIATION OF INSECT PUPAE
Radio Sci., Vol. 17, No. 5S, pp. 145-148 (1982)

Olsen, R.G. and W.C. Hammer
THERMOGRAPHIC ANALYSIS OF WAVEGUIDE-IRRADIATED INSECT PUPAE
Radio Sci., Vol. 17, No. 5S, pp. 95-104 (1982)

Pickard, W.F. and R.G. Olsen
DEVELOPMENTAL EFFECTS OF MICROWAVES ON TENEBRIO: INFLUENCES OF CULTURING PROTOCOL AND OF CARRIER FREQUENCY
Radio Sci., Vol. 14, No. 6S, pp. 181-185 (1979)

3.3.2 EFFECTS ON MAMMALS

3.3.2.1 RODENTS

Teratogenic effects of RFR in rodents have been reported in some studies, and negative findings in others. Among early studies of mice was that of Bollinger et al. (1974), who investigated the effects of exposure to RFR on growth and reproduction, in an experimental design involving C3H/He dams and successive generations thereof. The exposures were to 25-kHz synchronous, orthogonal electric and magnetic fields (the equivalent of plane CW RFR) in a combined capacitor and Helmholz-coil system. Some groups were exposed at 15 kV/m and 7.5 A/m, equivalent respectively to 59.5 and 2.12 W/sq cm ("full-power"). This level was selected to yield a 3-deg-C rectal-temperature rise in mouse carcasses in 1 hr. Other groups were exposed at 10.6 kV/m and 5.3 A/m, equivalent respectively to 29.8 and 1.06 W/sq cm ("half-power"). Durations of exposure at either level were 1 hr/day, 5 days/week, for a total of 50 hr. Control mice were sham-exposed. The results indicated that there were no statistically detectable effects of the RFR at either level on the growth, reproductive ability, and metabolism of neonates or on the growth of their subsequent offspring.

Bollinger et al. (1974) also sham-exposed and exposed groups of 4-day-old mice for 10, 20, 40, 70, or 100 hr at half-power or full-power, sacrificed them postexposure, and found no significant differences between RFR and sham groups in hematologic assays or major-organ weights, and no pathological changes in the organs. Also, cytological analysis revealed no obvious effects of the RFR on the number or the architecture of bone-marrow chromosomes. However, they reported that RFR exposure stimulated the uptake of tritiated thymidine in lymphocyte cultures and that the presence of common mouse parasites in RFR-exposed and control groups could not account for this effect. One other finding noted by the authors was no incidence of C3H/He-mouse mammary-tumor development up to 98 days of age.

Rugh et al. (1974, 1975), in two papers containing essentially the same information, reported first exposing groups of CF-1 female mice to 2.45-GHz CW RFR at 138 mW/sq cm for various durations in a waveguide system under controlled conditions of temperature, relative-humidity, and air-flow to determine the mean dose per unit mass (D/M) for lethality. The result was about 11 cal/g (10.65 for mice in estrus and 11.50 for mice in diestrus). They then exposed unrestrained timed-mated pregnant mice on gestation day 8.5 (time of greatest sensitivity to ionizing radiation) to the RFR at 123 mW/sq cm in the system at 25.0 deg C and 50% relative humidity for 2 to 5 min, corresponding to sublethal values of D/M ranging from about 3 to about 8 cal/g. From these dose-rate data, the SAR was about 110 W/kg. Most pregnancies were terminated on gestation day 18 and the mice were examined for resorptions and for dead, stunted, and malformed fetuses, all classed as anomalies, and for apparently normal fetuses.

In a plot of percentage of total anomalies of all types per litter vs

D/M, at least 40 litters (points too dense to count exactly) had 0% (all normal fetuses), spanning the exposure range from 3.4 to 7.8 cal/g; 5 litters had 100% (no normal fetuses), within the range from 5.8 to 7.7 cal/g; and the remaining litters (at least 140) had various intermediate percentages of anomalies, spread over the entire dose range. A plot of only the resorption percentages vs D/M showed at least 40 litters with 0%, from 3.3 to 7.7 cal/g; 3 with 100% resorptions, all above 5.9 cal/g; and the remaining litters (about 130) with intermediate percentages, spread over the entire dose range.

The percentages per litter of fetuses with exencephaly (brain hernia, produced consistently in CF-1 mice by ionizing radiation) vs D/M were plotted also. Exencephaly was absent in at least 45 litters, spanning the total dose range; 2 litters had 60%, the highest incidence, at about 7 cal/g; and the remainder (about 50 litters) had intermediate percentages, in the range 4.3-7.8 cal/g.

Apparently no control mice were studied, presumably under the assumption that the natural incidence of exencephaly is relatively rare. However, Chernovetz et al. (1975), in a similar study (discussed below) with C3H/HeJ rather than CF-1 mice, reported that about 20% of the fetuses from their control dams were abnormal. Also, despite statements by Rugh et al. about the absence of a teratogenesis threshold, our reanalyses of their data indicated thresholds of about 3.6 cal/g for occurrence of exencephaly and about 3.5 cal/g for resorptions.

Chernovetz et al. (1975), in the first of two regimens, exposed 4 groups of 5 pregnant C3H/HeJ mice to 2.45-GHz RFR for 10 min, 1 group each on gestation days 11, 12, 13, and 14 (totaling 20 dams). The mice in each group were concurrently exposed in a multimode, mode-stirred microwave cavity (at 22 deg C and 50% relative humidity) with the mice free to move about. At a mean SAR of 38 W/kg (estimated), the energy absorbed was 22.8 J/g or 5.44 cal/g. The authors noted that in a pilot study, 10-min exposures at 40 W/kg (24 J/g or 5.7 cal/g) were fatal to about 10% of a large number of pregnant mice, so 38 W/kg was just sublethal. Four other groups were similarly sham-exposed. In addition, 8 other groups were injected with cortisone (a teratogen); 4 of these groups were exposed to the RFR and the other 4 were sham-exposed.

Colonic temperatures were measured before and after RFR exposure for 10 cortisone-injected and 9 noninjected dams. The mean pre- and post-exposure values of the cortisone-injected dams were 34.59 and 39.93 deg C, respectively; the values for the noninjected dams were 38.58 and 40.60 deg C, respectively.

All mice were euthanized on gestation day 19, at which time the numbers of implantations and resorptions were counted and the fetuses were examined for structural abnormalities. For the noncortisone RFR and sham-exposed groups, there were no statistically significant differences in percentages of normal fetuses and structural abnormalities and no dependence on gestation day of treatment. However, the percentage of normal fetuses was 61% for the cortisone-with-sham-exposure and 50% for

the cortisone-with-RFR groups. The difference in these percentages was nonsignificant ($p>0.1$), but both percentages were significantly lower ($p<0.1$, the authors' criterion) than for the noncortisone RFR-exposed and sham-exposed groups (both 81%).

In the second regimen used by Chernovetz et al. (1975), the treatments were similar, but the exposures were done only on gestation day 14 and involved a total of 60 dams, 15 in each of the four treatment groups (RFR, sham-RFR, cortisone-with-RFR, cortisone-with-sham-RFR). All dams were allowed to carry to term, and the numbers of pups that survived to weaning at postpartum age 21 days were noted. (The behavior of the surviving pups was studied, and the findings thereof are discussed in Section 3.7.1.1.)

For the noncortisone groups, 81 pups from the sham-exposed dams and 93 pups from the RFR-exposed dams survived to weaning, a nonsignificant difference. For the cortisone groups, however, the results were 25 pups from the RFR-exposed dams and only 2 from those sham-exposed. These values were significantly lower than for the noncortisone groups and the difference between them was also significant.

These results of Chernovetz et al. (1975) indicated that absorption of about 5 cal/g of 2.45-GHz RFR is not teratogenic to mice, a finding that is at variance with those of Rugh et al. (1974, 1975). It is also noteworthy that dosage for lethality found by Chernovetz et al. (1975) was about 5.7 cal/g or about half the mean value found by Rugh et al. (1974, 1975), hence their conflicting characterizations of doses with respect to lethality. Possible reasons for these contradictory findings include the respective differences in exposure systems (cavity vs waveguide), use of multiple- vs individual animal exposures, gross uncertainties in actual doses, the mouse-strain difference (C3H/HeJ vs CF-1), variations in dam handling, and the differences in gestation day of treatment (day 11 through 14 vs day 8). As noted previously, Chernovetz et al. (1975) found fetal anomalies in about 20% of their control mice, whereas Rugh et al. (1974, 1975) apparently used no controls. Both groups of investigators indicated that extrapolation of their findings to higher mammalian species is an open question subject to experimental validation.

Berman et al. (1978) exposed pregnant CD-1 mice in 5x5, 7x4, or 3x5 arrays to far-field 2.45-GHz CW RFR at 20.2 deg C ambient temperature and 50% relative humidity for 100 min daily on gestation days 1 through 17 at 3.4, 13.6, or 14.0 mW/sq cm or gestation days 6 through 15 at 28 mW/sq cm. The SARs were determined by twin-well calorimetry. For 5x5 arrays exposed at 10 mW/sq cm, the SAR varied with location from 4.05 to 7.37 W/kg, with an array mean of about 5.9 W/kg, yielding 2.0, 8.1, and 8.3 W/kg for 3.4, 13.6, and 14.0 mW/sq cm, respectively. No data were given on spatial variations of SAR for the 7x4 or 3x5 arrays, but the mean SAR at 28 mW/sq cm was 22.2 W/kg (a value not twice the spatial mean for 14 mW/sq cm). Control mice were sham-exposed similarly. All mice were euthanized on day 18 and their uteri were examined for the number of resorbed and dead conceptuses and live fetuses. The live fetuses were examined for gross morphological alterations and weighed.

Ten types of anomalies were tabulated by numbers of litters affected. (The numbers of fetuses affected in each litter were not presented.) The investigators indicated that the number of litters with anomalies at each power density was not significantly different from zero, but that their sum over all power densities (7 of 318 RFR-exposed litters vs none of 336 sham-exposed litters) was significant.

A total of 27 of the 318 RFR-exposed litters, irrespective of power density, had 1 or more live abnormal fetuses, vs 12 of the 336 sham-exposed litters. For most of the individual anomalies, the numbers of litters affected were either too small for statistical treatment or no RFR-related pattern was apparent. To exemplify the latter, 4 litters exposed at 3.4 mW/sq cm (2.0 W/kg) exhibited hematoma, with none in the corresponding sham-exposed group; however, 2 litters exposed at 13.6 mW/sq cm (8.1 W/kg) and 3 sham-exposed litters were affected, and no litters were affected at 14.0 (8.3 W/kg) or 28.0 mW/sq cm (22.2 W/kg), compared with 1 litter in each of their corresponding controls. By contrast, cranioschisis (akin to exencephaly or brain hernia) was exhibited by 7 litters exposed to RFR, i.e., 1 litter each at 3.4 and 13.6 mW/sq cm (2.0 and 8.1 W/kg), 3 at 14.0 mW/sq cm (8.3 W/kg), and 2 at 28.0 mW/sq cm (22.2 W/kg), but by none of the control groups. In the latter case, though positive responses were obtained in the RFR groups, there was no discernible dose-dependence.

The mean live fetal weights of the litters exposed at 3.4, 13.6, or 14.0 mW/sq cm (2.0, 8.1, or 8.3 W/kg) were not significantly different from those of the corresponding sham-exposed litters; however, the mean weight of the litters treated at 28.0 mW/sq cm (22.2 W/kg) was significantly lower than that of the sham-exposed litters, possibly indicating the existence of a threshold for this effect.

Regarding abnormal fetuses, statistical treatment of the number of litters rather than the numbers of fetuses affected is of questionable validity. Also questionable is the summation of all litters exhibiting cranioschisis (irrespective of power density) to obtain statistical significance and ascribing such significance to RFR exposure.

In a similar investigation done subsequently, Berman et al. (1982a) exposed 2 5x5 arrays of time-bred CD-1 mice in individual vented plastic cages to 2.45-GHz CW RFR at 28 mW/sq cm (16.5-W/kg array mean, 4.5-W/kg standard deviation) at 20.2 deg C ambient temperature and 50% relative humidity for 100 min daily on gestation days 6 through 17. Two other arrays were similarly sham-exposed.

The mice in half of each group were examined on day 18. The incidence of pregnancy; the number of live, dead, and resorbed fetuses; and the total number of fetuses were found to be similar for the RFR-exposed and sham-exposed mice, findings at variance with those of their previous study (Berman et al., 1978). However, the mean body weight of the live fetuses in the RFR group was significantly smaller (by 10%) than those in the sham group, a finding consonant with their previous results (Berman et al., 1978). In addition, ossification of sternal centers was

significantly delayed in the RFR-exposed fetuses.

The mice in the other half of each group were permitted to come to term. At 7 days of age, the mean body weight of the suckling mice of the RFR-exposed group was also significantly smaller (by 10%) than for the sham-exposed group. The survival rates for the RFR and sham groups were comparable, but the investigators indicated that the growth retardation was permanent.

Berman et al. (1982b) exposed 8 Syrian hamsters dorsally in individual acrylic containers in a 3x3 array (with center position not used) to 2.45-GHz CW RFR at 20 mW/sq cm (6 W/kg) in an anechoic chamber at 22.2 deg C and 50% relative humidity for 100 min daily on gestation days 6-14. An array of 8 hamsters was similarly sham-exposed. RFR-exposure at this level, for which rectal temperatures were about 0.4 deg C higher than for sham-exposed hamsters, caused no significant change in fetal survival, body weight, skeletal maturity, or incidence of terata. By contrast, however, exposure at 30 mW/sq cm (9 W/kg), which elevated rectal temperatures about 1.6 deg C caused significantly higher fetal resorptions, lower fetal body weights, and delayed skeletal maturity. The authors, referring to Berman et al. (1978, 1982a), stated: "It appears that the hamster fetus may be more susceptible to microwave radiation than the mouse."

Nawrot et al. (1981) exposed groups of 12 CD-1 mice to far-field 2.45-GHz CW RFR in circular arrays in an anechoic chamber daily for 8 hr/day at 5 mW/sq cm (6.7 W/kg) during gestation days 1-15 or at 21 or 30 mW/sq cm (28.1 or 40.2 W/kg) during gestation days 1-6 or 6-15, all at an ambient temperature of 22 deg C and 55% relative humidity. Spatial variations of power density over the circular array were about 10%. Other groups were sham-exposed under the same conditions. Colonic-temperature increases for the latter two RFR levels were respectively 1 and 2.3 deg C. The same colonic-temperature increases were obtained in other groups sham-exposed in ambient temperatures of 30 and 31 deg C.

Two groups were used for each treatment, one group characterized as "handled" and the other as "nonhandled." The handled mice were transferred to Styrofoam cages (one per cage) for RFR-, sham-, or heat-exposure with no food or water available for the 4-hr periods 0800-1200 and 1300-1700, and were housed in polycarbonate shoe-box-type cages with food and water available during 1200-1300 and during 1700-0800. Nonhandled groups were housed in shoe-box-type cages with food and water available for the entire 24-hr period and were sham-exposed or heated concurrently with the handled groups. Dam body weights were recorded on gestation days 1, 6, 15, and 18. On day 18, the dams were killed, and implantation sites, resorptions, dead fetuses, and live fetuses were counted. Fetuses were sexed, weighed, and examined for malformations.

In the first of three experiments, 1 handled group was exposed at 5 mW/sq cm (6.7 W/kg) and 2 groups were sham-exposed (1 handled and 1 nonhandled). The pregnancy rates, maternal weight gains, and average fetal weights for both handled groups (RFR- and sham-exposed) were lower

than for the nonhandled-sham-exposed group, indicating that handling was the primary factor involved in the differences. The differences among the three groups for the other endpoints were nonsignificant.

In the second experiment, 1 handled group was exposed at 21 mW/sq cm (28.1 W/kg) and 22 deg C ambient temperature, another handled group was heated (without RFR) in ambient temperature 30 deg C (both yielding a rectal-temperature rise of about 1 deg C), and 1 handled group was sham-exposed at 22 deg C, all three groups during gestation days 1-6. One of 2 nonhandled groups was sham-exposed at 22 deg C and the other was heated at 30 deg C. The same procedure was used for other handled and nonhandled groups, but during gestation days 6-15. For the mice treated on days 1-6, significantly smaller maternal weight gains were obtained in the 3 handled groups (RFR-exposed, sham-exposed, heated) than in the 2 nonhandled groups (sham-exposed, heated). For those exposed on days 6-15, the maternal weight gain was smaller for the nonhandled-heated group as well, and the greatest decrease was for the handled-heated group. Thus, handling was again an important factor, but heating was as well. The other endpoints were not affected significantly.

The third experiment was similar to the second, but with treatment at 30 mW/sq cm (40.2 W/kg) or 31 deg C (both yielding mean rectal-temperature increases of 2.3 deg C). For the mice treated on days 1-6, the sham-exposed and heated groups of handled dams gained significantly less weight than the 2 nonhandled groups and the RFR-exposed group of dams lost weight, but the nonhandled heat group gained more weight than the nonhandled sham-exposed group. Also, the RFR-exposed group had significantly fewer implantation sites per litter than any of the other groups; he decreases in fetal weight for the RFR-exposed and handled-heated groups were comparable but were lower than for the nonhandled and handled sham-exposed groups and the nonhandled heat group. No increases in external, visceral, or skeletal malformations were seen in any group. The results for the mice treated on days 6-15 were similar except that the mean percentage of malformed fetuses for the RFR-exposed group was significantly larger than for any other group, with cleft palate the predominant malformation.

Based on the foregoing results, the authors concluded that the threshold for teratogenic effects in CD-1 mice is about 30 mW/sq cm (whole-body SAR of 40.2 W/kg).

Inouye et al. (1982) induced female CD-1 mice to superovulate and mated them. Groups were then sham-exposed or exposed for 3 hr on either gestation day 2 (during the 2-cell stage) or 3 (during the 4- to 8-cell stages) to far-field 2.45-GHz CW RFR at 9 or 19 mW/sq cm (11.7 or 24.7 W/kg) in circular arrays in an anechoic chamber at 22 deg C ambient temperature and 60% relative humidity. One group was exposed to 38 deg C ambient temperature and 60% relative humidity without RFR. No increase in colonic temperature was obtained at 9 mW/sq cm, 1 deg C increase occurred at 19 mW/sq cm, and at least 2.2 deg C occurred for the 38-deg-C heat treatment. On day 4, all mice were euthanized. The embryos were counted, examined for abnormalities, and classified by developmental

stage as: morula (9 or more blastomeres but no blastocoelic cavity), early blastocyst (small blastocoelic cavity), or blastocyst (large blastocoelic cavity). Abnormal embryos were defined as underdeveloped (less than 9 blastomeres) and as fragmented and/or collapsed embryos.

There were no statistically significant differences in the number of fertilized mice, the number of embryos per mouse, or the percentage of abnormal embryos (total and per dam) among all the groups. In addition, there were no significant differences in embryonic development or in abnormal embryos between RFR-exposed groups (at either power density) and sham-exposed groups for either treatment day. However, the heat treatment caused stunted embryonic development, i.e., significant increases in number of morulae and decreases in numbers of blastocysts compared with the numbers for sham-exposed mice on corresponding treatment days.

Direct comparisons of the results of this study with those of Nawrot et al. (1981), performed in the same laboratory with the same mouse strain (CD-1), are difficult because in the latter investigation, the dams were exposed for 8 hr/day over gestation days 1-6 or 6-15 (in contrast with a single 3-hr exposure on day 2 or 3), and the fetuses were examined at a much later stage of gestation (day 18 versus day 4). Moreover, the frequent handling of the dams was a significant factor in the earlier investigation. Nevertheless, the negative results for RFR exposure at 9 and 19 mW/sq cm (11.7 or 24.7 W/kg) obtained by Inouye et al. (1982) are consonant with the approximately 30 mW/sq cm threshold found by Nawrot et al. (1981). Also, fetal stunting occurred in both studies from exposure of the dams to elevated ambient temperatures without RFR.

Nawrot et al. (1985) performed experiments similar to the last one of Nawrot et al. (1981), i.e., exposures of groups of handled CD-1 mice to 2.45-GHz CW RFR at 30 mW/sq cm (40.2 W/kg) or to an ambient temperature of 31 deg C for 8 hr daily on gestation days 1-6 or 6-15, with groups of handled and nonhandled sham-exposed mice, a nonhandled heated group, and a cage-control group (maintained in animal quarters during pregnancy) for comparisons. As before, all dams were euthanized on day 18; the implantation sites were counted; the conceptus at each site was classed as resorbed, dead, or alive; and the live and dead fetuses were sexed, weighed, and examined for external anomalies. All live and dead fetuses were examined for skeletal alterations. Fetuses with external anomalies and stunted fetuses (weighing less than 0.5 g or less than two-thirds of their mean litter weight) were examined for visceral abnormalities. For the handled dams treated during gestation days 6-15, during which most prenatal brain development occurs, fetal brains were examined for histopathology and assayed for cholinesterase activity.

The mean pregnancy rate (determined on day 18) of the dams exposed to the RFR on days 1-6 was significantly lower than for the other groups treated on days 1-6. The mean maternal weight gains for the handled groups treated during this period (RFR-exposed, sham-exposed, heated) were significantly lower than for the corresponding nonhandled groups (sham-exposed, heated, cage-control). The mean fetal weights were lower

for all three handled groups than for the nonhandled groups, but the differences were significant only for the sham-exposed and heated groups. The highest incidence of external malformations (cleft palate, open eyes) occurred for the handled-sham-exposed group, but none of the differences was significant.

For the groups treated on days 6-15, the mean maternal weight gains were also smaller in the handled than the nonhandled groups. The mean fetal weights were smaller for the handled-RFR-exposed and handled-heated groups than for the other groups, but the difference was larger for the handled-heated group. There were no significant differences in the other teratologic endpoints among the groups treated on days 6-15. Mean cholinesterase activities assayed in fetuses from the three handled groups (RFR-exposed, heated, sham-exposed) did not differ significantly from one another. There were a few fetal abnormalities but none related to differences in treatment.

The authors suggested that the lower mean pregnancy rate in the group exposed to RFR on days 1-6 may have been due to preimplantation death and/or early postimplantation litter resorption, and that the absence of this effect in those exposed on days 6-15 may indicate that embryos in the earlier stage of gestation are more susceptible to the RFR. On the other hand, the authors noted that the decrease in mean pregnancy rate observed for mice exposed at 30 mW/sq cm on days 1-6 in the previous study (Nawrot et al., 1981) resulted from handling, but that combining the data from both studies yielded results indicating that the effect was not due to handling alone. They ascribed the contribution of the RFR to this effect to higher local temperatures in the uterine region because they had found that colonic temperature during exposure to the RFR rose about twice as fast than during treatment at the elevated ambient temperature used to attain the same final colonic temperature.

Stavinoha et al. (1975), in the first of two experiments, exposed groups of 4-day-old mice in plastic containers for 20 min to 10.5-, 19.27-, or 26.6-MHz RFR pulses (pulse duration and duty cycle not stated) in a rectangular-coaxial transmission-line (TEM) system (Mitchell, 1970) at an electric field strength of 5.8 kV/m. Control groups were kept in similar containers outside the exposure chamber. The mice were weighed daily for the next 21 days. Graphs of weight versus age at each frequency showed virtually no differences between exposed and control mice at corresponding ages.

In the second experiment, litters of 4-day-old pups from 20 mice were divided into three groups: (1) control pups, kept in individual cages; (2) thermal-control pups, held at 37 deg C for 40 min/day on five consecutive days; and (3) irradiated pups, exposed to 19-MHz CW RFR for 40 min/day on five consecutive days in a near-field synthesizer (Greene, 1974), in which the electric field was 8 kV/m, the magnetic field was 55 A/m, and the two fields were parallel (vertical) in coincident planes. After thermal or RFR treatment, the mean increase in rectal temperature was 1.5 deg C. The pups were weighed daily before each treatment and until they were 21 days old, at which time the males and females were

separated. The mice were then weighed weekly for 13 additional weeks.

Statistical analyses of growth curves showed no significant differences among the three groups of either sex. (The final weights of the males were somewhat higher than those of the females.) As the authors noted, although the fields used were very intense, relatively little RFR energy was absorbed by the mice because their sizes were much smaller than the wavelengths used. Thus, it would be inappropriate to apply these negative findings to humans exposed to RFR at frequencies in the same range.

The results of the second experiment above with mouse pups were also presented in Stavinoha et al. (1976), which included data on mortality after the 5-day treatment as well. Of 30-female and 30-male control mice, 1 female died; of 30 females and 29 males in the thermal-control group, there were 1 female and 6 male deaths; and of 40 females and 40 males in the RFR group, 2 females and 11 males died, i.e., relatively high death rates for males.

In addition, Stavinoha et al. (1976) had similarly treated adult mice in control, thermal-control, and irradiated groups, with the latter two treatments yielding a mean rectal-temperature increase of 1.6 deg C. Within 45 min after treatment, the mice were exposed to intense 2.45-GHz RFR for brain enzyme inactivation, which required 300 milliseconds, and various brain regions were assayed for adenosine 3':5'-cyclic phosphate (cyclic AMP). No significant differences among the three groups were reported.

Stavinoha et al. (1976) also had exposed rats to 19-MHz RFR in the near-field synthesizer (8 kV/m, 55 A/m) for 30-60 min/day (sufficient to increase rectal temperature by 1-1.5 deg C) on five days, with groups of control- and thermal-control rats for comparison. After brain enzyme inactivation, various brain regions were assayed for acetylcholine (ACh), norepinephrine, 5-OH tryptamine, adenosine diphosphate (ADP), adenosine triphosphate (ATP), and electrolyte concentrations.

The only significant difference in ACh concentration was in the cerebral cortex of the RFR group. There were no significant differences among the three groups in concentrations of norepinephrine, 5-OH tryptamine, or ATP. For the RFR group, the level of ADP was significantly lower in the cerebellum and cerebral cortex, and higher in the medulla-pons and thalamus, than in the corresponding regions of the other two groups. Differences among groups in various electrolyte concentrations were reported, with those for calcium most prevalent. Calcium concentration was higher in the medulla, hippocampus, striatum, and thalamus for the thermal-control group and in the medulla for the RFR group; it was lower in the heart for both the RFR and thermal-control groups and in the testicles and kidneys of the latter group.

Chernovetz et al. (1977) exposed pregnant rats for 20 min on only 1 day during gestation days 10 through 17 to 2.45-GHz RFR in a multimode, mode-stirred microwave cavity at a mean SAR of 31 W/kg in an ambient

temperature of 22 deg C and 50% relative humidity. They also exposed rats to infrared radiation (IR) in an incubator at 47 (+/- 7) deg C and 10-15% relative humidity. The incubator conditions were selected to produce the same colonic temperature rise of 3.5 deg C as the RFR exposure. Control groups were sham-exposed in the microwave cavity. Sixty-four pregnant rats (26 each in the RFR and IR groups and 12 in the control groups) were studied. Three dams died after exposure to IR, seven died after exposure to RFR, and none died in the control groups.

On day 19 of gestation, the 54 surviving dams were euthanized and the numbers of implantations and resorptions were counted. In addition, each fetus was examined for morphological abnormalities and its mass and viability were determined. The percentages of living fetuses per dam were about 98% each for the control and IR groups and 87% for the RFR group, a statistically significant decrease. The mean fetal mass for the control groups was 1.63 g, and the values for the IR and RFR groups were 1.53 and 1.54 g, respectively, both significantly lower than the mean for the control groups. No structural abnormalities were evident in any of the 468 formed fetuses, all of which were alive when taken, but severe edema and hemorrhagic signs were endemic in the IR and RFR groups.

The brains of 60 fetuses (20 each from control, IR, and RFR groups) were assayed for norepinephrine (NE) and dopamine (DA) in 4 groups of 5 pooled brains for each treatment. The mean NE level for the RFR group was significantly lower than for the controls, but only marginally lower than for the IR group. The averaged levels of DA ranked similarly, but the differences were not statistically significant.

The authors concluded that: "considered in sum, our findings could be taken as evidence that a brief but highly thermalizing application of 2,450-MHz microwaves or of infrared energy have biological effects both comparable and different when averaged colonic temperature changes are equal."

One problem with this investigation was the small number of rats studied (a point recognized by the authors), which necessitated averaging the data in each group over the 10- to 16-day gestation period, a procedure questionable both biologically and statistically. Perhaps a minor point was the use of the sham-RFR rats as controls for the IR group instead of a separate set of sham-IR controls, in view of the relative-humidity ambient-temperature differences. Because of such problems, the validity of either the positive or negative results of this investigation is difficult to assess.

Smialowicz et al. (1979a), in a study primarily on immunologic and hematologic effects, sham-exposed and exposed pregnant rats to 2.45-GHz CW RFR at 5 mW/sq cm (4.7-0.7 W/kg) for 4 hr/day, 7 days/week from gestation day 6 through term. Following birth, a group of male pups of each dam were similarly treated until age 20 days, at which time half were euthanized and the other half were treated until age 40 days and then euthanized. The dams and pups were weighed at selected intervals

to determine if the RFR affected growth. The SAR range 4.7-0.7 W/kg represents the decrease of mean SAR with increase in mean weight (with age) rather than variations among animals at any time. There were no significant differences in mean weight between exposed and control animals at any time. (The immunologic and hematologic results are discussed in Section 3.5.2.)

Berman et al. (1981) exposed 70 time-bred CD rats in groups of 8 in individual Plexiglas containers to 2.45-GHz CW RFR at 28 mW/sq cm (4.2 W/kg), 22.2 deg C ambient temperature, and 50% relative humidity for 100 min daily on gestation days 6 through 15. The containers were arranged in 3x3 rectangular arrays, with the central position unoccupied and the long axes parallel to the H-vector and perpendicular to the propagation direction. The mean colonic temperature at the end of each exposure period was 40.3 deg C. A group of 67 rats was similarly sham-exposed. Each rat was euthanized on gestation day 21, and the live, dead, and resorbed conceptuses were counted. Each live fetus was dried, examined for external morphology, weighed, fixed, and subsequently studied for internal morphology.

There were no statistically significant differences between RFR- and sham-exposed rats in pregnancy rates; mean litter values of live, dead, resorbed, or total fetuses; or live fetal weight. The numbers of ribs and sternal ossification centers were comparable. The types and indices of major and minor terata were similar in both groups of litters. No encephaloceles (brain hernias) were seen in any of these litters. These negative results were consonant with those of Chernovetz et al. (1977), who found no teratogenic effects from exposure to 2.45-GHz RFR at about 31 W/kg, which was lethal to about 27% of the dams.

Berman et al. (1981) surmised "that this lack of an effect may hold true at any exposure level less than that which will kill a significant number of the dams by hyperthermia (colonic temperature greater than 40 deg C)," and therefore concluded that the rat is an inappropriate model for determining whether RFR would be teratogenic to humans in exposure situations not lethal for the mothers. They then suggested that the mouse fetus is a more appropriate model for assessing such human risk.

Dietzel (1975) exposed 749 pregnant rats abdominally to 27.12-MHz RFR with a diathermy machine and applicator in three experimental groups at 55, 70, or 100 W once for up to 10 min between gestation days 1 and 16. The rectal temperature of each rat was monitored during exposure, and the rat was removed from the field when its temperature reached 39, 40.5, or 42 deg C (in lieu of any other dosimetry). On day 20, the fetuses were removed, counted, weighed, and examined for external malformations. Also, embryos in resorption and corpora lutea were counted, and the preimplantation losses were calculated by subtracting the numbers of mature and resorbed fetuses from the number of corpora lutea.

Typical predominant abnormalities included neurocranial malformations from exposure on days 9 and 10, kinked or short tails and "hand" defects for days 13 and 14, and cleft palate for day 15. The maximal numbers of

abnormalities occurred for exposure on days 13 and 14 and correlated well with rectal temperature, indicating that the abnormalities resulted from heating by the RFR.

The calculated preimplantation loss was about 55% for days 1 and 2, diminished rapidly to less than 20% for days 7 and 8, and was close to the control value of about 14% for most of the remaining gestation days of exposure. Postimplantation loss (after organogenesis) increased slowly from the 10% control value for exposure during days 1 through 6 and rose rapidly to about 22% for days 15 and 16. The higher values were ascribed to RFR-generated-heat accumulation in the amniotic sac. The lack of adequate dosimetry renders it difficult to compare these results with those of other investigators.

Dietzel (1975) also compared the effect of tumor treatment with 461-MHz RFR on DNA synthesis with treatment with X-rays. Tumor heating to 42 deg C with the RFR decreased the DNA-synthesis rate by about 13% at 2 hr post-treatment and by about 27% at 12 hr. The decrease produced by X-ray treatment was negligible at 2 hr and only about 7% at 12 hr.

Lary et al. (1982) exposed 8 groups of pregnant Sprague-Dawley rats to 27.12-MHz concurrent CW magnetic and electric fields at 55 A/m and 300 V/m (free-space equivalent power density about 138 mW/sq cm, SAR 11.1-12.5 W/kg) in a near-field synthesizer (Greene, 1974) in an ambient temperature of 23 deg C and relative humidity of 45%. Each rat was exposed individually while restrained in a perforated cylindrical Plexiglas holder with its frontal plane perpendicular to the magnetic field and parallel to the electric field.

One group each (16 to 28 rats) was exposed on gestation day 1, 3, 5, 7, 9, 11, 13, and 15 while colonic temperatures were monitored. Exposure of each rat was terminated when its colonic temperature reached 43.0 (+/- 0.1) deg C (duration 20-40 min). Colonic temperatures were also measured just before and after exposure. Eight control groups (each 10 to 13 rats) were sham-exposed for 30 min, one each on the same gestation days. A group (29 rats) maintained untreated in the animal quarters during gestation served as cage controls.

The exposure conditions were selected to deliver doses that were nearly hyperthermically lethal to the dams. In a pilot study, most malformed litters occurred in rats heated by RFR to 43.0 deg C or higher and no malformations were seen at less than 41.9 deg C; colonic temperatures exceeding 43.0 deg C were increasingly lethal, with no rat surviving above 43.5 deg C. In the main study, 26 (11%) of the RFR-exposed rats died from excessive hyperthermia during or shortly after exposure, and only 4 of these had a final temperature less than 43.0 deg C. No sham-exposed or cage-control rat died during the experiment.

All rats were euthanized on gestation day 20 (2 days before parturition) to avoid cannibalization of dead or malformed offspring by the dam. The numbers of implantations, live fetuses, and dead or resorbed conceptuses were determined. Also, the corpora lutea of pregnancy in

the cage controls were counted, as were those present during the preimplantation period (gestation days 1, 3, and 5) of the RFR- and sham-exposed groups. Each live fetus was sexed, weighed, measured for crown-rump length, and examined externally for gross malformations. One-third of the live fetuses from each litter were selected randomly, dissected, and examined for visceral abnormalities; the remaining fetuses were cleared and stained for skeletal examination.

The results for each group exposed to RFR on one of the preimplantation gestation days (1, 3, or 5) were compared with the combined results for the three groups sham-exposed on those gestation days; the results for each group exposed to RFR during early organogenesis (day 7, 9, or 11) were compared with the combined results for the groups sham-exposed on those gestation days; and the two groups exposed to RFR during late organogenesis (day 13 or 15) were similarly treated. To determine whether the sham-exposed rats were affected significantly by handling, transport, or restraint, their results were compared with those of the cage controls.

The results on embryotoxicity indicated that the cage controls and the sham-exposed rats did not differ significantly from one another at each gestation stage. Specifically, the percentages of preimplantation loss and dead or resorbed conceptuses for the rats sham-exposed during the preimplantation period were higher than for the cage controls, but the differences were not statistically significant, and neither were the differences in mean fetal weight and mean crown-rump length between the cage controls and the sham groups at each of the three gestation stages.

The mean fetal crown-rump lengths for the rats exposed to RFR on days 1, 3, and 5 were each slightly lower than for the combined groups of rats sham-exposed during that gestation stage, but only the differences for days 1 and 5 were significant. The percentages of dead or resorbed conceptuses for the rats exposed to RFR on gestation days 7, 9, and 11 were 29%, 49%, and 18%, respectively, as compared with 11% for the combined groups of rats sham-exposed on those days; only the differences of percentages for days 7 and 9 were significant. In addition, the fetal weights and crown-rump lengths for the RFR rats on each of these days were both significantly lower than for the combined sham groups. This was also true for the values of these two endpoints on days 13 and 15 relative to the means for the combined sham groups for that gestation stage. Thus, maximum embryotoxicity was induced by exposure to the RFR on gestation day 9.

Regarding the occurrence of terata, the differences in percentages of external, skeletal, or visceral abnormalities between the fetuses of the cage controls and those of the sham-exposed rats were nonsignificant with one exception: 4% of the fetuses of the rats sham-exposed during organogenesis (day 7, 9, or 11) exhibited major visceral abnormalities as compared with 0% of the cage-control fetuses, a significant difference. The percentages of fetal external abnormalities were 0 for all the sham groups, but significant percentages were found for the RFR groups on all days except 1 and 5, with the largest value (67%) for day

9. Significant differences between RFR and sham groups for major skeletal abnormalities were obtained for all days except 3, 5, and 13, with maximum value (60%) again on day 9. Skeletal variations were significant for all days, with day 9 once more yielding the largest value (83%). Major visceral abnormalities were significant only for day 9 (65%). No significant sex-related differences were found.

Only 3 preimplantation fetuses, 5 early-organogenesis fetuses, and 1 late-organogenesis fetus of the sham groups were abnormal, and only 3 cage-control fetuses were abnormal. In the RFR-exposed groups, more than 200 types of abnormalities were observed, most of which occurred only once. The greatest variety of abnormalities (17) occurred for exposure on gestation day 9. Microphthalmia or anophthalmia with associated small, narrow cranial orbits were present in 25-39% of all viable fetuses; exencephaly and the associated defects of protruding tongue and aplasia of the upper cranial bones were evident in 17-22% of the fetuses; and other severe malformations were seen in 6-14% of the fetuses.

Lary et al. (1983) subsequently sham-exposed or exposed 5 groups (each 30 to 41 rats) to 27.12-MHz fields at 55 A/m and 300 V/m (about 11 W/kg) on gestation day 9, which caused a relatively rapid increase in colonic temperature. Group I was sham-exposed for 2.5 hr. RFR-exposure of each rat in Group II was terminated when colonic temperature reached 41.0 deg C (duration 14-22 min). In Group III, 41.0 deg C was maintained for 2 hr more by on-off RFR-switching (total exposure time 137-144 min). Exposure of Group IV was terminated when colonic temperature reached 42.0 deg C (13-33 min). In Group V, 42.0 deg C was maintained for 15 min more by on-off switching of the RFR (34-55 min total exposure time).

About two-thirds of the rats bred and treated were actually pregnant at euthanasia on gestation day 20. There were no apparent differences in mating weight, exposure weight, or colonic temperature just prior to treatment between pregnant and nonpregnant rats or among the five groups of pregnant rats. The mean percentages of dead or resorbed conceptuses per litter for Groups II and III did not differ significantly from the mean for Group I, i.e., attaining or prolonging colonic temperature 41.0 deg C had no effect on this endpoint. Embryotoxicity was increased nonsignificantly by exposure to attain 42.0 deg C, but prolongation of exposure at that temperature for 15 min yielded a significant increase. Qualitatively similar results were obtained for mean fetal weights per litter and crown-rump lengths.

Comparing the five groups successively, there were monotonic increases in severity in both percentage of malformed fetuses and ratio of litters affected, with by far the largest change for prolongation of 42.0 deg C. Similar results were obtained for the percentages of live fetuses that had visceral malformations, the largest change again occurring for prolonged exposure at 42.0 deg C.

As in Lary et al. (1982), the authors ascribed the observed teratogenic effects to the hyperthermia induced by the RFR, citing the study by Edwards (1978), who demonstrated that excessive heat per se is a

teratogen. In addition, as noted by Lary et al. (1983), the existence of a colonic-temperature threshold for teratogenesis in the rat is supported by the in-vitro results of Cockcroft and New (1975), who subjected explanted rat embryos grown in culture during gestation days 10-12 to incubation at a temperature of 40 or 41 deg C (2-3 deg C above normal) for 12-46 hr. Nearly all of the embryos incubated at 41 deg C developed severe abnormalities, as compared with only about half of those incubated at 40 deg C.

Because of the high intensities of RFR used by Dietzel (1975) and Lary et al. (1982), the relevance of their findings to possible teratogenesis in humans exposed to much lower levels of RFR in the HF range might be questioned. However, Conover et al. (1980) surveyed industrial RFR plastic sealers operated (mostly by women) in the range 6-38 MHz and found that occupational exposure to the fields generated by many of the units (most at 27.12 MHz) exceeded the limits of electric and magnetic field specified in ANSI (1974), which were 200 V/m and 0.5 A/m. In ANSI (1982), the limits specified at 27.12 MHz are even lower, 70 V/m and 0.175 A/m.

In one of a pair of studies, Jensh et al. (1982a) exposed groups of up to 4 pregnant Wistar albino rats in individual Acrylite cages to 915-MHz CW RFR at 10 mW/sq cm for 6 hr/day without food and water in an anechoic chamber on gestation days 1 to 21. The mean maternal body weight over the gestation period was 0.28 kg, from which the authors derived a mean SAR of 3.57 W/kg. For this investigation, 11 pregnant rats exposed to the RFR comprised the "experimental" group and 4 sham-exposed rats comprised the "concurrent-control" group. In addition, 5 rats kept in home cages (the HC group) and 10 rats kept daily for 6 hr in the anechoic chamber (the AC group) served as two "baseline-control" groups.

The rats were euthanized on gestation day 22. The weights of maternal brain, liver, kidneys, and ovaries were measured and normalized to term body weights. No statistically significant differences in organ-to-body-weight ratios were found between the HC and AC baseline control groups or between the RFR-exposed and concurrent-control groups for any of the organs. However, significant differences were found between the baseline-control groups and the concurrent-control group, results ascribed to the significantly lower mean body weights of the baseline groups, which consisted of younger animals than in the RFR-exposed and concurrent-control groups. The unnormalized mean organ weights showed no significant differences among the four groups.

There were no statistically significant differences in mean litter size or mean 21-day-old fetal weight among the four groups. Only one fetus, in the AC baseline group, was abnormal. Resorption rates for HC and AC baseline groups were found to be 7.1% and 12%, respectively. For the RFR-exposed group, the resorption rate was 4.4%. In the concurrent-control group, an entire litter of 13 fetuses was resorbed by one of the rats; inclusion of these resorptions yielded a rate of 25.5%.

Not clear were the differences in treatment between the baseline-AC

and the concurrent-control (sham-exposed) groups. Also, the significant difference in mean body weights between these two groups tends to confound comparisons between them of the various biological endpoints studied. Thus, only the comparisons between the RFR-exposed and sham-exposed groups seem pertinent. The results for the latter two groups showed no statistically significant differences in any of the biological endpoints measured. These negative findings are consonant with those of Chernovetz et al. (1977) and Berman et al. (1981) at 2.45 GHz and of Lary et al. (1982) at 27.12 MHz, which showed that much higher SARs are necessary for teratogenic effects in rats.

In the companion study of this pair, Jensh et al. (1982b) similarly exposed groups of up to 4 rats (11 total) for 6 hr/day on gestation days 1 to 21 to 915-MHz CW RFR at 10 mW/sq cm (about 4 W/kg), with a group of 4 sham-exposed rats serving as concurrent controls. Again, an HC group of 5 rats kept in home cages and an AC group of 10 rats kept daily for 6 hr in the anechoic chamber without RFR served as baseline-control groups. After delivery of the initial litters (F1a offspring), neonatal weights were recorded weekly until age 87 days. These neonates were given the following four reflex tests, starting on the postnatal day indicated. The expected mean age for achieving criterion performance, based on results for 30 colony-control litters, is also indicated. The tests were: surface righting (day 3, criterion age 9.2 days), air righting (day 14, criterion age 14.0 days), auditory startle (day 7, criterion age 14.0 days), and visual placing (day 16, criterion age 23.7 days). The age for eye opening was also noted, starting on day 12. These neonates were weaned on day 30.

At age 60 days, the F1a offspring were given either a conditioned avoidance response (shuttle-box) test or a water T-maze test and two of the following four tests: open field, 24-hr activity wheel, forelimb hanging, swimming. At 90 days of age, half these offspring were killed and examined for histopathology. The remaining offspring were bred in four groups: control male to control female, control male to RFR-exposed female, RFR-exposed male to control female, and RFR-exposed male to RFR-exposed female. The resulting litters (F2) were examined prenatally for teratogenesis. Also, the original females were rebred 40 days after delivery of the F1a offspring (but not reexposed to RFR) and the resulting fetuses (F1b) were examined for teratogenesis.

Results for the initial pregnancy showed no significant differences in maternal weight, weight gain, or F1a mean litter size. Only one abnormal neonate, in the AC group, was found. The mean weekly weights of the RFR-exposed F1a neonates were significantly larger than for the concurrent-control neonates through age 24 days, after which the differences were statistically nonsignificant. There were also some significant weight differences, at various ages, among the baseline (HC and AC) groups and the concurrent-control group. In all four reflex tests, the RFR-exposed F1a neonates achieved criterion performance significantly sooner than the concurrent controls. However, there was no significant difference in mean age of eye opening. The behavioral tests at age 60 days yielded no significant differences among the four groups. Necrop-

sies of the F1a litters at 90 days showed no significant differences between the RFR-exposed and concurrent-control groups in organ weights or organ/body weight ratios.

The second breeding of the original females yielded no significant differences between the RFR- and concurrent-control groups in maternal weight or mean litter size, and no abnormal offspring were evident. Also, subsequent necropsies of these mothers showed no significant differences in mean organ weights or organ/body weight ratios. In the cross breeding of F1a males and females to obtain F2 fetuses, there were no significant RFR-related differences in maternal weight, percentage of resorptions, fetal weight, or litter size.

The Jensh et al. finding of significantly larger perinatal mean weekly weights for the RFR-exposed F1a neonate rats than for the concurrent controls is opposite to that found by Berman et al. (1982a) in mice exposed to 2.45-GHz RFR at 28 mW/sq cm (16.5 W/kg). This and the other minor effect found by Jensh et al. (earlier achievement of criterion performance in the reflex tests by the RFR-exposed rats) both appear to indicate that prenatal exposure of rats to relatively low levels of RFR may be beneficial, but such findings require independent verification.

Jensh et al. (1983a, 1983b) performed a similar pair of studies, but with 2.45-GHz RFR. In preliminary experiments involving exposures at up to 30 mW/sq cm, the authors found that 20 mW/sq cm was the highest level that yielded no significant increases in colonic temperature in near-term rats. They then exposed 11 pregnant rats in groups of up to 4 each daily for 6 hr/day throughout gestation at 20 mW/sq cm. From Durney et al. (1978), the authors estimated that the mean SARs during gestation days 0-1, 7-8, and 20 were 5.2, 4.8, and 3.6 W/kg, respectively. Three concurrent-control (sham-exposed) rats, 10 AC rats, and 5 HC rats served for comparisons. All of the rats were euthanized on gestation day 22, the numbers and positions of all live and dead fetuses were noted, and the fetuses were examined for abnormalities. There were no RFR-induced significant differences in maternal weight gain during pregnancy, term maternal organ weights (brain, liver, kidneys, ovaries), term fetal weight, resorption rate, or abnormality rate, which led the authors to conclude that protracted exposure of the dams throughout gestation to 2.45-GHz RFR at 20 mW/sq cm (5.2-3.6 W/kg) is not embryotoxic.

In the companion study, Jensh et al. (1983b) similarly treated other RFR (12), concurrent-control (8), and baseline-control (59) pregnant rats, but permitted them to come to term. The differences among groups for initial or term maternal weight or weight gain during pregnancy were not significant. Comparative ranking of growth rates of the F1a offspring during corresponding periods up to 87 days of age indicated that the RFR group had the highest growth rate, followed in succession by the AC, concurrent-control, and HC groups, but the differences were not statistically significant. Linear-regression analysis of these weight data also showed nonsignificance. Comparison of results on neonatal reflex tests (surface righting, air righting, auditory startle, visual placing) and on five of the six behavioral tests at age 90 days (water T-maze,

conditioned avoidance response, open field, forelimb hanging, swimming) showed no significant differences among groups. In the sixth behavioral test (activity wheel), both the males and females of the RFR group were significantly more active than their respective control groups. There were no significant differences among groups in the results of cross-breeding F1a offspring or in the results of teratologic examination of dams rebred 10 days after weaning the F1a offspring or of the resulting F2 offspring.

In the first of still another pair of studies, Jensh (1984a) exposed 10 pregnant rats (and 1 rat later found to be not pregnant) from above to 6-GHz RFR at 35 mW/sq cm, which did not increase colonic temperature significantly. From Durney et al. (1978), the author estimated the mean SAR to be 7.28 W/kg. Ten each concurrent-control and AC rats and 5 HC rats were used for comparison. On gestation day 22, half the dams of each group were decapitated. The remaining dams were used for postnatal analysis, (see Jensh, 1984b, below). In addition to the teratologic endpoints assessed in the previous studies, peripheral blood samples from the dams were analyzed on gestation day 22 for hematocrit and hemoglobin, and counts were made of total leukocytes and percentages of lymphocytes, monocytes, neutrophils, eosinophils, and basophils.

There were no significant RFR-induced differences in any of the teratologic endpoints studied except for mean fetal weight at term, which was significantly lower for the RFR group than for the concurrent-control (sham) group. However, so was the difference between the sham and AC groups and between the HC and AC groups, which could indicate that lower mean fetal weight of the RFR group may not have been RFR-related.

The blood analyses, presented for 7 of the RFR dams and 8 sham dams, showed no significant differences in hematocrit, hemoglobin, or white blood cell count. Also, the differential white blood cell counts showed no significant differences in neutrophils, eosinophils, or basophils. However, the mean monocyte count was significantly lower, and the mean lymphocyte count was almost significantly higher, for the RFR dams than the sham dams. (No blood-analysis data were presented for the HC or AC dams or for 3 of the RFR dams.)

Another point of conjecture is whether teratogenic effects would be expected for exposure from above to 6-GHz RFR at 35 mW/sq cm (estimated whole-body SAR of 7.28 W/kg). At this frequency, the penetration depth for muscle is about 0.7 cm, compared with about 2.4 cm at 915 MHz and 1.7 cm at 2.45 GHz. Therefore, the local SARs in the uteri may have been much lower at 6 GHz even though the whole-body SAR was much larger than in the earlier studies. In this context, it may be misleading to compare whole-body SARs for the three frequencies, and the author did not do so.

In the companion study, Jensh (1984b) culled each F1a litter of the remaining dams to 4 male and 4 female pups (total 124 pups), which were subjected to the four neonatal reflex tests noted above and to negative geotaxis. Starting at age 60 days, the behavioral tests noted above

were initiated on 121 pups. Starting at age 90 days, F1a offspring were bred within/across groups as before, and teratologic evaluations were completed on 659 F2 term fetuses. The original dams were rebred 10 days after weaning the F1a pups, and teratologic evaluations were completed on 263 F1b offspring. Organ weight analyses were completed on 17 original dams and 181 F1a adult offspring, and blood analyses on 21 of these dams and 131 of their offspring.

The difference in mean maternal weights of the RFR and sham groups on gestation day 0 of the first breeding was nonsignificant ($p>0.05$, t-test). On gestation day 21, the mean maternal weight for the RFR group was significantly smaller ($p<0.02$) than for the sham group, yielding mean weight gains of 42.1% and 45.2% respectively for the RFR and sham dams. However, the mean weight gain of the HC group was 45.8%, which was close to that of the sham group, but the mean for the baseline AC group was 42.8% or close to that of the RFR group. The mean litter size for the RFR dams was 9.55 fetuses, as compared with 12.00 for the sham group. The mean litter sizes for the HC and AC groups were respectively 12.40 and 11.20.

Examination of the F1a pups on postnatal day 3 revealed that 3 pups from one RFR-exposed dam had cataracts (unilateral in 2 pups and bilateral in 1 pup), 1 pup from a sham-exposed dam had bilateral cataracts, and 1 pup from an AC dam had a unilateral cataract. No other abnormalities were evident.

The mean weights of 68 RFR-exposed pups and 63 sham-exposed pups on day 3 were 9.1 and 9.9 g, respectively, a significant difference ($p<0.01$). In subsequent weekly weighings, the differences were progressively less significant, becoming nonsignificant ($p>0.05$) at about 38 days of age. On day 3, however, the mean weight of 111 AC pups was only 8.1 g and remained significantly lower than for the RFR-exposed pups throughout the subsequent weekly weighings (to age 87 days).

The mean ages for eye opening for 69 of the RFR-exposed and 55 sham-exposed F1a pups were 16.8 and 17.4 days, respectively, a significant difference. Although not mentioned in the text, the mean ages for visual placement shown in the tabulated results were 23.0 and 24.7 days, respectively, also a significant difference. (Comparative data were not presented for HC or AC offspring.)

The results for the adult behavioral tests were characterized by large variances for all groups. In the conditioned-avoidance-response test, the mean numbers of premature crossings on the 5th day of testing by 33 RFR-exposed and 29 sham-exposed rats irrespective of sex did not differ significantly from one another, but both values were significantly lower than for 48 baseline-control rats. Similar results were obtained on retest one week later. However, the author noted that the RFR-exposed females consistently made more premature crossings than the sham-exposed females. There were also no significant differences in mean numbers of shock avoidances on test and retest among the combined male and female RFR, sham, and baseline groups, but the author noted that the sham-

exposed females had significantly more shock avoidances and fewer shocks than the sham-exposed males.

There were no significant differences in mean time for the water T maze between males and females in either the RFR group or the sham group, or between the RFR and sham groups of either sex. However, 77% of the RFR-exposed females achieved criterion performance, compared with 100% for the sham-exposed females. The corresponding values for the males were 93% and 94%, yielding totals of 84% for the RFR-exposed rats and 96% for the sham-exposed rats.

Regarding the swimming tests, the author stated: "Statistical analyses invariably indicated that when significant differences ($P<0.05$) occurred between the baseline control and the irradiated groups, significant differences also occurred between the baseline and concurrent control [sham-exposed] groups."

The results of the open-field, hanging, and activity-wheel tests, presented without regard to sex, showed no significant differences between RFR- and sham-exposed rats, but both groups differed significantly from the baseline controls in hanging and activity.

The results of breeding the adult F1a rats were that the mean maternal weight increase during gestation of (in-utero) RFR-exposed females bred with RFR-exposed males (32.7%) was significantly less than for colony-control females bred with RFR-exposed males (44.7%) or for RFR-exposed females bred with colony-control males (37.0%) or for sham-exposed females bred with sham-exposed males (39.5%). Also significant was the weight-increase difference between the colony-control females mated with RFR-exposed males (44.7%) and RFR-exposed females mated with colony-control males (37.0%).

No data were presented on results of breeding colony-control rats with colony-control rats or with sham-exposed rats of either sex; however, the author stated: "The group in which only the mother was irradiated (irradiated female x colony control male) did not significantly differ ($P>0.05$) in weight gain from the colony control female x sham male group but did differ significantly ($P<0.05$) from the colony control female x irradiated male group as well as the sham female x sham male group ($P<0.01$)." (Reviewer note: by t-test, the last difference, 37.0% vs 39.5%, was not significant.)

Regarding the F2 offspring, the author stated: "Mean litter sizes differed significantly only between the irradiated female x irradiated male and the sham female x sham male groups ($P<0.05$). Both the litter size and the resorption rate varied inversely with the exposure groups. That is, the highest resorption rate (8.7%) and the smallest litter size (12.2) occurred in the irradiated female x irradiated male group, the two irradiated x colony control groups were intermediate, and the sham female x sham male group was the lowest in resorption rate (4.5%) and largest in litter size (14.8). Correlation coefficient analyses revealed a significant direct correlation between maternal weight gain and

mean litter size ($P<0.05$) in all groups." However, t-tests by the reviewer of the tabulated data indicated that the differences among the four groups in mean F2 litter size and mean fetal weight were not significant ($p>0.05$).

Mean organ-to-body weight ratios of RFR- and sham-exposed adult F1a males differed significantly ($p<0.05$) only for the left kidney and the right testis, with the mean values larger for the RFR group. However, the values for both groups were significantly larger ($p<0.01$) than for the baseline HC and AC groups. For the RFR- and sham-exposed females, the only significant ratio difference was for the liver ($p<0.02$), but again the values for both groups were significantly larger ($p<0.001$) than for the HC and AC groups.

The author summarized the results for hematocrit, hemoglobin, and white blood cell counts as follows:

"Nonpregnant females and pregnant term females also did not differ significantly ($P>0.05$) among all groups across the two generations. In every instance, when pregnant term females were compared with nonpregnant females, males from either of the two concurrent control groups (sham or colony control), and across two generations, there was a statistically significant difference ($P<0.05$), the pregnant females having markedly lower hematocrit values."

"Comparison of hemoglobin values indicated that these blood levels were significantly decreased in all pregnant females in all groups across two generations when compared to males ($P<0.001$) and all nonpregnant females ($P<0.05$) except the colony control rebred nonpregnant females."

"Statistical analysis of white blood cell counts indicated that F1a irradiated males had a significantly higher ($P<0.05$) count compared to concurrent control males or to irradiated or control females (pregnant or nonpregnant) across two generations. Statistical analysis of the differential white blood cell counts indicated that pregnant females had a significantly higher neutrophil count and a correspondingly lower lymphocyte count than nonpregnant females ($P<0.05$). Nonpregnant females had an average neutrophil count of 15 and an average lymphocyte count of 78. Neutrophil and lymphocyte counts of males were intermediate."

In his overall summary and conclusion, the author stated: "Several subtle psychophysiologic alterations occurred in animals exposed in utero to a 35 mW/sq cm power density level of 6000-MHz microwave radiation in the absence of morphologic alterations. The sexes appeared differentially affected by exposure to this radiation. Irradiated females exhibited decreased learning ability in the water T maze test but the males were unaffected. Irradiated females exhibited decreased activity levels, and males showed increased activity levels, in the open field test. [Note by reviewer: The last two statements appear to be contrary to the behavioral results discussed above.] Subtle shifts in the F1a population reproductive parameters indicate possible long-term

irradiation effects. These studies indicate that this power density level at this frequency may be deleterious to the rat, but that lower power density levels may not be. Functional evaluations are not conclusive in the absence of correlative structural data, since functional data are an addition to and not a substitute for structural data." [Note by reviewer: The statements regarding decreased female learning ability and activity appear to be contrary to the results reported in the body of the paper.]

A noteworthy point regarding the use of multiple behavioral tests on the same rats is an investigation (not involving RFR) by Jensh et al. (1981) showing that performance of a task by rat offspring does not alter significantly the subsequent performance of an unrelated task.

Perhaps the most important finding of this study was the absence of any terata in F1a, F1b, and F2 offspring from prolonged exposure of rats (8 hr/day throughout their first pregnancy) to 6-GHz RFR at 35 mW/sq cm (whole-body SAR of about 7 W/kg). (The few cataracts observed in the F1a offspring appeared to be unrelated to RFR exposure.) This finding is consonant with the results of Berman et al. (1981) on pregnant rats exposed to 2.45-GHz RFR for 100 min daily at 28 mW/sq cm (whole-body SAR of 4.2 W/kg) on gestation days 6 through 15.

Merritt et al. (1984) exposed 10 pregnant Sprague-Dawley rats, each unrestrained in a cylindrical Plexiglas cage within a circular-waveguide system (Guy et al., 1979), to circularly polarized 2.45-GHz pulsed RFR (8-microsecond pulses at 830 pps) for 24 hr/day starting on gestation day 2 and ending on gestation day 18. The power absorbed by each rat was determined from measurements of forward, reflected, and transmitted powers without and with the rat present. From Durney et al. (1980), p. 60, the incident average power density of circularly polarized RFR corresponding to 0.4 W/kg in a prolate-spheroidal model of a medium rat exposed end-on was estimated to be about 2 mW/sq cm. Based on this estimate and on power measurements on rat carcasses of different masses, the input power was varied to maintain the SAR constant at 0.4 W/kg for each dam as its mass increased during the exposure period. Ten rats similarly housed were concurrently sham-exposed. All 20 waveguides were in a room maintained at 24 +/- 2 deg C and 50-60% relative humidity. Water and food were provided freely during exposure via a bottle and food-pellet holder decoupled from each cage and waveguide by quarter-wavelength chokes to minimize external power losses.

All 20 rats were pregnant when they arrived on gestation day 2. They were weighed, immediately placed randomly in the 10 RFR- and 10 sham-exposure waveguides, and exposed. They were reweighed every fourth day. On gestation day 18, the dams were euthanized and the fetuses were removed. After each fetus was weighed, its brain was dissected out, weighed, homogenized, and assayed for RNA, DNA, and protein, with each of the latter three expressed in terms of both mg/brain and microgram/mg of brain tissue (totaling 8 endpoints). The difference between the two groups for each of the 8 endpoints was nonsignificant ($p>0.05$).

To determine the effects of RFR exposure on brain development, a regression of mean litter brain weight on mean litter body weight was calculated for the sham group and plotted. Scattered about the line were the mean values for the RFR group. Based on Edwards (1969), the criterion used for microencephalous litters was a regression line two SEMs below the regression line for the sham group. All RFR mean values were above the criterion line, i.e., no litter was micrencephalous.

It is interesting to note that all of the negative findings above were for rats. By contrast, RFR-induced teratogenesis (growth retardation) in the mouse and hamster was reported, for example by Berman et al. (1982a, 1982b). This effect appears to have been thermally induced, a conclusion supported by the results of Inouye et al. (1982) and Nawrot et al. (1981). These differences in response among the three species of rodents may be an indication that none is a satisfactory surrogate for humans with regard to possible RFR teratogenesis.

3.3.2.2 PRIMATES

As discussed in Section 3.7.1, Kaplan et al. (1982), in a study designed primarily for seeking possible effects of chronic exposure to RFR on mother-offspring behavioral patterns and the EEG, exposed 33 female squirrel monkeys near the beginning of the second trimester of pregnancy to 2.45-GHz RFR in multimode, mode-stirred microwave cavities at whole-body SARs of 0.034, 0.34, or 3.4 W/kg (respectively equivalent to 0.1, 1, and 10 mW/sq cm of plane-wave RFR) for 3 hr/day, 5 days/week, until parturition. Eight pregnant monkeys were sham-exposed for the same periods. After parturition, 18 of the RFR-exposed dams and their offspring were exposed to RFR for an additional 6 months; then the offspring were exposed without the dams for another 6 months.

Two of the dams exposed at 3.4 W/kg (10 mW/sq cm) and one dam exposed at 0.34 W/kg (1 mW/sq cm) died, all within a day or two after parturition. These dams comprised only 10% of the total exposed, but similar deaths had not occurred in more than 250 pregnancies recorded during the five previous years in the squirrel-monkey colony of that laboratory.

Live births were recorded for 30 of the 33 RFR-exposed dams and for all 8 sham-exposed dams. (The stillbirths were for two dams exposed at 0.034 and one at 3.4 W/kg.) The relative numbers of live births among RFR groups irrespective of when they were exposed were comparable: 2/9, 2/12, and 5/9 in the 0.034-, 0.34-, and 3.4-W/kg groups, respectively, vs 0/8 in the sham group. However, as discussed below, the relative numbers of infant deaths were not comparable.

Offspring were weighed weekly for the first 8 weeks of age and monthly thereafter until they were 1 year old. There were no significant differences between the groups at any age.

Developmental tests designed to assess perceptual and motor capabilities were given weekly, at ages 1-8 weeks. These tests were righting, orienting, climbing down, climbing up, and directed locomotion. There

were no significant differences among groups in the first four tests. In the fifth test, the infant was released into one end of a wire-mesh alleyway, with its mother visible at the other end. The alleyway was divided into six segments of equal length and the segment closest to the mother traveled by the infant within 30 seconds and the time taken to reach the mother if this occurred within 30 seconds were scored. With increasing age, infants generally moved closer to their mothers, and no significant differences were found among groups in distance traveled to mother. However, there were significant differences in the numbers of infants that reached the section nearest their mothers in the sixth, seventh, and eighth weeks. Of the sham-exposed infants, 88%, 100%, and 100% respectively did so. For the groups exposed only prenatally, the corresponding percentages were 100, 66, and 100 at 0.034 W/kg; 50, 50, and 100 at 0.34 W/kg; and 0, 0, and 50 at 3.4 W/kg. For the groups exposed prenatally and postnatally, the percentages were 60, 60, and 80 at 0.034 W/kg; 60, 75, and 75 at 0.34 W/kg; and 40, 40, and 40 at 3.4 W/kg.

Regarding infant mortality, of the infants exposed only prenatally and born alive, 2 of the 4 exposed at 0.034 W/kg died (at ages 32 and 83 days), none of the 6 exposed at 0.34 W/kg died, and 1 of the 4 exposed at 3.4 W/kg died (at age 4 days); of the 16 exposed both prenatally and postnatally, none of the 5 exposed at 0.034 W/kg died, 2 of the 6 exposed at 0.34 W/kg died (at ages 38 and 49 days), and 4 of the 5 exposed at 3.4 W/kg died (at ages 58, 78, 143, and 177 days). The annual mortality rate during the first year of life for the five previous years of the colony averaged 20-25%, so the numbers of infant deaths at 0.034 and 0.34 W/kg were not atypical; however, the 4 deaths of 5 infants in the 3.4-W/kg group exposed prenatally and postnatally were much larger than the normal mortality rate, and appeared to be a direct result of exposure to that level of RFR. None of the 8 sham-exposed infants died during the study, which was also atypical, and comparison of the two groups showed the difference to be statistically significant ($p<0.01$, Fisher exact probability test).

In all but one case, the infant deaths occurred without warning; each was found in its home cage in the morning. Necropsies had not been planned, were not performed on any of the adults, and were performed on only 4 of the 9 dead infants. In none of these cases could the cause of death be determined. However, as stated in a note added in proof to Kaplan et al. (1982), a followup study, with infant mortality as the major endpoint and sufficient numbers of animals for greater statistical validity, yielded negative results, i.e., no statistically significant differences in infant mortality between RFR and control groups.

Several epidemiologic studies were conducted on possible teratogenic effects of RFR in humans, notably by Peacock et al. (1971) and Burdeshaw and Schaffer (1977). The findings of these studies were discussed in Section 3.1.1.

REFERENCES:
ANSI (American National Standards Institute), C95.1-1974
SAFETY LEVEL OF ELECTROMAGNETIC RADIATION WITH RESPECT TO PERSONNEL
Published by the Institute of Electrical and Electronics Engineers, New York (1974)

ANSI, C95.1-1982
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
Published by the Institute of Electrical and Electronics Engineers, New York (1982)

Berman, E., J.B. Kinn, and H.B. Carter
OBSERVATIONS OF MOUSE FETUSES AFTER IRRADIATION WITH 2.45 GHZ MICROWAVES
Health Phys., Vol. 35, pp. 791-801 (1978)

Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF RAT FETUSES AFTER IRRADIATION WITH 2450-MHZ (CW) MICROWAVES
J. Microwave Power, Vol. 16, No. 1, pp. 9-13 (1981)

Berman, E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982a)

Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF SYRIAN HAMSTER FETUSES AFTER EXPOSURE TO 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 17, No. 2, pp. 107-112 (1982b)

Bollinger, J.N., R.L. Lawson, and W.C. Dolle
RESEARCH ON BIOLOGICAL EFFECTS OF VLF BAND ELECTROMAGNETIC RADIATION
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report SAM-TR-74-52 on Contract F41609-73-C-0035, submitted by Southwest Research Institute, San Antonio, Texas (1974)

Burdeshaw, J.A. and S. Schaffer
FACTORS ASSOCIATED WITH THE INCIDENCE OF CONGENITAL ANOMALIES: A LOCALIZED INVESTIGATION
Final Report, Report No. XXIII, 24 May 1973-31 March 1976, Contract No. 68-02-0791, EPA 600/1-77-016 (March 1977)

Chernovetz, M.E., D.R. Justesen, N.W. King, and J.E. Wagner
TERATOLOGY, SURVIVAL, AND REVERSAL LEARNING AFTER FETAL IRRADIATION OF MICE BY 2450-MHZ MICROWAVE ENERGY
J. Microwave Power, Vol. 10, No. 4, pp. 391-409 (1975)

Chernovetz, M.E., D.R. Justesen, and A.F. Oke
A TERATOLOGICAL STUDY OF THE RAT: MICROWAVE AND INFRARED RADIATIONS COMPARED
Radio Sci., Vol. 12, No. 6S, pp. 191-197 (1977)

Cockcroft, D.L. and D.A.T. New
EFFECTS OF HYPERTHERMIA ON RAT EMBRYOS IN CULTURE
Nature, Vol. 258, pp. 604-606 (1975)

Conover, D.L., W.E. Murray, Jr., E.D. Foley, J.M. Lary, and W.H. Parr
MEASUREMENT OF ELECTRIC- AND MAGNETIC-FIELD STRENGTHS FROM INDUSTRIAL RADIO-FREQUENCY (6-38 MHZ) PLASTIC SEALERS
Proc. IEEE, Vol. 68, No. 1, pp. 17-20 (1980)

Dietzel, F.
EFFECTS OF ELECTROMAGNETIC RADIATION ON IMPLANTATION AND INTRAUTERINE DEVELOPMENT OF THE RAT
Ann. N.Y. Acad. Sci., Vol. 247, pp. 367-376 (1975)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Durney, C.H., M.F. Iskander, H. Massoudi, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [THIRD EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-80-32 (1980)

Edwards, M.J.
CONGENITAL DEFECTS IN GUINEA PIGS: PRENATAL RETARDATION OF BRAIN GROWTH OF GUINEA PIGS FOLLOWING HYPERTHERMIA DURING GESTATION
Teratology, Vol. 2, pp. 329-336 (1969)

Edwards, M.J.
CONGENITAL DEFECTS DUE TO HYPERTHERMIA
Adv. Vet. Sci. Comp. Med., Vol. 22, pp. 29-52 (1978)

Greene, F.M.
DEVELOPMENT AND CONSTRUCTION OF AN ELECTROMAGNETIC NEAR-FIELD SYNTHESIZER
U.S. Department of Commerce, National Bureau of Standards, NBS Technical Note 652 (1974)

Guy, A.W., J. Wallace, and J.A. McDougall
CIRCULARLY POLARIZED 2450-MHZ WAVEGUIDE SYSTEM FOR CHRONIC EXPOSURE OF SMALL ANIMALS TO MICROWAVES
Radio Sci., Vol. 14, No. 6S, pp. 63-74 (1979)

Inouye, M., N. Matsumoto, M.J. Galvin, and D.I. McRee
LACK OF EFFECT OF 2.45-GHZ MICROWAVE RADIATION ON THE DEVELOPMENT OF PREIMPLANTATION EMBRYOS OF MICE
Bioelectromagnetics, Vol. 3, No. 2, pp. 275-283 (1982)

Jensh, R.P., A. Magaziner, and W.H. Vogel
EFFECTS OF MATERNAL ENVIRONMENT AND POSTNATAL MULTIPLE TESTING ON ADULT RAT OFFSPRING
J. Toxicol. Environ. Health, Vol. 7, Nos. 3-4, pp. 655-663 (1981)

Jensh, R.P., I. Weinberg, and R.L. Brent
TERATOLOGIC STUDIES OF PRENATAL EXPOSURE OF RATS TO 915-MHZ MICROWAVE RADIATION
Radiat. Res., Vol. 92, pp. 160-171 (1982a)

Jensh, R.P., W.H. Vogel, and R.L. Brent
POSTNATAL FUNCTIONAL ANALYSIS OF PRENATAL EXPOSURE OF RATS TO 915 MHZ MICROWAVE RADIATION
J. Am. Coll. Toxicol., Vol. 1, No. 3, pp. 73-90 (1982b)

Jensh, R.P., I. Weinberg, and R.L. Brent
AN EVALUATION OF THE TERATOGENIC POTENTIAL OF PROTRACTED EXPOSURE OF PREGNANT RATS TO 2450-MHZ MICROWAVE RADIATION: I. MORPHOLOGIC ANALYSIS AT TERM
J. Toxicol. Environ. Health, Vol. 11, pp. 23-35 (1983a)

Jensh, R.P., W.H. Vogel, and R.L. Brent
AN EVALUATION OF THE TERATOGENIC POTENTIAL OF PROTRACTED EXPOSURE OF PREGNANT RATS TO 2450-MHZ MICROWAVE RADIATION: II. POSTNATAL PSYCHOPHYSIOLOGIC ANALYSIS
J. Toxicol. Environ. Health, Vol. 11, pp. 37-59 (1983b)

Jensh, R.P.
STUDIES OF THE TERATOGENIC POTENTIAL OF EXPOSURE OF RATS TO 6000-MHZ MICROWAVE RADIATION--I. MORPHOLOGIC ANALYSIS AT TERM
Radiat. Res., Vol. 97, No. 2, pp. 272-281 (1984a)

Jensh, R.P.
STUDIES OF THE TERATOGENIC POTENTIAL OF EXPOSURE OF RATS TO 6000-MHZ MICROWAVE RADIATION--II. POSTNATAL PSYCHOPHYSIOLOGIC EVALUATIONS
Radiat. Res., Vol. 97, No. 2, pp. 282-301 (1984b)

Kaplan, J., P. Polson, C. Rebert, K. Lunan, and M. Gage
BIOLOGICAL AND BEHAVIORAL EFFECTS OF PRE- AND POSTNATAL EXPOSURE TO 2450 MHZ ELECTROMAGNETIC RADIATION IN THE SQUIRREL MONKEY
Radio Sci., Vol. 17, No. 5S, pp. 135-144 (1982)

Lary, J.M., D.L. Conover, E.D. Foley, and P.L. Hanser
TERATOGENIC EFFECTS OF 27.12 MHZ RADIOFREQUENCY RADIATION IN RATS
Teratology, Vol. 26, No. 3, pp. 299-309 (1982)

Lary, J.M., D.L. Conover, P.H. Johnson, and J.R. Burg
TERATOGENICITY OF 27.12-MHZ RADIATION IN RATS IS RELATED TO DURATION OF HYPERTHERMIC EXPOSURE
Bioelectromagnetics, Vol. 4, No. 3, pp. 249-255 (1983)

Merritt, J.H., K.A. Hardy, and A.F. Chamness
IN UTERO EXPOSURE TO MICROWAVE RADIATION AND RAT BRAIN DEVELOPMENT
Bioelectromagnetics, Vol. 5, No. 3, pp. 315-322 (1984)

Mitchell, J.C.
A RADIOFREQUENCY RADIATION EXPOSURE APPARATUS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-70-43 (1970)

Nawrot, P.S., D.I. McRee, and R.E. Staples
EFFECTS OF 2.45 GHZ CW MICROWAVE RADIATION ON EMBRYOFETAL DEVELOPMENT IN MICE
Teratology, Vol. 24, No. 3, pp. 303-314 (1981)

Nawrot, P.S., D.I. McRee, and M.J. Galvin
TERATOGENIC, BIOCHEMICAL, AND HISTOLOGICAL STUDIES WITH MICE PRENATALLY EXPOSED TO 2.45-GHZ MICROWAVE RADIATION
Radiat. Res., Vol. 102, No. 1, pp. 35-45 (1985)

Peacock, P.B., J.W. Simpson, C.A. Alford, Jr., and F. Saunders
CONGENITAL ANOMALIES IN ALABAMA
J. Med. Assoc. Ala., Vol. 41, No. 1, pp. 42-50 (1971)

Rugh, R., E.I. Ginns, H.S. Ho, and W.M. Leach
ARE MICROWAVES TERATOGENIC?
In P. Czerski et al. (eds.), BIOLOGICAL EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 98-107 (1974)

Rugh, R., E.I. Ginns, H.S. Ho, and W.M. Leach
RESPONSES OF THE MOUSE TO MICROWAVE RADIATION DURING ESTROUS CYCLE AND PREGNANCY
Radiat. Res., Vol. 62, pp. 225-241 (1975)

Smialowicz, R.J., J.B. Kinn, and J.A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

Stavinoha, W.B., A. Modak, M.A. Medina, and A.E. Gass
GROWTH AND DEVELOPMENT OF NEONATAL MICE EXPOSED TO HIGH-FREQUENCY ELECTROMAGNETIC WAVES
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report SAM-TR-75-51 on Contract F41609-74-C-0018, submitted by University of Texas Health Science Center, San Antonio, Texas (1975)

Stavinoha, W.B., M.A. Medina, J. Frazer, S.T. Weintraub, D.H. Ross, A.T. Modak, and D.J. Jones
THE EFFECTS OF 19 MEGACYCLE IRRADIATION ON MICE AND RATS
In C. C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8010, pp. 431-448 (1976)

3.3.3 CONCLUSIONS

Most studies of RFR-induced teratogenesis in Tenebrio molitor were done with RFR levels high enough to heat the subjects significantly, but the results of Carpenter and Livstone (1971) and Liu et al. (1975) appeared to indicate that RFR-induced teratogenesis is not entirely due to the heat produced by the RFR. However, Pickard and Olsen (1979) were unable to confirm such findings, and showed that the presence of uncontrolled non-RFR factors might account for such differences in findings. Also, Olsen and Hammer (1982) found large variations of local SAR in Tenebrio pupae, rendering inappropriate any comparisons of effects of RFR with those of radiant heat. Thus, there is no valid evidence for teratogenic effects in Tenebrio at nonthermogenic RFR levels.

A similar conclusion can be reached about the teratogenesis studies of McRee and coworkers with Japanese-quail eggs and about RFR-induced developmental abnormalities in hatched birds. On the other hand, Fisher et al. (1979) reported retardation of development in chicken embryos due to exposure of eggs to RFR at relatively low power densities (about 3.5 mW/sq cm average) at ambient temperatures selected to compensate for the rises in mean internal temperature, but the supposedly nonthermal basis for the effect is open to question because Clarke and Justesen (1983) showed that the internal temperature gradients within RFR-exposed eggs are much higher than in sham-exposed eggs.

Regarding the studies of RFR-induced teratogenesis and developmental abnormalities in mammals, the results for rodents were mixed. Though both positive and negative findings were obtained with mice, one effect, a significant retardation in postnatal growth due to RFR-exposure in utero was reported in several of the more recent studies (an effect found with hamsters as well). On the other hand, all of the studies with rats yielded negative results, an indication that the levels of RFR necessary to cause significant prenatal terata or postnatal growth or development retardation are close to, or above, the lethal level for the dams. This finding led Berman et al. (1981) to conclude that the mouse may be more suitable than the rat for studies of possible RFR-induced teratogenic effects in humans, a conclusion that appears specious in view of the large physiological differences between rodents and humans and among the three rodent species themselves. Clearly, such studies with nonhuman primates would be much more definitive. The negative findings of Kaplan et al. (1982) with squirrel monkeys are important, but firm conclusions should not be drawn on the basis of studies in one laboratory.

Overall, the findings of the investigations thus far of possible RFR-induced teratogenesis and developmental abnormalities appear to support the conclusion that such effects can occur from the heat produced by the RFR rather than from any special teratogenic properties of RFR, and that the likelihood of such effects occurring in humans from non-occupational exposure to RFR is negligible.

3.4 NERVOUS SYSTEM

Concern has been expressed that the interactions of RFR with the nervous system can give rise to various deleterious physiological effects. The RFR-auditory effect received early prominence because it had been cited as evidence that nonthermal effects can occur and because of an initial hypothesis that the effect could be due to direct RFR-stimulation of the central nervous system (CNS). Neither argument seems tenable, as noted above in Section 3.1.4.2. On the other hand, effects on the CNS may be manifested as alterations in behavior, fenestration of the blood-brain barrier that prevents passage of foreign agents from the vascular system of the brain into the surrounding tissue, changes in the histopathology and histochemistry of the CNS and of the EEG, and RFR-induced changes of efflux of calcium from brain tissue, the last being a subject of much controversy. These topics are discussed in the following sections.

3.4.1 BLOOD-BRAIN-BARRIER EFFECTS

The existence of a blood-brain barrier (BBB) in most regions of the brain has been established experimentally, but its specific morphology is still conjectural. This barrier normally provides high resistance to movements of large-molecular-weight, fat-insoluble substances (such as proteins or polypeptides) from the blood vessels into the surrounding cerebral extracellular fluid, to protect the brain from invasion by various blood-borne pathogens and toxic substances. Some investigators have reported that low levels of RFR can increase the permeability of the BBB to certain substances of large molecular weight. However, others were unable to confirm such effects.

Rodzilsky and Olszewski (1957) found that permeability changes in cerebral blood vessels could be induced by various non-RFR means, including those that produce heat necrosis.

Frey et al. (1975), in an endeavor towards defining the relationship between neural function and behavior, performed two experiments. In one, they studied the extent to which rats avoided exposure, in half of a shuttle box, to 1.2-GHz pulsed and CW RFR at the levels indicated below. The results of this behavioral experiment are discussed in Section 3.7. In the other experiment, they studied the effects of RFR exposure on the BBB. Ninety anesthetized male Sprague-Dawley rats in groups of 6 were exposed for 30 min to far-field 1.2-GHz pulsed RFR (0.5-ms pulses, 1000 pps) with heads toward the source at an average power density of 0.2 mW/sq cm or CW RFR at 2.4 mW/sq cm. For a prolate-spheroidal model of a medium rat in the K-polarization (Durney et al., 1978, p. 95), the corresponding SARs are estimated to have been about 0.04 and 0.5 W/kg. Sham-exposed rats served as controls. The tracer sodium fluorescein was injected into the femoral vein after exposure or sham exposure, and 5 min afterward, the rat was exsanguinated and the brain was removed, embedded in gelatin, refrigerated, and sectioned. The sections were viewed under ultraviolet light for fluorescence, the intensity of which was scored visually on a scale of 0 to 3 without

scorer knowledge about prior treatment.

Greater fluorescence was reported for the pulsed RFR (0.04 W/kg) than for the CW RFR (0.5 W/kg), but some control specimens also exhibited slight fluorescence. The authors regarded these results as evidence that exposure to RFR altered the BBB. However, the numbers of sections scored and the deviations from the means were not given, rendering it impossible to evaluate the statistical treatment of the data. Moreover, the use of a subjective scoring technique can be questioned, as well as the possibility of artifact because of the presence of fluorescein in some sham-exposed specimens.

Oscar and Hawkins (1977) exposed anesthetized rats for 20 min to 1.3-GHz RFR pulses (0.5 to 20 microseconds, 1000 to 5 pps) with heads toward the source at average power densities in the range 0.03-2 mW/sq cm (0.006-0.4 W/kg, Durney et al., 1978, p. 95) or to CW RFR at 0.3-3 mW/sq cm (0.06-0.6 W/kg). Controls were sham-exposed. Changes in permeability of the BBB to the C-14-labeled test substances D-mannitol (molecular weight 182.2 daltons), inulin (5000-5500 daltons), and dextran (60,000-75,000 daltons) were determined by the Oldendorf (1970, 1971) dual tracer technique: Following exposure, 0.2 ml of a mixture of the C-14 labeled test substance and tritiated water was injected rapidly into the rat's carotid artery as a bolus, the rat was decapitated 15 seconds later, each brain section was solubilized, liquid scintillation mixture was added, and the C-14 and H-3 radioactivities were assayed by liquid scintillation counting. The ratio of counts of C-14 to H-3 in samples of each brain region was normalized to a similar ratio for the injected solution. This normalized ratio (percentage) was defined as the brain uptake index (BUI), representing the relative amount of test substance lost to the brain in a single passage of the mixture through the brain's microcirculation.

For mannitol, the largest statistically significant changes in uptake occurred in the medulla, followed by the cerebellum and hypothalamus. In the medulla, the curve of mannitol uptake vs average power density was an inverted U for both pulsed and CW RFR. The maximum BUI for CW was about 9% (vs about 3.5% for the controls), at about 1 mW/sq cm (0.2 W/kg). For 0.5-microsecond pulses, 1000 pps, the maximum BUI was only about 7.5%, at about 0.4 mW/sq cm (0.08 W/kg); higher and lower power densities in each case yielded lower BUIs. For 10-microsecond pulses, 5 pps, BUIs of about 7% and 10% were obtained at only about 0.03 and 0.06 mW/sq cm (0.006 and 0.012 W/kg), respectively. Also indicated by these results was the possible existence of a power-density "window" within which BBB permeability is altered, but is not for power densities above or below the window. Similar results in the medulla were obtained for inulin, but the permeability changes for dextran were negligible.

To determine the duration of BBB permeability increases and recovery therefrom, Oscar and Hawkins (1977) similarly RFR- or sham-exposed unanesthetized rats. The rats were then anesthetized and injected with the mannitol mixture. Groups were euthanized at 8 min, 4 hr, or 24 hr after treatment and assayed for BUI. The results for the 8-min and 4-hr

groups were almost the same; both yielded statistically significant permeability increases over controls, with the largest changes again in the medulla. For the 24-hr groups, however, mannitol uptake did not differ significantly from controls in any brain region except for the medulla, in which the BUI was about 5.2% for the RFR group vs 3.8% for the controls, a significant increase.

The validity of these findings of RFR-induced BBB alterations by Oscar and Hawkins (1977) have been questioned on several grounds. In doubt are the assumptions underlying the Oldendorf (1970, 1971) methodology that tritiated water freely diffuses between the brain and its vascular system and that variations of cerebral blood flow (CBF) do not affect BUI values significantly. Moreover, injection of the dual-radiotracer mixture into a carotid rapidly as a bolus appears to be a prime source of artifact because of the high hydrostatic pressure produced.

Merritt et al. (1978) endeavored to replicate the studies of Frey et al. (1975) and Oscar and Hawkins (1977). They exposed rats for 30 min to 1.2-GHz pulsed RFR at peak power densities in the range from 2 to 75 mW/sq cm and 0.5 duty cycle, corresponding to average power densities of 1 to 38 mW/sq cm (0.2 to 7.6 W/kg, Durney et al., 1978, p. 95), or for 35 min to 1.3-GHz pulsed or CW RFR at average power densities in the range from 0.1 to 20 mW/sq cm (0.02 to 4 W/kg). They examined brain slices under ultraviolet light for transfer of fluorescein and under white light for transfer of Evans Blue dye (a visual tracer) across the BBB, and chemically analyzed various brain regions for their fluorescein content. They also measured the brain uptake of C-14-labeled D-mannitol and determined the BUIs. To validate these detection methods, they used hypertonic urea, known to alter the BBB, as an alternative agent to RFR. In addition, they heated rats for 30 min during sham-exposure in a 43-deg-C oven to appproximate the hyperthermia obtained at 38 mW/sq cm.

In their examination of brain slices, Merritt et al. (1978) found no evidence of fluorescein or Evans Blue dye transfer across the BBB of RFR-exposed rats, whereas penetration of the BBB was apparent for rats treated with urea instead of RFR. The analyses of fluorescein content corroborated these findings. However, fluorescein uptake was higher for the sham-exposed rats that were heated in the oven, an indication that hyperthermia of the brain is necessary to alter BBB permeability. In the C-14-mannitol study of the various brain regions, there were no significant differences in BUI between RFR- and sham-exposed rats, but BUI changes were evident for rats treated with urea. Also, the results (with 1.3-GHz CW RFR) showed no evidence of the power-density window reported by Oscar and Hawkins (1977).

The use of urea as a positive control (alternative agent to RFR) offers considerable weight to the negative findings by Merritt et al. (1978) on changes of BBB permeability by RFR in the absence of hyperthermia, especially the results of their chemical analyses of brain regions for fluorescein content. However, the basic uncertainties noted previously, whether significant artifacts were introduced by the kinds of biological techniques used, remain. Also, the effects on the overall

findings of the use of anesthesia in many animal experiments are difficult to ascertain. One well known consequence of anesthetizing rats is the induction of hypothermia, which could yield results that are different than those with thermonormic animals.

Preston et al. (1979) used C-14-labeled D-mannitol in a method similar to that of Oscar and Hawkins (1977), but with 2.45-GHz CW RFR instead of 1.3-GHz pulsed or CW RFR. In series 1, one anesthetized rat per day for 8 days was exposed (with head toward source) for 30 min at 0 (sham), 0.1, 0.5, 1, 5, or 10 mW/sq cm (0, 0.02, 0.1, 0.2, 1, or 2 W/kg, Durney et al., 1978, p. 95), totaling 48 rats. In series 2, one anesthetized rat per day for 6 days was exposed for 30 min at 0, 0.3, 1, 3, 10, or 30 mW/sq cm (0.06, 0.2, 0.6, 2, or 6 W/kg), totaling 36 rats.

Rectal temperatures measured before and after the 30-min exposures showed mean decreases ranging from 0.74 to 1.36 deg C for all groups except those exposed at 10 or 30 mW/sq cm; the mean temperature change was less than 0.1 deg C for the two 10-mW/sq-cm (2-W/kg) groups, and the 30-mW/sq-cm (6-W/kg) rats exhibited a mean increase of 1.5 deg C.

The results for both series showed nonsignificant differences ($p>0.05$, Student's t-test) between RFR- and sham-exposed rats in BUIs for each brain region. The mean BUIs for the cerebral cortex and diencephalon were about 22% irrespective of treatment. Those for the cerebellum and medulla were much higher and there was much more variability, related to the observation that both regions contained more C-14 and less H-3 than diencephalon or cortex.

Preston et al. (1979) also performed preliminary experiments to show that visible staining of the brain occurred with intravenous injection of Evans Blue dye as an indicator of disruption of the BBB by hypertonic solutions of propylene glycol. They then tested the BUI methodology by injecting 60% propylene glycol into the left common carotid (in lieu of RFR exposure), followed 2 min later by the C-14 mannitol/H-3 water injectate. For controls, saline was injected instead of propylene glycol. The results showed that propylene glycol greatly increased the mannitol BUIs (relative to saline); the highest BUIs were for the cortex and diencephalon.

Another experiment was performed to determine whether H-3 water injected intravenously would be distributed evenly in brain tissue or in the pattern obtained from intracarotid injection, i.e., highest uptake in the cerebrum and lowest uptake in the medulla. Rats were injected with 1 ml of 0.9% saline containing 10 microcuries of H-3 water. The rats were decapitated 1.5 min later and the concentrations of H-3 in the four brain regions were assayed. The highest and lowest concentrations were respectively in the diencephalon and cortex but none of the differences was significant. Thus, the lower H-3 concentrations found in cerebellum and medulla of rats injected via the common carotid were likely related to blood flow distribution, which led Preston et al. (1979) to believe that RFR-induced changes in CBF confounded the BBB results of earlier studies.

Rapoport et al. (1979) developed a method for measuring cerebrovascular permeability to C-14-labeled sucrose to obtain results independent of CBF rate. After anesthetizing each rat, catheters were inserted in a femoral vein and artery, C-14-labeled sucrose (5 microCuries) was injected intravenously, and arterial-blood samples were collected periodically during the next 10 min. The rat was then decapitated and the brain was dissected into the various regions. Liquid scintillation counting was used to determine the sucrose concentrations in the timed samples of whole blood and the plasma derived therefrom, and in each specific brain region.

Based on the assumptions that intravascular tracer diffuses into brain in proportion to the plasma concentration (C-plasma) at any sampling time and that back diffusion from brain is negligible during the 10-min sampling interval, the rate of tracer entry into any specific brain region at any sampling time is given by the product of C-plasma at that sampling time and PA, where P is the cerebrovascular permeability of that region and A is the capillary surface area of that region, neither of which is known separately. However, PA is given by the ratio of the measured tracer concentration in that brain region to the time-integral (obtained graphically) of the C-plasma values over the 10-min interval and is independent of cerebral blood flow rate. Regional blood volumes were determined in separate experiments, in which rats were euthanized 2 min and 40 min after tracer injection and similarly assayed.

To establish whether the method was useful for quantifying changes in BBB permeability, Rapoport et al. (1979), using intravenous Evans Blue as a visual tracer, osmotically opened the BBB of the rat by injecting hypertonic arabinose in a retrograde direction into the right external carotid artery for 30 seconds at a rate of 0.12 ml/s, intravenously injected C-14-labeled sucrose 5 min later, and treated the rat as described above. The results showed that the method is about 100 times more sensitive than dual-radiotracer techniques such as the BUI method.

Preston and Prefontaine (1980) used the method of Rapoport et al. (1979) to determine whether whole-body exposure of rats for 30 min to 2.45-GHz CW RFR with heads toward the source at 1 or 10 mW/sq cm (0.1 or 1 W/kg) alters BBB permeability to sucrose. They also used a specially designed applicator to expose only the head of the rat to the RFR for 25 min at estimated local SARs of 0.08, 0.3, or 1.6 W/kg. These authors obtained PA values for the rats exposed (whole-body or head only) to the RFR that were not significantly higher than for the sham-exposed rats, whereas the PA values for rats treated with arabinose were much higher.

Oscar et al. (1981), realizing the inadequacies of the BUI technique, also used another technique. They sham-exposed previously venous-catheterized but conscious rats for 5, 30, or 60 min, or exposed rats for 5, 15, 30, 45, or 60 min to 2.8-GHz RFR pulses (2 microseconds, 500 pps) at an average power density of 1 or 15 mW/sq cm (0.2 or 3 W/kg). Within 5 min after sham- or RFR exposure, they infused the rats with isotonic saline containing C-14-labeled iodoantipyrine through the catheter. They decapitated the rats 50 seconds after start of infusion,

excised the brain regions, and assayed each region for radioactivity, from which they calculated the local CBF (LCBF) by use of the Kety (1960) equation.

The results for the rats exposed at either power density showed LCBF increases of 10 to 144% in 16 of the 20 brain regions sampled. The largest statistically significant increases occurred in the pineal, hypothalamus, and temporal cortex of the rats exposed at 1 mW/sq cm (0.2 W/kg) and in the pineal, temporal cortex, inferior colliculus, and medial geniculate of the rats exposed at 15 mW/sq cm (3 W/kg). Because of these findings, the authors indicated that their previously reported BUIs (Oscar and Hawkins, 1977) may have been overly high. However, the C-14-iodoantipyrine results clearly demonstrated an alteration of brain activity at 15 mW/sq cm (3 W/kg).

In a subsequent study, Gruenau et al. (1982) used the method of Rapoport et al. (1979) to determine PA values for C-14-labeled sucrose in rats exposed for 30 min to 2.8-GHz pulsed RFR (2-microsecond pulses, 500 pps) at 0, 1, 5, 10, or 15 mW/sq cm (0, 0.2, 1, 2, or 3 W/kg) or to CW RFR at 0, 10, or 40 mW/sq cm (0, 2, or 8 W/kg). They found no significant alterations of PA in 11 separate brain regions from exposure to the RFR (pulsed or CW) at any of the levels used.

In a study by Ward et al. (1982), both the left and right femoral vein of the anesthetized rat were surgically exposed and a mixture of H-3 inulin and C-14 sucrose was injected into the right femoral vein. Five min later, a 0.4-ml blood sample was drawn from the left femoral vein. After another 5 min, each rat was exposed for 30 min at 0, 10, 20, or 30 mW/sq cm (0, 2, 4, or 6 W/kg) at an ambient temperature of 22 deg C or was subjected for 30 min to an environment at an ambient temperature of 22, 30, or 40 deg C. Rectal temperature was measured just before and after either 30-min treatment. Mean changes in rectal temperature were found to be linear with environmental temperature or power density, with a slope for the latter of 0.09 deg C per mW/sq cm.

Ten min after such treatment, (i.e., 50 min after tracer injection), another 0.4-ml blood sample was drawn by cardiac puncture. The blood samples were processed for liquid scintillation counting and the H-3 and C-14 activities were determined. The serum levels of each tracer at 0, 5, and 50 min were connected graphically with linear segments and the area under each resulting plot was used as an approximation to the integral, I, of the serum concentration over the 50-min period.

Eight rats were used for each treatment. Following cardiac puncture, the brain was perfused with saline for 10 min and removed, and eight samples each of cortex, hypothalamus, cerebellum, hippocampus, striatum, medulla, and midbrain were processed for H-3 and C-14 counting, yielding Tb, the amount of each tracer in each brain region at 50 min. Tracer permeations were expressed as blood-to-brain transfer constants, Ki, defined as the ratio Tb/I. The Ki values of each tracer in each brain region were treated by regression analysis for a total of 16 analyses.

The results for the RFR-exposed and environmentally treated rats were analyzed by two methods. First, regression analysis was used on the data for each tracer in each region for a total of 16 analyses. To avoid false-positive statistical significance from numerous analyses, Bonferroni's Inequality was applied; the $p<0.1$ for significance at the 5% level in a one-sided test was divided by 16, yielding $p=0.006$ as the level for significance. By this conservative test, no statistically significant increase in permeation was found for either tracer in any brain region of rats exposed to the RFR. For the environmentally treated rats, the only significant permeability increase was of sucrose in the hypothalamus of those heated at 40 deg C, possibly due to core-temperature elevation.

Second, a profile analysis was used to test for a general change in tracer uptake across all brain regions. Using this statistical method on the data for the RFR-exposed rats yielded a significant increase in permeation for sucrose but not for inulin. A factor was then derived from the environmentally treated rats to correct for the increase in permeation of the brain associated with change in body temperature. When this correction factor was applied to account for the thermally-induced permeability changes to sucrose by the RFR, no significant increase in permeation due to direct (nonthermal) action of the RFR on the brain was obtained.

For positive controls, 9 other rats were injected with hypertonic urea as a bolus into a common carotid artery, in lieu of RFR exposure, and comparisons were made of inulin permeation between ipsilateral and contralateral samples of each brain region. Because only one tracer was used in these rats, the level for significance was $p= 0.1/8 =0.013$. Significant increases of inulin permeation were obtained in the cortex, striatum, hypothalamus, and hippocampus of this group of rats, thus indicating that the method could detect increases in BBB permeation.

In the most recent (to date) endeavor to reproduce the results of Oscar and Hawkins (1977), Ward and Ali (1985) used exposure parameters similar to those of Oscar and Hawkins (1977), i.e., 30-min exposures to 1.7-GHz CW and pulsed RFR (0.5 microsecond pulses at 1000 pps). However, only the head of the rat was exposed, through a hole in the broad wall of a properly matched section of WR-430 waveguide, into which air at 28 deg C was pumped to prevent accumulation of carbon dioxide. The mean SAR, determined in a saline model of the head by both calorimetry and RFR- energy-absorption rate, was selected (by adjusting the forward power) to be 0.1 W/kg, at which Oscar and Hawkins (1977) reported maximal changes in permeability. In addition, the rat-processing methodology of Ward et al. (1982), discussed above, was used. No significant differences between RFR- and sham-exposed rats in uptake of either tracer were found in any of the eight brain regions.

Horseradish peroxidase (HRP), a high-molecular-weight protein, has been used frequently as a tracer that is detectable both morphologically and quantitatively. Normally, peroxidase is excluded from brain parenchyma except in the region of the choroid plexus and the median

eminence.

Albert (1977) sham-exposed or exposed unanesthetized Chinese hamsters for 2 or 8 hr to 2.45-GHz CW RFR at 10 mW/sq cm (SAR not determined in this study but subsequently estimated to be 2.5 W/kg), after which the animals were anesthetized, injected with HRP, and euthanized. Slices of various brain regions were prepared appropriately and scored visually by light microscopy for peroxidase leakage, which yields a dark-brown reaction product, and by electron microscopy. The author reported that the RFR exposure produced leakages of peroxidase in the microvasculature that were not confined to any particular brain region and that in control animals, extravascular reaction product was found only in brain regions normally lacking a BBB. The author also noted that some blood vessels from sham-exposed (as well as RFR-exposed) animals exhibited weak leakages, which he tentatively ascribed to the presence of endogenous peroxidase.

In a later study, Albert (1979) exposed 52 animals (34 Chinese hamsters and 18 rats) to 2.8-GHz RFR for 2 hr at 10 mW/sq cm (2 W/kg for the rat, Durney et al., 1978, p. 95; about 2.5 W/kg for the hamster). Of these, 30 were euthanized immediately, 11 at 1 hr after exposure, and 11 at 2 hr after exposure. Twenty animals (12 hamsters and 8 rats) were sham-exposed. Leakage of HRP was scored by two independent individuals on a 5-point scale.

Leakage of HRP in some brain regions was reported for 17 of the 30 animals euthanized immediately after RFR exposure and for 4 of the 20 sham-exposed animals. Fewer areas of increased BBB permeability were evident for animals euthanized 1 hr after RFR exposure, and except for one rat, virtually no leakage of HRP was seen for the animals euthanized 2 hr after RFR exposure. Albert also reported preliminary results with hamsters indicating that when HRP was injected after RFR exposure, some reaction product was seen in the extracapillary spaces of the iris, and that the cytoplasm of endothelial cells of the iris capillaries were filled with pinocytotic vesicles containing HRP.

The brain results indicated that increased BBB permeability due to RFR exposure at levels insufficient to denature brain tissue is a reversible effect. (Albert suggested that such changes in the BBB may be subacute clinically and would probably cause no lasting ill effects.) However, the increased BBB permeability seen in 4 of the 20 sham-exposed animals may indicate that factors other than RFR in the experimental procedure could have yielded the positive results. Moreover, no positive-control (BBB-altering) agent was used in these studies for comparative purposes. Also, as noted previously by Albert (1977) and in this study, a possible confounding point in the use of injected HRP as a tracer may be the presence of endogenous peroxidase, the detection of which could yield false-positive results.

Albert and Kerns (1981) exposed 51 Chinese hamsters to 2.45-GHz CW RFR for 2 hr at 10 mW/sq cm (2.5 W/kg). Thirty-nine of these were injected immediately with HRP and euthanized, and 6 each of the remaining 12 were

allowed to recover from exposure for 1 and 2 hr, respectively, before HRP injection and subsequent fixation. Equal numbers of hamsters were sham-exposed.

Gross observations of brain slices from the first group indicated the presence of reaction product in normally leaky areas of the posterior pituitary, median eminence, pineal gland, area postrema, choroid plexus, and the subfornical organ of both RFR- and sham-exposed animals. Also, randomly distributed lesions in other brain regions were found in about a third of the RFR-exposed animals, not only in the pons, cerebellum, thalamus, and areas around the fourth ventricle, but also in the hypothalamus, hippocampus, and cerebral cortex. Some of the sham-exposed animals also displayed a few random lesion areas, with a slight propensity for the thalamus. In the 1-hr-recovery groups, only 2 RFR-exposed animals and 1 sham-exposed animal showed evidence of lesions in the brain stem and cerebellum. No gross lesions were evident in the 2-hr-recovery groups.

Examination of lesion areas by light-microscopy showed that capillaries, venules, and some arterioles were often surrounded by reaction product. Leaky blood vessels were found to contain reaction product in the region of the basal lamina, around the pericytes or the smooth muscle of the microvasculature, and around nerve cell bodies. The concentration of reaction product was greatest in vascular walls and diminished with distance into the parenchyma.

By electron-microscopy, leaky vessels from RFR-exposed animals showed that reaction product was present in vesicular structures of endothelial cells, basal lamina, and surrounding pericytes. Tight junctions between endothelial cells appeared intact in all vessels examined, and complete transendothelial channels were not seen. However, endothelial cells of RFR-exposed animals appeared to have more pinocytotic vesicles with HRP than cells of sham-exposed animals (by a factor of 2-3), leading these investigators to suggest that the latter is the most likely transport mechanism across the RFR-disrupted BBB.

This study appears to be an extension of the one by Albert (1979), in which Chinese hamsters and rats were exposed to 2.8-GHz RFR at 10 mW/sq cm for 2 hr and given the same postexposure treatments and morphological examinations. The findings of RFR-induced BBB disruptions and their reversibility in the later study lend greater credence to the previous findings with Chinese hamsters. However, increased BBB permeability in sham-exposed animals was found again, an indication that non-RFR factors may have contributed to the positive results (such as the presence of endogenous peroxidase). On the other hand, Sutton and Carroll (1979), as discussed below, did not find endogenous peroxidase in their control animals, but their experimental species (rat), exposure regimen, and HRP methodology were vastly different.

Sutton and Carroll (1979), with a view toward use of RFR for selective hyperthermic treatment of brain tumors, experimentally determined the maximum temperatures and exposure durations that would not alter the

integrity of the rat BBB. They exposed the heads of normothermic rats (37 deg C) to 2.45-GHz CW RFR with a diathermy unit. A forward power of 80 W (power density or SAR not determined) was applied until the brain attained a temperature of 40, 42, or 45 deg C (measured by thermocouple inserted through the skull into the right cerebral hemisphere, with the leads perpendicular to the E-vector). At this time, they reduced the power to maintain that temperature for various durations.

For some normothermic rats, brain temperature was held at 40, 42, or 45 deg C for 10, 15, or 30 min. For others, brain temperature was held at 40 deg C for 45, 60, 90, or 120 min. Following exposure, the rats were euthanized by intracardial perfusion of polyvinylpyrrolidone (PVP) at mean arterial pressure for 2-5 min to clear the vascular tree of blood and peroxidase, and the brains were removed for assay. Control rats were euthanized for assay after 10, 15, 30, or 120 min of sham-exposure.

The authors also similarly exposed hypothermic rats (30 deg C) and held their brain temperature at 40, 42, or 45 deg C for 15, 30, or 45 min; 42 or 45 deg C for 10 min; 40 deg C for 60, 90, 120, or 180 min; or 45 deg C for 90 min. Control rats, with brain and body core both hypothermic, were euthanized after 180 min.

These investigators had found that the circulating half-time for HRP was about 22 min in mice, so they injected HRP either just before exposure into the rats exposed for less than 30 min, or 30 min before euthanizing the rats exposed for longer periods. After each rat was euthanized, its brain was removed, peroxidase activity in the left cerebral hemisphere and cerebellum were assayed by spectrophoto-fluorometry, and the values for the two regions were combined. (The right hemisphere was excluded from the assay because of the mild injury it sustained from insertion of the thermocouple.)

The results for normothermic rats showed no significant peroxidase activity in brains heated to 40 deg C for 10, 15, or 30 min, or to 42 deg C for 10 min. However, progressively higher activities were found in brains heated to 40 deg C for 60, 90, or 120 min. This was also true for brains heated to 42 deg for 15 or 30 min and for brains heated to 45 deg for 10, 15, or 30 min. By contrast, significant peroxidase activity was absent in brains of hypothermic rats heated to 40 deg C for 60, 90, or 120 min, indicating that the hypothermia was protective of the BBB. This was true to a lesser extent for hypothermia against 42 deg C; no significant activity was obtained for 10- or 15-min exposures, but the mean activities in hypothermic and normothermic rats exposed for 30 min were comparable. Hypothermia provided little BBB protection at 45 deg C for exposures of 15 min or longer. However, most normothermic rats were moribund after 30 to 60 min, whereas hypothermic rats readily survived for 3 hr.

As noted previously, Albert (1977, 1979) had suggested that endogenous peroxidase may confound results obtained with injected HRP. However, Sutton and Carroll (1979) found no endogenous peroxidase activity in

control rats perfused intracardially with PVP.

By using a small dielectrically loaded coaxial applicator, Lin and Lin (1980, 1982) were able to expose only the heads of anesthetized adult male Wistar rats to pulsed 2.45-GHz RFR (10 microseconds, 500 pps). The exposures were for 20 min at average power densities of 0.5 to 3000 mW/sq cm. The distribution of RFR energy absorbed within the head was determined by thermographic procedures, and average SARs were found to range from 0.04 to 240 W/kg. Following RFR- or sham-exposure, Evans Blue dye was injected into a catheterized femoral vein. Five min later, the animal was perfused via the left ventricle with normal saline. The brain was removed, examined, and scored for degree of tissue staining by the tracer. For average power densities up to and including 2.6 W/sq cm (200 W/kg), staining was not significantly different between exposed and control animals. For exposures at 3 W/sq cm (240 W/kg), extravasation of Evans Blue dye was seen in the cortex, hippocampus, and midbrain. The degree of staining decreased with increasing time interval between exposure and euthanasia, indicating that the effect was reversible.

In a later study by this group, Goldman et al. (1984) performed similar exposures to 2.45-GHz pulsed RFR (10 microseconds, 500 pps) directly to the left side of the head of the rat at an average power density of 3 W/sq cm (240 W/kg) for 5, 10, or 20 min (yielding brain temperatures up to 43 deg C) to ascertain the time course of BBB-permeability changes. Control rats were sham-exposed for 20 min. Because of the relatively low permeability of the tracer Rb-86 in regions with intact BBB, they used a version of the Sapirstein (1958) indicator-fractionation method, which permits determining both regional blood flow and cardiac output. After RFR- or sham-exposure, they intravenously injected a bolus of Rb-86-labeled RbCl in isotonic saline and collected arterial blood for 15 seconds to determine cardiac output. They then euthanized the rat, removed the brain, sectioned the exposed half into 13 parts, and assayed each part for Rb-86.

The results showed that within 5 min of RFR exposure, Rb-86 uptake was increased significantly in the hypothalamus, basal ganglia, midbrain, dorsal hippocampus, and occipital and parietal cortex relative to the uptake in the controls. Significant increases in other regions, such as the cerebellum and superior colliculum, occurred only after 20 min of exposure. Cardiac outputs, as well as blood pH and partial pressures of carbon dioxide and oxygen, were relatively unaffected for at least 5 min of exposure. By 10 min, however, cardiac output had significantly increased and hyperventilation was evident from elevated blood pH and oxygen partial pressure and correspondingly decreased carbon-dioxide partial pressure. These results correlated with the changes in brain temperature, which reached 43 deg C after 5 min of a 20-min RFR session and subsequently rose more slowly as thermoregulatory and heat-transfer processes became more effective. The authors noted that these findings were consonant with their previous ones (Lin and Lin, 1980, 1982) and with those of Sutton and Carroll (1979).

Chang et al. (1982) used a technique involving I-131-labeled albumin

to investigate alterations of the BBB in dogs. Prior to exposure, each dog was anesthetized, intubated, and placed on an artificial respirator. A femoral artery and vein were cannulated and a 19-gauge spinal needle was inserted into the cisterna magna. The dog was then injected with I-131-labeled human serum albumin via the femoral-vein catheter. The heads of dogs were sham-exposed or exposed to 1.0-GHz CW RFR at 2, 4, 10, 30, 50, or 200 mW/sq cm (SARs not determined). After RFR- or sham-exposure, 1-ml samples of venous blood and 0.2-ml samples of cerebrospinal fluid (CSF) were taken simultaneously every 20 min for 5 hr, at the end of which the dogs were in "satisfactory condition." Aliquots of CSF and blood-plasma samples were assayed for radioactivity by gamma counter, and the results were expressed as ratios of counts per min (CPM) in CSF x 1000 to CPM in plasma as a measure of albumin transfer across the BBB.

No significant differences in the CPM-CSF/CPM-plasma ratio were found between 11 sham-exposed dogs and 2 dogs each exposed at 2, 4, 10, 50, or 200 mW/sq cm. Two dogs were also exposed at 30 mW/sq cm. One of these exhibited increased albumin penetrance of the BBB, so 9 other dogs were exposed at this power density. Of the latter, 3 showed significantly higher BBB penetrance and the other 6 no significant differences from the controls. The positive results obtained for 4 dogs exposed at 30 mW/sq cm led the investigators to suggest the possible existence of a power density "window" in the vicinity of this value.

Measurements or estimates of SARs in the dog head might have been useful for comparing these result with those of other investigators (with other species), especially since the power densities were measured in the near field of a horn (with the dog absent). Also, the presence of the 19-gauge metal needle in the brain during RFR exposure may have affected the SAR in its vicinity.

Williams et al. (1984a), in one of four studies, compared the effects of RFR-exposure, ambient heat, and intravenously injected hyperosmolar urea on cerebral microvasculature permeability to systemically circulating sodium fluorescein, and determined the effect of hyperthermia on the circulating plasma levels of sodium fluorescein.

Fisher-344 male rats were housed in individual wire-mesh cages in animal quarters maintained at 23 +/- 1 deg C and normal 0600-1800 light cycle. Four to five days prior to each experiment, an indwelling catheter was inserted in the right jugular vein to permit the injection of solutions directly into the conscious animal. Each day from 0900 to 1200 for at least 7 days prior to exposure, the rats were acclimated to simulated-exposure conditions by placing each unrestrained within an individual Styrofoam box like those used for exposure. The treatment was continued until colonic temperature, taken at the end of each 3-hr daily session, was within the normal range for the rat (37-38 deg C).

After being acclimated on the day of an experiment, conscious rats were either sham-exposed or exposed dorsally to far-field 2.45-GHz CW RFR at 20 or 65 mW/sq cm (4 or 13.0 W/kg) for 30, 90, or 180 min within

an anechoic chamber maintained at 24 +/- 1 deg C ambient temperature and 55-68% relative humidity. Other similarly acclimated rats were exposed to heat for 30 or 90 (+/- 10) min in the anechoic chamber by raising the ambient temperature to 42 +/- 2 deg C. Still others were given an iv injection of hypermolar urea to open the BBB osmotically.

Within 15-30 seconds after such RFR-exposure, heat treatment, or iv injection, colonic temperature was measured and infusion of a solution of NaFl was begun within 2 min. The infusion took 1 min. The tracer was allowed to circulate for 5 min, after which the rat was anesthetized intravenously. Within 1-2 min of anesthesia, intracardiac perfusion with saline was performed; the brain was excised; and portions of the cerebral cortex, hypothalamus, cerebellum, and medulla were removed. Each was weighed, processed appropriately, and assayed for tracer by fluorescence spectrophotometer.

Significantly elevated levels of NaFl ($p<0.05$ when compared with brain samples from the same regions of sham-exposed animals) were found in the brains of rats exposed at 65 mW/sq cm (13 W/kg) for 30 or 90 min; for the urea (positive-control) animals; for the cortex, hypothalamus, and medulla, but not the cerebellum, of animals exposed to heat (42 +/-2 deg C); and for none of the brain samples of animals exposed at 20 mW/sq cm (4 W/kg) for 180 min. In general, ambient heat was not as effective as RFR energy in raising tracer concentration within the brain, and neither agent yielded elevations as great as the hyperosmolar solution of urea.

Studies were carried out on 3 additional rats to determine the effect of hyperthermia on circulating plasma levels of NaFl. Colonic temperatures were increased from normothermic levels (37-38 deg C) to 41.2-41.8 deg C in 30 min. Four other rats, treated identically but without exposure to hyperthermia, served as controls. Plasma concentrations were stated to be significantly higher for the 3 rats exposed to ambient heat than for the controls.

Using the argument that disruption of the BBB to NaFl would be expected to result in a significant relative increase of the NaFl concentration in brain tissue during the 5-min tracer-circulation period, the authors calculated the ratios of measured NaFl concentration of cerebral cortex, hypothalamus, cerebellum, and medulla brain to the integral of plasma concentration over that period in samples from each of the four sham- and three hyperthermic rats. The differences between ratios were found to be statistically nonsignificant when analyzed by the Mann-Whitney U-test. Because of this, the authors concluded that the increased levels of tracer found in the brains of rats rendered hyperthermic by ambient heat or by exposure to RFR were most likely the result of elevated circulating levels of NaFl due to reduced renal excretion.

The authors suggested that a second source of artifact might have been an increase in blood vascular space (BVS) in the brain resulting from moderate hyperthermia, but BVS was not determined in this experiment. Increases in circulating level of NaFl and BVS would both be expected to increase the residual amounts of tracer in the brain resulting from

either pinocytotic uptake during the 5-min circulation period or from incomplete clearance of fluorescein from the lumen and luminal wall surface of cerebral vessels. Thus, they concluded that the increased levels of the tracer in the brain were not the result of alteration of the BBB permeability to NaFl.

Williams et al. (1984b), in the second of the four studies, used HRP as the tracer in similarly treated rats. However, marked hypotension had been reported in some strains of rats 2-3 min after iv injection of HRP (5-10 mg HRP/100 g body weight). Other toxic effects observed included signs of erythema and edema of the paws, ears, and snout; lethargy; and prostration. The possible occurrence of such effects in Fisher-344 rats, which would be a potential source of artifact, was investigated by the authors. They inserted indwelling catheters into the right jugular vein and femoral artery of six rats. After recovery from anesthesia, four of the rats were exposed to RFR (65 mW/sq cm, 13 W/kg) for 30 or 90 min and the other two were sham-exposed. After exposure, femoral blood pressure was monitored for 1 min prior to injecting a 0.5-ml solution of HRP at 15 mg/100 g body weight and for up to 60 min after injection.

Mean blood pressure remained virtually unchanged in all six animals. The authors observed that the rats became noticeably less active on injection of the tracer, but did not display behavior indicative of illness, such as lowering of the head and sniffing. Toxicity was therefore not regarded a problem at the levels of HRP used.

For the study of BBB effects proper, rats were sham-exposed, exposed to dorsally to 2.45-GHz CW RFR at 20 mW/sq cm (4 W/kg) for 180 min or 65 mW/sq cm (13 W/kg) for 30 or 90 min, or heat-treated for 30 or 90 min by raising the ambient temperature to 42 +/- 2 deg C, as described above. Within 15-30 seconds after terminating treatment, colonic temperature was recorded. HRP, weighed and diluted in 0.5 ml of saline to give an injectable concentration of 15 mg/100 g body weight, was then injected iv at a constant rate of 0.6 ml/min and allowed to circulate for 60 min. The animal was then anesthetized, perfused intracardially with saline 1-2 min after anesthesia, and fixed by perfusion with glutaraldehyde in buffer. The brains were subsequently removed and 2-mm-thick sections of cerebral cortex, hypothalamus, cerebellum, and medulla were dissected, fixed, and prepared on glass slides for visualization of peroxidase reaction product. The pineal gland was also removed and similarly treated. Each of about 450 slides was renumbered with a code by an assistant beforehand to provide a single-blind format.

To evaluate each slide, 50 microvessels less than 30 microns in diameter were randomly selected and counted. The whole tissue section was then scanned, and evidence of HRP extravasation was recorded. Microvessels were assessed as positive or negative for the presence of HRP product in four categories: in microvessel- or surrounding perivascular structures; within microvessel endothelium (vesicles); within pericyte; around basement membrane or extravasation into surrounding neuropil. After all slides had been examined, code numbers were matched

with slide numbers (revealing the identity of each slide) and a ratio was calculated for each category with respect to the total number of vessels counted per slide. From the ratios for the four slides examined for each region, a mean ratio per category for each brain region was then calculated, and a mean of means (+/- SEM) for each category was obtained for each brain region by summing the means of all rats (n=4 or 5) in each respective exposure group.

Under light microscopy, the normally leaky pineal gland showed reaction product in both RFR- and sham-exposed rats. Of the other brain regions studied, none showed extracellular leakage of HRP attributable to RFR- or heat-induced breakdown of the BBB. A few microvessel endothelial cells with HRP-flooded cytoplasm were observed infrequently in 1-micron sections of brain from both RFR- and sham-exposed rats. HRP reaction product was seen more often within pericytes or immediately surrounding these cells at the bifurcation of small arterioles or precapillaries. Reaction product was sometimes present between the apposing folia of the cerebellum and immediately below the pial membrane in cerebral cortex. Reaction product was also seen around a few small vessels in the arcuate nucleus, and especially around vessels of the median eminence in both RFR- and sham-exposed rats. These findings were confirmed by electron microscopic examination of ultrathin sections of each brain region.

In the single-blind analysis, the mean ratios representing extravascular leakage of HRP into the surrounding neuropil were zero for the cortex, cerebellum, and medulla of all five groups (sham, RFR at 20 mW/sq cm for 180 min, RFR at 65 mW/sq cm for 30 min, RFR at 65 mW/sq cm for 90 min, and ambient heat for 90 min) and for the hypothalamus of the two 65-mw/sq-cm groups and the heat group. The hypothalamic ratios for the sham and 20 mW/sq-cm groups were small, comparable, and derived from a single rat in each group. The mean ratios for HRP-labeled pericytes obtained from cerebral cortex, hypothalamus, cerebellum, and medulla of the three RFR groups and the heat group were consistently lower than the corresponding values for the sham group. This was also true for the mean ratios of HRP-labeled endothelium.

In their discussion, the authors stated: "This study not only failed to show an increase in BBB permeability to HRP following exposure to ambient heat or microwaves, but actually showed a reduced uptake of the tracer by the brain, i.e., cerebral microvessels...This reduced uptake appears to be a direct result of decreased formation of pinocytotic vesicles. Lipid insoluble molecules, including sucrose, cross the microvessel endothelium by vesicular transport (appropriate references cited). The observed reduction in vesicular transport of HRP would, therefore, explain the reduced permeability-surface area product (PA) for C-14 sucrose noted in those rats exposed to microwaves at 65 mW/sq cm for 30 min (Williams et al., 1984c)." The authors also noted that significantly depressed ($p<0.05$) pinocytotic activity was only evident in rats exposed to RFR at 65 mW/sq cm (13 W/kg) for 30 or 90 min or to ambient heat (42 +/- 2 deg C) for 90 min, but that suppression may begin when brain temperatures exceed normothermic levels by as little as 1 deg

C or less.

In the third study, Williams et al. (1984c) used C-14-labeled sucrose as the tracer. Indwelling catheters were implanted into the right jugular vein and femoral artery 2-4 days before the experiments. Within 15-30 seconds after RFR-, sham-, or heat-exposure, colonic temperature was recorded and the conscious rat was rapidly transferred to a Styrofoam box, where the jugular catheter was attached to an injection syringe via a polyethylene extension tube containing a bolus of C-14 labeled sucrose and saline wash separated from the bolus by a small air bubble. The injections were performed 4-6 min after the end of treatment. After flushing the femoral catheter with saline, the catheter was attached to a transducer for recording the blood pressure before, during, and after bolus injection.

Within 5-10 seconds after injection, the catheter was disconnected from the transducer and 0.1-ml samples of whole blood were bled periodically into microcentrifuge tubes for 20 min (totaling less than 2 ml). After such bleeding, the rat was decapitated, its brain was removed, and the arachnoid-pial membrane was peeled off. Rectangular 3x6-mm strips of left and right cerebral cortex, the whole hypothalamus, half of the cerebellum, and a 4x4-mm strip of the medulla were removed and weighed. Each sample was solubilized, incubated, and assayed for radioactivity by liquid scintillation counting.

The counts per min for brain, plasma, and whole blood were converted to disintegrations per min (dpm) by the use of a separate quench curve for each region, and the following concentrations (C) of C-14 sucrose were determined for each rat: (1) brain-C,20 in dpm/g (at 20 min, the time at which the last blood sample was drawn and the rat decapitated) for the cortex, hypothalamus, cerebellum, and medulla; (2) integral of plasma-C over the 20-min period (dpm.s/ml), using the data from the periodically drawn samples; and (3) blood-C,20 (dpm/ml).

The blood vascular space (BVS) in ml of blood per gram of brain was calculated from rats in other experiments to correct for intravascular sucrose. In these experiments, rats were sham-exposed or heated to attain colonic temperatures approximating those obtained by exposure at 65 mW/sq cm (13 W/kg) for 30 or 90 min. However, blood samples were collected for only 5 min before decapitation. For each control- and heated rat, the ratio of brain-C,5 to blood-C,5 for each brain region was taken as an initial estimate of BVS for that region and a nonlinear least squares process was used reiteratively to obtain final BVS values. Lastly, mean BVS values obtained from averaged final values were used with data from RFR- and sham-exposed groups to calculate regional PA values for each group. The data from all studies were analyzed with the non-parametric Mann-Whitney U-test for differences in distribution.

The mean regional BVS values for the 30-min-heat group were slightly but consistently higher than the corresponding values for the sham and 90-min-heat groups. The mean values for the 90-min-heat group except for the cortex were lower than those for the sham group. However, none

of these differences were statistically significant. (The changes were nonmonotonic with increasing heat, so presumably they were not heat-induced.)

The regional PA values for the 30-min-RFR group were consistently lower than the corresponding values for the sham and 90-min-RFR groups. These decreases were significant for the hypothalamus, cerebellum, and medulla but the decreases for the cerebral cortex were not significant.

The differences between corresponding values for the 90-min-RFR and sham groups were not significant. However, the authors noted that two of the rats of this RFR group attained colonic temperatures below 42.5 deg C and yielded lower PA values than the other two rats in the group, whose colonic temperatures reached 43.0 and 43.4 deg C. Also, the lower PA values were within the range obtained for the 30-min-RFR group.

The authors indicated that as colonic temperature neared or exceeded about 41.5 deg C, plasma-sucrose levels increased significantly above those for the sham group. They illustrated this point with typical plots of plasma-sucrose concentration (from samples taken periodically for 20 min) vs time after injection for a rat exposed at 65 mW/sq cm (13 W/kg) for 90 min and a sham-exposed rat. The two curves were similar (both exponentially decreasing), with the one for the RFR rat above that for the sham rat. The authors noted that these increased levels of circulating sucrose constituted a potentially biasing artifact in calculations of PA and uptake ratio, and therefore they limited the 30-min-RFR group to those rats whose colonic temperatures remained below 41.3 deg C and whose concentration-vs-time profiles were within the range for sham-exposed rats. On this basis, the difference between the 30-min-RFR and sham groups was not significant, but the plasma levels for the rats in the 90-min-RFR group were significantly elevated above sham levels.

The authors did not discuss the blood-pressure or pulse results. By t-test, however, the mean blood pressures were significantly higher for both 90-min groups than for the sham group, but the only significant difference in pulse rate was a lower mean value for the 30-min-RFR group than for the sham group.

The authors indicated that consistently elevated plasma integrals and tracer concentrations in whole blood were found in the rats exposed to RFR or heat for 90 min, with colonic temperatures of all exceeding 41.5 and usually above 42 deg C, and that definite changes in renal function could occur at such temperatures. Thus, without discounting possible changes in sucrose distribution among the kidneys, liver, and muscle tissue, they ascribed increased circulatory levels of sucrose primarily to reduction of renal clearance. In support of this hypothesis, they determined endogenous creatinine levels in plasma samples collected from several sham-exposed and 90-min-hyperthermic (exceeding 42 deg C) rats as an index of renal function. The mean creatinine concentration for the sham-exposed group was significantly lower than for the 90-min hyperthermic group, which suggested significantly reduced glomerular filtration rates in these hyperthermic rats.

Because of the occurrence of impaired renal function in the severely hyperthermic rats, the authors regarded the BBB findings for these rats as unreliable, but indicated that this situation was avoided for the group rendered moderately hyperthermic. They therefore concluded that the arterial-integral method is a valid approach to calculating PAs in unrestrained conscious animals subjected to hyperthermic levels (by either heat or RFR) that do not impair renal function or alter tracer levels in plasma. They also stated:

"Our results, which confirm those previously reported by Gruenau et al. (1982) and Preston (1982), clearly demonstrate that exposure of conscious rats to 2450 MHz microwave energy at 20 or 65 mW/sq cm does not increase the permeability of the blood-brain barrier to sucrose."

Williams et al. (1984d) investigated the relationship of BBB alterations to colonic and regional brain temperatures in the fourth study. They measured the colonic temperature and local temperatures in the cortex, hypothalamus, cerebellum, and medulla of conscious rats within 30-90 seconds after completing the following treatments: sham-exposure; exposure to 2.45-GHz CW RFR at 20 mW/sq cm (4 W/kg) for 30, 90, or 180 min or at 65 mW/sq cm (13 W/kg) for 30 or 90 min; ambient heating at 42 deg C for 90 min. For this purpose, two nylon screws, each having a hole through its center, were surgically implanted and anchored under anesthesia in the head of each rat, one screw (5.0 mm long) 4.0 mm anterior to the lambdoid suture and 1.5 mm left of the midline, and the other (5.5 mm long) 3.0 mm posterior to the suture and 3.0 mm left of the midline. Recovery from surgery usually occurred within two weeks. Rats that exhibited altered behavior, high temperature, or continued weight loss by the end of this period were excluded from the study. Equilibration and handling were done daily as in the other studies.

The results revealed the presence of a thermal gradient within the rat brain; superficial regions of cerebral cortex and cerebellum were cooler than the deeper hypothalamus and medulla of all groups. Statistical analysis indicated that the mean regional brain temperatures for all five RFR groups were significantly higher than the corresponding values for the sham-exposed groups, as were the colonic temperatures. The difference (delta-t) between the mean temperature in each brain region and the mean colonic temperature was calculated. The values of delta-t for all nine groups were negative (mean colonic temperature higher than mean regional brain temperature) for the cortex and cerebellum, and positive for the hypothalamus and medulla. The delta-t values for the RFR- and heat-exposed groups did not differ significantly from those for the sham-exposed groups except for: the cortical value of the 65-mW/sq-cm (13-W/kg), 30-min group; the hypothalamic value of the 20-mW/sq-cm (4-W/kg), 180-min group; the cerebellar value of the 65-mW/sq-cm (13-W/kg), 90-min group; and the cerebellar and medullar values of the high ambient-temperature group.

For individual rats exposed to RFR at 20 or 65 mW/sq cm (4 or 13 W/kg) or to ambient temperature of 33 or 43 deg C, each of its regional brain temperatures was plotted against its colonic temperature. Collectively,

the points for each region showed that brain and colonic temperature were linearly related. Regression lines were calculated and used to estimate the mean regional brain temperatures for rats involved in the sodium-fluorescein (NaFl), horseradish-peroxidase (HRP), and C-14-sucrose studies (Williams et al., 1984a, b, c, discussed above). The Spearman rank correlation coefficient, rs, was then calculated and used to assess 'between-group' correlations of tracer levels within cerebral cortex, hypothalamus, cerebellum, and medulla with the regional brain temperature from groups sham-exposed or exposed to RFR at 20 or 65 mW/sq cm (4 or 13 W/kg) for 30, 90, or 180 min.

For the three groups assayed for NaFl concentrations after exposure at 20 mW/sq cm (4 W/kg) for 180 min or at 65 mW/sq cm (13 W/kg) for 30 or 90 min, the values of rs for the cortex, hypothalamus, cerebellum, and medulla were 0.800 ($p<0.01$), 0.720 ($p<0.01$), 0.623 ($p<0.05$), and 0.653 ($p<0.01$), respectively. (The critical values of rs at $p=0.05$ and $p=0.01$ were 0.456 and 0.645, respectively.) For the four groups assayed for HRP uptake after sham-exposure or exposure at 20 mW/sq cm (4 W/kg) for 180 min or exposure at 65 mW/sq cm (13 W/kg) for 30 or 90 min, the rs values for the cortex, cerebellum, and medulla were each 1.00 ($p<0.05$); the value for the hypothalamus, 0.800, was not significant ($p>0.05$). (The critical rs value at $p=0.05$ was 1.00.) For the two groups assayed for sucrose-permeability surface-area product (PA) after sham-exposure or exposure at 65 mW/sq cm (13 W/kg) for 30 min, the respective rs values were 0.399 (ns), 0.708 ($p<0.05$), 0.732 ($p<0.05$), and 0.851 ($p<0.01$). (The critical values of rs at $p=0.05$ and 0.01 were 0.643 and 0.833.) The corresponding rs values of C-14 uptake ratio for the same groups were 0.631 (ns), 0.708, 0.827, and 0.827, with the latter three significant ($p<0.05$).

In discussing their results, the authors stated the following: "An early consideration in this study, with regard to possible causes of increased BBB permeability reported in the literature, was that regional or whole brain loss of thermoregulatory ability might precede or accompany breakdown of the barrier. Conceivably, apparent changes in permeability to a substance may be concomitant with a measurable degree of tissue heating. Those regions of the brain presenting greatest change in BBB permeability might therefore exhibit a somewhat greater heat load following exposure to microwaves...Animals exposed to a relatively low power density (20 mW/sq cm) reflected a small, but significant increment in temperature of the colon and of each region of the brain studied. At this incident power level, tissue heating is effectively minimized by the animal's thermoregulatory capacity, even after an exposure lasting 180 min...With exposure of sufficient duration, the thermoregulatory response to a high intensity microwave field, such as 65 mW/sq cm is not adequate to maintain brain or colonic temperatures within the normal range."

They concluded that at 20 mW/sq cm (4 W/kg), physiological response mechanisms are more than adequate for maintaining body temperatures in the rat, including those of the brain, well within tolerable limits, but that exposure to intense fields (e.g., 65 mW/sq cm or 13 W/kg) for long

durations (90 min) could approach or exceed such limits.

In general, the use of conscious, unrestrained rats in these four studies represents a significant advance over previous methods used to ascertain the effects of RFR on the blood-brain barrier. The effects of stress arising from handling, the exposure environment, and colonic-temperature measurement were minimized by acclimating the animals to all procedures, before the actual experiments, until colonic temperatures at the end of the conditioning period were in the normal range for the rat.

In summary the uncertainties in most earlier research on this topic involve whether significant artifacts were introduced by the kinds of biological techniques used. Several investigators have indicated that exposure to RFR may alter the size of vascular and extravascular volumes and cerebral blood flow rate, thereby yielding changes in the BUI that were not necessarily related to BBB permeability alterations. Rapoport et al. (1979) developed a method for measuring the permeability of the cerebrovascular system to C-14-labeled sucrose that yielded results independent of cerebral blood flow rate. Blasberg (1979) reviewed many of the methods previously used for investigating BBB changes and the problems associated with these methods. As described earlier, Oscar et al. (1981) confirmed experimentally that LCBF is increased in the rat brain by exposure to pulsed RFR at 15 mW/sq cm average power density.

More recent findings such as those of Williams et al. (1984a, b, c, d) indicate that little quantitative confidence can be accorded to the results of early experiments on RFR-induced BBB alterations, such as those of Frey et al. (1975), Oscar and Hawkins (1977), and Albert (1977). Qualitatively, hyperthermic levels of RFR clearly can alter the permeability of the BBB. It is also possible that exposure at average power densities of the order of 10 mW/sq cm may result in randomly distributed, clinically subacute, reversible alterations.

REFERENCES:

Albert, E.N.
LIGHT AND ELECTRON MICROSCOPIC OBSERVATIONS ON THE BLOOD-BRAIN BARRIER AFTER MICROWAVE IRRADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 294-304 (1977)

Albert, E.N.
REVERSIBILITY OF MICROWAVE-INDUCED BLOOD-BRAIN BARRIER PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 323-327 (1979)

Albert, E.N. and J.M. Kerns
REVERSIBLE MICROWAVE EFFECTS ON THE BLOOD-BRAIN BARRIER
Brain Res. Vol. 230, pp. 153-164 (1981)

Blasberg, R.G.
PROBLEMS OF QUANTIFYING EFFECTS OF MICROWAVE IRRADIATION ON THE BLOOD-BRAIN BARRIER
Radio Sci., Vol. 14, No. 6S, pp. 335-344 (1979)

Chang, B.K., A.T. Huang, W.T. Joines, and R.S. Kramer
THE EFFECT OF MICROWAVE RADIATION (1.0 GHZ) ON THE BLOOD-BRAIN BARRIER IN DOGS
Radio Sci., Vol. 17, No. 5S, pp. 165-168 (1982)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Frey, A.H., S.R. Feld, and B. Frey
NEURAL FUNCTION AND BEHAVIOR: DEFINING THE RELATIONSHIP
Ann. N.Y. Acad. Sci., Vol. 247, pp. 433-439 (1975)

Goldman, H., J.C. Lin, S. Murphy, and M.F. Lin
CEREBROVASCULAR PERMEABILITY TO Rb-86 IN THE RAT AFTER EXPOSURE TO PULSED MICROWAVES
Bioelectromagnetics, Vol. 5, No. 3, pp. 323-330 (1984)

Gruenau, S.P., K.J. Oscar, M.T. Folker, and S.I. Rapoport
ABSENCE OF MICROWAVE EFFECT ON BLOOD-BRAIN BARRIER PERMEABILITY TO C-14-SUCROSE IN THE CONSCIOUS RAT
Exper. Neurobiol., Vol. 75, pp. 299-307 (1982)

Kety, S.S.
METHODS MED. RES., Vol. 8, pp. 228 (1960)

Lin, J.C. and M.F. Lin
STUDIES ON MICROWAVE AND BLOOD-BRAIN BARRIER INTERACTION
Bioelectromagnetics, Vol. 1, No. 3, pp. 313-323 (1980)

Lin, J.C. and M.F. Lin
MICROWAVE HYPERTHERMIA-INDUCED BLOOD-BRAIN BARRIER ALTERATIONS
Radiat. Res., Vol. 89, pp. 77-87 (1982)

Merritt, J.H., A.F. Chamness, and S.J. Allen
STUDIES ON BLOOD-BRAIN BARRIER PERMEABILITY AFTER MICROWAVE-RADIATION
Rad. and Environm. Biophys., Vol. 15, pp. 367-377 (1978)

Oldendorf, W.H.
MEASUREMENT OF BRAIN UPTAKE OF RADIOLABELED SUBSTANCES USING A TRITIATED WATER INTERNAL STANDARD
Brain Res., Vol. 24, pp. 372-376 (1970)

Oldendorf, W.H.
BRAIN UPTAKE OF RADIOLABELED AMINO ACIDS, AMINES, AND HEXOSES AFTER ARTERIAL INJECTION
Am. J. Physiol., Vol. 221, pp. 1629-1639 (1971)

Oscar, K.J. and T.D. Hawkins
MICROWAVE ALTERATION OF THE BLOOD-BRAIN BARRIER SYSTEM OF RATS
Brain Res., Vol. 126, pp. 281-293 (1977)

Oscar, K.J., S.P. Gruenau, M.T. Folker, and S.I. Rapoport
LOCAL CEREBRAL BLOOD FLOW AFTER MICROWAVE EXPOSURE
Brain Res., Vol. 204, No. 1, pp. 220-225 (1981)

Preston, E., E.J. Vavasour, and H.M. Assenheim
PERMEABILITY OF THE BLOOD-BRAIN BARRIER TO MANNITOL IN THE RAT FOLLOWING 2450 MHZ MICROWAVE IRRADIATION
Brain Res., Vol. 174, pp. 109-117 (1979)

Preston, E. and G. Prefontaine
CEREBROVASCULAR PERMEABILITY TO SUCROSE IN THE RAT EXPOSED TO 2,450-MHZ MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 49, No. 2, pp. 218-223 (1980)

Preston, E.
FAILURE OF HYPERTHERMIA TO OPEN RAT BLOOD-BRAIN BARRIER: REDUCED PERMEATION OF SUCROSE
Acta Neuropathol. (Berl.), Vol. 57, pp. 255-262 (1982)

Rapoport, S.I., K. Ohno, W.R. Fredericks, and K.D. Pettigrew
A QUANTITATIVE METHOD FOR MEASURING ALTERED CEREBROVASCULAR PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 345-348 (1979)

Rodzilsky, B. and J. Olszewski
PERMEABILITY OF CEREBRAL BLOOD VESSELS STUDIED BY RADIOACTIVE IODINATED BOVINE ALBUMIN
Neurology, Vol. 7, pp. 270-279 (1957)

Sapirstein, L.L.
REGIONAL BLOOD FLOW BY FRACTIONAL DISTRIBUTION OF INDICATORS
Am. J. Physiol., Vol. 193, pp. 161-168 (1958)

Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979)

Ward, T.R., J.A. Elder, M.D. Long, and D. Svendsgaard
MEASUREMENT OF BLOOD-BRAIN BARRIER PERMEATION IN RATS DURING EXPOSURE TO 2450-MHZ MICROWAVES
Bioelectromagnetics, Vol. 3, No. 3, pp. 371-383 (1982)

Ward, T.R. and J.S. Ali
BLOOD-BRAIN BARRIER PERMEATION IN THE RAT DURING EXPOSURE TO LOW-POWER 1.7-GHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 6, No. 2, pp. 131-143 (1985)

Williams, W.M., W. Hoss, M. Formaniak, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. A. EFFECT ON THE PERMEABILITY TO SODIUM FLUORESCEIN
Brain Res. Rev., Vol. 7, pp. 165-170 (1984a)

Williams, W.M., M. del Cerro, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. B. EFFECT ON THE PERMEABILITY TO HRP
Brain Res. Rev., Vol. 7, pp. 171-181 (1984b)

Williams, W.M., J. Platner, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. C. EFFECT ON THE PERMEABILITY TO C-14 SUCROSE
Brain Res. Rev., Vol. 7, pp. 183-190 (1984c)

Williams, W.M., S.-T. Lu, M. del Cerro, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. D. BRAIN TEMPERATURE AND BLOOD-BRAIN BARRIER PERMEABILITY TO HYDROPHILIC TRACERS
Brain Res. Rev., Vol. 7, pp. 191-212 (1984d)

3.4.2 HISTOPATHOLOGY AND HISTOCHEMISTRY OF THE CENTRAL NERVOUS SYSTEM

3.4.2.1 STUDIES OF EXCISED NEURAL TISSUES

In several studies, neural-tissue preparations were exposed to RFR in vitro. Among them was that of Courtney et al. (1975), who removed the right and left superior cervical ganglia from New Zealand white rabbits, stretched each across a vertical section of WR284 waveguide sealed at the bottom and filled with Ringer's solution, and exposed the ganglion to 2.45-GHz CW RFR from below. Temperature-controlled Ringer's solution was flushed through the waveguide section at 1 l/min. For impedance matching, the seal at the bottom of the waveguide was a dielectric plate of unstated thickness (presumably equivalent to a quarter-wavelength). The preganglionic end was connected to a set of stimulating electrodes external to the waveguide, and a silver lead wire within a suction syringe (external to the waveguide) was used to make contact with the postganglionic nerve via a glass capillary through the waveguide wall.

Forward and reflected powers were measured with a bidirectional coupler and power meters. Reflected powers were always less than 1% of forward powers. The mean power density incident on the ganglion and its mean SAR were calculated from the net (forward minus reflected) power, the waveguide cross section, the penetration depth for the Ringer's solution (1.75 cm at 2.45 GHz), and the distance of the ganglion from the bottom of the waveguide, which yielded 2.2 W/kg per mW/sq cm.

Prior to exposure, effects of temperature alone on synaptic transmission latencies through ganglia were measured. At 37 deg C, stimulation of the preganglionic nerve trunk with pulses 100 to 300 microseconds in duration at 1 pps and amplitude 4-8 V yielded a transient positive-going potential from the postganglionic nerve stump relative to the potential of the Ringer's solution, with a transmission latency of about 20 ms (B-fiber-mediated or short-latency response). Seen with higher stimulus amplitudes were C-fiber-mediated (long-latency) responses. Latencies for both responses increased about linearly with decreasing solution temperatures, yielding at 23 deg C about 40 ms and 65 ms for the short-latency and long-latency responses, respectively, which corresponded to change rates of about 3% per deg C for both.

Each ganglion was exposed to the RFR at power densities up to about 300 mW/sq cm (660 W/kg) for 1-min intervals, with 1 min between exposures for control measurements. During the exposure and control intervals, the ganglion was stimulated with an amplitude sufficient to excite both B and C fibers and the electrically evoked potentials were recorded with a computer of average transients. The authors stated: "Only at absorbed power densities [SARs] above 100 W/kg (50 mW/sq cm) did we observe temperature changes of 0.1 deg C or more in the solution just exiting the waveguide." However, they did not discuss the method for measuring such temperature changes.

Averaged short-latency and long-latency responses were plotted vs RFR level for each of three ganglia. These plots showed small differences

in latency between exposure and control periods for each ganglion. The authors gave no statistical treatment of the data but indicated that by t-test, such differences were nonsignificant ($p>0.05$) for either type of latency. The plots for two of these ganglia also showed temperature rises exceeding 0.2 and 0.4 deg C at the respective highest RFR levels.

The authors noted that some changes in response latencies over time were observed. They presented a plot of the short latencies at 36.5 deg C vs time for a ganglion in the absence of RFR, which showed a latency drift from about 15 ms initially to about 17 ms at 70 min. The short and long latencies were determined for a ganglion at 37 deg C for 35 min. This ganglion was exposed for five 1-min periods at 30 mW/sq cm (65 W/kg) alternating with 1-min control intervals during the middle 10 of the 35 min, which yielded no apparent effect on either latency. Thus, the latency drifts with time were not RFR-related.

Wachtel et al. (1975) exposed abdominal ganglia excised from the marine gastropod Aplysia to 1.5-GHz or 2.45-GHz CW RFR between center conductor and ground plane of a section of rectangular stripline, with the center conductor vertical. RFR was fed from the source through a circulator to the stripline section by coaxial cable. The section was terminated with a shorted stub, which reflected the energy not absorbed by the sample in transmission back through the sample for additional absorption. The remaining energy returned to the circulator, where it was absorbed by a dummy load. The forward and reflected powers were measured with a meter connected to a bidirectional coupler in the input coaxial cable. A few experiments were also conducted with 1.5-GHz and 2.45-GHz pulsed RFR.

Among the effects sought were RFR-induced changes in endogenous firing patterns of the two types of pacemaker neurons: "beating" pacemakers that have regular interspike intervals (ISIs) and "bursting" pacemakers, in which the action-potential (AP) bursts occur at regular interburst intervals (IBIs). Regarding pacemakers, the authors noted that the ISI of an unperturbed beating pacemaker neuron in an isolated ganglion of Aplysia usually varies less than 10% during several minutes and the IBI of a bursting pacemaker neuron was usually even more stable. Thus, RFR-induced changes exceeding about 10% were readily detected in this study, permitting determination of RFR thresholds for such changes. They also indicated that useful results were obtained from 41 separate neurons in about 25 "successful" experiments of 50.

For exposure, a ganglion was pinned with nonconductive cactus needles inside a small Plexiglas cylindrical chamber filled with seawater. The volume occupied by the various chambers used ranged from 0.3 to 0.8 ml (depending on the RFR frequency), all small relative to the volume of the stripline section. Intracellular microelectrodes were inserted through small holes in the ground-plane wall to stimulate neurons and record signals therefrom. The microelectrodes were filled with KCl solution, 2.5 M at the tip and 0.5 M in the barrel, yielding relatively low and high resistivities, respectively, with the latter rendering the barrel less susceptible to RFR and thereby reducing artifact potentials

to less than 1 mV.

With the simple geometry of the stripline (which propagated transverse electromagnetic waves) and the small sample size, SARs within the sample (expressed as absorbed powers in mW/cc) were calculated from the input power to the stripline, its cross-section, the dielectric properties and size of the Plexiglas chamber, and the volume and dielectric properties of the sample, as described in the appendix to the paper. The authors estimated that the values were incorrect by no more than 20%.

Temperature rises within the sample were monitored with a thermistor probe. The authors noted that by connecting the thermistor to a bridge circuit isolated from ground, previously observed temperature jumps indicating that the thermistor was functioning as an RFR sink were eliminated.

To illustrate the RFR-threshold-determination method, firing patterns for a beating pacemaker given a steady stimulus current to set its ambient ISI to 1 per second were presented. Each pattern covered about 1 min before and 1 min after exposure to 1.5-GHz CW RFR at 15, 30, or 45 mW/cc. No change in ISI was evident for 15 mW/cc, a slight ISI increase was observed several seconds after the onset of the RFR at 30 mW/cc, and the ISI increased by about 50% at 45 mW/cc. The authors concluded that 30 mW/cc was the threshold for this effect in this neuron.

Presented also were three illustrative bursting-pacemaker patterns. The first was a control pattern (2 min) to show the regularity of the IBI. The second was a 2-min pattern during the middle of which the neuron was exposed for about 25 seconds to 1.5-GHz CW RFR at 150 mW/cc, a level selected to yield a significant temperature rise (about 1 deg C) in the preparation. With RFR onset, the temperature rose linearly, and the second pattern showed an accompanying decrease in IBI (opposite to the RFR-induced increase in ISI for beating pacemakers). On termination of the RFR, the temperature decreased more slowly, and the IBI increased correspondingly. The third pattern was obtained with convective warm-air heating for about 25 seconds to obtain a temperature rise about the same as that induced previously by the RFR. The result was opposite to that with the RFR, an IBI increase (barely perceptible in the pattern) during heating. (Not clear was whether these patterns were for three distinct bursting-pacemaker neurons or for a single neuron given the RFR and convective-heat treatments in succession.)

The ISI thresholds for 14 beating pacemaker neurons tested were about 5 mW/cc for five, 10 mW/cc for four, 15 mW/cc for one, 25 mW/cc for one, and 30 mW/cc for three. For seven bursting pacemaker neurons, the IBI thresholds were 5 and 45 mW/cc for two at each level and 10, 25, and 30 mW/cc for one at each level.

In experiments with 1.5-GHz pulsed RFR (10-microsecond pulses at 1000 to 5000 pps) at 150 mW/cc (average), the percentage increases in ISI were comparable to those for 1.5-GHz CW RFR at the same level and convective heating. The authors noted that 10-microsecond pulses were very

short compared to the millisecond current pulses usually used to stimulate nerve cells, and that in a few experiments, "microwave pulses in the range of 10-100 msec may have increased efficacy in synchronizing firing patterns. A related effect has previously been reported in frog heart (Frey and Seifert, 1968)." (The latter finding is discussed in Section 3.6.3.) The authors noted that only a few experiments were performed with 2.45-GHz RFR for comparison with those with 1.5-GHz RFR and stated that: "...it is not possible to say that any difference in effects occurs at these two frequencies."

In their conclusions, the authors reiterated that the changes in firing patterns at RFR levels below 10 mW/cc were quite reproducible and they offered several inconclusive speculations regarding whether such effects would occur in cortical neurons of humans exposed at power densities between 1 and 10 mW/sq cm.

Chou and Guy (1978) designed a waveguide exposure system to study the effects of 2.45-GHz RFR on isolated tissues. Exposures were done from below in a vertical section of rectangular waveguide (inside dimensions 7.2 cm x 3.4 cm) filled with Ringer's solution to a height of 6 cm. A quarter-wavelength dielectric slab was used to match the impedance of the solution to that of air and to seal the bottom of the section. By measurement, the penetration depth of the solution was 1.65 cm at 2.45 GHz, so the 6-cm column of fluid was essentially equivalent to one of infinite length. A pump connected to inlet and outlet ports through the walls at the bottom of the section was used to circulate solution maintained externally at constant temperature.

Holes 3 mm in diameter were drilled in the four walls 1 cm above the dielectric slab, and Plexiglas chambers were glued to the outside walls against each hole. These chambers were used for holding stimulating and recording electrodes for specimens of isolated tissue mounted across the center of the waveguide either parallel or perpendicular to the electric field of the TE10 mode.

SARs of the Ringer's solution at the location of the isolated specimen were calculated from values of net forward (input minus reflected) power, the density of the solution, the cross-sectional area of the waveguide, and the attenuation constant of the solution. The authors noted that thin tissue preparations having dielectric properties close to those of the solution would not significantly perturb the fields therein. Thus, such calculated local SARs in the solution were deemed applicable to the tissues as well.

Using nonperturbing probes, SARs were also determined by measurements of temperature rises within specimens. Because of rapid heat convection in Ringer's solution, preparations were embedded in a jelly simulation of Ringer's solution. The results were in reasonable agreement with the calculated values (about 10% lower than the latter, possibly due to differences in properties of simulated and actual Ringer's solutions).

With this system, possible RFR effects on frog-sciatic and cat-

saphenous nerves, which contain mainly myelinated nerves, and on the rabbit vagus nerve, which consists of both myelinated and unmyelinated fibers, were sought. Also sought were effects on the superior cervical ganglion of the rabbit because it contains not only neuron cell bodies but also numerous synaptic junctions at which acetylcholine and norepinephrine are released.

Each vagus nerve or superior cervical ganglion was mounted within the waveguide (parallel or perpendicular to the E-vector), with one end passing through an appropriate hole in the waveguide wall to a pair of stimulation electrodes and the other end through the opposing hole to recording electrodes. Before, during, and after exposure to RFR, each specimen was stimulated with a 0.3-millisecond current pulse of 0.3-30 mA at 2-second intervals. The compound action potentials (CAPs) were recorded and their conduction velocity and amplitude were determined.

Vagus nerves were exposed to 1-microsecond RFR pulses at 1000 pps or 10-microsecond pulses at 100 pps for 10-min periods at average SARs of 0.3, 3, 30, and 220 W/kg or to CW RFR at the same SARs, with 5 min between exposures. The superior cervical ganglia were exposed for only 5-min periods because of their shorter lifetimes. Specimens were also exposed to pulsed RFR at an SAR of 220 W/kg average (220 kW/kg peak) and to CW RFR at 1500 W/kg in the absence of current-pulse stimulation to test for the possibility of direct RFR stimulation.

The temperature of the solution at the fluid outlet of the waveguide section was held constant at 37 +/- 0.02 deg C during exposure. At the higher RFR levels, however, the fluid temperature at the center of the mounted specimen (measured with a nonperturbing probe) rose by as much as 1 deg C because of the limited circulation rate of the pump. Frog-sciatic and cat-saphenous nerves were studied in similar fashion, but the frog preparations were immersed in amphibian Ringer's solution held at room temperature instead of mammalian Ringer's solution at 37 deg C.

For exposures of stimulated preparations to pulsed or CW RFR in either orientation relative to the E vector at SARs that did not increase the fluid temperature near the center of the specimen, no changes in either amplitude or conduction velocity of the CAP were observed. At the SARs that increased the fluid temperature by 1 deg C, a slight increase in conduction velocity was obtained, exemplified by the conduction velocity and peak CAP amplitude vs time, shown in Fig. 5 of the paper, for a cat saphenous nerve exposed to CW RFR at 1500 W/kg parallel to the E-vector. During exposure, the temperature increased by 1 deg C and the conduction velocity increased by about 2%, but the amplitude variations displayed were small and apparently not RFR-dependent. This conduction-velocity increase was reproduced by raising the temperature of the solution 1 deg C by non-RFR means.

Figure 6 of the paper showed CAP recordings for a stimulated rabbit vagus nerve before, during, and after exposure to 10-microsecond pulses (100 pps) at 220 kW/kg peak, and to CW RFR at 1500 W/kg, with the nerve perpendicular to the E-vector. For the pulsed-RFR case, the solution

temperature rose 0.3 deg C, which increased the conduction velocity slightly (from 117 to 118 m/s). For the CW case, the temperature rise of the solution was 1 deg C, which increased the conduction velocity from 117 to 135 m/s. An equivalent rise in solution temperature by non-RFR means yielded the same velocity increase.

The CAP recordings for a rabbit superior cervical ganglion mounted at right angles to the E-vector and exposed to 1-microsecond pulses (1000 pps) and to CW RFR at the same SARs as the vagus nerve were shown in Fig. 7 of the paper. For the pulsed RFR, the temperature rise of the solution was 0.3 deg C as before, but the latency time, 17 ms, remained unchanged. The temperature increase produced by the CW RFR was again 1 deg C, and the latency time decreased to 16 ms, a result reproduced by increasing the solution temperature 1 deg C by non-RFR means.

In the absence of stimulation by current pulses, no direct stimulatory effects of exposure were observed at the highest available SARs (pulsed RFR at 220 kW/kg peak or CW RFR at 1500 W/kg).

In addition to nerve preparations, Chou and Guy (1978) investigated the effects of RFR on contraction of rat diaphragm muscle. A muscle tension transducer was designed so that during contraction, a shutter between a light-emitting diode and a photoresistor would alter the transmission of infrared light from the diode to the resistor and hence the voltage across the resistor in proportion to the tension.

Diaphragm muscle with right and left phrenic nerves were excised and a section about 4 sq cm of the sternocostal portion of the muscle was dissected in Ringer's solution. Strings sutured on the central tendon and residual intercostal muscles were pulled through small opposing holes on the narrower walls of the waveguide. Two Plexiglas chambers attached to the exterior waveguide walls served to support the muscle under tension, and a third provided an access port for stimulating the phrenic nerve. The muscle was fixed at one end and connected to the tension transducer near the other end by the strings.

Current pulses 0.3 ms in width and 0.3-30 mA in amplitude were applied to the phrenic nerve once every 5 seconds for single-twitch experiments and 15-30 per second for tetanus experiments. The muscles were exposed to the pulsed or CW RFR at each SAR for 5 min, with intervals of 5-10 min between exposures.

A transient-averaging computer was used to obtain plots of mean tension vs time for 10 single twitches. The mean single-twitch tension for a muscle before, during, and after exposure to 1-microsecond pulses (1000 pps) at 220 kW/kg peak and to CW at 1500 W/kg were displayed in Fig. 8 of the paper. The pulsed RFR increased the solution temperature 0.2 deg C, but had little effect on twitch tension. The CW RFR increased the solution temperature by 1 deg C, a rise accompanied by a decrease in tension amplitude and a reduction of latency time. The postexposure values of tension amplitude and latency time were even smaller; however, these exposure and postexposure results were replica-

ted by a non-RFR-induced solution-temperature increase of 1 deg C.

Plots of mean tetanus tension for a muscle stimulated with 0.3-ms, 30-mA pulses at 15 pps and exposed to maximum pulsed and CW SARs (220 kW/kg and 1500 W/kg) during the decreasing phase of tetanic contraction were displayed in Fig. 9 of the paper. No RFR-induced changes were evident. Tests to determine whether the RFR at these SARs directly altered the tension of muscles not stimulated with current pulses also yielded no effects.

In their discussion, the authors noted that their negative results at SARs that did not increase the solution temperature were at variance with those of Kamenskii (1964, 1968), Rothmeier (1970), and Portela et al. (1975). However, the nerve preparations of Kamenskii and Rothmeier were exposed to RFR in air, so the SARs could have been high even though the incident power densities were low.

The authors also indicated that their negative findings in the absence of current-pulse stimulation do not support the hypothesis of direct neural stimulation proposed by Frey (1971) as the basis for the RFR-auditory effect or that RFR causes neurotransmitter release in isolated turtle hearts by excitation of nerve remnants (Tinney et al., 1976).

It is important to emphasize that the RFR fields were present within the preparations irrespective of their temperature equilibration with the Ringer's solution, i.e., even when the capabilities of the circulation system were adequate to avoid discernible temperature rises therein. Thus, a hypothesis that changes in neural CAPs or muscle tension might be produced by the fields per se (i.e., nonthermally) is negated by the absence of such effects at the SARs that yielded no measurable rises in solution temperature. On the other hand, the positive results at the SARs that increased the solution temperature were clearly thermal, as evidenced by their replication with non-RFR means. It is also likely that the preparations were heated by contact with the fluid rather than by RFR absorption, because these results were insensitive to orientation of the preparations relative to the E-vector.

The numbers of nerve and muscle preparations of each type studied were not indicated. Presumably the single results presented for each type were representative, but they provided no indication of how reproducible such results were. Representative results for the frog sciatic nerve were not presented.

McRee and Wachtel (1980) exposed isolated frog sciatic nerves to 2.45-GHz CW RFR from below in a waveguide system similar to that used by Chou and Guy (1978). Two thin-wall polyethylene tubes 2 mm in diameter were placed along a transverse centerline of the waveguide, presumably in the orientation parallel to the electric vector of the TE10 mode. One tube was located in proximity to the slab; the other was located 5 cm above the slab surface, where the intensity of the RFR was negligible because of the attenuation by the solution. One sciatic nerve from each frog was pulled through the lower tube for exposure and its mate was pulled

through the other tube as control. The tubes were used to preclude effects of toxic ions in the waveguide solution and to prevent leakages that could shunt the electrodes. Both tubes were filled with Ringer's solution. Stimulation electrodes were attached at one end of each nerve outside the waveguide, and recording electrodes were attached at the opposite ends.

SARs of the Ringer's solution at the lower nerve site were calculated as in Chou and Guy (1978). To determine whether the polyethylene tubes significantly altered the absorption characteristics of the solution, temperature-vs-time profiles were measured, during exposure at 100 W/kg for 60 min, with small glass-coated thermistors at locations within the tubes, just outside the tubes, and at the tube sites in their absence. The profile for the site next to the lower tube was slightly higher than for inside that tube, and the latter profile was slightly higher than for the site in the absence of the tube, but the differences were no greater than 0.1 deg C (at 100 W/kg). The differences among profiles for the control tube were negligible.

As noted by the authors, for a short period after a nerve is stimulated to fire by a current pulse, it is relatively refractory (less responsive to a second pulse). Thus, in the absence of fatigue, presentation of two pulses spaced at an interval longer than the refractory period would yield two compound-action-potential (CAP) responses of the same shape and magnitude. However, as a nerve fatigues from repeated stimulatory activity, its refractory period increases. Therefore, the amplitudes of CAP responses to second pulses (second-CAP responses) spaced from first pulses at intervals equal to the initial refractory period diminish with time relative to the amplitudes of the CAPs for the first pulses (first-CAP responses).

Since the refractory period for a healthy frog sciatic nerve is slightly longer than 5 ms, the exposed and control nerves were both stimulated with pairs of current pulses spaced 5 ms apart, so that the second pulse would occur at almost the end of the initial refractory period. Thus, time changes of the refractory period of the control nerve could be observed concurrently with possible alterations thereof in the nerve exposed to RFR. At the beginning of each experiment, both nerves were stimulated for 10 min with pulse pairs at a repetition rate of 5 pairs per second with no RFR present, allowing the nerves to stabilize. The repetition rate was then increased to 50 pairs per second and exposure to RFR at the desired SAR was begun.

In the first series of experiments, nerves were exposed at 100, 50, and 20 W/kg for 60 min at each SAR without circulation of the solution in the waveguide. As a consequence, the temperature-time profile for the exposed nerve at each SAR was higher than for the control nerve, with a difference of about 0.5 deg C at 100 W/kg. In this series, the stimulus magnitude of the pulse pair was set to yield maximal CAP amplitude for the first pulse and half-maximal CAP amplitude for the second pulse.

Representative recordings for 50 W/kg were displayed in Fig. 6 of the paper. The amplitudes of the first and second CAPs for the exposed nerve after 5 min of exposure were slightly smaller than corresponding values for the control nerve, with minor shape differences discernible. After 43 min, the CAPs of the control nerve had diminished slightly (retaining the 2:1 ratio between first and second amplitudes) but the CAPs of the exposed nerve had diminished much more. At 55 min, further diminution of the CAPs of the control nerve had occurred but the CAPs of the exposed nerve had become barely discernible on the scale used.

To quantify CAP changes and to account for vitality changes in control nerves, the "half-decay time ratio" (HDTR) for each CAP was defined as the time necessary for the CAP of the exposed nerve to decrease to half its value, divided by the half-value time for the corresponding CAP of the control nerve. Thus, values of HDTR less than unity indicated that the exposed nerve decayed faster than the control nerve, and vice versa for HDTRs larger than unity.

The HDTRs for the first series were given in Table I of the paper (adapted and presented below as Table 23).

TABLE 23: HALF-DECAY TIME RATIOS (HDTRs) FOR FIRST SERIES

EXPER.	SAR (W/kg)		FIRST-CAP HDTR	SECOND-CAP HDTR
5-23	100		0.99	0.48
5-24	100		0.56	0.35
8-30	100		0.80	0.83
9-8	100		1.00	0.25
		Means	0.79	0.39
6-1	50		0.96	0.79
6-7	50		0.82	0.50
6-8	50		0.79	0.86
6-17	50		0.23	0.21
9-18	50		0.71	0.78
9-19	50		0.40	0.61
		Means	0.51	0.49
6-14	20		1.00	0.59
6-16	20		0.67	0.50
9-20	20		1.00	1.00
9-22	20		0.70	0.74
		Means	0.82	0.66

The authors stated: "The times for the CAPs of the exposed nerves to decay to half amplitude for all SARs ... were less than for the CAPs of the unexposed nerves. Although no clear dose-response relationship could be detected for the first CAP decay, a faster decrease in amplitude of the second CAP did occur with increasing dose (SAR)."

It is noteworthy that presentation of the HDTRs for each nerve in Table 23 permitted not only a check of the means but also calculation of the standard deviations (SDs), not given in the paper. Surprisingly, all of the means shown in Table 23 were in error. The correct means and SDs are shown in Table 24:

TABLE 24: CORRECT MEAN HALF-DECAY TIME RATIOS FOR FIRST SERIES

SAR (W/kg)	FIRST-CAP HDTR (+/-SD)	SECOND-CAP HDTR (+/-SD)
100	0.84 +/- 0.21	0.48 +/- 0.25
50	0.65 +/- 0.28	0.63 +/- 0.24
20	0.84 +/- 0.18	0.71 +/- 0.22

The considerable variations among the individual results for each SAR were probably not RFR-related. By using the corrected values, dose-dependency was examined with the 1-tailed t-test, which showed that the differences among the first-CAP means for 100, 50, and 20 W/kg were statistically nonsignificant ($p>0.05$). This was also true for the second CAPs of the first series. At 100 W/kg, however, the mean second-CAP HDTR was significantly lower than the mean first-CAP HDTR.

Also performed in the first series were three experiments in which the temperature gradient between exposed and control nerves was reversed by using an infrared (IR) source to heat the control nerve (in the absence of RFR) to obtain the same differential level as that with RFR (but with the top nerve hotter than the bottom one). A reasonable simulation of the 100-W/kg temperature profile was achieved for the upper nerve in this manner. No CAP results for the IR experiments were presented, but the authors indicated that there was no significant difference in CAP decay time between the upper (IR-heated) and the lower (unheated) nerves. They therefore concluded: "From these results it would appear that the effects obtained are not due to a difference in temperature of the nerves but are specific to the microwave radiation." In their discussion, however, they stated: "Although elevating the temperature of the nerve did not have the same effect on vitality as microwaves, the conclusion that the effect on vitality is microwave specific does not preclude the possibility that nonuniform, localized heating or thermal gradients inside the nerves are the mechanisms producing the effect."

In the second series of experiments, the Ringer's solution within the waveguide was circulated through a temperature-controlled water bath. In this manner, the exposed and control nerves were maintained at 24 +/- 0.05 deg C for all SARs. The stimulus was set to produce equal maximal first and second CAPs. Exposures were done at 0, 5, 10, and 20 W/kg but only the results for 0, 5, and 10 W/kg were presented. (Two experiments of the second series were done at 20 W/kg; no data were presented, but the authors stated that since the results were basically the same as those of the first series at 20 W/kg, higher SARs were not used.)

Typical recordings for exposure 2, 50, 105, and 172 min at 10 W/kg

were presented in Fig. 7 of the paper. At 2 min, there was little difference between the first and second CAPs for either nerve or between the two nerves. At 50 min, the second CAP of the control nerve had diminished relative to its first CAP, indicating that the control nerve had lost some vitality. However, this effect was more pronounced for the exposed nerve. By 105 min, the first CAPs of both nerves and the second CAP of the control nerve had diminished, but the second CAP of the exposed nerve was no longer evident. By 172 min, the first and second CAPs of the control nerve had both decreased considerably, but both CAPs of the exposed nerve were absent.

The HDTRs obtained in the second series are shown in Table 25 (adapted from Table II of the paper). A check showed the means to be correct; the SDs are also shown.

TABLE 25: HALF-DECAY TIME RATIOS (HDTRs) FOR SECOND SERIES

EXPER.	SAR (W/kg)	FIRST-CAP HDTR	SECOND-CAP HDTR
5-24	0	1.40	1.57
7-11	0	1.21	1.00
7-13	0	1.11	1.04
	Means and SDs	1.24 +/- 0.15	1.20 +/- 0.32
6-28	5	1.21	1.19
7-05	5	0.75	0.68
7-07	5	1.91	0.97
7-16	5	1.07	1.22
	Means and SDs	1.24 +/- 0.49	1.02 +/- 0.25
5-19	10	0.64	0.50
6-21	10	0.35	0.55
6-22	10	0.36	0.40
7-12	10	0.74	0.17
	Means and SDs	0.52 +/- 0.20	0.41 +/- 0.17

In their discussion, the authors concluded that the SAR threshold was between 5 and 10 W/kg and that the effect was not reversible, since on termination of exposure, the nerves did not revitalize or increase their activity above that at the end of exposure.

It is interesting that the first-CAP means for 0 and 5 W/kg were both much larger than unity (1.24), indicating that the control nerves had decayed faster than the exposed nerves; however, the mean value at 10 W/kg was less than unity (0.52) and the decrease was significant by the 1-tailed t-test. Also, the second-CAP mean was larger than unity at 0 W/kg, about unity at 5 W/kg, and less than unity at 10 W/kg; the means for 0 and 5 W/kg did not differ significantly, but the mean for 10 W/kg was significantly lower than for 5 W/kg. Thus, these results support the existence of a threshold between 5 and 10 W/kg, but the occurrence of HDTRs larger than unity indicates that uncontrolled non-RFR factors

were present (ascribed by the authors to "natural variability of living nerves"). On the other hand, none of the HDTRs in the corrected results for the first series (Table 24) exceeded unity and all of the means were much less than unity, but the means showed no statistically significant SAR dependence (20 W/kg and higher). Thus, it is difficult to determine the relative importance of RFR and non-RFR factors in this study.

In a subsequent study, McRee and Wachtel (1982) used 2.45-GHz pulsed RFR (10-microsecond pulses at 50 pps) at an average SAR of 10 W/kg (20 kW/kg peak) in the same exposure system to study and compare the effects on frog sciatic nerves with those obtained previously with 2.45-GHz CW RFR at 10 W/kg (McRee and Wachtel, 1980).

In this as in the previous study, the stimulus was set such that the initial first and second CAPs were maximal and approximately equal in magnitude. At the start of each experiment, both nerves were stimulated for 10 min in the absence of RFR with pulse pairs at a repetition rate of 5 pairs per second, which allowed the nerves to stabilize. The repetition rate was then increased to 50 pairs per second (i.e., twin-pulse stimulation was done at 20-ms intervals) and RFR exposure was begun (at 10 W/kg average).

The 10-microsecond RFR pulses were delivered at 50 pulses per second, i.e., at 20-ms intervals. In one set of experiments, the RFR pulses were synchronous with the peak of the CAP. In another set, they were timed to arrive during the 15-ms quiescent intervals between successive 5-ms twin-pulse stimulations. In still another set, the RFR pulses were made to arrive asynchronously, i.e., at various times during the 5-ms stimulation intervals.

The authors did not present any representative CAP recordings, but they described the results qualitatively as follows: "During exposure the exposed nerves first underwent a prolongation of their refractory period as evidenced by a decrease in amplitude of the second CAP. This prolongation of the refractory period and decrease in the second CAP usually were observable after 20 to 30 min of exposure. Later in the exposure, severe decreases in maximal CAP amplitude occurred. During the same periods the control nerves showed little change in these characteristics."

As in the previous study, the HDTR (half-decay time ratio) was used to quantify RFR-induced effects on CAPs and to account for vitality changes in control nerves. The HDTRs for the first and second CAPs derived from five experiments with RFR pulses delivered in phase with the peak of the CAP are shown in Table 26 (Table I of this paper, in which the authors did include the SDs).

TABLE 26: HALF-DECAY TIME RATIOS (HDTRs) FOR RFR PULSES IN SYNCHRONY WITH THE PEAK OF THE COMPOUND ACTION POTENTIAL

EXPER.	FIRST-CAP HDTR	SECOND-CAP HDTR
12-3	0.72	0.74
12-7	0.76	0.71
12-12	0.35	0.60
12-14	0.26	0.43
12-19	0.30	0.49
Means and SDs	0.58 +/- 0.25	0.59 +/- 0.14

Surprisingly again, there were errors: the correct first-CAP mean and SD are 0.48 +/- 0.24; the second-CAP mean was correct but the correct SD is 0.13. However, these errors were not material because the difference in means was not significant in either case. All 10 individual ratios were less than unity, indicating that both the first and second CAP of each exposed nerve had decayed faster than its control nerve.

Tables 27 and 28 (Tables II and III of the paper) displayed the mean first- and second-CAP ratios and SDs for the five experiments with synchronous RFR pulses out of phase with the peak of the CAP and for the six experiments with asynchronous RFR pulses, respectively.

TABLE 27: HALF-DECAY TIME RATIOS (HDTRs) FOR RFR PULSES OUT OF PHASE WITH THE PEAK OF THE COMPOUND ACTION POTENTIAL

EXPER.	FIRST-CAP HDTR	SECOND-CAP HDTR
12-31	0.85	0.71
1-3	0.55	0.57
1-4A	0.93	0.73
1-4B	0.53	0.60
2-25	0.46	0.63
Means and SDs	0.66 +/- 0.21	0.65 +/- 0.07

TABLE 28: HALF-DECAY TIME RATIOS (HDTRs) FOR ASYNCHRONOUS RFR PULSES

EXPER.	FIRST-CAP HDTR	SECOND-CAP HDTR
2-26A	0.82	0.83
2-26B	0.31	0.93
2-27A	0.60	0.71
2-27B	0.36	0.33
2-28	0.44	0.61
2-29	0.45	0.76
Means and SDs	0.50 +/- 0.21	0.69 +/- 0.21

The means and SDs in Table 27 were correct and small errors in Table

28 were inconsequential. In both sets of experiments, all the ratios were also less than unity, but the first-CAP and second-CAP means did not differ significantly. The authors stated: "In all cases both CAPs of the exposed nerves lost their vitality in a shorter time than in the control nerves. Statistical examination of the data was performed using both the analysis of variance and the two-sided t test. In all cases the loss of vitality of the exposed nerve was highly significant ($P<=0.01$) when compared to that of the control nerve. However, no significant difference in loss of vitality was detected with different phasing of the microwave pulses with the CAPs." A minor comment about the statistical treatment is that perhaps the authors should have used the 1-tailed instead of the 2-tailed t-test, because the outcome sought was unidirectional (loss of nerve vitality).

The less-than-unity HDTRs displayed in the three tables of the paper clearly indicate that the vitality of every exposed nerve, as assessed from the first and second CAPs separately, diminished more rapidly than that of its control nerve. Not clear, however, is the interpretation of the observation that some of the second-CAP HDTRs were larger than their corresponding first-CAP HDTRs. For example, the first-CAP and second-CAP HDTRs obtained in one of the experiments with RFR pulses at the peak of the CAP response were respectively 0.35 and 0.60 (Table 26). One possible interpretation of this result is that the second-CAP time of the control nerve had not changed materially relative to its first-CAP time (as befits an adequate control) and that the second-CAP time of the exposed nerve had increased about 71% relative to its first-CAP time, a biologically unlikely result. A more tenable interpretation is that the second-CAP time of the control nerve had decreased materially while that of the exposed nerve also had decreased, but less so. If this had been the case, then there were uncontrolled non-RFR factors present in the experiment.

The case above is not unique. Specifically, the second-CAP mean HDTR for that set of experiments (0.59) was 23% larger than the (corrected) first-CAP mean (0.48); also, the first- and second-CAP means shown in Table 28 were 0.50 and 0.69, respectively. It is interesting that in the study with CW RFR (McRee and Wachtel, 1980), there were also a few isolated cases similar to those above, but all of the second-CAP means were smaller than their corresponding first-CAP means.

On the overall findings of this study, the authors noted: "It would seem reasonable that if pulse-microwave radiation had an immediate effect on the sciatic nerve, it would have been greater with the pulses delivered during the firing of the nerve. Our results showed that the increased rate of loss of vitality of the exposed nerves did not depend upon the phasing of the microwave pulses with the nerve action potential. Asynchronous microwave pulses which moved randomly through the action potential, pulses synchronized with the peak of the action potential, or pulses synchronized with the quiescent period of the action potential produced the same effect on vitality." They also noted that by analysis of variance, there were no significant differences in the effects on nerve vitality of 2.45-GHz CW and pulsed RFR at 10 W/kg.

The findings of the two studies by McRee and Wachtel (1980,1982) appear to be contrary to the negative results reported by Chou and Guy (1978) for exposure of isolated nerves from the cat and rabbit to CW and pulsed 2.45-GHz RFR. As previously noted, however, Chou and Guy (1978) did not present any data for the frog.

3.4.2.2 IN-VITRO HISTOCHEMICAL EFFECTS

Olcerst and Rabinowitz (1978) performed experiments to determine whether 2.45-GHz RFR alters the activity of the enzyme acetylcholinesterase (AChE) in purified form (at a concentration of 5 units per ml in 0.1 M phosphate buffer) or the activity of AChE in defibrinated rabbit blood. Enzyme assays of purified samples at room temperature and blood samples at 37 deg C were performed by recording spectrophotometer. The authors noted that changes in enzyme activity could affect the concentration of bivalent cations in blood serum. Such assays were performed by atomic absorption spectroscopy.

In each experiment, two 1.5-ml samples, each within a jacketed quartz cell, were placed within an anechoic chamber, one sample for exposure at a distance of 12.7 cm (about one wavelength) from the crossover of a horizontally directed diathermy antenna and the other sample at a site that was shielded from the RFR as a control. The exposure levels were calibrated by measuring the power densities at various distances from the crossover with an NBS power density meter for several values of source power (determined with a bidirectional coupler). For cooling during exposure, paraffin oil (dielectric constant about 2.0) was pumped in series through the two jackets to an external water bath maintained at 37 deg C. Sample temperatures were not monitored during exposure but were determined from cooling curves obtained after exposure termination with a thermistor probe. The authors indicated that the temperatures of control samples tracked those of the exposed samples to 0.5 deg C. In some experiments, samples were not cooled. Control runs with the RFR off were also made.

In one set of experiments, the mean initial velocity of enzyme activity (the amount of substrate cleaved per unit time just after exposure) was determined for samples of purified enzyme in buffer exposed to 2.45-GHz CW RFR at 0, 10, 15, 25, 50, 75, 100, or 125 mW/sq cm for 0.5 hr, or at 0 or 25 mW/sq cm for 3 hr. The results were tabulated as means and SDs and whether or not each result was statistically significant at the 95% confidence level (but the numbers of samples tested were not presented). Exposure at 125 mW/sq cm for 0.5 hr with the sample uncooled yielded the only result stated to be significant: a drop in mean initial velocity of enzyme activity.

In another set of experiments, the initial velocity of enzyme activity in defibrinated rabbit blood (the amount of substrate cleaved initially per unit time per red blood cell ccunted with a hemocytometer) was determined for samples maintained at 37 +/- 0.5 deg C and exposed for 3 hr to 2.45-GHz CW or square-wave-modulated RFR (0.75-ms pulses at 710 pps) at 0, 21, 35, and 64 mW/sq cm (average power densities). Tabulated

were results that appeared to be for one sample per exposure condition, i.e., with no indication of statistical treatment. These results showed no differences.

The release of bound calcium and magnesium from rabbit blood cells was investigated in a third set of experiments. Samples were sham-exposed or exposed to 2.45-GHz RFR (presumably CW) for 3 hr at 25 mW/sq cm, after which the serum concentrations of Ca and Mg ions were assayed. The means and SDs for each cation were presented with an indication that by t-test, none of the differences between exposed and control samples was significant (but the numbers of samples tested were not given).

Regarding their only positive finding, the authors noted that with the samples uncooled, the RFR power absorbed was sufficient to denature the enzyme, and that therefore the result was not relevant to possible in-vivo effects on AChE. However, they indicated their awareness of the limitations of postexposure assays.

Galvin et al. (1981c) investigated whether the activities of AChE and creatine phosphokinase (CPK) are altered by in-vitro exposure to RFR. They exposed AChE derived from the electric eel or CPK derived from rabbit muscle to 2.45-GHz CW RFR in a chamber consisting of a distilled-water-filled waveguide section. The input end of the section was sealed with a dielectric slab of quarter-wavelength thickness, to match the impedance of the section to that of air, and the output end was sealed with a short. For exposure to the RFR, a cylindrical tube holding 4.2 ml of sample was inserted adjacent to the dielectric slab through holes in the waveguide section (with the tube ends outside the waveguide); for control, another tube of sample was similarly inserted 9.5 cm along the propagation direction from the first tube, at which the RFR level was negligible because of the attenuation by the intervening water. The contents of each tube were stirred magnetically outside the waveguide and their temperatures were maintained at 37.25 +/- 0.25 deg C by water circulating continuously through the waveguide.

For treatment of AChE, 0.025 ml of the enzyme was added to 4.0 ml of phosphate buffer within each tube and the mixture was incubated for 5 min prior to exposure to equilibrate to 37 deg C within the waveguide. For treatment of CPK, 4.0 ml of substrate solution (CPK -1) in each tube was allowed to equilibrate for 5 min, 0.2 ml of CPK was then added, and the RFR was turned on. Exposures of each enzyme were at SARs of 1, 10, 50, or 100 W/kg. At the start of exposure and at every 2 min afterward for 10 min, 0.7-ml aliquots were taken from each tube and placed in test tubes at 0 deg C to stop the reaction. To maintain uniform exposure of the enzyme, each aliquot removed from the tubes was replaced with 0.7 ml of phosphate buffer.

Absorbance values for the aliquots of AChE and CPK were determined by spectrophotometry at 412 and 340 nm, respectively, with corrections for progressive dilution by buffer replacement of the withdrawn aliquots. Least-squares regression analysis was used on the data to obtain best-fit lines, and the paired 2-tailed t-test was used to compare reaction

rates of each RFR-exposed enzyme with its control. In an auxiliary experiment, the AChE and CPK activities of unexposed diluted samples (corrected for dilution) were compared with those of unexposed undiluted samples; the differences were found to be nonsignificant ($p>0.05$), thus confirming the validity of successive dilution in exposure experiments.

Typical plots of absorbance vs time for samples exposed at 50 W/kg and corresponding control samples showed almost coincident linear rises for each enzyme. The AChE and CPK activities for samples exposed at 1, 10, 50, and 100 W/kg, expressed as time rate of change in absorbance, did not differ significantly from their respective controls or from each other, thus revealing no effect of the RFR at any of the levels used.

Millar et al. (1984) sought possible changes in AChE from exposure to discrete RFR frequencies in the range 2.375-2.700 GHz, using a system designed to permit optical measurements of enzyme activity in a sample during exposure. The exposure system consisted basically of a microwave stripline with its short axis vertical. Mounted thereon was an 8-mm-square sample cell 3 mm thick, with one diagonal vertical and pipes fitted thereto to pump sample fluid into and out of the cell and to permit escape of bubbles in the sample. The normal flow rate was 10 ml/min, the sample volume was 0.192 ml, and the total volume of mixture circulated was about 4 ml, so the normal volume element residence time (cell volume/flow rate) was 0.0192 min (not seconds, as stated at the top of p. 171) or 1.15 seconds. SARs were calculated from measurements of forward, reflected, and transmitted powers and the sample volume.

For measurements of enzyme activity during exposure, a light beam from a monochromator (450 nm) was piped to the center of one of the sides of the cell by a quartz fiber-optic bundle. Light emerging at 180 deg from the center of the opposite side of the cell was similarly conveyed to another monochromator (450 nm) and thence to a photomultiplier with output fed to a photometer. Light emerging from the center of one of the other sides of the cell, scattered at 90 deg to the incoming beam by the sample, was similarly treated. Enzyme activities were determined alternately in the presence and absence of RFR with four fresh samples each, and the results were expressed as mean ratios (MRs) of activity with RFR present to activity with RFR absent and the SDs.

The AChE was derived from the electroplax of the ray fish, Narcine brasiliensis, and was rendered membrane-free. For most experiments, 50 microliters of enzyme mixed with about 20 ml of reaction solution was recirculated through the cell and through temperature-controlled jackets at 10 ml/min, which held the mixture at 25 or 37 deg C (+/- 0.2 deg C).

Exposures in one series of experiments were to 2.45-GHz pulsed RFR, with pulse durations of 4.8, 2.4, and 1.2 microseconds at repetition rates of 625, 1250, and 2500 pps, respectively, to yield a duty cycle of 0.003. About the mean (time-averaged) SARs for this series, the authors stated: "...the mean specific absorption rate (SAR) at the two absorbed power levels can be calculated as 2,460 W/kg and 4,290 W/kg, respectively. Peak power SAR is then 0.82 MW/kg and 1.43 MW/kg." The

latter values are consistent with the stated duty cycle. In Table 29 (adapted from Table 1 of the paper), which embodied the results for this series, the mean SARs cited were 2,460 W/kg and 4 (not 4,290) W/kg, a discrepancy that could not be resolved because the authors did not state the two absorbed power levels alluded to above.

TABLE 29: EFFECT OF 2.45-GHz RFR ON AChE ACTIVITY

	Mean SAR = 2460 W/kg			Mean SAR = 4 W/kg		
Pulse Width	4.8	2.4	1.2	4.8	2.4	1.2
Rep. Rate	625	1250	2500	625	1250	2500
MR at 25 deg C	1.00	1.00	1.03	0.98	1.04	1.01
+/- SD	0.012	0.026	0.018	0.036	0.003	0.010
MR at 37 deg C	1.00	0.980	0.985	1.00	0.993	1.00
+/- SD	0.001	0.020	0.010	0.005	0.012	0.003

All of the MRs were essentially unity, and the authors concluded: "At these levels, there is no significant effect of microwave irradiation on AChE activity."

In the next series of experiments, the effects on AChE activity of 2.45-GHz RFR at relatively low SARs were determined. Pulses 8 microseconds in duration at 50 pps were used (0.0004 duty cycle), and the temperature of the samples was 25 deg C. The results are displayed in Table 30, in which the mean absorbed powers (in mW) as well as SARs are stated:

TABLE 30: EFFECT OF LOW-INTENSITY 2.45-GHz RFR ON AChE ACTIVITY

Mean Absorbed Power	68	36	6.9	2.6
Mean SAR	330	180	34	13
MR	0.972	0.967	1.005	1.00
+/- SD	0.007	0.002	0.016	0.003

The authors indicated that by paired t-test, only the results for 330 and 180 W/kg (a loss of about 3% in AChE activity) were significantly different from unity ($p<0.001$). However, they questioned whether such a loss would measurably affect behavior or neurologic function.

Within the limits of the available RFR generator, possible effects of RFR frequency were sought. Pulses 16.7 microseconds in duration at 30 pps were used (0.0005 duty cycle), and the temperature of the samples was 25 deg C. The results, presented in Table 31, showed no significant departures from unity:

TABLE 31: EFFECT OF RFR FREQUENCY ON AChE ACTIVITY

Frequency (GHz)	2.375	2.425	2.500	2.550	2.625	2.700
Mean SAR	42	40	42	44	35	32
MR	0.999	0.999	0.998	0.997	1.002	0.998
+/- SD	0.003	0.003	0.002	0.002	0.004	0.003

Next, repetition rates of 10-90 pps (in steps of 10 pps) at a constant duty cycle of 0.0004 were used to determine whether this variable was im-portant. The mean SARs were all about 1900 W/kg and the sample temperature was 25 deg C. The MRs were presented graphically with SD bars with a view toward more readily revealing "EMR-effect windows," if present. [See Section 3.4.4.] From the graph, the minimum and maximum MRs were about 0.97 (at 50 pps) and 1.00 (at 40 pps) and most of the SD bars overlapped.

The authors stated that there was no distinguishable trend of increase or decrease in AChE activity, but since all but one MR was less than unity, the sign test indicated that: "the apparent treatment-associated decrease is significant within 95% confidence limits." They also noted, however: "While an oscillatory mode might be concealed in these data, the fact that the standard error bars overlap make us question the sign test as validly pointing to a significant EMR effect on enzyme activity. This view was supported by a Student's paired t-test that showed that only the 50- to 60-pulse experiments achieved confidence levels of .05 and .01, respectively. The remaining values clustered about confidence levels of .2--not significant. Nevertheless, the 50- to 60-pulse/s results are statistically significant. They fall in the exposure rates of known EMR windows, but the biological consequences of such small changes are moot at best."

The possibility that duty cycle might be important was considered also. For 2.45-GHz RFR at 1750 W/kg with pulses at 50 pps and duty cycles of 0.0008, 0.0016, and 0.0032, no change in AChE activity was observed; the MR was 0.996 +/- 0.005.

Last, the authors suggested the possibility (deemed unlikely) of RFR-initiated kinetic-reaction chains, particularly with regard to residence time of samples within the exposure cell, which might lead to cumulative or time-delayed effects. Experiments were done with 1.2-microsecond pulses at 2500 pps for a mean SAR of 483 W/kg, in which only the flow rate of mixture through the cell was varied. For residence times (cell volume/flow rate) of 0.44 to 2.09 seconds, MRs ranged nonmonotonically from 0.996 +/- 0.004 to 0.999 +/- 0.003, and the MR for zero flow rate was 1.00 +/- 0.01.

3.4.2.3 IN-VIVO HISTOLOGICAL AND HISTOCHEMICAL STUDIES

Tolgskaya and Gordon (1973) reported various effects in approximately 650 animals, predominantly rats, of exposure to RFR in the range 500 kHz to 100 GHz. The pathological effects of RFR in the "decimeter band"

(0.5-1 GHz) at "high intensity" (20 to 240 mW/sq cm) included multiple perivascular hemorrhages in the brain and other organs, apical-dendrite degeneration in the cortex, cloudy swelling of cytoplasm, cytoplasmic shrinkage, vacuole formation, unevenness of staining, disappearance of cytoplasmic structures, fatty degeneration, ribonucleoprotein decrease, and occasional karyocytolysis. These high intensities were capable of causing death of the animals since they produced signs of hyperthermia (temperature increases up to 42-45 deg C) in several minutes to several hours. Photographs of the exposure arrangement showed multiple animal exposures at the same time in a room that appeared to not have RFR-absorbing material on the walls. It is likely that the SARs for the individual animals under these conditions varied widely and that all effects were thermal in nature.

Exposures referred to as "low-intensity" were also performed. The authors defined the threshold field intensity for nonthermal effects ("intensity not raising body temperature") for decimeter microwaves as 40 mW/sq cm, and these exposures were generally at or slightly below 10 mW/sq cm for 60 min daily for 10 months. Investigation of the animals by ordinary morphological methods revealed practically no vascular disorders in the nervous system. "Delicate elective neurohistological methods" (not described), however, showed disappearance of spines from cortical dendrites; appearance of beading and irregular thickening of dendrites; swelling of cytoplasm of individual cells (with appearance of vacuoles) in the basal ganglia and hypothalamus; and focal and diffuse proliferation of microglial cells, with microglial processes showing initial signs of degeneration.

Many of these low-intensity effects were similar to those described for the high-intensity exposures. At 10 mW/sq cm, the whole-body SAR for a medium rat in the decimeter band (0.5-1 GHz) ranges from 6 to 8 W/kg (Durney et al., 1978, p. 95), and there were internal regions of higher local SARs that may have been enhanced in the multiple-animal exposure arrangement mentioned above. Thus, it seems likely that the described effects (more subtle than those of frank hyperthermia) were thermally induced also.

Shtverak et al. (1974) investigated whether 2.85-GHz pulsed RFR (2.7-microsecond pulses at 357 pps) at 30 mW/sq cm (average) would affect the responses to stimulation by bell of rats with an inherited disposition to sound-induced epileptic seizures. Starting on postnatal day 2, 24 such rats were exposed concurrently in perforated Perspex boxes to the RFR 4 hr daily (0800-1200) for 10 weeks excluding Saturdays and Sundays, and 16 were sham-exposed. (The exposure arrangement and animal spacing were not described, but the authors stated that the positions of the rats were changed stepwise for successive periods to obtain comparable exposures.) The absorption rates were not given, but the corresponding whole-body SAR of a small rat in either the E- or H-orientation would be about 9 W/kg (Durney et al., p. 94). During exposure, temperatures were monitored in two fixed boxes and were found to vary from 24.7 to 27.8 deg C and the temperature in the exposure room rose from 23 to 26 deg C.

Starting with postnatal week 4, the rats were weighed weekly and were tested with a bell once weekly for six weeks. If no change in behavior was observed after 1 min of uninterrupted ringing, the reaction of the rat was scored as null. For rats that responded with a motor reaction that ended in convulsions, the interval between initiation of ringing and onset of seizure was recorded. (Neither the duration of seizure nor the duration for recovery was assessed.) In addition, the number of rats that died was recorded. The results were expressed as percentages and were evaluated by t-test.

From postnatal weeks 4 to 10, the body weight of all the rats tended to increase, more so by males than females. Most mean weekly weights of the RFR-exposed males were smaller than for the sham-exposed males and similarly for the females, but the differences were nonsignificant. Two RFR-exposed rats and one sham-exposed rat died during the first 4 weeks.

Weekly sound tests yielded null reactions from about 70% of the RFR-exposed and about 20% of the sham-exposed rats, a significant difference ($p<0.05$). For those that responded positively, the mean time interval to seizure onset was higher in the RFR-exposed than sham-exposed rats. The authors stated that the difference between RFR and sham groups for week 6 was significant and not significant for the other weeks, but the error bars on the graph appear to overlap considerably for all weeks.

The authors concluded that exposure to the pulsed RFR tended to lower the sensitivity of rats to audiogenic seizure and increase the number of null reactions. They also noted that qualitatively similar results were obtained for rats exposed to a pulsed electrostatic field (800-V 10-microsecond pulses, 769.2 pps, at 130 V/cm, thus presumably exposed between electrodes spaced about 6 cm apart).

Albert and DeSantis (1975) sham-exposed or exposed a total of 60 adult male and female Chinese hamsters in individual vented Plexiglas chambers to far-field 2.45-GHz CW RFR within an anechoic chamber at 50 mW/sq cm for 30 min to 24 hr, or at 25 mW/sq cm 14 hr/day for 22 days. Hamsters exposed at 25 mW/sq cm were given one pellet of chow and 5 ml of water during each 14-hr exposure and ample food and water between exposures. Right after exposure at either level or after recovery for 1 to 2 weeks postexposure, hamsters were anesthetized and perfused with fixatives, and selected tissues were sectioned and stained for light- or electron-microscopic examination. Two of the animals were fixed with potassium dichromate and the brains were stained for showing degenerating myelin. Frozen sections of others were stained for revealing degenerating axons.

At the light-microscopic level, the cytoplasm of hypothalamic neurons from hamsters exposed at 50 mW/sq cm was markedly pale and displayed vacuolization and chromatolysis. Although the nuclear structure was unaltered, the cytoplasm often appeared frothy (probably an artifact called "frothy bloat," not seen by Albert in subsequent studies with modified techniques). In rare instances, vacuoles were detected within nuclei. Vacuoles were not present in the cytoplasm or nuclei of glial cells. At the electron-microscopic level, the preferential appearance

of vacuoles in the cytoplasm was evident for hamsters exposed at 25 mW/sq cm for 22 days. Vacuolization and chromatolysis in hypothalamic neurons were more prominent in animals euthanized immediately after exposure than in those euthanized 6-10 days after exposure, indicating some recovery.

Similar morphologic changes were observed in the subthalamus, but not in areas adjacent to the thalamus, i.e., the ventrobasal complex and the lateral geniculate nucleus. Also, the neurons in other regions of the central nervous system of hamsters exposed to either RFR level appeared unaltered relative to comparable tissues from control hamsters. At the light-microscopic level, no changes were found in Purkinje-cell bodies of the cerebellum, motor neurons in the ventral horn of the spinal cord, mesencephalic nuclei of the trigeminal nerve, or hippocampal pyramidal neurons. (Observations of these areas by electron microscopy were not reported in this paper.)

The authors reported some tentative evidence for axonal degeneration in RFR-exposed hamsters, but indicated that vagaries may occur with the staining method used; they stated: "The degenerated axons were widely scattered and did not seem to be confined to well-delineated pathways or distinct nuclear groups, as is customarily the case in animals with known lesions."

There was no evidence of myelin degeneration, gliosis, hemorrhage, or perivascular edema in the RFR-exposed hamsters. However, vascular stasis, or congestion, was observed in some animals.

The authors did not discuss SARs, but in the discussion printed with the paper, Dr. A.W. Guy noted that SARs as high as 4 W/kg per incident mW/sq cm were measured in his laboratory for animals of similar size, that the peak SARs (at 10 to 50 mW/sq cm) could have been 40 to 200 W/kg in some brain regions of the animals, and that this SAR range far exceeds that normally used for diathermy treatment in 20-min exposures of patients. He also noted that rectal temperature would not necessarily indicate the presence of high SARs in such local areas.

Dr. J.W. Frazer queried: "How do your histologic findings compare to those seen in animals that have experienced fevers of 4-5 deg C?" Dr. Albert's response was that: "Vacuolation and chromatolysis in the hypothalamus are typical responses of heated neurons."

Albert and DeSantis (1976) studied histological effects in the brains of 30 Chinese hamsters exposed to 1.7-GHz CW RFR at 10 or 25 mW/sq cm for 30 to 120 min. For each RFR level, each of 15 hamsters was paired with a sham-exposed hamster and both were otherwise similarly treated. Of the 15 hamsters in each RFR and sham group, 11 were euthanized right after exposure and the remaining 4 of each group were euthanized after 7 to 15 days for recovery. The whole animal was fixed and its brain was removed, further fixed, transversely cut into four blocks that included, respectively: forebrain, diencephalon and midbrain, pons and cerebellum, and medulla. Each block was dehydrated, embedded in paraffin, sectioned

and stained with hematoxylin-eosin or thionin. Serial sections were made through the diencephalon. Corresponding sections from each of the paired exposed and control hamsters were placed on the same slide prior to staining.

Eight of the hamsters exposed at 10 mW/sq cm and euthanized immediately after exposure exhibited greater cytological alterations in hypothalamic and subthalamic neurons than controls; for two of the other three, the appearance of these regions was similar to that of the controls; in the third exposed hamster, the histological changes were inconsistent. Of the four hamsters exposed at 10 mW/sq cm and euthanized after recovery, three displayed histological changes in the hypothalamus and subthalamus similar to those seen in the exposed hamsters euthanized right after exposure, and the fourth showed no changes relative to its control.

Seven of the 11 hamsters exposed at 25 mW/sq cm and euthanized right after exposure showed more extensive changes in the hypothalamic and subthalamic neurons than their controls; one hamster exhibited no differences and the other three an inconsistent histological pattern. Of the four hamsters allowed to recover after exposure, three showed more prominent changes than their controls and the other was similar to its control.

Regarding the hamsters exposed at 10 mW/sq cm, the authors noted: "Neurons of the hypothalamus and subthalamus were most dramatically affected in experimental animals that showed structural changes. More specifically, neurons of the medial part of the ventromedial as well as the dorsomedial and often the lateral nuclei of the hypothalamus were affected by irradiation. Areas of the subthalamus that were involved included the zona incerta and tegmental field, but not the subthalamic nucleus itself. Neurons of animals exposed to 10 mW/sq cm were swollen, their cytoplasm appeared vacuolated and stained less basophilic than their control counterparts...In all cases the cytological changes appeared to be restricted to the cytoplasm. Nuclei of neurons appeared normal. No evidence of pyknosis or eccentric position on the part of nuclei was observed. Similar morphological observations were made on brains of animals exposed to 25 mW/sq cm."

The authors indicated that the blood vessels in the affected brain areas appeared normal, with no evidence of hemorrhage or edema, and that no obvious histological alterations were seen in other parts of the central nervous system examined, including the cerebral cortex, cerebellum, medulla, and pons. They also noted that the findings were similar to the previous ones for 2.45-GHz RFR at 25 and 50 mW/sq cm (Albert and DeSantis, 1975), and stated: "Clearly, at those power densities one could suspect that the common factor might be the thermal effects. However, similar changes have now been observed at 10 mW/sq cm, and this power density may be non-thermal." The latter comment is questionable in the light of Guy's point above.

Albert et al. (1981a) sought effects of prenatal and postnatal expo-

sure of Sprague-Dawley rats to RFR on the Purkinje cells of the cerebellum. The authors noted that development of the mammalian brain is dependent on migration of nerve cells, the patterns of which are well understood for the cerebellum. Cerebellar Purkinje cells were selected for study because these cells provide a relay station for major input to, and output from, the cerebellum and because they are readily identifiable in the interface between the molecular and granular layers.

In experiment 1, six pregnant rats in individual ventilated Plexiglas containers were exposed concurrently in groups of three from above with a truncated horn to 2.45-GHz CW RFR at 10 mW/sq cm in one of two anechoic chambers. Six other rats were similarly treated but sham-exposed in the other anechoic chamber. Exposures were for 5 days, 21 hr/day, starting on gestation day 17. The rats were moved for 1.5 hr twice daily during each exposure period to conventional rat cages, where food and water were available ad libitum.

In experiment 2, six matched pairs of 6-day-old litter mates were used. One of each pair in a ventilated Plexiglas cage was exposed to 2.45-GHz CW RFR for 5 days, 7 hr/day, in one of the anechoic chambers while the other was sham-exposed in the other chamber. Daily exposure sessions were for 3.5 hr each in the morning and afternoon, with 1.5 hr between sessions for feeding. During all periods of no RFR- or sham-exposure, the pups were reunited with their dams in conventional cages.

In experiments 1 and 2, the rats were transported from George Washington University (GWU) to the Bureau of Radiological Health (BRH) for exposure and were returned to GWU for study after completion thereof. For these experiments, a nonperturbing probe was used to measure power densities within each empty Plexiglas cage with and without subjects in the other cages. The results indicated that the values varied with site within the cage and with time, due to rat movements in the other cages (no data presented). Thus, it was determined that at a mean power density of 10 mW/sq cm, the power density might vary with time from 4 to 30 mW/sq cm. From Durney et al. (1978), pp. 95-96, the corresponding time-averaged SAR for each pregnant rat in either the E- or H-orientation was about 2 W/kg, with a range from 0.8 to 6 W/kg.

In experiment 3, four pregnant rats were exposed concurrently to 100-MHz CW RFR at 46 mW/sq cm at the Environmental Protection Agency, North Carolina (EPA) in a transverse electromagnetic (TEM) cell described in Smialowicz et al. (1981b). Mean SARs ranged from 2 W/kg for pregnant rats to 3 W/kg for neonates, with intermediate values for older pups. The exposures were performed during 0800-1400 daily on gestation day 6 through term, after which the offspring were exposed 4 hr daily for 97 days. Four other pregnant rats and their pups were similarly treated but sham-exposed. The treated offspring were delivered to GWU 14 months after cessation of exposure.

In all three experiments, the brain of each RFR-exposed animal was processed concurrently with its corresponding sham-exposed control. After anesthesia, each rat was fixed with formalin by cardiac perfusion

and the cerebella were removed, divided in the midsagittal plane, embedded in paraffin, serially sectioned (10 micrometers thick), and stained. Six to nine parasagittal planes were selected and used as constant reference levels for matching cerebellar sections from RFR- and sham-exposed rats. Four to six serial sections were studied at each plane. Each section was projected, the boundaries of various regions were outlined, the geometric areas within the boundaries of interest were determined with a planimeter, and the Purkinje cells within the molecular-granular interface were counted. (Cells without visible nucleoli were not counted.) All cell counts were performed double blind by two individuals. Results were presented in terms of the mean density of Purkinje cells (number per sq mm) and standard error (SE) for the RFR- and sham-exposed groups.

In experiment 1, the pregnant rats delivered their pups within 12 hr after completion of their RFR- and sham-exposures and return to GWU. Three of the six pups exposed prenatally to RFR and three of the six pups sham-exposed prenatally were euthanized on postnatal day 1, and the remaining three pups of each group were euthanized 40 days after birth. The cerebella from the day-1 pups were not mature enough for clear discernment of the Purkinje cells, so no data were presented. The mean counts for the RFR-exposed 40-day pups were 35.87 +/- 1.71 cells/sq mm, as compared with 48.47 +/- 2.26 cells/sq mm for the sham-exposed 40-day pups. The 25.8% decrease for the RFR pups was significant ($p<0.01$).

In experiment 2, three pups exposed to RFR and three pups that were sham-exposed postpartum were euthanized immediately after return to GWU and the other three of each were euthanized 40 days after cessation of RFR- or sham-exposure. For the pups euthanized immediately, the mean counts were 87.46 +/- 4.62 cells/sq mm for the RFR-exposed pups and 115.68 +/- 5.30 cells/sq mm for the sham-exposed pups, a significant difference ($p<0.01$). For the 40-day pups, the mean counts were 31.61 +/- 1.22 and 33.98 +/- 1.05 cells/sq mm, respectively, a nonsignificant difference ($0.05<p<0.1$).

In experiment 3, the pups that were sham-exposed or exposed to 100-MHz RFR both in utero and postpartum were delivered to GWU 14 months after completion of the exposure regimen and were euthanized immediately. The mean counts were 24.74 +/- 0.71 and 28.33 +/- 1.21 for the RFR-exposed and sham-exposed pups, respectively, a significant difference ($p<0.05$).

The authors noted that the cerebellar rudiment and the Purkinje cells arise during the second half of gestation. They suggested that the significantly smaller Purkinje-cell counts obtained in experiments 1 and 3 (both of which involved exposure to RFR during that half of the prenatal period) could be due to reduction of the proliferative activity of the neuroepithelium by the RFR, or that the RFR could affect the migratory pattern of Purkinje cells and other microneurons in a manner that prevents the Purkinje cells from reaching the molecular-granular interface. The observation of smaller cell counts at both 40 days and 14 months after completion of RFR exposure was taken as indicating the permanence of this effect of prenatal exposure.

The results of experiment 2, in which significantly smaller Purkinje-cell counts were obtained for the pups exposed postnatally to RFR and euthanized immediately, and the nonsignificant difference in counts between the groups euthanized 40 days after RFR-and sham exposure, were taken as an indication of the reversibility of this effect. Presumably because brain cells are not regenerative, the authors suggested that postnatal exposure to RFR could temporarily affect the migration pattern of the Purkinje cells but not the proliferative activity of the external granular layer.

Although the positive results above appear to be statistically valid (from use of the t-test), they are questionable because the normalized SDs (ratio of SD to its mean value) for the RFR groups were virtually the same as for their respective sham-exposed groups. In view of the large variations in mean SAR at 2.45 GHz stated by the authors (0.8 to 6 W/kg), one would expect to observe some dose dependence of effect among the RFR-exposed animals that would be manifested as much larger values of normalized SDs than for the sham-exposed animals.

Albert et al. (1981b) conducted a similar study on squirrel monkeys that had been exposed perinatally elsewhere in an investigation of possible RFR-induced infant mortality described briefly in a note added in proof to a paper by Kaplan et al. (1982), discussed in Sections 3.3.2.2 and 3.7.1.2. In that infant-mortality study, Kaplan et al. (1982) exposed pregnant squirrel monkeys to 2.45-GHz amplitude-modulated RFR at a whole-body SAR of 3.4 W/kg (equivalent to plane-wave RFR at 10 mW/sq cm) 3 hr/day for 7 days/week, starting near the beginning of the first trimester of pregnancy. On parturition, each dam and its infant was exposed as a dyad for 6 months, and some offspring were exposed for 3 additional months without their dams. Albert et al. (1981b) obtained seven each of the RFR- and sham-exposed offspring used in that infant-mortality study.

These monkeys were weighed and anesthetized, and their brains were fixed with formalin by cardiac perfusion within 24 hr after receipt. The brains were removed and their weights and volumes were determined. The cerebella were dissected and the inferior vermis of each was separated and embedded in paraffin. The preparation was serially sectioned in the parasagittal plane at thicknesses of 10 micrometers and stained with hematoxylin-eosin. The uvula of the inferior vermis was selected for study because its mean cell density is representative of the mean cell density of the entire cerebellum.

Purkinje-cell density in each uvula was estimated by determining the area of the Purkinje cell layer and counting the number of cells therein by light microscopy, with the result expressed as the number of cells per sq mm. The linear density was also determined by counting the number of Purkinje cells per mm in the interface between the molecular and granular regions of each section and averaging the results over the sections. Only cells that displayed a visible nucleolus were counted. No significant differences between RFR- and sham-exposed groups were found in whole-body mass, brain mass, brain volume, or Purkinje-cell

counts per sq mm or per mm.

These negative results are at variance with those of the previous study with rats (Albert et al., 1981a), in which the mean density of Purkinje cells in the cerebella of rats exposed prenatally to 2.45-GHz or 100-MHz RFR at whole-body SARs of about 2 W/kg was significantly lower than for sham-exposed rats. Albert et al. (1981b) suggested that differences in species and in exposure methods, geometrical configurations of the head, and exposure protocols might account for the differences in findings. It is possible that local SARs in the rat brain may be higher than in the squirrel-monkey brain at comparable whole-body SARs. On the other hand, organogenesis in the squirrel monkey is completed within the first trimester of pregnancy, during which the brain may be more sensitive to exogenous agents (such as RFR) than subsequently. However, perhaps the negative results of Albert et al. (1981b) render this point moot.

Merritt and Frazer (1975) conducted a study to determine whether RFR altered whole-brain levels of specific neurotransmitters in the mouse. They exposed male Swiss-Webster mice individually at 19 MHz (HF) for 10 min to either an electric (E) field or a magnetic (H) field in plastic ventilated cages placed within a near-field synthesizer (Greene, 1974), with the long body axes of the mice perpendicular to the E-field. The synthesizer was calibrated with near-field electric and magnetic probes (Greene, 1975). With 400 W input, the E-field was 6 kV/m and the H-field associated with this E-field was 6.4 A/m; the H-field was 41 A/m and the associated E-field was 2 kV/m. The authors noted that exposure at these levels did not increase rectal temperature, measured with a thermistor probe. Control mice were sham-exposed in the synthesizer.

Fifteen minutes after exposure, the mice were euthanized by brain-enzyme inactivation with a 2.45-GHz industrial microwave oven modified by the addition of a section of shorted waveguide; the head of each mouse was inserted through a hole in the waveguide section at the maximum E-field location. By test, brain temperature rose 40-50 deg C in 1 second. A group of sham-exposed mice was similarly euthanized (microwave controls) and another group of sham-exposed mice was euthanized conventionally by cervical dislocation (conventional controls). Following euthanization, the brains were quickly removed, immediately frozen in liquid nitrogen, and homogenized in cold acidified (10 mM HCl) butanol. Each brain was assayed by spectrofluorometry for serotonin (5HT) and its metabolite 5-hydroxyindole acetic acid (5HIAA), dopamine (DA) and its metabolite homovanillic acid (HVA), and norepinephrine (NE). The normalized whole-brain mean concentrations (in nanograms per gram) and SDs are shown in Table 32 (adapted from Table 1 of the paper), with the number of mice in each group in parentheses:

TABLE 32: EFFECT OF E- AND H-FIELDS ON NEUROCHEMICALS

Treatment	5HT	5HIAA	DA	HVA	NE
E-field	745	780	1318	172	402
+/- SD	132 (5)	113 (5)	362 (5)	61 (5)	167 (5)
H-field	770	752	1487	182	533
+/- SD	79 (12)	62 (13)	374 (12)	44 (13)	123 (12)
Microwave Cont.	774	742	1355	184	468
+/- SD	50 (12)	121 (13)	287 (12)	62 (13)	88 (14)
Convent. Cont.	582	621	1025	184	367
+/- SD	86 (10)	75 (8)	108 (10)	62 (8)	38 (10)

By t-test, there were no statistically significant differences between the microwave controls and either E- or H-field-exposed animals in mean whole-brain concentrations for any of the neurotransmitters or their metabolites. However, the mean concentrations of all the neurochemicals except HVA were significantly higher ($p<0.02$) in the microwave controls than in the conventional controls. The authors suggested that these differences indicate that neurotransmitters were present having very rapid turnover and thus may be detectable after use of microwave- but not conventional brain-enzyme inactivation because of the shorter time required for the former.

The authors also noted that by frequency scaling, exposure of a mouse to 19-MHz RFR to obtain a specific whole-body SAR would require about 30-40 times higher incident power density than to obtain the same whole-body SAR in a human. On this basis, short-duration exposure of humans to 19-MHz E-fields up to about 150 V/m, or H-fields up to about 1 A/m may not have any detectable effects on the five neurochemicals studied.

Merritt et al. (1976) then sought to determine whether exposure to 1.6-GHz RFR would have any effect on the neurotransmitter concentrations in discrete regions of the rat brain. They inserted male Sprague-Dawley rats in individual ventilated cylindrical Plexiglas holders and placed each holder with its central axis upright and 43 cm along the axis of a horizontally radiating horn within an anechoic chamber. Exposures were for 10 min at 80 mW/sq cm. For hyperthermal controls, other rats were placed for 10 min in a chamber maintained at 78 deg C.

The mean rectal temperature rise in the rats exposed to the RFR was 4.09 +/- 0.55 (SE) deg C. The rise for the hyperthermal controls was 3.70 +/- 0.68 deg C. By scanning infrared thermography of a euthanized rat sectioned along a midsagittal plane and exposed at 200 mW/sq cm for 1 min, the temperature rise along the base of the brain was found to be comparable to the increase in core temperature in the intact rat.

The rats were euthanized by microwave brain-enzyme inactivation right

after either treatment, the brains were quickly removed, and discrete regions were dissected out. Each brain region was then frozen in liquid nitrogen, weighed in the frozen state, homogenized in acidified butanol, and assayed for the following: norepinephrine, dopamine, serotonin, and 5-hydroxyindole acetic acid in the hypothalamus, corpus striatum, midbrain, hippocampus, cerebellum, medulla, and cortex. Homovanillic acid, the metabolite of dopamine, was also assayed, but only in the corpus striatum because it cannot be detected in the other regions of the brain. The results were tabulated as mean concentrations (in ng/g) in each region, with SEs and numbers of determinations, and examined for statistical significance by t-test.

Regarding norepinephrine, the concentration in the hypothalamus of the RFR group was significantly lower ($p<0.01$) than in the control group, the only significant difference; the norepinephrine concentration in the hypothalamus of the hyperthermia group was 77% of that in the controls, but the difference was nonsignificant ($p>0.05$). Dopamine concentration in the corpus striatum of the RFR group was significantly lower ($p<0.05$) than in controls; it was also lower in the hypothalamus and labeled by the authors as significant ($p<0.05$), but a check of the p value showed it to be slightly larger than 0.05.

The concentrations of serotonin in the hippocampus of the RFR group and the cortex of the hyperthermia group were both significantly lower than in the controls ($p<0.02$ and $p<0.05$, respectively). All the differences in concentration of 5-hydroxyindole acetic acid in each brain region between RFR and control groups and between hyperthermia and control groups were nonsignificant. The mean homovanillic-acid concentrations in the corpus striata of the RFR- and hyperthermia groups were both significantly lower ($p<0.05$) than for the control group.

The authors concluded that: "the metabolism and/or transport of the putative neurotransmitters studied are altered by exposure of the rat to an environment that produces hyperthermia...The changes noted in the neurotransmitters in the brain areas were in the same direction for both the irradiated and hyperthermal animals. It then seems probable that these changes are a result of mechanisms involved in maintaining thermoregulation or a thermal effect on brain cells and not a direct effect of 1.6 GHz radiation on neural components."

Sanders et al. (1980) investigated the hypothesis whether exposure of brain tissue to RFR in vivo results in inhibition of the respiratory chain function followed by decreases in concentrations of adenosine triphosphate (ATP) and creatine phosphate (CP).

As indicated by the authors, the first entrance point to the electron transport chain, at which nicotinamide adenine dinucleotide (NAD) is reduced (by proton addition) to NADH, can be monitored continuously in situ by excitation at 366 nm and observation of NADH fluorescence at 460 nm with a time-sharing fluorimeter. Thus, if RFR imposes stresses on the cells that inhibit respiratory chain function or cell functions that utilize ATP and CP, the NADH level will increase (higher fluorescence);

conversely, RFR-induced enhancement of the respiratory chain or increase of cell functions that utilize ATP and CP will reduce the NADH level.

Male Sprague-Dawley rats were anesthetized with sodium pentobarbital (40-45 mg/kg), the scalp and muscles at the side of the skull were removed, and a 4x8-mm aperture was made through the skull, leaving the dura intact. The head of the rat was rigidly held in place, the light from a 366-nm excitation source was focused to a spot (1-2 mm) on the cerebral cortex, and a fiber-optic bundle was directed toward the focal spot. The other end of the fiber-optic bundle was terminated at a wheel that housed a 460-nm filter for NADH-fluorescence measurements and a 366-nm filter for measuring reflectance from the surface.

Following preparation, the rat was exposed to 591-MHz CW RFR at 3.0 cm from a 3.0-cm-square dielectrically loaded horn (in the far field), with the electric vector parallel to the long axis of the rat. The radiation pattern of the horn was such that only the head of the rat was exposed. A grounded Faraday shield was used to avoid RFR interference with the fluorimeter electronics. Incident power densities at the exposure site were measured with a Raham radiation detection meter, and theoretical models were used to estimate SARs. The maximum normalized SARs at the surface of a 2.0-cm diameter sphere and a semi-infinite plane of brain tissue were given as 0.026 and 0.16 W/kg per mW/sq cm, respectively.

Baseline NADH fluorescence and reflectance levels were determined in one rat before exposure. When both baselines were steady for 5 min, RFR-exposure for 5 min at 13.8 mW/sq cm was begun. The 366-nm reflectance trace showed no significant deviation from baseline during exposure, but the NADH trace began to increase on initiation of the RFR, reached a maximum at 30 seconds, and showed a compensatory partial return toward baseline during the next 2.5 min, followed by a slow rise again during the remaining 2 min. The authors ascertained that the changes in NADH fluorescence observed in the baseline experiment were not artifactual by using exposures at 18 mW/sq cm and several layers of opaque cloth to block excitation light from reaching the brain.

Groups of rats given the same pre-exposure treatment as in the baseline experiment were sham-exposed or exposed at 13.8 mW/sq cm for 0.5, 1, 2, 3, or 5 min, during which NADH fluorescence was measured. Right after RFR-or sham-exposure, the head and neck were immersed in liquid nitrogen for at least 2 min, and the frozen head was removed and stored in liquid nitrogen. Later, the frozen cerebral hemisphere near the aperture in the skull was extracted and pulverized, and duplicate aliquots were assayed for ATP and CP. Groups of rats were sham-exposed or exposed at 5.0 mW/sq cm for 0.5 or 1 min and similarly processed.

As in the baseline experiment, NADH fluorescence increased at initiation of 5-min exposures at 13.8 mW/sq cm. The levels reached maxima ranging from 4% to 12.5% above baseline at 30 seconds, decreased slowly to minima of about 2% above baseline in the next 2.5 min, and then again increased slowly to 5% above baseline at 5 min. The concentrations of ATP and CP for each duration of sham-exposure and exposure to RFR at

13.8 mW/sq cm were graphed as percentages of baseline level. The sham-exposures did not yield any significant changes in either ATP or CP. For exposure to RFR, however, the ATP level dropped to a minimum of about 75% by 30 seconds and rose to levels that did not exceed about 90%; the CP level dropped to a minimum of about 60% by 30 seconds and rose to a maximum of about 85%. By Student's t-test, all differences in levels of each biochemical between RFR- and sham-exposure groups for corresponding durations were significant, most at the $p<0.005$ level. The authors also noted that the decreases in ATP and CP levels were correlated with the relative increases in NADH level.

The mean ATP and CP levels (in micromoles/g), SEs, and numbers of rats are presented in Tables 33 and 34 (adapted from Tables 2 and 3 of the paper) for exposure at 0 (sham), 5, and 13.8 mW/sq cm for 0.5 and 1 min:

TABLE 33: ADENOSINE-TRIPHOSPHATE (ATP) CONCENTRATIONS

Power Density	0.5-Min Exposure	1-Min Exposure
0 mW/sq cm	2.48 +/- 0.06 (11)	2.48 +/- 0.05 (11)
5 mW/sq cm	1.89 +/- 0.06 (6)	2.17 +/- 0.07 (6)
13.8 mW/sq cm	1.93 +/- 0.17 (10)	2.19 +/- 0.09 (10)

TABLE 34: CREATINE-PHOSPHATE (CP) CONCENTRATIONS

Power Density	0.5-Min Exposure	1-Min Exposure
0 mW/sq cm	3.32 +/- 0.14 (11)	3.27 +/- 0.15 (11)
5 mW/sq cm	1.99 +/- 0.16 (6)	2.17 +/- 0.31 (6)
13.8 mW/sq cm	2.17 +/- 0.30 (10)	2.11 +/- 0.31 (10)

Regarding these results, the authors stated: "Even the 5.0 mW/sq-cm were above threshold for decreasing brain ATP and CP levels. This does not imply that a threshold power level would not be found if the microwave exposure power level continued to be decreased." However, by t-test of the ATP results above, the decreases for exposure at 5 mW/sq cm for 0.5 and 1 min were highly significant ($p<0.001$ and $p<0.01$, respectively), but the differences between exposure at 5 and 13.8 mW/sq cm for either duration were nonsignificant ($p>0.05$). This was also true for the CP results. Both statistical findings appear to indicate the absence of dose-dependence, at least for exposure levels above the threshold postulated by the authors, or that a plateau had been reached.

Temperatures at 2-3 mm below the surface of the brain were also measured in this study. For this purpose, a thermistor was placed perpendicular to the electric vector immediately under the dura but on top of the brain, adjacent to the focal spot of the excitation light. Rats other than those used in the NADH, ATP, and CP assays were exposed at 0, 13.8, 18.0, 30.0, 40.0, and 47.0 mW/sq cm for 5 min. Rectal temperatures were also recorded. With sham-exposure, the heat sink due

to the aperture in the skull was found to cause a decrease in brain temperature of 0.7 deg C (from 36.9 initially to 36.2 deg C at the end of the 5-min interval). For exposure at 13.8 mW/sq cm, the initial and final brain temperatures were 35.2 and 34.6 deg C, a decrease of 0.6 deg C. Decreases in brain temperature were also observed for exposure at 18.0 and 30.0 mW/sq cm, 0.5 and 0.1 deg C, respectively, but increases of 0.2 and 0.1 deg C were obtained at 40.0 and 47.0 mW/sq cm, respectively. Rectal temperatures remained constant at all exposure levels.

The authors concluded that because brain temperatures did not increase during RFR exposure at 5 or 13.8 mW/sq cm, the observed changes in NADH, ATP, and CP levels could not be ascribed to general tissue hyperthermia (but did not rule out local hyperthermia). Instead, the data support the hypothesis of RFR inhibition of electron transport chain function in brain mitochondria and results in decreased energy levels in the brain.

Subsequently, Sanders and Joines (1984) investigated the effects of hyperthermia alone and in conjunction with RFR. Male Sprague-Dawley rats were anesthetized with urethane (1250-1350 mg/kg ip) [instead of sodium pentobarbital] "to avoid barbiturate effects on brain energy metabolism." Rat preparation was similar to that in the previous study, except that the fiber-optic bundle was bifurcated near the measurement end; one arm served to convey 460-nm light from the brain to apparatus for measuring NADH fluorescence and the other arm conveyed 549-nm light to apparatus for measuring general brain fluorescence. Measurements of the latter were to permit correction of NADH fluorescence data for the effects of hemoglobin-content changes in the brain region studied, but no changes in 549-nm fluorescence were observed during and after RFR exposure, rendering such corrections unnecessary and showing that normal respiration rates were maintained in the rats during RFR exposure.

Groups of anesthetized rats were exposed to 591-MHz CW RFR for up to 5 min at 13.8 mW/sq cm. The upper and lower limits of spatial-average SAR in the brain were estimated in this paper to be 0.42 and 0.18 W/kg per mW/sq cm, based on prolate-spheroidal models having volumes of 110 and 25 cu cm in the E-polarization (Durney et al., 1978, pp. 94, 99), which yielded limits of 5.8 and 2.5 W/kg at 13.8 mW/sq cm. Also, temperatures were measured with a thermistor at a point about 2 mm below the surface of the brain during exposure at 60 and 100 mW/sq cm, and the rates of temperature increase were used (with 0.88 cal/g per deg C for brain-tissue specific heat) to estimate the local normalized SAR. The results for the two power densities were 0.613 and 0.626 W/kg per mW/sq cm, yielding a local SAR of about 8.5 W/kg for 13.8 mW/sq cm.

Other groups were subjected only to brain hyperthermia and still other groups to combined hyperthermia and RFR. In both sets of hyperthermia experiments, brain temperatures were held constant by use of heater pads and a temperature regulator. However, the method used to maintain brain temperatures constant was not described. At the end of the paper, the authors stated only that: "The temperature regulator was adjusted so that power would turn off when the selected temperature (35.6 or 37 or 39 deg C) was reached.

In an auxiliary experiment, ATP and CP assays in urethane-anesthetized RFR-exposed rats were compared with similar assays in pentobarbital-anesthetized RFR-exposed rats with the brains of both groups held at 35.6 deg C. The maximum deviation was 4.5%.

In the hyperthermia-only experiments, brain temperatures of the first 10 urethane-anesthetized, sham-exposed rats were maintained at 35.6 deg C. The assays of ATP and CP yielded mean concentrations of 2.47 +/- 0.03 (SE) and 3.44 +/- 0.11 micromoles/g, respectively. As indicated by the authors, these values did not differ significantly from those reported by Sanders et al. (1980) (for 0 mW/sq cm in Tables 33 and 34). The authors then sham-exposed groups with brain temperatures maintained at 37.0, 39.0, or 41.0 deg C and plotted the mean ATP and CP concentrations vs brain temperature as percentages of the concentrations at 35.6 deg C. The percentages of both ATP and CP declined monotonically with increases in brain temperature, with the rate of decline for CP higher. At 39 deg C, ATP and CP decreased to about 90% and 70%, respectively; at 41 deg C, the decreases were to about 70% and 45%, respectively.

Rats with brain temperatures held at 35.6 deg C were exposed for 0.5, 1, 2, 3, or 5 min at 13.8 mW/sq cm, and the percentage increase in NADH and mean percentages of ATP and CP (relative to the concentrations at 35.6 deg C for sham-exposed rats) were plotted vs exposure duration. These results, displayed in Fig. 3 of the paper, were evidently the same as those shown in Fig. 1 of Sanders et al. (1980), i.e., ATP decreased to about 75% and CP to about 60% in the first half-min. A similar set of experiments was performed with brain temperatures held at 39.0 deg C (RFR plus hyperthermia). At 0 min, the ATP and CP levels respectively were about 90% and 70%, decreases ascribed to the hyperthermia, and the levels declined further to minima of about 60% and 45% by 1 min of exposure. By 5 min, the ATP level rose linearly to about 80% and the CP level rose nonmonotonically to about 50%.

A group of sham-exposed rats with brain temperatures at 35.6 deg C was rendered hypoxic by giving them air consisting of 2% oxygen and 98% nitrogen for 0.5, 1, or 2 min. At 0.5 and 1 min, the mean ATP level of these rats remained 100% but dropped to about 85% at 2 min; by contrast, the mean CP level dropped to 80% and 60% at 0.5 and 1 min, and further to about 25% at 2 min. The authors stated: "Note that in the hypoxic animals brain ATP did not decrease until CP decreased below 59% of control levels. This illustrated the functional role of CP as a support system for maintaining ATP within narrow limits. Brain CP will decrease to levels of approximately 55-60% of control levels at normothermic conditions before any significant decrease in ATP can be observed."

The general conclusion was: "The decreases in ATP and CP in the 39 deg C brain during microwave exposure were significant and resulted in ATP and CP being much lower than observed at 35.6 deg C. Thus, at 39 deg C when the brain metabolic rate was increased, subsequent microwave exposure rapidly induced further decreases in ATP and CP, similar to the 35.6 deg C microwave exposure data, ie, without a further increase in brain temperature; [these results] are consistent with the concept of

direct microwave inhibition of energy metabolism." The latter statement seems open to question, however, because with an estimated local SAR of 8.5 W/kg at 13.8 mW/sq cm, considerable heating must have occurred.

In another paper, Sanders et al. (1984) described the results of similar experiments, but with frequencies of 200 MHz and 2.45 GHz in addition to 591 MHz. In this study, rats (surgically prepared as in the previous studies) were exposed to RFR in a horizontal microstrip transmission line system having a 6-cm plate separation, with the anesthetized rat placed on the ground plane. Precautions were taken to ensure that RFR-induced artifacts in NADH fluorescence were negligible. Incident power densities at the position of the rat's head (in the absence of the rat) were measured with a Raham radiation hazard meter.

Local SARs at a depth of 2-3 mm below the top surface of the brain of a dead rat were determined from measurements of temperature rise vs time with a Vitek isotropic probe during exposure of the carcass to each frequency at 60 and 100 mW/sq cm. The normalized SARs at 200, 591, and 2450 MHz were 0.046, 0.185, and 0.368 W/kg per mW/sq cm.

Brain temperature at the same depth was measured with the Vitek probe in urethane-anesthetized rats. The authors noted that the concentrations of ATP and CP did not significantly change when brain temperature varied by 0.4 deg C (Sanders and Joines, 1984) and that urethane anesthetic lowers the rat's body temperature to about 35.5 deg C. They stated: "Consequently, the brain temperature in these experiments was maintained at 35.6 +/- 0.3 deg C using a hot air blower which was directed into the microstrip toward the animal. The blower cycled on and off when the brain temperature reached 35.3 and 35.8 deg C, respectively. Occasionally, the brain temperature would increase to 35.9 deg C. Without the blower, we found that the brain temperature in sham-exposed animals would decrease from 35.6 deg C to 35.1 deg C in 5 min. In RF-exposed animals the brain temperature did not decrease as rapidly and the blower ran less often. On average, the temperature of the brain in RF-exposed animals was somewhat lower than in sham-exposed animals, ie, in the RF-exposed animals the brain temperature was between 35.4 and 35.6 deg C much of the time."

The authors indicated that brain fluorescence varied widely from rat to rat because of differences in brain vasculature and noted: "Therefore, the fluorescence data for different animals should not be averaged; each animal must be used as its own control." For this reason, the percent changes in NADH level for six individual rats exposed to 200-MHz RFR at power densities in the range 0.5-40.0 mW/sq cm (0.02-1.84 W/kg) and for six other rats exposed to 591-MHz RFR in the same power-density range (0.09-7.40 W/kg) were tabulated in the paper. At 200 and 591 MHz, there was a dose-response relationship for each rat in the percentage change in NADH for levels up to 10 mW/sq cm (0.46 and 1.85 W/kg, respectively). Above this power density, the NADH responses showed plateaus. At 2.45 GHz, significant NADH changes were not observed, leading the authors to suggest that the effect was frequency-dependent.

The authors also suggested that the important exposure parameter may be the electric field intensity in brain tissue, and using the dielectric constant and conductivity for each frequency, they converted incident power densities to tissue field strengths, obtaining 12.5, 22.5, and 20.7 V/m per mW/sq cm for 200, 591, and 2450 MHz, respectively. In addition, by extrapolating the 200- and 591-MHz curves for maximum and minimum NADH change to zero (the abscissa where the two curves met), they estimated that the threshold field for effect was 3-5 V/m.

The curves for percent NADH increase and percentage changes in ATP and CP vs duration for exposure to 591 MHz at 13.8 mW/sq cm (2.6 W/kg, 311 V/m) were stated to be the same as those given in Fig. 1 of Sanders et al. (1980). For 200 MHz (0.63 W/kg, 173 V/m), the NADH fluorescence curve and percentage concentrations of ATP were qualitatively similar to those for 591 MHz, but the changes were smaller: at 0.5 min, the NADH fluorescence increased to a maximum only about 5% above controls and ATP concentration dropped to about 80% of controls; however, the changes in CP concentration were nonsignificant for all durations (up to 5 min). For 2.45 GHz (5.1 W/kg, 286 V/m), no changes were seen in NADH level (as noted above) and the percentage changes in ATP and CP concentrations were statistically nonsignificant.

Last, rats were exposed to 591-MHz RFR at 13.8 mW/sq cm for durations up to 20 min. The data for durations up to 5 min were the same as those in Fig. 1 of Sanders et al. (1980). Beyond 5 min, the NADH level continued to slowly rise linearly, to a level 10% above baseline at 20 min (about equal to the maximum level at 0.5 min). The ATP concentration continued to decrease linearly, from 88% of controls at 5 min to 65% at 20 min. The CP concentration, 65% of controls at 5 min, dropped to a minimum of 45% at 10 min and rose to 60% at 20 min.

In their discussion the authors noted: "Adenosine triphosphate [ATP] is a key compound in energy metabolism because it is the carrier of energy to the processes in living cells. The relationship of ATP to CP and NADH in the metabolic pathway of energy production has been described in detail elsewhere (Siesjo, 1978). Briefly, NADH is oxidized to produce ATP in the mitochondria. In addition, brain ATP concentration is maintained at the expense of CP. Siesjo (1978) has shown in the hypoxic rat that brain ATP was maintained at control levels when the CP concentration had decreased to 62.4% of control CP levels. Also, when the CP concentration had decreased to 35.3% of control levels, brain ATP had decreased to only 77.8% of control levels. Therefore, when demand for ATP is higher than the mitochondrial production capacity, CP is rapidly converted to ATP by CP-kinase to sustain ATP levels, and significant decreases in CP levels are observed prior to any decrease in ATP." Thus, in interpreting their results, the authors stated:

"In the experiments presented here, increased NADH levels suggest an inhibition of mitochondrial oxidative phosphorylation. This reversible effect occurs during irradiation at 200 MHz and 591 MHz but not at 2.45 GHz...at 591 MHz the CP concentration drops more rapidly than the ATP concentration, which is expected. However, the ATP concentration

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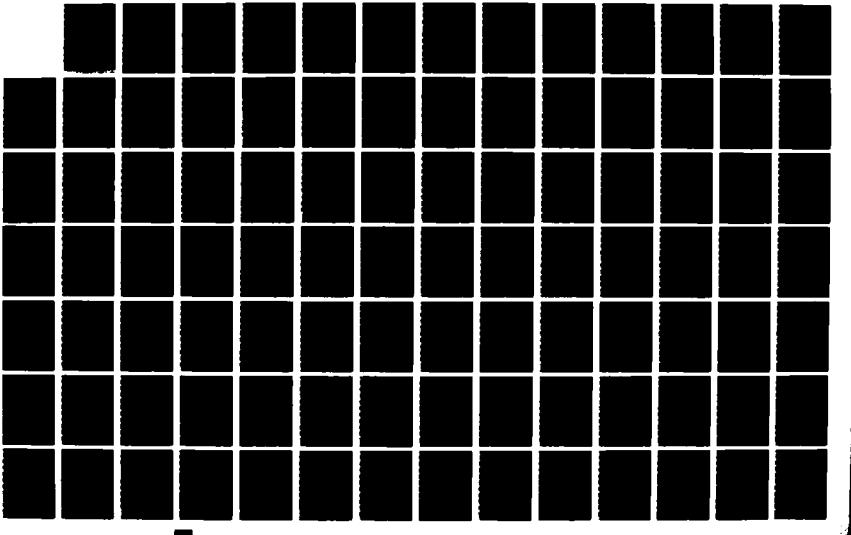

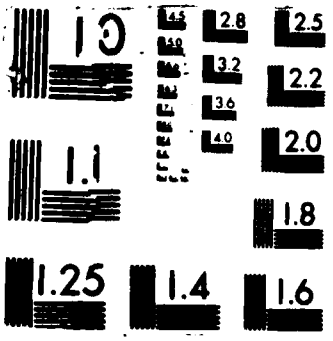
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be maintained until the CP concentration drops below 60% of normal levels. This is clearly not the case here, where the microwave exposures resulted in a decrease in ATP levels to 75% of controls when CP levels are no lower than 60% of controls. During the 200-MHz exposures, brain ATP levels decreased to 80-90% of controls even though CP levels were not significantly decreased. These results are not consistent with normal energy metabolism where ATP levels are maintained at the expense of CP, and suggest that at 200 MHz there is RF inhibition of the CP-kinase reaction converting CP to ATP."

In still another study, Sanders et al. (1985) compared the effects of CW, sinusoidal-amplitude-modulated, and pulsed 591-MHz RFR on NADH fluorescence and concentrations of ATP and CP in the brains of rats prepared as in the previous studies and exposed in the microstrip system. The initial temperature in the brain of the anesthetized rat was 35.6 deg C and decreased by 0.27 deg C during 5-min exposure at 13.8 mW/sq cm. No increase in brain temperature was seen during any of the RFR exposures. As in Sanders et al. (1984), because of the brain vascularity differences among rats, each rat served as its own control for NADH fluorescence, i.e., changes were expressed as percentages of its preexposure (baseline) NADH level.

In the sinusoidal-modulation experiments, the modulation was essentially 100% at frequencies ranging from 4 to 32 Hz in 4-Hz increments, and the exposures were for 5 min at average power densities of 10 and 20 mW/sq cm (1.8 and 3.6 W/kg). Mean percentage increases in NADH fluorescence vs modulation frequency were plotted (with SE bars) separately for the two RFR levels. At 20 mW/sq cm, NADH fluorescence was about 9% higher than baseline for modulations at 4 and 8 Hz, it increased to a maximum of 11% at 24 Hz, and decreased to slightly less than 9% at 32 Hz. The changes at 10 mW/sq cm were qualitatively similar but smaller, ranging from about 4.5% above baseline at 4 Hz to a relatively flat maximum of about 5.5% at 16 Hz. The SEs at both RFR levels were about 10% of the means. By analysis of variance (ANOVA) and comparison of treatment to control, the effect of exposure and difference in exposure levels were both statistically significant ($p<0.001$). However, although the data on modulation frequencies appeared to indicate a trend, the difference across modulation frequency was nonsignificant ($p>0.1$).

In the pulsed-RFR experiments, the pulses used were 5 microseconds in duration at 250 or 500 pps and the average power densities ranged from 0.5 to 13.8 mW/sq cm (0.09 to 2.5 W/kg). The percentage increases in NADH fluorescence were plotted vs average power density for each of four rats given 500 pps. At 13.8 mW/sq cm (2.5 W/kg), the largest and smallest increases in NADH fluorescence were about 8% and 4%, but the thresholds for all four rats were within the range 0.4-0.5 mW/sq cm (0.07-0.09 W/kg). Also shown was the curve for one of two rats given 250 pps. At 13.8 mW/sq cm, its increase in NADH fluorescence was about 5%, but its threshold was within the range 1.8-1.9 mW/sq cm (0.33-0.34 W/kg), about fourfold higher than for the rats given 500 pps. Analyses of variance of the NADH data for rats given 250 and 500 pps (six each) indicated a significant effect of exposure for each type of modulation.

The effects of CW, 16-Hz amplitude-modulated, and pulsed (500 pps) 591-GHz RFR, all at 13.8 mW/sq cm (2.5 W/kg) for durations of 0 (sham), 0.5, 1, and 5 min on the mean ATP and CP concentrations were tabulated for comparison. Multivariate ANOVA indicated a highly significant effect of exposure ($p<0.001$, Hotelling-Lawley) on the joint ATP-CP response and that the partial correlation between ATP and CP was high ($p<0.001$). The authors noted that this correlation was expected because the function of the CP-creatine phosphokinase system is to maintain ATP levels. The ATP and CP levels of all treated rats except one differed significantly from the levels for sham-exposed rats ($p<0.05$, Dunnett's test). The ATP level for one rat exposed to the pulsed RFR for 5 min was the exception. The authors stated: "The significance levels associated with the CP data should be viewed with some caution, however, since Bartlett's test showed unusual variability in the standard deviations."

From the tabulated data, the mean ATP or CP concentrations for exposure to CW, amplitude-modulated, and pulsed RFR did not differ significantly for corresponding durations.

The authors stated in their discussion: "The change in brain temperature was found to be -0.1 to -.04 deg C compared to preexposure temperatures during all exposures; ie, from the initial temperature of 35.6 deg C the final brain temperature was in the range of 35.2 to 35.5 deg C after a 5-min exposure. Thus the observed changes in brain NADH fluorescence and ATP and CP concentrations cannot be attributed to microwave-induced brain hyperthermia. The changes are consistent with the hypothesis of direct microwave inhibition of ATP production in the mitochondria, possibly by microwave-induced molecular dipole oscillations in the divalent metal-containing enzymes and/or electron transfer sites; such action could compromise the conformation and/or stereospecificity requirements for normal function."

In overall conclusion, RFR can cause observable histopathological and histochemical changes in the central nervous system of animals, but most of the positive findings were evidently thermally induced. The studies by Sanders and coworkers, however, are of considerable interest because their positive results were obtained in the absence of measurable tissue hyperthermia. The significance of their findings (direct-RFR-inhibition of respiratory chain function) with regard to possible hazards to human health is not clear at present.

REFERENCES:

Albert, E.N. and M. DeSantis
DO MICROWAVES ALTER NERVOUS SYSTEM STRUCTURE?
Ann. N.Y. Acad. Sci., Vol. 247, pp. 87-108 (1975)

Albert, E.N. and M. DeSantis
HISTOLOGICAL OBSERVATIONS ON CENTRAL NERVOUS SYSTEM
In C.C. Johnson and M.L. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8010, pp. 299-310 (1976)

Albert, E.N., M.F. Sherif, N.J. Papadopoulos, F.J. Slaby, and J. Monahan
EFFECT OF NONIONIZING RADIATION ON THE PURKINJE CELLS OF THE RAT CEREBELLUM
Bioelectromagnetics, Vol. 2, No. 3, pp. 247-257 (1981a)

Albert, E.N., M.F. Sherif, and N.J. Papadopoulos
EFFECT OF NONIONIZING RADIATION ON THE PURKINJE CELLS OF THE UVULA IN SQUIRREL MONKEY CEREBELLUM
Bioelectromagnetics, Vol. 2, No. 3, pp. 241-246 (1981b)

Chou, C.-K. and A.W. Guy
EFFECTS OF ELECTROMAGNETIC FIELDS ON ISOLATED NERVE AND MUSCLE PREPARATIONS
IEEE Trans. Microwave Theory Tech., Vol. 26, No. 3, pp. 141-147 (1978)

Courtney, K.R., J.C. Lin, A.W. Guy, and C.-K. Chou
MICROWAVE EFFECT ON RABBIT SUPERIOR CERVICAL GANGLION
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 10, pp. 809-813 (1975)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Frey, A.H. and E. Seifert
PULSE MODULATED UHF ENERGY ILLUMINATION OF THE HEART ASSOCIATED WITH CHANGE IN HEART RATE
Life Sci., Vol. 7, No. 10, Part II, pp. 505-512 (1968)

Frey, A.H.
BIOLOGICAL FUNCTION AS INFLUENCED BY LOW-POWER MODULATED RF ENERGY
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 153-163 (1971)

Galvin, M.J., D.L. Parks, and D.I. McRee
INFLUENCE OF 2.45 GHZ MICROWAVE RADIATION ON ENZYME ACTIVITY
Radiat. Environ. Biophys., Vol 19, pp. 149-156 (1981c)

Greene, F.M.
DEVELOPMENT AND CONSTRUCTION OF AN ELECTROMAGNETIC NEAR-FIELD SYNTHESIZER
U.S. Department of Commerce, National Bureau of Standards, NBS Technical Note 652 (1974)

Greene, F.M.
DEVELOPMENT OF ELECTRIC AND MAGNETIC NEAR-FIELD PROBES
U.S. Department of Commerce, National Bureau of Standards, NBS Technical Note 658 (1975)

Kamenskii, Yu.I.
THE EFFECT OF MICROWAVES ON THE FUNCTIONAL STATE OF THE NERVE
Biophys., Vol. 9, No. 6, pp. 758-764 (1964)

Kamenskii, Yu.I.
EFFECT OF MICROWAVES ON THE KINETICS OF ELECTRIC PARAMETERS OF A NERVE IMPULSE
In SOCIETY OF NATURALISTS, Moscow, Vol. 28, pp. 164-172 (Engl. Trans., 1968)

Kaplan, J., P. Polson, C. Rebert, K. Lunan, and M. Gage
BIOLOGICAL AND BEHAVIORAL EFFECTS OF PRENATAL AND POSTNATAL EXPOSURE TO 2450-MHZ ELECTROMAGNETIC RADIATION IN THE SQUIRREL MONKEY
Radio Sci., Vol. 17, No. 5S, pp. 135-144 (1982)

McRee, D.I. and H. Wachtel
THE EFFECTS OF MICROWAVE RADIATION ON THE VITALITY OF ISOLATED FROG SCIATIC NERVES
Radiat. Res., Vol. 82, pp. 536-546 (1980)

McRee, D.I. and H. Wachtel
PULSE MICROWAVE EFFECTS ON NERVE VITALITY
Radiat. Res., Vol. 91, pp. 212-218 (1982)

Merritt, J.H. and J.W. Frazer
EFFECT OF 19 MHZ RF RADIATION ON NEUROTRANSMITTERS IN MOUSE BRAIN
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-75-28 (August 1975)

Merritt, J.H., R.H. Hartzell, and J.W. Frazer
THE EFFECTS OF 1.6 GHZ RADIATION ON NEUROTRANSMITTERS IN DISCRETE AREAS OF THE RAT BRAIN
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-76-3 (February 1976)

Millar, D.B., J.P. Christopher, J. Hunter, and S.S. Yeandle
THE EFFECT OF EXPOSURE OF ACETYLCHOLINESTERASE TO 2,450-MHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 165-172 (1984)

Olcerst, R.B. and J.R. Rabinowitz
STUDIES ON THE INTERACTION OF MICROWAVE RADIATION WITH CHOLINESTERASE
Radiat. Environ. Biophys., Vol 15, pp. 289-295 (1978)

Portela, A., et al.
TRANSIENT EFFECTS OF LOW-LEVEL MICROWAVE IRRADIATION ON BIOELECTRIC MUSCLE CELL PROPERTIES AND ON WATER PERMEABILITY AND ITS DISTRIBUTION
In FUNDAMENTAL AND APPLIED ASPECTS OF NONIONIZING RADIATION, Plenum Press, N.Y., pp. 93-127 (1975)

Rothmeier, J.
EFFECT OF MICROWAVE RADIATION ON THE FROG SCIATIC NERVE
In THE NERVOUS SYSTEM AND ELECTRIC CURRENTS, Plenum Press, N.Y., Vol. 1, pp. 57-69 (1970)

Sanders, A.P., D.J. Schaefer, and W.T. Joines
MICROWAVE EFFECTS ON ENERGY METABOLISM OF RAT BRAIN
Bioelectromagnetics, Vol. 1, No. 2, pp. 171-181 (1980)

Sanders, A.P. and W.T. Joines
THE EFFECTS OF HYPERTHERMIA AND HYPERTHERMIA PLUS MICROWAVES ON RAT BRAIN ENERGY METABOLISM
Bioelectromagnetics, Vol. 5, No. 1, pp. 63-70 (1984)

Sanders, A.P., W.T. Joines, and J.W. Allis
THE DIFFERENTIAL EFFECTS OF 200, 591, AND 2,450 MHZ RADIATION ON RAT BRAIN ENERGY METABOLISM
Bioelectromagnetics, Vol. 5, No. 4, pp. 419-433 (1984)

Sanders, A.P., W.T. Joines, and J.W. Allis
EFFECTS OF CONTINUOUS-WAVE, PULSED, AND SINUSOIDAL-AMPLITUDE-MODULATED MICROWAVES ON BRAIN ENERGY METABOLISM
Bioelectromagnetics, Vol. 6, No. 1, pp. 89-97 (1985)

Shtverak, I., K. Marha, and G. Pafkova
SOME EFFECTS OF VARIOUS PULSED FIELDS ON ANIMALS WITH AUDIOGENIC EPILEPSY
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 141-144 (1974)

Siesjo, B.K.
BRAIN ENERGY METABOLISM
John Wiley and Sons, New York (1978)

Smialowicz, R.J., J.S. Ali, E. Berman, S.J. Bursian, J.B. Kinn, C.G. Liddle, L.W. Reiter, and C.M. Weil
CHRONIC EXPOSURE OF RATS TO 100-MHZ (CW) RADIOFREQUENCY RADIATION: ASSESSMENT OF BIOLOGICAL EFFECTS
Radiat. Res., Vol. 86, pp. 488-505 (1981b)

Tinney, C.E., J.L. Lords, and C.H. Durney
RATE EFFECTS IN ISOLATED TURTLE HEARTS INDUCED BY MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 24, No. 1, pp. 18-24 (1976)

Tolgskaya, M.S. and Z.V. Gordon
PATHOLOGICAL EFFECTS OF RADIO WAVES
(Translated from the original Russian text published by Meditsina Press, Moscow, 1971), Consultants Bureau, New York-London (1973)

Wachtel, H., R. Seaman, and W. Joines
EFFECTS OF LOW-INTENSITY MICROWAVES ON ISOLATED NEURONS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 46-62 (1975)

3.4.3 ALTERATIONS OF THE ELECTROENCEPHALOGRAM AND EVOKED RESPONSES

Various studies have been conducted on the effects of exposure of animals to RFR on the electroencephalogram (EEG) and/or stimulus-evoked responses (ERs). In many early studies, metallic electrodes were either attached to the scalp or implanted in the brain prior to exposure of the animal to RFR and were present during exposure. Johnson and Guy (1972) pointed out that such metallic electrodes can grossly perturb the fields and produce greatly enhanced absorption of energy in the vicinity of the electrodes, thereby yielding false or misleading results.

Examples of the magnitude of such enhancement were given in a National Academy of Sciences publication (NAS, 1979): For an implanted insulated wire, with the end of the conductor in direct contact with the tissue and a length-to-radius ratio of the wire of 100:1, the SAR enhancement factor is of the order of 100,000. Such enhancements can result in transient heating of the tissue volume in the immediate vicinity of conductive implants exposed to RFR with time-averaged power densities greater than 0.001 mW/sq cm. In such volumes, the greatly enhanced fields *per se* are also likely to cause artifacts in nervous-system-tissue function because of the sensitivity of such tissue to electrical stimulation by induced currents.

Such biological artifacts should not be confused with possible recording artifacts in EEGs or ERs produced by pickup of fields by the electrodes and leads during exposure of the animal. Recording artifacts have been avoided by making the recordings before and after exposure, but at the expense of missing effects that may occur solely or have significantly different characteristics during exposure. Moreover, such artifacts can usually be rendered negligible by appropriate filtering, but the field-enhancement biological artifacts cannot. It should be noted also that many EEG and ER studies were performed on heavily sedated animals, with barbiturates as the usual drugs. Hence, the responses reported may not necessarily reflect those expected in normal alert animals.

Frey et al. (1968) described a coaxial electrode designed to convey and record potentials evoked in the brain stem of the cat during exposure to RFR in the UHF range. The device was fabricated from an Amphenol 27-8 subminiature coaxial connector, into which a section of stainless-steel tubing (20-gauge) was inserted and fastened, to serve as the outer coaxial conductor and electrical shield for the electrode proper. The electrode was a length of 30-gauge stainless-steel wire in coaxial alignment within the shield, with one end fastened to the center pin of the connector and the other end for implantation in the subject.

Tyazhelov et al. (1977) discussed the artifact problems and pointed out that even for the coaxial electrode developed by Frey et al. (1968), in which the end of the inner conductor is the recording electrode and is shielded from the RFR by the outer conductor, diffraction of the RFR is still a major source of error because of the outer electrode's metallic nature and large dimensions. To diminish the problems, Tyazhelov et

al. (1977) developed electrodes of high linear resistance (>100 kilohms/m) and used appropriate filtering of the recorded signals. In this paper, they also indicated that Soviet investigators were aware of questions about the validity of data and conclusions from experiments conducted in the U.S.A. as well as the USSR with animals having indwelling metallic electrodes during exposure.

Lambert et al. (1972) studied the effects of exposure to 2.45-GHz CW RFR at 176 and 88 mW/sq cm ("full dose" and "half-dose") on performance of young beagles trained to traverse a runway for food reward and on their EEGs and ECGs. Twenty-four beagles (12 each male and female) 10 weeks old were trained to seek Hills Canned Dog Food in a runway 9.4 m long and 0.6 m wide, entered from a start box via a guillotine gate. Since the dogs preferred this food over their usual diet of dry kibble and because the dogs developed a social bond with the investigators, the latter found it unnecessary to train the dogs on a food deprivation schedule for motivation. Radio programs served as random background noise, and the start-box ventilation fan provided more-uniform noise.

In a 4-day initial "shaping" of responses, the time each dog spent in the start box before the gate to the runway was opened was increased from 1 min on the first day to 20 min on the fourth day. At the end of this stage, the dogs "were approaching the reward with eagerness, i.e., total time to traverse the runway was between 4 and 10 seconds." In a 3-day final stage of shaping, the procedure was similar but an auditory cue consisting of a double knock on the wall of the start box signaled the opening of the gate. At the end of the final stage, the traverse times of all dogs were in the range 3.8 to 7.9 seconds. Because the performance times varied only slightly and appeared to be uniformly distributed, the dogs were randomly assigned to three treatment groups (8 dogs each): (a) sham-control, (b) half-dose, and (c) full-dose.

A standard-gain horn was mounted above the start box so that the center of the body of a standing dog was about 0.5 m from the neck of the horn, and blocks of RFR-absorption material were placed under the box. With 176 mW/sq cm at 0.5 m along the horn axis, the horizontal spatial variation of power density within the start box at that distance was mapped with a Narda radiation survey meter. At 10 cm radially off-axis, the power densities were about half the on-axis value, so the spatial mean power density was less than the nominal (on-axis) value, and dog movements within the box created uncertainties in time-averaged values. The source power was halved for exposures at 88 mW/sq cm (on-axis). For a prolate-spheroidal model of a beagle, the normalized whole-body SARs in the E- and H-polarizations are respectively about 0.04 and 0.05 W/kg per mW/sq cm (Durney et al., 1978, p. 91), so the SARs corresponding to the two on-axis power densities were about 8 and 4 W/kg. Each treatment group was tested under the following three conditions:

(I) Each dog was retained in the start box for 20 min and given the treatment specified for the group (sham-exposure, half-dose, or full-dose). At the end of the 20 min, the auditory cue was given, the gate was raised, the treatment was halted, and the interval for the dog to

reach the food pan at the end of the runway after raising the gate was determined with a manually operated timer. All 24 dogs were tested under Condition I in one day.

(II) The dogs were tested similarly, except for increase of treatment duration to 1 hr. Condition II was started on the day following tests under Condition I and required four days to complete. On the day after completion (presumably the day after each dog was tested under this condition), all dogs were examined for residual effect from the previous treatments by testing each again after no treatment.

(III) Two days after the intercondition control run, the dogs in each group were treated for 15 min, but the task was rendered more difficult by placing the food reward in the start box after the dog was released, to enhance possible performance differences among the RFR- and sham-exposed groups.

By analysis of variance, the differences in performance times among the three groups were not significant under each condition or among the three conditions or the intercondition control run. The authors noted: "Although the dogs were confined to a relatively small space in the start box, it was possible for them to easily turn around, stand up, lie down, and be facing toward or away from the start gate. This procedure had the disadvantage regarding the irradiation exposure, but an advantage regarding the restraint of the animals. Since the subjects were randomly assigned to the treatment groups and none was handled or 'shaped' preferentially, it could be assumed that the probabilities for the contingencies within the start box, except for the independent variable of exposure, are the same for each group."

Eight days after the performance tests, all of the dogs were examined clinically for effects of the RFR exposures and found to be normally healthy. Eye examinations with an ophthalmoscope showed no signs of cataracts. EEGs and ECGs were then recorded, with the identity of the three groups retained. For this purpose, each dog was intravenously anesthetized to a light surgical level with sodium pentobarbital. Ten min later, recordings of monopolar EEGs from the left and right frontal and occipital (LF, RF, LO, and RO) sites were started on magnetic tape with EEG amplifiers having an upper frequency limit of 100 Hz and a lower cut-off filter at 0.35 Hz. Also recorded was a Lead-II ECG. All of the subcutaneous needle electrodes were kept in place throughout the experiment. Normal activities were recorded for 5 min before normal visual evoked responses (VERs) and auditory evoked responses (AERs) were elicited. The VER for each site was the average of the EEG responses to 100 diffuse light flashes, and the AER for each site was the average of the EEG responses to 100 presentations of a 70-dB, 2-kHz tone.

After 5 min of recording normal VERs and AERs, the heads of the dogs in each group (with vertex on the horn axis) were given the appropriate treatment for that group (sham- , half-dose, or full-dose exposure) for 20 min. After the first 5 min of treatment, a VER was recorded followed by an AER. Post-treatment, VERs were obtained at 1, 8, and 15 min, and

AERs at 3, 10, and 17 min. A special-purpose digital-type correlator was used to analyze the EEGs. Autocorrelation and probability-density functions were calculated for each site, and crosscorrelation functions were calculated for the RF and LO sites with the RF function delayed.

Stated in a footnote: "The authors were keenly aware of the possibility that metal recording electrodes within the exposure field could produce undesirable perturbations of the microwave field...A preliminary experiment with dogs was conducted in which EEGs and their functions were compared after having been recorded: (1) with the scalp electrodes in place during the exposure and (2) with the scalp electrodes placed at the termination of the exposure. Little difference could be noted in the results and no heating of the electrodes was detected...In a similar fashion, records of brain temperatures were compared. An artifact associated with the thermistor was noted when the microwave generator was turned 'on' and 'off'. However, when the temperature curve was corrected for the step at 'on', it was similar to the curve recorded by placing the thermistor at one minute intervals with the generator 'off' to make the reading. No problems were associated with the electrocardiogram, since the subcutaneous needle electrodes were at the periphery or outside of the exposure field."

A control dog that died accidentally during anesthesia induction was used immediately to record RFR heating effects in the head. Thermistor probes were placed under the scalp, on the dura, and subdermally under the head, and temperatures were recorded at full-dose exposure. The resulting temperatures were corrected for the RFR-probe interaction mentioned in the footnote. The temperature at the cortical surface rose from 37 to about 41 deg C during the first 5 min, and then more slowly linearly to about 45 deg C at 16 min of exposure. During that period, the temperature changes at the other two sites did not exceed about 1 deg C. Also monitored was the dog's body temperature with an esophageal probe, and was found to not vary appreciably. In addition to the dead control dog, one dog from the half-dose group died from unexplainable causes on the day after anesthesia induction.

The EEG autocorrelograms obtained for each site before and after head treatment were compared for the mean square relative amplitude and the periodicity of the function. The pre-treatment and post-treatment autocorrelograms for the sham group differed little, and the differences among the pre-treatment autocorrelograms for the three groups were small. However, the autocorrelograms for both RFR groups showed sizable increases in mean square amplitude and variable reaction in periodicity. (Pre- and post-treatment autocorrelograms at the RF and LO sites for representative dogs of the three treatment groups were shown.)

The crosscorrelograms for the RF and LO sites showed post-exposure differences in peak amplitude and time of peak correlation (relative to pre-treatment values). The mean changes for the sham, half-dose, and full-dose groups were -0.05, +0.01, and +0.15 (volts-squared per cm), respectively; the corresponding differences in time of highest peak correlation were 1.44, 0.64, and 4.0 milliseconds. The pre- and post-

treatment probability-density functions of the EEGs did not differ significantly for the sham group, but these functions for the two RFR groups showed significant differences, with larger changes for the full-dose group. (Pre- and post-treatment probability-density functions for representative dogs of the three groups were displayed.)

Regarding evoked responses, the authors stated: "The effect of the microwave irradiation on the specific components of the VERs and AERs were difficult to assess. Latency and amplitude comparisons did not unequivocally demonstrate an effect. It appeared that the problem here was the variable nature of the response to the microwave irradiation, sometimes increasing the amplitude and latency and other times decreasing them. The presence of the evoked responses was not affected at any time during and up to 20 minutes after exposure." Data on mean latencies of the first positive peaks and peak-to-peak amplitudes of the AERs and VERs (with SDs) were presented in Tables 2-5 of the paper to support this assessment.

Heart rates were determined for 20 min of treatment plus 15 min post-treatment and the "combined" means for the 35 min of each group were compared with their respective means (in beats per min) for 8 min of pretreatment. The means and SDs for the three groups are shown in Table 35 (adapted from Table 1 of the paper):

TABLE 35: RFR EFFECTS ON MEAN HEART RATE (MHR)

Group	Sham		Half-dose		Full-dose	
Treat. Time	Pre-	Combined	Pre-	Combined	Pre-	Combined
MHR	197.89	186.64	200.55	192.97	180.54	187.40
SD	14.95	10.04	11.58	14.28	11.68	19.13

The means for the 35-min combined duration were slightly lower for the sham and half-dose groups than for their respective pretreatment periods and the combined-duration mean for the full-dose group was higher than its pretreatment mean. A trend analysis was performed, for which the authors discarded the data for one dog randomly selected from the full-exposure group to maintain equal group size (7 dogs each). The results showed that the effect of treatment only was nonsignificant, but that the effect of anesthesia and of treatment-anesthesia interaction were significant ($p<0.05$ and $p<0.01$, respectively). However, the authors noticed that the full-dose pretreatment mean was significantly lower ($p<0.02$, analysis of variance) than the pretreatment means for the sham and half-dose groups, and stated: "This result implied a residual effect from the previous microwave exposures in the behavioral experiment."

To check whether the observed bradycardia could be ascribed to unequal anesthesia, an analysis of variance on the amounts of anesthetic per unit of body weight was performed, which showed no significant effect. The authors, noting that the bradycardia was observed in the full-dose (176-mW/sq-cm) but not in the half-dose (88-mW/sq-cm) group, indicated

that the finding was consonant with the results of Kaplan et al. (1971), who found that exposure of rabbits at RFR levels greater than 100 mW/sq cm was necessary for bradycardia (see Section 3.6.3).

In overall summary of this study, the authors stated: "In view of the unresponsiveness of the EEG to arousal stimuli in animals under pentobarbital anesthesia, the dissociation (time wise) between sites as suggested by the crosscorrelograms, and the increase in the voltage amplitude as indicated by the probability density functions, imply a paradoxical arousal, and would be comparable to the increase in number of slow, high amplitude waves. The results of the behavioral test and the evoked responses support this view. The irradiated animals did not exhibit a decrease in alertness related performance, and the specific components of the sensory evoked responses were not materially affected by the head irradiation."

Goldstein and Cisko (1974) studied EEGs of sedated rabbits to determine whether RFR exposure would evoke arousal. "In order to reduce the presence of metals in the pathway of the microwaves," three electrodes, each consisting of an "extremely thin" (0.01-inch) Formvar-coated stainless-steel wire, were surgically implanted, one each above the right and left somatosensory cortices and one within the nasal bone as the common reference electrode. Following recovery, the animals were trained to sit quietly unrestrained in an anechoic chamber and to accept intravenous injections administered by remote control via a catheter inserted in one of the marginal ear veins.

At the outset, the authors noted: "The main complicating feature of these studies is that, under everyday conditions, the EEG patterns of rabbits are quite variable. The animals oscillate between sedation and arousal unpredictably. It is therefore difficult, when a change from one state to another state occurs in animals exposed to microwaves, to be confident that the shift would have not taken place spontaneously in the absence of treatment. One way to deal with this problem is to induce a sustained, stable baseline state."

Based on the foregoing and their prior observation that 9.3-GHz RFR is stimulatory, their procedure was as follows. At the start of each experimental session, the rabbit was left disturbed in the anechoic chamber for 5-10 min, after which recording of its EEG was started. Following a 10-min baseline recording period, the rabbit was sedated with sodium pentobarbital (4 mg/kg in 0.1 ml/kg). Five minutes later, the head of the rabbit, at about 45 cm from a horn antenna, was sham-exposed or exposed for 5 min to 9.3-GHz RFR at 0.7 to 2.8 mW/sq cm as measured with a Narda monitor, and recording of the EEG was continued for 30-60 min. From Durney et al. (1978), p. 92, the range of whole-body SARs is estimated to have been 0.07-0.28 W/kg.

Ninety experiments were run on 13 rabbits; 55% of the experiments were with RFR-exposure and 45% with sham-exposure, with most rabbits serving as their own controls. The brain electrical activity of each rabbit was recorded directly on paper and concurrently processed through electronic

integrators, which measured on-line amplitudes of unfiltered brain waves continuously and numerically expressed the results over time for preset, fixed intervals.

The first finding was no detectable changes in EEG patterns, their integrated counterparts, or animal behavior during the 5 min of exposure to RFR. The second finding was that after a postexposure latent period of 3 to 12 min, a sudden arousal lasting an average of 3 min occurred, followed by a return to sedation and a second arousal 3-5 min later that lasted 2 to 10 min. The authors indicated that alternating periods of sedation and arousal occurred up to four times in some experiments. The two findings were illustrated with a representative example for exposure at 0.72 mW/sq cm (0.07 W/kg), which also showed a brief (1-min) arousal about 6 min after the end of exposure. In an example for exposure at 2 mW/sq cm (0.2 W/kg), the chronology was similar. There was a decrease in overall amplitudes and a sixfold decrease in the standard deviation of the distribution of amplitudes during sustained arousal.

The authors noted that very similar decreases of mean amplitudes and variability were observed in rabbits treated with hallucinogenic drugs but that hyperstimulation with such drugs was sustained, whereas it waxed and waned with RFR. However, they also stated: "As a matter of fact, arousals do occur in control experiments without microwave exposure, but they are most often of short duration, at most 1 min." Such occurrences in control rabbits render it difficult to interpret the results with RFR. In addition, it seems unlikely that use of 0.01-inch metal electrodes reduced artifact significantly, because this thickness was much greater than the metal's "skin depth" at 9.3 GHz and because thickness reduction increases the length-to-diameter ratio and hence field enhancement (NAS, 1979).

The authors also observed: "In the course of the experiments reported, it was found that the microwave effects disappeared when the relative humidity reached or exceeded 40%. It may be that transmission of the waves through the fur is impaired in rabbits whose long hairs are known to adsorb water. Further experimentation is planned in which this environmental factor will be controlled."

Dumanskij and Shandala (1974) conducted experiments to determine the effects of chronic exposure to 6-m (50-MHz) CW RFR, 12-cm (2.5-GHz) CW RFR, or 3-cm (10-GHz) pulsed RFR (1-microsecond pulses at 1000 or 20 pps) on white rats and rabbits. Exposures to 50 MHz were for 10-12 hr daily at 10, 2.4, 1.9, 0.06, 0.01, and 0.0006 microwatts/sq cm in "shortened wave guides" and involved 128 white rats and 28 rabbits. Exposures to 2.5-GHz CW RFR were for 8 hr daily at 10, 5, 1, or 0.5 microwatts/sq cm, and those to 10-GHz pulsed RFR were also for 8 hr daily at 10, 5, or 1 microwatts/sq cm; 100 rats and 32 rabbits were used. The duration for all three frequencies was 120 days with a postexposure followup of 60 days.

The authors noted that exposure to RFR at all three frequencies during the first 10-12 days resulted in some changes in the general status of

the animals, that they were somewhat excited and reacted to switching-on of the RFR. These changes led the authors to study the conditioned reflexes of the animals, and periodic changes thereof were reported; the latent periods were longer, reflex reactions to positive stimuli were weakened, and the numbers of missing reactions were increased. They gave no data on conditioned reflexes, but stated that the levels of RFR that yielded statistically significant changes were 1.9-10 microwatts/sq cm for 50 MHz and 5-20 microwatts/sq cm for the other two frequencies. Data on EEG studies of the rabbits at 50 MHz were then presented. The results, determined before exposure and after 2, 10, 30, and 60 days of exposure, were expressed as means and SDs of "slow, intermediate, and fast" biocurrent rhythms for rabbit groups (of unstated size) exposed at 10, 1.9, and 0.01 microwatts/sq cm and for controls.

For the controls and the group exposed at 0.01 microwatts/sq cm at the successive time periods, all three biocurrent rhythms showed relatively small increases and decreases, but presumably the changes were not statistically significant. For the group exposed at 1.9 microwatts/sq cm, however, there were nonmonotonic changes in slow-wave biocurrents at 2, 10, and 30 days of exposure, followed by a sharp increase at 60 days to a mean almost threefold higher than the mean pre-exposure value. The slow-rhythm results for the 10-microwatts/sq-cm group were qualitatively similar. Both groups showed relatively large but nonmonotonic changes in intermediate-rhythm currents. These results were described by the authors as follows:

"At the beginning (2-14 days), activation of the biocurrents in the brain was observed, testifying to some increase in the excitation process. With increasing duration of exposure an initial stage of inhibition developed, characterized by synchronization of the cortical rhythms. Thus, upon prolonged irradiation, the strength of the process of inhibition within the brain hemisphere cortex was appreciably increased, as evidenced by the appearance of slow rhythms in the electroencephalograms. The observed changes in bioelectric activity of the brain cortex of rabbits confirmed previously reported results of studies on conditioned reflex activity of animals and showed that electromagnetic energy in the UHF range [50 MHz] and 0.06-10 microwatts/sq cm intensity, as well as in the SHF range [2.5 and 10 GHz] and 5-20 microwatts/sq cm intensity, was indeed active biologically according to the results of statistical analysis."

The rather sketchy description of the study precluded any definitive evaluation of the results. Absent in this paper were details on the exposure arrangements and the method used to record and process the EEGs. Specifically, not indicated was whether indwelling electrodes had been used. Presumably they were, however, because such electrodes were used in a later study, Shandala et al. (1979), discussed below.

Shandala et al. (1979) exposed 24 rabbits from above in the far field of a cylindrical horn to 2.375-GHz CW RFR at 0.01, 0.05, and 0.5 mW/sq cm 7 hr/day for 3 months in a chamber lined with RFR-absorption materials. From Durney et al. (1978), p. 92, the whole-body SARs are

estimated to have been 0.0014, 0.007, and 0.07 W/kg in the E- and H-polarizations. The animals were exposed within four plastic cages on the floor of the chamber. The EEGs were taken with electrodes implanted in the mammillary region of the posterior hypothalamus, the central medial nucleus of the thalamus, and the sensory and visual zones of the neocortex, with the indifferent electrode attached to the nasal bone. An 8-channel encephalograph was used to record the EEGs. At the start of each experiment, baseline data were obtained with a "functional load" consisting of stimulation with light at 5, 8, and 12 Hz. The EEGs were recorded every 10 days during the 3-month exposure period and every two weeks post-exposure until complete recuperation. Each EEG recording was for 4-50 min.

The authors noted that the results showed great variability and stated that the EEGs "did not proceed identically in the subcortical and cortical regions of the various animals. Nevertheless in statistically processing the data it was possible to determine definite regularities associated with changes in the bioelectric processes taking place in the studied structures."

Cited as an example was a reliable increase ($p<0.05$) observed in the alpha-rhythm index in the sensory-motor and visual cortex after 1 month of exposure at 0.01 mW/sq cm, ascribed to suppression of the slow EEG components. *The increase in* bioelectric activity developed somewhat later (40 days of exposure) in the subcortical regions (thalamus and hypothalamus). The total amplitude of the biocurrent increased by 22.5% relative to its initial value. For exposure at 0.05 mW/sq cm, the theta rhythm in the subcortical regions registered clearly after two weeks and its amplitude increased (presumably subsequently) by 10-11 microvolts and by 40 microvolts in some cases.

Regarding the baseline evoked potentials, the authors indicated that: "the subcortical structures of the brain in the initial state do not master a given light flash rhythm as well as the sensory-motor and visual zone of the cortex," and that two weeks of exposure at 0.05 mW/sq cm "increased the capacity of the neurons to react adequately to discontinuous photostimulation, since unlike the control studies, the rabbits of this test group showed a wider frequency band to which the brain could readjust its own electric oscillation frequency."

After 3 weeks of exposure at 0.05 mW/sq cm, the identity of the EEG components was disturbed. "Some rabbits showed a greater manifestation of earlier evoked changes in bioelectric activity, others showed some restoration of the initial EEG indices, and still others showed a slowing down of the basic rhythm down to three oscillations per second with some synchronization of processes at that frequency." After 30 days of exposure, the majority of these rabbits showed gradual increases in the density of slow waves in the range 1-3 Hz.

The initial changes in bioelectric activity in the 0.05-mW/sq-cm group were noticed after 2 weeks of exposure. However, the changes were more intense in the cortex than in the subcortical structures. The cortical

effect was a disturbance of the EEG frequency spectrum, consisting of a verifiable decrease in the number of delta-range oscillations and an increase in the alpha- and beta-range potentials. In the sensory-motor and visual regions, the delta-rhythm index fell by averages of 6.1% and 7.7%, respectively, while the alpha-rhythm index rose by averages of 9.2% and 9.7%. No quantitative changes were seen in the theta range. The authors stated that adaptation to the rhythms of 5-, 8-, and 12-Hz visual stimuli appeared more pronounced than initially.

For the group exposed at 0.5 mW/sq cm, suppression of bioelectric activity was manifested as an increase in slow delta waves of high amplitude in the cortex after 2 weeks of exposure, an effect that was different than for exposure at 0.01 and 0.05 mW/sq cm.

The questions previously raised about the possibility that the metallic electrodes caused artifacts are applicable as well to both Dumanskij and Shandala (1974) and Shandala et al. (1979).

Baranski and Edelwejn (1975) indicated that personnel exposed to RFR in various occupations for durations of 0-1, 1-3, 3-5, 5-10, and more than 10 years were given clinical examinations. Among their findings, the authors stated: "Those personnel who had the longest occupational exposure history and the highest exposure levels generally exhibited flat EEG recordings (Figure 3)." Displayed in Fig. 3 were the EEGs for a person who had been "occupationally exposed for 5 years to microwaves while working in a repair shop." Except for fluctuations of about a few microvolts (possibly noise), the EEG tracings were indeed essentially flat, but reminiscent of those for a brain-dead individual. It seems possible that the gain of the amplifiers was set incorrectly for these recordings. In general, the authors stated: "No firm conclusions could be drawn, however, due to the complexity of environmental occupational factors and the lack of adequate control groups," which led them to conduct an EEG study in animals under controlled conditions.

They exposed rabbits to far-field 2.95-GHz CW or pulsed (1-microsecond pulses at 1200 pps) RFR at the same average power density, either once at 5-30 mW/sq cm (0.7-4.2 W/kg; Durney et al., 1978, p.92) or 2 hr/day for 3-4 months at 5 mW/sq cm (0.7 W/kg). The EEGs in nine brain regions were recorded with leads of unstated design or composition on completion of exposure, so RFR-induced recording artifacts were absent. However, the leads undoubtedly were present during the exposures, so the question about possible enhancement of the local fields remains.

Regarding the results, the authors stated: "The most salient changes were obtained in animals exposed to pulsed microwaves. In the long-term-exposed rabbits, desynchronized high-voltage recordings were obtained. This finding may be interpreted to result from chronic stimulation of brain stem structures, probably the reticular formation. No such phenomena were noted in animals subjected to single exposures. Only slight differences were detected at high exposure levels (about 30 mW/sq cm) and these may be explained as thermal effects." Quantitative data were not presented; instead, representative sets of recordings from

the nine brain regions were presented for three rabbits, one exposed 3 hr/daily for a total of 200 hr to the pulsed RFR at 5 mW/sq cm, another exposed once for 2 hr to the pulsed RFR at 25 mW/sq cm, and the third exposed once for 2 hr to the CW RFR at 25 mW/sq cm.

Bruce-Wolfe and Justesen (1979) investigated the effects of RFR-induced hyperthermia on the visually evoked electrocortical response (VER) in five Hartley albino female guinea pigs. After anesthetizing the animals with sodium pentobarbital (30 mg/kg, ip), two electrodes were implanted 2 mm anterior to the lambdoid junction, one each at 6 mm to the left and right of the midsagittal suture. The reference electrode was implanted 2 mm to the right of the midline and 1 mm posterior to the bregmate junction. Each electrode was a small, stainless-steel screw penetrating the calvarium to make contact with the dura. Also, a thermistor was implanted in contact with the dura 2 mm to the left of the midline and 1 mm posterior to the bregmate suture for measuring brain temperature.

After surgery, each animal was habituated 30 min daily for 5 days to restraint in a cylindrical Plexiglas holder. The animal was then placed in restraint with its head about 50 cm from a photic stimulator adjusted to produce a 0.025-ms flash of light, and sessions of VER recording were conducted until latencies did not vary by more than 2.0 ms. Baseline cortical and rectal temperatures (the latter with a thermistor inserted 4 cm into the colon) were recorded prior to each experimental session.

The animals, presumably under restraint, were exposed in a multimode, mode-stirred cavity to 2.45-GHz RFR, amplitude-modulated at 60 Hz by the power supply and 12 Hz by the mode stirrer (Justesen et al., 1971). The SAR was in the range 30-40 W/kg and the durations ranged from 4 to 15 min, with an average of 8.5 min. At the end of exposure, each animal was moved quickly to a nearby shielded chamber for recording its VERs. During the VER elicitation period, a polygraph was used to produce a crude continuous EEG record and to provide a filtered and balanced amplified signal to an averaging computer. The information stored in the computer was used to produce graphic VERs by X-Y plotter. As rectal or cortical temperature fell, the photic stimulator and the signal-averaging computer were triggered manually during a series of measures, each of which involved a set of eight stimulations. Each VER was initiated by light flashes at a mean rate of one every three seconds during artifact-free periods determined from the crude EEG. X-Y plots were then made of summed VERs extending 250 ms from onset of photic stimulation.

Eleven sessions of RFR-exposure were conducted. During sessions 1-5, the VERs of all five animals were recorded, and before and after each set of photic stimulations, cortical temperature was recorded from three of the animals and rectal temperature from the other two animals. The successive increments of temperature (cortical or rectal) induced in the five sessions were 1.25, 2.50, 3.75, 2.50, and 1.25 deg C. Thus, with mean cortical and rectal baseline temperatures of 37.4 and 39.4 deg C, respectively, exposure raised these temperatures to as high as 41 and 43 deg C.

Sessions 6-10 were devoted solely to concurrent measurements of cortical and rectal temperatures in all five animals, using the same succession of increments. In session 11, rectal temperatures of all five animals were raised by an average of 4.75 deg C to 44.0 deg C, after which the VERs were recorded.

The primary characteristic of the VER examined was the latency time from the onset of photic stimulation to the N1 peak, "an inverse index of conduction velocity of primary visual fibers". The latencies were determined for each animal for its cortical or rectal temperatures at the times of VER recording after exposure, and its values at each such temperature for sessions 1-5 were pooled and plotted vs temperature (without error bars).

The plots for the three guinea pigs whose cortical temperatures were measured were roughly similar; these plots indicated that N1 latency is inversely related to temperature. Some latency displacements among the three curves were seen because of differences in baseline values and in latencies at 41.0 deg C, the highest temperature at which the VERs were recorded. The authors indicated that for these three animals, the mean baseline latency (at a cortical temperature of 37.0 deg C) was 42.84 ms and that it diminished to 37.68 ms at 40.5 deg C, corresponding to a 12% total increase in conduction speed or 3.4% mean increase per incremental deg C. The plots for the two animals whose rectal temperatures were measured also showed latencies inversely related to temperature. The mean values were not stated, but from the plots were about 46.6 ms at 38.5 deg C and 39.5 ms at 43 deg C. The authors noted that latencies were progressively more variable as the temperature increments were increased, but that overall correlation between latency and temperature was high and reliable (all $p<0.001$).

Cortical and rectal temperatures obtained in successive measurements after raising rectal temperature to 44.0 deg C (during session 11) were presented in bar graphs for each temperature at corresponding times. The results indicated that the two temperature measures were highly correlated and that rectal temperature was about 3 deg C higher than cortical temperature shortly after exposure but decreased slightly more rapidly than cortical temperature to yield a difference of about 2 deg C. Four of the five guinea pigs died between the second and third hour after cessation of exposure.

In their discussion, the authors stated: "Interpretation of our findings must be tempered by the condition of irradiation--electrodes were in contact with the animals' brains during exposure to microwaves--but we doubt that the observed relation between temperature increment and reduced latency of the VER was either quantitatively or qualitatively affected." Studies by Hetschel (1979) and Bruce-Wolfe et al. (1979) on endogenous warming of normal human subjects were cited, which yielded approximately the same VER latencies per incremental degree as for the guinea pigs, but the citations were not included in their reference list. They also stated: "We would not argue that local brain damage from demodulated currents at the junction of electrode and cortex does

not result from exposure to intense microwave radiation. This is a possibility we are exploring both behaviorly and histologically in the rat and guinea pig."

It should be noted that relatively few animals were used in this study, particularly since four of the five died under the severe hyperthermia (44 deg C). Moreover, in addition to the qualifying statements above by the authors, the relevance of the results to possible effects of RFR on the VERs of humans is open to question.

Takashima et al. (1979) studied the effects of amplitude-modulated electric fields on the EEGs of rabbits. Male rabbits were exposed to frequencies in the range 1-30 MHz between two 30x30-cm square aluminum plates spaced 20 cm apart at fields in the range 0.5-1 kV/m. A circuit for impedance matching was used between the plates and the source to minimize reflected powers. As noted below, EEGs were recorded before, after, and in some experiments, during exposure, with stainless-steel electrodes chronically implanted along the midline in the central and posterior regions of the brain; scalp electrodes were used in other experiments.

EEG signals were fed to a preamplifier having a pass band of 3-100 Hz and a 60-Hz notch filter. In initial experiments, the authors found it difficult to interpret unprocessed time-domain signals. Consequently, such signals were sampled at 5-ms intervals (1024 points), digitized, converted to frequency-domain complex spectra by the fast-Fourier-transform (FFT) technique, and thence to power spectra. Smoothing of the power spectra was required in order to resolve discrete frequency components. Hann's function was applied to autocorrelograms, the autocorrelograms were Fourier-transformed to obtain the smoothed power spectra, and sequential displays of smoothed power spectra (usually 17 spectra at 3-min intervals) were examined for time-invariant features.

Typical pre-exposure power-spectra sequences from anesthetized rabbits (sodium pentobarbital, 30 mg/kg ip) showed frequency components between 5 and 15 Hz that varied during each sequence, indicating the absence of a dominant component. The authors denoted such EEGs as "normal".

To determine the effects of short-term exposure, anesthetized animals were exposed once (acute exposure) to fields modulated at 60 Hz. In one set of such experiments (5 animals), stainless-steel electrodes had been implanted in the brain and were allowed to remain in the cranial cavity during exposure. The sequential set of power spectra obtained following exposure showed a clustering of amplitude peaks in the range 2-5 Hz that persisted over the postexposure recording period (40-60 min). Reduction of high-frequency components was also noted. Similar patterns were seen with the modulation absent (CW), but to a lesser extent.

In a second set of such experiments (2 animals), the EEG electrodes were removed prior to exposure and reinserted after exposure. (Not clear was whether surgery was involved in removal and reinsertion and if so, the effects thereof.) The resulting power spectra were said to re-

semble normal EEGs as defined above; no clustering of spectral components was seen. Therefore, the EEG alterations in the first set of acute-exposure experiments were attributed by the authors to the local field created by the presence of metal electrodes in the cranial cavity.

To investigate the effects of chronic exposure, 4 unanesthetized animals were exposed 2 hr/day to 1.2-MHz fields modulated at 15 Hz for 6 weeks. EEGs were recorded using silver electrodes placed directly on the skull before and after periods of exposure. The EEGs were monitored every 2 weeks. A sequential display of power spectra taken after 4 weeks of exposure showed ordering of low-frequency spectral peaks and reduction of high-frequency components similar to the acute-exposure data taken with intracranial electrodes. The abnormal patterns began to appear after 2-3 weeks of exposure. The authors constructed histograms from power-spectrum sequences derived from 4-week exposures and normal EEGs. The histogram for the exposed animals showed major peaks at 2 and 10 Hz, whereas the major peaks for the normal EEGs were at 4.5, 8, and 11.5 Hz.

In the chronic-exposure experiments, although the electrodes were not present during exposure, the description of electrode placement before and after exposure is confusing. In the text, attachment to the "skull" was described, whereas in Table 1 of the paper, "scalp" was used to describe the electrode arrangement. Again, not clear is whether surgery was involved.

Assuming that the rabbit head (without intracranial metal electrodes) could be modeled as a homogeneous conducting sphere immersed in a 10-MHz field of 500 V/m, the authors calculated that the current density within the head was 0.082 mA/sq cm. Consequently, they regarded the positive results as a nonthermal effect. However, adequate dosimetry data were not presented, particularly measurements or estimates of SARs in the head, so it is questionable to characterize any of the positive findings as thermal or nonthermal. Also not clear is why 60 Hz was used as the modulation frequency in the acute-exposure experiments, since the EEG signals were passed through a 60-Hz notch filter.

Although the authors claimed enhancement of low-frequency components and increase in high-frequency activity after 3 weeks, the data presented do not support this conclusion, and the authors themselves stated that the results presented were incomplete. However, they did note that for acute exposure, "enhanced slow waves and unusually low high-frequency activities were due to the local field created by the presence of the metal electrodes in the cranial cavity."

In this study, the rabbits were used as their own control group, in that data obtained during and after exposure were compared with "normal" (preexposure) data from the same group. The absence of a similarly treated but sham-exposed group, however, makes it difficult to assess whether the reported EEG changes were the result of exposure per se, or perhaps of adaptation to the repetitive aspects of the experimental procedures, such as handling and recording.

When power spectra for EEGs taken at short time intervals (3 min) in a sequence are highly variable relative to one another, it is difficult to quantitatively assess differences among sequences. Autoregressive spectral estimation techniques may be more appropriate for analysis of EEG data than FFT techniques, since interval definition is problematic for nonstationary data. Qualitatively, nevertheless, their chronic-exposure results appear to show enhancement of low-frequency power-spectral components and reduction of high-frequency activities. On the other hand, comparison of data from the anesthetized animals used in the acute experiments with data from the unanesthetized animals used in the chronic experiments lacks analysis of the effects of anesthesia as a possible confounding factor. Also, it is not clear why they presented the data taken after 4 weeks, and not after 2 and 6 weeks, of exposure.

Chou and Guy (1979a) investigated two types of nonperturbing electrodes for recording EEGs during chronic exposure to RFR. One type consisted of a fine carbon-loaded-Teflon wire (4 S/m conductivity) used as a conductive lead and as a subcortical electrode; the electrode end of the wire was passed through and fastened with epoxy to a glass pipette 2.5 cm long for support, emerging from the pipette for a distance of 0.5 mm to serve as the electrode proper. The other type, used as a cortical electrode, consisted of a screw (2-56 or 4-40) 4.5 mm long machined from carbon-loaded Teflon (1 S/m conductivity), with a carbon-loaded-Teflon lead squeezed tightly onto the screw by a nylon nut, using conductive glue to ensure good electrical contact. The other end of the lead from either type was attached with conductive glue to a metal pin, the latter to permit quick connection to a head plug. The authors noted that the glass-pipette carbon-loaded-Teflon configuration is the same as that in the Vitek 101 non-perturbing temperature probe (Bowman, 1976).

For electrode implantation, rabbits were anesthetized with sodium pentobarbital (30 mg/kg iv), a small hole was drilled in the calvarium and threaded. One carbon-loaded-Teflon screw (2-56) was placed near the sensory-motor cortex (3 mm anterior to the horizontal line and 3 mm to the right of the center line); another carbon-loaded-Teflon screw (2-56 or 4-40) was placed in the area of the nasal bone as the reference electrode. The subcortical carbon-loaded-Teflon electrode was implanted so that its tip entered the ventro-medial hypothalamus. All the metal pins at the other ends of the leads were connected to a Winchester plug.

Both stainless-steel and carbon-loaded-Teflon electrodes were implanted in one rabbit, carbon-loaded-Teflon electrodes only were implanted in three rabbits, and stainless-steel electrodes only were implanted in two rabbits. For the rabbits with metal electrodes, one set of Vitalic screws (3 mm) and monopolar electrodes were placed in the same or contralateral locations. The rabbits were restrained in a wooden box and placed within a dark, sound-attenuated room. The head plug was connected by flexible cable to a differential amplifier with frequency response from 0.6 to 60 Hz. A 60-Hz notch filter was used in several cases as discussed below. The EEG signals were recorded on graph paper directly from the amplifier and also fed to a spectrum analyzer for processing, amplification, and recording. The total

sampling period was only 20 seconds due to equipment limitations.

Presented were cortical EEGs and the resulting spectra recorded without and with the 60-Hz filter for two rabbits five months after metal and carbon-loaded-Teflon electrodes were implanted. These recordings were made prior to exposing the rabbits to RFR. The authors stated: "Due to the high resistance of the carbon-loaded Teflon, it was impossible to record the EEG via these electrodes without the 60-Hz filter. The EEGs and spectra of both types of electrodes were similar when the 60-Hz filter was in operation...The 60-Hz noise interfered with the main frequency components of the EEG. The amount of interference was correlated with the resistance of the electrode."

The authors also indicated that for the EEGs recorded via the metal electrodes, the 60-Hz filtering of the spectra had no effect on major frequency components. In particular, a slight high-frequency noise was seen in both the EEG and its spectrum when no filter was used. When a variable resistance was added in series with the metal electrode, more noise appeared in the EEG that distorted the spectrum, and recording was impossible with 90 kilohms. The spectrum was depressed when no filter was used, but showed no effect when the filter was turned on, a result similar to that with the carbon-loaded-Teflon electrode. These results showed that "with proper recording conditions, a carbon-loaded-Teflon electrode with resistance less than 90 kilohms can be used for EEG recordings if a 60-Hz filter is used."

The subcortical EEGs and spectra, shown for rabbits implanted with metal and carbon-loaded-Teflon electrodes but only with the 60-Hz filter in operation, were highly similar. The authors also noted that the EEG amplitude and pattern remained similar for periods up to six months.

Exhibited (in Fig. 5) for a rabbit implanted with carbon-loaded-Teflon electrodes were subcortical EEGs and spectra before and during exposure of its head to 2.45-GHz RFR. RFR from a diathermy machine was directed to the right eye at a power density of 100 mW/sq cm. The corresponding SAR in the hypothalamus was about 25 W/kg. The authors stated: "There was no obvious RF interference picked up by the carbon-loaded-Teflon electrode. Within the short recording time, no obvious difference can be seen in this figure."

Four to six months after electrode implantation, the rabbits were perfused, the brain regions near the cortical electrodes were examined visually, and the brain regions near the subcortical electrode track were sliced (50-micron sections), stained with cresyl violet, and examined with a light microscope. For electrodes longer than skull thickness, a small indentation always occurred at the cortex. However, no infection or hemorrhage was evident in the dura or the cortex. The cells around the tip of the subcortical-electrode track did not differ from the cells at other locations. Other than the electrode track, there was no observable tissue damage. The authors noted that they did not investigate the stainless-steel electrodes for tissue compatibility, but that such electrodes are conventionally used in electrophysiological

experiments for chronic recordings and would be expected to have good tissue compatibility.

Their general conclusion was: "It has been shown that electrodes made of carbon-loaded Teflon with conductivity close to that of high-water-content tissue are useful for chronic EEG recording in animals exposed to microwave radiation. With a 60-Hz filter, the EEG recorded from carbon-loaded Teflon electrodes is indistinguishable from that recorded from metal electrodes."

Chou et al. (1982) implanted carbon-loaded Teflon electrodes in the sensory-motor, occipital, and nasal areas of 18 young adult New Zealand rabbits (9 males, 9 females), with the electrodes in contact with the dura. The rabbits were divided into three equal groups. Those of one group were exposed individually from above to 2.45-GHz far-field CW RFR at 1.5 mW/sq cm 2 hr/day between 0830 and 2030, 5 days/week, for 90 days within a miniature anechoic chamber (Guy, 1979). For exposure, each rabbit was placed in a Plexiglas cage with its long body axis parallel to the electric vector. The second group was exposed to 2.45-GHz pulsed RFR (10-microsecond pulses at 100 pps) at 1.5 mW/sq cm average power density in a similar chamber for the same periods. By thermographic measurements in the sagittal plane of a euthanized rabbit, there were two "hot spots," one in the sinus area and the other on the back. The peak SARs in these regions were respectively 2.1 and 1.6 W/kg at 1.5 mW/sq cm. The third group was sham-exposed in still another chamber of the same kind for the same durations.

Body weights were measured every other day and were found to increase almost linearly during the 3-month treatment period, at which time the weights were reaching a plateau. By least-squares linear regression and analysis of variance, there were no significant differences among the three groups. The results of hematological, chemical, and morphological tests of blood samples taken monthly were tabulated. These showed no significant differences among groups. Eyes were examined with a slit lamp before and after the 3-month treatment. No cataracts developed in any of the 18 rabbits.

EEGs and evoked potentials were recorded via the implanted electrodes every Friday after the 2-hr treatment. The animals were restrained in wooden boxes with their heads protruding to permit connection of the electrodes to the recording equipment. For each recording session, three rabbits were enclosed in a light-proof and sound-proof chamber, with the animals visually separated from one another. A strobe light and a loudspeaker within the chamber were used for inducing VERs and AERs. The recording leads were connected to differential amplifiers each having a frequency response of 0.6-60 Hz, and a line filter was used to eliminate 60-Hz noise pickup by the high-resistance electrodes. The outputs of the amplifiers were fed to an 8-channel FM magnetic tape recorder and monitored on a 6-channel oscilloscope.

After 5-10 min of adaptation, the EEGs from the sensory-motor and occipital areas of each animal were recorded for 20 min. Then, VERs

stimulated at 1 flash per second were recorded from the occipital cortex for 5 min. In the final 5 min of testing, AERs stimulated by 70-dB 0.1-ms clicks at 1 click per second were recorded from the sensory-motor cortex. The EEG data were analyzed off-line for frequency spectrum and averaged amplitudes with a computer, and the ERs were reduced on a computer of average transients. VERs and AERs for one rabbit of each group were displayed.

The authors indicated that the frequency spectrum varied considerably from rabbit to rabbit and from one recording session to another for each rabbit, rendering it impossible to compare each individual frequency. Instead, the power spectra were integrated. The weekly integrated power-spectrum means and SDs from each cortical area for each group were tabulated for the 3 months. The authors noted that despite the large differences among the means and the large SDs, there was a trend toward decreased amplitude during the later part of the experiment, a trend ascribed to acclimatization of the animals. However, statistical tests revealed no significant differences among the three groups.

Also tabulated were the weekly means and SDs of the amplitudes taken over a 1-s period of each 20-min recording session. Great variability also made comparisons difficult, but again no statistically significant differences among the groups could be discerned. Regarding the VERs and AERs, the authors indicated that the waveforms varied from animal to animal and with time, with no consistent amplitude or latency useful for comparison, and noted that the large variability of the VERs appeared to be contrary to the findings of Baranski and Edelwejn (1975).

At the end of the study, apomorphine in doses of 1, 2, or 4 mg/kg was injected into the animals to determine differences in induced behavioral excitation and hyperthermia. However, 5 rabbits (one each in the CW and sham groups and three in the pulsed group) died during the experiment, so no results were presented. Finally, the 13 rabbits that survived the drug study were euthanized, and the lungs, heart, vessels, stomach, small and large intestines, pancreas, liver, gall bladder, adrenal gland, kidneys, bladder, testes or ovaries, bone marrow, spleen, and brain were examined microscopically for pathology.

Regarding the necropsies, the authors presented the following findings and stated: "To summarize, for the small number of animals (N=13), the histopathological study did not show any consistent, significant differences in tissue damage." One rabbit exposed to the CW RFR showed linear focus of necrosis with moderate mononuclear infiltration in the zona fasciculata of the adrenal cortex. Three of the rabbits exposed to CW and two sham-exposed rabbits had dilated collecting tubules in the renal cortex of the kidney. One other sham-exposed rabbit had foci of chronic interstitial nephritis. One each of the CW and sham groups had moderate amounts of glycogen deposits in hepatocytes. One CW rabbit showed hepatic coccidiosis with biliary hyperplasia and ectasia in the liver. A single subcapsular focus of hepatic coagulation necrosis occurred in one rabbit of the sham group. The most common lesion was mild periportal fibrosis, which occurred in one rabbit exposed to the CW

RFR and two rabbits each of the sham and pulsed groups.

In the lung, there was peribronchiolar lymphoid proliferation in four rabbits of the CW group, one rabbit of the pulsed group, and three rabbits of the sham group; subacute suppurative bronchopneumonia in one of the rabbits of the sham group; and mild suppurative bronchitis in one of the rabbits of the pulsed group. Macrophages in the sacculus robundus of cecum were seen in two rabbits each of the CW and pulsed groups and in five rabbits of the sham group. One rabbit each of the pulsed and sham groups had myofibrillar degeneration of the heart. All other tissues investigated appeared normal. The authors noted that the peribronchiolar lymphoid proliferation and several other minor abnormalities in sham-exposed rabbits were common lesions in older animals housed in a conventional nonpathogen-free environment. They concluded that, "for the small number of animals (N=13), the histopathological study did not show any consistent, significant differences in tissue damage."

Kaplan et al. (1982) performed a study primarily of possible effects on infant behavior of perinatal exposure of the squirrel monkey to 2.45-GHz RFR (see Section 3.7.1.2), but also recorded EEGs and VERs. From the beginning of the second trimester of pregnancy, squirrel monkeys were exposed to 2.45-GHz pulsed RFR in 12 multimode, mode-stirred cavity modules. Within each module, an opaquely partitioned dielectric cage housed two adult monkeys. Groups of 10, 12, and 11 pregnant females were exposed at respective whole-body mean SARs of 3.4, 0.34, and 0.034 W/kg (plane-wave equivalents of 10, 1, and 0.1 mW/sq cm) for 3 hr/day, 5 days/week until parturition. Eight pregnant monkeys were similarly sham-exposed in the same modules. Eighteen RFR-exposed mothers were exposed with their offspring for 6 months after parturition, and then the offspring were exposed alone for another 6 months after weaning.

Baseline EEGs and VERs were obtained from mothers and infants of all groups at the time of weaning (when the infants were 6 months old), and at 9 and 12 months of age from infants that had been perinatally sham-exposed or exposed to RFR at the three levels. At stimulus frequencies of 6, 10, and 16 flashes per second, blocks of 20 trials each were presented to each subject in a single session. Each trial consisted of 4 seconds of baseline EEG recording followed by 4 seconds of visual stimulation. The interstimulus interval was 20-30 seconds and the order of presentation of the three frequencies was counterbalanced across subjects for the separate recording sessions.

No chronically attached or indwelling electrodes were used during exposure. Instead, one or two days before testing, the heads of the monkeys were shaved and cleaned with a depilatory. At testing time, each monkey was sedated lightly with sodium pentobarbital (10-15 mg/kg intramuscularly) to reduce movement, and adhesive collars were used to attach biominiature Ag-AgCl electrodes at the occipital and frontal regions of the scalp. The frontal site was used as a reference and an electrode attached at the vertex was grounded.

The analog occipital records were digitized and subjected to spectral

analysis on a computer. After spectral analysis, the 20 trials for each of the three flicker frequencies were averaged together, and a special program was used to compute nine spectral parameters for each of the EEG frequency bands selected. Six bands were evaluated: the three 3-Hz-wide bands encompassing the flicker frequencies (5-7, 9-11, and 15-17 Hz) and bands for delta activity (0.5-4 Hz), alpha activity (8-13 Hz), and beta activity (15-23 Hz). To determine the extent of photic driving at each flicker rate, the flicker-to-baseline-EEG ratios were calculated.

No data were presented, but the authors indicated that statistical analyses of the data for the seven groups of mothers revealed no differences on any of the obtained measures (Kruskal-Wallis analysis of variance by ranks). Moreover, no differences were found after combining mothers from the three exposure levels into two groups consisting of those treated during gestation only and those treated during gestation plus 6 months after parturition. Also, no differences were seen between groups of infants treated prenatally only and treated prenatally plus postnatally irrespective of treatment level. The authors noted that, as would be expected, all groups of infants (including those sham-exposed) had consistently larger values of slow-wave activity than the adults at each of the ages tested. A comparison of delta-to-beta, delta-to-alpha, and alpha-to-beta ratios between mothers and infants at each age tested showed that infants had a relatively greater amount of delta activity ($p<0.01$, t-tests).

In summary, the use of indwelling metallic electrodes, wires, or screws in studies of the effects of RFR on the EEG and/or ERs may be questioned as a procedure likely to induce artifactual effects in the preparations under study, as well as in the recordings themselves. Moreover, the influence on the findings of anesthesia, used in many experiments, could not be assessed. In more recent studies, occurrence of artifacts was minimized by use of electrodes and leads appropriately designed from materials having high resistivities comparable to those for tissue. When such electrodes were implanted prior to exposure and were present during exposure, or when conventional metallic (or high-resistivity) electrodes were used after exposure, no statistically significant differences in EEGs or evoked responses between control and RFR-exposed animals were obtained. An important finding of Guy and coworkers was that for rabbits, so often used in such studies, the EEGs and ERs can vary widely among control animals not under anesthesia and with time for each animal (and likewise for animals exposed to RFR). As previously noted, large variations in the rabbit EEG were observed by Goldstein and Cisko (1974) also.

REFERENCES:

Baranski, S. and Z. Edelwejn
EXPERIMENTAL MORPHOLOGIC AND ELECTROENCEPHALOGRAPHIC STUDIES OF MICROWAVE EFFECTS ON THE NERVOUS SYSTEM
Ann. N.Y. Acad. Sci., Vol. 247, pp. 109-116 (1975)

Bowman, R.R.
A PROBE FOR MEASURING TEMPERATURE IN RADIO-FREQUENCY HEATED MATERIAL
IEEE Trans. Microwave Theory Tech., Vol. 24, No. 1, pp. 43-45 (1976)

Bruce-Wolfe, V. and D.R. Justesen
MICROWAVE-INDUCED HYPERTHERMIA AND THE VISUALLY EVOKED ELECTROCORTICAL RESPONSE OF THE GUINEA PIG
Radio Sci., Vol. 14, No. 6S, pp. 187-191 (1979)

Chou, C.-K., and A.W. Guy
CARBON-LOADED TEFLON ELECTRODES FOR CHRONIC EEG RECORDINGS IN MICROWAVE RESEARCH
J. Microwave Power, Vol. 14, No. 4, pp. 399-404 (1979a)

Chou, C.-K., A.W. Guy, J.B. McDougall, and L.-F. Han
EFFECTS OF CONTINUOUS AND PULSED CHRONIC MICROWAVE EXPOSURE ON RABBITS
Radio Sci., Vol. 17, No. 5S, pp. 185-193 (1982)

Dumanskij, J.D. and M.G. Shandala
THE BIOLOGIC ACTION AND HYGIENIC SIGNIFICANCE OF ELECTROMAGNETIC FIELDS OF SUPERHIGH AND ULTRAHIGH FREQUENCIES IN DENSELY POPULATED AREAS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 289-293 (1974)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Frey, A.H., A. Fraser, E. Siefert, and T. Brish
A COAXIAL PATHWAY FOR RECORDING FROM THE CAT BRAIN DURING ILLUMINATION WITH UHF ENERGY
Physiol. and Behav., Vol. 3, pp. 363-364 (1968)

Goldstein, L. and Z. Cisko
A QUANTITATIVE ELECTROENCEPHALOGRAPHIC STUDY OF THE ACUTE EFFECTS OF X-BAND MICROWAVES IN RABBITS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 128-133 (1974)

Guy, A.W.
MINIATURE ANECHOIC CHAMBER FOR CHRONIC EXPOSURE OF SMALL ANIMALS TO PLANE-WAVE MICROWAVE FIELDS
J. Microwave Power, Vol. 14, No. 4, pp. 327-338 (1979)

Johnson, C.C., and A.W. Guy
NONIONIZING ELECTROMAGNETIC WAVE EFFECTS IN BIOLOGICAL MATERIALS AND SYSTEMS
Proc. IEEE, Vol. 60, No. 6, pp. 692-718 (1972)

Justesen, D.R., D.M. Levinson, R.L. Clarke, and N.W. King
A MICROWAVE OVEN FOR BEHAVIOURAL AND BIOLOGICAL RESEARCH: ELECTRICAL AND STRUCTURAL MODIFICATIONS, CALORIMETRIC, DOSIMETRY, AND FUNCTIONAL EVALUATION
J. Microwave Power, Vol. 6, No. 3, pp. 237-258 (1971)

Kaplan, I.T., W. Metlay, M.M. Zaret, L. Birenbaum, and S.W. Rosenthal
ABSENCE OF HEART-RATE EFFECTS IN RABBITS DURING LOW-LEVEL MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 168-173 (1971)

Kaplan, J., P. Polson, C. Rebert, K. Lunan, and M. Gage
BIOLOGICAL AND BEHAVIORAL EFFECTS OF PRENATAL AND POSTNATAL EXPOSURE TO 2450-MHZ ELECTROMAGNETIC RADIATION IN THE SQUIRREL MONKEY
Radio Sci., Vol. 17, No. 5S, pp. 135-144 (1982)

Lambert, P.D., R.C. Nealeigh, and M. Wilson
EFFECTS OF MICROWAVE EXPOSURES ON THE CENTRAL NERVOUS SYSTEM OF BEAGLES
J. Microwave Power, Vol. 7, No. 4, pp. 367-380 (1972)

NAS (National Academy of Sciences)
ANALYSIS OF THE EXPOSURE LEVELS AND POTENTIAL BIOLOGIC EFFECTS OF THE PAVE PAWS RADAR SYSTEM (1979)

Shandala, M.G., U.D. Dumanskii, M.I. Rudnev, L.K. Ershova, and I.P. Los
STUDY OF NONIONIZING MICROWAVE RADIATION EFFECTS UPON THE CENTRAL NERVOUS SYSTEM AND BEHAVIOR REACTIONS
Environ. Health Perspectives, Vol. 30, pp. 115-121 (1979)

Takashima, S., B. Onaral, and H.P. Schwan
EFFECTS OF MODULATED RF ENERGY ON THE EEG OF MAMMALIAN BRAINS
Rad. and Environm. Biophys., Vol. 16, pp. 15-27 (1979)

Tyazhelov, V.V., R.E. Tigranian, and E.P. Khizhniak
NEW ARTIFACT-FREE ELECTRODES FOR RECORDING OF BIOLOGICAL POTENTIALS IN STRONG ELECTROMAGNETIC FIELDS
Radio Sci., Vol. 12, No. 6S, pp. 121-123 (1977)

3.4.4 CALCIUM EFFLUX

Adey, Bawin, and their colleagues have reported extensively on studies of changes in calcium efflux from preparations of neonate chick brain and cat cortex due to exposure of such preparations to very specific frequencies and intensities of unmodulated sub-ELF fields or to specific levels of VHF and UHF RFR amplitude-modulated at very specific sub-ELF frequencies, using the radioactive-calcium ion Ca-45++ as the tracer. Confirmation of the basic phenomenon was obtained by some investigators, and others reported negative or contradictory results. Representative papers selected from the literature on the subject are discussed below.

Bawin et al. (1975), in an early paper on calcium efflux, described the experimental protocol for chick brains in detail. Five hundred neonatal chicks in the age range 2-7 days were used. After decapitating each chick, its forebrain was quickly excised and each cerebral hemisphere was incubated for 30 min in 1.0 ml of physiologic medium and 0.2 ml of saline containing 0.2 microcurie of Ca-45++, within a polyallomer test tube. Following incubation, the samples were washed three times in nonradioactive solution. They were then immersed in 1 ml of physiologic medium for 20 min, during which one hemisphere of each chick was exposed to RFR with the other hemisphere as its control.

The exposures were to a 147-MHz field between two 4100-sq-cm triangular aluminum plates within an environmental chamber adapted for use of VHF fields and maintained at 37 deg C and 35% relative humidity. The field was modulated at 0.5, 3, 6, 9, 16, 20, 25, or 35 Hz at depths between 80% and 90% or was unmodulated. The RF from the source was applied to the narrow apices of the plates via an antenna coupler. The power was monitored with two in-line wattmeters and an RF ammeter and was adjusted to yield intensities in the range 1-2 mW/sq cm.

Sets of 10 brains (10 each exposed and control hemispheres) were treated concurrently for each field condition and control. Each field condition was tested at least three times, to provide large enough populations for statistical analysis. In each experiment, four series of 10 samples each were treated, i.e., one series each was exposed to fields modulated at three different modulation frequencies and one series of unexposed samples served as controls. On treatment completion, a 0.2-ml aliquot of each bathing solution diluted in 11 ml of Packard "Instagel" was assayed for radioactivity by liquid scintillation counting. Regarding treatment of the data, the authors stated: "The radioactivities (cpm) of all samples were related to the mean value of the counts obtained with the 10 control samples, taken as 100. All normalized data within each condition were then statistically compared with matched samples of control values." (No unnormalized data were presented.)

The results for the unmodulated field and each modulation frequency were plotted as bar graphs of mean percentage increases (with SEs) of Ca-45++ concentration (effluxes) relative to the mean value in the absence of the field. The unmodulated field and those modulated at 0.5, 3, 6, 9, and 16 Hz yielded progressively larger increases in the per-

centage of calcium efflux, with a maximum of about 19% (to 119% of control) for 16 Hz. The results for 0 (unmodulated), 0.5, and 3 Hz were statistically not significant ($p>0.05$); those for 6 and 9 Hz were significant at the 5% level, and those for 11 and 16 Hz were significant at the 1% level. Above 16 Hz, calcium efflux percentage declined progressively with increasing modulation frequency, with the mean efflux significant ($p<0.05$) for 20 Hz and not significant ($p>0.05$) for 25 or 35 Hz.

Forty other chick brains were used to compare the effects of exposure on calcium efflux from brains in physiologic medium with those in brains poisoned by incubation with 0.0001-M sodium cyanide. Four sets, each consisting of five poisoned samples and five normal samples, were assayed, with the samples of each set treated simultaneously: One set each was tested for the effects of exposure to fields modulated at 0 (unmodulated), 0.5, and 16 Hz and one set was tested without exposure. The results are shown in Table 36, adapted from Table 1 of the paper.

TABLE 36: PERCENTAGE CALCIUM EFFLUX FROM NORMAL AND POISONED BRAINS

Exposure Condition	% Efflux +/- SE (N) Normal Brain	% Efflux +/- SE (N) Poisoned Brain
Control	100.0 +/- 4.0 (15)	96.7 +/- 3.6 (15)
Unmod.	103.7 +/- 6.0 (10)	102.3 +/- 5.3 (10)
0.5-Hz Mod.	100.5 +/- 4.6 (10)	98.7 +/- 5.0 (10)
16-Hz Mod.	114.2 +/- 6.4 (10)*	118.9 +/- 7.7 (10)*

*$p<0.05$

As seen above, the difference in mean percentages of calcium efflux between poisoned and normal brains for each exposure condition was not significant. The authors stated: "The field effects observed previously were not altered by the cyanide treatment, which strongly suggests that the Ca-45++ effluxes from the cerebral tissues are independent of any ongoing metabolism."

The authors did not state what type of statistical analysis they used; their statements regarding data treatment, quoted above, do not indicate whether the paired t-test was used on the assays for each exposed brain hemisphere and its contralateral control hemisphere, which would seem to be an appropriate statistic. Regarding the 16-Hz value in Table 36 for normal brains (114.2%), which was labeled significant by them, it is interesting that by unpaired t-test, $t=1.99$, which is significant under the 1-tailed criterion ($0.025<p<0.05$), but is just outside the level of significance under the 2-tailed criterion ($0.05<p<0.1$). Also, that mean was smaller than the 119% obtained previously, but the difference presumably was not significant.

Also performed were preliminary experiments on possible calcium efflux from skeletal muscles (lateral head of the gastrocnemius). Muscle and cerebrum excised from the same chicks were tested concurrently for 20-

min exposures to fields modulated at 6 or 16 Hz and no field. The results are shown in Table 37 (from Table 2 of the paper):

TABLE 37: PERCENTAGE CALCIUM EFFLUX FROM BRAIN AND MUSCLE

Exposure Condition	% Efflux +/- SE (N) Brain	% Efflux +/- SE (N) Muscle
Control	100.0 +/- 5.4 (10)	100.0 +/- 5.8 (10)
6-Hz Mod.	115.0 +/- 4.2 (10)*	105.1 +/- 9.8 (10)
16-Hz Mod.	119.1 +/- 6.2 (10)*	100.1 +/- 3.9 (15)

*$p<0.05$

As seen above, the results for muscle exhibited much greater variability than those for brain tissue, but neither exposure condition had any significant effect on mean percentage calcium efflux therefrom.

The cerebral-calcium-efflux results of this study constitute evidence for the existence of a quite subtle RFR effect. The absence of the effect for unmodulated RFR and for modulation frequencies outside the range reported is an indication that heating of the preparation by the RFR is unlikely to be involved. Rather, some nonlinear mechanism may exist in the preparation that is capable of recovering and/or responding to one polarity of the modulation envelope. Such a mechanism would also have to have a time constant comparable to that for 16 Hz, at which the effect is near maximum.

The authors speculated that such slow undulations of the extracellular electric field could affect the binding of calcium to the neuronal membrane, and that a small displacement of calcium ions would result in cooperative interaction between modified adjacent binding sites, thus producing propagation and amplification of local electrical events.

Bawin and Adey (1976a,b), to ascertain whether calcium efflux induced by amplitude-modulated 147-MHz fields was due to the carrier frequency or the modulation per se, performed similar experiments with excised tissue from chicks (cerebral and muscle) and cats (cerebral only), but exposed the preparations to sinusoidal fields at discrete frequencies in the extremely-low-frequency (ELF) and sub-ELF ranges (1-75 Hz). Exposures were done between two parallel metal plates 1 square meter in area and spaced 50 cm apart in a chamber held at 36 deg C. Brain samples in 1 ml of physiologic medium were exposed for 20 min to 1, 6, 16, or 32 Hz at peak fields (in air) of 5, 10, 56, and 100 V/m. The muscle preparations were exposed for 20 min to a 16-Hz field at 20 V/m.

Cerebral and muscle samples from the chick were prepared and the 0.2-ml aliquots of bathing solutions were assayed for radioactivity following treatment as in the previous study. In addition, each brain sample was dissolved overnight in a digestive medium and assayed for radioactivity as a check. Cortical samples were dissected from the visual,

auditory, somatosensory, and suprasylvian areas of anesthetized cats. Each sample was bisected and the pia mater removed before weighing. Half of each bisected sample for each field condition was exposed after incubation with Ca-45++, with the other half kept concurrently in a bath at 36 deg C as the control. Experiments were also done in which samples were sham-exposed, and the results were compared with those of controls.

About statistical treatment of the data, Bawin and Adey (1976b) stated: "Our pilot studies with radio frequency fields demonstrated that sample counts more than 40% above or below the mean of any set of 10 samples can be discarded as aberrations due to experimental errors in washing the tissue after incubation or in collecting the supernatant following the test period. In the present study, two statistical criteria applied to each set of data confirmed our previous observations. Extreme counts in any set more than 1.5 standard deviations away from the mean also satisfied the probability levels (0.1 to 0.01) in a statistical method based on the range of values [maximum ratio of extreme ranking observations (Dixon, 1951)]. Therefore, such extreme values were eliminated from the sets (fields as well as controls) before final analysis of the data. The radioactivities (cpm/g) of all samples (supernatant and digested tissues) were referred to the mean value of the counts obtained in control effluxes. This allows direct comparison between the amounts of Ca-45++ taken up by the tissues and subsequently released during the experimental conditions. All normalized data were statistically compared (t test) with matched samples of control values.

"The results are expressed in terms of the mean of all samples within a condition, plus or minus the standard error of the mean (m +/- sem). 340 neonate chicks and 39 adult cats were used in this study."

The mean chick-brain ratio m +/- SE for each of the four frequencies and field intensities (F) and for the controls (C) were presented in Table 1 of Bawin and Adey (1976b), shown adapted as Table 38. Also given were the numbers of samples (n) and the values of t. (These means and SEs were also displayed in Fig. 1 of the paper as bar graphs, but the SE bars were erroneously half the values given in Table 38.)

TABLE 38: MEAN CALCIUM-EFFLUX RATIOS FROM CHICK FOREBRAIN

Mod.	m +/- SE (F)	m +/- SE (C)	n	t
		5 V/m		
6 Hz	0.923 +/- 0.036	1.000 +/- 0.038	30	1.450
16 Hz	0.933 +/- 0.041	1.000 +/- 0.041	27	1.144
32 Hz	0.945 +/- 0.038	1.000 +/- 0.041	27	0.974
		10 V/m		
1 Hz	0.943 +/- 0.041	1.000 +/- 0.038	26	1.021
6 Hz	0.866 +/- 0.029	1.000 +/- 0.037	26	3.069**
16 Hz	0.849 +/- 0.026	1.000 +/- 0.031	38	3.726**
32 Hz	0.913 +/- 0.038	1.000 +/- 0.037	27	1.633
		56 V/m		
1 Hz	1.028 +/- 0.042	1.000 +/- 0.038	26	0.515
6 Hz	0.882 +/- 0.032	1.000 +/- 0.030	37	2.681*
16 Hz	0.889 +/- 0.035	1.000 +/- 0.028	36	2.489*
32 Hz	0.942 +/- 0.031	1.000 +/- 0.038	26	1.518
		100 V/m		
6 Hz	0.928 +/- 0.028	1.000 +/- 0.029	36	1.735*
16 Hz	0.995 +/- 0.037	1.000 +/- 0.037	28	0.092

*p<0.05; **p<0.01

The results above indicate that the effect with ELF and sub-ELF fields was opposite to that with amplitude-modulated 147-MHz RFR (Bawin et al., 1975), i.e., mean ratios of less than unity (decreases rather than increases of calcium efflux) were obtained for all conditions except with 1 Hz at 10 V/m, with maximum effect with 6 and 16 Hz at 10 V/m. In addition, the data indicate the existence of a field-amplitude "window" (as well as a frequency window), i.e., with 6 and 16 Hz, the decreases were statistically significant at 10 V/m ($p<0.01$) and 56 V/m ($p<0.05$) but not at 5 or 100 V/m. The results for the chick-muscle preparations indicated no effect of field exposure, in consonance with the previous negative finding with amplitude-modulated 147-MHz RFR.

About the brain-tissue assays, the authors stated: "Tissue counts from exposed brain tissues were not statistically different from the control values. Each field condition was tested against the corresponding no field control to insure that the decrease seen in the Ca-45++ release was not due to an accidentally low tissue uptake. The mean uptake obtained for all brain samples (across all field conditions), expressed as a ratio with respect to the mean efflux of all controls, was 3.076 with a standard error of 0.104; the control values were 3.167 and 0.090. Thus the ratio of Ca-45++ uptake in the brain tissues versus the Ca-45++ released in the bathing fluid was three to one."

The results for the cat-cortex preparations are displayed in Table 39:

TABLE 39: MEAN CALCIUM-EFFLUX RATIOS FROM CAT CORTEX

Mod.	m +/- SE (F)	m +/- SE (C)	n	t
		10 V/m		
6 Hz	0.948 +/- 0.023	1.000 +/- 0.032	23	1.296
16 Hz	0.982 +/- 0.037	1.000 +/- 0.034	29	0.302
32 Hz	1.006 +/- 0.054	1.000 +/- 0.036	16	0.108
		56 V/m		
1 Hz	0.974 +/- 0.054	1.000 +/- 0.036	23	0.386
6 Hz	0.855 +/- 0.034	1.000 +/- 0.043	21	2.600*
16 Hz	0.874 +/- 0.025	1.000 +/- 0.026	24	3.402**
32 Hz	0.909 +/- 0.034	1.000 +/- 0.040	21	1.704
75 Hz	0.932 +/- 0.026	1.000 +/- 0.033	22	1.600
		100 V/m		
6 Hz	1.000 +/- 0.025	1.000 +/- 0.032	21	0.016
16 Hz	0.965 +/- 0.033	1.000 +/- 0.025	29	0.830

*p<0.05; **p<0.01

As seen above, decreases in calcium efflux were obtained under almost all exposure conditions, but the only significant changes were at 56 V/m for 6 Hz ($p<0.05$) and 16 Hz ($p<0.01$), again indicating the existence of an amplitude window. The authors noted that no significant differences were found between different cortical regions, and that removal of the pia mater was essential for consistent effects in neocortical samples. They also found no differences in results for samples sham-exposed and samples placed in the heated bath, or between samples tested at 30 and 36 deg C.

The field amplitudes cited were those in air between the two exposure plates. Regarding the magnitudes of the induced internal field, the authors stated: "Tissue gradients were not directly measured, but in related studies, gradients of the order of 0.1 microvolt/cm were induced in a phantom monkey head by fields of similar geometry (Miller et al., 1974)." However, the description of the work on the phantom monkey head was obscure; also, it is difficult to understand the extrapolation from the results for the phantom monkey head to the brain preparations used in these experiments.

On the other hand, as with the study by Bawin et al. (1975), heating of the preparations by the ELF or sub-ELF fields was most unlikely to be involved. Instead, some nonlinear mechanism capable of rectifying the sinusoidal field with a time constant within those for the frequency range where the effect occurs may exist in the preparations. However, why decreases of calcium efflux were found for sub-ELF fields and increases were found for sub-ELF-modulated 147-MHz RFR is not readily explainable. The authors speculated on possible mechanisms for the basic phenomenon, including triggering of cooperative interactions at

the cell membrane surface. In Bawin et al. (1978), a more complete discussion of possible mechanisms was presented. Also included therein were data on increases of calcium efflux from chick-brains exposed to 16-Hz-modulated 450-MHz RFR; these results indicated the existence of a power-density window in the range 0.1-1.0 mW/sq cm.

Regarding the statistical treatment of the numerical results, the validity of discarding extreme values a posteriori rather than because of foreknowledge that an experimental error may have occurred in any specific sample is questionable, and weakens the credibility of the results. It is noteworthy that since the opposite effect (decreases rather than increases in calcium efflux) was presumably not predicted before the results were obtained, use of the 2-tailed (rather than the 1-tailed) significance criterion was appropriate.

Sheppard et al. (1979) similarly prepared and exposed chick-brain halves to 450-MHz RFR sinusoidally modulated at 16 Hz only, this being the frequency for maximum effect in prior studies with 147-MHz RFR (Bawin et al., 1975). The exposures were for 20 min at 36 deg C and about 40% relative humidity to a TEM field within a tapered chamber fitted with RFR-absorbing material on the back and side walls. The incident average power densities were 0.05, 0.10, 1.0, 2.0, and 5.0 mW/sq cm. Following exposure, 0.2-ml aliquots of supernatant were assayed for Ca-45++ by liquid scintillation counting; the brains were dissolved overnight and also assayed for Ca-45++. Eight runs involving five each exposed and control half-brains per run were performed at each power density except 5 mW/sq cm, at which only six runs were done, for a total of 190 chick brains. Mean supernatant radioactivities of each exposure group were normalized to the mean values for the corresponding control groups, and the 2-tailed t-test was used. The normalized mean (m) and SE, number (N) of paired samples, and value of t for each RFR level are shown in Table 40, adapted from Table 1 of the paper, the asterisk indicating significance ($p<0.05$):

TABLE 40: CALCIUM EFFLUX FROM CHICK BRAINS

RFR LEVEL mW/sq cm	EXPOSED m +/- SE	CONTROL m +/- SE	N	t
0.05	0.937 +/- 0.025	1.0 +/- 0.030	40	1.615
0.10	1.080 +/- 0.026*	1.0 +/- 0.026	40	2.13
1.0	1.112 +/- 0.032*	1.0 +/- 0.026	40	2.68
2.0	1.035 +/- 0.030	1.0 +/- 0.023	40	0.339
5.0	1.022 +/- 0.030	1.0 +/- 0.034	30	0.484

The authors stated: "With attention to the important experimental steps (consistency in the pH and osmolarity of the physiological solution, and careful rinsing of the brains after incubation with the radioactive solution) it was possible to reduce the occurrence and magnitude of extreme values so that no data points were discarded. Significant results were found at the $P<0.05$ level, with statistical

significance estimated by the two-tailed t-test."

Tissue counts for dissolved brains showed that the proportion of Ca-45++ remaining in the tissue was greater than in the supernatant; the ratio of the normalized counts in tissue to the counts per ml in supernatant was 3.5:1. The difference between mean tissue counts for exposed and control brains was not significant.

The authors proposed a model for the interaction of weak electric fields with neuronal membranes, which describes amplification of weak signals by the cooperative behavior of glycoprotein-bound ions in the membrane under the influence of field enhancement by polarization of surrounding unbound ions. They suggested that field-triggered cooperative behavior of the bound ions could change the calcium binding and give rise to the effects found and stated: "Adey has suggested that the sub-ELF envelope impressed on the RF carrier is detected at the polyanionic surface due to a strong asymmetry in charge distribution with respect to that surface. The charge asymmetry at the borders of glycoprotein-dense regions may allow demodulation much as in the case of a semiconductor diode but further details of the mechanism and its coupling to the cooperative system have not been developed."

Allis and Fromme (1979) pointed out that calcium is also transported across biological membranes by energy-dependent processes, suggesting specifically that amplitude-modulated RFR may directly stimulate the membrane to transport calcium (or stimulate calcium-sequestering sites within the cell to release or bind calcium), thus altering the quantity of calcium ions transferred across the membrane. With this hypothesis, they performed experiments in which specially prepared membrane-bound enzyme systems were exposed to almost 100% amplitude-modulated 2.45-GHz RFR in a spectrophotometric apparatus that was equipped with a slotted-waveguide applicator, thus permitting measurement of enzyme activity during exposure (Allis et al., 1975).

Two enzyme systems were selected for study: sodium-potassium adenosine triphosphatase (ATPase) from the erythrocyte's plasma membrane, which transports sodium and potassium ions across the membrane as adenosine triphosphate (ATP) is hydrolyzed (and may be responsible for maintaining the sodium-potassium balance in the cell); cytochrome oxidase, which is contained in the inner membrane of mitochondria (and is the final enzyme in the electron-transport chain of oxidative phosphorylization). Both preparations were derived from the rat.

Exposure was started after initiating the specific reaction for each enzyme system, and the reaction and exposure were continued for 15 min, during which the reaction rate was measured spectrophotometrically at the appropriate wavelengths. Three RFR-exposure and three control assays were made per day, with each set performed first on alternate days. From heating and cooling curves, the SAR was 26 W/kg (Allis et al., 1977). The sinusoidal modulation frequencies used were 16, 30, 90, and 120 Hz.

The membrane preparations for the ATPase system were found to vary in enzyme activity per gram of total protein, so membranes from a single preparation were used on each day (presumably for one frequency), but more than one preparation was necessary to complete several runs at each frequency. For this reason, the activities of the samples exposed to RFR each day were averaged and compared with the mean activity of that day's control samples. Paired t-tests of the results showed that the differences in enzyme activities were nonsignificant ($p>0.1$) at any modulation frequency. An analysis of variance was also performed on the mean values of each day's results. A nested design was used because the daily variation in results was nested within the effect of modulation frequency. The effects of treatment vs control, variation of modulation frequency, and frequency-treatment interaction were all nonsignificant.

The reaction rate of the cytochrome-oxidase system proved to be too high to permit direct measurements of its specific activity. Therefore, this assay was run under conditions for which the apparent first-order rate constant could be measured. Use of statistical techniques similar to those for the ATPase system yielded no significant differences between RFR-exposed and control samples.

However, as Allis and Fromme (1979) pointed out, the results of this study were not definitive, because: the membranes were tested for two functions under highly artificial conditions, e.g., the resting electrical potential across the membrane was not maintained in the in-vitro preparations used; the exposure levels were much higher than the power-density window found in the previously cited research; and of the four modulation frequencies used, only 16 Hz was within the frequency window found for nerve-tissue effects.

Blackman et al. (1979) performed experiments toward reproducing the 147-MHz chick-brain results of Bawin et al. (1975). After decapitating each chick, its forebrain was removed and divided at the midline to provide an exposure-control pair. After four brain-tissue pairs were prepared, each tissue sample was weighed. Each specimen was then immersed in 1 ml of physiologic medium labeled with Ca-45++ and agitated for 30 min at 37 deg C. The radioactive solution was then aspirated and the tissues were rinsed as follows: Two ml of medium was added to each tube and then was poured off with the tissues into small plastic sieves. Each sample was rinsed successively in two 250-ml volumes of nonradioactive medium, to render it free of any loosely associated Ca-45++, and was placed in a clear plastic tube containing 1 ml of medium for exposure.

Samples were exposed to 147-MHz RFR for 20 min in a rectangular TEM cell (Crawford, 1974; Weil, 1978) that was enclosed in a foamed polystyrene chamber maintained at 37 +/- 0.2 deg C. The sample-containing tubes in Lucite racks were arranged symmetrically on each side of the center conductor of the TEM cell while similar racks were placed on shelves within the chamber alongside the cell in a region where the field strength was more than 30 dB lower than in the cell. Two series of exposures were done. In one series, the power density was held

constant at 0.75 mW/sq cm and the modulation frequencies were 0, 3, 9, 16, and 30 Hz. In the other series, the modulation frequency was held constant at 16 Hz and the power densities were 0 (sham), 0.5, 0.75, 1.0, 1.5, and 2.0 mW/sq cm.

Following RFR- or sham-exposure, 0.2-ml aliquots of bathing medium were assayed for radioactivity by liquid scintillation counting. The counts-per-min (CPM) value for each specimen was normalized to the weight of the specimen, and the difference, V, in normalized values between the exposed half-brain and its control was treated as the variable for statistical analysis. Preparation and exposure of four brain-tissue pairs were repeated nine times for each condition of frequency and power density, and a nested one-way analysis of variance was used for each series. For those values of the F statistic that were significant, a multiple-comparison procedure (sequential Newman-Keuls) was used to determine where significant differences existed between means.

The mean values of V for the constant-power-density series (0.75 mW/sq cm) and for sham-exposure were displayed in Fig. 2 of the paper as bar graphs with SEs. All mean values were positive (increases in calcium efflux); those for sham-exposure and 30 Hz were close to zero, which was well within their SEs; the values of (V-SE) for the other frequencies were all positive, but only the mean value of V for 16 Hz was labeled significant ($p<0.05$). The analysis of variance yielded a significant effect of frequency [$F(5,48)=3.32$, $p<0.02$]. The multiple-comparison procedure showed that V for 16 Hz was significantly higher than for sham-exposure or for 30 Hz, but that all the other values of V were nonsignificant ($p>0.05$), including the difference between the means for those exposed to the unmodulated RFR and those sham-exposed.

The mean values of V for the constant-modulation-frequency series (16 Hz) were similarly displayed in Fig. 3 of the paper. All mean values of V except for 0.75 mW/sq cm were close to zero. (Those for 0, 0.5, and 2.0 mW/sq cm were slightly positive and those for 1.0 and 1.5 mW/sq cm were slightly negative.) For 0.75 mW/sq cm, however, V was positive and labeled significant ($p<0.01$). Analysis of variance showed a significant power-density effect [$F(5,48)=5.77$, $p<0.001$]. The multiple-comparison procedure indicated that the mean V for 0.75 mW/sq cm was significantly higher ($p<0.01$) than the values for the other five power densities.

The authors stated: "Our results indicate that the modulation-frequency window in which calcium-ion flux is enhanced only occurs within a restricted range of power densities. Our initial attempts to reproduce the modulation-frequency window were hampered by the dramatic character of the power-density effect, of which we were initially unaware. These results indicate a maximal power-density effect at 0.75 mW/sq cm and no enhancement at levels plus or minus 0.25 mW/sq cm of this value. The narrow width of this window was not observed in the preliminary study in which intermediate values for enhanced efflux were found at 0.5 and 1.0 mW/sq cm."

They also noted: "In the experiments performed at 147 MHz, no differ-

ence could be detected in the measured values of incident and transmitted power [in the TEM cell]. This means that the rate of absorption of RF energy by the samples is low; i.e., less than the approximately 0.4 mW/g that can be resolved within the +/- 1% of full-scale uncertainty specified for our power meters. In measurements performed at a higher frequency of 500 MHz, where the ratio of sample size to wavelength is considerably greater than that existing at 147 MHz, an SAR of 1 mW/g was obtained in a 10 mW/sq cm field. Thus, at 500 MHz, an incident field of 0.75 mW/sq cm would be expected to produce an SAR of 0.075 mW/g, which doubtless represents an upper limit of the SAR in our experiments. This rate of energy deposition is too low to produce measurable heating by any readily available method (Allis et al., 1977; Blackman and Black, 1977; Kinn, 1977)."

The results of Blackman et al. (1979) appear to confirm the existence of the calcium-efflux phenomenon in excised chick brains, at least for 147-MHz RFR amplitude-modulated at 16 Hz. As noted by the authors, however, the power density window found is narrower than the windows found by Bawin and coworkers for modulated 450-MHz RFR (Sheppard et al., 1979) and sinusoidal sub-ELF fields (Bawin et al., 1976a,b).

Blackman et al. (1980a) extended this work with amplitude-modulated 147-MHz RFR, to determine whether the width of the power-density window depends on the number of brain samples exposed simultaneously in their system (a possible artifact) and whether the modulation frequency used affects the location or width of the power-density window. For this purpose, the experimental design was improved by obtaining, for each exposure condition, a companion set of results for sham-exposure under otherwise identical conditions.

Brain tissues were obtained from chicks 1 to 7 days old and processed as in the previous study. Lucite racks holding the tissue samples to be exposed were arranged symmetrically on each side of the center conductor of the TEM cell in the calculated uniform-field region and similar racks containing the control samples were placed on shelves outside the cell. Exposures were for 20 min to 147-MHz RFR sinusoidally modulated with 0, 9, or 16 Hz at power densities of 0.11, 0.55, 0.83, 1.1, 1.38, and 1.66 mW/sq cm. The authors noted that the 0.83-mW/sq-cm level represented a correction to the 0.75 mW/sq cm used in the previous study and was based on a more accurate calibration. Half of each chick brain was exposed to the RFR, and the other half, which was neither exposed nor sham-exposed, served as its control. Halves of other brain pairs were sham-exposed in the TEM cell, and the corresponding halves served as controls.

In one series of runs, four brain samples were treated concurrently per run in the TEM cell (with the corresponding controls outside the cell). In another series, six tubes containing equivalent amounts of unlabeled medium only (dummy loads) were placed in the Lucite racks together with four tubes containing brain samples (10 tubes total per run). In a third series, conducted to determine the influence of temperature only, Lucite racks holding four tubes containing brain halves were placed in water baths for 20 min at 32, 37, or 41 deg C

while the complementary halves were held for 20 min at 37 deg C.

The relative quantity of Ca-45 ions released by each tissue pair was defined as the ratio, Vt/Vc, of the CPMs for the treated and control samples. Time and replication effects, sought by analysis of variance for a partially nested design, were not found, so analysis of variance for a one-way design was done for each combination.

Statistically significant differences in values of Vt/Vc were found between RFR- and sham-exposed tissues for eight combinations of power density, modulation frequency, and number of tubes/run (brains only or brains plus dummy loads). One combination that yielded a significant difference at the $p<0.001$ level was for 4 tubes/run with 16 Hz at 0.83 mW/sq cm; the corresponding differences for 4 tubes/run with 16 Hz at 0.55 and 1.11 mW/sq cm were nonsignificant ($p>0.05$), indicating the existence of a narrow power-density window. These results were similar to those found in the previous study. For 10 tubes/run with 16 Hz at 0.83 mW/sq cm, the difference in mean values for RFR- and sham-exposed tissues was significant ($p<0.001$), but so were the differences for 0.55, 1.11, and 1.38 mW/sq cm ($0.01<p<0.05$), implying that the power-density window was broadened by the presence of the dummy loads. This effect was provisionally ascribed by the authors to greater interaction among samples that distorted the fields in the vicinity of the brain samples.

The difference for 10 tubes/run with 9 Hz at 0.83 mW/sq cm was also significant ($p<0.001$), as were those for 10 tubes/run with 9 Hz at 0.55 and 1.11 mW/sq cm ($0.01<p<0.05$), thus indicating that the modulation-frequency window was relatively broad. (A series for 9 Hz with 4 tubes per run was not done.) The authors noted that although the differences in Vt/Vc between the RFR- and sham-exposed samples for the remaining combinations of power density, modulation frequency, and number of tubes/run were nonsignificant, the values of Vt/Vc for the RFR-exposed samples were all inexplicably larger than for their corresponding sham-exposed samples.

For the exposures to unmodulated RFR at 0.83 mW/sq cm (10 tubes/run), the differences in Vt/Vc between RFR- and sham-exposed samples were nonsignificant ($p>0.05$). For the tissues held at other temperatures than 37 deg C, the efflux was 9% lower at 32 deg C and 15% higher at 41 deg C than at 37 deg C. However, the authors excluded the possibility of RFR-induced temperature increases as a factor in the positive results above because the maximum SAR was undoubtedly less than 0.075 W/kg.

Blackman et al. (1980b) also conducted experiments with 16-Hz-modulated 50-MHz RFR in a TEM cell, to determine whether changes in carrier frequency altered the range of power densities effective in producing statistically significant increases in calcium efflux. The exposure conditions and protocol were similar to those previously used by these investigators. Ten tubes were treated concurrently per run (4 brain samples and 6 dummy loads), to broaden the power-density window as for 147 Mhz. The results are given in Table 41 (Table 2 of the paper):

TABLE 41: MEAN CALCIUM-EFFLUX RATIOS (Vt/Vc) VERSUS POWER DENSITY (PD)

PD		SHAM-EXPOSURE		RFR-EXPOSURE		
(mW/sq cm)	n	Vt/Vc	SE	Vt/Vc	SE	P
0.37	32	1.063	0.044	1.053	0.036	0.863
0.72	47	1.148	0.047	1.089	0.032	0.301
1.44	32	1.014	0.035	1.159	0.044	0.013
1.67	64	1.026	0.023	1.182	0.034	<0.001
2.17	36	1.119	0.036	1.138	0.040	0.730
3.64	64	1.054	0.029	1.165	0.033	0.014
4.32	28	1.058	0.050	1.079	0.051	0.778

As seen above, the maximum value of Vt/Vc (1.182) occurred at 1.67 mW/sq cm and was significantly higher ($p<0.001$) than the corresponding Vt/Vc for sham-exposure (1.026). Significant increases in calcium efflux (about 16%) were also obtained at 1.44 and 3.64 mW/sq cm ($p=0.013$ and 0.014). Exposure at the intermediate level 2.17 mW/sq cm yielded 1.138, only marginally higher than 1.119 for sham-exposure, a nonsignificant difference ($p=0.738$). The value of Vt/Vc for RFR-exposure at 0.72 mW/sq cm, though greater than unity (1.089), was nonsignificantly lower ($p=0.301$) than for sham-exposure (1.148). For the remaining power densities, the differences, some of which were negative (decreases in calcium efflux), were also nonsignificant ($p>0.05$).

The authors stated: "Instead of a power-density window centered at 0.83 mW/sq cm [for 147-MHz], the results at 50 MHz indicated that there are at least two ranges of power densities that can induce enhanced calcium-ion efflux; one range spans 1.44 to 1.67 mW/sq cm and is bounded by 'no-enhancement' results at 0.72 and 2.17 mW/sq cm; the other range includes 3.64 mW/sq cm and is bounded by 2.17 and 4.32 mW/sq cm." This argument appears specious, however, in view of the two relatively large values of Vt/Vc for sham-exposure noted above (possibly indicative of the presence of uncontrolled non-RFR factors). If those values had been as close to unity as the other sham-exposure values, perhaps the increase in calcium efflux for exposure at 2.17 mW/sq cm also would have been significant, thus yielding a single relatively broad power-density window centered at 1.67 mW/sq cm.

Joines and Blackman (1980) modeled the chick-brain hemisphere bathed in buffer solution as a sphere within the field of uniform incident RFR, in an endeavor to account for the dependence of calcium-efflux increase on carrier frequency in the results for 16-Hz amplitude-modulated RFR at 450 MHz by Bawin et al. (1978) and Sheppard et al. (1979) and at 147 and 50 MHz by Blackman et al. (1980a,b). This theoretical analysis showed that the average electric-field intensity within such a spherical model can be made the same at the three carrier frequencies by adjusting the incident power density to compensate for the frequency dependence of the complex permittivity and internal wavelength of the sample.

Examination of the experimental data on this basis showed that all of

the positive and negative results obtained at these three frequencies, when compared by average electric-field intensity within the sample, were in basic agreement and that no result, positive or negative, was contradicted by a corresponding experimental result at a different carrier frequency. However, the model did not take into account the amplitude-modulation frequencies per se. Because not all modulation frequencies are effective, comparisons among average electric-field intensities within the samples cannot be extended to other modulation frequencies.

Athey (1981) challenged the analysis above. He pointed out that there were uncertainties in the values of the electrical properties (complex permittivity) of brain material, that actual samples were predominantly saline and therefore different from the brain material assumed in the model, and that the simple homgeneous spherical geometry assumed may have been too unrealistic, all of which led to uncertainties that were too large to permit meaningful conclusions. He recommended that further work be based on experimental dosimetry to diminish such uncertainties.

In rebuttal, Joines and Blackman (1981) reported results on an improved model, that of a layered sphere. They performed calculations with the new model for various worst-case situations, which showed that the relationship of incident power density to internal field is relatively insensitive to small uncertainties in permittivity. A key aspect of the calcium-efflux effect, however, its dependence on modulation frequency (and its absence with unmodulated RFR), remained unanswered. Also among the observations not yet accounted for are why calcium efflux increases for modulated 147- and 450-MHz RFR and decreases for sinusoidal sub-ELF fields, and why the phenomenon only occurs within an amplitude or power-density window.

In two recent studies, Blackman et al. (1985a,b) reviewed prior work by Blackman and coworkers on the effects of fields at frequencies in the ELF range (defined by them for convenience as 1-300 Hz) on calcium efflux from chick brains in vitro. Among the findings were windows of frequency and field intensity within which calcium efflux was enhanced, and outside of which alterations of calcium efflux were nonsignificant. However, Blackman et al. (1985b) noted that their calcium-efflux changes (enhancements) were opposite in direction to the reductions found by Bawin and Adey (1976b) at frequencies in the same range.

A major difference between the two studies was the use, by Bawin and Adey (1976b), of AC electric fields only, whereas Blackman et al. (1985a) used AC fields having a magnetic component as well as an electric component. Therefore, Blackman et al. (1985b) hypothesized that the AC magnetic component could significantly influence changes in calcium efflux and that a DC magnetic field such as the local geomagnetic field (LGF) might also have a role.

The exposure apparatus used by Blackman et al. (1985b) consisted of a transmission line terminated with a 50-ohm load, a function generator to provide an AC electromagnetic field, and instrumentation (Bell Model

SAB4-1808 probe, Bell Model 640 gaussmeter, and Hewlett-Packard Model 3582A spectrum analyzer) to measure the frequency and intensities of the field components. In consonance with the authors' usage, values cited below of AC electric field are peak-to-peak and those of AC magnetic field are rms. To obtain an electric field only, the 50-ohm load was removed. Specifically, with the load present and the field components adjusted to 40 V/m and 59.5 nanoteslas (nT), removal of the load reduced the magnetic component to a residual level of about 15 picoteslas (pT).

For exposure of samples to either type of AC field under altered LGF conditions, a pair of 18-inch-radius Helmholtz coils spaced 18 inches apart was oriented to produce a DC magnetic field parallel to the LGF (which was inclined at 85 deg), and the transmission line was placed within the coils. The gaussmeter was used to set the desired level of DC field within the transmission line in the absence of samples, and introduction of samples did not change the level. The authors assumed that sample magnetization was negligible, so the magnetic-field levels within and outside tissue were taken to be the same.

Sample preparation was similar to that used in previous studies. Also, in an endeavor to keep the procedures invariant, four tubes containing chick-brain-halves were treated concurrently with six tubes containing equivalent dummy loads (10 tubes total) as in Blackman et al. (1980b). Field exposures (including sham-exposures) were for 20 min at 37 deg C, with the corresponding half-brains held at the same temperature within a water bath. The following series of exposures were performed and the post-treatment assay for Ca-45++ in each field- or sham-exposed half-brain was normalized to the value for its control half-brain:

(1) Ten tubes were exposed to a 16-Hz electric field alone at 6, 10, or 40 V/m (peak-to-peak in air) and 10 other tubes were sham-exposed. The exposure at each level and the corresponding sham-exposure comprised a set. Exposure sets for 6 and 40 V/m were done eight times and sets for 10 V/m seven times. In addition, eight sets for 40 V/m were repeated eight months later.

(2) To compare effects of an AC electric field alone with those of an AC electromagnetic field, nine sets, each comprised of an exposure to a 16-Hz electric field at 40 V/m and an exposure to a 16-Hz electromagnetic field at 40 V/m, 59.5 nT, were performed (sham-exposures omitted).

(3) A similar design was used for determining the possible influence of the LGF (given as 38 microteslas, presumably at the experimental site). Eight sets were performed, each consisting of two exposures to a 15-Hz, 40-V/m, 59.5-nT field, one with the normal LGF present and the other with the LGF reduced to 19 microteslas by the Helmholtz coils. Also, the eight sets were repeated one week later.

(4) Sets of exposures to a 30-Hz, 40-V/m, 59.5-nT field, but for several integral and fractional multiples of the LGF, including negative values representing field reversal. In each set, comparison was made of the

results for the altered LGF with those of the normal LGF, and some sets were replicated one week later.

The normalized data collected for each series above were subjected to a two-way analysis of variance for a replication main effect and for a replication-by-exposure-group interaction. Neither replication effect was found to be significant, so a one-way analysis of variance was used to compare the combined normalized results for the different conditions in each series.

The results for series (1) yielded nonsignificant differences ($p>0.2$) between field- and sham-exposed sets for any level or for the combined initial and repeated 40-V/m set. By contrast, Blackman and coworkers had found that 16-Hz electromagnetic fields at 6 V/m, 8.9 nT and at 40 V/m, 59.5 nT enhanced calcium efflux significantly ($p<0.05$), whereas Bawin and Adey (1976b) had reported significant reduction ($p<0.05$) for a 16-Hz electric field at 10 V/m.

Direct comparison of the results of series (2) for an AC electric field only vs an AC electromagnetic field showed that calcium efflux for the latter was significantly larger than for the former ($p=0.011$). The authors stated: "The data demonstrate that the AC magnetic component [59.5 nT] must be present in the 6- and 40-V/m fields to induce an enhanced efflux."

The results for series (3) and (4) are shown in Table 42, adapted from Table 3 of the paper:

TABLE 42: MEAN CALCIUM-EFFLUX RATIOS
FOR VARIOUS MULTIPLES OF THE NORMAL LGF

Net LGF	N	Mean Efflux Ratio	SE	P
For 15 Hz:				
1.0	32	1.199	0.054	
0.5	32	1.045	0.049	0.043*
1.0	32	1.236	0.046	
0.5	32	0.997	0.042	<0.001*
For 30 Hz:				
1.0	32	1.040	0.038	
2.0	32	1.309	0.078	0.003*
1.0	32	1.048	0.037	
1.33	32	1.058	0.049	0.870
1.0	40	1.020	0.038	
0.67	40	1.248	0.054	<0.001*
1.0	32	0.981	0.042	
0.67	28	1.208	0.033	<0.001*
1.0	32	1.041	0.032	
-0.67	32	1.143	0.048	0.085
1.0	32	1.065	0.040	
-0.67	32	1.323	0.068	0.002*
1.0	32	1.028	0.035	
-2.0	32	1.300	0.089	0.006*
1.0	32	1.002	0.049	
-2.185	32	1.076	0.036	0.226

*Significantly different at the indicated level from the mean for 1.0

The authors stated: "The results demonstrate that a normally effective 15-Hz signal is ineffective when the net density of the LGF is reduced to half the ambient, and an ineffective 30-Hz signal is effective when the net density is changed to .67x or 2.0x ambient but not when it is increased to 1.33x or to 2.185x ambient...increased efflux resulted at LGFs +0.67x ambient and of +/- 2.0x ambient when compared to the lack of enhancement for ambient conditions...A slight increase in the density of the LGF from -2.0x to -2.185x the ambient was sufficient to remove the enhancement conditions."

The results above with changes in the LGF appear to indicate that the DC geomagnetic field is fundamentally involved in alterations of calcium

efflux, but as is evident in the quotation above, the relation between the magnitudes of the LGF changes and the presence or absence of effect, if any, is obscure. Also not clear is the absence of effect in series (1), in which the AC magnetic field was absent but the LGF was present, since the magnitude of the normal LGF (38 microteslas) is about 600-fold larger than the AC magnetic component (59.5 nT rms) used in all series except (1). It seems plausible that the latter would have been swamped by the former. Moreover, the negative findings for series (1) do not gainsay the positive findings of Bawin and Adey (1976b) in the absence of an AC magnetic component.

Dutta et al. (1984) exposed monolayer cultures of human neuroblastoma cells in T-flasks to 16-Hz-amplitude-modulated (80%) 915-MHz RFR in a TEM exposure chamber at SARs ranging from 0.01 to 5 W/kg, and studied the effects of such exposure on calcium efflux from the cells. The SARs were determined by measurements of forward, reflected, and transmitted powers with: the TEM cell empty, empty flasks in the cell, and samples in flasks within the cell (Dutta et al., 1982).

Human neuroblastoma cells were grown to confluent monolayers within T-flasks (25 sq cm of growth surface), each containing 5 ml of minimum essential medium (MEM) supplemented with other necessary elements. The monolayer in each flask was then incubated in 5 ml of MEM containing 2 microliters of Ca-45++ (specific activity 5 Ci/l) for 1 hr to establish steady-state calcium-ion equilibrium within the cells. This incubation period was selected on the basis of preliminary experiments showing (in Fig. 2 of the paper) that Ca-45++ uptake rises linearly during the first hour to a plateau, with no difference in uptake between the first and second hours.) The labeled cells were washed with nonradioactive medium three times without disturbing the monolayer, to remove excess Ca-45++. After washing, 6 ml of MEM was added to the culture and mixed, and 1 ml was removed for determining the initial radioactivity (400-600 cpm/ml).

One flask was placed on each side of the center plane of the TEM cell within an incubator at 37 deg C and exposed for 30 min at 0.01, 0.05, 0.075, 0.1, 0.5, 0.75, 1.0, 1.5, 2, or 5 W/kg. Two control flasks for each exposure were kept concurrently at 37 deg C within the incubator, but outside the TEM cell. Sham-exposures were also conducted, but no significant differences in calcium efflux were found between control and sham-exposed cultures. At exposure end, a 1-ml sample of the medium was withdrawn from each flask. For calcium-efflux assay, the 1-ml pre- and post-exposure samples were centrifuged at 500g for 1 min to remove any cells or large debris, and 0.5 ml of each supernatant was added to 4 ml of scintillation cocktail and counted. A series of exposures was also conducted at 0.05 W/kg with modulation frequencies between 3 and 30 Hz.

RFR-induced changes of calcium influx into cells were also investigated. Monolayers were grown in medium that contained Ca-45++ instead of normal medium, and immediately exposed for 30 min to 16-Hz-modulated RFR at 0.05 or 0.1 W/kg, with similarly grown controls outside the TEM cell. After such treatment, the cells were washed three times as before and suspended in 0.5 ml of 0.25 M ethylenediaminetetracetic acid (EDTA) to

detach the cells from the flask without affecting cell integrity. The cell suspensions were then assayed for radioactivity.

The results for the series of exposures at 0.05 W/kg with various modulation frequencies were graphed (in Fig. 3 of the paper) as the percentage increases of calcium efflux vs modulation frequency. This graph showed a sharp maximum of about 50% at 16 Hz, compared with about 35% at 14 Hz and 28% at 18 Hz, with much lower percentages above and below these frequencies.

The calcium-efflux results with 16-Hz modulated RFR are shown in Table 43, adapted from Table 1 of the paper. The differences between treated and control samples were assessed for significance by the two-tailed Student t-test.

TABLE 43: EFFECTS OF 16-HZ MODULATION ON CALCIUM EFFLUX

SAR (W/kg)	N(a)	Control (cpm/ml) Mean Efflux +/- SE	Exposed (cpm/ml) Mean Efflux +/- SE	% Increase
0.00(b)	6	691 +/- 25	689 +/- 20	-0.3
0.01	4	703 +/- 11	704 +/- 24	0.1
0.05	6	694 +/- 33	1074 +/- 76**	54.7
0.075	6	627 +/- 14	695 +/- 43	10.8
0.10	4	596 +/- 23	650 +/- 37	9.1
0.50	4	653 +/- 22	619 +/- 14	-5.2
0.75	4	653 +/- 21	729 +/- 16*	11.6
1.0	8	684 +/- 16	866 +/- 28**	16.6
1.5	4	606 +/- 23	621 +/- 26	2.5
2.0	6	630 +/- 33	733 +/- 36	16.3
5.0	6	665 +/- 36	641 +/- 14	-3.6

(a) N = number of flasks; (b) sham-exposure; *p<0.05; **p<0.001

As seen above, significant increases in calcium efflux were obtained at 0.05 and 1.0 W/kg (both p<0.001) and at 0.75 W/kg (p<0.05) but not for intermediate SARs or those outside the range 0.05-1.0 W/kg. For comparison, results for exposure to unmodulated (CW) 915-MHz RFR at 0.05 and 1.0 W/kg are shown in Table 44 (Table 2 of the paper):

TABLE 44: EFFECTS OF UNMODULATED (CW) RFR ON CALCIUM EFFLUX

SAR (W/kg)	N	Control (cpm/ml) Mean Efflux +/- SE	Exposed (cpm/ml) Mean Efflux +/- SE	% Increase
0.05	6	633 +/- 16	655 +/- 19	3.5
1.0	4	675 +/- 20	833 +/- 38	19.8 (p<0.01)

Regarding the differences among the control values above, the authors stated: "The variations in calcium ion efflux in the control cultures

shown in Tables 1 and 2 [43 and 44] could be due to the minor variation in cell numbers and uptake of Ca-45++ by the cells. However, since the exposed and control cultures used for experiments at any given SAR come from the same parental stock, there should not be a consistent bias."

The percentage reduction of Ca-45++ uptake by cells exposed to the 16-Hz-modulated RFR at 0.05 and 0.1 W/kg are given in Table 45 (Table 3 of the paper):

TABLE 45: EFFECTS OF 16-HZ MODULATED RFR ON CALCIUM UPTAKE

SAR (W/kg)	N	Control (cpm/ml) Mean Uptake +/- SE	Exposed (cpm/ml) Mean Uptake +/- SE	% Reduction
0.05	4	5768 +/- 048	5382 +/- 027	7.0 ($p<0.01$)
0.10	4	4666 +/- 139	4875 +/- 172	---

In summary, the authors stated: "Human neuroblastoma cells in culture show similar patterns of calcium ion efflux at 16 Hz AM as has been found in freshly isolated brain tissues (Bawin et al, 1975). Studies reported here indicate the presence of a narrow range of absorbed powers at which a significant increase in the efflux of calcium ions occurs from human neuroblastoma cells in culture. Similar intensity regions for radiofrequency fields were first noted in freshly removed chicken brain by Blackman and his colleagues...In the present studies, although we have actually measured SARs of samples (medium + cells), the energy absorbed by the neuroblastoma cells alone is not known. Thus it is difficult to compare our results with the effective radiofrequency power densities obtained for chicken brains."

They also noted: "The present study reveals that an unmodulated [915-MHz] carrier wave can induce calcium ion efflux at an SAR of 1 mW/g." (This finding is contrary to those of the chick-brain studies).

Lastly, they stated: "The uptake studies suggest that specific microwave intensities known to cause enhanced net efflux of calcium ions from prelabeled cells can also reduce the net uptake of calcium ions when the cells are exposed during the labeling period. Because the exposure time during the uptake studies [0.5 hr] was not long enough for equilibrium to be reached [at least 1 hr], there can be no comparison between the uptake and efflux results."

Shelton and Merritt (1981) investigated whether RFR pulses at repetition rates comparable to the modulation frequencies used in the chick-brain studies would elicit alterations in calcium efflux from the rat brain. After rats were euthanized by cervical dislocation, their brains were excised rapidly, the olfactory bulbs were removed, a vertical cut was made to extract about one-third of the cerebrum, and the pia mater was removed. In each experiment, three pairs of cerebral-hemisphere samples were processed together for RFR- and sham-exposure. Each tissue sample (about 100 mg) was immersed in 4 ml of medium containing 2 micro-

curies of Ca-45++ within a 50-ml glass beaker, in which it was incubated for 20 min at 37 deg C. The bicarbonate concentration in the medium was 26 mM (that of mammalian cerebrospinal fluid instead of 2.4 mM in the chick-brain studies).

Following incubation, samples were washed once with 1-ml portions of medium that was free of Ca-45++, and were transferred to clean 50-ml beakers containing 2-ml aliquots of the radioactivity-free medium for RFR- or sham-exposure. Because the Ca-45++ concentration could be affected by the extent of tissue washing, the samples in one experiment were washed with 1-ml portions of radioactivity-free medium five times instead of once.

Six beakers containing cerebral samples thus treated were placed in two parallel rows of three each below, and in the far field of, a standard-gain horn within an anechoic chamber. The exposures in four experiments were for 20 min to 20-ms pulses of 1-GHz RFR, 16 pps (0.32 duty factor), a repetition rate analogous to the 16-Hz amplitude modulation used in the chick-brain experiments; the average power densities were 0.5, 1.0, 2.0, or 15 mW/sq cm, selected to search for the reported power-density window. In two other experiments, samples were exposed for 20 min to 10-ms pulses, 32 pps pulses (same duty factor), at 1.0 or 2.0 mW/sq cm. Sham-exposures were conducted in similar fashion for each experiment. Four groups each of RFR-exposed and sham-exposed samples comprised the population for each experiment.

In a seventh experiment, samples washed five times instead of once were exposed to 20-ms pulses, 16 pps, at 1.0 mW/sq cm (or sham-exposed) as in the second experiment. In still another experiment (with samples washed only once), the exposure parameters used were the same as in the second experiment again, but the exposure was interrupted for about 1 min each after 4, 8, and 12 min of exposure, and 0.5-ml aliquots of incubation medium were taken and assayed for possible time-dependent effects and replaced with fresh medium.

On completion of exposure, a 0.5-ml aliquot of each incubation medium was transferred to a counting vial. The tissue samples were washed once with 1-ml portions of medium free of Ca-45++ and also placed in counting vials, to which 2 ml of Soluene was added for overnight digestion at 37 deg C. Dimilume was added to all vials, and the radioactivities of the media and tissue samples were assayed by liquid scintillation counting.

The authors defined "efflux value" as the ratio (in percent) of the CPM of the medium to the sum of the CPMs in tissue and medium, a measure of efflux that differed from that used by other investigators, and the mean values (and SDs) were compared by Student's t-test. The results for cerebral tissue from 143 rats used in the first six experiments showed statistically nonsignificant ($p>0.05$) differences between any of the mean Ca-45++ effluxes when RFR-exposed samples were compared with their corresponding sham-exposed control samples. The mean efflux values for RFR- and sham-exposure in the seventh experiment (24 rats, five washings instead of one) also did not differ significantly from one

another, but both means were higher than those obtained in the first six experiments. The results of the time-dependence experiment (presumably 24 rats also) showed successive rises in efflux at the three epochs, but again the differences in means for RFR- and sham-exposed samples at corresponding times were nonsignificant.

Thus, the findings of Shelton and Merritt (1981) were negative, but, as pointed out by the authors, no direct comparisons can be made between their results and those of the investigators on chick brains discussed above because in addition to the difference in species, the samples were actually exposed (with a duty factor of 0.32) for only a third of the 20-min period (at correspondingly higher peak levels), and because the spectral distribution of energy for the 16-pps repetition rate differed markedly from that in the sidebands for 16-Hz amplitude-modulated RFR.

Merritt et al. (1982) performed experiments in vivo as well as in vitro on possible pulsed-RFR-induced alterations of calcium efflux from the rat brain. For both types of experiment, brain tissue was loaded with Ca-45++ by injection directly into the right lateral ventricle of ether-anesthetized male Sprague-Dawley rats (175-225 g).

In the in-vitro experiments, cervical dislocation was used to euthanize the rats after intraventricular injection of Ca-45++. Six brain-tissue samples excised as in the previous study were exposed concurrently for 20 min to 20-ms pulses, 16 pps, of 1-GHz RFR at 1 or 10 mW/sq cm (SAR 0.29 or 2.9 W/kg) or of 2.45-GHz RFR at 1 mW/sq cm (SAR 0.3 W/kg), with a like number of samples sham-exposed as controls. The incident power densities at the sample sites were measured with a Narda Microwave Corp. Model 8316B RF monitor and 8323 probe, but the method for measuring the SARs of the samples was not described.

Although the radioactivities of the incubation media and digested tissue samples were assayed by liquid scintillation counting, results were not given in terms of the efflux values as defined in Shelton and Merritt (1981); instead, the mean disintegrations per min per gram of tissue (DPM/g) and SDs were presented. By 2-tailed t-test, the difference in mean DPM/g values between the RFR- and sham-exposed samples was not statistically significant for any of the three exposure conditions.

For the whole-animal exposures, two hours after the rats were injected intraventricularly with Ca-45++, each rat was gently squeezed between two Styrofoam sides of a Plexiglass holder to maintain its body axis constant during exposure, and groups of 12 rats each were exposed for 20 min to 2.06-GHz RFR with long axes parallel to the E-field. One group each was exposed to CW at 0.5, 1.0, 5.0, or 10.0 mW/sq cm and one group each to 10-ms pulses at 8, 16, or 32 pps and average power density of 0.5, 1.0, 5.0, or 10.0 mW/sq cm (16 groups total). For controls, a 17th group was sham-exposed. Each rat was assigned randomly to an exposure condition, and exposure conditions were presented randomly to eliminate time-of-day effects. The normalized SAR, measured in muscle-equivalent rat models by calorimetry (Allen and Hurt, 1979), was 0.24 W/kg per

mW/sq cm or 0.12, 0.24, 1.2, and 2.4 W/kg for the four power densities.

After exposure, the rats were euthanized by cervical dislocation and the brains were quickly removed, rinsed in physiologic medium, blotted dry, weighed, and solubilized in Soluene. An aliquot of solubilized tissue of each rat was transferred to a counting vial containing Dimilume and assayed for 45-Ca++ by liquid scintillation counting. Statistical tests performed on the 17 treatment combinations (4x4 RFR-exposures, 1 sham-exposure) showed that difference between the sham group and the combined RFR groups and the differences between the sham group and the individual RFR groups were statistically nonsignificant.

A control series of experiments was conducted on 12 rats to obtain baseline Ca-45++ levels. These rats were treated in the same manner as the sham-exposed rats, i.e., they were injected intraventricularly with Ca-45++ and allowed to stabilize for 2 hr. However, their brains were assayed immediately after the 2-hr period to ascertain the amount of Ca-45++ at the beginning of the 20-min period used for the sham- and RFR-exposed rats. This experiment yielded a mean concentration of 0.944 +/- 0.033 (SD) ng-atoms/g of brain tissue, whereas for the 12 sham-exposed rats, the mean value at the end of sham-exposure was 0.659 +/- 0.156 ng-atoms/g, indicating that there was a mean net efflux of 0.285 ng-atoms/g from the brain during the 20-min period.

This paper, like the previous one, described an attempt to determine whether changes in calcium efflux reported to be induced in chick brains by in-vitro exposure to amplitude-modulated RFR might also be seen in rats from in-vitro or in-vivo exposure to pulse-modulated waveforms. No RFR-induced calcium-efflux changes were found. However, in addition to the previously noted differences in species, carrier frequency, and waveform, there were others:

1) Loading of the brain with Ca-45++ was done by injection into the right ventricle of the brain of the intact animal, whereas external bathing media containing Ca-45++ were used in the other studies. The dynamics of regional uptake of Ca-45++ by this intraventricular method were not described, but measurements of calcium diffusion in the other studies indicated that their reported RFR-induced changes were probably obtained from the outer mm or so of cortical tissue. Not reported was whether the intraventricular technique loaded cortical tissue; indeed, it is not clear whether this technique may have resulted in passage of Ca-45++ from the cerebrospinal fluid directly into the bloodstream in addition to the assumed perfusion from cerebrospinal fluid into brain tissue. No measurements were given of Ca-45++ levels in the blood.

2) Also not stated was whether only the right cerebral hemisphere or both hemispheres were used to provide tissue samples for the in-vitro exposures. Injection only into the right hemisphere might have provided asymmetrical loading. For the in-vivo exposures, apparently the whole brain was solubilized. It is unclear what the effect of any Ca-45++ still remaining in the ventricular fluid might have had on the liquid-scintillation-counting results. Additional characterization of the

intraventricular technique, originally developed for injecting tritiated norepinephrine into the lateral ventricle of the rat, was required for the present application.

3) As in the other in-vitro studies, great variability was found in the liquid-scintillation-counting results. In those other studies, the technique of normalizing the results of an RFR-exposed half-brain to the results of a matched, sham-exposed half-brain was used to reduce the overall variability. The Ca-45++ brain-loading technique used in the present study did not permit such normalization.

4) In other studies (both in vivo and in vitro), alterations in calcium efflux have been detected as alterations in the concentration of Ca-45++ in the incubating medium, but not in solubilized brain tissue. In the in-vitro part of the present study, measurements were made on samples of bathing medium as well as for solubilized brain case, but only results for the latter were given. However, the control series of experiments in vivo did show that the Ca-45++ concentration in whole brain decreased by about 30% during the 20-min exposure period. Under the experimental conditions described, such a decrease could have occurred by uptake into the bloodstream and distribution to the rest of the body. The presence of Ca-45++ in the blood could have yielded erroneous readings in whole-brain liquid-scintillation counts, a possibility that could be studied by perfusion of the animals with saline following euthanasia.

Adey et al. (1982) presented results of a study of Ca-45++ efflux in vivo from the cortex of the paralyzed but awake cat. A 12-mm-diameter trephine hole centered over the right suprasylvian cortex was drilled under ether anesthesia. The dura mater was carefully removed and a plastic cylindrical well was fitted in the aperture so as to make gentle contact with the surface of the pia. Nonradioactive physiologic medium was added to the well and all skin incisions and pressure points were infiltrated with local anesthetic. Use of ether was then discontinued, the cat was paralyzed with gallamine triethiodide IV, and artificial respiration was maintained with a tracheotomy. The end-tidal level of CO2, a measure of the CO2 level in the blood, was monitored and normally maintained at 4%, but was changed during episodes of hypoventilation and hyperventilation imposed to alter the state of arousal.

During recovery from ether anesthesia, the fluid level in the well was replaced at 10-min intervals for 30 min, to ensure that the fluid was clear. Incubation was then begun with 1.0 ml of medium that contained 20 microcuries of Ca-45++, and was continued for 90 min, at the end of which the fluid was replaced with nonradioactive medium. At 10-min intervals throughout the remainder of the experiment, the fluid was exchanged completely with fresh medium by pipetting, and 0.2-ml aliquots of each solution removed were diluted with Dimilume and assayed for Ca-45++. All samples were counted twice, once during the experiment and again to a stated accuracy of 1% within 24 hr.

Twenty-three female cats (2.8-3.6 kg) were used. Starting at different times following completion of incubation of the cortex with

Ca-45++, the cats were individually sham-exposed or exposed for 60 min to 450-MHz RFR 85% amplitude-modulated at 16 Hz, and intervals ranging from 80 to 120 min were tested for possible differences in efflux patterns. Exposures were done with a horn about seven wavelengths long within an anechoic chamber maintained at 28 deg C and 30-40% relative humidity. Each cat was placed in a plastic stereotaxic headholder, with body axis at right angles to the incident field and with the right cerebral cortex nearest the RFR source. The power density was 3.0 mW/sq cm, for which the electric field in the interhemispheric fissure was found by Adey et al. (1981) to be 33 V/m, which corresponded to an SAR of 0.29 W/kg.

Description of the data-analysis methods used was rather obscure. The authors indicated that the relative Ca-45++ efflux data taken at 10-min intervals in the absence of RFR could be fitted by a time-dependence equation involving the sum of two exponential terms (but not clear was how the actual radioactivity data were normalized to obtain relative Ca-45++ effluxes). Accordingly, they log-transformed such data and used linear regression to obtain an idealized curve of relative efflux vs time. Though not displayed, this idealized curve was said to consist of two linear branches, one of large negative slope indicating that the rate of decrease in relative efflux during approximately the first hour of successive 10-min measurements is rapid, and the other of smaller negative slope showing that the rate of relative efflux decrease is less rapid during the remainder of the measurement period.

The authors then quantified the results for RFR-exposed cats in terms of the means of the relative squared deviations of experimental data from the idealized curve at the sampling points, and similarly with the results for sham-exposed cats. By this analysis, the total variance for the preexposure periods was found to be the same for data from the RFR- and sham-exposed animals, but the total variance in the data from the RFR-exposed cats for the exposure- and post-exposure period was higher than for the sham-exposed cats. A 1-tailed binomial probability test was used to show that this exposure- and post-exposure increase in variance was significant ($p<0.05$), i.e., that the results for the RFR- and sham-exposed cats were from statistically different populations. Experiments with imposed hypoventilation and hyperventilation showed that the effect was not a consequence of alteration of end-tidal CO2 levels, i.e., not secondary to raised cerebral CO2 levels.

Next, they paired experimental curves of relative Ca-45++ efflux vs time from RFR- and sham-exposed cats. (The pairing criteria used were rather involved, but were designed to ensure the best matching of the available data.) The data for a representative pair of cats, for which RFR- and sham-exposure were initiated 90 min into the measurement period, were exhibited in Fig. 1 of the paper. By eye, the average slopes of the two curves were approximately the same up to about the first 60 min of the measurement period (corresponding to the period of rapid decrease noted above). Beyond this interval (during and after RFR- or sham-exposure), both slopes were smaller (corresponding to the lower rate of decrease above), but the average slope for the RFR-exposed

cat was less negative than for the sham-exposed cat and exhibited cyclic variations ("waves of increased Ca-45++ efflux") having a periodicity of about 25 min.

No experimental data for RFR- and sham-exposed animals were presented (other than mention of their use in the curve-fitting method as noted above) or were directly compared for significant differences, and as noted previously, no information on how the radioactivity data were normalized was given. Absence of such data seemed to imply that the important difference between the calcium efflux curves for the RFR- and sham-exposed cats was in the oscillations about the idealized straight-line fit to the data, and not between values themselves at corresponding measurement times or their means. Only amplitude modulation at 16 Hz was used in this study. Whether CW or other modulation frequencies would also be effective in causing the Ca-45++ efflux oscillations noted above is unknown.

In overall summary, there is a large volume of work by Bawin, Adey, and coworkers, and by Blackman and coworkers on changes of calcium efflux from chick brain resulting from in-vitro exposure to various regimens of electromagnetic fields at specific frequencies in the sub-ELF range and at 50-, 147- and 450-MHz RFR carriers sinusoidally amplitude-modulated at specific sub-ELF frequencies. Only a few studies involving in-vivo exposure were performed, notably those of Adey et al. (1982) with cats and of Merritt et al. (1982) with rats. The findings of some of the studies are corroborative, those of others appear to be contradictory, and those of still others negative (no effect). Noteworthy was the study by Dutta et al. (1984), which yielded a significant increase of calcium efflux from human neuroblastoma cells from in-vitro exposure to unmodulated 915-MHz RFR (as well as for 16-Hz modulated RFR at specific SARs). Thus, the occurrence of RFR-induced calcium efflux changes may depend on a complex function of incident power density and modulation frequency.

Calcium is known to play a major role in the regulation of not only secretion of neurotransmitters by nerve cells, but also of proteins by endocrine and exocrine glandular cells (Schramm, 1967). Myers and Ross (1981) performed a comprehensive and detailed critical analysis of the studies (to that date) on the RFR-induced calcium-efflux phenomenon, in which they raised some doubts about certain aspects of the methods used, statistical treatments of the data, and interpretations of the results. Disageement with their conclusions has been expressed by some of the researchers who studied the effect experimentally, with little if any likelihood that the controversy will be resolved in the near future.

In spite of the differences in findings among the various investigators, there appears to be substantial common agreement that the calcium-efflux phenomenon may be worthy of further study to further elicit the basic mechanisms of interaction of electromagnetic fields with biological entities at the microscopic level, but that the effect is not of concern with regard to possible hazards to humans from in-vivo exposure to RFR.

REFERENCES:
Adey, W.R., S.M. Bawin, B.F. Burge, H.I. Bassen, and K.E. Franke,
ELECTRIC FIELDS IN CAT BRAIN EXPOSED TO 450 MHZ CW FIELDS IN SEMI-FAR FIELDS
In Abstracts of Bioelectromagnetics Symposium, Washington, D. C., p. 35 (August 1981)

Adey, W.R., S.M. Bawin, and A.F. Lawrence
EFFECTS OF WEAK AMPLITUDE-MODULATED MICROWAVE FIELDS ON CALCIUM EFFLUX FROM AWAKE CAT CEREBRAL CORTEX
Bioelectromagnetics, Vol. 3, No. 3, pp. 295-307 (1982)

Allen, S. and W. Hurt
CALORIMETRIC MEASUREMENTS OF MICROWAVE ENERGY ABSORPTION BY MICE AFTER SIMULTANEOUS EXPOSURE OF 18 ANIMALS
Radio Sci., Vol. 14, No. 6S, pp. 1-4 (1979)

Allis, J.W., C.M. Weil, and D.E. Janes, Jr.
A CROSSED-BEAM APPARATUS FOR SIMULTANEOUS SPECTROPHOTOMETRIC OBSERVATION AND MICROWAVE EXPOSURE OF BIOCHEMICAL SAMPLES
Rev. Sci. Instrum., Vol. 46, pp. 1344-1349 (1975)

Allis, J.W., C.F. Blackman, M.L. Fromme, and S.G. Benane
MEASUREMENT OF MICROWAVE RADIATION ABSORBED BY BIOLOGICAL SYSTEMS: I. ANALYSIS OF HEATING AND COOLING DATA
Radio Sci., Vol 12, No. 6S, pp. 1-8 (1977)

Allis, J.W. and M.L. Fromme
ACTIVITY OF MEMBRANE-BOUND ENZYMES EXPOSED TO SINUSOIDALLY MODULATED 2450-MHZ MICROWAVE RADIATION
Radio Sci., Vol. 14, No. 6S, pp. 85-91 (1979)

Athey, T.W.
COMPARISON OF RF-INDUCED CALCIUM EFFLUX FROM CHICK BRAIN TISSUE AT DIFFERENT FREQUENCIES: DO THE SCALED POWER DENSITY WINDOWS ALIGN?
Bioelectromagnetics, Vol. 2, No. 4, pp. 407-409 (1981)

Bawin, S.M., L.K. Kaczmarek, and W.R. Adey
EFFECTS OF MODULATED VHF FIELDS ON THE CENTRAL NERVOUS SYSTEM
Ann. N.Y. Acad. Sci., Vol. 247, pp. 74-81 (1975)

Bawin, S.M. and W.R. Adey
INTERACTIONS BETWEEN NERVOUS TISSUES AND WEAK ENVIRONMENTAL ELECTRIC FIELDS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 323-330 (1976a)

Bawin, S.M. and W.R. Adey
SENSITIVITY OF CALCIUM BINDING IN CEREBRAL TISSUE TO WEAK ENVIRONMENTAL ELECTRIC FIELDS OSCILLATING AT LOW FREQUENCIES
Proc. Nat. Acad. Sci., Vol. 73, No. 6, pp. 1999-2003 (1976b)

Bawin, S.M., A. Sheppard, and W.R. Adey
POSSIBLE MECHANISMS OF WEAK ELECTROMAGNETIC FIELD COUPLING IN BRAIN TISSUE
Biochemistry and Bioenergetics, Vol. 5, pp. 67-76 (1978)

Blackman, C.F. and J.A. Black
MEASUREMENT OF MICROWAVE RADIATION ABSORBED BY BIOLOGICAL SYSTEMS: II. ANALYSIS BY DEWAR-FLASK CALORIMETRY
Radio Sci., Vol 12, No. 6S, pp. 9-14 (1977)

Blackman, C.F., J.A. Elder, C.M. Weil, S.G. Benane, D.C. Eichinger, and D.E. House
INDUCTION OF CALCIUM-ION EFFLUX FROM BRAIN TISSUE BY RADIO-FREQUENCY RADIATION: EFFECTS OF MODULATION FREQUENCY AND FIELD STRENGTH
Radio Sci., Vol. 14, No. 6S, pp. 93-98 (1979)

Blackman, C.F., S.G. Benane, J.A. Elder, D.E. House, J.A. Lampe, and J.M. Faulk
INDUCTION OF CALCIUM-ION EFFLUX FROM BRAIN TISSUE BY RADIO-FREQUENCY RADIATION: EFFECT OF SAMPLE NUMBER AND MODULATION FREQUENCY ON THE POWER-DENSITY WINDOW
Bioelectromagnetics, Vol. 1, No. 1, pp. 35-43 (1980a)

Blackman, C.F., S.G. Benane, W.T. Joines, M.A. Hollis, and D.E. House
CALCIUM-ION EFFLUX FROM BRAIN TISSUE: POWER DENSITY VERSUS INTERNAL FIELD-INTENSITY DEPENDENCIES AT 50-MHZ RF RADIATION
Bioelectromagnetics, Vol. 1, No. 3, pp. 277-283 (1980b)

Blackman, C.F., S.G. Benane, D.E. House, and W.T. Joines
EFFECTS OF ELF (1-120 HZ) AND MODULATED (50 HZ) RF FIELDS ON THE EFFLUX OF CALCIUM IONS FROM BRAIN TISSUE
Bioelectromagnetics, Vol. 6, No. 1, pp. 1-11 (1985a)

Blackman, C.F., S.G. Benane, J.R. Rabinowitz, D.E. House, and W.T. Joines
A ROLE FOR THE MAGNETIC FIELD IN THE RADIATION-INDUCED EFFLUX OF CALCIUM IONS FROM BRAIN TISSUE IN VITRO
Bioelectromagnetics, Vol. 6, No. 4, pp. 327-337 (1985b)

Crawford, M.L.
GENERATION OF STANDARD EM FIELDS USING TEM TRANSMISSION CELLS
IEEE Trans. Electromagn. Compat., Vol. 16, No. 4, pp. 189-195 (1974)

Dixon, W.J.
RATIOS INVOLVING EXTREME VALUES
Ann. Math. Stat., Vol. 22, pp. 68-78 (1951)

Dutta, S.K., J. Choppalla, M.A. Hossain, T.N. Bhar, and H.S. Ho
DOSIMETRIC MEASUREMENT AND BIOEFFECT STUDIES OF LOW LEVEL 915 MHZ CW MICROWAVES USING TEM CRAWFORD CELL
J. Basic Appl. Sci., Vol. 2, pp. 43-52 (1982)

Dutta, S.K., A. Subramoniam, B. Ghosh, and R. Parshad
MICROWAVE RADIATION-INDUCED CALCIUM ION EFFLUX FROM HUMAN NEUROBLASTOMA CELLS IN CULTURE
Bioelectromagnetics, Vol. 5, No.1, pp. 71-78 (1984)

Joines, W.T. and C.F. Blackman
POWER DENSITY, FIELD INTENSITY, AND CARRIER FREQUENCY DETERMINANTS OF RF-ENERGY-INDUCED CALCIUM-ION EFFLUX FROM BRAIN TISSUE
Bioelectromagnetics, Vol. 1, No. 3, pp. 271-275 (1980)

Joines, W.T. and C.F. Blackman
EQUALIZING THE ELECTRIC FIELD INTENSITY WITHIN CHICK BRAIN IMMERSED IN BUFFER SOLUTION AT DIFFERENT CARRIER FREQUENCIES
Bioelectromagnetics, Vol. 2, No. 4, pp. 411-413 (1981)

Kinn, J.F.
WHOLE BODY DOSIMETRY OF SMALL ANIMALS: THE EFFECT OF WEIGHT AND EXPOSURE GEOMETRY
Radio Sci., Vol 12, No. 6S, pp. 61-64 (1977)

Merritt, H., W.W. Shelton, and A.F. Chamness
ATTEMPTS TO ALTER 45-CA++ BINDING TO BRAIN TISSUE WITH PULSE-MODULATED MICROWAVE ENERGY
Bioelectromagnetics, Vol. 3, No. 4, pp. 475-478 (1982)

Miller, D.A., A.R. Valentino, and M. Benedick
Tech. Memorandum No. 2, Project No. IIT RIE-6249, U. S. Naval Electronic Systems Command, Washington, D. C. (1974)

Myers, R.D. and D.H. Ross
RADIATION AND BRAIN CALCIUM: A REVIEW AND CRITIQUE
Neurosci. Biobehav. Rev., Vol. 5, No. 4, pp. 503-543 (1981)

Schramm, M.
SECRETION OF ENZYMES AND OTHER MACROMOLECULES
Ann. Rev. Biochem., Vol. 36, pp. 307-320 (1967)

Shelton, W.W., Jr. and J.H. Merritt
IN VITRO STUDY OF MICROWAVE EFFECTS ON CALCIUM EFFLUX IN RAT BRAIN TISSUE
Bioelectromagnetics, Vol. 2, No. 2, pp. 161-167 (1981)

Sheppard, A.R., S.M. Bawin, and W.R. Adey
MODELS OF LONG-RANGE ORDER IN CEREBRAL MACROMOLECULES: EFFECTS OF SUB-ELF AND OF MODULATED VHF AND UHF FIELDS
Radio Sci., Vol. 14, No. 6S, pp. 141-145 (1979)

Weil, C.M.
THE CHARACTERISTIC IMPEDANCE OF RECTANGULAR TRANSMISSION LINES WITH THIN CENTER CONDUCTOR AND AIR DIELECTRIC
IEEE Trans. Microwave Theory Tech., Vol. 26, pp. 238-242 (1978)

3.4.5 CONCLUSIONS

Many of the findings on the effects of RFR on the blood-brain barrier must be discounted because of the presence of significant artifact due to the biological methodology used or to interpretation of RFR-induced changes in the relative sizes of vascular and extravascular volumes in the brain as alterations of the BBB. In recent studies, in which the occurrence of artifact was substantially reduced and perhaps rendered negligible, the results indicate that RFR can affect the BBB, but only at hyperthermic levels.

With the notable exception of the recent work by Sanders and co-workers, most of the findings on histopathological and histochemical changes in the nervous system induced by RFR were evidently thermally based. The finding of Sanders et al. (1985), that inhibition of respiratory chain function was induced by RFR at levels that did not produce measurable tissue hyperthermia, should be investigated further.

Until relatively recently, work on possible effects of RFR on EEGs and evoked responses suffered from artifact introduced by use of metallic electrodes, during exposure, that perturbed or were perturbed by the RFR. This problem was ameliorated greatly by Guy and coworkers, who developed high-resistance, carbon-loaded-Teflon electrodes that were tissue-compatible and thus chronically-implantable, thereby permitting measurements of EEGs and evoked responses during RFR exposure of animals without anesthesia. When such electrodes were used, differences between responses of RFR- and sham-exposed animals were nonsignificant. Guy and coworkers also found that for rabbits, so often used for such studies, the EEGs and evoked responses varied considerably among unanesthetized control animals, as well as with time for individual rabbits, rendering suspect the findings of previous investigators. In the squirral-monkey study by Kaplan et al. (1982), one of the few on RFR-induced changes in EEGs and visually evoked responses in primates, metallic electrodes were used but the animals were exposed before and after (and not during) RFR-exposure. No significant effects of the RFR were observed.

The controversy regarding the calcium-efflux phenomenon in its various manifestations (and apparent contradictions) appears unlikely to be resolved in the near future. However, there is essentially no concern that the effect is directly relevant to potential human hazards of RFR-exposure.

3.5 IMMUNOLOGY AND HEMATOLOGY

Many reports indicated that RFR has definite effects on the mammalian immune system. Most reported effects were detected after exposure at power density levels of about 10 mW/sq cm and higher; a few have been detected following exposure to power densities as low as about 0.5 mW/sq cm; and in some cases, effects obtainable with the higher power-density range were not found at lower power densities. In most of the studies, the mechanisms for the effects seen were not investigated, and many of the results were not consistent with one another. Because of the many complexities of the immune system and the variety of test procedures used, the representative studies discussed in this section are grouped into appropriate categories.

3.5.1 IN VITRO STUDIES

An important question is whether exposure to RFR can stimulate human or animal lymphocytes to transform into lymphoblasts (mitotically active form of lymphocytes) and to undergo mitosis (cell division). In-vitro studies directed toward this question were those in which lymphocytes were removed from the body, cultured, exposed to RFR (or exposed, then cultured), and examined for RFR-induced effects. Usually, such cells were cultured in the presence of a mitogen, an agent (usually chemical) that stimulates blastic transformation (i.e., lymphocyte to lymphoblast) and mitosis. The effects of in-vitro exposure of erythrocytes to RFR were also studied by several investigators.

3.5.1.1 LEUKOCYTE STUDIES

One of the early studies was by Stodolnik-Baranska (1967, 1974). In one of two series of experiments, lymphocyte suspensions from peripheral human blood were incubated for various periods and exposed to 2.95-GHz RFR (1-microsecond pulses, 1200 pps) either 4 hr/day for 3 or 5 days at 7 mW/sq cm (average power density) or 15 min/day for 3 or 5 days at 20 mW/sq cm, both groups without the mitogen phytohemagglutinin (PHA). In the second series, PHA was added and the following exposures were done with 4 groups. Specimens of group 1 were exposed at 20 mW/sq cm for 0, 5, 10, 15, 20, or 40 min. Those of group 2 were exposed at 7 mW/sq cm for either 3 or 4 hr. Group 3 was exposed 4 hr/day for 3 days at 7 mW/sq cm. Those of Group 4 were exposed for 10 min at 20 mW/sq cm.

The author tabulated only the results for 20 mW/sq cm with PHA (Groups 1 and 4 of the second series). Those for Group 1 showed no significant changes in the percentage of blastoid forms, but a significant decrease of the percentage of lymphocytes with exposure duration. The mitotic index (MI) for this group changed from 12.0% for no exposure to RFR to: 13.7 for 5 min of exposure, 17.2 and 17.9 respectively for 10 and 15 min, and 23.5 and 25.0 respectively for 20 and 40 min. The author stated that similar results were obtained for Group 2 (at 7 mW/sq cm).

The results for Group 4 indicated increases in MI from 12.0 for 0 hr of incubation to 15.6 for 59 hr and to 17.0 for 64 hr of incubation. MI

decreases to 10.2 and 11.0 were obtained respectively for 70 and 71.5 hr of incubation. Also reported were increases in chromosomal aberrations with exposure duration for Group 1, including stickiness of chromosomal arms, dicentrics, hypoploidy, hyperploidy, and chromatid breaks, with each type illustrated by a micrograph. The author indicated that the most unusual results obtained were alterations in chromosomal morphology that suggested changes in spiralization.

Regarding exposures of specimens without PHA, the author stated: "It should be stressed that irradiation of lymphocytes without PHA addition induces the appearance of blastoid forms and macrophage-like cells." The point was illustrated by one micrograph, but no data were given.

The results at 20 mW/sq cm with PHA-containing cultures showed a trend toward increase of mitotic index with exposure duration, decrease of the percentage of lymphocytes with duration, but no significant changes in the percentage of blastoid forms. Thus, it is difficult to understand how the results suggest that RFR may have mutagenic effects, as stated by the author. The changes found may have been of thermal origin rather due to any intrinsic effect of RFR, because the author indicated that exposure at 20 mW/sq cm for 20 min resulted in a 1-deg-C rise in the cultures, showing that culture temperature was not well controlled.

As part of a larger study primarily involving exposure of animals to RFR in vivo, preliminary work was done by Czerski (1975) in which cultures of human lymphocyte were exposed in vitro (power densities and durations not specified), with a view toward reproducing the results of Stodolnik-Baranska (1974). After cultures were exposed to RFR and incubated for 72 hr, the percentage of blast cells was determined. In addition, after incubation for 24 hr, such cultures were used to test for inhibition of macrophage migration in mouse spleen fragments. Unexposed samples or samples incubated for 1 hr with PHA served as controls.

Although a few positive results were obtained, Czerski noted that he encountered difficulties in obtaining reproducible results. This work was discussed on p. 133 of Baranski and Czerski (1976), who implicated uncontrolled RFR-induced temperature increases in the specimens (which were not cooled during exposure). They stated that: "exposures at power densities between 5 and 15 mW/sq cm, if continued till the moment when the temperature of the medium attained 38 deg C, could induce lympho-blastoid transformation; no such phenomenon could be obtained by exposure below 5 mW/sq cm."

Szmigielski (1975) exposed suspensions of rabbit granulocytes in thin-wall plastic tubes to far-field 3-GHz CW RFR at 1 or 5 mW/sq cm for 15, 30, or 60 min in an anechoic chamber. The suspension temperatures were checked before and after exposure. Control suspensions were stored in a separate chamber at room temperature. In some suspensions, the dead cells were then stained with nigrosine and counted for percentages by light microscopy; in others, the live cells were stained with neutral red and janus green B and counted by phase-contrast microscopy. Also

determined in supernatants after centrifugation of suspensions were the acid phosphatase and lysozyme activities (by one type of granule inside granulocytes) and the alkaline phosphatase and lysozyme activities (by another type of granule within granulocytes).

The author indicated that suspension temperature was not altered by exposure at either power density, and that nevertheless, suspensions exposed at 5 mW/sq cm for 30 or 60 min exhibited higher percentages of dead cells than either controls or those exposed at 1 mW/sq cm. Also, numerous vacuoles stained with neutral red were visible under phase-contrast microscopy in cells exposed to 5 mW/sq cm for 30 or 60 min (but no vacuoles stained with janus green B were detected). Liberation of acid phosphatase and lysozyme from granulocytes was observed in cells exposed to either power density and exhibited time- and dose-dependence. Suspensions exposed at 5 mW/sq cm for 60 min yielded acid phosphatase and lysozyme activities of about 90% and 85% relative to controls, but a total alkaline phosphatase activity of only 35%. At 1 mW/sq cm, only acid phosphatase and lysozyme activities were observed. Thus, the two granular species reacted differently to RFR exposure. Szmigielski et al. (1975a) reported effects of RFR on granulocytes of rabbits exposed in vivo, as discussed in Section 3.5.3.

Mayers and Habeshaw (1973) prepared monolayer cultures, on coverslips, of mouse macrophages that were continuously perfused with suspensions of human erythrocytes and exposed them to 2.45-GHz RFR at 50 mW/sq cm in a section of waveguide terminated with a water load, under strict control of culture temperature. The authors reported that the exposed cultures exhibited depressed erythrophagocytosis compared with unexposed control cultures. However, the data presented were sparse and the statistical treatment thereof was obscure.

Smialowicz (1976) prepared suspensions of mouse-spleen cells and exposed them to 2.45-GHz CW RFR at 10 mW/sq cm (SAR about 19 W/kg) for 1, 2, or 4 hr. Similar cell suspensions held at 37 deg C (without RFR exposure) for the same periods served as controls. Specimens after each treatment were cultured with or without one of four different mitogens (including PHA). Although changes in the extent of blastic transformation with exposure duration were seen, there were no statistically significant differences between corresponding values for each duration from RFR-exposed and control specimens. This was true both for specimens not stimulated with mitogen and for those stimulated with any of the four mitogens. Also measured were the temperature and percentage viability of the specimens immediately after each treatment, and no significant differences were found between RFR-exposed and control specimens for each treatment period.

Hamrick and Fox (1977) exposed rat lymphocyte cultures with and without PHA to far-field 2.45-GHz CW RFR at 5, 10, or 20 mW/sq cm (0.7, 1.4, or 2.8 W/kg) for 4, 24, or 44 hr and monitored lymphocyte-to-lymphoblast transformation by the uptake of tritiated thymidine. The differences in thymidine uptake between PHA-stimulated and nonstimulated cultures were large at each exposure level and duration, but the

differences between RFR-exposed and control cultures in each case were nonsignificant.

Roberts et al. (1983) concurrently sham-exposed and exposed cultures of human mononuclear leukocytes to 2.45-GHz CW RFR for 2 hr at 0.5 to 4 W/kg in a waveguide system within an incubator (Lu et al., 1981a). The upper SAR was chosen because it is the basis (with a safety factor of 0.1) for the 1982 American National Standards Institute guideline for human exposure to RFR (ANSI, 1982). No attempt was made to remove any heating due to the RFR. Other cultures external to the waveguide system served as controls. The cultures were then incubated at 37 deg C and assessed for percentage viability by their ability to exclude trypan blue dye and ethidium bromide on days 1 through 7 after treatment. The mean percentage viability decreased (nonmonotonically) with time after treatment for all three groups, but the postexposure differences between the group exposed at 4 W/kg and the other groups were not significant. Similar results (not shown) were obtained at the lower SARs.

Roberts et al. (1983) also stimulated control, sham-exposed, and RFR-exposed leukocyte cultures with PHA and assayed them daily for DNA, RNA, and total protein synthesis by cellular uptake of tritiated thymidine, uridine, and leucine. Unstimulated cultures were similarly assayed. There were no significant differences between the unstimulated group exposed at 4 W/kg and the other two unstimulated groups or among the three groups stimulated with an optimal PHA concentration. Similar results were obtained for suboptimal PHA concentrations and lower SARs.

These authors also measured the spontaneous production of interferon by RFR-exposed, sham-exposed, and control cultures; their production of influenza-virus-induced alpha-interferon; and their production of PHA-induced gamma-interferon, at 1 and 3 days after induction. Spontaneous production of interferon did not occur. By 24 hr, virtually all of the virus-induced alpha-interferon was present in the group exposed at 4 W/kg and in the other two groups, with no significant differences among the three groups. PHA-induced gamma-interferon, usually produced by 48-72 hr, was not detected at 24 hr, but was present by 72 hr in all PHA-induced cultures, with no significant differences among the RFR, sham, and control groups.

Lin and Peterson (1977) exposed suspensions of human-skin fibroblasts (two lines) and human lymphoblasts (two lines) to 2.45-GHz CW RFR for 15 min at 10 to 500 mW/sq cm in a special fluid-filled waveguide system (Lin, 1976c) in which the fluid of the system was maintained at 37 deg C. Corresponding SARs ranged from 24 to 1200 W/kg, with no measurable temperature rise in the suspensions. For comparisons, some suspensions were sham-exposed and others (controls) were not placed in the exposure system. After treatment and incubation in growth medium for 6 days, the viable fraction of cells was determined for each suspension with trypan blue. There were no significant differences in viability among the control, sham, and RFR groups. The authors surmised that RFR-induced effects on cell suspensions reported by other investigators might have been due to local temperature increases despite precautions to avoid

such increases.

Lin et al. (1979a) prepared suspensions of colony-forming-units-in-culture (CFU-c) bone-marrow cells from mice and sham-exposed or exposed such suspensions to 2.45-GHz RFR for 15 min in the same system at 30 to 1000 mW/sq cm (60 to 2000 W/kg). Immediately after treatment, there were no significant differences in the numbers of viable cells from sham-exposed suspensions and suspensions exposed at 500 mW/sq cm (1000 W/kg). Cell samples were then treated with a colony-stimulating factor, were permitted to grow in an appropriate medium, and were examined on days 5, 6, or 7 and 12, 13, or 14 after exposure. For samples examined on days 5-7, no significant differences were found between the number of colonies from sham-exposed samples and from the samples exposed at 30 mW/sq cm (60 W/kg). However, at higher power densities, the ratio of the number of colonies from RFR-exposed to sham-exposed samples was found to decrease with increasing power density. Similar results were obtained for days 12-14.

Harrison et al. (1980) determined the survival rates (the colony-forming abilities) of Chinese-hamster-ovary (CHO) cells heated to 43, 44, and 45 deg C and of bacterial cells (Serratia marcesens) heated to 48, 49, and 50 deg C within a fluid-filled waveguide exposure chamber similar to that of Lin (1976c). Heating was done in the absence of RFR and with the addition of 2.45-GHz pulsed RFR (0.01 duty cycle) at up to 550 mW/sq cm average power density for 5-60 min. Exposure at 550 mW/sq cm yielded a 0.37-deg-C incremental temperature rise in the specimens. Following each treatment, specimens of CHO cells were planted and incubated in growth medium at 37.5 deg C for about 1 week, after which the surviving colonies were counted. For each treatment temperature with and without RFR, linear regression analysis was done on the semilog of the survival fraction (relative to controls) vs treatment duration. Bacteria samples for each treatment were planted on agar and incubated overnight at 37.5 deg C, after which the survival-fraction data were similarly analyzed.

For the CHO cells, the slopes of the regression lines for 45 deg C (with RFR, presumably at 550 mW/sq cm, and in its absence) were far steeper than those for 43 deg C (indicating significantly higher survival rates at the lower temperature). At each temperature, the slope for the RFR-exposed cells was slightly but significantly steeper than for those not exposed. The authors ascribed this slope difference to the incremental temperature increase from the RFR. The results for the bacteria at 48 and 50 deg C were qualitatively similar to those for the CHO cells, but the slope difference between RFR and non-RFR plots at each temperature was not significant.

In an investigation similar to that of Lin et al. (1979a), Ottenbreit et al. (1981) sham-exposed or exposed bone-marrow specimens from children with acute leukemia in remission or other disorders at 31, 62, 125, 250, 500, or 1000 mW/sq cm (62-2000 W/kg) for 15 min. As before, the fluid of the exposure system was held constant at 37 deg C. In this study, the sample colonies from each treatment were stained to determine

the subpopulations of cells.

It was found that irrespective of sham- or RFR exposure at any of the power densities, the cell colonies consisted of 86-90% pure neutrophils, with the remainders consisting of macrophages (0-3%), mixtures of neutrophils and macrophages (7-10%), and unclassifiable cells (1-2%). Cells treated with a colony-stimulating factor and grown were examined on days 6-7 and 12-14. The variations of the data among the series of experiments performed under each set of conditions were large. For this reason, presumably, results were expressed as the ratio of mean numbers of colonies from RFR-exposed specimens to mean numbers of colonies from sham-exposed specimens in each series. For either examination period, the results showed no significant reductions in this ratio for those exposed at 31 or 62 mW/sq cm (62 or 124 W/kg). Above the latter power density, the ratio tended to decrease with increasing power density.

To ascertain whether the ratio reductions were due to specimen heating by the RFR, one set of experiments was performed at 1000 mW/sq cm (2000 W/kg) with the fluid of the exposure system held at 7, 22, or 37 deg C, and another set at 37 or 41 deg C. Reductions in ratio were obtained irrespective of the fluid temperature, a possible indication that the effect was not due to specimen heating by RFR exposure. However, the results for the two sets at 37 deg C were inconsistent: for the data taken at this temperature on days 6-7, the ratios for the first and second sets differed considerably from one another, possibly indicating the presence of uncontrolled experimental factors.

Cain et al. (1981) labeled hamster PARA-7 fibrosarcoma cells with the tracer Cr-51 and heated cell suspensions for 30 to 180 min to specific temperatures (+/- 0.1 deg C) in the range 37 to 44 deg C in a controlled water bath or they exposed cell suspensions to 2.45-GHz CW RFR at 100 mW/sq cm (105 W/kg) in a saline-cooled arrangement within an anechoic chamber. Following such treatments, the spontaneous release of Cr-51 in the supernatants vs treatment duration were determined by scintillation counting. Although Cr-51 release increased with treatment duration and temperature, the differences between RFR-exposed and water-bath-heated specimens maintained at the same temperature for the same durations were not significant.

Cain et al. (1981) also studied the effect of heating suspensions of Cr-51-labeled PARA-7 cells to various temperatures for various durations in the presence and absence of RFR, on the toxicity of antibody-complement (Ab-C) to such cells. Two methods were used. In one, cell suspensions reacted with Ab-C were heated (with and without RFR present) and assayed subsequently for Cr-51 release, such release being a measure of cell-membrane disruption. In the other, the colony-forming (CF) efficiencies of cell suspensions reacted with Ab-C were determined after heating (in the presence and absence of RFR), to ascertain the extent to which the treatment reproductively inactivated cells without affecting membrane integrity. Both methods results indicating that loss of cell viability and sensitization to Ab-C cytotoxicity were dependent on temperature and treatment duration, but again, there were no significant

differences between RFR-exposed and water-bath-heated specimens maintained at the same temperature for the same durations. However, the CF method proved to be far more sensitive than the Cr-51-release method.

Lyle et al. (1983) studied the effects of amplitude-modulated RFR at 1.5 mW/sq cm (SAR not stated) on the allogeneic cytotoxicity of the murine CTLL-1 T-lymphocyte line for H-2d B lymphoma MPC-11 cells. In a series of 5 experiments (6 replicates each), cytotoxicity assays were performed by gamma counting for 4 hr of specific mixtures of target cells labeled with Cr-51 and effector cells in the presence of 450-MHz RFR amplitude-modulated at 60 Hz. Such RFR exposure resulted in mean inhibition of 17-24% of the cytotoxicities observed in the respective controls for each experiment. Similar suppression percentages (15-25%) were observed in 4-hr assays performed in the absence of RFR but in which the effector cells had been exposed to the RFR for 4 hr before mixing them with the target cells, a result that led the authors to surmise that the changes in cytotoxicity were due to actions of the RFR on the effector cells. Lyle et al. (1983) also exposed effector cells to the RFR for 4 hr and performed the 4-hr assays (in the absence of the RFR) at 1, 4, 9, and 12.5 hr after exposure. They obtained respectively 20%, 13%, 12%, and no inhibition at these intervals.

Last, Lyle et al. (1983) performed similar 4-hr cytotoxicity assays in the presence of RFR that was modulated at 0 (unmodulated), 3, 16, 40, 80, and 100 Hz and compared the results with those obtained with 60 Hz. Inhibition was negligible with unmodulated RFR, was maximal with 60 Hz, and was significant (but smaller) with 80 and 100 Hz.

Sultan et al. (1983a) investigated the effects of combined in-vitro RFR-exposure and hyperthermia on the ability of normal B-lymphocytes to cap surface immunoglobulin (Ig) following the binding of specific anti-Ig molecules. They exposed suspensions of normal mouse B-lymphocytes at temperatures of 37, 41, and 42.5 deg C to 2.45-GHz CW RFR for 30 min at power densities of 5, 10, 25, 50, and 100 mW/sq cm (2.25, 4.5, 11.25, 22.5, and 45 W/kg). Control suspensions at each temperature were sham-exposed concurrently with the RFR suspensions. After treatment, the exposed cells and the unexposed controls were incubated at 4 deg C for 10 min with fluorescein-isothiocyanate-labeled goat anti-mouse Ig (FITC-anti-Ig) to permit antibody binding to surface Ig and were transferred to a 37-deg-C environment for 9 min to allow antigen-antibody capping to occur. Fluorescence microscopy was then used to test the preparations for capping.

Capping was seen in more than 90% of the cells heat-treated at 37 deg C, but in less than 60% of those treated at 41 deg C and in less than 5% of those treated at 42.5 deg C. The authors concluded that the mechanisms responsible for inhibition of capping in their experiments are thermal in origin, with no apparent effects of 2.45-GHz CW RFR if RFR-exposed and control samples are held at the same temperature.

Sultan et al. (1983b) reported similar results with cell suspensions exposed for 30 min to 147-MHz RFR amplitude modulated at 9, 16, or 60

Hz. The average power density ranged from 0.1 to 48 mW/sq cm (0.004-2.0 W/kg). Again, capping inhibition increased with temperature and no significant differences were obtained between RFR-exposed and control specimens held at the same temperature. These authors also found that for temperatures not exceeding 42 deg C, cytotoxicity and capping returned to normal levels 2 hr after heat treatment.

Liburdy and Wyant (1984) used liquid gel chromatography (LGC) to study whether RFR would affect the separation of immunoglobulin (Ig) and of T- and B-lymphocytes, based on the hypothesis that the field might alter the orientation of dipolar molecules as they diffuse through the column. Human serum was fractionated into IgM, IgA, and IgG classes with an ascending LGC column between a vertical pair of plates that provided a 10-MHz electric field perpendicular to the column. This frequency was selected because it corresponds to the rotational relaxation time for large freely diffusing macromolecules in solution. The field intensity used was 8500 V/m, which yielded an estimated field of 20.5 V/m in the gel core. By calculation, the SAR was less than or equal to 0.13 W/kg. With the geometry and flow rate used, complete fractionation required about 6 hr. Temperature rises within the column did not exceed 0.05 deg C. For reference data, LGC was performed before and after exposure of the column to the field. The IgM, IgA, and IgG peaks in the elution profiles (absorbency vs effluent volume) obtained in the presence of the field were all shifted toward lower effluent volumes relative to the peaks in the absence of the field. This shift also occurred for a serum albumin peak that appeared after IgG elution.

Liburdy and Wyant (1984) also investigated whether RFR would affect the separation of Ig-bearing (Ig+) lymphocytes from Ig- lymphocytes by immunoaffinity cell chromatography (ICC), a method that is based on the immunospecific binding of Ig+ cells to Ig-derivatized agarose beads. They hypothesized that a 2.5-GHz RFR field might alter bound water and dipolar amino acid side chains involved in cell surface interactions. Suspensions of mouse spleen cells 99% free of erythrocytes were loaded onto vertical ICC columns of Ig-derivatized agarose beads and exposed to horizontally polarized far-field RFR at 10 mW/sq cm (194 V/m), which yielded an SAR of 0.117 W/kg. During the 15 min needed for lymphocyte separation, no temperature excursions exceeding 0.03 deg C were found. For reference data, ICC columns were sham-exposed. Three successive ICC separations were made. The first served to collect non-absorbed (Ig-) cells, yielding a fraction that contained T-lymphocytes. The second separation was an intermediate wash that yielded a fraction containing relatively few cells because the Ig+ cells remained bound to the agarose beads. The third separation served to displace the bound Ig+ cells (fraction 3). Each fraction was assayed for Ig+ cells (B-lymphocytes), theta+ cells (T-lymphocytes), and Ig- and theta- cells (null cells), and the fractions obtained from each separation were summed by cell class.

For the RFR- and sham-exposed columns, fraction 1 consisted mostly of theta+ and null cells; the percentages were 36.1 and 35.3 for theta+ cells, respectively, and were 26.4 and 28.0 for null cells; in either case, the difference was not significant. The corresponding percentages

of Ig+ cells in this fraction were respectively only 3.1 and 1.2, but the difference was significant. By contrast, the respective percentages of Ig+ cells in fraction 2 were only 5.3 and 1.1 (a difference that was significant), but were larger than for the other classes, 1.6 and 1.4 for theta+ cells, and 1.7 and 1.3 for null cells (both nonsignificant differences). As expected, fraction 3 contained the largest percentages of Ig+ cells, 23.0 and 28.8 for the RFR and sham cases, respectively, a significant difference. The corresponding values were 1.1 and 1.3 for the theta+ cells and 2.0 and 1.2 for the null cells (both differences nonsignificant).

The authors concluded that RFR at levels below the 0.4-W/kg basis for the 1982 American National Standards Institute guide for human exposure to RFR (ANSI, 1982) can accelerate the elution of immunoglobulins by LGC and can reduce the immunospecific adsorption of B-lymphocytes during ICC, but they expressed caution regarding extrapolation of such in-vitro results to in-vivo exposures.

Cleary et al. (1985) exposed samples of rabbit peritoneal neutrophils to 100-MHz CW RFR for 30 or 60 min at field strengths ranging from 250 to 410 V/m (120 to 341 W/kg) or for 60 min to 100-MHz RFR 95% amplitude-modulated at 20 Hz (331 W/kg), within a temperature-controlled coaxial exposure chamber (Guy, 1977). For controls, they sham-exposed other samples and held still others concurrently outside the exposure chamber at the same temperature as the sham-exposed samples. The results showed that the viability and phagocytotic ability of the neutrophils were not affected by such RFR exposures, i.e., no significant differences were found among the groups for each exposure regimen. These negative findings are questionable, however, because of the relatively large variabilities among the two control groups in each case, an indication of the possible presence of uncontrolled non-RFR factors.

3.5.1.2 ERYTHROCYTE STUDIES

In a study by Peterson et al. (1979), suspensions of rabbit red blood cells (RBCs) were conventionally heated ("CH" groups) or heated with RFR ("MWH" groups), the latter with 2.45-GHz RFR at 10 to 140 mW/sq cm (46-644 W/kg) or with RFR in selected 0.5-GHz swept-frequency regions in the 12.5-18 GHz range at 31 to 124 mW/sq cm (SARs not stated). The sample temperatures were monitored continuously with a nonperturbing liquid-crystal, optic-fiber temperature probe. Following either treatment, the samples were examined for loss of hemoglobin (Hb) and potassium ions (K+). In all experiments, MWH groups were directly compared with CH groups at corresponding temperatures and with RBCs maintained at room temperature ("RT" groups).

For RBCs warmed only to 3.7 deg C above room temperature by 2.45-GHz RFR at 10 mW/sq cm (46 W/kg) or by conventional heating for 45 min, no additional Hb or K+ was released into the supernatant. By contrast, when RBCs were rapidly warmed from room temperature to 37 deg C by either technique, the heated erythrocytes lost significantly more of both Hb and K+ than RBCs maintained at room temperature. In addition,

RBCs warmed to 41.5 deg C by either technique lost far more Hb and K+ than those warmed to 37 deg C.

Groups of RBC samples were also heated from room temperature (21-24 deg C) to 37 deg C by exposure to each of the 0.5-GHz-wide swept-frequency bands in the Ku region at 124 mW/sq cm, and were held at 37 deg C by exposure at 31 mW/sq cm. As before, CH and RT groups were used for comparison. For each band, the differences between the MWH and CH groups for each endpoint were not significant and the means for both groups were significantly larger than for the RT group. There were also apparently significant interband differences among the various MWH groups for each endpoint, but these differences probably were not RFR-related because similar differences were evident for the CH and RT comparison groups for each band.

In all experiments, Hb and K+ were lost in equal amounts by RFR-heated and conventionally-heated erythrocytes warmed at the same rate to the same final temperature. Thus, at all the frequencies and power levels tested, the increased losses of either Hb or K+ from RFR-exposed RBCs were ascribed to thermal effects on the stability and/or permeability of the erythrocyte membrane, with a threshold well above 46 W/kg.

The authors noted that their results were in agreement with those of Liu et al. (1979), who reported no significant differences in loss of Hb or K+ from rabbit RBCs heated to 37 deg C by 2.45-, 3-, or 3.95-GHz RFR or conventional techniques, and with similar results of Hamrick and Zinkl (1975) with 2.45- and 3 GHz and conventional heating. However, the authors indicated that their findings differed from those of Baranski et al. (1971, 1974) and Ismailov (1971), who reported increased hemolysis and efflux of K+ from rabbit RBCs exposed to 1- or 3-GHz RFR at power densities as low as 1 mW/sq cm.

Peterson et al. (1979) also heated groups of samples of human RBCs to 37 deg C by exposure to 2.45-GHz RFR at 90 mW/sq cm (412 W/kg) for 8 min and held them there for 37 min by exposure at 30 mW/sq cm (137 W/kg). Unlike the results for rabbit RBCs, no significant differences among the MWH, CH, and RT groups were obtained in either hemolysis (about 0.6%) or K+ release (about 6%). Absence of hemolysis and K+ release for human RBCs heated to 37 deg C can be taken as an indication that RFR-induced changes in rabbit blood may not be reflected in similar effects with human blood.

Olcerst et al. (1980) found that in the absence of RFR, Arrhenius plots of the passive efflux rates of sodium-22 and rubidium-86 from the RBCs of rabbits in vitro have four separate linear regions of negative slope, with transitions (regions of positive slope) at 8-13, 22.5, and 36 deg C. They then measured the sodium and rubidium effluxes after exposures for 1 hr to 2.45-GHz RFR in a waveguide system, described by Rabinowitz et al. (1977), that maintained samples at predetermined temperatures. The efflux rates with RFR exposure were identical to the control rates, except at the critical temperatures, where exposure increased the efflux of both cations. The effluxes measured at the

22.5-deg-C transition for SARs of 100, 190, and 390 W/kg were found to be significantly higher than those obtained without RFR. Similar increased cation efflux was also observed near the transitions at 8-13 and 36 deg C.

The authors stated that at all three SARs, the cation effluxes were statistically greater than one would predict from a "macrothermal" response (not clearly defined by the authors) and that the response does not increase monotonically as a function of absorbed power. They suggested that the existence of an intermediate configuration within the RBC membrane is necessary for the observation of increased efflux and that this could be either the simultaneous existence of two phases or an intermediate protein configuration. However, coexistence of two phases in a phase transition implies the requirement for absorption or release of latent energy (without temperature change) to complete transformation from either phase to the other, so the interaction mechanism cannot be characterized readily as nonthermal.

Allis and Sinha (1981) used the fluorescent probe, 1,6-diphenyl-1,3,5-hexatriene (DPH) to investigate the effects of in-vitro exposure of human erythrocytes to 1.0-GHz CW RFR on the internal viscosity of the cell membranes, based on the concept that the functional properties of biological membranes are influenced by changes in the fluidity of their lipid portions. They noted that the fluidity of membrane lipid rises with increasing temperature, envisioned as an enhanced ability of the hydrocarbon tails of the phospholipids to move within their environment in the membrane. They reasoned that since most membrane lipid species are dipolar, RFR might alter the molecular motion in a way that would change their fluidity-vs-temperature profile.

Human erythrocyte membranes were prepared from outdated blood-bank blood and processed to obtain hemoglobin-free ghosts. The membranes were then suspended in hypotonic sodium phosphate buffer (20 mM, pH 7.4) at a protein concentration of 2.5-3.0 mg/ml. The processing and storage were done at 3 deg C, and the suspensions were used within 24 hr. Each day, DPH was dissolved in tetrahydrofuran to a concentration of 2 mM, and was diluted to 0.001 mM with the hypotonic phosphate buffer; equal volumes of 0.001-mM DPH solution and a 1:12 dilution (in the hypotonic phosphate buffer) of membrane suspension were mixed and incubated at 37 deg C for 90 min to ensure membrane penetration by the DPH. Non-probe-containing suspensions were prepared by substituting hypotonic phosphate buffer for the DPH solution, similarly incubated, and used as the light-scattering blanks for the fluorescence measurements.

A spectrofluorometer was used to measure fluorescence depolarization of DPH. The excitation wavelength was 360 nm and fluorescence intensity at 425 nm was measured in planes parallel and perpendicular to that of the exciting light. The measurements were converted to apparent viscosity of the lipid portion of the membrane, based on the theory of fluorescent probe depolarization applied to membrane systems (references cited by the authors). One set of measurements was done versus temperature and another set as a function of exposure duration at 23 deg C.

Exposure durations for the temperature set were not explicitly stated.

Two pairs of suspensions were used for fluorescence measurements, each pair consisting of cuvettes of membrane suspension with and without DPH (exactly 3.5 ml in each). One pair was exposed to RFR and the other pair served as control. Exposures were done in a small rectangular TEM cell mounted vertically at the front of the fluorometer. Special optics were used that permitted fluorescence measurements of a suspension pair (with and without DPH) placed within the TEM cell, one of each pair on each side of the center conductor. The long axis of each cuvette was parallel to the center conductor and orthogonal to both the electric and magnetic vectors, with the top of the cuvette facing the source. Each cuvette occupied the central two-thirds of the distance between center conductor and ground plane without contact with either.

A sweep generator set at 1.0-GHz CW was the RFR source; the signal was fed through an amplifier and dual directional coupler to the TEM cell. Incident and reflected powers were monitored at the dual directional coupler and transmitted power was monitored at the lower end of the TEM cell via a 20-dB attenuator. SARs were determined by calculation from such power readings with and without suspension-bearing cuvettes in the TEM cell.

Membrane-suspension temperatures were maintained to within +/- 0.2 deg C during fluorescence measurements by circulating water from a constant-temperature bath through thin-wall Tygon tubing in contact with the TEM cell walls, so only the air surrounding the cuvettes provided thermal contact thereto. Membrane-suspension temperature was adjustable over the range 15-40 deg C. The control pair was maintained in a water bath at the same temperature as the exposed pair. Temperatures of exposed and control samples were measured periodically with a Yellow Springs Instrument Co. (YSI) Model 46 TUC telethermometer and a YSI Model 520 non-metallic thermistor probe; however, neither fluorescence nor dose measurements were made with the probe in the RFR field.

A Vitek probe, made available after the experiments were completed, was used to measure the temperature at 15 locations within a sample exposed at 15 W/kg. The temperatures were within 0.1 deg C except at the top and bottom of the sample column, where variations of 0.2-0.3 deg C were often found. These results imply that energy deposition was reasonably uniform in the central portion of the sample where the fluorescence measurements were taken.

The rotational motion of DPH in the lipid portion of the membrane is dependent on the degree to which its surroundings allow movement and is therefore a direct measure of the local viscosity of the membrane interior. With Ipa and Ipp representing the fluorescence intensities respectively parallel and perpendicular to the excitation plane, DPH rotation is characterized by the anisotropy parameter r given by:

$$r = (Ipa - Ipp)/(Ipa + 2Ipp). \qquad (1)$$

The apparent microviscosity v indicated by DPH can be calculated from r by a modified version of the Perrin equation simplified for DPH:

$$v = 2.4r/(0.362 - r). \qquad (2)$$

The logarithm of the viscosity of a homogeneous medium is normally a linear function of the inverse absolute temperature (an Arrhenius plot). The authors noted that the variation of membrane lipid viscosity with temperature may also be characterized in this way, but that since the membrane is not a homogeneous medium, the result may apply only to the microviscosity in the immediate neighborhood of the probe molecule.

Representative Arrhenius plots for the approximate temperature range 4-49 deg C were presented for samples exposed at 0.6, 2.0, and 15 W/kg and their respective controls. All six plots were essentially linear, with only minor differences in slope, obtained by a least-squares fit. The results of each of four experiments at each SAR were tabulated. By analysis of variance, the differences in slope between the exposed and control samples were nonsignificant.

Also measured were changes in DPH anisotropy (r) for exposure durations of 1, 2, 3, 4, and 5 hr at 0.7, 2.9, and 14 W/kg (and for corresponding controls), and mean r and SD for each set of conditions were plotted. At 0.7 and 2.9 W/kg, no statistically significant differences between exposed and corresponding control specimens and no significant effect of exposure duration were found; however, the results for both measures at 14 W/kg were significant ($p<0.02$). The authors suggested that the most probable explanation of the latter results was that the temperatures of the exposed and control samples were the same (22.8 +/- 0.5 deg C) for the two lower SARs, but were 3.2 deg C higher for the samples exposed at 14 W/kg. Moreover, use of the slope for any of the Arrhenius plots in equation (2) showed that a temperature rise of 3.2 deg C would decrease r by 0.004, and that if the latter were used to compensate the 14-W/kg results, the difference between the exposed and control samples would be rendered nonsignificant. Thus, the authors stated: "The anisotropy of DPH was found to be independent of the duration of exposure, and from this we may infer with confidence that the Arrhenius-type plots are not skewed by exposure duration."

The authors, noting that the slope of an Arrhenius plot is proportional to the activation energy for the process, indicated that the RFR had not induced a fundamental change in motion of the hydrocarbon tails of the lipid molecules, and that this conclusion applies to the mixed lipids of the red-cell membrane presumably in the liquid-crystalline state above the phase-transition temperature from the gel-like state. They also indicated that their mean activation energy was consistent with those of others obtained with fresh blood.

Last, the authors cited the findings of Olcerst et al. (1980) on the RFR-induced efflux of cations from rabbit erythrocytes, who suggested two possible mechanisms for their results: the existence of two lipid phases separated laterally in the erythrocyte membrane or conformational

transitions of the membrane proteins at key temperatures. Allis and Sinha (1981) noted that their results argued against lateral separation of lipid phases and favored the hypothesis that the observed efflux of cations is due to interaction of RFR with membrane protein, perhaps in combination with limited amounts of associated water or membrane lipid.

Allis and Sinha (1982) used DPH and associated apparatus to study the effects of 1.0-GHz RFR on multilamellar dimyristoylphosphatidylcholine (DMPC) vesicles, phospholipids that exhibit a highly cooperative phase transition in which hydrocarbon chains in the interior of the membrane undergo a sharp decrease in the degree of order, with a corresponding increase in chain mobility. Multilamellar DMPC vesicles were prepared by dissolving the lipid in 2 ml of chloroform and placing the solution in a 50-ml round-bottom flask attached to a rotating flash evaporator. The flask was suspended in a 30-deg-C water bath and rotated for 3-4 hr under vacuum. As the chloroform evaporated, a thin film of lipid was left on the flask walls. Sufficient KCl-Tris-sucrose buffer was added to obtain a final concentration of 5 mg of lipid per ml of buffer, and the suspension was rotated for 3-4 hr more in a 30-deg-C water bath to form the vesicles.

Each experimental day, equal volumes of 0.001-mM DPH and a 1:24 dilution (in the same buffer) of the DMPC membrane suspension were mixed and incubated at 37 deg C for 60 min to facilitate penetration of the lipid by DPH. Suspensions in which buffer was substituted for DPH were also prepared, similarly incubated, and used as the light-scattering blanks for the fluorescence measurements. For positive controls, vesicles were prepared in similar fashion except that 0.030 ml of chloroform was added to 9.6 ml of vesicle suspension before the 60-min incubation.

As described in Allis and Sinha (1981), fluorescence measurements were made in planes parallel and perpendicular to that of the exciting light, and the measurements were converted to apparent viscosity. Two pairs of samples in cuvettes were used for each set of measurements; one pair was exposed in a TEM cell, and the other pair was maintained at the same temperature in a water bath as the control.

The authors noted that a viscosity Arrhenius plot will yield a straight line if no phase transition is involved. However, their results for the control suspensions without chloroform yielded a plot consisting of two linear regions separated by a transition (from the liquid-crystalline phase of relatively low viscosity to the gel phase of higher viscosity) at about 25 deg C; for the chloroform-treated positive controls, the transition temperature was about 5 deg C lower, but the shape of the curve was not affected substantially.

Temperature profiles were obtained for the samples exposed at 1, 5, 15, or 30 W/kg. The profile for the samples exposed at each level did not differ significantly from that of its corresponding control plot, i.e. the two sets of data could be fitted to the same Arrhenius plot. This point was illustrated by the Arrhenius plots for 5 and 30 W/kg, which appeared to be similar within the limits of experimental error.

Thus, no RFR-induced temperature shifts in phase transition were found.

Measurements were also made for samples exposed at various SARs at two constant temperatures, 23.5 and 25.5 deg C, which corresponded to log-viscosities of about 0.7 and 0, respectively, approximate values that bounded the phase-transition region. The mean microviscosities and SDs at each temperature were plotted vs SAR. Analyses of variance yielded no significant effect of SAR at either temperature.

The authors noted that to obtain such data, it was necessary to expose a single sample for several hours on a given day. Therefore, they did an another set of experiments, in each of which a single sample was exposed for 5 hr/day, with measurements made every hour, and the results of which were compared with those for a control sample maintained at the same temperature. Such experiments were performed at each of four SARs between 1 and 25 W/kg and each of two temperatures, 23.5 and 25.5 deg C. For each case, analysis of variance showed no significant trend over exposure duration.

Shnyrov et al. (1984) studied the effects of RFR on the heat capacity of human erythrocyte ghost suspensions by use of scanning differential microcalorimetry. They exposed suspensions to 330-MHz CW RFR at 9.2 W/kg in a silica chamber placed between two capacitor plates. Exposure for 20 min increased the suspension temperature by 0.8 deg C.

Liburdy and Penn (1984) reported the occurrence of increased sodium passive transport at a membrane phase transition temperature within 17-19 deg C for rabbit RBCs exposed to 2.45-GHz RFR at 60 W/kg. They indicated that maximum effect occurred for hypoxia and hyperoxia (relative to atmospheric pO2), induced by bubbling appropriate O2/N2 mixtures through samples, a parameter not controlled by previous investigators. They noted that with the same apparatus and procedures used by Olcerst et al. (1980) but with better control and measurement of sample temperature (to +/- 0.05 deg C), they were unable to reproduce the regions of positive slope found by the latter for control RBCs. Though apparently not recognized by Liburdy and Penn, however, their data for RFR-exposed RBCs appeared to indicate a small but analogous positive-slope region.

Liburdy and Vanek (1985) further demonstrated RFR-induced changes in erythrocyte cation permeability that they occur only at temperatures within the phase-transition region (18-22 deg C), by using cholesterol to inhibit the phase transition. An Arrhenius plot of Na-22 influx over the temperature range 13-43 deg C for sham-exposed rabbit erythrocytes having the normal concentration of cholesterol exhibited two linear regions of differing slopes, with the slope change (phase transition) in the region 17.5-19.5 deg C. The Na-22 influx for such erythrocytes that were exposed to 2.45-GHz RFR at 100 W/kg, was significantly higher (by 75-100%) than for sham-exposed cells only within the phase-transition region. The slope for the temperature range above the transition was smaller than for the temperature range below the transition, with the slope for the latter corresponding to about twice the activation energy than the former (14 vs 6.5 kcal/mole), consonant with results by Allis

and Sinha (1981).

Erythrocytes were enriched in membrane cholesterol by incubation in mixtures of sonicated cholesterol/phosphatidylcholine liposomes in the presence of albumin. As expected, the Arrhenius plot for sham-exposed cholesterol-enriched erythrocytes was linear, with a single slope over the entire temperature range 13-43 deg C, signifying the absence of a phase transition. The slope was the same as for erythrocytes of normal cholesterol concentration in the temperature range above the transition region, indicating that the cholesterol enrichment yielded the liquid-crystal state (Allis and Sinha, 1981) in the temperature range below, as well as above, the transition region for normal erythrocytes. Moreover, the data for the RFR-exposed cholesterol-enriched erythrocytes fitted the Arrhenius plot for sham-exposed cholesterol-enriched erythrocytes very well, indicating absence of an RFR effect for such erythrocytes.

Kim et al. (1985) also sought effects of RFR on erythrocyte membranes, but used the fluorescence probes 1-anilinonaphthalene-8-sulfonic acid (1,8-ANS), 2-toluidinylnaphthalene-6-sulfonate (2,6-TNS), pyrene, and perylene for studies on erythrocyte ghosts. In addition, they used the nonfluorescent covalent label 2,4,6-trinitrobenzene sulfonic acid (TNBS) for studies on whole erythrocytes.

The authors noted: The probes 1,8-ANS and 2,6-TNS were chosen because they are mainly localized in the lipid-water interface of the membrane. Perylene is localized in the hydrocarbon layer, concentrating mainly near fatty acid residues, while pyrene is characterized by a uniform distribution over the hydrocarbon layer. The probe TNBS was selected because it allows the study of protein shielding of lipids. At room temperatures, TNBS does not penetrate the erythrocyte membrane, and therefore the information obtained with TNBS relates to the outer surface of the membrane; at 37 deg C, the membrane becomes permeable to TNBS, and so the labeling of phospholipids at this temperature depends on both protein shielding and permeation.

Blood from five rats was collected in 220 ml of 0.9% NaCl (free from anticoagulants) at 0 deg C. After centrifugation for 10 min at 0 deg C, the supernatant and the layer of lymphoid cells above the erythrocyte sediment were aspirated, and the erythrocytes were washed three times with 0.9% NaCl. The erythrocyte ghosts for the fluorescence aspects were obtained by hemolysis, with 1 mM EDTA added to the erythrocyte-hemolysis medium, and were kept at -20 deg C and used within 2 days.

For the TNBS aspects, 9 ml of medium containing 2 mM of TNBS was added to 1 ml of freshly isolated and packed erythrocytes, and incubated with continuous stirring for 1 hr; the cells were washed free of unreacted dye, and the phospholipids were extracted. The phospholipids were separated by chromatography and the amounts of phosphatidylethanolamine (PEA) and trinitrophenylphosphatidylethanolamine (TNPE) were determined, TNPE being the reaction product of PEA and TNBS, and the fraction F of PEA available for TNBS incorporation into PEA was calculated from:

$$F = \text{PEA-reacted/PEA-total.} \qquad (3)$$

From the results, the ratio R was determined, given by:

$$R = \text{TNPE}/(\text{PEA} + \text{TNPE}), \qquad (4)$$

representing the degree of trinitrophenylation of erythrocyte PEA.

The TNBS studies were performed in a rectangular thermostat cell with horizontal inner dimensions 30x30 mm, a height of 60 mm, and a bottom of 1 mm thickness. A suspension height of 9 mm yielded a total thickness of 10 mm. The cell and stirrer immersed in the suspension were made of Plexiglas. The suspensions were exposed to 900-MHz RFR at 10 mW/sq cm through the bottom from a horn below the cell. The authors noted that field nonuniformity did not exceed 3% in the 30x30-mm exposure area. Sample temperature was measured a short time after the RFR was shut off. The SAR was not estimated. Incubation of suspensions was also done in a water bath at 10, 15, 20, 25, and 30 deg C to determine the temperature dependence of TNBS labeling.

In each experiment, a sample was exposed to the RFR during the 1 hr of incubation, with a paired sample as the control. The initial sample temperature before exposure and in the control was 22 deg C. After 5 min of RFR-exposure, the temperature rose by about 3 deg C to a plateau of 25 deg C for the remaining 55 min. The results for three experiments were shown in Table 46 (adapted from Table 1 of the paper):

TABLE 46: EFFECT OF RFR-EXPOSURE ON THE RATIO R

Experiment	R for RFR-exposed sample	R for paired control
1	0.025	0.021
2	0.029	0.024
3	0.025	0.022
Mean and SE	0.026 +/- 0.004	0.022 +/- 0.001

It is seen that in each experiment, the RFR yielded a higher R than the control, with a mean increase of 0.004. (Although the authors noted that $p>0.1$ by Student's t-test, they appeared to regard the mean increase in R as significant.)

For five experiments at each temperature in the range 10-30 deg C, a plot of the mean fraction F (TNBS incorporation into PEA of erythrocyte membranes) vs temperature was shown in Fig. 2 of the paper. The graph was linear, and by estimation therefrom, the slope was 0.0012 per deg C. Thus, for a 3.5-deg-C temperature rise induced by RFR, the increase in F would be 0.004, indicating that the effect of the RFR was thermal.

For each fluorescence experiment, erythrocyte ghosts were suspended in 15-mM phosphate buffer, pH 7.4 (protein concentration 100 mg/ml), and sonicated for 15 s at 22 kHz and 0.5 A. To the suspension, 1,8-ANS and

2,6-TNS were added to a final concentration of 10 mM, and pyrene and perylene respectively up to 2.5 and 0.2 mM. The measurements were done with a spectrofluorimeter, using excitation wavelengths of 360 nm for 2,6-TNS; 380 nm for 1,8-ANS; 330 nm for pyrene; and 436 nm for perylene. Fluorescence wavelengths were 430 nm for 2,6-TNS; 480 nm for 1,8-ANS; 390 nm (monomer) and 480 nm (dimer) for pyrene; and 474 nm for perylene.

Perylene fluorescence anisotropy, A, in the membrane was estimated by measuring the relative fluorescence yield at parallel and perpendicular orientation of the optical axis of polaroids when irradiating the specimen with polarized light. The following equation was used:

$$A = (Fpa - G.Fpp)/(Fpa + 2G.Fpp), \qquad (5)$$

where Fpa and Fpp are respectively the fluorescence intensities of the parallel and perpendicular components, and G is the grating factor.

In initial fluorescence measurements of specimens during exposure to RFR at various frequencies, including 900 MHz, pickup of strong stray fields by the fluorimeter electronics was obtained except at frequencies near 340 MHz, so that frequency was chosen for the fluorescence aspects. The cell used for the fluorescence measurements and exposure was rectangular with opposite walls spaced 10 mm apart. The cell frame and two of the walls were made of Plexiglas, quartz was used for the walls at the site of fluorescence excitation and emission measurements, and the bottom was of 1-mm-thick Plexiglas.

One of two silver condenser plates (9.5x9.5 mm) was placed under the bottom (on the outside) of the cell. The bottom of the other plate was isolated with an etched polyethylene film to minimize light reflection, a vertical support rod was attached to its top surface and affixed to a horizontal cell cover, and the plate was placed within the cell at 6 mm above the first plate. The cell was filled with suspension to the level of the upper plate. A G3-20 high-frequency generator (made in the USSR) was used to deliver energy to the two condenser plates.

Suspension temperatures were measured by microthermistor (MMT-4, made in the USSR) of time constant not exceeding 0.3 s. The authors indicated that its calibration curve within the range 10-50 deg C was linear. For such measurements, the RF field was switched off, the cell cover with the attached upper condenser plate was removed, and the microthermistor was inserted, all requiring a time interval of 5-6 s. Suspension SARs at cell center and by the wall were respectively 100 +/- 9 and 96 +/- 11 W/kg. However, the authors stated: "One cannot exclude the probability that removal of the top condenser plate caused the agitation of the suspension and lowering of its temperature."

The results for 1,8-ANS; 2,6-TNS; and pyrene were plotted as the mean relative fluorescence intensity and SE for each probe vs temperature, attained by either RFR-exposure or heating in the thermostat. All of the graphs were linear with negative slopes, indicating decreases in fluorescence intensity with increasing temperature. In each case, the

slope for the RFR graph was slightly more negative than the slope for its corresponding thermostat graph, but the authors indicated that the differences were not significant ($p>0.1$), thus demonstrating that the RFR caused no other effect than heating. The relative intensity for pyrene decreased more strongly at 390 nm (monomeric form) than at 480 nm (dimer form), indicating that pyrene dimerization rose with temperature. Analogous results for fluorescence anisotropy of perylene were obtained.

Based on the aforementioned properties of TNBS and that the erythrocyte temperature did not exceed 25 deg C, the authors concluded that protein shielding was the primary contributor to the results with that probe, and that the results considered together with those for the fluorescence probes, showed the following: (1) an increase in fluidity of the lipid phase in the sites of probe localization, (2) changes in the state of the lipid-protein contact region, and (3) a decrease in the shielding of the lipid bilayer by proteins. They also stated:

"When compared with results from the temperature control, the observed alterations in the erythrocyte membrane under microwave radiation are qualitatively and quantitatively similar to those produced by its thermalizing action. In all cases the significance level exceeded 0.1. A nonthermal effect of this radiation was not found with the techniques used in this study."

It should be noted, however, that the temperature range used by Kim et al. (1985) was 22-36 deg C, above the phase-transition region within which RFR-induced alterations of cation permeability were reported in other investigations such as those discussed above.

REFERENCES:

Allis, J.W. and B.L. Sinha
FLUORESCENCE DEPOLARIZATION STUDIES OF RED CELL MEMBRANE FLUIDITY. THE EFFECT OF EXPOSURE TO 1.0-GHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 2, No. 1, pp. 13-22 (1981)

Allis, J.W. and B.L. Sinha
FLUORESCENCE DEPOLARIZATION STUDIES OF THE PHASE TRANSITION IN MULTILAMELLAR PHOSPHOLIPID VESICLES EXPOSED TO 1.0-GHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 3, No. 3, pp. 323-332 (1982)

ANSI (American National Standards Institute)
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
Published by the Institute of Electrical and Electronics Engineers, New York (1982)

Baranski, S. and P. Czerski
BIOLOGICAL EFFECTS OF MICROWAVES
Dowden, Hutchinson & Ross, Inc., Stroudsburg, Pennsylvania (1976)

Baranski, S., H. Ludwicka, and S. Szmigielski
THE EFFECT OF MICROWAVES ON RABBIT ERYTHROCYTE PERMEABILITY
Medycyna Latnicza Z., Vol. 39, pp. 75-79 (1971)

Baranski, S., S. Szmigielski, and J. Moneta
EFFECTS OF MICROWAVE IRRADIATION IN VITRO ON CELL MEMBRANE PERMEABILITY
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 173-177 (1974)

Cain, C.A., G.V. Rama Rau, and W.A.F. Tompkins
ENHANCEMENT OF ANTIBODY-COMPLEMENT CYTOTOXICITY AGAINST VIRUS-TRANSFORMED HAMSTER PARA-7 CELLS TREATED WITH HEAT AND MICROWAVE RADIATION
Radiat. Res., Vol. 88, No. 1, pp. 96-107 (1981)

Cleary, S.F., L.-M. Liu, and F. Garber
VIABILITY AND PHAGOCYTOSIS OF NEUTROPHILS EXPOSED IN VITRO TO 100-MHZ RADIOFREQUENCY RADIATION
Bioelectromagnetics, Vol. 6, No. 1, pp. 53-60 (1985)

Czerski, P.
MICROWAVE EFFECTS ON THE BLOOD-FORMING SYSTEM WITH PARTICULAR REFERENCE TO THE LYMPHOCYTE
Ann. N.Y. Acad. Sci., Vol. 247, pp. 232-242 (1975)

Guy, A.W.
A METHOD FOR EXPOSING CELL CULTURES TO ELECTROMAGNETIC FIELDS UNDER CONTROLLED CONDITIONS OF TEMPERATURE AND FIELD STRENGTH
Radio Sci., Vol. 12, No. 6S, pp. 87-96 (1977)

Hamrick, P.E. and S.S. Fox
RAT LYMPHOCYTES IN CELL CULTURE EXPOSED TO 2450 MHZ (CW) MICROWAVE RADIATION
J. Microwave Power, Vol. 12, No. 2, pp. 125-132 (1977)

Hamrick, P.E. and J.G. Zinkl
EXPOSURE OF RABBIT ERYTHROCYTES TO MICROWAVE IRRADIATION
Radiat. Res., Vol. 62, pp. 164-168 (1975)

Harrison, G.H., J.E. Robinson, D. McCulloch, and A.Y. Cheung
COMPARISON OF HYPERTHERMAL CELLULAR SURVIVAL IN THE PRESENCE OR ABSENCE OF 2.45 GHZ MICROWAVE RADIATION
Proc. URSI Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 41-45 (June-July 1980)

Ismailov, E.S.
MECHANISM OF THE EFFECT OF MICROWAVES ON THE PERMEABILITY OF ERYTHROCYTES FOR POTASSIUM AND SODIUM IONS
Biol. Nauki (Engl. Trans.), Vol. 3, pp. 58-60 (1971)

Kim, Y.A., B.S. Fomenko, T.A. Agafonova, and I.G. Akoev
EFFECTS OF MICROWAVE RADIATION (340 AND 900 MHZ) ON DIFFERENT STRUCTURAL LEVELS OF ERYTHROCYTE MEMBRANES
Bioelectromagnetics, Vol. 6, No. 3, pp. 305-312 (1985)

Liburdy, R.P. and A. Penn
MICROWAVE BIOEFFECTS IN THE ERYTHROCYTE ARE TEMPERATURE AND pO2 DEPENDENT: CATION PERMEABILITY AND PROTEIN SHEDDING OCCUR AT THE MEMBRANE PHASE TRANSITION
Bioelectromagnetics, Vol. 5, No. 2, pp. 283-291 (1984)

Liburdy, R.P. and A. Wyant
RADIOFREQUENCY RADIATION AND THE IMMUNE SYSTEM. PART 3. IN VITRO EFFECTS ON HUMAN IMMUNOGLOBULIN AND ON MURINE T- AND B-LYMPHOCYTES
Int. J. Radiat. Biol., Vol. 46, No. 1, pp. 67-81 (1984)

Liburdy, R.P. and P.F. Vanek, Jr.
MICROWAVES AND THE CELL MEMBRANE II. TEMPERATURE, PLASMA, AND OXYGEN MEDIATE MICROWAVE-INDUCED MEMBRANE PERMEABILITY IN THE ERYTHROCYTE
Radiat. Res., Vol. 102, pp. 190-205 (1985)

Lin, J.C.
A NEW SYSTEM FOR INVESTIGATING NONTHERMAL EFFECT OF MICROWAVES ON CELLS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. II, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8011, pp. 350-353 (1976c)

Lin, J.C. and W.D. Peterson, Jr.
CYTOLOGICAL EFFECTS OF 2450 MHZ CW MICROWAVE RADIATION
J. Bioeng., Vol. 1, pp. 471-478 (1977)

Lin, J.C., M.J. Ottenbreit, S.-L. Wang, S. Inoue, R.O. Bollinger, and M. Fracassa
MICROWAVE EFFECTS ON GRANULOCYTE AND MACROPHAGE PRECURSOR CELLS OF MICE IN VITRO
Radiat. Res., Vol. 80, No. 2, pp. 292-302 (1979a)

Liu, L.M., F.G. Nickless, and S.F. Cleary
EFFECTS OF MICROWAVE RADIATION ON ERYTHROCYTE MEMBRANES
Radio Sci., Vol. 14, No. 6S, pp. 109-115 (1979)

Lu, S.-T., N.J. Roberts, Jr., and S.M. Michaelson
A MODIFIED WAVEGUIDE EXPOSURE FACILITY FOR EXAMINING EFFECTS OF MICROWAVES ON IMMUNOCOMPETENT AND HEMATOPOIETIC CELLS
In J.C. Mitchell (ed.), AEROMEDICAL REVIEW: USAF RADIOFREQUENCY RADIATION BIOEFFECTS RESEARCH PROGRAM--A REVIEW., USAF School of Aerospace Medicine, Brooks Air Force Base, TX, Review 4-81, pp. 159-183 (1981a)

Lyle, D.B., P. Schechter, W.R. Adey, and R.L. Lundak
SUPPRESSION OF T-LYMPHOCYTE CYTOTOXICITY FOLLOWING EXPOSURE TO SINUSOIDALLY AMPLITUDE-MODULATED FIELDS
Bioelectromagnetics, Vol. 4, No. 3, pp. 281-292 (1983)

Mayers, C.P. and J.A. Habeshaw
DEPRESSION OF PHAGOCYTOSIS: A NON-THERMAL EFFECT OF MICROWAVE RADIATION AS A POTENTIAL HAZARD TO HEALTH
Int. J. Radiat. Biol., Vol. 24, No. 5, pp. 449-461 (1973)

Olcerst, R.B., S. Belman, M. Eisenbud, W.W. Mumford, and J.R. Rabinowitz
THE INCREASED PASSIVE EFFLUX OF SODIUM AND RUBIDIUM FROM RABBIT ERYTHROCYTES BY MICROWAVE RADIATION
Radiat. Res., Vol. 82, No. 2, pp. 244-256 (1980)

Ottenbreit, M.J., J.C. Lin, S. Inoue, and W.D. Peterson, Jr.
IN VITRO MICROWAVE EFFECTS ON HUMAN NEUTROPHIL PRECURSOR CELLS (CFU-C)
Bioelectromagnetics, Vol. 2, No. 3, pp. 203-215 (1981)

Peterson, D.J., L.M. Partlow, and O.P. Gandhi
AN INVESTIGATION OF THE THERMAL AND ATHERMAL EFFECTS OF MICROWAVE IRRADIATION ON ERYTHROCYTES
IEEE Trans. Biomed. Eng., Vol. 26, No. 7, pp. 428-436 (1979)

Rabinowitz, J.R., R.B. Olcerst, and W.W. Mumford
THE DESCRIPTION OF A SYSTEM TO IRRADIATE CELLS IN CULTURE WITH MICROWAVES
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 216-229 (1977)

Roberts, N.J.Jr., S.-T. Lu, and S.M. Michaelson
HUMAN LEUKOCYTE FUNCTIONS AND THE U. S. SAFETY STANDARD FOR EXPOSURE TO RADIO-FREQUENCY RADIATION
Science, Vol. 220, pp. 318-320 (15 April 1983)

Shnyrov, V.L., G.G. Zhadan, and I.G. Akoev
CALORIMETRIC MEASUREMENTS OF THE EFFECT OF 330-MHZ RADIOFREQUENCY RADIATION ON HUMAN ERYTHROCYTE GHOSTS
Bioelectromagnetics, Vol. 5, No. 4, pp. 411-418 (1984)

Smialowicz, R.J.
THE EFFECT OF MICROWAVES ON LYMPHOCYTE BLAST TRANSFORMATION IN VITRO
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8010, pp. 472-483 (1976)

Stodolnik-Baranska, W.
LYMPHOBLASTOID TRANSFORMATION OF LYMPHOCYTES IN VITRO AFTER MICROWAVE IRRADIATION
Nature, Vol. 214, pp. 102-103 (1967)

Stodolnik-Baranska, W.
THE EFFECTS OF MICROWAVES ON HUMAN LYMPHOCYTE CULTURES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 189-195 (1974)

Sultan, M.F., C.A. Cain, and W.A.F. Tompkins
EFFECTS OF MICROWAVES AND HYPERTHERMIA ON CAPPING OF ANTIGEN-ANTIBODY COMPLEXES ON THE SURFACE OF NORMAL MOUSE B LYMPHOCYTES
Bioelectromagnetics, Vol. 4, No. 2, pp. 115-122 (1983a)

Sultan, M.F., C.A. Cain, and W.A.F. Tompkins
IMMUNOLOGICAL EFFECTS OF AMPLITUDE-MODULATED RADIO FREQUENCY RADIATION: B LYMPHOCYTE CAPPING
Bioelectromagnetics, Vol. 4, No. 2, pp. 157-165 (1983b)

Szmigielski, S.
EFFECT OF 10-CM (3 GHZ) ELECTROMAGNETIC RADIATION (MICROWAVES) ON GRANULOCYTES IN VITRO
Ann. N.Y. Acad. Sci., Vol. 247, pp. 275-281 (1975)

Szmigielski, S., J. Jeljazewicz, and M. Wiranowska
ACUTE STAPHYLOCOCCAL INFECTIONS IN RABBITS IRRADIATED WITH 3-GHz MICROWAVES
Ann. N.Y. Acad. Sci., Vol. 247, pp. 305-311 (1975a)

3.5.2 IN VIVO STUDIES: EFFECTS OF EXPOSURES ON IMMUNOLOGICAL PARAMETERS

Investigations of immunological effects of RFR in vivo can be divided into those in which changes in specific immunological parameters were sought, the subject of this section, and those in which effects of RFR on the health of the subjects and their resistance to disease were studied, discussed in the next section.

Several studies were performed with Japanese quail as subjects. Hamrick et al. (1977) sham-exposed and exposed fertile Japanese quail eggs in 6x5 arrays for 24 hr/day during the first 12 days of embryology to 2.45-GHz far-field CW RFR at 5 mW/sq cm (SAR about 4 W/kg), and reared the birds for 5 weeks after hatching. At this age, the levels of antibodies against sheep red blood cells (SRBC) were determined before, and 4 days after, challenge with SRBC. The differences between antibody levels for the quail from RFR-exposed eggs and control-quail were not significant, either before or after challenge. Also, no significant differences were found in the weights of the bursa of Fabricius (source of B lymphocytes in birds) or the spleen.

In a teratological study of Japanese quail from eggs similarly exposed, McRee and Hamrick (1977) reported RFR-induced higher hemoglobin levels and lower monocyte counts but no statistically significant changes in hematocrits, red blood cells, total white blood cells, lymphocytes, heterophils, basophils, or eosinophils. However, the differences of mean temperature from egg to egg in the arrays were relatively large (up to 0.5 deg C), rendering it difficult to specifically associate the two positive findings with RFR exposure.

In a later investigation by this group, Galvin et al. (1981a) exposed eggs similarly and reared the quail for 22 weeks after hatching, along with nonexposed controls. From 6 weeks of age, the exposed quail were housed as male-female pairs in mating cages; control quail were housed similarily. In one set of experiments, the quail were immunized with chukar (partridge) red blood cells (CrRBC) at 22 weeks; blood samples were drawn on days 0, 4, and 7 following immunization and assayed for anti-CrRBC hemagglutinins (antibodies) as a measure of humoral response, and total and differential leukocyte counts were made on days 0 and 7. In another set of experiments, each quail was administered the mitogen PHA intradermally in one wing web and saline in the other wing web, and the ratio of skin thickness 18 hr after PHA injection to the thickness before injection was the indicator of cell-mediated immune potential.

The results showed that immediately prior to immunization, the exposed quail of both sexes had significantly higher levels of nonspecific antibodies, however, there were no significant differences in the levels of anti-CrRBC antibodies between exposed and control birds of either sex on days 4 and 7 after immunization. The PHA web index data yielded no significant differences between exposed and control males, but the mean for the exposed females was significantly greater than for the control females. In addition, the saline web index data showed no significant differences. The total and differential leukocyte counts were found

be significantly increased (leukocytosis) only in the exposed females. The investigators were unable to account for these response differences between the sexes. However, the occurrence of leukocytosis in this investigation (in which birds were immunized when 22 weeks old) and its nonoccurrence in the birds immunized when 5 weeks old (Hamrick et al., 1977) was attributed to the fact that the hematologic system of the adult bird differs from that of the neonatal bird.

Among early studies with mammals was that of Rotkovska and Vacek (1975), who exposed mice to 2.45-GHz CW RFR at 10 mW/sq cm for 5 min. Based on a prolate-spheroidal model of a mouse (Durney et al., 1978, pp. 97-99), the corresponding whole-body SAR was about 10 W/kg. Other mice were heated for 5 min in a ventilated chamber held at 43 deg C. Mean rectal temperatures increased by 2.3 and 2.5 deg C, respectively, for the two groups. The leukocyte counts for the circulating blood of both groups increased, reaching maxima at 4 and 7 days after treatment for those exposed to RFR and at 4 days for those heated in the chamber. This effect was accompanied by increases in the numbers of nucleated cells in the spleen and the bone marrow of the femur over the same time period after treatment.

Czerski (1975) exposed 100 mice to pulsed 2.95-GHz RFR (1-microsecond pulses, 1200 pps) at 0.5 mW/sq cm average power density (about 0.5 W/kg, Durney et al., pp. 97-99) for 6 weeks, and another 100 for 12 weeks (2 hr/day, 6 days/week). Following exposure, the mice were immunized by injection of sheep red blood cells (SRBC). For controls, 100 unexposed mice were immunized and 2 other groups of 100 each were exposed for 6 or 12 weeks but not immunized. Five of the mice in each group were then euthanized on days 4, 6, 8, 12, and 20. Sera were collected, lymph nodes were excised, suspensions of cells therefrom were prepared, and the percentages of lymphoblasts and plasmocytes in the latter were determined. The number of antibody-forming cells was determined as a measure of immune response. Also, serum hemagglutinins were estimated.

For the three immunized groups, the percentage of blast cells rose from an initial value of about 5%, reached maxima on day 6 after injection of SRBC, and diminished to approximately baseline values by day 20. The lowest maximum, about 27%, was for the unexposed group; the next at 32%, was for the group exposed for 12 weeks; and the highest, at 45%, was for those exposed for 6 weeks. Smaller rises to maxima on day 6 were obtained for the two nonimmunized groups, with the 6-week group again yielding a higher maximum than the 12-week group. The patterns for the percentage of plasmocytes and the number of antibody-forming cells were similar.

In another series, Czerski (1975) also exposed 12 rabbits to the same RFR at 5 mW/sq cm (at about 2.5 W/kg, Durney et al., 1978, p. 92) for 6 months. Each month, peripheral blood was obtained, lymphocyte cultures were prepared and incubated for 3 days at 37 deg C, and the percentage of blast cells was counted. The results showed an increase from about 5% initially to 9 and 12% respectively for months 1 and 2 of exposure, after which the percentage returned to baseline. A smaller increase, to

about 6%, was also seen for month 7 (1 month after exposure cessation) and a return to baseline for months 8 and 9.

In general, the results of this investigation indicate that in-vivo exposure to RFR at the frequency and power densities used does alter the immune system, but the significance of such findings with respect to possible RFR effects on the human immune system are difficult to assess.

Huang et al. (1977) exposed groups of five Chinese hamsters to 2.45-GHz RFR for 15 min/day on 5 consecutive days at power densities of 5, 15, 30, or 45 mW/sq cm. The whole-body SARs, measured calorimetrically in dead animals, were 2.3, 6.9, 13.8, and 20.7 W/kg. Control animals were sham-exposed. One hour after exposure, blood was drawn and cultured for 1 day if not mitogen-stimulated or for 3 days if stimulated with PHA.

Cultures not stimulated with PHA exhibited variation of Transformation Index (TI, the percentage of transformed cells relative to the total number) with power density. The curve was in the shape of an inverted U; values peaked at 30 mW/sq cm (13.8 W/kg) and then gradually returned to control values. Cell counts done when blood was collected showed no net gain of lymphocytes from other sources, such as the lymph nodes or the spleen, and no significant changes in differential leukocyte counts; these differential counts support the contention that RFR does not cause lymphocytosis. As discussed later, however, Liburdy (1977) reported RFR-induced complementary lymphopenia and neutrophilia in mice.

Regarding the inverted-U relationship between TI and power density for the nonstimulated cultures, the authors suggested that two unspecified controlling mechanisms may have been involved, one operating at lower power densities and the other that quenches the first at higher power densities. They stated that the quenching mechanism is probably related to the temperature of the animal, but indicated that it was not possible to discern whether the TI increases at 5 and 15 mW/sq cm (2.3 and 6.9 W/kg) were due to heating or some athermal RFR interaction. However, because SAR distributions in animals at 2.45 GHz are far from uniform, power densities as low as 5 mW/sq cm could have produced significant local internal heating. Other unknown factors may have contributed to the results. For example, a 0.2-deg-C decrease occurred in mean rectal temperature after sham exposure, an indication of some non-RFR-induced physiological change.

For cultures stimulated with PHA, Huang et al. (1977) found that the mean value of the Mitotic Index (percentage of cells in mitosis relative to the total number of lymphocytes) diminished from 3% for controls to about 0.04% and 0.05% for the 30 and 45 mW/sq-cm (13.8- and 20.7-W/kg) exposure groups, respectively.

The decrease of mean Mitotic Index with power density for PHA-stimulated cultures was significant, but equally interesting was that the large scatter of values for the controls (0 to 9%) also diminished rapidly with power density, tending to further confirm that RFR does

inhibit mitogen stimulated mitosis. However, the scatter was sizable for 5 mW/sq cm (2.5 W/kg), which can be taken as evidence that the effect was of thermal origin.

Huang and Modak (1980) exposed mice to 2.45 GHz RFR at [illegible] mW/sq cm [illegible] W/kg) 10 min/day for [illegible] days after which the spleens were removed and cells therefrom were cultured for [illegible] with or without the T cell mitogens PHA (Phytohemagglutinin A) or A or the B cell mitogen lipopolysaccharide (LPS). Tritiated thymidine, a radioactively labeled substance the uptake of which is a measure of DNA synthesis during cell proliferation, was added 4 hr before the end of the culture period. The cells were then harvested and assayed for thymidine uptake. Plots of uptake versus exposure duration showed biphasic or variable responses for cells from both mitogen stimulated and nonstimulated cultures from the RFR exposed mice. The investigators suggested that such variations could account for the differences in results from various laboratories. However, similar plots for the sham exposed mice also showed variations, evidently resulting from factors other than RFR, such as thread and rhythms and estrus cycle changes in female mice. Therefore, the proliferative effects of RFR per se could not be ascertained. In another part of the study, exposure at 5 mW/sq cm (2.5 W/kg) for 7 days (10 min/day) did not diminish the cytotoxic activity of lymphocytes on leukemic cells injected after or concurrently with the last exposure.

Hagan et al. (1981) concurrently sham exposed and exposed groups of 8 mice each to 2.88 GHz pulsed RFR (2 microsecond pulses at 100 pps) at average power densities of 5 or 10 mW/sq cm (2.25 or 4.50 W/kg).

Three groups were exposed at 5 mW/sq cm (2.25 W/kg), 7.5 hr/day for 10 days and blood samples were assayed for various hematologic and serum chemistry indices, including volume of packed red cells; counts of red cells, white cells, reticulocytes, and platelets; hemoglobin, protein, and triglyceride concentrations; and the number of nucleated femoral bone marrow cells (femoral marrow cellularity). The values of femoral marrow cellularity were higher for two of the three RFR-exposed groups than their corresponding sham-exposed groups, yielding a significantly higher ($p<0.01$) pooled mean than for the three sham-exposed groups. The differences between RFR- and sham-exposed groups in any of the other indices measured were nonsignificant.

Six groups were exposed at 10 mW/sq cm (4.50 W/kg), one group 7.5 hr/day for 10 days, two groups 3 hr/day for 20 days, two groups 7 hr/day for 27 days, and one group 7 hr/day for 51 days. Significant differences were obtained in several indices between some RFR-exposed groups and their sham-exposed groups, but no consistent pattern across groups. In the group exposed 7.5 hr/day for 10 days, mean bone marrow cellularity was reduced significantly ($p<0.05$), a finding opposite to that for those exposed at 5 mW/sq cm. Comparisons of all of the sham-exposed groups indicated relatively large variations among their mean values for the hematologic and serum-chemistry indices studied.

Ragan et al. (1983) also reported that no effects were seen on bone-marrow granulocyte/macrophage colony-forming units (CFU) after exposure at 5 mW/sq cm (2.25 W/kg). There was a significant increase in one of four groups exposed at 10 mW/sq cm (4.50 W/kg): the number of CFU for this group was larger than for its control group ($p<0.05$). However, as stated by the investigators, the coefficient of variation (about 40%) was more a reflection of large differences among animals than among plates from individual mice.

At 10 mW/sq cm (4.50 W/kg), there were no significant effects on in-vivo and in-vitro assays of cell-mediated immune functions. In addition, no exposure related histopathologic lesions were found in examination of several tissues and organs.

Lin et al. (1979c) exposed groups of 4 mice each to 148-MHz CW RFR at 0.5 mW/sq cm (0.013 W/kg) 1 hr/day, 5 days/week, for 10 weeks in a TEM cell beginning on the 4th to 7th day post-partum. Controls were sham-exposed. Ambient temperature and humidity were between 25 and 35 deg C and 35 to 65%, respectively. The mice were weighed daily from the beginning of exposure through the 10-week exposure period and weekly thereafter up to 600 days of age. The differences in weights between RFR and sham exposed mice at corresponding times were not significant.

Blood (less than 0.045 ml per sampling) was drawn from tail vessels at 28 and 70 days of age (during the 10-week exposure period) and at 100, 250, 300, 360, and 600 days of age (post-exposure). No significant differences between RFR-exposed and sham-exposed groups were found for hematocrit, hemoglobin, leukocyte counts or erythrocyte counts. There were also no significant differences in differential blood-cell counts (but only data on lymphocytes and segmented neutrophils were presented).

Wiktor-Jedrzejczak et al. (1977) exposed CBA/J mice to 2.45-GHz RFR in a waveguide at a mean SAR of 14 W/kg for either a single 30-min session or three such sessions, one per day, 3 days apart. Control mice were sham-exposed. Following exposure, the spleens were removed and tested for various effects of the RFR.

First, the relative numbers of T and B lymphocytes in the spleens of the RFR-exposed mice were compared with those in the control mice. The results indicated that the total numbers of T cells were unaffected by either the single-session or triple-session exposures. However, the single exposures produced statistically significant increases in the population of one subclass of B cells (complement-receptor-positive, or CR+) but not in another subclass of B cells (immunoglobulin-positive, or Ig+), whereas the triple exposures yielded increases in both types of B cells.

Next, spleen cells from RFR- and sham-exposed mice were cultured with various added T-cell-specific or B-cell-specific mitogens, and the numbers of cells undergoing blastic transformation were determined. Both single and triple exposures resulted in significant increases in blastic transformation of B cells but had nonsignificant corresponding

effects on T cells.

Last, mice were inoculated with the antigen SRBC, which induces the production of antibodies by B cells if T cells are also present, or with an antigen (DNP-lys-Ficoll) that does not require the presence of T cells for antibody production by B cells. The mice were then given triple-session RFR- or sham-exposures, after which their spleens were removed and assayed for antibody production. RFR-induced decreases of mean antibody production in response to both antigens were observed, but only the difference for SRBC was statistically significant.

Taken together, the results of Wiktor-Jedrzejczak et al. (1977) indicate that acute exposures to the thermogenic levels of RFR used can have weak stimulatory effects on splenic B cells but none on T cells. The authors reasoned that the observed increases in the numbers of CR+ B cells and of B cells undergoing blastic transformation either were manifestations of RFR-induced proliferation of the B-cell populations, which would be consonant with the findings of Stodolnik-Baranska (1967, 1974) and of Czerski (1975), or were a result of RFR stimulation of immature B cells already present. In a later paper, Wiktor-Jedrzejczak et al. (1980) presented data that support the latter hypothesis.

Sulek et al. (1980) reported on threshold values for the increases in CR+ B cells. They exposed groups of mice once to 2.45-GHz RFR at a mean SAR of 11.8 W/kg for 5 to 120 min or for 30 min at SARs from about 2 to 18 W/kg, and determined the numbers of CR+ cells on days 3 and 6 after exposure. They obtained significant increases in CR+ cells on day 6 for single exposures at 11.8 W/kg for a minimum of 15 min, and on day 3 (as well as 6) for single exposures of 30 min at 5.0 W/kg, or a threshold energy absorption of about 10 J/g. They also observed that multiple exposures at subthreshold values were cumulative if the exposures were done within 1 hr of one another but did not increase the numbers of CR+ cells if spaced 24 hr apart, even if the sum of the energy-absorption values exceeded the threshold.

Schlagel et al. (1980) presented results indicating that the RFR-induced increases in CR+ B cells are dependent on genetic factors: Strains of mice having the histocompatibility H-2k haplotype (e.g., CBA/J) showed marked increases in CR+ cells due to RFR exposure, whereas those bearing H-2a, H-2b, and H-2d haplotypes did not. Moreover, athymic H-2k mice responded similarly to RFR exposure, indicating that the effect was not regulated by the T-cell population.

Wiktor-Jedrzejczak et al. (1981), noting the genetic control over the increases in CR+ cells found by Schlagel et al. (1980), suggested that the effect might be mediated by a humoral factor. Diffusion chambers permeable to soluble factors but not cells were surgically implanted in peritoneal cavities of host CBA/J mice. The authors then either derived donor CBA/J-mouse spleen cells from mice exposed to 2.45-GHz RFR at 14 W/kg for 30 min and cultured the cells in diffusion chambers within sham-exposed mice or derived donor CBA/J-mouse spleen cells from sham-exposed mice and cultured them in chambers within mice similarly exposed

to the RFR. For controls, cells from sham-exposed donors were also cultured in chambers within sham-exposed host mice. Assays for CR+ spleen lymphocytes circulating in the host mice and within the implanted diffusion chambers were performed 6 days after RFR- or sham-exposure.

For either the donor or the recipient mice exposed to the RFR, the mean frequencies of CR+ cells, both circulating in the hosts and within the diffusion chambers, were significantly higher than their respective mean control values. These results support the hypothesized existence of a humoral factor and indicate that the effect is not due to RFR-induced alterations of CR+ lymphocyte circulation patterns.

Smialowicz et al. (1981c) exposed CBA/J mice 10-12 weeks old once to 2.45-GHz CW RFR at 15, 20, 30, or 40 mW/sq cm (11, 14, 22, and 29 W/kg) for 30 min in an anechoic chamber having an ambient temperature held constant at 22 deg C and 50% relative humidity. (The authors stated that the mice exposed at 40 mW/sq cm were clearly under thermal stress and that a 60-min exposure at this power density is lethal.) Six days later, the percentage of CR+ spleen cells and the number of nucleated spleen cells were determined. No significant differences in these two endpoints were found between sham-exposed mice and mice exposed at any of the RFR levels. Thus, Smialowicz et al. (1981c) could not confirm the RFR-induced CR+ increases found by Wiktor-Jedrzejczak and coworkers.

On the assumption that older mice may be more responsive, Smialowicz et al. (1981c) exposed mice 14, 16, and 24 weeks old at 30 or 40 mW/sq cm for 30 min. Only the 16-week-old group exposed at 40 mW/sq cm yielded significantly higher percentages of CR+ cells and smaller numbers of nucleated spleen cells than the corresponding group of sham-exposed controls. The authors suggested that the internal SAR distributions in mice exposed in their anechoic chamber were considerably different than for mice exposed at the same whole-body SARs in the waveguide system used by Wiktor-Jedrzejczak and coworkers.

Liburdy (1977) exposed rats in a TEM cell to 26-MHz CW RFR at field intensities of 5780 V/m and 6.71 A/m for 4 to 7 min to induce a body-temperature increase of 2-4 deg C. The author stated that the value of ExH was 8.62 W/sq cm and that the whole-body SAR was 23 W/kg. Control rats were sham-exposed. Other rats were heated in a vented, dry-air oven at 79 deg C for 8 to 12 min to match the body-temperature increases produced by the RFR. To induce inflammatory responses, SRBCs were then subcutaneously injected into one footpad of each rat and saline into the contralateral footpad. The thicknesses of both footpads were measured 4 hr later. The footpads of the sham-exposed rats showed a mean thickness increase of about 0.23 cm compared with about 0.01 cm for the saline-injected footpads of the same rats. By contrast, the SRBC-injected footpads increased only about 0.18 cm for the rats treated with warm air, and about 0.10 cm for the RFR-exposed rats. Thus, RFR exposure and warm-air treatment yielded significant suppression of SRBC-induced inflammatory response, but suppression was greater for the RFR.

In similar experiments with mice, Liburdy (1977) obtained lymphocyte,

neutrophil, and total leukocyte counts immediately before and at regular intervals after sham-exposure or exposure to 26-MHz RFR at the same E and H levels (ExH=8.62 W/sq cm), for which the whole body SAR was 12.9 W/kg, or to warm-air treatment to produce comparable body-temperature increases. It should be noted that this SAR is at variance with those for the mouse cited in Liburdy (1979), discussed below. Inflammatory responses were then induced by incision across a tail vein. Both sham exposure and warm-air treatment yielded significant leukocytosis, which persisted for about 96 hr. Differential counts were made of circulating lymphocytes and neutrophils, which yielded about twofold increases for both, with no significant differences between the two treatments. By contrast, pronounced lymphopenia and complementary neutrophilia that summed to a substantially constant total leukocyte count over the 96 hr period were obtained for the RFR-exposed mice. Maximum lymphopenia and neutrophilia (both fourfold changes from initial values) occurred 3 hr after treatment, followed by gradual diminution of both effects during the remainder of the period.

In a later study, Liburdy (1979) exposed mice to 26 MHz RFR at 80 mW/sq cm, corresponding to 5.6 W/kg ("thermogenic" RFR), for 15 min. These exposures produced core-temperature increases of 2 to 3 deg C. For comparison, mice were heated in a dry air oven at 61 deg C for the same period to obtain approximately the same increase in core temperature. Lymphopenia and neutrophilia were evident in the RFR-exposed mice, effects that persisted for about 12 hr after exposure. These effects could be sustained and the recovery period prolonged by additional RFR exposures at 3-hr intervals. By contrast, the effects were only slight for the mice heated in the oven. A qualitatively similar time course of sustained peripheral-blood lymphopenia and neutrophilia was obtained by a single injection of the glucocorticosteroid methyl prednisolone sodium succinate, but the injection also led to a decrease in total leukocyte population.

The effects were absent for mice exposed to 26-MHz RFR at 50 mW/sq cm or to 5-MHz RFR at 800 mW/sq cm, both of which yielded a whole-body SAR of 0.36 W/kg ("nonthermogenic" RFR) or about one-sixteenth of the SAR used previously. Because heating may result in significant stress, Liburdy determined the plasma corticoid levels after acute and chronic (longer-term, lower-level) RFR exposure, and found about a threefold increase in corticoid level relative to controls, whereas acute and chronic warm-air heating produced modest, statistically insignificant increases.

Because steroid injection yielded results qualitatively similar to those for the thermogenic RFR, Liburdy concluded that a causal relationship exists between RFR hyperthermia, steroid release, and alterations of lymphocyte distribution and function. The suggested mechanisms involves RFR stimulation of the hypophyseal-hypothalamic-adrenal axis through heating, which triggers release of adrenal steroids that act directly on the lymphocytes to alter their distribution and function.

Also ascertained in this study was delayed type hypersensitivity (DTH), done by sensitizing mice with SRBC by injection, challenging the mice 4-5 days later by SRBC injection into the right rear footpad and saline injection into the left rear footpad, and measuring the swelling of the right footpad relative to the left one 24 hr after challenge. The mice were chronically exposed to the thermogenic RFR or warm air from 5 days prior to sensitization to the day of challenge. The warm air treatment yielded DTH results comparable to those for sham exposed controls, but chronic RFR exposure markedly depressed the DTH response.

Liburdy (1980) injected mice with radioactively labeled (^{51}Cr) spleen lymphocytes and sham exposed or exposed the mice to far field 2.6 GHz CW RFR in an anechoic chamber for 1 hr at 5 or 25 mW/sq cm (3.8 or 19 W/kg) immediately after injection. Other injected mice were heat treated at 41 deg C for 1 hr. Rectal temperatures were monitored continuously. At 1, 6, or 24 hr after injection, the lungs, liver, spleen, and long bones of the rear legs were removed and relative populations of lymphocytes in those tissues were determined by scintillation counting. For positive controls, other mice were injected with methyl prednisolone sodium succinate in lieu of RFR or warm air treatment.

Exposure at 25 mW/sq cm (19 W/kg) produced a core temperature increase of 2 deg C during the first 15 min, to a thermoregulatory plateau of 39 deg C. Heating at 41 deg C yielded the same plateau but at a slower rate of rise. Exposure at 5 mW/sq cm (3.8 W/kg) did not increase the core temperature. The lymphocyte counts indicated that normal lymphocyte migration patterns were obtained for the mice exposed at 5 mW/sq cm or heated to 41 deg C. However, for the mice exposed at 25 mW/sq cm, the number of lymphocytes that normally migrate from the lungs to the spleen decreased by 37% and the number of lymphocytes entering the bone marrow increased threefold. Qualitatively similar results were obtained for the steroid-treated group. Liburdy suggested that RFR at relatively high levels (e.g., 25 mW/sq cm or 19 W/kg) can affect the immune system indirectly as a nonspecific stressor that induces steroid release.

Guy et al. (1980b) sham-exposed and exposed four rabbits each to 2.45-GHz CW RFR for 23 hr/day on 180 consecutive days. The power densities at the head and body were 10 and 7 mW/sq cm, respectively; the estimated peak SAR in the head was 17 W/kg, and the average SAR of the whole body was 1.5 W/kg. The eyes were examined periodically, and no differences were found between the two groups. Also evaluated were hematologic (as well as other physiological) parameters, and the results for 0, 1.5, 3, 4.5, and 6 months of exposure were presented. The differences in values for RFR- and sham-exposed animals were found to be nonsignificant except for a decrease in the percentage of eosinophils at 6 months, but the investigators noted that this parameter varies widely among animals.

McRee et al. (1980) did hematologic and clinical-chemistry evaluations of the same animals (in another laboratory) shortly after completion of exposure and 1 month later, at which time the animals were euthanized and necropsies were performed. Again, the mean eosinophil percentage at completion of exposure was lower for the RFR- than sham-exposed rabbits;

however, there was no significant eosinophil depression 1 month after exposure. Regarding clinical chemistry values, the only statistically significant results at completion of exposure were increases in albumin and calcium. However, 1 month after completion of exposure, the mean total globulin percentage had increased and the mean albumin percentage had decreased, both nonsignificantly, but the ratio of the latter to the former showed a statistically significant decrease.

At necropsy, tissue examinations showed no lesions attributable to RFR exposure. Samples of spleen tissue were cultured, stimulated with the mitogens PHA, Con A, or pokeweed mitogen (PMW, a mitogen that stimulates both T and B lymphocytes), each in three different concentrations, and assessed for response by uptake of tritiated thymidine. Lower responses for the RFR exposed animals were obtained with all three mitogens, but the differences were statistically significant only for PMW (at all three concentrations).

Smialowicz et al. (1979a) exposed rats to 2.45 GHz RFR at 5 mW/sq cm for 4 hr/day, 7 days/week, on day 6 of pregnancy until term. On birth, pups were exposed until age 20 days; then half of these were exposed until age 40 days. Corresponding numbers of pregnant rats and pups were sham exposed for controls. The mean SARs for the pups, determined by twin well calorimetry, decreased with age from 4.7 to 0.7 W/kg due to growth. Blood counts were made at ages 20 and 40 days, and blastogenic responses of blood and lymph node lymphocytes were determined by measuring uptake of tritiated thymidine after stimulation of cell cultures with T and B cell mitogens. Two such experiments with distinct exposure arrangements were performed. The mean leukocyte counts at 20 days were found to be significantly lower for the RFR-exposed pups than for the controls in the first experiment but not in the second, and the values were not significantly different from controls at 40 days in either experiment. The results for the mitogen-stimulated cultures were widely scattered, with no consistent pattern evident. Increases in thymidine uptake were seen in several cases, mostly for the cultures from the 40-day-old rats; such results are difficult to interpret because the mean SAR had dropped by more than a factor of two relative to that at age 20 days, and by a factor of five since the first few days of exposure.

Galvin et al. (1984) exposed groups of 12 pregnant CD-1 mice to 2.45-GHz CW RFR at 30 mW/sq cm (22 W/kg) for 8 hr/day during gestation days 1-6 (preimplantation embryogenesis) or 6-15 (organogenesis), to study the effects of such exposure on hematopoiesis during these periods. The exposures, performed in an anechoic chamber at an ambient temperature of 22 deg C and 55% relative humidity, produced a mean rectal-temperature increase of 2 deg C. Therefore, a group was sham-exposed at 32 deg C and 55% humidity to obtain a comparable rise in rectal temperature, and a control group was sham-exposed at 22 deg C.

On gestation day 18, the authors obtained samples of peripheral blood from the tail and bone marrow from the sternum and assayed the blood samples for total-leukocyte and differential-leukocyte counts and the bone-marrow samples for erythroid- and myeloid mitotic indices. They

found no significant differences in hemopoietic results between the two sham groups or between the RFR and sham groups.

Smialowicz et al. (1981b) performed a study having several biological endpoints. They exposed 20 time-bred pregnant rats to 100-MHz CW RFR in a transmission-line system at about 22 deg C ambient temperature and 50% relative humidity for 4 hr daily from day 6 of pregnancy to parturition. On birth, four male pups of each litter were exposed for 4 hr each day of the first 14 days at 27 deg C (approximate nest temperature) and then at 22 deg C for the remainder of the exposure regimen. Two pups of each exposed litter were removed for tests at age 20-22 days and a third pup at 40-42 days; the remaining pup was exposed until 97 days of age. The SARs varied with body mass, with the mean ranging from 2.02 W/kg for the pregnant dams to 2.96 W/kg for the neonatal rats, and intermediate SARs for the pups as they grew. Another group of 20 pregnant rats and their pups were sham-exposed but otherwise similarly treated.

The blood samples taken at ages 22 and 42 days showed no significant differences between RFR- and sham-exposed rats in: erythrocyte and leukocyte counts; differential counts of lymphocytes, macrophages, and polymorphonuclear cells; hematocrit; or hemoglobin. There were also no significant differences in lymphocyte response to stimulation by T- or B-cell mitogens. The pups removed at age 22 days were immunized with purified pneumococcal polysaccharide, and blood samples taken 5 days later were assayed for serum antibody titers. The differences between samples from RFR- and sham-exposed pups were not significant.

During the exposure regimen, the mean body weight of RFR exposed pups was consistently larger than for the sham-exposed pups at corresponding ages, but the differences were generally nonsignificant. Differences in ages for startle response and righting reflex were also nonsignificant, as were locomotor activity in a residential maze at ages 35 and 84 days. However, the mean age for complete opening of both eyes of RFR-exposed pups was almost 1 day older than for sham-exposed pups, a finding that was consonant with the larger sizes of the RFR-exposed pups.

At 90 days of age, each RFR- and sham-exposed rat (male) was mated with a pair of normal, virgin, unexposed females for 1 week. Dominant lethal assays of the females 11 days later yielded no significant differences in preimplantation losses or the numbers of live fetuses between the two groups, indicating that RFR-exposure of the males was not mutagenic.

Regional brain weights of rats, determined at ages 22, 40, and 90 days, showed that the mean weight of the medulla oblongata of the RFR-exposed rats was significantly larger than for the sham-exposed rats at age 40 days but not at 22 or 90 days. No other significant regional-brain-weight differences were found. Acetylcholinesterase (AChE) activity was lower in the striatum and medulla of the 22-day-old RFR-exposed rats and in the midbrain of the 40-day-old rats, but no significant differences in AChE activity were found in any brain region of the 97-day-old rats. The authors surmised that these transient

changes may have been due to local alterations of cation concentrations.

Smialowicz et al. (1981d) exposed 16 rats individually in circularly polarized waveguides to 970-MHz RFR for 22 hr/day at 2.5 W/kg for 69-70 consecutive days. Another group of 16 rats was similarly sham-exposed. Blood samples were taken from eight rats of each group on day 69, after which the rats were euthanized and their spleens were removed. The remaining rats were treated in the same manner on day 70.

There were no significant differences between RFR- and sham-exposed rats in erythrocyte count, leukocyte count, mean cell volume of erythrocytes, hematocrit, or hemoglobin concentration, or in differential leukocyte counts of lymphocytes, monocytes, eosinophils, or polymorphonuclear leukocytes. Also, spleen cells removed from the RFR- and sham-exposed rats and cultured with various mitogens did not show any significant differences in responses. However, blood serum chemical analysis showed levels of triglyceride, albumin, and total protein concentration that were significantly higher for the RFR-exposed group. The higher levels of albumin and protein concentration were within the normal ranges for this strain of rat and were not consonant with the absence of changes in erythrocyte assays, indicating that the rats may have been dehydrated. The authors noted that an SAR of 2.5 W/kg is about half the basal metabolic rate of an adult rat, and suggested that the increases in triglyceride level may have been due to thermal stress induced by the exposure to RFR. At 970 MHz, there probably were regions within the rat where the local SARs were much larger than 2.5 W/kg, and such higher SARs could have affected the endocrinological system of the rat (see Section 3.6.2).

Smialowicz et al. (1982a) exposed pregnant rats to 425-MHz CW RFR within a temperature-controlled multimode rectangular strip transmission line for 4 hr/day from day 12 of gestation to parturition. Four male pups born to each dam were then exposed for 20-21 days of age, at which time 2 pups per litter were bled and euthanized. The remaining 2 pups per litter were exposed until 40-41 days of age, bled, and euthanized. The SARs ranged from 3.1 to 6.7 W/kg. Equal numbers of dams and pups were sham-exposed. At selected times, rats were weighed to determine if the RFR exposure affected growth. There were no significant differences in pup weight at each age.

The blood samples collected were assayed for erythrocyte count, total and differential leukocyte counts, mean cell volume of erythrocytes, hematocrit, and hemoglobin concentration. No consistent changes in the peripheral blood picture were observed between RFR- and sham-exposed rats. Cultures of blood and lymph-node lymphocytes were stimulated with the T-cell mitogen phytohemagglutinin (PHA) or concanavalin A (Con A), or with the B-cell mitogen lipopolysaccharide of E. coli (LPS) or purified protein derivative of tuberculin (PPD), or with nonspecific pokeweed mitogen (PWM), each in several concentrations. Tritiated thymidine was added to each culture 24 hr before harvesting and its uptake in DNA as a measure of cell proliferation was determined by liquid scintillation counting.

In two experiments, the results for RFR-exposed pups showed consistently significant increases in stimulated lymph-node lymphocytes for all the mitogens, but nonsignificant changes for blood lymphocytes. Also, the nonstimulated cultures did not yield significant differences between the RFR- and sham-exposed pups. However, the results for a replicate of the two experiments showed no significant differences between RFR- and sham-exposed rats in lymph-node lymphocytes; the only significant result was an increase of PHA-stimulated blood lymphocytes for pups 40-41 days old.

Smialowicz et al. (1982b) exposed 5x5 arrays of time-bred pregnant mice to 2.45-GHz CW RFR at 28 mW/sq cm (16.5 W/kg) for 100 min daily from day 6 to day 18 of pregnancy. At 3 and 6 weeks of age, the offspring were assessed for development of primary immune response to SRBC; lymphocyte proliferation by in-vitro stimulation with PHA, Con A, PWM, and LPS; and natural killer (NK) cell activity against subline YAC-1 lymphoma cells in vitro. No consistent significant difference between RFR- and sham-exposed mice was observed in any of the endpoints.

Deschaux et al. (1984) discussed two experiments in which they exposed male BALB/c mice within individual containers concurrently in groups of 20 to 2.45-GHz CW RFR at 5, 10, 15, or 20 mW/sq cm (5, 7.5, 11, or 14 W/kg) 4 hr/day for 4 days within an anechoic chamber under controlled environmental conditions. Such exposures yielded no significant core-temperature increases. Other groups were similarly sham-exposed. After treatment, the mice were euthanized and spleen lymphocytes were assayed for T-cell cytotoxicity against syngeneic-virus-SV40-induced mouse sarcoma and for NK-cell activity against human B16-melanoma cells.

Both experiments yielded a significant decrease, relative to controls, in T-cell cytoxicity against SV40 sarcoma for exposure at 20 mW/sq cm (14 W/kg) but not at the lower power densities. By contrast, both experiments showed a significant increase in NK-cell activity against melanoma cells for exposure at 15 mW/sq cm (11 W/kg) but not at 20, 10, or 5 mW/sq cm (14, 7.5, or 5 W/kg). The authors noted that cytotoxic T cells react preferentially against histocompatible target cells, whereas NK-cell activity appears to be independent of antigenic sensitization. However, they did not offer any comments on why the increase in NK-cell activity occurred at 15 mW/sq cm but not at the higher or lower levels.

Smialowicz et al. (1982c) exposed groups of female BALB/C mice to either CW or pulse-modulated (1-ms pulse width, 250 pulses/s) 425-MHz RFR in a rectangular strip-transmission line at average forward powers of 78, 17.7, or 5 W for CW and 17.7, 5, or 1.25 W for pulse modulation. For a forward power of 70 W, the mean SAR, measured by twin-well calorimetry, was 7.7 W/kg. No differences in the mitogen-stimulated response of lymphocytes or in the primary antibody response to sensitization with polyvinylpyrrolidone (PVP) or SRBC were observed between RFR- and sham-exposed mice, nor between mice exposed to CW and pulse-modulated RFR.

Smialowicz et al. (1983) sham-exposed or exposed mice for 1.5 hr/day on 2 or 9 consecutive days in diamond arrays of 4 mice each to 2.45-GHz

CW RFR at 5, 15, or 30 mW/sq cm (3.5, 10.5, or 21 W/kg). Hydrocortisone or saline was injected in mice for positive controls. Spleen cells from treated mice were assayed in vitro for NK-cell activity by cytotoxicity against Cr-51-labeled mouse lymphoma (YAC-1) cells. Significant but transient suppression of NK-cell activity was observed for mice exposed at 30 mW/sq cm (21 W/kg) but not at 15 or 5 mW/sq cm (10.5 or 3.5 W/kg). NK-cell activity returned to normal within 24 hr after the last exposure to RFR. In-vivo NK-cell activity, determined by injecting mice with I-125-labeled YAC-1 cells and measuring tumor cell clearance from lungs and spleens, was suppressed in mice exposed at 30 mW/sq cm (21 W/kg), with return to normal several days after the last exposure. Injection of hydrocortisone caused suppression of NK cell activity both in vitro and in vivo.

Spleen-cell suspensions were also stimulated with PHA, LPS, and PWM, and the amounts of tritiated thymidine into DNA were determined. There were no consistent differences in mitogenic response between RFR and sham-exposed mice. The phagocytotic capabilities of resident peritoneal macrophages against chicken erythrocytes, determined immediately after last exposure, were enhanced for mice exposed at 30 mW/sq cm (21 W/kg).

Yang et al. (1983) concurrently sham-exposed and exposed groups of hamsters to far-field 2.45-GHz CW RFR at 15 mW/sq cm (8.0 W/kg) for 1 hr/day on 5 successive days or once for 1 hr at 25 mW/sq cm (13.3 W/kg) in an anechoic chamber at an ambient temperature of 22.5 deg C and 55% relative humidity. Some groups given the five successive daily sham-exposures or exposures at 15 mW/sq cm were intraperitoneally immunized with vaccinia virus immediately after the second exposure. Some groups given the single exposure were immunized 4 days before exposure. Other groups were not immunized. After exposure, populations of NK cells were prepared from the spleens of the hamsters and tested as effector cells against targets consisting of Cr-51-labeled cultures of baby hamster kidney (BHK) cells, BHK cells infected with herpes simplex virus (BHK-H), transformed hamster embryo fibroblasts (PARA-7), or PARA-7 cells infected with herpes (PARA-7-H), using gamma counting for the assays.

The multiple exposures at 15 mW/sq cm (8.0 W/kg) had no significant effect on natural levels of spleen-cell NK activity against BHK targets. Similarly, repeated exposure at 15 mW/sq cm over a 5-day period did not have any demonstrable effect on the induction of spleen NK activity by vaccinia-virus immunization; comparable levels of NK activity were induced in untreated and RFR-exposed animals.

By contrast, the single exposures at 25 mW/sq cm (13.3 W/kg) caused a significant suppression in induced spleen NK activity. Similar but less marked decreases in NK activity were seen in the sham-exposed animals. Moreover, the effects of sham-exposure were not predictable and appeared to represent large individual animal variations in response to stress factors. Depressed spleen NK activity was evident as soon as 4 hr post-RFR treatment and returned to normal levels by 8 hr.

Core temperatures were measured in hamsters under various conditions,

[illegible] in each animal [illegible] repeated stress from the [illegible] In one group of untreated hamsters [illegible] temperatures were measured in the animal room. In another group, temperatures were taken immediately after transportation from the animal room to the exposure room for treatment. The temperatures in these groups that were RFR or sham exposed for 2 hr or more were measured immediately after treatment. Subgroups treated for 30 min were removed at various times to determine cooling rates after cessation of treatment. The temperatures in groups transported to the exposure room but otherwise not treated (ten rats as a "minimum handling" group) were used as controls in all experiments.

The results indicated that the single exposures at 25 mW/sq cm (13.3 W/kg) for 2 hr increased the mean core temperature by about 1 deg C and initiated a transient increase in serum glucose (stress) level and a transient suppression of NK cell activity. Accompanying these effects were transient lymphopenia and neutrophilia findings consistent with the results of earlier studies. Sham exposed rats, RFR and mice injected with corticosteroids, but were at variance with the NK cell results of Smialowicz et al. (1981) discussed above.

In another study by this group, Rama Rao et al. (1981) found that single 2 hr exposures of hamsters at 25 mW/sq cm (13.3 W/kg) caused activation of peritoneal macrophages that were significantly more viricidal to vaccinia virus than macrophages from sham exposed or minimum handling controls. However, RFR exposure for 2 hr at 25 mW/sq cm (13.3 W/kg) did not activate macrophages and 40 mW/sq cm (21.3 W/kg) was fatal to some hamsters. Macrophages from hamsters exposed at 25 mW/sq cm (13.3 W/kg) became activated as early as 6 hr after exposure and remained activated for up to 12 days. Such activation by exposure to RFR paralleled the macrophage activation after vaccinia virus immunization. Activated macrophages from vaccinia-immunized hamsters did not differ in their viricidal activity for hamsters that were RFR or sham exposed.

Average maximum core temperatures in the 25 mW/sq-cm (13.3 W/kg) and sham groups were 40.5 deg C and 38.4 deg C, respectively. Heating of macrophages in vitro to 40.5 deg C was not as effective as exposure to RFR in vivo in activating macrophages to the viricidal state.

The macrophages from minimally-handled, sham-exposed, and RFR-exposed hamsters were not morphologically different from one another, and they all phagocytosed India-ink particles. Moreover, the cytotoxicity of the macrophages from vaccinia-immunized hamsters for virus-infected or noninfected target cells was not suppressed in the 25-mW/sq-cm group relative to sham-exposed controls, an indication that the peritoneal macrophages were not functionally suppressed or injured by RFR-induced hyperthermia.

The comparisons of minimum-handling groups with sham-exposed groups by Yang et al. (1983) indicated that the sham-exposed and RFR-exposed hamsters were subjected to some degree of non-RFR-related stress that probably affected the functions of their immune systems, but to extents that

were difficult to quantify. This statement also applies to the study by Rama Rau et al. (1983). For this reason, the effects of RFR-exposure per se in both studies must be deduced from comparisons of the results from the RFR- and sham-exposed animals only, under the tacit assumption that their non-RFR stresses were comparable. On this basis, the results on PM viricidal activity, against vaccinia, of nonimmunized hamsters exposed at 25 mW/sq cm (13.3 W/kg) and the lack of effect at 15 mW/sq cm (8.0 W/kg) appear unequivocal.

Rama Rau et al. (1984) also found that exposure of hamsters to 2.45-GHz RFR at 25 mW/sq cm (13.3 W/kg) for 1 hr activated peritoneal macrophages to a viricidal state that aborted vesicular stomatitis virus (VSV) in vitro and rendered hamsters more resistant to in-vivo lethal challenge with VSV.

Rama Rau et al. (1985) studied the effects of single exposure of groups of 6 hamsters each for 1 hr to 2.45-GHz RFR at 0, 5, 10, 15, or 25 mW/sq cm (0, 2.7, 5.3, 8.0, or 13.3 W/kg) on the IgM-antibody response of spleen cells to SRBC. Some RFR- and sham-exposed groups of hamsters were immunized by injection with SRBC immediately after treatment; for comparison, other groups were injected with saline. Four days after injection of SRBC or saline, the spleens were removed and assayed for IgM-antibody plaque-forming cells (PFC).

The saline-injected sham- and 25-mW/sq-cm (13.3-W/kg) groups yielded no PFC; however, the PFC for the SRBC-injected 25-mW/sq-cm (13.3-W/kg) group were about threefold higher than for the SRBC-injected sham-exposed group. At 5 and 10 mW/sq cm (2.7 and 5.3 W/kg), there were no significant differences in PFC between SRBC-injected RFR- and sham-exposed groups. At 15 mW/sq cm (8.0 W/kg), however, the PFC for the RFR group were about 35% higher than for the sham group, a significant rise.

In another experiment, PFC assays were performed for SRBC-injected 25-mW/sq-cm and sham-exposed groups on successive days after exposure. PFC levels for the sham group were highest between days 4 and 5 and returned to baseline values by day 9. For the RFR group, the levels of PFC were elevated significantly only on days 4 and 5. Thus, the RFR augmented the IgM-antibody response to SRBC but not its onset or duration. In an analogous experiment, the period between exposure and injection with SRBC was varied. Significantly higher PFC levels were found for those injected as long as 4 days after exposure at 25 mW/sq cm (13.3 W/kg). In a converse experiment, exposures at 25 mW/sq cm (13.3 W/kg) were done immediately, and on days 0.5, 1, 2, 3, and 4, after SRBC injection. The results showed maximum PFC level for immediate exposure and a monotonic decrease in level to baseline for exposure on day 4.

For 1-hr exposure at 25 mW/sq cm, the mean core temperature was [illegible] deg C. Sham-exposure yielded a mean core temperature of 38.[illegible] deg ascertain whether the results above were thermally induced, a group of hamsters was exposed for 1 hr in an environmental chamber to an ambient temperature of 41 deg C, which yielded a mean core temperature [illegible] deg C, and another group was exposed to 37 deg C (resulting mean [illegible]

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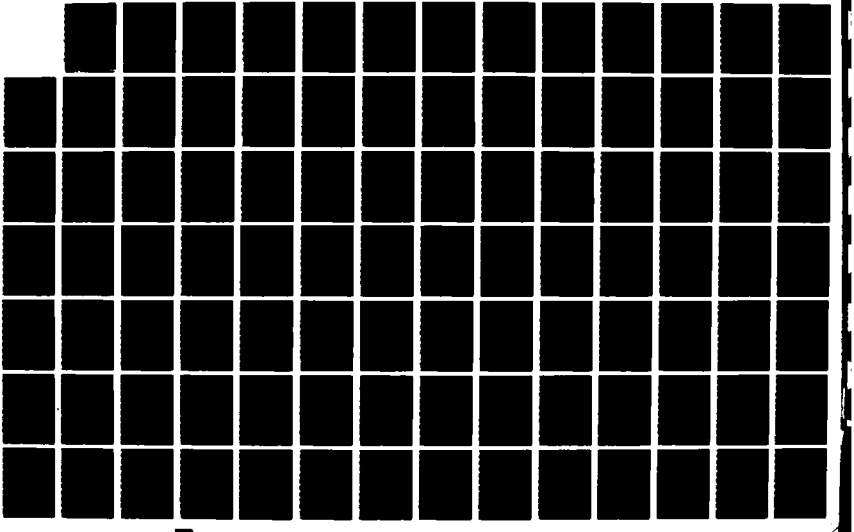

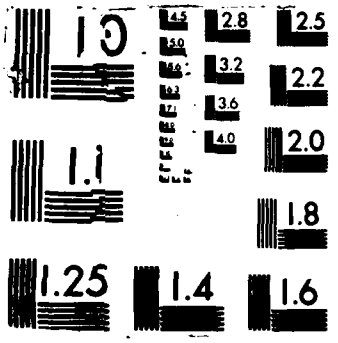
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temperature not stated). The hamsters were injected with SRBC right after treatment and as before, their spleens were assayed for PFC 4 days later. The mean PFC levels for the 41-deg-C and 37-deg-C groups were higher than the mean control level by factors of about 2.27 and 1.52, respectively, with both differences significant, thus supporting the thermal hypothesis.

In the first of three studies, Ortner et al. (1981a) concurrently exposed rats in groups of 8 to 2.45-GHz CW RFR for 8 hr at 2 or 10 mW/sq cm (0.44 or 2.2 W/kg). Within 5-15 min after exposure, 6 of the 8 rats of each group were decapitated, and peritoneal mast cells were extracted and divided into two equal subgroups, one subgroup for determining the histamine release from mast cells induced by Con A and the other for the histamine release induced by compound 48/80 (a condensation product of p-methoxy-N-methyl phenethylamine and formaldehyde).

Histamine secretion was determined as the percentage released into each supernatant based on the total histamine originally present in each aliquot of cells. Cell viability was determined as the percentage of peritoneal cells that excluded trypan blue. The percentage of mast cells was calculated by counting those stained metachromatically with toluidine blue. The average mast-cell size for each group was measured microscopically with an eyepiece micrometer grating.

The results for several mast-cell parameters showed no significant differences among the groups exposed at 0, 2, and 10 mW/sq cm in percentage of cell viability, percentage of cells, amount of histamine per cell, and cell diameter (about 12.5 microns, with a range 18-10 microns). These findings were in accord with previous in-vitro RFR data (Sawicki and Ostrowski, 1968; Ortner and Galvin, 1980). The authors noted that the absence of effect on toluidine blue metachromasia or histamine content per cell indicated that normal uptake, metabolism, and storage of histamine and heparin were unimpaired, a finding contrary to that of Sawicki and Ostrowski (1968), who reported reduced metachromasia after 10 min of in-vitro exposure through air at 3 mW/sq cm. Ortner et al. (1981a) never found giant mast cells (30-48 microns in diameter), an effect reported by Valtonen (1966a, 1966b) for RFR close to the LD-50 level. The absence of this effect was in agreement with the in-vitro findings of Sawicki and Ostrowski (1968) and Ortner and Galvin (1980), leading Ortner et al. to suggest that this effect may only occur in vivo under conditions approaching lethality.

The other two rats of each group were anesthetized with pentobarbital immediately after RFR- or sham-exposure and their aortas were cannulated for blood-pressure measurements. Blood pressures and heart rates were recorded. After stabilization (1 hr), 48/80 was injected intravenously simultaneously into both rats and they were monitored for 2 hr. The authors stated: "The initial blood pressures and heart rates did not differ between the control and irradiated groups. The hypotensive response to 48/80 varied among the individuals; however, there were no significant differences due to irradiation of the animals."

The second study, by Abhold et al. (1981), was on the effects of RFR exposure on thyroid and adrenal hormones, and is discussed in Section 3.6.2. In the third study, Galvin et al. (1982b) similarly exposed groups of rats, after which the rats were decapitated and blood samples were collected for determination of hematocrit, hemoglobin, red and white cell count, and differential white cell percentages. The total red and white cell counts were not affected by 8-hr exposure at either 2 or 10 mW/sq cm (0.44 or 2.2 W/kg), nor were blood-hemoglobin levels or percentages of lymphocytes and neutrophils relative to those of the sham group. The other cell types were also unchanged by RFR. None of the serum biochemistries assayed (beta-glucuronidase, alkaline phosphatase, total protein concentration, lactic dehydrogenase activity, sodium and potassium concentrations, and cholinesterase), was affected by either RFR level.

Wong et al. (1985) noted that relatively few studies had been conducted in the HF band (3-30 MHz), that most such studies indicated that for acute exposure, thermogenic levels of RFR were necessary to obtain significant effects, but that possible effects of prolonged exposure to low levels of RFR in this frequency range were not investigated. Toward the latter purpose, they conducted a study consisting of two experiments with rats, using a large rectangular TEM chamber (4.75 x 9.25 x 30 ft) with 6-ft center conductor (Mitchell, 1970) that was driven at 20 MHz.

In Experiment 1, 200 male Sprague-Dawley rats (280-300 g) were divided into 40 groups of 5 rats each, with each group housed in a conventional plastic cage (55 x 31.5 x 20 cm) with wire-mesh top. Of these groups, 20 were randomly selected and concurrently exposed to the 20-MHz RFR for 6 hr/day, 5 days/week, with the other 20 groups as controls. The cages (each containing 5 rats) were spaced 30 cm apart within the TEM chamber and were periodically rotated through each position. During nonexposure periods, the rats were allowed access to food and water ad libitum. For exposure, the water bottles were removed, the conventional wire tops of the cages were replaced with plastic-screen tops, and halved apples were provided instead of food and water. The 100 control rats were treated similarly except for being loaded onto a holding rack just outside the TEM chamber during the exposure periods. After 8 days of exposure, 6 cages each of exposed and control rats were terminated and samples were taken; this procedure was repeated for 7 cages of each after 22 days of exposure and for 7 cages of each after 39 days of exposure. In each procedure, the cages removed were replaced with empty cages.

In Experiment 2, 24 rats of about the same age and size as in Experiment 1 were randomly divided into control and exposed groups of 12 each, but each rat was housed in a separate cage and all of them were terminated and sampled after a 6-week exposure schedule.

Power measurements were performed with an NBS 10-cm dipole and NBS loop antennas. Measurements within the TEM chamber at each of the 20 cage sites with empty cages at the other 19 sites yielded an average vertical E field of 2686.5 +/- 163.6 (SD) V/m, from which the calculated incident power density was 1920 mW/sq cm. SAR measurements for live

moving rats could not be made because of the low absorption rate, but from Durney et al. (1980), the authors calculated that the SARs for a 320-g rat exposed at 1920 mW/sq cm are 0.12, 0.17, and 2.49 W/kg in the H-, K-, and E-polarizations, respectively. The rats showed no preference between the H- and K-polarizations, but they spent less than 5% of the exposure time upright (E-polarization). On this basis, the time-averaged maximum SAR was calculated to be 0.26 W/kg for individual rats and 0.3 W/kg for the worst-case huddling of the 5 rats in a cage.

Blood was collected from the rats by cardiac puncture under anesthesia in standard 2-ml EDTA-containing tubes. Counts of RBCs and WBCs and hemoglobin concentrations were determined. Measurements of packed cell volumes were done for blood in heparinized microhematocrit tubes, and methemoglobin concentration was assayed. Hypotonic lysis was used to determine RBC fragility. Blood-chemistry assays were done, including serum Na, K, and Ca; alkaline phosphatase; bilirubin; creatinine; and serum glutamic pyruvic transaminase (SGPT).

The spleens were excised and extraneous tissues were removed before weighing. Cells were collected into Hanks' balanced salt solution that contained Hepes buffer. Each suspension was centrifuged to remove any remaining tissue. Contaminating RBCs were lysed before counting the WBCs. In Experiment 2, nonspecific spleen-cell chemiluminescence was measured by liquid scintillation counting after incubating 1 ml of spleen-cell suspension with 100 million luminol-labeled rat RBCs at 37 deg C.

Four control rats and four exposed rats of each group in Experiment 1 and three each control and exposed rats in Experiment 2 were submitted for histopathology. Tissues from the upper respiratory passages, lungs, kidneys, liver, lymph nodes, salivary and Harderian glands, eyes, ears, small and large intestines, pancreas, and central nervous system were examined.

In Experiment 1, 16 parameters were determined. For data analysis, each cage was considered a sample unit and the mean of each biochemical or hematological value for the rats therein was regarded as a single datum, except for values of splenic mass or splenic white-cell counts, which were taken for a randomly selected rat of each cage. Nine parameters were determined for each rat in Experiment 2. In Experiment 1, two-way analysis of variance was used to compare data for exposed vs control groups, days of sampling, and group-day interaction (how both groups varied over the sampling period). The power to detect a difference of one standard deviation in exposed vs control rats was 0.85-0.89. When warranted by the analysis results, differences in means between exposed and control values on specific days were analyzed by unpaired Student's t-test. For the results of Experiment 2, the unpaired Student's t-test was used.

The authors stated that overall differences between exposed and control mean values for hematology and blood chemistry in Experiment 1 were not significant. In Table 1 of the paper, the mean RBC count for the

rats terminated after 39 days of exposure was significantly higher and the mean hemoglobin content was significantly lower ($p<0.05$ by t-test) than for the control group, but the analysis of variance revealed that these differences could be ascribed to significant (respectively $p<0.05$ and $p<0.025$) group-day interactions for these two parameters. The authors stated: "This trend suggested that significant differences might have occurred if exposure time had been extended beyond Day 39. For this reason, measurement of these blood parameters on Day 42 of exposure was performed in Experiment 2." However, no significant differences in RBC count and hemoglobin content or in any of the other hematology and blood chemistry parameters were found in Experiment 2.

In Experiment 1, the differences in mean splenic mass between exposed and control rats were significant on Day 22 and in mean ratio of spleen-to-body mass were significant on Days 22 and 39. However, in Experiment 2, in which the spleens and body masses were sampled only on Day 42, the differences in splenic mass and spleen/body mass ratios between exposed and control groups were nonsignificant. In both experiments, spleen cell density did not differ between exposed and control rats. Spleen cell peroxidative activity against particulate antigens, as determined by the chemiluminescence assay in Experiment 2, was not significantly different in exposed and control rats.

Regarding histopathology, the authors stated: "Prior to the initiation of Experiment 1, rats examined for quality control were histologically normal. By Day 8, rats had minimal to moderate pulmonary congestion and edema, rhinitis, and peribronchiolar and pulmonary perivascular lymphoid proliferation. In addition, emphysema and atelectasis were present in some rats killed on Day 22. No pattern of lesions was associated with irradiation. On Day 39, in a sample of four rats examined from the exposed group, the tissues varied from essentially normal to those with focal disseminated pneumonia. The four control animals killed on Day 39 had lesions varying from rhinitis only to focal disseminated pneumonia, cholangitis, and nephritis. Of the 200 rats used in Experiment 1, only one had any clinical signs of illness--epistaxis. In Experiment 2, the rats were histologically normal at the end of the 6-week period of exposure."

The statistically significant differences noted above in splenic mass and spleen/body mass ratios were interpreted by the authors as implying that an asynchronous splenic response was occurring in the exposed and control rats. The histopathological results of Experiment 1 indicated progressive respiratory mycoplasmosis, a finding noted by the authors to be apparently contrary to that of Prausnitz and Susskind (1962), who reported higher resistance to spontaneous pneumonia in mice chronically exposed to 9.3-GHz pulsed RFR.

The authors presumed that mycoplasmosis was exacerbated by the presence of ammonia, so they took extraordinary measures to prevent accumulation of environmental ammonia in Experiment 2, e.g., the rats were housed individually and the bedding was changed daily. These measures yielded the nonsignificant differences in splenic response noted above

between exposed and control rats as well as the absence of mycoplasmosis by Day 42 in these rats. The authors cautioned that: "Investigators measuring sensitive parameters in RFR experiments in rats must be aware of the insidious nature of rat mycoplasmosis. In particular, they must realize its widespread latent presence in commercially available rats and its initiation by mild to moderate ammonia stress."

Guy and coworkers have conducted a study in which 100 rats were exposed for 22 hr/day over their entire lifetimes to 2.45-GHz RFR at up to 0.4 W/kg in individual circular waveguides under controlled environmental conditions and 100 control rats were concurrently sham-exposed. The health of the rats was monitored, their longevity was assessed, and various biological endpoints were determined (including immunological and hematological assays). The results are discussed in Section 3.5.3.

REFERENCES:

Abhold, R.H., M.J. Ortner, M.J. Galvin, and D.I. McRee
STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHZ MICROWAVE RADIATION: II. EFFECTS ON THYROID AND ADRENAL AXES HORMONES
Radiat. Res., Vol. 88, No. 3, pp. 448-455 (1981)

Czerski, P.
MICROWAVE EFFECTS ON THE BLOOD-FORMING SYSTEM WITH PARTICULAR REFERENCE TO THE LYMPHOCYTE
Ann. N.Y. Acad. Sci., Vol. 247, pp. 232-242 (1975)

Descheux, P., T. Douss, R. Santini, P. Binder, and R. Fontanges
EFFECT OF MICROWAVE IRRADIATION (2450 MHZ) ON MURINE CYTOTOXIC LYMPHOCYTE AND NATURAL KILLER (NK) CELLS
J. Microwave Power, Vol. 19, No. 2, pp. 107-110 (1984)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22, (1978)

Durney, C.H., M.F. Iskander, H. Massoudi, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [THIRD EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-80-32 (1980)

Galvin, M.J., D.I. McRee, C.A. Hall, J.P. Thaxton, and C.R. Parkhurst
HUMORAL AND CELL-MEDIATED IMMUNE FUNCTION IN ADULT JAPANESE QUAIL FOLLOWING EXPOSURE TO 2.45-GHZ MICROWAVE RADIATION DURING EMBRYOGENY
Bioelectromagnetics, Vol. 2, No. 3, pp. 269-278 (1981a)

Galvin, M.J., M.J. Ortner, and D.I. McRee
STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHZ MICROWAVE RADIATION--III. BIOCHEMICAL AND HEMATOLOGIC EFFECTS
Radiat. Res., Vol. 90, pp. 558-563 (1982b)

Galvin, M.J., G.L. MacNichols, and D.I. McRee
EFFECT OF 2450 MHZ MICROWAVE RADIATION ON HEMATOPOIESIS OF PREGNANT MICE
Radiat. Res., Vol. 100, pp. 412-417 (1984)

Guy, A.W., P.O. Kramar, C.A. Harris, and C.-K. Chou
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: METHODOLOGY AND EVALUATION OF OCULAR AND PHYSIOLOGIC EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 37-44 (1980b)

Hamrick, P.E., D.I. McRee, P. Thaxton, and C.R. Parkhurst
HUMORAL IMMUNITY OF JAPANESE QUAIL SUBJECTED TO MICROWAVE RADIATION DURING EMBRYOGENY
Health Phys., Vol. 33, pp. 23-33 (1977)

Huang, A.T., M.E. Engle, J.A. Elder, J.B. Kinn, and T.R. Ward
THE EFFECT OF MICROWAVE RADIATION (2450 MHZ) ON THE MORPHOLOGY AND CHROMOSOMES OF LYMPHOCYTES
Radio Sci., Vol. 12, No. 6S, pp. 173-177 (1977)

Huang, A.T. and N.G. Mold
IMMUNOLOGIC AND HEMATOPOIETIC ALTERATIONS BY 2,450-MHZ ELECTROMAGNETIC RADIATION
Bioelectromagnetics, Vol. 1, No. 1, pp. 77-87 (1980)

Liburdy, R.P.
EFFECTS OF RADIO-FREQUENCY RADIATION ON INFLAMMATION
Radio Sci., Vol. 12, No. 6S, pp. 179-183 (1977)

Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHYOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979)

Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: II. MODULATION OF IN VIVO LYMPHOCYTE CIRCULATION
Radiat. Res., Vol. 83, pp. 66-73 (1980)

Lin, J.C., J.C. Nelson, and M.E. Ekstrom
EFFECTS OF REPEATED EXPOSURE TO 148-MHZ RADIO WAVES ON GROWTH AND HEMATOLOGY OF MICE
Radio Sci., Vol. 14, No. 6S, pp. 173-179 (1979c)

McRee, D.I. and P.E. Hamrick
EXPOSURE OF JAPANESE QUAIL EMBRYOS TO 2.45-GHZ MICROWAVE RADIATION DURING DEVELOPMENT
Radiat. Res., Vol. 71, No. 2, pp. 355-366 (1977)

McRee, D.I., R. Faith, E.E. McConnell, and A.W. Guy
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: EVALUATION OF HEMATOLOGICAL AND IMMUNOLOGICAL EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 45-52 (1980)

Mitchell, J.C.
A RADIOFREQUENCY RADIATION EXPOSURE APPARATUS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-70-43 (1970)

Ortner, M.J. and M.J. Galvin
THE EFFECT OF 2450 MHZ MICROWAVE RADIATION ON RAT PERITONEAL MAST CELLS
Cell Biophys., Vol. 2, pp. 127-138 (1980)

Ortner, M.J., M.J. Galvin, and D.I. McRee
STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHZ MICROWAVE RADIATION--I. MAST CELLS AND BASOPHILS
Radiat. Res., Vol. 86, pp. 580-588 (1981a)

Prausnitz, S. and C. Susskind
EFFECTS OF CHRONIC MICROWAVE IRRADIATION ON MICE
IRE Trans. Bio-Med. Electron., pp. 104-108 (1962)

Ragan, H.A., R.D. Phillips, R.L. Buschbom, R.H. Busch, and J.E. Morris
HEMATOLOGIC AND IMMUNOLOGIC EFFECTS OF PULSED MICROWAVES IN MICE
Bioelectromagnetics, Vol. 4, No. 4, pp. 383-396 (1983)

Rama Rao, G., C.A. Cain, J. Lockwood, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. II. PERITONEAL MACROPHAGE FUNCTION
Bioelectromagnetics, Vol. 4, No. 2, pp. 141-155 (1983)

Rama Rao, G., C.A. Cain, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. III. MACROPHAGE RESISTANCE TO VESICULAR STOMATITIS VIRUS INFECTION
Bioelectromagnetics, Vol. 5, No. 4, pp. 377-388 (1984)

Rama Rao, G.V., C.A. Cain, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. IV. SPLEEN CELL IgM HEMOLYTIC PLAQUE FORMATION
Bioelectromagnetics, Vol. 6, No. 1, pp. 41-52 (1985)

Rotkovska, D. and A. Vacek
THE EFFECT OF ELECTROMAGNETIC RADIATION ON THE HEMATOPOIETIC STEM CELLS OF MICE
Ann. N.Y. Acad. Sci., Vol. 247, pp. 243-250 (1975)

Sawicki, N. and K. Ostrowski
NON-THERMAL EFFECT OF MICROWAVE RADIATION IN VITRO ON PERITONEAL MAST CELLS OF THE RAT
Amer. J. Phys. Med., Vol. 17, pp. 225-234 (1968)

Schlagel, C.J., K. Sulek, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE. II. STUDIES ON THE MECHANISMS CONTROLLING SUSCEPTIBILITY TO MICROWAVE-INDUCED INCREASES IN COMPLEMENT RECEPTOR-POSITIVE SPLEEN CELLS
Bioelectromagnetics, Vol. 1, No. 4, pp. 405-414 (1980)

Smialowicz, R.J., J.B. Kinn, and J.A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)

Smialowicz, R.J., J.S. Ali, E. Berman, S.J. Bursian, J.B. Kinn, C.G. Liddle, L.W. Reiter, and C.M. Weil
CHRONIC EXPOSURE OF RATS TO 100-MHZ (CW) RADIOFREQUENCY RADIATION: ASSESSMENT OF BIOLOGICAL EFFECTS
Radiat. Res., Vol. 86, pp. 488-505 (1981b)

Smialowicz, R.J., P.L. Brugnolotti, and M.M. Riddle
COMPLEMENT RECEPTOR POSITIVE SPLEEN CELLS IN MICROWAVE (2450-MHZ)-IRRADIATED MICE
J. Microwave Power, Vol. 16, No. 1, pp. 73-77 (1981c)

Smialowicz, R.J., C.M. Weil, P. Marsh, M.M. Riddle, R.R. Rogers, and B.F. Rehnberg
BIOLOGICAL EFFECTS OF LONG-TERM EXPOSURE OF RATS TO 970-MHZ RADIOFREQUENCY RADIATION
Bioelectromagnetics, Vol. 2, No. 3, pp. 279-284 (1981d)

Smialowicz, R.J., C.M. Weil, J.B. Kinn, and J.A. Elder
EXPOSURE OF RATS TO 425-MHZ (CW) RADIOFREQUENCY RADIATION: EFFECTS ON LYMPHOCYTES
J. Microwave Power, Vol. 17, No. 3, pp. 211-221 (1982a)

Smialowicz, R.J., M.M. Riddle, R.R. Rogers, and G.A. Stott
ASSESSMENT OF IMMUNE FUNCTION DEVELOPMENT IN MICE IRRADIATED IN UTERO WITH 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 17, No. 2, pp. 121-126 (1982b)

Smialowicz, R.J., M.M. Riddle, C.M. Weil, P.L. Brugnolotti, and J.B. Kinn
ASSESSMENT OF THE IMMUNE RESPONSIVENESS OF MICE IRRADIATED WITH CONTINUOUS WAVE OR PULSE-MODULATED 425-MHZ RADIO FREQUENCY RADIATION
Bioelectromagnetics, Vol. 3, No. 4, pp. 467-470 (1982c)

Smialowicz, R.J., R.R. Rogers, R.J. Garner, M.M. Riddle, R.W. Luebke, and D.G. Rowe
MICROWAVES (2,450 MHZ) SUPPRESS MURINE NATURAL KILLER CELL ACTIVITY
Bioelectromagnetics, Vol. 4, No. 4, pp. 371-381 (1983)

Stodolnik-Baranska, W.
LYMPHOBLASTOID TRANSFORMATION OF LYMPHOCYTES IN VITRO AFTER MICROWAVE IRRADIATION
Nature, Vol. 214, pp. 102-103 (1967)

Stodolnik-Baranska, W.
THE EFFECTS OF MICROWAVES ON HUMAN LYMPHOCYTE CULTURES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 189-195 (1974)

Sulek, K., C.J. Schlagel, W. Wiktor-Jedrzejczak, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE: I. THRESHOLD CONDITIONS FOR THE INDUCTION OF THE INCREASE IN COMPLEMENT RECEPTOR POSITIVE (CR+) MOUSE SPLEEN CELLS FOLLOWING EXPOSURE TO 2450-MHZ MICROWAVES
Radiat. Res., Vol. 83, pp. 127-137 (1980)

Valtonen, E.J.
GIANT MAST CELLS--A SPECIAL DEGENERATIVE FORM PRODUCED BY MICROWAVE RADIATION
Exp. Cell Res., Vol. 43, pp. 221-224 (1966a)

Valtonen, E.J.
THE EFFECTS OF MICROWAVE RADIATION ON THE CELLULAR ELEMENTS IN THE PERITONEAL FLUID AND PERIPHERAL BLOOD OF THE RAT
Acta Rheumatol. Scand., Vol. 12, pp. 291-299 (1966b)

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
IMMUNE RESPONSE OF MICE TO 2450-MHZ MICROWAVE RADIATION: OVERVIEW OF IMMUNOLOGY AND EMPIRICAL STUDIES OF LYMPHOID SPLENIC CELLS
Radio Sci., Vol. 12, No. 6S, pp. 209-219 (1977)

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
EFFECT OF MICROWAVES (2450-MHZ) ON THE IMMUNE SYSTEM IN MICE: STUDIES OF NUCLEIC ACID AND PROTEIN SYNTHESIS
Bioelectromagnetics, Vol. 1, No. 2, pp. 161-170 (1980)

Wiktor-Jedrzejczak, W., C.J. Schlagel, A. Ahmed, W.M. Leach, and J.N. Woody
POSSIBLE HUMORAL MECHANISM OF 2450-MHZ MICROWAVE-INDUCED INCREASE IN COMPLEMENT RECEPTOR POSITIVE CELLS
Bioelectromagnetics, Vol. 2, No. 1, pp. 81-84 (1981)

Wong, L.S., J.H. Merritt, and J.L. Kiel
EFFECTS OF 20-MHZ RADIOFREQUENCY RADIATION ON RAT HEMATOLOGY, SPLENIC FUNCTION, AND SERUM CHEMISTRY
Radiat. Res., Vol. 103, No. 2, pp. 186-195 (1985)

Yang, H.K., C.A. Cain, J. Lockwood, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. I. NATURAL KILLER CELL ACTIVITY
Bioelectromagnetics, Vol. 4, No. 2, pp. 123-139 (1983)

3.5.3 IN VIVO STUDIES: EFFECTS OF CHRONIC EXPOSURE ON HEALTH, LONGEVITY, AND RESISTANCE TO DISEASE

Relatively few investigations have been conducted to determine whether chronic exposure to RFR affects the general health or longevity of animals, or alters the resistance to, or the severity of, diseases accidentally acquired or purposely given to animals. Such studies have been difficult to perform, and consistent or reliable results have been hard to achieve. Representative examples of such investigations follow.

In an early study, Prausnitz and Susskind (1962) exposed 200 male mice in groups of 10 for 4.5 min/day, 5 days/week, for 59 weeks to 9.3-GHz pulsed RFR (2-microsecond pulses, 500 pps) at 100 mW/sq cm average power density, which caused a mean body-temperature rise of 3.3 deg C. Based on a prolate-spheroidal model of a mouse (Durney et al., 1978, pp. 97-99), the SAR was about 45 W/kg. The body-temperature rise sufficient to cause death in half the animals (LD-50) was 6.7 deg C, attained in 12 min at 100 mW/sq cm. Thus, exposure for 4.5 min at this power density was sublethal. Controls consisted of 100 sham-exposed mice.

Among the results were liver abcesses in some mice at necropsy, but because some tissues were lost by autolysis, the relative incidence in RFR-exposed and control mice could not be determined. Another finding was that the death rate was greater in the sham-exposed than in the RFR-exposed mice; at completion of the exposure series, 50% of the control mice and 65% of the RFR-exposed mice were still alive. The deaths were attributed to a pneumonia infection introduced accidentally into the colony during the experiment, and the authors suggested that the better survival of the RFR-exposed mice was due to the protective effect of the daily rise in temperature ("fever") induced by the RFR. The explanation is plausible, but not proven; RFR in vivo can have effects on the immune system, as discussed previously in Section 3.5.2.

These authors reported that some of the mice developed leukosis (also spelled leucosis), which was described in the paper as a "cancer of the white blood cells," and that the incidence of leukosis was greater in the RFR-exposed than in the control mice. This effect was real but its interpretation by the authors was probably faulty. In dictionaries of medicine and pathology, leukosis is defined as an abnormal rise in the number of circulating white blood cells. It is not regarded as a form of cancer, though such dictionaries give detailed definitions of various types of leukemia, which are cancers of the circulatory system. Various factors can give rise to leukosis, including stress, disturbances of the endocrine system, and infection such as pneumonia, which may have caused the observed liver abscesses.

Two other points should be considered as well. First, the incidence of leukosis in the RFR-exposed mice relative to the controls was higher but their percentage of survivors was also greater, a finding that would be considered unusual for most forms of leukemia in the mouse. Second, the incidence of leukosis in the RFR-exposed mice was higher during, but not following, exposure, with the implication that spontaneous remission

of the "cancer" had occurred after the RFR-exposure series was completed. For true cancer, such remission would be considered quite improbable. Overall, the data from this study do not provide evidence as to whether or not chronic exposure of animals to RFR induces any form of cancer.

The conclusion above is supported by a reanalysis of the primary data of Prausnitz and Susskind (1962). Roberts and Michaelson (1983), noting that the results of Prausnitz and Susskind had been presented without statistical analyses, restated the data as follows:

The first sacrifice, performed 7 months into the study, consisted of 10 mice of the RFR group and 5 of the control group. The second sacrifice, done at 16 months (1 month after completion of exposure), consisted of 20 RFR mice and 10 control mice. At 19 months (4 months after exposure completion), the surviving mice, which consisted of 67 RFR mice and 19 control mice, were all sacrificed. The respective totals of sacrificed RFR and control mice were 103 of 200 (52%) and 66 of 100 (66%). The remaining 97 RFR and 34 control mice had died at various times during the study. Of these, 60 of the RFR group and 40 of the control group were necropsied; the remainder had suffered excessive autolysis.

The incidences of leukosis in the first groups sacrificed had not been reported. In the second groups sacrificed, 6/20 (30%) RFR mice and 1/10 (10%) control mice had been reported as having leukosis. Roberts and Michaelson indicated that the difference was nonsignificant ($p>0.05$ by chi-square analysis). In the third groups sacrificed, 12/67 (18%) and 4/19 (21%) had leukosis, also a nonsignificant difference. By contrast, 67/200 (34%) of the RFR mice and 19/100 (19%) of the control mice had been alive just before the third sacrifice, a significant difference ($p<0.01$, chi-square analysis). Roberts and Michaelson (1983) concluded that the report "does not support a link between exposure to microwave radiation and the development of neoplasia," and they stated: "Thus, an equally plausible case could be made for the concept that the study by Prausnitz and Susskind (1962) demonstrated microwave-induced beneficial, rather than detrimental effects."

Prausnitz and Susskind (1962) also gave results of such exposure on the testes of the mice. These results are discussed in Section 3.6.2.

Pautrizel et al. (1975) reported that exposure of mice to RFR (frequency or intensity not reported) conferred protection against an otherwise fatal challenge with Trypanosoma equiperdum.

The experiments performed by Szmigielski (1975) on rabbit granulocytes exposed to RFR in-vitro were discussed in Section 3.5.1. Szmigielski et al. (1975a) also studied the effects on granulocytes of exposing rabbits to RFR in-vivo followed by infection with Staphylococcus aureus. One group of 5 rabbits was exposed to 3-GHz RFR at 3 mW/sq cm 6 hr/day for 6 weeks and another group of 5 rabbits to the same RFR for 12 weeks. From a prolate-spheroidal model of a rabbit (Durney et al., 1978, p. 92), the SAR was about 0.4 W/kg. Controls consisted of an unexposed group of 5

rabbits. After such treatment, the rabbits were infected intravenously with S. aureus and the effects on granulopoiesis were assessed. The results were presented graphically, without uncertainty bars or other statistical treatment.

In the control rabbits, granulocyte counts in peripheral blood increased (granulocytosis) to a maximum about 1.9 times the initial value by day 6 after injection with S. aureus and diminished less rapidly to about 50% above initial value by day 44. For the rabbits exposed to the RFR for 6 weeks and infected, granulocytosis also reached maximum on day 6, about 2.2 times the initial value, but dropped sharply by day 10 to a plateau less than the initial value, an indication of RFR-induced granulocytosis depression. Granulocytosis was almost completely suppressed in rabbits exposed to the RFR for 3 months.

Mobilization of granulocyte reserves in bone marrow was determined by challenging the rabbits with Staphylococcus endotoxin and counting the peripheral-blood granulocytes 6 hr after endotoxin injection. For the control group, the count vs time-interval after initial infection rose monotonically to about double its initial value on day 44. By contrast, the count for each RFR group declined during the same period, but the effect was larger for the 3-month group.

The blood-serum lysozyme activity of the control group increased from initial to maximum value by a ratio of about 6 on day 4 and declined but remained well above initial value to day 44. The activity for the 6-week RFR group increased by a maximum ratio of about 5, also on day 4, and declined but remained above initial value to day 44. The rise for the 3-month RFR group was only by a factor of 2, followed by decline to slightly above initial value on day 44.

In the first part of a later study, Szmigielski et al. (1980) exposed male BALB/c mice and male rabbits to 2.45-GHz RFR, CW or pulsed (1- or 2-microsecond pulses, peak power density or duty cycle not stated), at average power densities of 5 or 15 mW/sq cm 2 hr/day for either 6 or 12 weeks before injecting the animals with S. aureus. For the mice, the SARs were stated to be 2-3 and 6-9 W/kg. No SARs for the rabbits were given, but are estimated from a prolate-spheroidal model (Durney et al., 1978, p. 92) to have been about 0.8 and 2.3 W/kg. During exposures at 5 or 15 mW/sq cm, no rectal-temperature increases were detected in either species. Hence the authors characterized the exposures as "nonthermal." In the second part of the study, mice and rabbits were exposed at 30-40 mW/sq cm ("hyperthermic" RFR) 2 hr/day for 4, 7, 10, or 14 days before injecting them with S. aureus. The estimated SARs at 35 mW/sq cm were about 18 W/kg for mice and 5.3 W/kg for rabbits.

The dose of S. aureus given the mice was selected to be lethal for 40% of control mice in 3 days. (The text stated 60% lethality, but the data shown in the accompanying figure showed 60% survival for controls.) The mice exposed at 5 or 15 mW/sq cm (2-3 or 6-9 W/kg) for 6 or 12 weeks comprised 4 groups of 20 each. Of the control group (also 20 mice), 5 died on day 1 after injection, 2 more on day 2, and 1 more on day 3,

yielding the 60% 3-day survival rate. Of those exposed at 5 mW/sq cm (2-3 W/kg) for 6 weeks prior to injection, 4 died on day 1 and none during days 2 and 3, for an 80% survival rate. Of the mice exposed at 5 mW/sq cm for 12 weeks, 6 died on day 1, 5 more on day 2, and none on day 3, for a 45% survival rate. The authors denoted the differences between these two RFR groups and the control group as nonsignificant. The 3-day survival rates for the groups exposed at 15 mW/sq cm (6-9 W/kg) for 6 or 12 weeks were only 25% (5 mice) and 5% (1 mouse), respectively.

Phagocytosis of S. aureus by isolated peritoneal macrophages was lower in mice exposed at 15 mW/sq cm (6-9 W/kg) for 12 weeks than in controls, but was higher in mice exposed at 5 mW/sq cm (2-3 W/kg) for 6 weeks. The differences between the other two RFR-exposed groups and the control group were not significant. Neither were the differences among the four RFR groups and the controls in delayed hypersensitivity to oxazolone.

In the infected control rabbits and those exposed at 5 or 15 mW/sq cm (0.8 or 2.3 W/kg) for 6 weeks before infection, rectal temperatures and peripheral-blood granulocytosis were elevated, release of bone-marrow granulocytes stimulated by staphylococcal endotoxin was increased, and higher lysozyme activity occurred during the 5-7 days after injection of S. aureus, with spontaneous recovery by day 10-14 and no animal deaths. By contrast, peripheral-blood granulocytosis, mobilization of bone-marrow granulocytes, and serum lysozyme activity were suppressed in the rabbits exposed for 12 weeks before injection.

Groups of 20 mice each were studied in the hyperthermia part of the investigation. Exposures at 30-40 mW/sq cm (18 W/kg) 2 hr/day for 4, 7, 10, or 14 days before injection with S. aureus caused a mean rectal-temperature rise to 41.5 deg C. Again, the S. aureus dose used was for a 3-day survival rate of 60% in controls. For the group exposed for 4 days before injection, the 3-day survival rate was 75% (15 mice), i.e., higher than for the controls. Again, the authors deemed the difference nonsignificant. The 3-day survival rates for the groups exposed for 10 and 14 days were 30% and 5%, respectively, both significantly lower than for the controls.

The authors did not present data for the rabbits given RFR hyperthermia. Instead, they cited Roszkowski et al. (1980a, b, c, d) and stated that exposure of rabbits at 30-40 mW/sq cm (5.3 W/kg) 2 hr/day for 10 or 14 days before injection with S. aureus reduced the phagocytotic capacity of the macrophage-monocyte system and weakened phagocytosis of P-32-labeled staphylococci by isolated peritoneal macrophages in vitro.

They concluded: "The two investigated factors--long-term exposure to low-level microwave fields and repeated sessions of whole body microwave hyperthermia--resulted in lowering of natural antibacterial resistance, suppression of non-specific immune reactions and finally in increased mortality from experimental acute staphylococcal infections." They also noted that the 2-hr exposures may have been "stressogenic," because the animals exhibited temporary discomfort during the exposures. They did not discuss the higher 3-day survival rate and phagocytotic capacity of

the mice exposed at 5 mW/sq cm (2-3 W/kg) relative to the values for the controls, presumably because the differences were not significant, but did not present any statistical treatment of these data.

Liddle et al. (1980) performed initial analyses of blood samples from mice for red and white blood cell counts, hematocrit, and hemoglobin, and differential leukocyte counts. One week later, groups of 4 mice were immunized by injection with a killed bacterin of Streptococcus pneumoniae type III, other groups were immunized by injection of type III purified pneumococcal polysaccharide (PPS), and still another group was injected with equal quantities of saline to serve as cage controls. Each group (except the cage controls) was then either sham-exposed or exposed to 9-GHz pulsed RFR (1-microsecond pulses at 970-1000 pps) at 10 mW/sq cm average power density for 5 days, 2 hr/day. SAR was calculated to be 3.3 W/kg for a multilayered spherical model (Weil, 1975) or 4.7 W/kg for a prolate spheroid model (Durney et al., 1978, pp. 97-99).

Rectal temperatures were taken just before and after treatment on the second day. On the day after completion of treatment (day 6 after immunization), blood samples were analyzed for hemagglutination with SRBC and for hematology. On that day, the mice were also challenged with an injection of an LD-50 dose of virulent S. pneumoniae type III and day of death was recorded for 10 days after challenge. The saline-injected controls were similarly challenged.

The hemagglutination titers for the RFR-exposed mice were significantly higher than for the sham-exposed mice. No antibody titers were detected in the saline-injected controls. Within the 10 days after challenge, 47.2% of the RFR-exposed and 50.0% of the sham-exposed mice had died; the difference was statistically nonsignificant. None of the saline-injected (non-immunized) controls survived the challenge. The last death occurred on day 7 in the RFR-exposed mice and on day 6 in the sham-exposed mice. In addition, the greatest number of deaths in one day occurred on day 6 after challenge (10 mice) for the RFR-exposed mice and on day 3 after challenge (14 mice) for the sham-exposed mice. The mean day of death was 5.58 for the RFR-exposed mice and 4.78 for the sham-exposed mice, but the difference was nonsignificant ($p=0.073$, Mann-Whitney U-test). The longer survival times of the RFR-exposed mice, though not statistically significant, were qualitatively similar to those of Prausnitz and Susskind (1962) and of Pautrizel et al. (1975), discussed previously.

Guy and coworkers have completed a study in which 100 cesarean-derived, barrier-reared, male Sprague-Dawley rats were exposed unrestrained for 21 hr per day for durations up to 25 months (virtually their entire lifetimes) to circularly polarized, 2.45-GHz RFR (10-microsecond pulses at 800 pps, square-wave modulated at 8 Hz) at an average power density of 0.48 mW/sq cm in individual circular waveguides (Guy and Chou, 1976; Guy et al., 1979) under controlled-environmental and specific-pathogen-free conditions. The facility was maintained at an ambient temperature of about 21 deg C and a relative humidity of 55%. This relatively low temperature was selected to ensure that the thermo-

regulatory responses of the rats to the RFR would be limited primarily to variations in their metabolic heat production. Concurrently sham-exposed within the same facility were 100 similarly derived control rats.

The overall objective was to determine how such chronic exposure would affect the general health and longevity of the rats. Exposure values were selected to simulate, by scaling considerations, chronic exposure of humans to 450-MHz RFR at whole-body SARs up to but not exceeding 0.4 W/kg, the basis for the 1982 ANSI exposure guideline (ANSI, 1982). Nine final reports have been issued: Guy et al. (1983a, 1983b), Chou et al. (1983b), Johnson et al. (1983), Kunz et al. (1983), Kunz et al. (1984), Johnson et al. (1984), Kunz et al. (1985), and Guy et al. (1985).

The exposure criteria, experimental design, animal facility, exposure system, rationale of biological assessment, and data acquisition system were described in the first report (Guy et al., 1983a). The exposure frequency and average power density were selected to yield about the same size-to-wavelength ratio and SAR as a human exposed at 450 MHz. Use of amplitude modulation was prompted by the calcium-efflux effect discussed in Section 3.4.4 above; 8 Hz was selected because it is near the dominant EEG frequency of the rat.

Described in the second report (Guy et al., 1983b) were:

(1) Estimation of whole-body SARs for humans exposed to 450-MHz RFR under free-space conditions in various body orientations and postures, by calorimetry with one-fifth-scale models made of synthetic biological materials and exposed to 2.45-GHz RFR (approximately 5x450 MHz).

(2) Determination of SAR distributions in such models (again in various orientations and postures) corresponding to free-space exposure at 450 MHz, by the use of thermography with a specially developed interactive computer for analyzing and processing thermographs.

(3) Establishment of the exposure parameters for rats to simulate human exposure to 450-MHz RFR.

In the discussion on p. 101 of whole-body SARs (41 measurements on the models of humans), Guy et al. (1983b) stated: "From these data we can assume that regardless of the exposure conditions for man--whether the polarization is vertical, horizontal, or circular; or the posture is erect, supine, or sitting; or the arms are extended or not--the average SAR remains relatively constant at a level of approximately .05 W/kg for a 1-mW/sq-cm exposure level [at 450 MHz]. This SAR level is a factor of 8 below the level [0.4 W/kg] used as a basis for the ANSI C95.1-1982 RFR standard."

Since whole-body SARs of rats vary with age (weight), several exposure options were considered. The one selected was to ensure that the rats would be exposed at 0.4 W/kg at some period during the exposure regimen but that this level would not be exceeded. Regarding SAR distributions in the models of humans, they found that local SARs could be as high as

about 4 times the average in the head and about 15 times the average in the wrist or perineum. Comparable ratios would also occur in the rat. Actual measurements of whole-body SARs and SAR distributions in rats exposed within circular waveguides as the rats grew from 200 to 700 g were given in detail in the third report (Chou, et al., 1983b). The whole-body SARs ranged from about 0.4 W/kg for a 200-g rat to 0.15 W/kg for an 800-g rat.

The sole behavioral endpoint included in the study, an assessment of open-field activity, and the apparatus and procedures therefor were described in the fourth report (Johnson et al., 1983). The criteria used to select this test were that it:

(1) not jeopardize the health of the rats
(2) not lead to obvious stress reactions or differential experience
(3) be done easily within the confines of the specific-pathogen-free facility and during the schedule of daily maintenance procedures
(4) not be subject to experimenter bias
(5) have a history of reported sensitivity to RFR in prior studies.

The results, discussed in detail in Section 3.7, showed no significant differences between RFR- and sham-exposed rats during corresponding test sessions.

The exposure regimen was begun when the rats were 8 weeks old and was continued for 25 months. As discussed in the fifth report (Kunz et al., 1983), ten each of the RFR-exposed and sham-exposed rats were killed after 13 months of exposure (interim kill) and exsanguinated, and their spleens were removed. The 12 RFR-exposed and 11 sham-exposed rats that survived to the end of the 25-month exposure regimen were euthanized (terminal kill) and 10 of each group were similarly processed.

After each kill, suspensions of splenic cells from the RFR and sham groups were prepared and assayed for populations of T- and B-cells, complement-receptor-positive (CR+) cells, and plaque-forming cells in response to SRBC vs saline. In addition, suspensions of splenic cells were stimulated with the T-cell mitogen phytohemagglutinin (PHA) or Concanavalin A (Con A), the B-cell mitogen purified protein derivative of tuberculin (PPD) or lipopolysaccharide (LPS) of E. Coli, or the nonspecific pokeweed mitogen (PMW). Prior to cell harvest, tritiated thymidine was added to the cultures, and the stimulation index, defined as the ratio of mean counts per min (cpm) for each stimulated culture to the mean cpm for unstimulated cultures, was determined.

The population results for the interim kill showed significantly higher counts ($p<0.05$, Student t-test) of splenic T- and B- lymphocytes for the RFR-exposed rats than for the sham-exposed rats, an indication that the RFR had stimulated the lymphoid system. By contrast, however, there were no significant differences in T- and B-cell populations between the RFR and sham groups of the terminal kill. The authors suggested that the latter result may indicate the onset of immunosenescence due to age.

The CR+ values for the RFR groups of both the interim and terminal kills were lower than for the corresponding sham groups, but the differences were nonsignificant ($p>0.05$, Student t-test), indicating no differences between RFR and sham groups in lymphocyte maturation. The percentages of plaque-forming cells for the SRBC-immunized rats was nonsignificantly higher for the RFR group than for the sham group in the interim kill, but was nonsignificantly lower in the terminal kill.

The mitogen-stimulation results for the RFR group of the interim kill showed higher responses than the sham group to the T-cell mitogens PHA and Con A, but only the difference for the latter was significant. The responses of the RFR group to the B-cell mitogens LPS and PPD were respectively significantly higher and lower than for the sham group. The RFR group also yielded significantly higher response to nonspecific PWM than the sham group. The authors stated (Kunz et al., 1983, p. 38): "These results suggest a selective effect of RFR on the response of the lymphoreticular system to mitogen stimulation." No mitogen-stimulation results were obtained for the terminal kill because the lymphocyte cultures failed to grow and respond to any of the mitogens.

As described in the sixth report (Kunz et al., 1984), blood samples (1.8-2.0 ml each) were drawn periodically for analyses from all rats quickly under anesthesia by the retro-orbital technique (selected primarily because of its lack of adverse effect on the animals). Light anesthesia was used to avoid stress-induced corticosterone elevation. The first sampling was done 4 weeks prior to the start of the exposure regimen to provide baseline data. Other samplings were done after 7 weeks of exposure, at subsequent 6-week intervals during the first year of exposure, and at 12-week intervals during the second year (for a total of 15 samplings). However, the numbers of rats sampled decreased with time because of withdrawal and mortality.

Assays of the blood samples from the 15 sessions were made for the 11 hematologic parameters listed below. Also evaluated for the 15 sessions were serum chemistry and protein electrophoretic patterns. However, after the the second bleeding session (first session after the start of exposure), the corticosterone and thyroxine (T4) levels were determined only at 12-week intervals, and corticosterone was not assayed after the tenth session except at the last session prior to the terminal kill and again at the time of terminal kill.

The 11 hematologic parameters assayed were: white-blood-cell count (WBC), red-blood-cell count (RBC), hematocrit (HCT), hemoglobin (Hgb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and counts of neutrophils, lymphocytes, eosinophils, and monocytes. Multivariate analyses of the data sets from the 15 sessions (for decreasing numbers of rats) with the Hotelling T-square statistic showed no significant overall difference between the RFR- and sham-exposed rats. In intrasession comparisons of each hematologic parameter by t-test, the absolute eosinophil count of the RFR group for the second bleeding session was significantly lower, and the absolute neutrophil counts for the second and third sessions

were marginally significantly lower, than for the sham group. No other differences were significant. Kunz et al. (1983) stated (p. 99): "These findings indicate that, despite the 25-month duration of exposure, no detectable effects were produced in the bone marrow erythropoietic cells or in the juxtaglomerular apparatus of the kidney and its production of erythropoietin." They also stated (p. 38): "The significant decrement in eosinophil count during session 2 is interesting in light of the significant elevation of corticosterone during this session and the eosinopenic effect of elevated corticosteroids." However, no data on corticosterone levels were presented in this report.

The serum-chemistry assays were of: glucose, blood urea nitrogen (BUN), creatinine, sodium, potassium, chloride, carbon dioxide, uric acid, total and direct bilirubin, calcium, phosphorus, alkaline phosphatase, lactate dehydrogenase (LDH), serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic-pyruvate transaminase (SGPT), cholesterol, triglycerides, total protein, albumin, and globulin. From examination of the data, the authors deemed multivariate analysis unnecessary. Comparisons of results for each parameter between the RFR- and sham-exposed rats by t-test yielded significant differences ($p<0.05$) for only a few isolated cases, and no coherent pattern was discernible.

Results for serum-protein electrophoresis, analyzed by t-test, showed nonsignificant ($p>0.05$) differences between the RFR- and sham-exposed rats. Kunz et al. (1983) stated (p. 92): "This indicates that the level of RFR exposure had no apparent effect on various organ-system functions that contribute to serum protein concentrations. Production of neither albumin by the liver nor globulin fractions by the lymphoreticular system was altered. Normal levels of alpha fractions reflect none of the increases usually seen in tissue destruction nor the decreases often associated with renal glomerular damage."

T4 levels were determined by radioimmunoassays, using I-125-labeled T4 as the tracer. By t-test, the differences between RFR- and sham-exposed rats at each bleeding session were nonsignificant ($p>0.05$), indicating that the RFR had no effect on the entire hypothalamic-pituitary-thyroid feedback mechanism. As expected, however, the T4 levels of both groups decreased significantly with age.

In the seventh report (Johnson et al., 1984), the analyses of growth and metabolism and the results of the necropsies done after the interim and terminal kills were presented. Rapid growth was evident for the RFR- and sham-exposed rats during the early part of the exposure regimen, but there were no significant differences between the groups in daily body weight, food and water consumption, oxygen consumption, carbon dioxide production, or respiratory quotient at corresponding times.

At the interim and terminal kills, the hearts, brains, livers, kidneys, testicles, and adrenals of the RFR- and sham-exposed rats were weighed. Also, the composition, fatty acid profile, and mineral content of the carcasses were analyzed. At the interim kill, there were no significant differences between RFR- and sham-exposed rats in the mass of

any organ. At the terminal kill, however, the mean adrenal mass for the RFR-exposed rats was 75% higher than for the sham-exposed rats, with no significant differences for the other organs.

Seven of the 12 RFR-exposed rats and 4 of the 11 sham-exposed rats necropsied at the terminal kill were found to have benign adrenal tumors. (No adrenal tumors were found in the 20 rats of the interim kill.) When the rats of both groups with adrenal tumors were excluded, the difference in mean adrenal mass was found to be nonsignificant. Johnson et al. (1984) stated (p. 31): "This analysis indicated that the increased adrenal weight was related to the tumors and irrelevant to the metabolic processes in the rats. It was noticed that the mean adrenal mass in the exposed animals without tumors was slightly heavier, but statistically insignificant as compared with those of the sham group. This increase in weight was due to one animal with a hyperplastic adrenal cortex that was secondary to a pituitary tumor."

Discussed in the eighth report (Kunz et al., 1985) was that 157 rats had died spontaneously or were terminated in extremis during the exposure period. (Twenty of the remaining 43 rats comprised the interim-kill groups and the other 23 were the survivors at the end of the exposure period, which comprised the terminal-kill groups). Evaluation of the cumulative survival curves showed that the median survival times for the RFR- and sham-exposed rats were respectively 688 and 663 days. However, comparison of the curves by the log-rank statistic showed no significant difference between the groups at any age. Also indicated was that no significant infections had occurred to complicate or produce erroneous results in the gross or histopathological evaluations.

Gross and histopathological examinations were performed on the rats, including various organs and tissue specimens. The primary cause of death of each rat (31 specific causes, 1 unknown-cause category, and the 2 kills) was determined and the results were tabulated separately for the RFR and sham groups. The numbers of deaths for most of the causes were small, so the table was collapsed to four specific major causes (defined as having at least 5 deaths), the "kills" category, and a category comprising all the other causes.

Glomerulonephritis was the largest specific category, with 17 deaths in the RFR group and 15 in the sham group; next was urinary tract blockage, with 9 and 19 deaths in the RFR and sham groups, respectively; third was atrial thrombosis, with 7 and 9 deaths; fourth was pituitary adenoma, with 4 and 8 deaths. There were 22 and 21 rats in the two kill groups. The all-other category had 41 deaths in the RFR group and 28 in the sham group. Analysis by chi-square statistic showed no association between cause of death and exposure condition. In addition, use of the log-rank statistic indicated no significant differences between the RFR and sham groups in survival times for glomerulonephritis, atrial thrombosis, or pituitary adenoma; the RFR group had significantly longer survival times than the sham group for urinary tract blockage.

The lesions found in the various organs and tissues during necropsies

were characterized as nonneoplastic or neoplastic, and the latter were subdivided into benign and malignant neoplasms. Of the nonneoplastic lesions, glomerulonephropathy was the most prevalent. Analysis of the data (chi-square statistic) by incidence, age, and treatment (RFR or sham) indicated that significantly fewer of such lesions occurred in the RFR group. There were no significant differences between RFR and sham groups for nine other major types of nonneoplastic lesions.

Only 3 benign neoplasms occurred in rats younger than 1 year and these were in the sham group. The incidences of benign neoplasms increased rapidly with age during the second year for both the RFR and sham groups, but the differences between the groups at each age of death were nonsignificant.

No primary malignant lesions were found in rats younger than 1 year. Primary malignant lesions were found in 2 RFR-exposed and 2 sham-exposed rats at ages 13-18 months, in 9 of the RFR group and 1 of the sham group at ages 19-24 months, and in 7 of the RFR group and 2 of the sham group at ages 26-30 months. The totals without regard to age were 18 and 5 for the RFR and sham groups, respectively. Kunz et al. (1985) stated: (p. 36): "To summarize the above results, primary malignancies are somewhat more likely to be present in exposed animals than in the sham exposed. This should not be considered as some artifact of the data, since different analyses led to similar results."

On the other hand, Kunz et al. (1985) also stated (p. 39): "There is statistical evidence that the mean number of primary malignancies was higher in the exposed animals than in the sham exposed, but the biological significance of this difference is reduced by several factors. First, detection of this difference required the collapsing of sparse data without regard for the specific type of malignancy or tissue of origin. Also, when the incidence of the specific primary malignancies in the exposed animals is compared with specific tumor incidence reported in the literature, our exposed animals had an incidence similar to that of untreated control rats of the same strain, maintained under similar SPF [specific-pathogen-free] conditions. It is important to note that no single type of primary malignancy was enhanced in the exposed animals. From the standpoint of carcinogenesis, benign neoplasms have considerable significance under the assumption that the initiation process is similar for both benign and malignant tumors. The fact that treatment groups showed no difference in benign tumor incidence is an important element in defining the promotion and induction potential of microwave radiation for carcinogenesis."

The foregoing results were also summarized in the ninth report (Guy et al., 1985). The authors concluded (p. 19): "In summary, no defendable trends in altered longevity, cause of death, or spontaneous aging lesions and neoplasia can be identified in the rats exposed to this long-term low-level radiofrequency radiation exposure."

REFERENCES:
ANSI (American National Standards Institute)
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
Published by the Institute of Electrical and Electronics Engineers, New York (1982)

Chou, C.-K., A.W. Guy, and R.B. Johnson
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 3. SAR IN RATS EXPOSED IN 2450-MHZ CIRCULARLY POLARIZED WAVEGUIDE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-19 (1983b)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22, (1978)

Guy, A.W. and C.-K. Chou
SYSTEM FOR QUANTITATIVE CHRONIC EXPOSURE OF A POPULATION OF RODENTS TO UHF FIELDS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. II, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8011, pp. 389-410 (1976)

Guy, A.W., J. Wallace, and J.A. McDougall
CIRCULARLY POLARIZED 2450-MHZ WAVEGUIDE SYSTEM FOR CHRONIC EXPOSURE OF SMALL ANIMALS TO MICROWAVES
Radio Sci., Vol. 14, No. 6S, pp. 63-74 (1979)

Guy, A.W., C.-K. Chou, R.B. Johnson, and L.L. Kunz
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 1. DESIGN, FACILITIES, AND PROCEDURES
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-17 (1983a)

Guy, A.W., C.-K. Chou, and B. Neuhaus
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 2. AVERAGE SAR AND SAR DISTRIBUTION IN MAN EXPOSED TO 450-MHZ RFR
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-18 (1983b)

Guy, A.W., C.-K. Chou, L.L. Kunz, J. Crowley, and J. Krupp
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 9. SUMMARY
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-85-64 (1985)

Johnson, R.B., D. Spackman, J. Crowley, D. Thompson, C.-K. Chou, L.L. Kunz, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 4. OPEN-FIELD BEHAVIOR AND CORTICOSTERONE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-42 (1983)

Johnson, R.B., L.L. Kunz, D. Thompson, J. Crowley, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 7. METABOLISM, GROWTH, AND DEVELOPMENT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-84-31 (1984)

Kunz, L.L., K.E. Hellstrom, I. Hellstrom, H.J. Garriques, R.B. Johnson, J. Crowley, D. Thompson, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 5. EVALUATION OF THE IMMUNE SYSTEM'S RESPONSE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-50 (1983)

Kunz, L.L., R.B. Johnson, D. Thompson, J. Crowley, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 6. HEMATOLOGICAL, SERUM CHEMISTRY, THYROXINE, AND PROTEIN ELECTROPHORESIS EVALUATIONS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-84-2 (1984)

Kunz, L.L., R.B. Johnson, D. Thompson, J. Crowley, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 8. EVALUATION OF LONGEVITY, CAUSE OF DEATH, AND HISTOPATHOLOGICAL FINDINGS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-85-11 (1985)

Liddle, C.G., J.P. Putnam, J.S. Ali, J.Y. Lewis, B. Bell, M.W. West, and O.H. Lewter
ALTERATION OF CIRCULATING ANTIBODY RESPONSE OF MICE EXPOSED TO 9-GHZ PULSED MICROWAVES
Bioelectromagnetics, Vol. 1, No. 4, pp. 397-404 (1980)

Pautrizel, R., A. Priore, P. Mattern, and A.N. Pautrizel
STIMULATION OF THE DEFENSES OF MICE WITH TRYPANOSOMIASIS BY EXPOSURE TO RADIATION ASSOCIATED WITH A MAGNETIC FIELD AND ELECTROMAGNETIC WAVES
Compt. Rend. D., Vol. 280, No. 16, pp. 1915-1918 (1975)

Prausnitz, S. and C. Susskind
EFFECTS OF CHRONIC MICROWAVE IRRADIATION ON MICE
IRE Trans. Bio-Med. Electron., pp. 104-108 (1962)

Roberts, N.J.,Jr. and S.M. Michaelson
MICROWAVES AND NEOPLASIA IN MICE: ANALYSIS OF A REPORTED RISK
Health Phys., Vol. 44, No. 4, pp. 430-433 (1983)

Roszkowski, W., J.K. Wremble, K. Roszkowski, M. Janiak, and S. Szmigielski
DOES WHOLE-BODY HYPERTHERMIA THERAPY INVOLVE PARTICIPATION OF THE IMMUNE SYSTEM?
Int. J. Cancer, Vol. 25, p. 289 (1980a)

Roszkowski, W., J.K. Wremble, M. Janiak, and S. Szmigielski
THE SEARCH FOR AN INFLUENCE OF WHOLE BODY MICROWAVE HYPERTHERMIA ON ANTITUMOR IMMUNITY
Clin. Exp. Oncol., in press (1980b)

Roszkowski, W., J.K. Wremble, M. Janiak, and S. Szmigielski
EFFECT OF WHOLE BODY HYPERTHERMIA AND DELAYED CUTANEOUS HYPERSENSITIVITY TO OXAZOLONE
Clin. Exp. Immunol., in press (1980c)

Roszkowski, W., S. Szmigielski, M. Janiak, J.K. Wremble, and W. Hryniewicz
EFFECT OF HYPERTHERMIA ON RABBIT MACROPHAGES
Zbl. Bakt. Hyg. Infekt., Vol. 1, No. 1 (1980d)

Szmigielski, S.
EFFECT OF 10-CM (3 GHZ) ELECTROMAGNETIC RADIATION (MICROWAVES) ON GRANULOCYTES IN VITRO
Ann. N.Y. Acad. Sci., Vol. 247, pp. 275-281 (1975)

Szmigielski, S., J. Jeljazewicz, and M. Wiranowska
ACUTE STAPHYLOCOCCAL INFECTIONS IN RABBITS IRRADIATED WITH 3-GHZ MICROWAVES
Ann. N.Y. Acad. Sci., Vol. 247, pp. 305-311 (1975a)

Szmigielski, S., W. Roszkowski, M. Kobus, and J. Jeljaszewicz
MODIFICATION OF EXPERIMENTAL ACUTE STAPHYLOCOCCAL INFECTIONS BY LONG-TERM EXPOSURE TO NON-THERMAL MICROWAVE FIELDS OR WHOLE BODY HYPERTHERMIA
Proc. URSI Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 127-132 (June-July 1980)

Weil, C.M.
ABSORPTION CHARACTERISTICS OF MULTILAYERED SPHERE MODELS EXPOSED TO UHF/MICROWAVE RADIATION
IEEE Trans. Biomed. Eng., Vol. 22, No. 6, pp. 468-476 (1975)

3.5.4 CONCLUSIONS

Much early work toward seeking possible effects of RFR on suspensions of various classes of leukocytes exposed in vitro suffered from the lack of adequate control of cell temperature during exposure. In later studies, considerable effort was expended toward development of exposure systems that permitted maintenance of cell temperature constant at optimum value during exposure or deliberate temperature increases to predetermined values for comparison. Many studies with such systems were devoted to effects on lymphocyte proliferation (without and with stimulation by various mitogens) or to their functional characteristics as components of the immune system. In those studies where exposed cultures were held at the same temperature during exposure as control cultures, nonsignificant differences in results between exposed and control cultures were obtained, and where the findings were positive, the effects on the exposed cultures were clearly of thermal origin.

In early studies on the effects of in-vitro exposure of erythrocytes to RFR, significant hemolysis and efflux of K+ were reported for rabbit erythrocytes exposed to RFR at average power densities as low as 1 mW/sq cm. In later studies, however, the hemoglobin and K+ losses from rabbit erythrocytes by heating with RFR from room temperature to 37 deg C did not differ significantly from the losses due to conventional heating; the threshold SAR for effect was found to exceed 46 W/kg. Also found was absence of significant hemolysis and K+ loss from human erythrocytes that were heated by either means to 37 deg C, an indication that RFR may not induce similar changes in rabbit and humar blood. It is noteworthy, however, that the temperatures investigated in those studies were above the phase transition region (detected as changes in slope of Arrhenius plots) within which RFR was reported to have significant effects but not above or below the region. The investigators described several possible mechanisms for such effects.

Immunological effects sought by exposing animals to RFR in vivo yielded mixed results. In studies with Japanese quail, RFR-related differences in antigenic responses were not found, except when elevated temperature was implicated. Some investigators reported that exposure of mammals to RFR increased proliferation of leukocytes or production of antibodies (relative to controls), but with few exceptions, measured or estimated SARs were well in excess of 1 W/kg. In the more recent studies, subtle effects on the mammalian immune system were sought, using advances in assay methods, with some investigations directed toward the effects of RFR on the activity of natural killer (NK) cells and with attention to the possible effects of non-RFR stress. The results of such studies again showed that SARs much higher than 1 W/kg were necessary.

More directly relevant to possible effects of RFR-exposure on the human immune system would be studies in which animals are chronically exposed to RFR (preferably over virtually their entire lifetimes), to determine whether such exposure adversely affects their health, longevity, and resistance to natural disease or experimental challenge with various microorganisms or toxins therefrom. Because of limitations in funding,

however, few such studies were done or repeated by other laboratories.

The findings of various investigators were not fully consistent with one another. Some showed apparent diminution of immune responses to RFR, but with no clear dependence on RFR level; others appeared to indicate that survival was extended by exposure to RFR. The most comprehensive chronic study was that of Guy and coworkers, who exposed 100 rats to RFR and concurrently sham-exposed 100 other rats for essentially their full lifetimes (except for those withdrawn for interim tests and those that expired before the end of the exposure regimen). Tests of 10 each RFR- and sham-exposed rats withdrawn after 13 months of treatment (interim kill) showed significantly higher counts of splenic T- and B-lymphocytes for the RFR group than the sham group, an effect ascribed by the authors to stimulation of the lymphoid system by the RFR. However, this effect was absent in similar tests on completion of treatment, provisionally ascribed to immunosenescence. Longevity was not affected by the RFR at corresponding times during the regimen.

No primary malignancies were found at the interim kill (in rats younger than one year). However, probably the most controversial finding of the entire study was that for the rats older than one year, a total of 18 of those RFR-exposed and only 5 of those sham-exposed had various kinds of primary malignant lesions. The authors gave several cogent arguments to discount the biological significance of this finding, including points that the difference between the RFR- and sham-exposed rats in the number of cases of each type of malignancy was nonsignificant and that because of the smallness of the numbers, statistical significance was attained only by combining them, an oncologically dubious procedure. To date, nevertheless, the issue has not been resolved.

3.6 PHYSIOLOGY AND BIOCHEMISTRY

The literature on physiological and biochemical effects associated with RFR is extensive. Many of the reported effects were associated with other events (e.g., changes in hormonal levels or stress adaptation), some are questionable for various reasons, and the medical significance of others is unclear.

3.6.1 METABOLISM AND THERMOREGULATION

Among several investigations for possible effects of exposure to RFR on the autonomic or involuntary thermoregulatory mechanisms of warm-blooded animals, and specifically of primates to RFR in the HF range, was the study by Bollinger (1971). He concurrently exposed tranquilized rhesus monkeys in groups of three in a rectangular TEM cell (Mitchell, 1970) to 10.5- or 19.3-MHz RFR for successive time intervals at increasing power densities up to 600 mW/sq cm or to 26.6-MHz RFR at up to 300 mW/sq cm. Based on a prolate-spheroidal model for a sitting rhesus monkey (Durney et al., 1978, p. 87), the whole-body SARs for 600 mW/sq cm at 10.5 and 19.3 MHz are about 0.2 and 0.6 W/kg, respectively; the SAR for 300 mW/sq cm at 26.6 MHz is also 0.6 W/kg. Deep-body (esophageal) temperatures and EKGs were taken during exposure. No obvious indications of thermal stress, increases of heart rate, or other influences on the electrical events of the heart cycle due to the RFR were found.

In another part of this study, he exposed rhesus monkeys concurrently in groups of 12 to 10.5- or 26.6-MHz pulsed RFR for 1 hr at average power densities of 200 or 105 mW/sq cm (0.06 or 0.2 W/kg), respectively, or to 19.3-MHz RFR for 14 days, 4 hr/day, at 115 mW/sq cm (0.1 W/kg). For each frequency, a group was sham-exposed as controls. Hematologic and blood-chemistry analyses were performed before and after exposure. The results showed no significant differences between exposed and control monkeys for most of the cellular components of the blood. Significant differences in mean monocyte and eosinophil counts were obtained, but were ascribed to conditions not related to RFR exposure. Similar conclusions were reached for the blood-chemistry parameters. Gross pathological and histopathological (microscopic) examinations of these animals showed no abnormalities ascribable to RFR exposure.

Frazer et al. (1976) exposed male rhesus monkeys to 26-MHz CW RFR at 500, 750, or 1,000 mW/sq cm (1.0, 1.5, or 2.0 W/kg) for 6 hr in the same TEM cell. Control monkeys were maintained just outside the exposure chamber. The ambient temperature was 22.2 deg C. Rectal and skin temperatures were measured. At the highest power density, the skin and rectal temperatures increased during the first half hour by 2.5 and 1.3 deg C, respectively, and decreased during the next hour to 1.1 and 0.7 deg C above their respective initial values. Rectal temperature stayed essentially constant during the remainder of the exposure period, but the skin temperature increased again slightly until the fifth hour and then declined during the last hour to 0.1 deg C above the initial value. Similar but smaller changes were found at the two lower power densities. These results indicated that even at the highest power density, the mon-

keys were in thermal equilibrium; i.e., they were able to dissipate the additional heat induced by the RFR, and their thermoregulatory mechanisms were quite efficient in doing so. The authors calculated that exposure of a 3.6-kg monkey to 26-MHz RFR at 1,000 mW/sq cm is about equivalent to exposing a human 1.8 m tall to 26-MHz RFR at 400 mW/sq cm.

Krupp (1977) performed similar experiments, exposing rhesus monkeys for 3 hr at frequencies of 15 and 20 MHz and power densities ranging from 760 to 1,270 mW/sq cm (0.6-1.3 W/kg). The results again indicated that the additional heat induced by the RFR was readily accommodated by the thermoregulatory mechanisms of the animals. The authors calculated that exposure of a monkey to 20-MHz RFR at 1,270 mW/sq cm is about equivalent to exposure of a human at 225 mW/sq cm. The equivalence for 15 MHz at 1,025 mW/sq cm is 205 mW/sq cm.

Krupp (1978) also did a follow-up study of 18 rhesus monkeys that had been exposed 1 to 2 years previously to 15-, 20-, or 26-MHz RFR for up to 6 hr on at least two occasions at power densities in the 500 to 1270 mW/sq-cm range. Hematologic and biochemical blood indices were measured and physical (including ophthalmologic) examinations were performed. No variations from normal values or conditions that could be attributed to RFR exposure were found.

Adair and Adams (1980a) trained three squirrel monkeys to regulate the environmental temperature (Ta) behaviorally by adjusting air flows of different temperature into an anechoic exposure chamber. The normal thermoregulatory behavior produces tight control over environmental and body temperatures; most monkeys select a Ta of 34-36 deg C. The monkeys were then exposed to 2.45-GHz CW RFR for 10-min periods at incident power densities ranging from 1 to 22 mW/sq cm (0.15 to 3.3 W/kg). For control data, the same monkeys were sham-exposed or exposed to infrared radiation (IR) of equivalent power density. Exposure to the RFR at 6-8 mW/sq cm or higher stimulated all animals to select a lower Ta. This threshold represents a whole-body SAR of 1.1 W/kg or about 20% of the resting metabolic rate of the monkey. Thermoregulatory behavior was highly efficient, and skin and rectal temperatures remained stable, even at 22 mW/sq cm (3.3 W/kg) where the preferred Ta was lowered by as much as 4 deg C. No comparable reduction in selected Ta below control levels occurred during exposure to the IR.

Adair and Adams (1980b) equilibrated squirrel monkeys for a minimum of 2 hr to constant environmental temperatures (22 to 26.5 deg C) cool enough to ensure that the cutaneous blood vessels in the tail and extremities were fully vasoconstricted (an effect produced by the thermoregulatory system to minimize heat loss). The monkeys were then exposed to 2.45-GHz RFR for 5-min periods at successively higher power densities in the range 2.5 to 4 mW/sq cm (0.4-0.6 W/kg), until vasodilation in the tail occurred, as evidenced by an abrupt and rapid temperature increase for the tail skin. For example, a monkey equilibrated to 25 deg C exhibited tail vasodilation when exposed to RFR at 10 mW/sq cm (1.5 W/kg), but it did not when exposed to IR at the equivalent power density, indicating that the effect resulted from stimulation of thermo-

sensitive elements of the thermoregulatory system by the RFR rather than from heating of the tail skin. To cause tail vasodilation in monkeys equilibrated to lower environmental temperatures required RFR exposure at higher power densities. Specifically, an increase of 3 to 4 mW/sq cm was found necessary for every 1-deg-C reduction in environmental temperature.

Adair (1981) also exposed four squirrel monkeys to 2.45-GHz CW RFR in warm ambient temperatures ranging from 32 to 35 deg C. After an initial 90-min or longer equilibration period, each monkey was exposed for 10-min periods to power densities in an increasing sequence from 2.5 to 20 mW/sq cm (0.4-3.0 W/kg), with sufficient time between the exposures for reequilibration. The rectal temperature and the skin temperature at the abdomen, tail, leg, and foot were monitored continuously. The metabolic heat production was determined from the oxygen deficit in the expired air. Also determined was thermoregulatory foot sweating by sensing the dewpoint of the air in a special boot over the foot. The results showed that at ambient temperatures below about 36 deg C, at which sweating in a sedentary monkey may occur spontaneously, the threshold power density (or SAR) for initiating thermoregulatory foot sweating decreased with decreasing ambient temperature.

In another study, Adair and Adams (1982) exposed three equilibrated squirrel monkeys to 2.45-GHz RFR at successively higher power densities from 2.5 to 10 mW/sq cm (0.4-1.5 W/kg) for 10-min intervals at constant ambient temperature (Ta) of 15, 20, or 25 deg C. Reductions in the metabolic heat production (M), calculated from oxygen deficits in the expired air of the monkeys, were initiated at all three values of Ta by two monkeys at 4 mW/sq cm (0.6 W/kg) or higher and at 6 mW/sq cm (0.9 W/kg) or higher in the third monkey. Above the threshold, the reduction in M was linearly related to power density. Rapid rebound of M occurred on termination of exposure. However, the reduction in M was always greater than the RFR energy absorption rate (by a factor of about 2.5) without any significant reduction in rectal temperature.

The authors noted that response time for rectal-temperature changes was too long to be manifested during a 10-min exposure, so they also exposed the three monkeys for 90-min intervals at 20 deg C, one monkey each at 6, 8, and 10 mW/sq cm (0.9, 1.2, and 1.5 W/kg), with three such sessions per monkey. The 90-min exposures were found to be long enough for the monkeys to achieve a new thermoregulatory steady state, and the reduction in M was equivalent to the RFR energy-absorption rate.

Adair and Adams (1983) also examined the effect of exposure duration at threshold power density on voluntary thermoregulation. Two squirrel monkeys were trained to control the Ta by selecting between sources of cold (10-15 deg C) and warm (50-55 deg C) air. In one of two series, they were exposed to 2.45-GHz RFR at 4 or 10 mW/sq cm for successive periods of 5, 10, 15, 20, and 25 min, with corresponding intervals between exposures, and 4-hr sham-exposures for control data. In the other series, the monkeys were exposed for 150 min at 10 or 20 mW/sq cm. No change in thermoregulatory behavior occurred at 4 mW/sq cm (0.6 W/kg)

irrespective of duration. At 10 and 20 mW/sq cm (1.5 and 3.0 W/kg), the monkeys selected Ta values 1.5 and 3.0 deg C cooler than control levels, respectively. Except during the first exposure of a series or during the early minutes of the 150-min exposures, duration had no significant effect on Ta selection or body temperatures achieved.

Adair et al. (1984a) implanted a pair of Teflon reentrant tubes in the medial preoptic nucleus of the anterior hypothalamic area (PO/AH) of squirrel monkeys trained to regulate Ta, PO/AH being the brainstem region considered to control normal thermoregulatory processes. After recovery from surgery, a Vitek temperature probe was inserted into one of the tubes to measure PO/AH temperature continuously while changes in voluntary thermoregulation were induced by successive 10-min (brief) unilateral exposures to 2.45-GHz CW RFR at 4 to 14 mW/sq cm (0.6-2.1 W/kg), with 10 min between exposures, or 150-min (prolonged) exposures at 20 mW/sq cm (3.0 W/kg). The rectal- and four representative skin temperatures were also monitored, as was the Ta selected by each animal.

Brief exposures at 8 mW/sq cm (1.2 W/kg) and higher induced each monkey to select a cooler Ta. The PO/AH temperature rose about 0.3 deg C but seldom more. Lower power densities usually produced smaller increases in PO/AH temperature and no reliable alteration of thermoregulatory behavior. Rectal temperature remained constant while PO/AH temperature rose only 0.2-0.3 deg C during the 150-min exposures at 20 mW/sq cm (3.0 W/kg) because the Ta selected was 2-3 deg C cooler than was normally preferred. Thus, a PO/AH temperature rise of 0.2-0.3 deg C accompanying RFR exposure appears to be both necessary and sufficient to modify the thermoregulatory behavior, which ensures that no greater temperature excursions occur in this hypothalamic thermoregulatory center.

The authors also noted, however, that the requisite RFR-induced rise in PO/AH temperature did not always induce voluntary thermoregulation, and therefore they suggested that thermosensitive tissues other than the hypothalamus, such as cutaneous thermodetectors, may also contribute to thermoregulatory behavior. To support this hypothesis, they presented preliminary results of an experiment in which perfusion of the other tube implanted in the PO/AH with a heated nonaqueous fluid was used to manipulate the PO/AH temperature in the absence or presence of RFR. In the experiment, a monkey was given four 20-min treatments with 20-min intervals between them. Treatments 1 and 3 were exposures at 20 mW/sq cm (3.0 W/kg), treatment 2 was heating the PO/AH with the fluid while the animal was exposed to the RFR, and treatment 4 was heating the PO/AH with the fluid only.

Results showed Ta reductions during treatments 1 and 3 similar to those obtained before. Concurrently, PO/AH-, rectal-, and skin temperatures rose approximately linearly during each treatment. Also noteworthy was a sharp rise in foot-skin temperature, particularly during treatment 1, an indication of the occurrence of peripheral vasodilation. The authors surmised that this process could stimulate the cutaneous thermodetectors and thereby furnish a peripheral cue for altering the thermoregulatory behavior. By contrast, dips in Ta were

much deeper during treatments 2 and 4, to a minimum of about 23 deg C for treatment 2 (concurrent RFR and fluid) and 27 deg C for treatment 4 (fluid only). Moreover, the PO/AH temperature rose sharply by well in excess of 0.3 deg C to a peak within the first few minutes of each treatment and then declined about linearly during the remainder of the period to below initial value. These changes were accompanied by linear decreases in rectal and skin temperature. The authors concluded that localized PO/AH heating (by thermode, for example) stimulates vigorous heat-loss responses, whereas whole-body heating by RFR can result in heat storage.

It may be significant to emphasize that hypothalamic temperature rises were evident at all the subthreshold power densities (or corresponding whole-body SARs) used. Obviously the local SARs in the hypothalamus were considerably higher than the whole-body SARs, as the authors noted. However, absence of voluntary thermoregulation indicates that exposure at such whole-body SARs is well within the capabilities of the autonomic thermoregulatory system of that primate species.

In another study by this laboratory, Candas et al. (1985) investigated the thermal adjustments made by three squirrel monkeys exposed to high levels of RFR in a cold environment. Baseline experiments done on each monkey consisted of one 4-hr sham-exposure at the thermoneutral Ta of 32 deg C, to determine the resting rate of metabolic heat production of each monkey, and three sham-exposures for 4 hr each at a Ta of 20 deg C.

In the RFR-exposure experiments, the monkeys were equilibrated for 90 min at a Ta of 20 deg C, after which they were given two series of exposures to 2.45-GHz CW RFR at successively higher levels. Series 1, involving all three monkeys, consisted of 10-min periods at 10, 14, 19, and 25 mW/sq cm (1.5, 2.1, 2.9, and 3.8 W/kg), with recovery periods of 30, 35, and 40 min. In each experimental session of series 2, which involved only two of the monkeys, each monkey was exposed for two 30-min periods at 30 and 35 mW/sq cm (4.5 and 5.3 W/kg) or 40 and 45 mW/sq cm (6.0 and 6.8 W/kg), with 70 min between periods. As in the earlier studies, PO/AH-, rectal, and skin temperatures were measured. Also, oxygen uptake was used to calculate metabolic heat production (M).

Metabolic heat production by the monkeys during the 90-min baseline period at 20 deg C to achieve equilibrium was found to be about 11 W/kg. Decreases in tail, leg, and foot temperatures during this period were reflections of peripheral vasoconstriction to preclude excessive heat loss, which resulted in a constant rectal temperature of 38.3 deg C.

The results for the 10-min exposures showed that M decreased during each exposure to a value below that observed at the end of the stabilization period and that the reductions were dependent on power density (or SAR), as were increases in skin temperatures, with small concomitant rises in rectal temperature. During the two sequential 30-min exposures at 40 and 45 mW/sq cm (6.0 and 6.8 W/kg), M decreased to the resting level (determined at 32 deg C), and, at end of each exposure, increased slowly toward the stable pre-exposure level at a rate that was dependent

on the RFR level.

Analysis of the results of both series showed that for 10-min exposures at a Ta of 20 deg C, the power density necessary to reduce M to resting level was 35 mW/sq cm (5.3 W/kg), and that for longer exposures at 30 mW/sq cm (4.5 W/kg) or higher, reduction of M to its lowest level took about 20 min. Vasodilation occurred at the latter RFR levels and was sufficient to prevent large increases in thermal-energy storage by the body, and vasoconstriction returned on termination of the RFR, thus confirming the influence of both peripheral and internal inputs to thermoregulation in squirrel monkeys in a cool environment.

Lotz (1985) sham-exposed and exposed five restrained rhesus monkeys in 4-hr sessions during the daytime in the E-orientation (long axis of the body parallel to the electric vector) to 225-MHz RFR (a frequency near body resonance) at 1.2, 2.5, 5.0, 7.5, 10.0, and 15.0 mW/sq cm (0.8, 1.7, 3.4, 5.1, 6.8, and 10.2 W/kg) in an anechoic chamber. In other 4-hr sessions, the monkeys were exposed at night in the E-orientation to 225-MHz RFR at 5 mW/sq cm (3.4 W/kg) and, during the daytime, in the H-orientation (long axis of the body parallel to the magnetic vector) to 225-MHz RFR at 5 mW/sq cm (1.2 W/kg) and to 1.29-GHz RFR (a frequency well above resonance) at 20, 28, and 38 mW/sq cm (2.9, 4.0, and 5.4 W/kg). Rectal temperatures were monitored continuously during every session and blood samples for cortisol analysis were taken hourly during the 225-MHz E-orientation sessions. The criterion for RFR tolerance was defined as a rectal temperature not exceeding 41.5 deg C.

Average rectal-temperature increases for 4-hr daytime exposures to 225-MHz RFR in the E-orientation at 2.5 and 5.0 mW/sq cm (1.7 and 3.4 W/kg) were 0.4 and 1.7 deg C. However, the monkeys were unable to tolerate exposure (as defined above) to 225-MHz RFR in this orientation at 7.5 mW/sq cm (5.1 W/kg) or higher for more than 90 min. No changes in circulating cortisol levels were found for exposures at 5 mW/sq cm (3.4 W/kg) or less. Night-time exposures to 225-MHz RFR in the E-orientation at 5 mW/sq cm (3.4 W/kg) and daytime exposures to 225-MHz RFR in the H-orientation at 5 mW/sq cm (1.2 W/kg) yielded mean rectal-temperature increases of 2.1 and 0.2 deg C, respectively. For exposures to 1.29-GHz RFR at 20, 28, and 38 mW/sq cm (2.9, 4.0, and 5.4 W/kg), the mean rises in rectal temperature were 0.4, 0.7, and 1.3 deg C. These results confirmed that RFR-hyperthermia production is most effective by exposure to a frequency near resonance (225-MHz in the E-orientation for the rhesus monkey).

Among the studies of RFR-induced alterations of thermoregulation in nonprimate mammals was that of Phillips et al. (1975), who exposed rats to 2.45-GHz RFR at an SAR of 0, 4.5, 6.5, or 11.1 W/kg for 30 min in a microwave cavity. Colonic temperatures were measured immediately after exposure, and measurements of colonic and skin temperatures, oxygen consumption, carbon dioxide production, respiratory quotient, and heart rate were recorded continuously for 5 hr starting 10 min after exposure. Control rats were sham-exposed.

The mean colonic temperature of the control rats immediately after sham exposure was 38.6 deg C and it diminished gradually over the test period to a final value of about 38.0 deg C. For the rats exposed at 4.5 W/kg, initial colonic-temperature increases to 40.0 deg C occurred, followed by decreases to mean control values in 20 min and continuation at such levels for the remainder of the period. For those exposed at 6.5 W/kg, the initial colonic temperature rises were slightly larger (to 40.5 deg C) and were followed by rapid decreases to levels significantly below the control values, which persisted for the remainder of the period. For the rats exposed at 11.1 W/kg, the initial colonic temperatures were much higher (42.4 deg C), but diminished more slowly to values well below those for the 6.5-W/kg group by 3 hr after exposure; they then increased again to control values by the end of the 5-hr period.

Dose-rate-dependent elevations of skin temperature were observed shortly after exposure; temperatures diminished to normal values within 50 min. For the rats exposed to 4.5 and 6.5 W/kg, normal values persisted for the remainder of the period. However, for the group exposed at 11.1 W/kg, skin temperature continued to decrease during the next hour, finally leveling off at well below control values for the rest of the period. Oxygen consumption and carbon dioxide production by the 4.5-W/kg group were comparable to control values, but they were lower for the two groups exposed at the higher levels. Phillips et al. (1975) also described the cardiovascular effects of the RFR on these animals, as discussed in Section 3.6.3.

Ho and Edwards (1979) used the oxygen-consumption rate as a biological indicator of stress. They exposed mice to 2.45-GHz RFR in a waveguide system that permitted continuous monitoring of the RFR absorption rate during exposure (Ho et al., 1973). The animals were exposed under the following controlled environmental conditions: 24 deg C temperature, 55% relative humidity, and 78 ml/min airflow rate. The forward power levels ranged from 0 to 3.3 W; the corresponding range of mean SARs was 0 to 44.3 W/kg. The exposures were for 30 min, during which the oxygen-consumption and RFR-absorption rates were determined at 5-min intervals; these values were converted into specific metabolic rates (SMRs) and SARs, respectively, expressed in the same units (W/kg). The oxygen-consumption rate was also measured at 5-min intervals for 30 min before and after exposure. Sham-exposed mice served as controls.

At the highest power used, the SAR (averaged over 16 mice) decreased during exposure from 56 to 39 W/kg, and the SMR decreased from 17.5 to 14 W/kg, thereby decreasing the total thermal burden from about 74 to 54 W/kg. (The values for individual mice varied more widely.) Apparently the mice tried to decrease their thermal burdens by altering their body configurations during exposure to minimize the RFR-absorption rates; they also reduced their oxygen consumption. Similar but smaller changes were obtained at forward powers of 1.7 and 0.6 W (23.6 and 10.4 W/kg), and insignificant changes were noted at 0.3 and 0.09 W (5.5 and 1.6 W/kg). Thus, the onset of such RFR-induced thermal stresses were about the same as the basal metabolic rate of the mouse (9 W/kg). Oxygen

consumption rates returned to normal on completion of RFR exposure.

The SAR-dependent decreases of SMR, obtained for SARs of 10.4 W/kg and higher but not for 5.5 W/kg and lower, were ascribed to thermal stress. These results support the finding of RFR-induced reductions of metabolic rate by Phillips et al. (1975).

Gordon (1982) reported measuring whole-body evaporative water loss (EWL) as determinative of whole-body evaporative heat loss (EHL) in mice during a 90-min exposure to 2.45-GHz CW RFR at 0-44 W/kg in an ambient temperature of 20 deg C, and in unexposed mice maintained at ambient temperatures of 20, 25, 30, 33, and 35 deg C. Plots of EWL vs SAR for 27 points taken with 9 mice were displayed in the paper. Regression-line segments were drawn by the author; one segment was essentially horizontal for the EWL points at SARs below 23 W/kg and another segment had an indicated positive slope of 0.68 for the EWL points at SARs from 28 to 44 W/kg. (There were no points in the range 23-28 W/kg.) The intersection of the two segments was at about 26 W/kg.

From the results, the author stated: "At an ambient temperature of 20 deg C, whole-body EHL was relatively constant between SARs ranging from 0 to 29 W/kg. Above 29 W/kg, the mouse underwent a linear elevation in EHL with increasing SAR. The slope of the regression line--0.65 W/kg evaporated heat per W/kg absorbed heat--implies that 65% of the absorbed microwave energy was dissipated by evaporation while the remaining 35% was dissipated passively." He concluded: "When mice were maintained at 20 deg C, an SAR of 29 W/kg was required to significantly raise EHL (the microwave heat load was equivalent to approximately 290% of the resting metabolic heat production of the mouse). That EHL did not increase below 29 W/kg indicates that thermal homeostasis can be maintained by passive dissipation of the entire absorbed microwave energy, mainly through radiative and convective heat loss." Thus, RFR at 29 W/kg is a threshold for loss of thermoregulatory ability by the mouse at 20 deg C.

The results for the mice maintained at 20, 25, 30, 33, and 35 deg C but not exposed to RFR were EHL values of 2.49, 2.10, 2.02, 6.06, and 5.25 W/kg, respectively. The first three values did not differ significantly from each other; the last two values were significantly higher than the value for 30 deg C and were about twice the resting EHL. Thus, a Ta of about 30 deg C represents a threshold for loss of thermoregulatory ability in the absence of RFR.

The author also used published data on reported RFR-induced effects on thermoregulation and the endocrine system of various laboratory animals, derived from 10 references, to predict similar effects in humans. From results for a number of biological endpoints in various species studied at ambient temperatures in the range 20-30 deg C and mostly at 2.45 GHz, he abstracted and plotted the minimum SAR found to alter the specific physiological response studied vs the representative body mass of each species. He stated that the best fit was a regression line indicating the existence of an inverse relationship between log of threshold SAR and log of body weight, from which it would be possible to extrapolate a

threshold SAR measured in a small mammal to a threshold SAR for humans. As an example, he predicted that a threshold SAR of 29 W/kg in a 0.034-kg mouse would be equivalent to an SAR of 0.25 W/kg in a 70-kg man.

Adair et al. (1983) took issue with the basic premises of this paper. Among their major comments were: Because the threshold for any thermoregulatory response depends directly on the Ta as well as the internal body temperature, there is no single threshold SAR for EHL and attempts to generalize measurements of RFR-induced EHL at one Ta (20 deg C) are in error. There are several inconsistencies regarding the two regression segments. They intersect at 25 W/kg, not at 29 W/kg, and the slope of the segment above 25 W/kg, stated as 0.65 in the text and as 0.68 in the figure is actually 0.58. Also, the interpretation of the 0.65 slope ignored the resting metabolic heat production of the adult mouse, conservatively estimated as about 10 W/kg at thermoneutrality, and therefore yielded much higher than actual percentages of aggregate heat dissipation by EWL. At SARs of 25 and 40 W/kg, the values should have been 8.6% and 22%, respectively. That the measurements of EWL at 40 W/kg could account for only 22% of a heat load that was about five times the resting metabolism indicates that the mice were undergoing substantial heat stress, which would have elevated body temperatures considerably (not measured).

Adair et al. (1983) also stated that the the extrapolation scheme based on thresholds derived from the 10 references is deceptively simple in concept in that various not necessarily related physiological responses were involved. Some of the investigators cited had presented rigorous definitions of "threshold" but others gave no definition. Some of the values were incorrectly used or were of questionable relevance and other values that were relevant were not included. Among the problems with the concept is the great variability among the different assessments of threshold, even in the same species, and that such threshold values depend strongly on ambient temperature. Gordon (1983) and Adair et al. (1984b) are respectively a rebuttal and a counter-rebuttal.

Apart from the foregoing arguments, the statistical reliability of the regression lines is open to question because of the paucity of data (no correlation coefficients were presented). Moreover, no data for body masses exceeding 4 kg were included by Gordon, so the extent to which the regression lines can be extrapolated to larger body masses (such as those of humans) and even whether the relationship is linear in the latter range are highly questionable.

Putthoff et al. (1977) investigated various drugs for rendering several species of mammals ectothermic, i.e., disabling their thermoregulatory capabilities without pronounced soporific or anesthetic effects, with a view toward using such animals as biological RFR dosimeters based on colonic temperature. The authors performed screening tests on male and female pigmented and albino (Long-Evans and Sprague-Dawley) rats, guinea pigs, and rabbits with sodium salicylate as the potential ectothermic agent injected in a range of doses, and with saline for control. The results indicated that salicylate could induce reliable hypothermia

in the albino rat, but was less effective in the pigmented rat and was essentially ineffective in the guinea pig or rabbit.

The other agent studied was cortisone acetate. A 3x4 factorial design with 36 albino (Sprague-Dawley) rats was used, with ambient temperature and drug dose as the factors. The ambient temperatures were 37.5 deg C (hot), 4 deg C (cold), and 22 deg C (neutral) and the cortisone doses (injected i.p.) were 0, 100, 200, and 400 mg/kg. Colonic temperatures were recorded just before injection and at 15-min intervals for three hours after injection.

At 37.5 deg C, the colonic temperatures of the control rats rose to a stable level about 2 deg C above baseline. For the cortisone-injected rats, small declines in colonic temperature were seen at the end of the first 15 min, followed by rises to plateaus about 2 deg C above baseline by 90 min, with some dependence on dose. At 22 deg C, the colonic temperatures of the control rats initially rose slightly and declined slowly to about 1 deg C below baseline at the end of the 3-hr period. By contrast, the temperatures of the cortisone-injected rats declined relatively quickly during the initial 30 min to dose-dependent plateaus between about 1 and 2 deg C below baseline (the latter for the highest dose). The results at 4 deg C were more pronounced; the declines to plateaus were again dose-dependent for 0, 100, and 200 mg/kg, but the temperatures of the rats given 400 mg/kg declined almost linearly with time to about 10 deg C below baseline by the end of the 3-hr period.

To determine the dosimetric utility of rats rendered ectothermic by cortisone, Putthoff et al. (1977) studied four groups of female albino rats; group 1 was injected with cortisone and exposed to 2.45-GHz RFR in a modified microwave oven (Justesen et al., 1971); group 2 was injected with cortisone and sham-exposed; group 3 was not injected with cortisone but was exposed to the RFR; and group 4 was not injected but was sham-exposed. Colonic temperatures were measured 30 min before, and just before, cortisone injection (300 mg/kg). The temperatures were measured again 30 min after injection, at which time the rats were sham- or RFR-exposed for 300 seconds, the latter at 40 W/kg. The ambient temperature was 22 +/- 2 deg C and the relative humidity ranged between 45% and 55%. Colonic temperatures were measured once more on completion of exposure.

The mean colonic temperature for the sham-exposed, non-injected group remained essentially at baseline throughout the entire measurement period, as did the value for the non-injected RFR group until the start of RFR exposure; by the end of exposure, the mean temperature of the latter group had risen to about 40.2 deg C. The mean temperature of both cortisone-injected groups declined from baseline at injection time to about 36 deg C at the start of exposure; it remained at the same level for the sham-exposed group but returned to baseline for the RFR group by the end of exposure. Analyses of variance showed the results to be reliable. As noted by the authors, the dosimetric findings are pertinent only to whole-body exposure.

In a study by Smialowicz et al. (1980), rats rendered hypothermic by

parenteral administration of bacterial endotoxin were maintained in a controlled environment at 22 deg C and 50% relative humidity and exposed for 90 min to 2.45-GHz CW RFR at 1, 5, or 10 mW/sq cm (0.2, 1.0, or 2.0 W/kg). Significant increases were observed in body temperature compared with endotoxin-treated, sham-exposed rats. The response magnitude was related to power density (magnitudes: 10 mW/sq cm > 5 mW/sq cm > 1 mW/sq cm). Saline-injected rats exposed for 90 min at 5 mW/sq cm (1 W/kg) showed no significant increase in body temperature compared with saline-injected, sham-exposed rats. Endotoxin-induced hypothermia in rats was also found to be affected by ambient temperature alone (in the absence of RFR), i.e., increases of ambient temperature above 22 deg C yielded concomitant increases in body temperature.

The results of this investigation indicate that relatively low RFR power densities or SARs (of the order of 1 mW/sq cm or 0.2 W/kg) are absorbed in the rat as heat that is not manifested as an increase in colonic temperature in normothermic animals but that can be detected in rats rendered hypothermic by endotoxin injection. These findings support the contention that RFR interaction at such RFR levels is primarily thermal.

Smialowicz et al. (1981a) also rendered unrestrained, unanesthetized mice hypothermic by injecting them with 5-hydroxytryptamine (5-HT) in a controlled environment of 22 deg C and 50% relative humidity. Mice injected with saline were used as controls. Colonic temperatures were measured prior to injection. Following injection, groups of mice were exposed to 2.45-GHz CW RFR for 15 min at 10, 5, or 1 mW/sq cm (SAR of 7.2, 3.6, or 0.7 W/kg) or were sham-exposed, after which their colonic temperatures were measured again. The experiments were performed with BALB/C and CBA/J mice.

For saline-injected mice of either type, there were no significant rectal-temperature differences between mice exposed at 10 mW/sq cm and sham-exposed mice. For BALB/C mice rendered hypothermic with 5-HT, the rectal temperatures were significantly higher for those exposed at all three power densities than those sham-exposed, and the differences rose monotonically with power density. The results for the CBA/J mice were similar, but the increases were statistically significant only at 5 and 10 mW/sq cm. The investigators concluded that subtle heating by RFR can alter the thermoregulatory capacity of mice rendered hypothermic by 5-HT, whereas the colonic temperature of normal (saline-injected) mice was not significantly altered by exposure at 10 mW/sq cm.

Lai et al. (1983) studied the effects of various psychoactive drugs in rats exposed for 45 min to 2.45-GHz pulsed RFR (2-microsecond pulses, 500 pps) at 1 mW/sq cm average power density (0.6 W/kg). Apomorphine-induced hypothermia and stereotypy were enhanced by the RFR exposure. Amphetamine-induced hyperthermia was attenuated while stereotypy was unaffected. Catalepsy and lethality induced by morphine were enhanced by the RFR at certain dosages of the drug. Because these drugs have different modes of action on central neural mechanisms and the effects of microwaves depend on the particular drug studied, these results show

the complex nature of the effect of RFR exposure on brain functions.

In a similar investigation, Lai et al. (1984a) performed two series of experiments to study the effects of acute exposure (45 min) to the same RFR on the actions of pentobarbital in the rat. In the first series, rats were exposed to RFR first and then injected with pentobarbital immediately. Exposure did not significantly affect the extent of the pentobarbital-induced fall in colonic temperature. However, recovery from the hypothermia was at a significantly slower rate in the RFR-exposed rats and they also took a significantly longer time to regain their righting reflex.

In the second series, rats were anesthetized with pentobarbital first and then exposed to RFR with their heads either pointing toward the RFR source (anterior exposure) or pointing away (posterior exposure). In either orientation, exposure significantly retarded the pentobarbital-induced fall in colonic temperature. However, recovery from hypothermia was significantly faster in posterior-exposed animals compared to the recovery of anterior-exposed and sham-exposed animals. Furthermore, the posterior-exposed rats took a significantly shorter time to regain their righting reflex than both the anterior-exposed and sham-exposed rats.

Similar results were obtained by Lai et al. (1984b) on the effects of acute exposure to the same RFR on ethanol-induced hypothermia. The authors also found that the RFR did not affect the consumption of a 10% sucrose (w/v) solution by water-deprived rats, but it enhanced the consumption of a solution of 10% sucrose (w/v) + 15% ethanol (v/v) by water-deprived animals, as discussed in more detail in Section 3.8.1.

Voluntary thermoregulation to changing ambient environments can also be altered by exposure to RFR. Stern et al. (1979) trained rats with fur clipped to press a lever that turned on an infrared lamp while in a cold chamber. When the trained rats were exposed to 2.45-GHz CW RFR for 15-min periods, the rate at which they turned on the lamp decreased as a function of the RFR power density, which ranged between 5 and 20 mW/sq cm (1-4 W/kg). The authors concluded that the rat responds to maintain a nearly constant thermal state. In the absence of RFR, the lamp is the sole heat source. With RFR present, the rat compensates by reducing the response rate, thereby reducing the infrared-heat contribution. Thus, voluntary thermoregulation is an index of the thermal burden contributed by RFR. The rapidity of this behavioral response is such that it cannot be mediated by deep-body (colonic) temperature rise, and indeed there was no change in colonic temperature at 5 mW/sq cm (1 W/kg).

In summary, the thermal basis for the various reported effects of RFR on the autonomic thermoregulatory systems of mammals and their behavioral thermoregulatory responses to RFR is clearly evident. Noteworthy are the results for the primates because of their far greater similarities to humans than the other laboratory animals studied. Based on these results, it is unlikely that humans chronically exposed to RFR at whole-body SARs of the order of 1 W/kg or lower will be adversely affected.

REFERENCES:

Adair, E.R. and B.W. Adams
MICROWAVES MODIFY THERMOREGULATORY BEHAVIOR IN SQUIRREL MONKEY
Bioelectromagnetics, Vol. 1, No. 1, pp. 1-20 (1980a)

Adair, E.R. and B.W. Adams
MICROWAVES INDUCE PERIPHERAL VASODILATION IN SQUIRREL MONKEY
Science, Vol. 207, pp. 1381-1383 (21 March 1980b)

Adair, E.R.
MICROWAVES AND THERMOREGULATION
In J.C. Mitchell (ed.), USAF RADIOFREQUENCY RADIATION BIOEFFECTS RESEARCH PROGRAM--A REVIEW, Aeromed. Rev. 4-81, Report No. SAM-TR-81-30, pp. 145-158 (1981)

Adair, E.R. and B.W. Adams
ADJUSTMENTS IN METABOLIC HEAT PRODUCTION BY SQUIRREL MONKEYS EXPOSED TO MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiology, Vol. 50, No. 4, pp. 1049-1058 (1982)

Adair, E.R. and B.W. Adams
BEHAVIORAL THERMOREGULATION IN THE SQUIRREL MONKEY: ADAPTATION PROCESSES DURING PROLONGED MICROWAVE EXPOSURE
Behav. Neurosci., Vol. 97, No. 1, pp. 49-61 (1983)

Adair, E.R., D.E. Spiers, J.A.J. Stolwijk, and C.B. Wenger
TECHNICAL NOTE: ON CHANGES IN EVAPORATIVE HEAT LOSS THAT RESULT FROM EXPOSURE TO NONIONIZING ELECTROMAGNETIC RADIATION
J. Microwave Power, Vol. 18, No. 2, pp. 209-211 (1983)

Adair, E.R., B.W. Adams, and G.M. Akel
MINIMAL CHANGES IN HYPOTHALAMIC TEMPERATURE ACCOMPANY MICROWAVE-INDUCED ALTERATION OF THERMOREGULATORY BEHAVIOR
Bioelectromagnetics, Vol. 5, No. 1, pp. 13-30 (1984a)

Adair, E.R., C.B. Wenger, and D.E. Spiers
TECHNICAL NOTE: BEYOND ALLOMETRY
J. Microwave Power, Vol. 19, No. 2, pp. 145-148 (1984b)

Bollinger, J.N.
DETECTION AND EVALUATION OF RADIOFREQUENCY ELECTROMAGNETIC RADIATION-INDUCED BIOLOGICAL DAMAGE IN MACACA MULATTA
Final report submitted by Southwest Research Institute, San Antonio, Texas, to the USAF School of Aerospace Medicine, Brooks AFB, Texas (February 1971)

Candas, V., E.R. Adair, and B.W. Adams
THERMOREGULATORY ADJUSTMENTS IN SQUIRREL MONKEYS EXPOSED TO MICROWAVES AT HIGH POWER DENSITIES
Bioelectromagnetics, Vol. 6, No. 3, pp. 221-234 (1985)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22, (1978)

Frazer, J.W., J.H. Merritt, S.J. Allen, R.H. Hartzell, J.A. Ratliff, A.F. Chamness, R.E. Detwiler, and T. McLellan
THERMAL RESPONSES TO HIGH-FREQUENCY ELECTROMAGNETIC RADIATION FIELDS
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-76-20 (September 1976)

Gordon, C.J.
EFFECTS OF AMBIENT TEMPERATURE AND EXPOSURE TO 2450-MHZ MICROWAVE RADIATION ON EVAPORATIVE HEAT LOSS IN THE MOUSE
J. Microwave Power, Vol. 17, No. 2, pp. 145-150 (1982)

Gordon, C.J.
NOTE: FURTHER EVIDENCE OF AN INVERSE RELATION BETWEEN MAMMALIAN BODY MASS AND SENSITIVITY TO RADIO-FREQUENCY ELECTROMAGNETIC RADIATION
J. Microwave Power, Vol. 18, No. 4, pp. 377-383 (1983)

Ho, H.S., E.I. Ginns, and C.L. Christman
ENVIRONMENTALLY CONTROLLED WAVEGUIDE IRRADIATION FACILITY
IEEE Trans. Microwave Theory Tech., Vol. 21, No. 12, pp. 837-840 (1973)

Ho, H.S. and W.P. Edwards
THE EFFECT OF ENVIRONMENTAL TEMPERATURE AND AVERAGE DOSE RATE OF MICROWAVE RADIATION ON THE OXYGEN-CONSUMPTION RATE OF MICE
Radiat. Environ. Biophys., Vol. 16, pp. 325-338 (1979)

Justesen, D.R., D.M. Levinson, R.L. Clarke, and N.W. King
A MICROWAVE OVEN FOR BEHAVIORAL AND BIOLOGICAL RESEARCH: ELECTRICAL AND STRUCTURAL MODIFICATIONS, CALORIMETRIC, DOSIMETRY, AND FUNCTIONAL EVALUATION
J. Microwave Power, Vol. 6, No. 3, pp. 237-258 (1971)

Krupp, J.H.
THERMAL RESPONSE IN MACACA MULATTA EXPOSED TO 15- AND 20-MHZ RADIOFREQUENCY RADIATION
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-77-16 (September 1977)

Krupp, J.H.
LONG-TERM FOLLOWUP OF MACACA MULATTA EXPOSED TO HIGH LEVELS OF 15-, 20-, AND 26-MHZ RADIOFREQUENCY RADIATION
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-78-3 (January 1978)

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
PSYCHOACTIVE-DRUG RESPONSE IS AFFECTED BY ACUTE LOW-LEVEL MICROWAVE IRRADIATION
Bioelectromagnetics, Vol. 4, No. 3, pp. 205-214 (1983)

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
EFFECTS OF ACUTE LOW-LEVEL MICROWAVES ON PENTOBARBITAL-INDUCED HYPOTHERMIA DEPEND ON EXPOSURE ORIENTATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 203-211 (1984a)

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
ETHANOL-INDUCED HYPOTHERMIA AND ETHANOL CONSUMPTION IN THE RAT ARE AFFECTED BY LOW-LEVEL MICROWAVE IRRADIATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 213-220 (1984b)

Lotz, W.G.
HYPERTHERMIA IN RADIOFREQUENCY-EXPOSED RHESUS MONKEYS: A COMPARISON OF FREQUENCY AND ORIENTATION EFFECTS
Radiat. Res., Vol. 102, pp. 59-70 (1985)

Mitchell, J.C.
A RADIOFREQUENCY RADIATION EXPOSURE APPARATUS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-70-43 (1970)

Phillips, R.D., E.L. Hunt, R.D. Castro, and N.W. King
THERMOREGULATORY, METABOLIC, AND CARDIOVASCULAR RESPONSE OF RATS TO MICROWAVES
J. Appl. Physiol., Vol. 38, No. 4, pp. 630-635 (1975)

Putthoff, D.L., D.R. Justesen, L.B. Ward, and D.M. Levinson
DRUG-INDUCED ECTOTHERMIA IN SMALL MAMMMALS: THE QUEST FOR A BIOLOGICAL MICROWAVE DOSIMETER
Radio Sci., Vol. 12, No. 6S, pp. 73-80 (1977)

Smialowicz, R.J., K.L. Compton, M.M. Riddle, R.R. Rogers, and P.L. Brugnolotti
MICROWAVE RADIATION (2450 MHZ) ALTERS THE ENDOTOXIN-INDUCED HYPOTHERMIC RESPONSE OF RATS
Bioelectromagnetics, Vol. 1, No. 4, pp. 353-361 (1980)

Smialowicz, R.J., M.M. Riddle, P.L. Brugnolotti, R.R. Rogers, and K.L. Compton
DETECTION OF MICROWAVE HEATING IN 5-HYDROXYTRYPTAMINE-INDUCED HYPOTHERMIC MICE
Radiat. Res., Vol. 88, No. 1, pp. 108-117 (1981a)

Stern, S., L. Margolin, B. Weiss, S.-T. Lu, and S.M. Michaelson
MICROWAVES: EFFECT ON THERMOREGULATORY BEHAVIOR IN RATS
Science, Vol. 206, pp. 1198-1201 (7 December 1979)

3.6.2 ENDOCRINOLOGY

Exposure of animals to RFR has produced somewhat inconsistent effects on the endocrine system of mammals. In general, the effects produced are apparently related to either the heat load associated with the RFR or the stress induced in the animals by the RFR and possibly by other experimental circumstances. Some effects also appear to be related to alteration of the circadian rhythm by RFR. Effects clearly demonstrated to be associated with nonthermogenic stimulation of the endocrine system or the associated parts of the CNS are not evident.

Because of the known sensitivity of the testes to heat, studies were conducted on the effects of RFR on gonadal function in animals. As discussed in Section 3.5.3, Prausnitz and Susskind (1962) exposed mice to 9.3-GHz RFR at 100 mW/sq cm for 4.5 min/day (which increased mean body temperatures by 3.3 deg C) for 5 days/week over 59 weeks (SAR about 45 W/kg). Testicular degeneration was found in 40% of the RFR-exposed and in 8% of the control mice that had died during the course of the experiment. However, no endocrinological data were presented.

Lancranjan et al. (1975) studied 31 men (mean age 33 years) who were occupationally exposed to RFR in the 3.6- to 10-GHz range at power densities ranging from tenths to hundredths of a mW/sq cm for 1 to 17 years (a mean of 8 years). By questionnaire, potential subjects having endocrinologic diseases, venereal infections, varicocel, hydrocel, trauma of the testes, and other conditions affecting spermatogenesis were eliminated. Semen volume was measured and counts of total, mobile, and abnormal sperm per ml were made for each subject after at least 3 days of sexual inactivity. The total neutral 17-ketosteroids (17-ks) and total gonadotropins (TG) in 24-hr urine were determined for 19 of the subjects. Controls consisted of 30 unexposed men (mean age 34 yrs) for semen analyses, 8 for 17-ks analyses, and 10 for TG analyses.

The authors stated that 23 (74%) of the exposed subjects exhibited alterations of spermatogenesis, but provided no details except mean values for the entire group relative to those for the controls. The mean total sperm count for the subjects was 50 +/- 24 (SD) million per ml. The corresponding value for the controls was 60 +/- 34 million per ml. The authors stated that the difference was significant with the t-test ($p<0.02$), but calculation shows that t was 1.33, yielding $p>0.1$ for the 2-tailed test or $p>0.5$ for the 1-tailed test.

The mean numbers of motile and normal sperm for the exposed group were 36 +/- 10 and 70 +/- 6 million/ml, respectively, and the corresponding values for the control group were 54 +/- 19 and 82 +/- 7 million/ml. Both differences were statistically significant ($p<0.001$), as stated by the authors.

There was no significant difference between the mean 17-ks elimination for the 19 exposed subjects and the 8 controls. Also, 14 subjects had normal values of TG elimination, 4 had higher values, and 1 had a value below the lower limit of the normal range; this man (age 33 yrs) had

been exposed to RFR for 14 yrs and also exhibited azoospermia. The authors interpreted the normal and higher values of TG as ruling out the possibility that spermatogenesis alteration was secondary to a central diencephalo-pituitary disorder that induced a decrease in gonadotropic stimulation, but rather as due to direct effect of RFR on the germinal epithelium of the gonads.

The authors also stated that 80% of the exposed subjects suffered from asthenic syndrome, which included complaints of decreases of libido and of erection, ejaculation, and/or other orgasm disturbances. They also noted that reinvestigation after three months of interruption of RFR exposure showed improved spermatogenesis in two-thirds of the subjects, but gave no data.

As in other studies of possible effects of occupational exposure to RFR, accurate information was lacking on intensities and exposure durations. The authors did indicate that the intensity "varied according to the working process, the existence of some shielding systems, and the power installations," but did not give other details on the various exposure situations. Moreover, it is difficult to determine the influence of physiological and emotional factors not related to RFR exposure in the occupational environment or in the personal lives of the subjects, especially with so few subjects. Such factors could adversely affect spermatogenesis and give rise to the subjective complaints mentioned, and removal from the occupational environment for three months could produce improvement. Therefore, these findings are open to question.

Muraca et al. (1976) exposed the testes of anesthetized Sprague-Dawley rats to 2.45-GHz RFR at 80 mW/sq cm. Colonic temperature was monitored during exposure with a thermocouple probe. The temperature of the right testis was measured with a needle thermistor and was used to switch the RFR source on and off to permit automatic attainment and maintenance of any desired testicular temperature for appropriate time periods. In preliminary experiments, it was found that testicular temperature rise to 40 deg C by single exposures for 10 to 73 min caused degenerative changes. Therefore, testicular temperature rises to 36, 38, 40, and 42 deg C were selected for study. Groups of rats were given single or five consecutive daily exposures to RFR to attain these temperatures and the testes of other groups were subjected to water bath submersion at these temperatures for comparison. Five days after treatment, the rats were euthanized and their testes were fixed, sectioned, stained, and examined for histological changes (classed 0 to 3, with 0 for normal histology).

For the single RFR exposures to attain testicular temperatures of 36, 38, 40, and 42 deg C, the corresponding treatment times were 60, 60, 27, and 10 min, which respectively yielded testicular damage in 33%, 22%, 20%, and 80% of the rats. Five consecutive daily RFR exposures for the same durations yielded damage in 100%, 40%, 100%, and 100% of the rats. Single submersions in a water bath at these temperatures for the same durations produced testicular damage respectively in 17%, 18%, 40%, and 60%. The corresponding values for five consecutive daily immersions were 66%, 50%, 50%, and 50%.

No statistical analyses of the results were presented. However, the authors noted that multiple treatments nearly always produced damage in larger percentages of rats than the corresponding single treatments and that exposure to the RFR may cause an increase in damage not seen in comparable water-immersion heating, probably because of the greater heating efficiency of RFR.

Cairnie and Harding (1981) exposed arrays of up to 10 conscious mice urestrained within cages to 2.45-GHz CW RFR at a spatial average power density of 37 mW/sq cm for 16 hr per day for 1 to 30 days. When mice were exposed for more than one day (16 hr/day), the location of each mouse in the array was shifted daily. The exposure arrangements and dosimetry were presented in detail in Cairnie et al. (1980).

In Cairnie et al. (1980), whole-body SARs were determined in mouse carcasses for various exposure orientations by calorimetry. The mean values for 27-g mice in the E, K, and H orientations were 1.204, 0.632, and 0.587 W/kg per mW/sq cm, respectively, consonant with calculations by Durney et al. (1978), p. 99, for a 25-g prolate-spheroidal model of a mouse. Thus, the corresponding mean whole-body SARs at 37 mW/sq cm were 44.6, 23.4, and 21.7 W/kg. Relative energy-deposition patterns in the sagittal plane of mouse carcasses were determined by thermography after exposure in various orientations. In each orientation, absorption in the abdomen was markedly greater than in the testis but not as high as in parts of the head or hindquarters. Local temperatures in the abdomen and testis of mouse carcasses were variable, but were summarized as 0.4 W/kg per mW/sq cm or less in the testis, independent of orientation, or 14.8 W/kg at 37 mW/sq cm. Also, the ratio of the SAR in the abdomen to the SAR in the testis was 11.9 +/- 3.7 (SE) for the E orientation.

Cairnie et al. (1980) also measured rectal and testis temperatures in 14 mice euthanized after unanesthetized exposure for 16 hr at 50 mW/sq cm (60 W/kg) and in 10 mice after similar sham-exposure, and used cooling curves to determine the temperatures immediately after cessation of exposure. The mean rectal temperatures for the RFR and sham groups were 36.19 and 34.83 deg C, respectively, a significant difference. However, the mean testis temperatures for the RFR and sham groups were 34.44 and 34.05 deg C, respectively, a nonsignificant difference, indicating that the testis thermoregulatory system was able to fully compensate for the increased thermal burden from RFR at close to lethal level.

The tests used for assessing damage were described in Cairnie and Leach (1980). Damaged testicular cells in a suspension made from fresh testis were identified by their uptake of trypan blue, scored by phase-contrast microscopy. For sperm counts, aliquots of sperm suspensions obtained from each epididymis were counted separately. Percentages of abnormal sperm in suspensions obtained from each epididymis were scored for abnormal heads or tails. All scorings were performed blind, i.e., without knowledge regarding prior treatment of each mouse.

In experiment 1, male mice of the B6C3F1 strain were exposed in groups of 12 concurrently. From the power-density distribution in the array,

seven of the mice were exposed at 21 mW/sq cm (whole-body SAR 25.3 W/kg, 8.4 W/kg in the testes) and the other five mice at 34 mW/sq cm (whole-body 40.9 W/kg, 13.6 W/kg in the testes). The authors stated that since there were no significant differences within or between the subgroups, the data for the 12 mice in each group were combined.

In the first part of this experiment, one group was exposed to the RFR for 1 hr (9 to 10 am), another for 2 hr (9 to 11 am), another for 4 hr (9 am to 1 pm), still another for 8 hr (7 am to 1 pm), and the fifth group for 20 hr (5 pm to 1 pm the next day); the sixth group was sham-exposed for 20 hr. The mice in all six groups were euthanized at 1 pm. In the second part, four groups were exposed to the RFR for 16 hr/day (5 pm to 9 am): one group for one day only, another on two successive days, another on four successive days, and still another on eight successive days; a fifth group was sham-exposed 16 hr/day for eight days. These five groups were euthanized at 9 am on the last treatment day.

The mice treated in both parts of experiment 1 were assayed only for uptake of trypan blue by damaged testicular cells. The mean percentages of cells for the groups in the first part, i.e., exposed to the RFR for 1, 2, 4, 8, or 16 hr, or sham-exposed for 16 hr, were 1.38, 0.95, 1.33, 2.36, 4.06, and 1.62, respectively. By t-test, the difference between each RFR group and the sham group was not significant. The results for the mice in the second part were 1.55, 1.73, 1.63, and 19.3 for those exposed to the RFR for 1, 2, 4, and 8 days, respectively, and 1.38 for the group sham-exposed for 8 days. The differences among these values were not significant.

In experiment 2, 70 B6C3F1-strain mice were exposed to the RFR 16 hr/day for 4 days. Groups of five mice each were euthanized at intervals from immediately to 10 weeks after exposure and assayed for sperm counts and percentages of abnormal sperm. The results showed a nonmonotonic but significant increase of sperm count with time interval after exposure, consistent with the maturation of the mice, a result similar to that obtained previously by Cairnie and Leach (1980) without RFR exposure. Also, there were no significant differences in percentages of abnormal sperm among the groups euthanized at the various intervals.

Experiment 3 was performed to ascertain whether the B6C3F1 strain is especially resistant to testicular damage, based on results by Bruce et al. (1974) indicating that this strain has a low background level of abnormal sperm (about 1%). In the first part of this experiment, 10 mice each of strains B6C3F1, C3H/HeB, Balb/c, C57Bl/6B, and Swiss-Webster were treated in a water bath at 40 deg C for 2 hr. Five of each group were euthanized 4 hr after treatment and assayed for percentage of damaged testicular cells, sperm count, and percentage of abnormal sperm. The other five mice of each group were kept in the animal facility for 2 weeks after treatment, at which time they were euthanized and assayed for sperm count and percentage of abnormal sperm. Control values were obtained from mice of each strain kept overnight in the anechoic chamber but not exposed to RFR or treated in the water bath.

The percentages of damaged testicular cells did not differ significantly among the control groups for the five strains. However, significant differences in sperm counts and percentages of abnormal sperm were seen between some control groups. More important, the mean sperm count for each strain euthanized 4 hr after treatment was smaller than for its control group, with the differences for the B6C3F1 and C3H/HeB strains significant, and the counts for the groups euthanized 2 weeks after treatment were all markedly lower than for their respective control groups. The differences in percentages of abnormal sperm between the groups euthanized 4 hr after treatment and their respective control groups were nonsignificant. For the groups euthanized 2 weeks after treatment, however, the abnormal-sperm percentages for four of the strains were markedly higher than for their control groups. The exception was the C3H/HeB strain; its percentage was nonsignificantly higher than for its control group. Thus, most of the results for this part of experiment 3 indicated that the treatment with water at 40 deg C for 2 hr was deleterious.

Three groups of 10 mice of each strain were used in the other part of experiment 3. One group of each strain was exposed at about 27 mW/sq cm for 2 hr (5 am to 7 am), the second group was exposed at about the same power density for 16 hr (5 pm to 9 am), and the third group was sham-exposed for 16 hr. Five mice of each group were euthanized at 9 am for the three assays and the others of each group were kept in the animal facility for 2 weeks before being euthanized and assayed. None of the means for the RFR groups differed significantly from the means for their respective sham groups. The authors concluded: "Thus, the changes seen after 2 hr in a water bath at 40 deg C could not be replicated by exposure to microwaves for 2 or 16 hr at an exposure rate of 27 mW/sq cm." They also concluded that the B6C3F1 strain does not have any peculiar resistance to RFR damage.

In experiment 4, two groups of 18 mice each (of the B6C3F1 strain) were exposed to RFR at 37 mW/sq cm for 30 consecutive days, 16 hr/day. For this experiment, a second array of cages was added closer to the antenna (at about half the conventional distance to the far-field boundary) and an RFR source of higher power was used, which permitted exposure of 18 mice in locations that differed in power density at most by a ratio of about 2. Moreover, the mice of each group were rotated daily through the array positions, thus providing substantially the same time-average power density for each. Two control groups of 18 mice from the same batches were maintained in individual cages in the same animal facility. Six mice of each group were used for reproductive trials (results not reported in this paper), two mice were assayed at exposure end for percentage of trypan-blue staining, and 10 were assayed for percentage of abnormal sperm at half-week intervals up to 8 weeks after completion of exposure. None of the results showed any significant differences ascribable to the RFR.

In their discussion, the authors noted that for study of possible RFR-induced testicular damage, the mouse is an inadequate model for man, because the dimensions of the mouse are much smaller, it is a quadruped,

its scrotum is nonpendulous, and its testes migrate freely through the inguinal canal between scrotum and abdomen, the latter point implying that testicular function is adapted to temperature elevations to 37 deg C for at least short periods.

Saunders and Kowalczuk (1981) exposed the rear halves of anesthetized mature male mice to 2.45-GHz RFR in a waveguide system for 30 min. The half-body SARs ranged from 18 to 75 W/kg. The corresponding rectal temperatures at the end of exposure ranged from 35.3 to 42.2 deg C. Other anesthetized mice were sham-exposed, which yielded a mean rectal temperature of 32.6 deg, about 4-5 deg C lower than for conscious mice. For comparison, the rear halves of still other anesthetized mice were heated for 30 min in a water bath to 37, 41, 43, or 45 deg C, which resulted in rectal temperatures from 36.4 to 40.7 deg C. Six days after treatment, sections of testes were scored for cell damage and sperm counts were made.

Extensive degeneration of the spermatogenic epithelium was evident for RFR exposure at 75 W/kg and for direct heating to 45 deg C. At SARs of 57 and 46 W/kg or temperatures of 43 and 41 deg C, marked depletion of spermatids and spermatocytes but not spermatogonia was observed. At lower SARS (0-37 W/kg) or at 37 deg C, no effects were seen. Testicular temperatures taken with probes implanted in the testes of other groups of mice were found to be SAR-dependent, and indicated the existence of a threshold of about 39 deg C for depletion of spermatocytes and of about 41 deg C for 50% cell death after 6 days of RFR exposure or direct heating. The corresponding SARs for these two thresholds were 20 and 30 W/kg, respectively.

Lebovitz and Johnson (1983) exposed 14 unanesthetized male Sprague-Dawley rats to pulsed-modulated circularly polarized RFR (1-microsecond pulses of 1.3-GHz RFR, 600 pps) 6 hr/day for 9 days during a 2-week period concurrently in individual cylindrical waveguides. The whole-body SAR was 6.3 W/kg, which produced a mean core-temperature rise of 1.5 deg C. A group of 15 rats was similarly sham-exposed.

Deep rectal temperatures were measured hourly in three sham-exposed rats and four rats exposed at 6.3 or 6.9 W/kg for 6 hr and otherwise handled in the same fashion as those used in the testicular experiments. The mean rise of core temperature for the 6.3-W/kg group was 1.5 to 2 deg C. The rise was attained during the first hr and was stable for the rest of the period. The mean rise for the 6.9-W/kg group was slightly but not significantly higher than for the 6.3-W/kg group. Thus, the rats were able to accommodate (attain an elevated but stable body temperature) to these levels of exogenous thermogenesis. There were no significant core-temperature changes in the sham-exposed rats.

The rats were weighed and decapitated at 6.5, 13.0, 26.0, or 52 days after the last treatment day, corresponding to 0.5, 1.0, 2.0, or 4.0 cycles of spermatogenesis. Testes were separated from the epididymides before weighing each testis and epididymis and the seminal vesicles. The right testis was decapsulated, the tunica albuginea weighed, and the

testis homogenized. The spermatids resistant to homogenization were enumerated by phase-contrast cytometry. Daily sperm production (DSP) per testis was calculated by dividing the number of resistant spermatids by the 6.3-day life span. DSP/g of parenchyma was obtained by dividing DSP/testis by the difference between testis and tunic weights. The number of sperm in the right epididymis was determined from epididymal homogenates. The left testis was fixed, osmicated, sectioned, stained, and examined by bright-field microscopy.

The results showed some trend toward lower testicular and epididymal weights and toward lower levels of DSP/testis for the RFR-exposed rats compared to the sham-exposed rats, but by two-way analysis of variance, the differences were not significant. No significant differences for RFR- vs sham-exposure were found, and the interactions between treatment and spermatogenic cycle were also not significant.

The RFR-exposed rats examined on day 6.5 after treatment (0.5 cycle of spermatogenesis) yielded 87.6% normal sperm compared with 95.8% for the corresponding sham-exposed rats, a significant difference. However, most of the abnormal sperm in the former group were derived from one rat that yielded 45.5% abnormal sperm, rendering the finding suspect. Since spermatogenic cycle at time of sacrifice was not a significant factor, the data for all cycles were pooled. No significant differences were found in pooled values of any endpoint for RFR- and sham-exposed rats.

The weight of seminal vesicles was taken as a measure of testicular endocrine function. The nonsignificant differences between values for the RFR- and sham-exposed rats indicated that RFR exposure at 6.3 W/kg was not deleterious to the production of testosterone. This finding was supported by the histological evaluations by light microscopy, which showed similarities in: structure of seminiferous tubules, abundance of all types of developing germ cells, and structure of Leydig cells.

The authors noted that exposure of rats at 6.3 W/kg yielded not only an unambiguous core-temperature elevation, but also immediate alterations in food-reinforced behavior (Lebovitz, 1981; see Section 3.7.1.1), and that both effects were fully reversible. They suggested that if these effects were due solely to the RFR acting as an added thermal burden and a sensory stimulus or cue, there would be little basis for considering such exposures as harmful.

Regarding other endocrinologic effects, Todorovich et al. (1965) exposed three groups of five male white rats to "microwaves" (frequency not indicated), one group each at 20, 40, and 60 mW/sq cm, for 10 min at 7 to 9 cm from a dish antenna in the dorso-ventral direction, using a "filter" to restrict exposure to the adrenal area. A fourth group of rats served as controls. Blood samples drawn from the tail 24 hr before exposure and at 2 and 24 hr after exposure were assayed for sugar level. Samples were also drawn daily for 6 to 24 days post-exposure, depending on power density and effects found. The rats were euthanized after the last blood sample was drawn and the concentrations of ascorbic acid in the adrenal cortex were determined by impregnating it with acidic silver

nitrate and staining and counting the argyrophyllous granules (capable of binding silver salts) in the cells.

For the rats exposed at 20 mW/sq cm, the mean blood-sugar level at 2 hr after exposure was almost 10% higher than for controls, a significant rise, but dropped to levels not significantly different from controls at 1, 3, and 6 days post-exposure. The mean levels for those exposed at 40 mW/sq cm were about 18% and 16% above mean control level at 2 and 24 hr, respectively, both significant rises, and diminished to levels that were nonsignificantly higher than for controls at 3, 6, and 9 days post-exposure. For those exposed at 60 mW/sq cm, the mean blood-sugar level rose to 36% (its maximum) above mean control level at 2 hr, decreased slightly at 24 hr, and gradually diminished to about 24% above control level (a difference still significant) by 24 days after exposure.

For the rats exposed at 20 mW/sq cm and euthanized six days later, the mean number of stained granules in the adrenal cortex did not differ significantly from the control mean. However, for those exposed at 40 mW/sq cm and euthanized nine days later and for those exposed at 60 mW/sq cm and euthanized 24 days later, the granule counts diminished by about 24% and 36%, respectively, both significant changes.

The authors stated: "As the amount of ascorbic acid in the adrenal cortex is an indication of its function, it follows that the microwaves had a stimulating effect. Therefore, the greater blood sugar level may also be ascribed to greater hormone, i.e., cortisone and hydrocortisone secretion by the adrenal cortex. These hormones, together with the hormones of the anterior lobe of the pituitary, have an inhibitive effect on the enzyme hexokinase, causing changes in the metabolism of carbohydrates."

Milroy and Michaelson (1972) exposed three groups of male rats to 2.45-GHz RFR. The 16 rats comprising one group were exposed once at 100 mW/sq cm, 4 rats each for 10, 20, and 30 min and 4 rats for 40 min or more; the 10 rats in another group were exposed at 10 mW/sq cm, 8 hr per day, for 8 weeks; and the 10 rats in the third group were exposed at 1 mW/sq cm continuously for 8 weeks. Of three control groups, one group comprised of 10 rats was maintained in stock cages under conditions similar to those for the exposed groups; another group (15 rats) was exposed to infrared radiation (IR) at a level sufficient to yield body-temperature increases comparable to those with the RFR, 4 rats each for 10, 20, and 30 min and 3 rats for 40 min or more; the 5 rats comprising the third group were sham-exposed. From a prolate-spheroidal model of a medium rat (Durney et al., 1978, p. 95), the whole-body RFR SARs at 100, 10, and 1 mW/sq cm were about 20, 2, and 0.2 W/kg.

The gross behavior of the rats during exposure was observed. The body weights and body temperatures were monitored throughout the exposure and post-exposure periods. Blood samples were drawn from the tail at 4-week intervals during the exposure and post-exposure periods and assayed for triiodothyronine (T-3) uptake, thyroxine (T-4), and thyroid-stimulating hormone (TSH). Following the post-exposure period, half the surviving

rats were tested for radioactive-iodine uptake. The remaining rats were euthanized and their pituitaries, thyroids, and adrenals were examined for histopathology. The eye lenses of all surviving rats were examined for opacities.

A plot of body temperature vs duration of exposure to RFR showed an approximately linear rise from 38.3 to about 42 deg C by the 38th min. A similar plot for IR showed little change during the first few minutes, followed by a relatively steep rise from 37.5 to about 42 deg C by the 25th min. The difference in curve shape was clearly due to the greater penetration depth of the RFR. Of the 66 rats in the study, 5 deaths occurred in the untreated rats and 21 died during the experimental period, with none during exposure. The exposures to RFR or IR for 40 min or more yielded body temperatures that exceeded 42.3 deg C and produced irreversible changes and death in 6 rats within hours of exposure. The remaining deaths occurred randomly.

No significant body-weight changes occurred in any group. No unusual behavioral changes were noted among the sham-exposed rats or those exposed at 1 mW/sq cm (0.2 W/kg). Rats in the 10-mW/sq-cm (2-W/kg) group decreased their activity and did not huddle when the RFR was on, but resumed their normal activity and huddled for warmth when the RFR was off. The rats exposed at the higher RFR or IR levels became increasingly agitated as body temperature rose; they urinated and salivated on themselves for cooling and became prostrate when body temperature reached 42 deg C.

No significant direct effects of RFR on thyroid function were observed. In the 100-mW/sq-cm RFR (20-W/kg) and IR groups, no differences in T-3 uptake or T-4 level were detected relative to each other or to the normal range (mean +/- 1 SD) for controls. In the 10-mW/sq-cm (2-W/kg) and 1-mW/sq-cm (0.2-W/kg) groups, the T-3 uptake decreased to values significantly below the normal range for controls, but so did the T-3 uptake of the sham-exposed group. The T-4 levels of the 10-mW/sq-cm and 1-mW/sq-cm groups were near the upper limit of the normal range for controls, but the levels for the sham-exposed group were significantly above that range. No changes in circulating levels of TSH were detected for any group, but the authors noted that decreases in TSH levels were not detectable with the assay method used. In the radioactive-iodine-uptake tests, no significant differences among groups were seen.

The necropsies showed varying degrees of thyroid destruction in all groups. The thyroids of the rats exposed at lethal RFR or IR levels showed massive destruction of autolytic appearance, but the extent to which such destruction occurred by post-mortem autolysis or by pre-terminal hyperexia could not be determined. There were no specific pathological changes in the pituitaries or adrenals af any of the rats. Of 90 lenses (45 pairs) examined, 89 were free of opacities; the other lens, from a rat exposed at 10 mW/sq cm (2 W/kg), had a suture defect that was probably congenital.

Parker (1973) sham-exposed and exposed groups of male Sprague-Dawley

rats to far-field 2.45-GHz CW RFR at 10, 15, 20, or 25 mW/sq cm in an anechoic chamber for 4, 16 or 60 hr. The whole-body SARs are estimated to have been about 2, 3, 4, and 5 W/kg (Durney et al., 1978, p. 95). Rectal temperatures were measured immediately after exposure. The mean value for the rats exposed for 16 hr at 10 and 20 mW/sq cm and for 60 hr at 15 mW/sq cm did not differ significantly from the mean for the sham-exposed rats, but was significantly higher for the rats exposed at 25 mW/sq cm (5 W/kg) for 16 hr.

Adrenal epinephrine level and phenylethanolamine-N-methyltransferase (PNMT) activity were determined after adrenal removal. Plasma and adrenal corticosterone were assayed for rats decapitated within 30 seconds after gentle removal of each rat from the exposure arrangement. The ability of the thyroid to concentrate iodide was determined by using the radiotracer I-131 to measure the thyroid/serum (T/S) ratio of iodide in euthanized rats. Serum was analyzed for protein-bound iodine (PBI) and thyroxine (T-4) levels. Blood samples were taken for determining hematologic indices.

The rats exposed at 10 mW/sq cm (2 W/kg) for 4 hr showed no significant differences in adrenal weights, PNMT activity, or epinephrine level relative to controls. Adrenal weights were unaltered for those exposed at 10 mW/sq cm for 16 hr and there were no significant alterations in adrenal or plasma corticosterone levels, but epinephrine level was lowered and PNMT activity was increased significantly. There were no significant differences in hematocrit or in counts of total leukocytes, lymphocytes, or eosinophils between this 16-hr group and controls.

For the rats exposed for 16 hr at 10, 20, or 25 mW/sq cm (2, 4, or 5 W/kg), there were no significant differences in serum PBI or T-4 levels or in T/S ratio relative to controls, but all three were significantly lowered for 60-min exposure at 15 mW/sq cm (3 W/kg), an indication of thyroid function suppression. The author surmised that the effects were due to stress from the whole-body heat load or selective stimulation of discrete anatomical areas such as the brain or thyroid.

Mikolajczyk (1976) exposed groups of 35-day-old male Wistar rats to far-field 2.9-GHz RFR for 6 hr/day, 6 days/week over 6 weeks at 10 mW/sq cm (about 2 W/kg, Durney et al., 1978, p. 95) in an anechoic chamber. For controls, other groups were similarly sham-exposed. On the day after exposure completion, the rats were weighed and decapitated, and the anterior pituitary, thyroid, adrenals, prostate, and testes were excised and weighed. No significant differences between RFR- and sham-exposed rats were found in the mean body weight or in the mean weight of each organ. Thus, RFR exposure had no significant effect on growth.

The anterior lobe of the pituitary gland (hypophysis) of each rat was homogenized and centrifuged, and the supernatant was used for assays of follicle-stimulating hormone (FSH), growth hormone (GH), and luteinizing hormone (LH). These assays were done by injection of supernatant into 30-day-old male and female rats that had been hypophysectomized, with saline injection for control. Body weights and weights of the adrenals

and ovaries of the hypophysectomized females before and after injection were measured, and body weights and weights of the adrenals, prostate, and testes of the hypophysectomized males prior to and after injection were also measured. By this assay method, the mean amounts of FSH and GH in the RFR and sham groups were found to be comparable, but the mean amount of LH for the RFR group was significantly higher than for the sham group.

Guillet and Michaelson (1977) exposed 18 neonatal Long-Evans rats for 5 min daily at ages 1 through 6 days to far-field 2.45-GHz CW RFR at 40 mW/sq cm in an anechoic chamber maintained at 34 deg C, corresponding to the ambient temperature in the home cage in the immediate vicinity of the dam surrounded by her pups. By calorimetry with water loads, the SAR was 9-10 W/kg. Each pup was weighed daily before exposure. Colonic temperature was taken every second day just after exposure. Eighteen pups were stated to be sham-exposed but actually were placed in an incubator at 34 deg C for 5 min daily and otherwise similarly treated.

At 7 days of age, in a test for adrenal responsiveness, subgroups of six pups each of the RFR and "sham" groups were given adrenocorticotropic hormone (ACTH) i.p., other subgroups of each group were exposed to the RFR for 5 min and these 24 pups were decapitated 20 min after these treatments. For controls, the remaining pups from both groups were euthanized immediately after removal from the nest. Trunk blood was collected from each pup, the serum was assayed for corticosterone, and the adrenals were excised, weighed, and preserved for future study.

The curves for colonic temperature vs age for the two groups were similar in shape, but mean values for the RFR group were 1.5 to 2.5 deg C higher than for the sham group at corresponding ages. Despite the colonic-temperature elevations, the curves of mean pup weight vs age through 7 days for the RFR and sham groups were also similar and the mean weights at corresponding ages were comparable, thus yielding no manifest effect of the RFR on growth, at least during this period.

In the adrenal-responsiveness test, there were no significant plasma-corticosterone differences between the RFR and sham subgroups euthanized immediately on day 7 (control subgroups) or between the RFR and sham subgroups given ACTH and then euthanized; however, the corticosterone concentration for the RFR subgroup exposed to the RFR (again) on day 7 was higher than for the sham group exposed to the RFR on day 7. Also, although the corticosterone concentration for sham group exposed to the RFR on day 7 did not differ significantly from the mean for the control sham subgroup, the means for the RFR subgroups given ACTH or the extra exposure were higher than for the control RFR subgroup, but did not differ significantly from each other. The means of adrenal mass and ratio of adrenal-to-body mass for the RFR group were significantly higher than for the sham group. In the absence of detailed statistical treatment of the corticosterone and weight data, such as by analysis of variance, it is difficult to interpret these results.

Magin et al. (1977a, 1977b) surgically exposed the two thyroid glands

of anesthetized dogs and used a diathermy unit and special applicator to irradiate one gland in vivo with 2.45-GHz RFR for 2 hr at 72, 162, or 236 mW/sq cm. The corresponding SARs in the gland were 58, 131, and 190 W/kg, and the resulting temperatures therein were about 39, 41, and 45 deg C. The other thyroid gland served as control. The release rates of the hormones thyroxine (T-4) and triiodothyronine (T-3) into the blood were measured for both glands.

The mean T-4 release rates for the three exposure levels were found to be higher by respective factors of 150, 350, and 1000% for the glands exposed to the RFR than for the control glands. The T-3 release rates were smaller than those of T-4, but the time courses of release of the two hormones were similar. In addition, the mean blood flow rates in the thyroids exposed at 162 or 236 mW/sq cm (131 or 190 W/kg, yielding mean gland temperatures of 41 and 45 deg C) were higher by 140 and 170%.

Lotz and Michaelson (1978) first "gentled" rats for 2 weeks prior to exposure by weighing and handling them at least 4 times per week and equilibrating each rat for exposure by taking its colonic temperature and placing it in an exposure cage for 3 to 5 hr on 3 of the last 4 days before use. The activity of the adrenal axis during equilibration was determined by placing groups of rats in the exposure chamber for 30, 60, 90, 120, 150, or 180 min, measuring colonic temperature before and after this interval, and assaying the blood for corticosterone (CS) level. The results indicated a rapid rise of both colonic temperature and CS level during the first half hour to an approximate plateau, followed by a return to baseline values by the end of 3 hr, thus demonstrating the need for such an equilibration period prior to exposure.

The authors then exposed groups of unanesthetized gentled rats to 2.45-GHz CW RFR for 30, 60, or 120 min at 0, 13, 20, 30, or 40 mW/sq cm or for 30 or 60 min at 50 or 60 mW/sq cm, and measured colonic temperatures and CS levels after exposure. The SARs, determined calorimetrically in water phantoms, were 0.16 W/kg per mW/sq cm. Plots of post-exposure colonic temperature vs exposure duration at each power density showed a small but statistically significant temperature rise after 30 min of exposure at 13 mW/sq cm (2.1 W/kg); exposures for the same duration at higher levels yielded temperature increases approximately proportional to power density. Up to 40 mW/sq cm (6.4 W/kg), exposures for 60 min produced temperature increases not significantly greater than those for 30 min, but the temperature rises for 60-min exposures at 50 and 60 mW/sq cm (8.0 or 9.6 W/kg) were significantly larger than those for 30 min. Increases in CS level above baseline values were nonsignificant for durations of up to 120 min at 13 mW/sq cm (2.1 W/kg), up to 60 min at 20 mW/sq cm (3.2 W/kg), and 30 min at 30 mW/sq cm (4.8 W/kg). All other CS increases were significant and highly correlated with colonic-temperature rises.

Threshold values for adrenal-axis stimulation were estimated to be about 30-50 mW/sq cm (4.8-8.0 W/kg) for 60-min exposures and 15-20 (2.4-3.2 W/kg) mW/sq cm for 120-min exposures. The latter range is somewhat less than half the resting metabolic rate of the rat.

Lotz and Michaelson (1979) exposed hypophysectomized ("hypox") rats, sham-hypox rats (given the same surgical procedure without removing the hypophysis), and intact rats to 2.45-GHz RFR for 60 min at 60 mW/sq cm (9.6 W/kg). Before exposure, the rats were gentled as described above. After exposure, blood-plasma samples were assayed for CS level. For comparison, similar groups were sham-exposed and assayed for CS level.

To verify adrenal functional integrity of hypox rats during RFR exposure, other groups of unexposed hypox, sham-hypox, and intact rats were injected with ACTH and assayed 1 hr later for blood-plasma CS. The differences in CS level among the ACTH groups were not significant.

For the intact, hypox, and sham-hypox groups that were sham-exposed, the differences in mean colonic temperature were nonsignificant. For the RFR-exposed groups, the only significant difference in mean colonic temperature was between the hypox and sham-hypox rats, with the value for the latter lower than for the former.

For the sham-exposed groups, the mean plasma-CS level of the hypox rats was barely detectable and significantly lower than for the intact or sham-hypox rats; the difference between the latter two groups was not significant. For the RFR-exposed groups, the CS levels of the intact and sham-hypox rats were both much higher than for their respective sham-exposed groups and did not differ significantly from each other, but again the level for the hypox rats was barely detectable.

To determine whether RFR stimulation of the rat pituitary-adrenal axis could be blocked by pretreatment with exogenous glucocorticoids, dexamethasone in doses in the range 0.56-10 (microgram/100 g of body weight) were injected into groups of intact rats, after which the rats were exposed at 50 mW/sq cm (8.0 W/kg) for 60 min and assayed for CS. Doses of 3.2 or 5.6 were injected into other groups followed by exposure at 70 mW/sq cm (11.2 W/kg) for 60 min. For controls, other rats were injected with saline and exposed. Exposure at 50 mW/sq cm (8.0 W/kg) after dexamethasone injection produced highly significant dose-dependent reductions in CS level, with doses of 3.2 or larger almost totally blocking any increases in CS level during exposure. However, doses of 3.2 or 5.6 did not fully suppress CS-level increases during subsequent exposure at 70 mW/sq cm (11.2 W/kg). Mean colonic temperatures for the rats exposed at 50 mW/sq cm (8.0 W/kg) after dexamethasone injection ranged from 39.8 to 40.1 deg C; the differences among the various dose groups were not statistically significant.

From the barely detectable CS levels in the hypox rats exposed at 60 mW/sq cm (9.6 W/kg) for 60 min and the high levels in the hypox rats injected with ACTH (which stimulated adrenal secretion of CS in these rats), Lotz and Michaelson (1979) concluded that RFR exposure does not stimulate the adrenal gland primarily. Instead, the observed increases in CS level in intact rats during RFR exposure must have been due to adrenal stimulation by endogenous ACTH from the pituitary during RFR exposure. The results of the dexamethasone experiments comprise additional evidence that adrenal response is due to ACTH stimulation during

exposure, and the moderate doses needed to inhibit RFR-induced ACTH secretion indicate that exposure at 50 mW/sq cm (8.0 W/kg) for 60 min is a relatively mild stimulus for such secretion. Based on their results, Lotz and Michaelson hypothesized that RFR-induced secretion of ACTH is a systemic integrative process due to general hyperthermia.

Lu et al. (1977) subjected rats first to a 2-week gentling period, and then sham-exposed or exposed them to 2.45-GHz RFR at 1, 5, 10, or 20 mW/sq cm for 1, 2, 4, or 8 hr starting at the same time and day of the week. From colonic-temperature measurements in anesthetized rats, the corresponding SARs were 0.25, 1.25, 2.5, and 5.0 W/kg. The rats were decapitated after treatment, blood was collected, and body mass and rectal temperature were measured. The blood-serum levels of CS, T-4, and GH were assayed. In addition, the pituitary, adrenal, and thyroid glands were weighed.

For the sham-exposed rats, rectal temperature increased with treatment duration, an effect ascribed to circadian rhythmicity. The mean rectal temperatures of the RFR-exposed rats varied in an inconsistent manner. For example, for the 1-hr exposures, increases in temperature were noted for the groups exposed at 5 and 20 mW/sq cm (1.25 and 5.0 W/kg), but not for those exposed at 1 and 10 mW/sq cm (0.25 and 2.5 W/kg).

The CS level increased with treatment duration for the sham-exposed rats and was correlated with rectal temperature increase. CS-level increases occurred in the RFR-exposed rats but were not significantly correlated with rectal temperature. The only significant changes in T-4 level were an increase for 4-hr exposure at 1 mW/sq cm (0.25 W/kg) and decreases for 4-hr and 8-hr exposures at 20 mW/sq cm (5.0 W/kg). No significant changes in GH level due to RFR exposure were noted. Neither body mass nor pituitary mass (normalized to body mass) were affected by RFR exposure. Several statistically significant alterations of thyroid and adrenal masses were observed, but no obvious pattern related to power density, exposure duration, or circadian rhythmicity was apparent.

The large variations seen for each endpoint in the rats sham-exposed for various durations presumably resulted from unknown differences in residual stress reactions after gentling as well as circadian changes. Such uncontrolled variations render it difficult to discern any clear-cut effects ascribable to RFR exposure per se in these studies. The authors in recognizing such difficulties stated: "In spite of these constraints, we were able to show that exposure of rats to 2450-MHz CW microwaves at 20 mW/sq cm for eight hours depressed serum CS levels."

Indeed their results that show a statistically significant lower mean CS value for the 4 rats thus exposed than for the 6 rats that were sham-exposed for the same duration. Also, comparisons between groups exposed to RFR at other power densities and groups sham-exposed for the same durations showed both increases and decreases of CS level, but none of these changes were statistically significant. However, large changes (primarily increases) in CS level with exposure duration at constant power density were evident for most groups, including those that were

sham-exposed. Therefore, possible RFR-induced changes, if any, would probably be masked by the non-RFR-induced changes, and the significant result cited above was probably a statistical anomaly.

In general, the number of rats used for each exposure regimen was too small to lend much biological credence to any of the statistically significant differences between RFR- and sham-exposed rats. The authors used the Mann-Whitney U-test on the CS values and the Student t-test on the rectal temperatures without stating their justification for doing so. This point is mentioned because had they used the t-test on the 20-mW/sq cm, 8-hr CS data relative to the corresponding controls, they would have found the CS depression to be nonsignificant ($p>0.05$).

Lu et al. (1980b) also exposed gentled rats to the same frequency at power densities ranging from 1 to 70 mW/sq cm (equivalent SARs of 0.21 to 14.7 W/kg) for 1 to 8 hr at an environmental temperature maintained at 24 deg C. Sham-exposed rats were used as controls. After treatment, the rats were decapitated, colonic temperatures were taken, and blood was collected for assays of T-4, TSH, GH, and CS.

For 1-hr exposures, colonic temperatures increased with power density at 20 mW/sq cm (4.2 W/kg) and higher, but consistent elevation of serum CS did not occur below 50 mW/sq cm (10.5 W/kg). Lower serum TSH and GH levels also occurred at this and higher power densities. Significant serum T-4 elevations were noted at 40 and 70 mW/sq cm (8.4 and 14.7 W/kg), but they were not consistently related to power density values. For sham exposures and exposures at 1-20 mW/sq cm (0.21-4.2 W/kg) for longer durations (2-8 hr), the results were rather equivocal, presumably because such exposures encompassed significant portions of the circadian cycle. Specifically, in the sham-exposed rats, the level of T-4 did not change significantly with exposure duration and significant increases of CS and decreases of TSH and GH were seen, so it was difficult to discern consistent changes in these hormones ascribable to RFR exposure. The authors suggested that the divergent responses may be due to different mechanisms that are dependent on RFR intensity and the timing of the exposures relative to circadian rhythms.

The most sensitive parameter measured proved to be colonic temperature. For example, for rats exposed at 20 mW/sq cm (4.2 W/kg), increases in colonic temperature were consistent for any exposure duration, and smaller increases were noted for exposures at 10 mW/sq cm (2.1 W/kg) for 2 hr and at 1 mW/sq cm (0.21 W/kg) for 4 hr.

In a later study by Lu et al. (1981b), unanesthetized, equilibrated male rats were exposed to 2.45-GHz RFR for 1 hr at 1-70 mW/sq cm (0.25-14.7 W/kg) or for 4 hr at 0.1-40 mW/sq cm (0.021-8.4 W/kg), or were sham-exposed. The authors reported that for the RFR-exposed rats, TSH varied inversely while the CS level increased with power density or colonic temperature. Similar relationships between TSH and CS with colonic temperature were obtained for the sham-exposed rats. The authors also reported that exposure to RFR at 20 mW/sq cm (4.2 W/kg) or less for 4 hr inhibited normal circadian elevation of adenocortical

function if the exposure occurred during the diurnal CS elevation.

Liburdy (1979), in a study primarily on the effects of RFR on the immune system (see Section 3.5.2), found that for a single exposure of mice to "thermogenic" 26-MHz CW RFR, i.e., 800 mW/sq cm (SAR of 5.6 W/kg) for 15 min, which produced core-temperature rises of 2-3 deg C, the levels of plasma corticoid were severalfold higher than for sham-exposed mice or mice in which similar core-temperature elevations were produced by warm-air heating. Moreover, mice exposed to "nonthermogenic" RFR, i.e., to either 26-MHz RFR at 50 mW/sq cm (0.36 W/kg) or 5-MHz RFR at 800 mW/sq cm (same SAR) for 1 or 20 15-min/day sessions did not show this effect. As noted by the author, these results support the hypothesis that the heat generated by thermogenic RFR triggers the ultimate release of adrenal steroids.

Abhold et al. (1981) sham-exposed or exposed rats in individual vented Styrofoam cages to far-field, 2.45-GHz CW RFR in groups of 8 arranged in a circular pattern with their long axes parallel to the E-vector in an anechoic chamber held at 23 deg C and 65% relative humidity. Exposures were at 2 or 10 mW/sq cm (0.44 or 2.2 W/kg) continuously for 8 hr within the period from about 0030 to 0845, during which food and water were not provided. Untreated rats served as controls.

The rats were then decapitated and blood was collected in centrifuge tubes and allowed to clot. After centrifugation, sera from pairs of similarly treated rats were combined, thereby yielding 4 pooled samples each from 8 untreated rats (cage controls), 8 sham-exposed rats, and 8 rats exposed at each power density (a total of 16 pooled samples from 32 rats). Aliquots of the pooled samples were assayed for T-4, T-3, the percentage of T-3 uptake (T-3u), and CS. The free thyroxine index (FTI), defined as the product of T-4 and T-3u, and adjusted thyroxine (AT-4), defined as the product of T-4 and the ratio of T-3u for treated rats to T-3u for control rats, were calculated.

The differences in T-4, T-3, T-3u, FTI, and AT-4 were not statistically significant among the cage-control, sham, and RFR groups. The serum-CS mean value for the rats exposed at 2 mW/sq cm (0.44 W/kg) was almost the same as for the sham group and the means for both of these groups were significantly higher than for the cage controls. However, the mean CS for the rats exposed at 10 mW/sq cm (2.2 W/kg) did not significantly differ from the value for the cage controls.

The authors indicated that the negative findings for T-4, T-3, T-3u, FTI, and AT-4 were consistent with those of Lu et al. (1977 and 1980b). About the CS results, they stated: "Although the 10- mW/sq-cm exposure group had lower corticosterone levels than either the 2 or 0 mW/sq-cm group, the 10 mW/sq-cm group had levels which were similar to those of the untreated controls. These data suggest that the experimental protocol stimulated the HHA [hypothalamo-hypophyseal-adrenal] axis, and that this effect could be counteracted by exposure to microwaves at 10 mW/sq cm." The meaning of "experimental protocol" in the last statement is unclear; presumably it is meant to account for the significant dif-

ference between the mean CS values for the untreated-control and sham-exposed groups, which is an indication that uncontrolled factors were present. Also, their results are not consonant with the the later CS results of Lu et al. (1980b), who controlled for stress factors that would otherwise have elevated CS levels, and who obtained nonmonotonic, nonsignificant CS changes in the rats exposed for 8 hr at 5 or 10 mW/sq cm (relative to sham-exposed rats) and a significant CS depression for the rats exposed for 8 hr at 20 mW/sq cm.

In general, it is difficult to distinguish alterations of hormonal levels ascribable to RFR exposure in the 0-10 mW/sq-cm range for periods that are substantial fractions of the circadian cycle from alterations associated with the circadian cycle and/or other uncontrolled factors.

In a more recent paper, Lu et al. (1985), noting the inconsistencies in findings among various investigators, described studies with male Long-Evans rats of ages 36-41 days totaling 353 from two suppliers, Charles River Breeding Laboratories (CR) and Blue-Spruce Farms (BS). After the rats were acclimated and gentled, including 4 to 11 days of observation, 2 weeks of handling, and 3 to 5 days of simulated exposure, they were exposed dorsally from above concurrently in groups of four in individual Styrofoam cages to far-field, 2.45-GHz RFR amplitude-modulated at 120 Hz in an anechoic chamber held at 23-25 deg C and 50-60% relative humidity. The minimum separation between rats was 18 cm.

Whole-body SARs were determined from changes in colonic temperature in rats anesthetized with sodium pentobarbital and encased in a Styrofoam jacket. In 20 determinations at 60 mW/sq cm, the mean SAR was 11.26 +/- 1.79 (SD) W/kg for four rats exposed concurrently in an array and 11.21 +/- 1.72 W/kg with only one rat present. Thus, the normalized SAR was 0.19 W/kg per mW/sq cm, a value close to that previously obtained in the authors'laboratory (0.21).

Exposure protocols (A)-(G) below were used. The rats were given a 3-hr equilibration period before the start of exposure. Except as indicated, endpoints were sampled immediately after completion of exposure; the rats were decapitated and trunk blood was collected, processed, and assayed for serum T-4 concentration. Student's t-test was used for comparing RFR- and sham-exposed groups. Analysis of variance was also used on the experimental design.

(A) 1-hr exposures ending at 1230: BS rats at 0 to 70 mW/sq cm (13.3 W/kg).
(B) 2-hr exposures ending at 1330: BS rats at 0 to 20 mW/sq cm (3.8 W/kg); CR rats at 0 to 40 mW/sq cm (7.6 W/kg).
(C) 4-hr exposures ending at 1530: BS rats at 0 to 20 mW/sq cm (3.8 W/kg); CR rats at 0 to 40 mW/sq cm (7.6 W/kg).
(D) 8-hr exposures ending at 1930: BS rats at 0 to 20 mW/sq cm (3.8 W/kg).
(E) 24-hr delayed measure of endpoints after 4-hr exposure of CR rats at 0 to 40 mW/sq cm (7.6 W/kg); 17 hr after exposure, these rats were sham-exposed for 7 hr.

(F) three consecutive daily 4-hr exposures: CR rats at 0 to 55 mW/sq cm (10.45 W/kg).
(G) 10 consecutive daily 4-hr exposures, 5 days/week, for 2 weeks: CR rats at 0 to 40 mW/sq cm (7.6 W/kg).

The results for the 1-hr exposures of BS rats (A) showed significantly higher T-4 levels for those exposed at 40 or 70 mW/sq cm (7.6 or 13.3 W/kg), but not for those exposed at 1, 5, 10, 20, 50, or 60 mW/sq cm (0.19, 0.95, 1.9, 3.8, 9.5, or 11.4 W/kg). For the 2-hr exposures (B), the pooled mean levels of T-4 for the rats from both suppliers were higher after exposure at 25, 30, or 40 mW/sq cm (4.75-7.6 W/kg), but not at 1, 5, 10, or 20 mW/sq cm (0.19-3.8 W/kg). However, the normal T-4 concentrations for the CR rats were found to be higher than for the BS rats, so these and subsequent results were reevaluated by separately comparing the T-4 levels for the RFR-exposed rats from each supplier with the sham-exposed rats from the same supplier. When this was done for the 2-hr exposures, there were no significant changes in T-4 concentration for any RFR level.

For the 4-hr exposures (C), the mean T-4 levels of the BS rats were significantly higher after exposure at 1 mW/sq cm (0.19 W/kg), and were significantly lower after exposure at 20 mW/sq cm (3.8 W/kg), than after sham-exposure, but no changes were seen for 5 or 10 mW/sq cm (0.95 or 1.9 W/kg). (The 4-hr results for the CR rats were not reported.) The results for the remaining protocols showed no significant RFR-induced alterations of T-4 level, except for the CR rats exposed for three consecutive daily 4-hr periods (F) at 40 mW/sq cm (7.6 W/kg), for which the T-4 level was significantly lower than for shams.

The authors performed the foregoing comparisons with the t-test because it was used in many previous studies. However, their use of two-way analysis of variance as well, confirmed the finding of no significant changes in T-4 concentration for 2-hr exposures at any RFR level when comparisons were made between RFR- and sham-exposed rats from the same supplier. In addition, analysis of variance on the sham-exposed groups confirmed that the normal mean T-4 level of the CR rats was higher than for the BS rats and that the time when exposures were completed was not a significant factor. As the number of sham-exposures increased from 4 to 15, however, the mean T-4 level rose monotonically and significantly.

In their discussion, the authors noted that "conceptually, response of the thyroid gland to a change in the internal or external environment can be a specific reaction to the demand of thermoregulation (or energy metabolism) or a nonspecific reaction to a stressful stimulus," and that thyrotropin, the thyroid-stimulating hormone (TSH), should be considered in conjunction with thyroid responses. They referenced their previous finding (Milroy and Michaelson, 1972; Lu et al., 1981b) that TSH had decreased unequivocally and consistently with increasing levels of RFR exposure and that the decreases could be correlated with increases of colonic temperature. Thus, they had expected that irrespective of which mechanism (thermogenic or nonspecific stimulus) was involved, the levels

of T-4 would also decrease.

Because of the design of their protocols, they believed that they had avoided possible nonspecific reactions to stressful stimuli, but not those from repeated sham-exposures. They concluded that: "Obviously, our data and discussion do not resolve the precise mechanism for the results obtained by us, nor do they define the degree of responsiveness of thyroxine level to microwave exposure." and "From the viewpoint of environmental health, changes in serum thyroxine cannot be used as an indicator of a past history of microwave exposure due to its limited magnitude of response and its sensitivity to extraneous factors."

In a study with primates, Lotz and Podgorski (1982) monitored the levels of cortisol, T-4, and GH before, during, and after RFR exposure. Prior to exposure, a catheter was surgically implanted in the internal jugular vein (into the superior vena cava) of six male rhesus monkeys; the other end was threaded subcutaneously over the shoulder and was passed through the skin at the middle of the back. Two weeks or more were allowed for recovery from the surgery.

The experimental session was 42 hr long, starting on the afternoon preceding the start of data collection. Each monkey was seated in a Styrofoam restraint chair in the far field of a vertically polarized, horizontally propagating horn within an anechoic chamber at about 24 deg C and 55% relative humidity. On the following morning, the monkey was fed at 0730, just before the chamber was closed and data collection was begun. During the next 24 hr, water was provided ad libitum from a reservoir outside the chamber through a vinyl tube. At each hour from 0800 to 0800 the following day, blood samples were drawn through tubing connected to the catheter and routed to the outside of the chamber, and colonic temperature was measured with an indwelling thermistor probe. The lights were on from 0600 to 2200 in the chamber and home-cage room. A video camera mounted in the chamber was used to observe the monkey being treated.

Each monkey was given 8-hr sessions (from 1200 to 2000) of exposure to 1.29-GHz pulsed RFR (3-microsecond pulses at 337 pps) at average power densities of 20, 28, and 38 mW/sq cm. (The corresponding peak power densities were about 20, 28, and 38 W/sq cm.) The SARs, determined by Olsen et al. (1980) for a muscle-equivalent model of a sitting rhesus monkey, were about 2.1, 3.0, and 4.1 W/kg. The authors noted that the resting metabolic rate (RMR) of a rhesus monkey is about 2.4 W/kg. Each monkey was given a total of three sessions at each level of RFR, which were alternated with sham-exposure sessions at intervals of 10-14 days for recovery.

After each blood sample (2.5 ml) was collected, it was heparinized and centrifuged, the plasma was aseptically removed, and the erythrocytes were resuspended in sterile physiological saline and returned to the monkey via the catheter. Hematocrit and hemoglobin, monitored before and after each session, showed no significant decline. Plasma samples were assayed for cortisol, T-4, and GH. The data collected from the

monkeys for the same clock periods of each of the three sessions at each RFR level were averaged, to yield a 24-hr temporal series of mean values for each condition.

For the control sessions (those that involved sham-exposure), the mean hourly rectal temperature exhibited a slight 24-hr periodicity, with minimum values during the lights-off interval (2200-0600). For the RFR-exposure sessions, the mean rectal-temperature time profile during the preexposure period was similar to that for control sessions (about 38 deg C), but rose within 2 hr after the start of exposure to plateaus that were dependent on power density, e.g., to 39.7 deg C for exposure at 38 mW/sq cm (4.1 W/kg), and returned to the control profile within 2 hr after exposure end.

The hourly mean plasma-cortisol level for the control sessions showed a slow but steady decline to a minimum at the start of the dark period, after which it recovered slightly more rapidly to almost initial levels by 0800. For the sessions involving exposure at 20 and 28 mW/sq cm (2.1 and 3.0 W/kg), the hourly means did not significantly differ from the corresponding values for the sham-exposure sessions, i.e., they had a similar decline and recovery profile. At 38 mW/sq cm (4.1 W/kg), the mean plasma-cortisol level had a corresponding preexposure profile, but rose to significantly above control level within about 2 hr after the start of exposure, remained above control level during the rest of the exposure period. The cortisol level then diminished to control profile, also with a delay of about 2 hr after exposure end, indicating that the effect was transient (reversible).

The mean plasma-GH time profiles for all exposure conditions rose and fell periodically during the 24-hr period, but at corresponding times, there were no significant differences between control values and those for any RFR level. The mean T-4 profile for the control sessions showed little change over the 24-hr period, and the profiles for the three RFR levels were similar, with no significant differences from control means at corresponding times.

In their discussion, the authors noted that the increases in circulating cortisol level for exposure at 38 mW/sq cm and the absence of this response at 20 and 28 mW/sq cm indicates the existence of a threshold between 28 and 38 mW/sq cm (3.0 and 4.1 W/kg) and that the increases were associated with rectal-temperature elevations of about 1.7 deg C. Thus, the results support the hypothesis that RFR adrenocortical effects are thermally induced. The authors also noted that the SAR necessary to elicit similar rectal-temperature increases and adrenocortical responses in rats was about 4 W/kg as well, but that this SAR is about half the RMR for the rat but almost twice the RMR for the rhesus monkey. They ascribed this difference in SAR/RMR to the different internal spatial distributions of SAR and to differences in thermoregulatory capability.

The authors also indicated that the dose-response relationship for behavioral effects observed by de Lorge (1976) in rhesus monkeys (see Section 3.7.1.2) is highly consistent with that obtained in the present

study; in the earlier study, 1-hr exposures of rhesus monkeys to 2.45-GHz RFR also yielded rectal-temperature increases proportional to power density and that the threshold for behavior disruption was about 4.7 W/kg, i.e., close to the 4.1 W/kg for significant cortisol increase.

In summary, although some effects of RFR exposure on the endocrine system appear to be relatively straightforward and predictable from physiological considerations, other, more subtle effects may be worthy of further study, notably those related to the interactions among the pituitary, adrenal, thyroid, and hypothalamus glands and/or their secretions. Part of the problem in interpreting results appears to arise from uncertainties regarding stress mechanisms and accommodations thereto. Animals placed in novel situations are much more prone to exhibit stress responses than animals that have been adapted to the situation. However, there may be large variations in adaptation among animals in a given situation or among experimental situations in different laboratories. Moreover, the use of sham-treated controls may not always reduce the problem.

Because the reported effects of RFR on the endocrine systems of animals are largely ascribable to increased thermal burdens, stresses engendered by the experimental situation, or both, there is no evidence that such effects would occur in humans exposed to RFR at power densities that do not produce significant increases in body temperature.

REFERENCES:

Abhold, R.H., M.J. Ortner, M.J. Galvin, and D.I. McRee
STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHZ MICROWAVE RADIATION: II. EFFECTS ON THYROID AND ADRENAL AXES HORMONES
Radiat. Res., Vol. 88, No. 3, pp. 448-455 (1981)

Bruce, W.R., R. Furrer, and A.J. Wyrobek
ABNORMALITIES IN THE SHAPE OF MURINE SPERM AFTER ACUTE TESTICULAR X-IRRADIATION
Mutat. Res., Vol. 23, pp. 381-386 (1974)

Cairnie, A.B. and K.E. Leach
QUANTITATIVE STUDIES OF CYTOLOGICAL DAMAGE IN MOUSE TESTIS PRODUCED BY EXPOSURE TO HEAT
Can. J. Genet. Cytol., Vol. 22, pp. 93-102 (1980)

Cairnie, A.B., D.A. Hill, and H.M. Assenheim
DOSIMETRY FOR A STUDY OF EFFECTS OF 2.45-GHZ MICROWAVES ON MOUSE TESTIS
Bioelectromagnetics, Vol. 1, No. 3, pp. 325-336 (1980)

Cairnie, A.B. and R.K. Harding
CYTOLOGICAL STUDIES IN MOUSE TESTIS IRRADIATED WITH 2.45-GHZ CONTINUOUS-WAVE MICROWAVES
Radiat. Res., Vol. 87, pp. 100-108 (1981)

de Lorge, J.O.
THE EFFECTS OF MICROWAVE RADIATION ON BEHAVIOR AND TEMPERATURE IN RHESUS MONKEYS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 158-174 (1976)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22, (1978)

Guillet, R. and S.M. Michaelson
THE EFFECT OF REPEATED MICROWAVE EXPOSURE ON NEONATAL RATS
Radio Sci., Vol. 12, No. 6S, pp. 125-129 (1977)

Lancranjan, I., M. Maicanescu, E. Rafaila, I. Klepsch, and H.I. Popescu
GONADIC FUNCTION IN WORKMEN WITH LONG-TERM EXPOSURE TO MICROWAVES
Health Phys., Vol. 29, pp. 381-383 (1975)

Lebovitz, R.M. and L. Johnson
TESTICULAR FUNCTION OF RATS FOLLOWING EXPOSURE TO MICROWAVE RADIATION
Bioelectromagnetics, Vol. 4, No. 2, pp. 107-114 (1983)

Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHYOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979)

Lotz, W.G. and S.M. Michaelson
TEMPERATURE AND CORTICOSTERONE RELATIONSHIPS IN MICROWAVE-EXPOSED RATS
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 44, No. 3, pp. 438-445 (1978)

Lotz, W.G. and S.M. Michaelson
EFFECTS OF HYPOPHYSECTOMY AND DEXAMETHASONE ON RAT ADRENAL RESPONSE TO MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 47, No. 6, pp. 1284-1288 (1979)

Lotz, W.G. and R.P. Podgorski
TEMPERATURE AND ADRENOCORTICAL RESPONSES IN RHESUS MONKEYS EXPOSED TO MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 53, No. 6, pp. 1565-1571 (1982)

Lu, S.-T., N. Lebda, S.M. Michaelson, S. Pettit, and D. Rivera
THERMAL AND ENDOCRINOLOGICAL EFFECTS OF PROTRACTED IRRADIATION OF RATS BY 2450-MHZ MICROWAVES
Radio Sci., Vol. 12, No. 6S, pp. 147-156 (1977)

Lu, S.-T., N. Lebda, S. Pettit, and S.M. Michaelson
DELINEATING ACUTE NEUROENDOCRINE RESPONSES IN MICROWAVE-EXPOSED RATS
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 48, No. 6, pp. 927-932 (1980b)

Lu, S.-T., N. Lebda, S. Pettit, and S.M. Michaelson
MICROWAVE-INDUCED TEMPERATURE, CORTICOSTERONE, AND THYROTROPIN INTERRELATIONSHIPS
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 50, No. 2, pp. 399-405 (1981b)

Lu, S.-T., N. Lebda, S.M. Michaelson, and S. Pettit
SERUM-THYROXINE LEVELS IN MICROWAVE-EXPOSED RATS
Radiat. Res., Vol. 101, pp. 413-423 (1985)

Magin, R.L., S.-T. Lu, and S.M. Michaelson
MICROWAVE HEATING EFFECT ON THE DOG THYROID GLAND
IEEE Trans. Biomed. Eng., Vol. 24, No. 6, pp. 522-529 (1977a)

Magin, R.L., S.-T. Lu, and S.M. Michaelson
STIMULATION OF DOG THYROID BY LOCAL APPLICATION OF HIGH INTENSITY MICROWAVES
Am. J. Physiol., Vol. 233, No. 5, pp. E363-E368 (1977b)

Mikolajczyk, H.J.
MICROWAVE-INDUCED SHIFTS OF GONADOTROPIC ACTIVITY IN ANTERIOR PITUITARY GLAND OF RATS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 7-8010, pp. 377-382 (1976)

Milroy, W.C. and S.M. Michaelson
THYROID PATHOPHYSIOLOGY OF MICROWAVE RADIATION
Aerospace Med., Vol 43, No. 10, pp. 1126-1131 (1972)

Muraca, G.J., Jr., E.S. Ferri, and F.L. Buchta
A STUDY OF THE EFFECTS OF MICROWAVE IRRADIATION OF THE RAT TESTES
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 7-8010, pp. 484-494 (1976)

Olsen, R.G., T.A. Griner, and G.D. Prettyman
FAR-FIELD MICROWAVE DOSIMETRY IN A RHESUS MONKEY MODEL
Bioelectromagnetics, Vol. 1, No. 2, pp. 149-160 (1980)

Parker, L.N.
THYROID SUPPRESSION AND ADENOMEDULLARY ACTIVATION BY LOW-INTENSITY MICROWAVE RADIATION
Am. J. Physiol., Vol. 224, No. 6, pp. 1388-1390 (1973)

Prausnitz, S., and C. Susskind
EFFECTS OF CHRONIC MICROWAVE IRRADIATION ON MICE
IRE Trans. Bio-Med. Electron., pp. 104-108 (1962)

Saunders, R.D. and C.I. Kowalczuk
EFFECTS OF 2.45 GHZ MICROWAVE RADIATION AND HEAT ON MOUSE SPERMATOGENIC EPITHELIUM
Int. J. Radiat. Biol., Vol. 40, No. 6, pp. 623-632 (1981)

Todorovich, P., R. Gensi, and M. Kosanovich
ON THE INFLUENCE OF MICROWAVES ON RAT ADRENALS
Arkhiv. Bioloshkih Nauka, Vol. 17, No. #, pp. 121-128 (1965)

3.6.3 CARDIOVASCULAR EFFECTS

Few investigations were carried out on possible effects of RFR on the human heart. Among these was the occupational study by Hamburger et al. (1983), discussed in Section 3.1.1. By contrast, various studies of the effects of RFR on animal hearts were performed in vivo, and others were done in vitro, i.e., on hearts (or parts thereof) excised from animals.

Among the early investigations in vivo were two studies on the rabbit by Presman and Levitina (1962a,b), one with 2.4-GHz CW RFR at 7-12 mW/sq cm and the other with 3-GHz pulsed RFR (1-microsecond pulses, 700 pps) at 3-5 mW/sq cm average power density, 4.3-7.1 W/sq cm pulse power density. In both studies, each rabbit was used repeatedly as follows: the head only or the back only (each in dorsal or ventral aspect) or the entire surface (dorsal or ventral aspect) was exposed for two 20-min periods in each aspect. During each 20-min exposure and for 10 min preceding and following the exposure, the EKGs of the rabbits were recorded with plate electrodes. For control data, the same rabbits were sham-exposed once prior to, and once after, the series of RFR exposures.

Exposure of the entire dorsal surface did not yield either significant tachycardia or bradycardia during the exposure period per se. However, tachycardia was seen during the first half of the post-exposure period, changing to bradycardia toward the end of that period. By contrast, exposure of the dorsal aspect of the head or back produced significant tachycardia during the exposure period, with the former yielding the greater effect. The tachycardia increased to peak values at about 5 min post-exposure and declined to nonsignificant values by the end of that period. Bradycardia was seen during exposure in all three ventral aspects; it persisted to the end of the exposure period and was followed by returns toward normal heart rates during the first half of the post-exposure period. It was most pronounced and was manifested earliest for exposure of only the head.

The authors summarized the differences in results for pulsed and CW RFR as follows: "Above all, it must be noted that the effect of impulse irradiation was basically more manifest than the effect of continuous irradiation, despite the fact that the mean intensity with impulse irradiation was approximately half as great. This is not difficult to understand if it is taken into consideration that the impulse intensity exceeded the mean by 1400 times."

In general, the findings of these two papers were difficult to assess because no actual data were presented, only the relative differences of means (rendering it difficult to estimate variabilities among rabbits or the time variations of the heart-beat rate of each rabbit in the absence of RFR), and the statistical treatment of the results was obscure. A more fundamental question is whether use of metal electrodes to record EKGs during RFR exposure introduced artifacts of sufficient magnitude to render the results meaningless because the presence of such electrodes and their conductive leads could have significantly altered the local fields. This possibility is supported by the results of Kaplan et al.

(1971) and Birenbaum et al. (1975) in one laboratory, and Chou et al. (1980b) in another laboratory, discussed below. These investigators found that exposure of rabbits to average power densities of at least 80 mW/sq cm was necessary to affect their heart rates significantly.

In the first of two experiments, Kaplan et al. (1971) endeavored to replicate the CW study by Presman and Levitina (1962a), except that Kaplan et al. recorded the EKG of each rabbit with small curved surgical needles subcutaneously implanted in the left chest, right chest, and left hip, with these needles and their lead wires shielded from the incident RFR by an absorbent panel. Recording sessions (40 min) were 20 min of exposure at 10 mW/sq cm preceded and followed by 10 min without RFR. Using the same method as Presman and Levitina to calculate heart-rate changes, Kaplan et al. found no significant difference between the heart rate of each animal during or after exposure and its heart rate during a control condition of no exposure. Analysis of the variability in the heart-rate data from this experiment led Kaplan et al. to suggest that the heart-rate effects reported by Presman and Levitina might have been chance variations.

In the second experiment, Kaplan et al. (1971) recorded, concurrently with heart rate, the respiration rate with a strain gauge around the thorax and body temperature with a subcutaneous hypodermic thermistor near the midline of the lower back, for each of two rabbits during once-weekly 40-min sessions. During the 20-min exposure intervals, each rabbit was exposed in the dorsal aspect of the head only. The levels ranged from 0 to 100 mW/sq cm (in 20 mW/sq-cm increments). Respiration rate increased during exposure at 40 mW/sq cm and body temperature rose at 80 mW/sq cm, but heart rate increased only at 100 mW/sq cm.

Birenbaum et al. (1975), in another endeavor to replicate the results of Presman and Levitina, concurrently recorded EKGs, respiration rates, and subcutaneous temperatures, as described above. In one experiment, two unanesthetized rabbits were exposed in the dorsal aspect of the head tc 2.4-GHz CW RFR at 0 to 80 mW/sq cm (in 20-mW/sq-cm increments). All three indices increased with increasing power density in qualitatively similar fashion, but the mean respiration-rate increases were 20 times greater than the heart-rate increases. In another experiment, Birenbaum et al., (1975) exposed the entire dorsal surface of each rabbit to 2.8-GHz RFR (CW or 1.3-microsecond pulses at 1000 pps) at an average power density of 20 mW/sq cm and found no significant difference between the CW and pulsed responses for each index. In still another experiment, the backs of rabbits were exposed for 1 hr to 2.4-GHz CW RFR or infrared radiation (IR) at 0, 10, and 20 mW/sq cm. Although the respiration and heart rate changes were substantially the same for the RFR and IR, the subcutaneous temperature increased more rapidly and rose to higher values for the IR case.

Chou et al. (1980b) exposed three rabbits dorsally or ventrally 20 min per day for 10 days to 2.45-GHz RFR, CW or pulsed (1-microsecond pulses, 700 pps), at 5 mW/sq cm (average). For dorsal exposure at this level, the maximum SARs were 0.86 W/kg in the brain and 0.09 W/kg in the heart;

for ventral exposure, the corresponding values were 0.24 and 0.30 W/kg. The same animals were also exposed dorsally to 10-microsecond pulses, at a pulse power density of 13,700 mW/sq cm, that were synchronized to the heart rate with 0-, 0.1-, or 0.2-s delay times relative to the R wave of the EKG (which was measured with carbon-loaded Teflon electrodes; Chou and Guy, 1979a). The rabbits were acclimated for several weeks before the experiments and for at least 15 min before and after each exposure. No significant differences were observed between heart rates during the periods of exposure and nonexposure to RFR. In addition, no cumulative effects on heart rate were observed over four months of such exposures. The rabbits were also exposed to CW RFR at 80 mW/sq cm. The resulting heat stress disturbed them sufficiently to render heart-rate recording difficult. Heart rates increased for such exposure, but returned to normal about 20 min after termination of exposure.

In a study mostly on effects of RFR on metabolism and thermoregulation (see Section 3.6.1), Phillips et al. (1975) exposed rats to 2.45-GHz RFR at SARs of 0, 4.5, 6.5, or 11.5 W/kg for 30 min. Bradycardia was seen in the 4.5-W/kg group, but was statistically nonsignificant; mild but statistically significant bradycardia developed within 20 min for the 6.5-W/kg group, with recovery in about 2 hr; and pronounced bradycardia developed abruptly for the 11.1-W/kg group, after which the heart rates increased to values well above those of controls and persisted at these levels to the end of the test period. The bradycardia was accompanied by irregular heart rhythms, and incomplete heart block was evident for most of the rats exposed at the highest level, but the rats recovered within 60 min after cessation of exposure. The heart block was surmised to be caused by release of toxic materials, elevated serum potassium, or myocardial ischemia, all from excessive heat.

Galvin and McRee (1981a) studied the influence of exposure to RFR on the functioning of the intact heart of the cat with and without myocardial ischemia (MI). MI was induced in two groups of cats by occluding the left anterior descending coronary artery. The hearts of one group were exposed for 5 hr with a dielectrically loaded waveguide applicator to 2.45-GHz CW RFR at an SAR of 30 W/kg, and those of the other group were sham-exposed for the same duration. At 30 W/kg, heart temperature of dead cats increased at an initial rate of 0.43 deg C per min. However, no increases in aortic blood temperature occurred in live cats during RFR exposure. For comparison, the coronary arteries of two other groups were isolated but not occluded, and the hearts were similarly RFR- or sham-exposed.

The mean arterial blood pressure, cardiac output, heart rate, and EKG were measured before and during the 5-hr period. Arterial blood samples were drawn just prior to occlusion or isolation and hourly afterward, and assayed for plasma protein concentration and creatine phosphokinase (CPK) activity. After the 5-hr period, the hearts were excised. The left ventricle of each cat with the occluded artery was divided into ischemic-myocardium (IM) and nonischemic-myocardium (NIM) parts, and anatomically equivalent tissue samples were derived from the hearts of other cats. The heart samples were assayed for tissue CPK activity,

expressed as the ratio of CPK activity in the first part to that in the second part of each heart.

In both ischemic and nonischemic cats, the results showed no significant differences in mean arterial blood pressure, cardiac output, or heart rate between RFR- and sham-exposed groups, and no synergism of ischemia and RFR exposure for these cardiovascular indices. The EKG of the IM groups showed significant elevation of the S-T segment during the five hours, which did not occur for the NIM groups, but the differences in each case between RFR- and sham-exposed groups were nonsignificant. In addition, plasma CPK activity in the IM groups increased about ninefold in the 5-hr period, whereas it increased only about threefold in the NIM groups, but again, the differences between RFR- and sham-exposed groups were nonsignificant. Last, the ratio of myocardial tissue CPK activity in the two heart parts was about 0.8 for the ischemic RFR- and sham-exposed hearts and about unity for the nonischemic RFR- and sham-exposed hearts. These results indicated that local exposure of either the undamaged or the ischemic heart to CW RFR in vivo had no effect on the myocardium or its neural components. These findings are at variance with those obtained from isolated hearts exposed to RFR in vitro.

Hamrick and McRee (1980) exposed Japanese quail embryos 8-13 days old to pulsed and CW 2.45-GHz RFR at SARs of 0.3-30 W/kg to study the effects of such exposures on heart rate. No effects were detected that could not be attributed to temperature changes. In another study, Galvin et al. (1980a) exposed Japanese quail embryos during the first eight days of development to 2.45-GHz CW RFR at 5 or 20 mW/sq cm (SARs of 4.0 and 16.2 W/kg). The ambient temperature for each exposure was adjusted to maintain the embryonated eggs at 37.5 deg C. (This did not preclude the presence of thermal gradients in the exposed embryos since the RFR may not have been uniformly absorbed.) No changes were induced in either morphology of the embryonic heart or ultrastructure of the myocardial cells. Analysis of the enzymatic activities of lactate dehydrogenase, glutamic oxaloacetic transaminase, and creatine phosphokinase did not reveal any statistically significant differences between nonexposed controls and those groups exposed at either 5 or 20 mW/sq cm.

Among the in-vitro investigations was that of Frey and Seifert (1968), who exposed isolated frog hearts to 1.425-GHz pulsed RFR at a peak power density of 60 mW/sq cm and a pulse duration of 0.01 ms. The pulses were triggered at the peak of the P wave of the EKG and at 100 ms and 200 ms after the peak, so the average power density was negligible. Results were inconclusive for no delay and for the 100-ms delay, but significant tachycardia was seen for the 200-ms delay.

Clapman and Cain (1975) exposed 14 groups of isolated frog hearts for 1 min each to 1.42- or 3-GHz pulsed RFR. A 15th group served as controls. Three of the groups were exposed to 1.42-GHz, 0.01-ms pulses at a peak power density of 60 mW/sq cm and triggered at 0, 100, or 200 ms relative to the P wave (i.e., the same values used by Frey and Seifert, 1968, but each group was exposed at only one of the delays). Three other groups were similarly exposed, but with 0.15-ms instead of 0.01-ms

pulses. The other eight groups were exposed to 3-GHz RFR at a peak power density of 5,500 mW/sq cm. For three of these, 0.01-ms pulses were used; 0.002-ms pulses were used for another three. For one of the remaining groups, 0.002-ms pulses were triggered at the initial rise of the QRS complex of the EKG. The last group was exposed to unsynchronized 0.002-ms pulses at 500 pps, which yielded an average power density of 5.5 mW/sq cm. The results showed no significant differences in heart rate between any of the groups exposed to RFR and the control group.

Liu et al. (1976) also endeavored to obtain effects similar to those of Frey and Seifert (1968). In one set of experiments, frog hearts were isolated and exposed to 0.1-ms pulses of 1.42-GHz RFR triggered either by the P wave to begin 200-250 ms after the P-wave peak or by the R wave without significant delay. The time intervals between successive P-wave peaks were measured in the former, and those between successive R-wave peaks in the latter. The results for both showed no significant time-interval variations. In the other set of experiments, the thorax of the frog was opened, and the heart was exposed in situ to 0.1-ms pulses of either 1.42- or 10-GHz RFR. Again, negative results were obtained.

Lords et al. (1973) exposed isolated turtle hearts submerged in Ringer's solution to 960-MHz CW RFR, typically for 30 min, in a capacitor system at applied powers in the range from 0 to 500 mW. Bradycardia was seen for the range from about 50 to 200 mW, and tachycardia at higher powers. They estimated that about 3.3% of the applied power was absorbed by the heart and that the temperature increase in the heart at 100 mW was about 0.2 deg C.

Lords et al. (1973) also found that heating the solution (without RFR) yielded tachycardia, so they hypothesized that the bradycardia observed in the lower power range resulted from RFR-induced neurotransmitter release by the remnants of the sympathetic and parasympathetic nervous systems in the heart preparation. Tinney et al. (1976) subsequently obtained confirmation of this hypothesis. They demonstrated that when propranolol hydrochloride (which blocks the sympathetic system) or atropine (which blocks the parasympathetic system) was added to the Ringer's solution, RFR-exposure did not produce bradycardia. Reed et al. (1977) produced bradycardia in isolated rat hearts exposed to the same frequency for 10 min in the SAR range from 1.5 to 2.5 W/kg; no bradycardia was observed when the same blocking agents were used.

Galvin et al. (1981b) isolated cardiac muscle cells from the Japanese quail heart and exposed them in suspension to 2.45-GHz CW RFR within a special water-filled-waveguide system at 37 deg C. The impedance of the waveguide was matched to that of free space by a quarter-wave dielectric plate, and the specimen to be exposed was placed against the immersed surface of the plate. As a control, another similarly prepared specimen was concurrently mounted in the waveguide at 9.5 cm from that surface of the plate, and thus received essentially no RFR because of attenuation by the intervening water. Exposures were for 90 min at mean SARs of 1, 10, 50, or 100 W/kg, determined from time-temperature profiles.

After exposure, aliquots of the suspensions were examined for integrity of the cardiac cells using the trypan-blue exclusion test. (An intact cell will exclude this vital stain.) The remainder of each suspension was centrifuged at 250g for 30 min, the supernatants were assayed for release of the enzymes creatine phosphokinase (CPK) and lactic acid dehydrogenase (LDH), and the pellets were resuspended. The latter suspensions were centrifuged at 10000g for 15 min and assayed for bound enzyme. The pellets from some experiments were cooled to 4 deg C and fixed, dehydrated, embedded, sectioned, and examined with an electron microscope.

Trypan-blue exclusion was unaffected by exposure at 1 W/kg, but the suspensions exposed at 10, 50, and 100 W/kg showed successively larger increases in percentages of cells permeable to the stain relative to their respective control suspensions. CPK release was unaffected at any SAR. However, LDH release increased monotonically with SAR, but the increases relative to controls were nonsignificant except at 100 W/kg. The ultrastructural appearance of heart cells exposed at 1, 10, and 50 W/kg, as well as control cells appeared normal. However, cells exposed at 100 W/kg showed increased cytoplasmic vacuolization and chromatin clumping, but the intercellular junctions remained intact.

Galvin et al. (1982a) also isolated atria of spontaneously beating rat hearts, suspended the atria in glass tubes continuously perfused with aerated Krebs Henseleit solution, and exposed the specimens individually for 30 min to 2.45-GHz CW RFR at an SAR of 2 or 10 W/kg in the special water-filled-waveguide system at 37 or 22 deg C. As before, a similarly prepared specimen concurrently mounted in the waveguide at 9.5 cm from the first served as a control. The atria were equilibrated for 30 min before exposure and allowed to recover for 30 min after exposure.

Contractile force and beat rate were recorded with a cardiotachometer periodically before, during, and after exposure. At 37 deg C, the average beat rate for both exposed and control atria was 230 beats per minute for 2 W/kg and 215 beats per minute for 10 W/kg. However, the beat rate of each specimen expressed as a percentage of its own rate at the start of exposure was not significantly different from 100%. The average contractile force at 37 deg C was 640 mg for the control atria and for those exposed at 2 and 10 W/kg. At 22 deg C, the average beat rates at 2 and 10 W/kg were 102 and 106 beats per minute, respectively, and there were no significant differences between these values and their corresponding control values expressed as percentages of initial rates. The average contractile force at 22 deg C was 1,200 mg. These findings for isolated heart atria support the conclusion of Galvin and McRee (1981a) that in-vivo exposure of intact animals to CW RFR at the stated power densities or SARs has no influence on the myocardium or its neural components.

The question about possible electrode artifacts was studied further by Yee et al. (1984), who divided 102 isolated frog hearts into ten groups, placed them individually in a waveguide filled with Ringer's solution, and exposed them to 2.45-GHz CW RFR at 2 and 8.55 W/kg. Heart rate was

recorded using one of the following methods: 3-M KCl glass electrode, ultrasound probe, tension transducer, Ringer's solution glass electrode, and a metal wire inserted in the Ringer-solution electrode. Accelerated decrease of heart rate was observed only in those groups recorded using the 3-M KCl electrode and the metal wire Ringer's solution electrode. No effect was found in the other groups. These results indicate that bradycardia in isolated hearts could be caused by electrode artifacts resulting from intensification of the electromagnetic fields.

In summary, results of studies of the effects of RFR on heart-beat rate in which EKGs were recorded with electrically conductive electrodes that were not shielded from the RFR during exposure are open to question with regard to possible presence of artifact. On the other hand, results of the studies done with shielded or nonperturbing electrodes indicate that heart rate is altered by RFR only at levels that produce significant temperature elevations or otherwise add thermal burdens to the animal. Also, the experimental evidence that RFR pulses that are synchronous with various phases of the EKG alter heart rate appears to be weak at best; most of the results were negative.

REFERENCES:

Birenbaum. L., I.T. Kaplan, W. Metlay, S.W. Rosenthal, and M.M. Zaret
MICROWAVE AND INFRA-RED EFFECTS ON HEART RATE, RESPIRATION RATE AND SUBCUTANEOUS TEMPERATURE OF THE RABBIT
J. Microwave Power, Vol. 10, No. 1, pp. 3-18 (1975)

Chou, C.-K. and A.W. Guy
CARBON ELECTRODES FOR CHRONIC EEG RECORDINGS IN MICROWAVE RESEARCH
J. Microwave Power, Vol. 14, No. 4, pp. 399-404 (1979a)

Chou, C.-K., L.F. Han, and A.W. Guy
MICROWAVE RADIATION AND HEART-BEAT RATE OF RABBITS
J. Microwave Power, Vol. 15, No. 2, pp. 87-93 (1980b)

Clapman, R.M. and C.A. Cain
ABSENCE OF HEART-RATE EFFECTS IN ISOLATED FROG HEART IRRADIATED WITH PULSE MODULATED MICROWAVE ENERGY
J. Microwave Power, Vol. 10, No. 4, pp. 411-419 (1975)

Frey, A.H. and E. Seifert
PULSE MODULATED UHF ENERGY ILLUMINATION OF THE HEART ASSOCIATED WITH CHANGE IN HEART RATE
Life Sci., Vol. 7, No. 10, Part II, pp. 505-512 (1968)

Galvin, M.J., D.I. McRee, and M. Lieberman
EFFECTS OF 2.45-GHZ MICROWAVE RADIATION ON EMBRYONIC QUAIL HEARTS
Bioelectromagnetics, Vol. 1, No. 4, pp. 389-396 (1980a)

Galvin, M.J. and D.I. McRee
INFLUENCE OF ACUTE MICROWAVE RADIATION ON CARDIAC FUNCTION IN NORMAL AND MYOCARDIAL ISCHEMIC CATS
J. Appl. Physiol: Respiratory, Environmental, and Exercise Physiol., Vol. 50, No. 5, pp. 931-935 (1981a)

Galvin, M.J., C.A. Hall, and D.I. McRee
MICROWAVE RADIATION EFFECTS ON CARDIAC MUSCLE CELLS IN VITRO
Radiat. Res., Vol. 86, pp. 358-367 (1981b)

Galvin, M.J., M.S. Dutton, and D.I. McRee
INFLUENCE OF 2.45-GHZ CW MICROWAVE RADIATION ON SPONTANEOUSLY BEATING RAT ATRIA
Bioelectromagnetics, Vol. 3, No. 2, pp. 219-226 (1982a)

Hamburger, S., J.N. Logue, and P.M. Silverman
OCCUPATIONAL EXPOSURE TO NON-IONIZING RADIATION AND AN ASSOCIATION WITH HEART DISEASE: AN EXPLORATORY STUDY
J. Chron. Dis., Vol. 36, No. 11, pp. 791-802 (1983)

Hamrick, P.E. and D.I. McRee
THE EFFECT OF 2450 MHZ MICROWAVE IRRADIATION ON THE HEART RATE OF EMBRYONIC QUAIL
Health Phys., Vol. 38, pp. 261-268 (1980)

Kaplan, I.T., W. Metlay, M.M. Zaret, L. Birenbaum, and S.W. Rosenthal
ABSENCE OF HEART-RATE EFFECTS IN RABBITS DURING LOW-LEVEL MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 168-173 (1971)

Liu, L.M., F.J. Rosenbaum, and W.F. Pickard
THE INSENSITIVITY OF FROG HEART RATE TO PULSE MODULATED MICROWAVE ENERGY
J. Microwave Power, Vol. 11, No. 3, pp. 225-232 (1976)

Lords, J.L., C.H. Durney, A.M. Borg, and C.E. Tinney
RATE EFFECTS IN ISOLATED HEARTS INDUCED BY MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 21, No. 12, pp. 834-836 (1973)

Phillips, R.D., E.L. Hunt, R.D. Castro, and N.W. King
THERMOREGULATORY, METABOLIC, AND CARDIOVASCULAR RESPONSE OF RATS TO MICROWAVES
J. Appl. Physiol., Vol. 38, No. 4, pp. 630-635 (1975)

Presman, A.S. and N.A. Levitina
NONTHERMAL ACTION OF MICROWAVES ON CARDIAC RHYTHM--COMM. I: A STUDY OF THE ACTION OF CONTINUOUS MICROWAVES
Bull. Exp. Biol. Med., Vol. 53, No. 1, pp. 36-39, (1963a) (Engl. Transl. of pp. 41-44 of 1962a Russ. publ.)

Presman, A.S. and N.A. Levitina
NONTHERMAL ACTION OF MICROWAVES ON THE RHYTHM OF CARDIAC CONTRACTIONS IN ANIMALS--REP. II: INVESTIGATION OF THE ACTION OF IMPULSE MICROWAVES
Bull. Exp. Biol. Med., Vol. 53, No. 2, pp. 154-157 (1963b)
(Engl. Transl. of pp. 39-43 of 1962b Russ. publ.)

Reed, J.R.III, J.L. Lords, and C.H. Durney
MICROWAVE IRRADIATION OF THE ISOLATED RAT HEART AFTER TREATMENT WITH ANS BLOCKING AGENTS
Radio Sci., Vol. 12, No. 6S, pp. 161-165 (1977)

Tinney, C.E., J.L. Lords, and C.H. Durney
RATE EFFECTS IN ISOLATED TURTLE HEARTS INDUCED BY MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 24, No. 1, pp. 18-24 (1976)

Yee, K.C., C.K. Chou, and A.W. Guy
EFFECT OF MICROWAVE RADIATION ON THE BEATING RATE OF ISOLATED FROG HEARTS
Bioelectromagnetics, Vol. 5, No. 2, pp. 263-270 (1984)

3.6.4 OCULAR AND AUDITORY EFFECTS IN ANIMALS

Studies of ocular effects and of perception of RFR pulses as sound by animals were discussed in Sections 3.1.4.1 and 3.1.4.2, respectively.

3.6.5 CONCLUSIONS

The finding that the thermoregulatory systems of nonhuman primates can readily compensate for high RFR levels is most significant relative to possible hazards of human exposure, because of the closer similarities in anatomies and physiological characteristics among human and nonhuman primates than between those of humans and any other laboratory species.

Most of the studies of possible RFR-induced effects on the endocrine system were conducted on rodents. Those that yielded positive findings indicated that the effects were largely due to increases in the thermal burdens of the animals. In many of the studies, the alterations in endocrine function may have been influenced significantly by stresses in the animals. For this reason, the studies by Michaelson and coworkers are notable for the efforts toward reducing stress by acclimating the animals to handling and to the experimental situation. Nevertheless, some of the subtle effects of RFR on the endocrine system are worthy of further study.

Regarding effects of RFR on the heart, some early studies were conducted in which excised hearts were exposed to RFR, and others in which the whole animal was exposed in vivo. The positive findings reported in most of these studies (bradycardia, tachycardia, or both) were suspect because of the use of attached or indwelling electrodes that probably introduced significant artifact in the results. Later studies involving the use of electrodes that were not perturbed by, or did not perturb, the RFR yielded results indicating that heart rates were altered only at RFR levels that caused significant body-temperature rises or otherwise added to the thermal burden of the animal.

Also investigated, both in excised animal hearts and in vivo, was the possibility that pulsed RFR at repetition rates synchronous with various periodic characteristics of the EKG could alter the heart rate. Frey and Seifert (1968) had reported that tachycardia was induced in isolated frog hearts by RFR pulses in synchrony with the EKG, but this finding was not confirmed by other investigators in isolated hearts (Clapman and Cain, 1975; Liu et al., 1976) or in intact animals (Chou et al., 1980b).

Other investigators (Phillips et al., 1975; Chou et al., 1980b) showed that for CW RFR, levels well in excess of 1 mW/sq cm or 1 W/kg were necessary for significant alterations of heart rate. The results of another important study (Galvin and McRee, 1981b) indicated that the functioning of hearts already damaged from other causes is not affected by exposure to CW RFR at levels of 10 mW/sq cm or lower.

3.7 BEHAVIOR

Numerous investigations have been conducted on possible effects of RFR exposure on various forms of animal behavior. The papers discussed in Section 3.7.1 represent most of the studies performed on naturalistic behavior, reflex activity, learning, and performance of trained tasks by rabbits, rodents, and nonhuman primates. Interactive effects of RFR and drugs on behavior and physiological responses are discussed in Section 3.7.2. Effects of RFR on behavioral thermoregulation are not included below because they were discussed in Section 3.6.1, "Metabolism and Thermoregulation."

3.7.1 RFR EFFECTS ON NATURALISTIC BEHAVIOR, REFLEX ACTIVITY, LEARNING, AND PERFORMANCE OF TRAINED TASKS

3.7.1.1 RABBITS AND RODENTS

Justesen and King (1970) exposed six Sprague-Dawley male rats within a modified commercial microwave oven (Justesen et al., 1971) to 2.45-GHz RFR (modulated at 60 Hz from the magnetron high-voltage power supply and at 12 Hz by the mode stirrer) in chamber temperatures ranging from 22 to 26 deg C. Each session consisted of alternating 5-min intervals of RFR and no RFR (0.5 duty cycle) for a total time of 60 min. The silhouette-surface-area equivalent power density, time-averaged over an exposure session, was 2.5, 5, 10, or 15 mW/sq cm, with the level during any session never exceeding 30 mW/sq cm. By calorimetry with distilled-water phantom loads in the oven, the corresponding mean SARs were about 7.5, 15, 30, or 45 W/kg, but data were presented only for SARs of 0 (sham), 1.5, 3.1, and 4.6 W/kg (0, 0.5, 1.0, and 1.5 mW/sq cm).

Prior to exposure, the rats were food-deprived to 85% of median control weight and trained on a fixed-ratio (FR) schedule of reinforcement, the learning task being to lick a specially designed nozzle a prescribed number of times (usually 40, termed an FR-40 schedule) to be rewarded with a drop of dextrose-water solution. Each lick was detected as an interruption of a light beam by the tongue. The FR schedules were made more complex by use of a 525-Hz tone as alternating reinforcement and extinction components presented at random intervals during a session, with "tone-on" for three of the rats and "tone-off" for the other three rats signifying the availability of reward. These rats served as their own controls at all RFR levels, i.e., the same group was exposed, during various sessions, at each of the time-averaged RFR levels noted above.

The mean number of responses during the reinforcement periods diminished monotonically from about 6400 per session at 0 W/kg to about 2500 at 4.6 W/kg. Visual observations of the rats by the authors showed that the decreases in total numbers of responses did not arise from lower licking rates when the rats were responding, but from cessation of responding, especially near session end, probably associated with warming of the rats. The authors indicated that the rats exhibited extreme flaccidity, "as if injected with a curariform drug," on examination at session end, but that they recovered fully within 5 to 10

min, with no aversion for the chamber on the next day.

In subsequent experiments, first the rats were trained readily (in 2 or 3 sessions) to respond reliably on FR-20 complex schedules to the fixed-interval presence or absence of light illumination (from a house-lamp) in lieu of the 525-Hz tone as the cue. The responses of the rats to the presence or absence of the RFR at 0.8 or 1.6 W/kg as the cue were then determined. Even after 13 sessions, none of the rats responded much above baseline levels. The authors defined the discrimination ratio as the total number of responses per session by a rat during reinforcement divided by its responses during extinction. With light as the cue, the ratios were high (e.g., about 20), but were low (about 2) for either RFR level as the cue. Moreover, reversal of the reinforcement cue from "on" to "off" midway through sessions markedly diminished the ratio for the light, but had no significant effect for the RFR cues.

Near the completion of the behavioral studies, deep rectal temperatures were taken just before and after 60-min sessions at 0, 1.5, and 4.25 W/kg and after 19 min at 4.25 W/kg. During sham-exposure, four of the rats had initial temperatures less than 38 deg C and showed temperature rises exceeding 1 deg C; the initial temperatures of the other two rats exceeded 38 deg C and showed slight decreases. The results at 1.5 W/kg were presented for only three rats: Two of these showed rises of more than 1 deg C; the third rat, which had an initial temperature of almost 39 deg C, showed essentially no change. At 4.25 W/kg, the temperatures of five of the six rats rose by more than 2 deg C in 60 min, and the temperatures of three of these rats rose more than 1.5 deg C in 19 min.

At the end of the behavioral studies, the RFR-exposed rats as well as a group of 7 food-deprived rats and a group of 5 normal-weight rats that were neither RFR-exposed nor behaviorally conditioned were euthanized, and their brains were removed and shipped to another laboratory for histological examination. No significant differences indicative of adverse effects of RFR were found.

In a later paper, King et al. (1971) provisionally ascribed the absence of response to the RFR as a cue to possibly inadequate sensitivity of a behavioral paradigm based on appetite, and suggested that rats may be more responsive to the technique of conditional suppression. In this technique, a subject is reinforced after it makes an operant response; the subject is then reinforced on an intermittent schedule until it responds frequently and consistently; when this status is achieved, a Pavlovian conditioning regime is superposed, in which a warning signal always terminated with a brief but aversive unconditional stimulus is presented at various times until the subject responds stably in the absence of the warning signal but does not respond when it is presented.

The operant response used was tongue licking for dextrose solution (as in the previous study) and the aversive unconditional stimulus was an electric shock to the feet. The efficiency of the 525-Hz tone as a warning stimulus was compared with cueing RFR (2.45-GHz RFR modulated at

60 and 12 Hz, in the modified microwave oven) at 1.2, 2.4, 4.8, or 6.4 W/kg. Discriminative Efficiency (DE) was defined as the percent ratio (S-W)/S, S being the number of responses per session in the absence of warning and W the number of responses when warning was presented. For the tone, DE exceeded 90%. For the RFR, mean DE at 1.2 W/kg was about 25%, a value barely significant statistically at the 5% level; mean DEs increased with SAR to a maximum of about 80% at 6.4 W/kg. Thus, the effect had a threshold of about 1.2 W/kg. The corresponding silhouette-surface-area equivalent power density was about 2.5 mW/sq cm.

Nealeigh et al. (1971) set up a horizontal Y- maze with one side of its start box on the axis of a horizontally pointed standard-gain horn at a distance of 1 m and with the rest of the maze essentially outside the field of the horn. Twenty Sprague-Dawley female rats were placed on a 23.5-hr deprivation schedule for 13 days, during which they were handled and placed in the maze for familiarization. At the end of the schedule, each of 10 of the rats was held in the start box for 20 min while it was exposed to 2.45-GHz CW RFR at a maximum of 50 mW/sq cm (value on horn axis). From Durney et al. (1978), p. 95, the SAR is estimated to have been about 10 W/kg. The remaining 10 rats were similarly sham-exposed.

Each rat was then released to run the maze and to select either the right or left arm. Once the rat entered either arm, it was kept in that arm for about 20 seconds to eat a food reward if present. Trial 1 was completed when the rat found the reward for the first time. The next correct response was the alternate arm. Each rat was given 50 trials per day on three consecutive days. The percentages of correct responses on each day were recorded and were transformed to arcsin of square-root of percentage (expressed in deg) before they were tested for statistical significance by analysis of variance and trend analysis.

There was no significant difference in behavior between the two groups during the 20 min of RFR- or sham-exposure; neither group appeared to be stressed. Rectal temperatures taken on two male rats during 20 min of RFR exposure each increased approximately linearly by about 1.5 deg C.

The performance data in the maze for the RFR group yielded mean angles (transformed percentages) of 52.5, 60.7, and 71.2 deg for days 1, 2, and 3, respectively, an almost linear increase in learning. The results for the sham group were 56.1, 56.5, and 65.2 deg, respectively. Based on the statistical analyses, the RFR had a stimulatory effect, i.e, it improved the performance of the rats.

Lobanova (1974), in the first of several series of experiments, trained rabbits to respond to a sound or light stimulus by pulling on a ring attached to a food-dispensing trough. The author then exposed the rabbits 60 min daily for 4 months to centimeter-range RFR (wavelength not stated, but presumably 10 cm, used in subsequent experiments) at 10 mW/sq cm. For a prolate-spheroidal model of a 1-kg rabbit exposed to 3-GHz (10-cm) RFR at this level in the E- or H-polarization, the SAR would be about 1.4 W/kg (Durney et al., 1978, p. 92). Exposure during the

first 3 months led to only slight weakening of the conditioned reflexes (to about 90% of baseline) as shown by increased latency or absence of response and failure to recognize the conditioned stimulus. During the fourth month, however, the conditioned reflexes dropped to about 40% of baseline. Full recovery to baseline occurred in the second month after exposure cessation, with an intermediate recovery to 70% in the first post-exposure month.

In the second series, outbred non-stock rats were trained to push a lever to obtain food, after which they were exposed to the RFR at 10 mW/sq cm 60 min daily for 6 months. In the third series, inbred rats (K-M strain, characterized as being more sensitive to CNS excitation) were similarly treated. The SAR for a prolate-spheroidal model of a medium (320-g) rat exposed to 3-GHz RFR at this level is about 2 W/kg (Durney et al., 1978, p. 95). Unexposed rats served as controls. Prior to exposure, all three groups of rats performed at close to baseline level. The performance of the inbred group diminished to about 87% and 76% respectively during the first and second months of exposure, rose to 91% during the third month, and decreased to 83% by the sixth month. By contrast, the performance of the outbred group varied somewhat above and below the 70% level during the entire six months of exposure.

In other series of experiments, the author reported various performance differences between the inbred and outbred rats, with no clear patterns discernible. In still other experiments, significant differences were found in reactions to intense sound stimulation for rats exposed to 3-GHz pulsed or CW RFR at 1 and 10 mW/sq cm (0.2 and 2 W/kg). From the results for the latter experiments, the author concluded: "It follows that 10 mW/sq-cm, 15 min irradiation does not influence significantly the level of excitability of the CNS, while 1 mW/sq cm, 15 min somewhat increases it." However, the nonmonotonic time variations of responses in the second series may be indicative of the presence of uncontrolled non-RFR factors, which would render questionable all of the results of this investigation.

Thomas et al. (1975) placed each of 4 Sprague-Dawley albino male rats, maintained at 80% of their free-feeding weights, in a behavioral chamber having two levers, with a red light over one and a blue light over the other. A yellow light mounted within the chamber served as the house light. A food hopper was mounted midway between the levers. First, the rats were trained by the method of successive approximations to press each of the levers to obtain a food pellet. They were then required to learn the following multiple fixed-ratio, differential reinforcement of low rate (mult FR DRL) schedule. Whenever the red light above the right lever was on and the house light was off, the rat was required to press the right lever 20 times for a pellet (FR-20 schedule); whenever the blue light over the left lever and the house light were on, a pellet was delivered by the second of two presses of the left lever separated by at least 18 but not more than 24 seconds, comprising a DRL-18 schedule with limited-hold (LH-6) contingency.

The rats performed for 6 days per week in 1-hr sessions, during which

the FR-20 and the DRL-18, LH-6 schedules were each for 3 min and were alternated at random times. Inserted between each pair of successive schedules was a 30-second time-out period, during which all lights were off and response on either lever extended the time-out for 30 seconds. Each rat performed at baseline for about 60 sessions on the multiple schedule before exposure experiments were initiated. Then, on 1 or 2 days a week just before the performance session, each rat in a sleeve holder was exposed for 30 min in an anechoic chamber to vertically polarized far-field RFR of one of the following types: 2.86- or 9.6-GHz 1-microsecond pulses at 500 pps or 2.45-GHz CW, each at average power densities up to 20 mW/sq cm, with sham-exposure for every third session. Presuming that the long axis of the rat was perpendicular to the E- and propagation vectors (H-polarization), the SARs are estimated from Durney et al. (1978), p. 95, to have been about 0.2 W/kg per mW/sq cm at all three frequencies.

During baseline sessions, the rats exhibited high and constant response rates on the FR schedule. All three types of RFR affected performance. The mean response rate on the FR schedule after exposure to the 9.6-GHz pulses at 3 mW/sq cm (0.6 W/kg) was about 120% of mean control level, but fell to values between 90% and 98% at higher power densities. The mean response rates on the FR schedule to the other two types of RFR varied nonmonotonically with power density, but were all 90% or lower, falling to about 10% for 2.86-GHz pulses at 20 mW/sq cm (4 W/kg). The response rates on the DRL schedule, in percentage of the performance for the sham-exposure session just preceding the RFR session, also varied nonmonotonically with power density to values well above and below the baseline. The 9.6-GHz pulses yielded larger percentage increases than the other two types of RFR at corresponding levels up to 15 mW/sq cm (3 W/kg), but the largest increase was for the 2.86-GHz pulsed RFR at 20 mW/sq cm (4 W/kg).

The mean response rate during time-outs between FR and DRL schedules on sham-exposure days was about 420% of baseline, with a range of 200-600%. The plots of response rates vs power density were roughly inverted-U in shape, with maxima of 2300% after exposure to 2.45-GHz CW RFR at 7 mW/sq cm (1.4 W/kg), 1150% after exposure to 2.86-GHz pulses at 10 mW/sq cm (2 W/kg), and 900% after exposure to 9.6-GHz pulses at 5 mW/sq cm (1 W/kg).

The authors noted that "the low rates of responding produced by the DRL schedule increased after irradiation, and the high rates of responding produced by the FR schedule decreased after irradiation. Responding also increased during time-out periods between the component schedules as a result of microwave exposures." However, only four rats were studied, which may have precluded valid statistical treatment of the data (no treatment presented), and the nonmonotonic variations of performances with power density may have been due at least in part to uncontrolled non-RFR factors.

In another study, Thomas et al. (1976) trained four male albino rats to perform on a reinforcement schedule in which each rat was required to

press one lever (at right) at least eight consecutive times before a response on another lever (at left) would produce a pellet. When the rat switched to the left lever in fewer than eight times, the count was restarted. Each daily session lasted until 60 food reinforcements were delivered. The session was then terminated by inactivating the lever switches and extinguishing the houselight. The sessions were conducted for 6 months to ensure stability in baseline performance.

The rats were then individually exposed broadside in the near-field of a horn (at about a third or half the conventional boundary of the far-field distance), with head on the horn's axis, to vertically polarized 2.45-GHz pulsed RFR (1-microsecond pulses at 500 pps) for 30 min one day a week at 5, 10, or 15 mW/sq cm (1, 2, or 3 W/kg). The sessions on the reinforcement schedule were started 5-10 min after exposure. Each rat was exposed at each level twice or three times in semirandom sequence, with sham-exposures every day between RFR-exposures. Core temperatures, taken during and immediately after exposure, were found to be within normal variations and not correlated with RFR exposure. The results for the last two exposures at each RFR level and the last two sham-exposures were presented.

The mean running rate (number of responses per second) of the four rats showed no systematic changes with power density. However, the mean percentage of runs in each session that were long enough to produce reinforcement dropped from close to 80% after sham-exposures to about 60% after exposures at 5 or 10 mW/sq cm (1 or 2 W/kg) and to less than 50% after exposures at 15 mW/sq cm (3 W/kg). By F-test, these decreases were significant. There was also a significant, approximately linear decrease with power density in the mean number of responses on the right lever between responses on the left lever (run length), from about 10 to less than 8 responses, changes directly associated with increases in the number of run lengths less than the required 8 right-lever presses.

Frey et al. (1975) performed two experiments directed toward determining the relationship between neural function and behavior. In one, they sought effects of RFR exposure on the blood-brain barrier. The results of this experiment were discussed in Section 3.4.1. In the other, they sham-exposed or exposed female Sprague-Dawley rats dorsally to 1.6-GHz CW RFR at 2.4 mW/sq cm or to pulsed RFR (0.5-ms pulses, 1000 pps) at 2.1 mW/sq cm peak and 0.2 mW/sq cm average (6 rats per condition) within a shuttle box, half of which was shielded against the RFR. The SAR at 1.2 GHz for a prolate-spheroidal model of a medium rat (Durney et al., 1978, p. 95) is about 0.3 W/kg per mW/sq cm (the mean of the values for the E- and H-polarizations), yielding estimated SARs for the CW and pulsed RFR of about 0.7 and 0.06 W/kg, respectively. Each rat was treated for 30 min/day on 4 successive days, and the fraction of the time it spent in the unshielded half of the shuttle box during each session was recorded.

The authors reported that all three groups spent approximately 60% in the unshielded half during the first two daily sessions and that the differences among groups were not statistically significant. For the other two daily sessions, however, the pulsed group spent only 30% in

the unshielded half, the CW group 64%, and the sham group 52%. The difference in time spent between the CW and the sham groups was not significant, but the differences between the pulsed and the other two groups were significant, indicating that the rats tended to avoid the pulsed RFR. Because the pulse characteristics were well below those necessary to produce the RFR-auditory effect (see Section 3.1.4.2) in either the rats or the walls of the shuttle box, it seems unlikely that this effect was involved.

The behavioral data presented were insufficient to permit analysis of the validity of the avoidance conclusion. Specifically, it is unclear why the authors presented only the combined data for the first two days and for the second two days instead of the data for each day. Also, because all three groups spent about 60% of the session time in the unshielded half of the shuttle box during the first two days (which might indicate some preference for that half of the box irrespective of the presence or absence of the CW or pulsed RFR), it is difficult to draw any inferences regarding why the pulsed group spent only 30% there during the second two days.

In another study, Frey and Feld (1975) again reported avoidance of RFR by rats in a shuttle box. In the first of two experiments, four rats were exposed horizontally two at a time in two shuttle boxes to 30-microsecond 1.2-GHz pulses at 100 pps in seven daily sessions of 90-min duration. The right side of one box (A) and the left side of the other box (B) were shielded against the RFR to control for possible side preference. Peak and average power densities in the unshielded half of box A were 133 and 0.4 mW/sq cm (0.08 W/kg for K-polarization, Durney et al., 1978, p. 95). The values in the unshielded half of box B were 300 and 0.9 mW/sq cm (0.18 W/kg). A group of four rats was similarly sham-exposed. The rats were maintained in home cages with reversed 12-hr day/night cycle and were habituated to handling for at least one week before exposure.

The authors noted that most rat activity occurred during the first 30 min of each session and they used the Mann-Whitney U-test on the data for that part of each session. The authors stated (without presenting actual data) that the pulsed-RFR group averaged 29% of the time in the unshielded half as compared with 57% for the sham group, a significant difference ($U=0$, $p=0.014$). They also stated: "An aversive effect was apparent within 15 min, since the respective proportions of time spent in the illuminated side within the first 15 min were 32% and 54% for experimental and control groups, respectively ($U=1$, $p=.029$). The effect was consistent over 7 days of testing, and the animals responded similarly in Boxes A and B, even though the boxes' unshielded halves differed in the amount of energy that illuminated them." They also indicated that the mean number of crossings per session was 7 for the RFR group and 15 for the sham groups ($U=0$, $p=0.014$).

For the second experiment, the shuttle-box design was improved, only one shuttle box was used but each half was shielded alternately on a random basis, a CW group was included, and four daily sessions of only

30 min each were conducted on each rat. The pulsed group (6 rats) was exposed to 0.5-millisecond pulses, 1000 pps, at peak and average levels of 2.1 and 0.2 mW/sq cm (0.06 W/kg), and the CW group (6 rats) at 2.4 mW/sq cm (0.48 W/kg).

The authors stated: "We expected that avoidance would not appear as soon as it did with the higher power levels used in Experiment 1. This may be noted by comparing the three exposure groups during the first two sessions and comparing them again during the last two sessions of the four-session sequence." The average times spent in the unshielded half by the pulsed, CW, and sham groups during the first two days were 60%, 64%, and 58%, respectively (nonsignificant differences). For the second two days, the corresponding values were 30%, 64%, and 52%. Significant differences ($U=4$, $p=0.0.13$) were found between the pulsed and CW groups and between the pulsed and sham groups, but not between the CW and sham groups ($U=13$, $p>0.05$). Again, no actual data were presented.

It is not clear whether the 7 crossings per session (mean) for the RFR group and 15 per session for the sham group in the first experiment were for the 90 min or the first 30 min thereof. In either case, such rates of avoidance of a noxious stimulus seem low. (Corresponding values for the second experiment were not given.) The general reviewer comments presented above relative to Frey et al. (1975) seem applicable to this paper as well, except that the characteristics of the pulses used in the first but not the second experiment described in the latter paper might have been adequate to produce the RFR-auditory effect.

Hunt et al. (1975), in a three-part study, exposed male Wistar rats for 30 min to 2.45-GHz RFR pulses (quasi-sinusoidal, 2.5-ms half-amplitude duration, 120 pps) in a cylindrical confining holder made of expanded bead polystyrene (Polyfoam) and Lucite rods within a modified commercial microwave oven (Justesen et al., 1971) maintained at 24 deg C and 20-40% relative humidity. Based on the weight of each rat, the input power was adjusted to yield 6.3 W/kg for an exploratory behavioral test used in the first part of the study, 6.3 or 11 W/kg for a swimming test in the second part, and 6.5 or 11 W/kg for a discrimination test in the third part. All rats were repeatedly confined to the holder, and sham-exposed when appropriate, prior to treatment. From Justesen et al. (1971), the corresponding silhouette-surface-area equivalent power densities were about 2.1, 2.2, and 3.7 mW/sq cm.

In the first part, designed to test for effects of RFR on exploratory activity, each rat was exposed to the RFR and then placed for the first time in its life in a chamber within which its exploratory movements were recorded with a commercial activity meter (calibrated to exclude most non-exploratory movements such as scratching or grooming). The number of movements was counted during the first 15 min and during each 30-min interval afterward for sessions lasting either 45 or 105 min. In one set of three replications, the activity test was started immediately after exposure. In another set, each rat was held undisturbed within a metal cage similar to its home cage for 1 hr after exposure before the test was started. In a third set similar to the second, deep colonic

temperatures were measured immediately after exposure and again just before starting the test.

Mean activities of the rats in the first set of replications decreased with elapsed time after either RFR- or sham-exposure, but the values after RFR-exposure were generally lower during most of each test period than after sham-exposure and became comparable for the two treatments toward session end. From observations through a window, the RFR-exposed rats were likely to be in sleeping positions during the middle part of a session. Qualitatively similar behavior was observed for the sets in which the rats were tested 1 hr after treatment. Following treatment in the last replication, the mean rectal temperatures of the RFR- and sham-exposed rats were 40.3 and 38.6 deg C, respectively. One hour later, their respective mean temperatures were 37.8 and 38.0 deg C.

In the second part of this study, Hunt et al. (1975) trained rats by immersion to swim a 6-m-long channel of water (at 24 deg C) repeatedly forth and back during a 24-hr period, with rests of 20 or 30 seconds at each end of the channel. Each rat's performance vs time was scored as its median swim speed for each successive block of 20 traverses. After training, the rats were given a pretreatment test and distributed into RFR and sham groups on the basis of equal proficiency. In one of three experiments, the pretest was for 3 hr; one day later, the rats were exposed at 6.3 W/kg (or sham-exposed) for 30 min and a 5-hr test was given right after treatment to determine prompt effects. In the second and third experiments, the pretest consisted of 200 traverses, the rats were exposed at 11 W/kg (or sham-exposed), and the post-treatment test was 400 traverses, given 2 days after pretest, either immediately after treatment or after a 1-day delay. Colonic temperatures were measured immediately after treatment and before and after swimming sessions. The results showed that the rats exposed at 11 W/kg were rendered severely hyperthermic (41 deg C or higher), with some relief by immersion during the post-treatment test for those tested immediately after exposure.

For the sham-exposed groups in all three experiments, the performances in the pretest sessions were comparable: high initial speeds, quick drops and rises to plateau speeds of 36-38 cm/s for about 100 traverses, followed by steady declines until session end. In the post-treatment sessions, all three groups exhibited initial speeds comparable to the values in the pretest sessions, but the sham-exposed groups for the second and third experiments showed successively steeper drops and lower plateaus than the sham-exposed group for the first experiment. By about 250 traverses, the mean speeds of all three control groups were again comparable.

The performance of the group exposed at 6.3 W/kg was essentially similar to that of their control group for about 200 traverses, but was below mean control speed for about the next 100 traverses, at which point the performances of the two groups became comparable again. Similar results were obtained for the group exposed at 11 W/kg and tested 1 day later. However, the performance of the group exposed at 11 W/kg and tested with no delay was initially significantly below that of the con-

trol group; it recovered and remained at control performance during about the first 100 traverses, but diminished to well below control performance for most of the remaining session period. The performance of this RFR group was clearly impaired by the hyperthermia despite the partial relief obtained from immersion, but the authors noted that other factors associated with hyperthermia (e.g., thermoregulatory overcompensation, lower metabolic rate, cardiovascular changes) may have contributed to impairment. By contrast, the other 11-W/kg-group had recovered from the hyperthermia when tested 1 day later.

The last part of the study was designed to test rat performance of a complex vigilance-discrimination task for 30 min immediately after a 30-min sham-exposure or exposure at 6.5 or 11 W/kg. Rats were maintained on a 23-hr water-deprivation cycle and were reinforced for each correct response (lever press when appropriate) by the delivery of 0.08 ml of saccharin-flavored water. In the test procedure, a light flash (S+) signaled the availability of a single reinforcement, and a brief burst of sound (S-) indicated that a "time-out" punishment would follow a lever response. Either cue was presented at the start of 5-second intervals, with S+ given randomly at 12.5% of the intervals (about 45 times during the 30-min test period). A failure to respond in time to an S+ constituted an error of omission. Responses to S- presented at all other intervals constituted errors of commission. Either type of error resulted in punishments consisting of a 15-second time-out, during which the house light was extinguished and no cues were presented. More than one response during an S+ interval also produced a 15-second time-out, but few such errors occurred after extensive training.

On each session day, each rat was first given 10 min of practice on the discrimination task, then confined in the holder within the cavity for 30 min, after which it was given the 30-min discrimination test. After the rats had achieved stable performance levels under this schedule, each was tested on five consecutive days. On the first day, all groups were sham-exposed. During the next four days, each group was exposed for one 30-min period each at 6.5 and 11 W/kg and two periods of sham-exposure, i.e., each rat received all three treatments. However, the treatment sequence was varied among groups, with at least one of the sham-exposure days between the two RFR-exposure days.

The results were presented graphically for each treatment as the mean percentages of omission and commission errors vs elapsed time during testing (at the 5-, 15-, and 25-min epochs). For the test sessions following the sham-exposures, the mean omission errors were in the 10-15% range at all three epochs. For the session following exposure at 6.5 W/kg, the mean of omission errors was about 36% at 5 min, but was in the 10-15% (sham-exposure) range at 15 and 25 min. Following exposure at 11 W/kg, however, the respective omission-error percentages at 5, 15, and 25 min were 75, 50, and 40. Thus, the rats were missing or ignoring S+ cues early in the sessions following exposure to RFR at either level, but the effect was more severe for 11 W/kg and was well above the sham-exposure range by session end. The commission-error results were in the 1-2.5% range at all three epochs, with no significant differences among

the treatments.

Chernovetz et al. (1975), in a study devoted primarily to teratogenic effects of RFR (Section 3.3.2.1), exposed three groups of five pregnant C3H/HeJ mice to 2.45-GHz RFR, each group concurrently in a multimode, mode-stirred cavity at 38 W/kg for 10 min on gestation day 19. Three other groups were sham-exposed. Another six groups were injected with cortisone (as a teratogen), three groups of which were then exposed to the RFR and the other three groups were sham-exposed. All 60 dams were allowed to come to term.

At 38 days of age, nine pups from the non-injected sham-exposed groups, 15 from the non-injected RFR-exposed groups, and 11 from those that received cortisone and RFR were selected and their ability to learn to swim a cold-water (16 deg C) Lashley-III maze in one direction and to subsequently learn to swim the maze in the reverse direction (reversal learning) were studied. The motor abilities of the three treatment groups were essentially the same. Also, statistical analysis of the errors made in the original learning showed no significant differences between the two non-cortisone groups, but higher error scores for the combined-treatment group. All three treatment groups showed significant changes in their respective error scores for reversal learning. Thus, exposure of the dams to a nearly lethal level of RFR had no discernible effect on the motor abilities or behavior of the pups.

Moe et al. (1976) pair-matched 16 male Wistar rats by weight (range 360-410 g). They then concurrently exposed one of each pair for 10 hr each night for three weeks (total exposure time 210 hr) unrestrained in an individual Plexiglas cage within a cylindrical waveguide (Guy and Chou, 1976) to circularly polarized 918-MHz CW RFR at 10 mW/sq cm (4 W/kg). Food and a 0.1% sodium saccharin solution were available ad libitum in a manner that precluded absorption of RFR energy therein. The other rats were sham-exposed but otherwise similarly treated.

For three weeks prior to the start of exposure, rats were adapted to the waveguides by maintaining them therein from 1700 to 0800 each day, at the end of which they were returned to their home cages. The RFR- and sham exposures were then performed from 2200 to 0800, i.e., during the active part of the rat's diurnal cycle, after which the rats were weighed and their consumption of food and saccharin in the waveguide were measured. Core temperatures were taken aperiodically at 0800.

During exposure, the behavioral repertoire of each rat (divided into the mutually exclusive categories: eating, drinking, grooming, activity, and at rest) was sampled five times for about 1 second each time in sessions at 2230, 0300, and 0730. The at-rest category was divided into "curled-up" and "stretched-out", and the orientation relative to the propagation direction was noted. To determine the basal and ether-stress-induced corticosterone levels of each rat, 2 cc of blood was obtained by cardiac puncture under light ether anesthesia at exposure end; 15 min later, the rats were lightly anesthetized again and another 2-cc sample was taken. In addition, four 0.05-cc samples were taken

from the tail at intervals of 6 hr starting immediately after drawing the first cardiac sample, and were assayed for blood glucose levels.

By analysis of variance, there were no significant differences between the RFR- and sham-exposed rats in body weights, core temperatures, basal and ether-stress-induced corticosterone levels, or in daily saccharin consumption. Daily food consumption (averaged over 5-day blocks) by the two groups was comparable during adaptation and diminished comparably under ether stress. However, consumption by the sham group recovered to pretreatment levels, whereas it remained low for the RFR group. Mean blood glucose levels at 1200, 1800, 2400, and 0600 were presented for both groups, times that appear to have been different than those when blood was drawn from the tail (0700, 1300, 1900, 0100). The values varied nonmonotonically with time of day, but were significantly lower for the RFR- than the sham group at corresponding times.

The behavior of the sham group, presented as mean activity responses at 2230, 0300, and 0730, were about 3.6, 3.2, and 1.2, respectively, a monotonic decrease. The corresponding values for the RFR group were about 1.3, 1.8, and 0.2, indicating an increase in activity at 0300, but all were significantly lower than the respective values for the sham group. In addition, the rats in both groups spent virtually all of their resting time in the stretched-out position at 2230; at 0300 and 0730, however, the sham group spent only about 30% of the time stretched out (70% in the curled-up position), whereas the RFR group spent about 83% and 75% stretched out at these times.

In discussing the results, the authors, noting that the SAR was about 82% of the rat's basal metabolic rate, suggested that the reduction in food intake and activity but not of saccharin solution by the RFR group may have been independent responses toward coping with the thermal load induced by the RFR. Regarding the blood-glucose decrease, however, they stated: "It would be too hasty to similarly attribute the effect as a caloric (energy) trade-off induced by the heating effects of microwaves, or as a consequence of the microwave-induced reduction in eating."

They also concluded that: "the reduction is probably not a metabolic consequence of some other microwave-induced bio-effect, e.g., pituitary-adrenal stress response. Indeed, we found no differences in either basal or ether-stress-induced corticosterone levels for the two groups of rats. In point of fact, the corticosterone data are quite consistent with our interpretations of the food intake and general activity reductions--namely, that the animal is changing its behavior to cope with the thermal loading brought about by microwave exposure, and that this behavioral coping is sufficient to preclude the development of a hyperthermic stress response. Regardless of the eventual accuracy of this interpretation, we are not convinced, at this time, that the chronic drop in blood glucose levels is attributable to the direct heating effects of exposure to microwave radiation."

Monahan and Ho (1976) endeavored to determine whether mice would try to orient themselves to minimize their absorption of CW RFR under expo-

sure conditions that did not permit them to escape. In one experiment, CF1 male mice (30-34 g) were exposed singly for 15 min in a holder that permitted relatively free movement within a waveguide system (Ho et al., 1973) to 2.45-GHz CW RFR at forward powers of 0.4, 0.8, 1.6, 2.4, 3.2, 4.0, and 4.8 W (10 mice per level) in an ambient temperature held at 24 +/- 0.5 deg C. Mean SAR and percentage of forward power absorbed were measured at 5-min intervals, and rectal temperature was measured right after exposure. A second experiment was similar except that two mice per level were used, exposures were limited to 10 min, and absorptions were sampled and recorded at 12-second intervals. The results at each level for the two experiments were presented as averages over the time intervals 0-5, 5-10, and 10-15 min. Visual observations of the mice were not possible during either experiment.

In the first experiment, no significant changes in percentage of power absorbed or SAR were observed during the 15 min at mean forward powers of 0.43 and 0.85 W; mean SARs at these levels were 7.8 and 15.4 W/kg. At 1.66 W, however, the absorption percentage declined from 55.2% for the first 5 min to 48.2% during the second 5 min and to 47.4% during the last 5 min; the respective SARs were 28.4, 25.0, and 24.4 W/kg. Thus, the largest changes occurred after 5 min of exposure. At the higher power levels, even larger decreases were observed. Rectal temperatures were highly variable, a finding ascribed to the naivety of the mice, but no consistent increase was observed at less than 4 W, at which the mean increase was 0.4 deg C.

At 0.4 W in the second experiment, measurements at 12-second intervals indicated that the mice were moving essentially randomly within the holder, with no significant decrease in percentage absorption or SAR over the 10 min. The respective means were 53.9% and 15.0 W/kg. At 2.4 W, however, representative results showed a decrease in absorption from about 65% to 46% within 3.5 min and fluctuations around this value for the remaining 6.5 min of exposure. The mean percentage absorption and SAR for the 10 min were 46.2% and 44.0 W/kg. The results at 4 W were more dramatic; the percentage absorption dropped from about 65% to about 30% during the first 1.5 min and remained well below 40% during the rest of the exposure. The mean percentage absorption and SAR for the 10 min were 40.6% and 35.1 W/kg.

The results of both experiments clearly demonstrated that the mice did orient themselves to reduce their percentages of RFR energy absorbed and SARs when the forward power was about 1.7 W (initial SAR about 28 W/kg) or higher at an ambient temperature held at 24 deg C.

In a subsequent study, Monahan and Ho (1977) exposed 17 groups of 6 CF1 male mice each for 20 min at various forward powers and temperatures in the waveguide exposure system, with the relative humidity maintained at 50 +/- 1.5%. At each power level and temperature, the SARs (calculated from the net energy absorption rate by each mouse and its mass) were averaged over the entire 20-min exposure period and over each successive 5-min interval thereof, and the latter were expressed as percentages of forward power absorbed.

First, groups were exposed at 20 deg C, one at a forward power of 1.62 W, another at 2.31 W, a third at 3.28 W, and a fourth at 3.84 W. The corresponding mean SARs for the entire 20-min exposure period were 30.7, 43.6, 56.3, and 63.8 W/kg, respectively. At 1.62 W (30.7 W/kg), the percentages of incident power absorbed at successive 5-min intervals did not differ significantly from one another, and no downward (or upward) trend with time was observed. At 2.31 W (43.6 W/kg), the differences in absorption percentages between successive 5-min intervals did not differ significantly, but a highly significant ($p<0.001$) downward trend with time was evident; absorption had decreased from about 61% during the first 5 min to about 52% during the last 5 min. At 3.28 W (56.3 W/kg), the percentages for successive intervals were 57, 44, 50, and 44; the sequential differences were significant but no trend was discernible. At 3.84 W (63.8 W/kg), the successive percentages were 53, 39, 38, and 37, with only the first drop significant.

Next, one group each was exposed at 24 deg C to a forward power of 1.12, 1.70, 2.39, or 3.11 W, corresponding to mean SARs of 20.6, 30.1, 43.5, and 51.3 W/kg. Significant downward trends in power absorption were evident for all but the lowest power level. One group each was exposed at 30 deg C to 0.415, 0.736, 1.62, or 2.45 W, yielding mean SARs of 7.3, 12.7, 25.8, and 40.2 W/kg. Downward trends in power absorption were significant at all four power levels. At all levels but the lowest (0.415 W, 7.3 W/kg), the largest drop occurred between the first and second 5-min intervals. One each of the last five groups was exposed at 35 deg C to 0.004, 0.035, 0.075, 0.21, or 0.4 W, yielding mean SARs of 0.06, 0.6, 1.2, 3.7, and 6.7 W/kg. Downward trends were obtained at all levels, with the drops significant at 0.035 W (0.6 W/kg) and higher.

Several mice of the last five groups were similarly exposed at 35 deg C, but with no flow of air, to ascertain whether they had been orienting themselves so as to minimize the flow of the hot air rather than their SARs. The results for 0.6 W/kg were about 56% and 57% absorption during the first and second 5-min intervals (a nonsignificant change), and 49% and 38% respectively during the last two 5-min intervals. By contrast, the corresponding results at this ambient temperature and SAR but with air flowing were about 51%, 43%, 41%, and 39%. The authors concluded that the use of air flow did affect percentage of absorption initially but not after the mice had reoriented to minimize their SARs.

In summary, Monahan and Ho (1977) found that the lowest (threshold) RFR level at which the mouse significantly altered its SAR at 24 deg C was about 2.4 W (43.5 W/kg), corresponding to about 40 mW/sq cm (estimated by dividing the forward power by the cross section of the waveguide, about 60 sq cm); at 30 deg C, the threshold values were 1.62 W (25.8 W/kg) and 27 mW/sq cm; and at 35 deg C, they were 0.035 W (0.6 W/kg) and 0.6 mW/sq cm.

Gage et al. (1979a) also investigated whether animals would reorient themselves to minimize absorption of RFR. They exposed 6 CD male rats (260-360 g) individually in either a ventilated Plexiglas cylindrical container or a Styrofoam cuboid container, and 6 CD1 male mice (25-33 g)

in the latter container for 1 hr from above to far-field 2.45-GHz CW RFR at 15 mW/sq cm within an anechoic chamber illuminated with incandescent light and maintained at 22 or 28 deg C and 50% relative humidity. By twin-well calorimetry, the ranges of SARs for the rats were 2.1-2.6 W/kg and 3.2-3.6 W/kg respectively in the cylindrical and cuboid containers, and 6.5-11.1 W/kg for the mice in the cuboid container. Each animal was studied for 2 hr, during which its behavior was videotaped every 30 seconds for 2-3 seconds. The animals were exposed to RFR only during the second hour of the session.

The videotaped records were scored by noting the numbers of times each animal assumed positions in which its long axis was parallel to the electric (E) vector, parallel to the magnetic (H) vector, and other orientations during the 2-3-second sampling periods. These numbers were summed over each of the eight 15-min periods (30 samples per period) of its 2-hr session.

Observations of the rats at ambient temperature 22 deg C showed that after exploratory activity during the first 15 min, they generally became less active and usually adopted curled positions that were not preferentially oriented relative to either the E- or H-vector, and they appeared to be sleeping in such curled positions. Turning-on the RFR during the second hour did not alter their behavior significantly. The sums of occurrences of each orientation during each 15-min period were averaged for the 6 rats. In the cylindrical container, the mean values for the E- and H orientations ranged from 1 to 6 occurrences per period, with no statistically significant differences between these orientations or for RFR vs no RFR. By contrast, the mean numbers of occurrences of orientations in the "other" category ranged from 19 to 26, but again no significant RFR-induced differences. Comparable results were obtained for the rats in the cuboid container. At 28 deg C, the rats frequently stretched out on their backs during RFR exposure, but again with no preference for the E- or H orientation.

The results for the 6 mice (studied only in the cuboid container) at 22 deg C were qualitatively similar to those for the rats. The mean number of occurrences for the E orientation rose about linearly from about 1 to 4 during the 2-hr session; the mean for the H orientation was less than 1 for periods 1-5, rose to 4 for period 6, and diminished linearly to 0 during periods 7-8. For the "other" category, the values decreased from 29 to 27 for periods 1-5, dropped to 22 for period 6, and rose to 25 for periods 7-8, nonsignificant changes. Raising the temperature to 28 deg C rendered the mice more active, and their means for both the E- and H orientations rose sharply during periods 3-6 from less than 3 to the range 8-12 while the mean for the "other" category dropped from 30 to within the 8-12 range. Analysis of variance showed that although the presence of the RFR produced larger numbers of E- and H orientations, the differences between these two orientations were not significant.

Based on the results, the authors suggested that perhaps rodents do not sense or respond differentially to 2.45-GHz CW RFR at 15 mW/sq cm

(2.1-3.6 W/kg for rats, 6.5-11.1 W/kg for mice) during the first hour of exposure. Not stated were angular limits within which the animals were considered to have taken the E- or H orientation; actual counts for each such orientation would depend on the size of the angular sectors; more importantly, the size would determine the ratios of counts in these two orientations to those in the "other" orientation category. Also not discussed was the rationale for sampling the behavior of the rodents for only 2-3 seconds of every 30-second interval in the 2-hr sessions, and how representative were such samples. These comments are directed more toward the quantitative aspects rather than the qualitative findings.

The finding that the mice did not endeavor to reduce their whole-body SARs by appropriate orientation appears to be at variance with the results of Monahan and Ho (1976, 1977). However, unlike the far field used by Gage et al. (1979a), the field within the waveguide was neither transverse-electromagnetic nor uniform over the waveguide cross-section. Also, the propagation direction in the latter system was parallel rather than transverse to the long axis of the mouse. Thus, whole-body SAR may be more sensitive to orientation in a waveguide than under far-field conditions. Moreover, the internal distribution of local SAR may have differed significantly for the two exposure methods. For these reasons, the validity of such comparisons of findings is open to question.

Monahan and Henton (1977a) used another approach to determining whether mice avoided RFR. They exposed five CF1 male mice individually to 2.45-GHz CW RFR at 46 W/kg (about 45 mW/sq cm) within a waveguide system held at 24 deg C and 40-50% relative humidity. Three mice were sham-exposed. Each mouse was in a ventilated opaque Plexiglas container large enough to permit free movement. A light beam was shone, through a set of aligned holes appropriately located in the side walls of the waveguide and mouse container, to a photosensor; beam interruption constituted the basic response of the mouse. Paired with the RFR (or sham-exposure) was a 2900-Hz tone.

Behavioral sessions were for 30 min. The procedure was to turn on the RFR and tone or sham-RFR and tone 12 seconds after the beginning of a session. The stimuli remained on as long as no response was made. Once on, a beam-interruption response by the mouse terminated the stimuli, which then remained off for 12 seconds in the absence of another beam interruption during the period. Such behavior was characterized as an escape response. If the mouse interrupted the beam again during the 12-second absence of stimuli, each such response would delay the onset of stimuli for 12 seconds. Such double responses were characterized as avoidance behavior.

The escape responses of each mouse exposed to the RFR, averaged over eight sessions, yielded mean cumulative exposures (total durations of RFR and tone) that ranged between 11 and 17 seconds per session, with relatively small standard deviations (about 3 seconds). Whenever the RFR was turned on, these mice terminated the RFR by a response within 20 seconds. By contrast, the mean cumulative exposures (durations of tone) for the sham-exposed mice were much larger and differed greatly from one

another (36, 136, and 342 seconds). Thus, the mice exposed to the RFR (in the presence of the tone) were responding so as to minimize their cumulative exposure times per session, which were significantly smaller than for the sham-exposed mice.

The authors displayed the mean percentages of escape responses by RFR-exposed mice 1-5 and the mean number of avoidance responses per escape response of each. Mouse 3 exhibited nearly 30% escape responses and only 2 avoidance responses per escape response, so its behavior was categorized as primarily "escape." Mice 4 and 5 showed less than 10% escape responses, but 18 and 13 avoidance responses per escape response, respectively, so their behavior was classified as primarily "avoidance." The escape responses of mice 1 and 2 were about 15% of their total responses and they performed about 6 avoidance responses per escape response, so their behavior was categorized as "mixed." Corresponding data for sham-exposed mice 6-8 were not presented, presumably because their total response rates were too low and inconsistent.

The authors concluded that RFR can be an aversive stimulus. However, characterizing the behavior of the mice as "escape," "avoidance," or "mixed" is difficult to interpret, especially since so few mice were used. The authors did state that each mouse maintained rather than altered its response pattern, but that the determinants governing the individual patterns were dependent on the available contingencies and not on the RFR itself.

In still another approach, Monahan and Henton (1977b) exposed three groups of eight Sprague-Dawley male rats individually to 915-MHz CW RFR, each rat restrained in a ventilated Plexiglas holder within a waveguide system. The rats were housed in their home cages with food available freely. Water was provided for 15 min/day except on exposure days, when a 10% (by weight) sucrose solution was substituted. At end of sucrose presentation, each rat was exposed for 15 min and immediately returned to its home cage. After 24 hr, each rat was given a 1-bottle preference test for 15 min, and the amount of sucrose consumed was compared with the quantity of liquid consumed on the previous day.

One group was exposed at a forward power of 5.0 W, another at 9.1 W, and the third at 19.0 W. Air at 38 l/min was forced through the waveguide. The temperature of the exhaust air ranged from 23 to 26 deg C, and the relative humidity was 40-50%. A fourth group was sham-exposed.

SARs were determined for the entire 15-min exposure period and for the three successive 5-min intervals thereof, and the latter were expressed as percentages of the incident (forward) power absorbed. The results at 5.0 W were 7.1 W/kg for each 5-min interval and for the entire period, i.e., the SARs (about 50% of the forward power absorbed) did not vary with time at this RFR level. At 9.1 W, the SARs for the successive 5-min intervals were 10.5, 9.5, and 8.7 W/kg, with a mean of 9.6 W/kg for the entire period. These values corresponded to about 49%, 44%, and 41% of the forward power. At 19.0 W, the corresponding values were 18.5, 16.9, and 16.5 W/kg (57%, 53%, and 52% of the forward power), with a

mean of 17.3 W/kg. The power densities at 5.0, 9.1, and 19.0 W (mean SARs of 7.1, 9.6, and 17.3 W/kg) were estimated to be 16.3, 29.6, and 61.8 mW/sq cm.

The largest SAR changes at 9.1 W and 19.0 W occurred during the second 5-min interval. As indicated by the authors, these time-dependent SAR reductions in rats were consonant with similar results in mice exposed to 2.45-GHz RFR (Monahan and Ho, 1976) and with the dependence of the effect on the ambient temperature (Monahan and Ho, 1977). Absence of the effect at 7.1 W/kg may indicate a threshold SAR between 7.1 and 9.6 W/kg or a power-density threshold between 16 and 30 mW/sq cm.

Mean sucrose consumption 24 hr after exposure at 0 W (sham), 5.0 W (7.1 W/kg, 16 mW/sq cm), or 19.0 W (17.3 W/kg, 61.8 mW/sq cm) was slightly higher than for the previous day in each case, and at 9.1 W (9.6 W/kg, 29.6 mW/sq cm) was slightly lower than for the previous day, but none of the differences was significant. Thus, the results yielded no evidence of conditioned aversion to sucrose engendered by RFR exposure.

Carroll et al. (1980) studied whether 20 mature female Long-Evans rats would try to escape from a region, within a multimode cavity, of intense (60 W/kg) 918-MHz RFR to a region of lower intensity (40, 30, 20, or 2 W/kg) by performing a simple locomotor response. The cavity was mode-stirred, producing amplitude modulation at 3 Hz with a peak-to-average power ratio of about 5. The ambient temperature and relative humidity were 21.1 deg C and 53%. Air flow through the cavity was at a rate of 0.1 m/second. The authors used faradic shock on 10 other rats within the unpowered cavity as an alternative agent (positive control).

For the studies on escape from RFR, the cavity was equipped with a false floor of white, opaque Plexiglas on which the boundary of a rectangular "safer" region about 25% of the total floor area was marked with black tape. Movement from the unsafe to the safer area was the simple escape response required. The safer area was not a region of intrinsically lower intensity relative to the unsafe area, but was rendered safer by the experimenters who reduced the input RFR power to the cavity by a predetermined percentage each time a rat entered that area. Recrossing by a rat to the unsafe area triggered restoration of the initial power to the cavity. A crossing in either direction was defined as when half the body traversed the boundary.

A false floor with a similarly marked boundary and with 22 parallel, equidistant 5-mm stripes of conductive silver painted on the "unsafe" area was used for the faradic-shock studies; alternate stripes were connected to form 2 poles, to which the shock source was fed.

Whole-body SARs were determined calorimetrically with saline solution in foamed polystyrene vessels exposed at the center of the unsafe area, and by measuring colonic temperature increases in similarly exposed live rats previously rendered hypothermic by i.p. injection of cortisone or pentobarbital.

In a pilot study on dose lethality, rats were exposed for a succession of five 2-min periods timed 2-min apart, one rat at 50 W/kg, three at 60 W/kg, one at 75 W/kg, and one at 120 W/kg. The latter two rats expired. The four rats exposed at 60 W/kg or lower exhibited symptoms of severe hyperthermia but survived because of the cooling between exposures. For the three rats exposed at 60 W/kg, mean colonic temperature increase at the end of the five exposures was 3.5 deg C. Based on this pilot study, 60 W/kg was adopted as the maximum SAR. The exposure regimen used in the formal studies consisted of alternating 2-min exposures and respites for a total session time of 22 min per day for 6 days.

The first formal experiment was done in 3 consecutive phases of 6 days each at 40-hr intervals. In the first phase (involving 10 rats), each crossing of a rat to the safer area during each 2-min exposure resulted in a SAR reduction from 60 to 40 W/kg, with restoration of 60 W/kg for each reverse crossing and at the start of each period. In the second phase, the reduction was to 30 W/kg for 5 of the rats and to 20 W/kg for the other 5 rats. For the third phase (all 10 rats), the reduction was to 2 W/kg.

For each rat, the numbers of entries into the safer area during the periods of exposure and nonexposure and the times spent there were recorded independently by two observers. To obtain preexposure and postexposure baseline data, sham exposures were performed during the first daily session of each phase and during an additional session 40 hr after completion of the 3 phases.

The numbers of entries per session by each rat into the safer area were measures of locomotor activity rather than of escape learning. For the periods of RFR exposure, the mean number of entries and SE by all 10 rats in all 3 phases of experiment 1 was 7.9 +/- 0.7 per session or an average of about 1.6 times per rat per 2-min exposure, for a grand mean of 119 entries per rat during the 75 periods of RFR exposure. For the 2-min nonexposure periods, the corresponding values were 5.6 +/- 0.4 per session, 0.93 times per period, and a grand mean of 70 entries per rat. The differences were significant ($p<0.05$), indicating greater activity during RFR exposure. During the exposure periods, the animals exhibited hyperthermic behavior similar to that seen in the pilot study, i.e., initial hyperactive locomotion followed by salivary grooming and usually by immobilization and collapse. In general, complete recovery occurred within 30-60 seconds of the next nonexposure period.

For the nonexposure intervals, there were no statistically significant intraphase or interphase differences in mean entries; the means were comparable to baseline values. For the RFR-exposure intervals, there were no significant intraphase differences in activity, but the mean phase activity diminished significantly with successive phases.

Despite the significantly higher levels of activity during RFR exposure, the mean times spent in the safer area during the periods of exposure and nonexposure did not differ significantly from baseline values or from each other either intraphase or interphase. Irrespective

of the experimental conditions, the rats spent only about 10% of the session times in the safer area, and specifically, the absence of an interphase effect indicated that the level of RFR in the safer area (obtained by the respective percentages of SAR reduction from 60 W/kg) was not a significant factor.

In the second formal experiment, 10 of 20 naive rats were treated in a manner similar to that used for phase 3, i.e., each crossing into the safer area during exposure produced reduction of the SAR from 60 to 2 W/kg. The other 10 rats were similarly scheduled, but faradic shock (about 800 microamperes) was given instead of RFR, and each crossing to the safer area while the source was activated produced reduction of the intensity to zero. Six daily sessions of 22 min each were performed, of which the first day was for acquiring baseline data.

The mean number of entries per session into the safer area by the RFR-exposed rats during the exposure periods (3.3 +/- 0.7) was significantly lower ($p<0.05$) than for the rats during phase 3 of experiment 1. Also, the mean percentages of time spent in the safer area by the RFR-exposed rats (about 5% both during and between exposure periods of each daily session) were smaller than the baseline mean (about 10% for all 20 rats), with a trend toward diminution in successive sessions.

By contrast, during the first and second days of faradic shock, the rats so treated occupied the safer area for averages of 89% and 95% of the respective source-on periods, and most of the time spent in the unsafe area occurred during the source-off periods. In addition, they probed the unsafe area frequently during the first day and quickly retreated to the safer area; they also actively resisted placement within the cavity on the second day. Because of these decisive results, the remaining shock sessions were cancelled.

Analysis of this study revealed a flaw in the design of the exposure apparatus. The unsafe area of the false floor used for the faradic-shock aspects was readily distinguishable visually from the safer area by the conductive stripes, which may have provided tactile differences also. The safer area of the false floor used for the RFR aspects of the study, however, was not visually distinguishable from the unsafe area; the only visual cue was the boundary per se. Thus, the rats exposed to RFR may have had a more difficult task to learn than those given faradic shock. This flaw could have been avoided by using, on the unsafe area of the RFR floor, nonconductive stripes of reflective characteristics and texture approximating those of the faradic floor, a measure taken in a subsequent investigation (Levinson et al., 1982) discussed below.

It should be noted also that although the safer area was 25% of the total floor area in each case, the data indicated that the rats actually spent only about 10% of the time there during baseline sessions. Was there some repelling factor associated with that region of the cavity?

Despite the points above, the finding that rats do not learn to escape from potentially lethal levels of RFR appears unequivocal. The results

obtained by Levinson et al. (1982) support this finding.

In the discussion by the authors, they considered the argument that the use of the alternating 2-min cycles of RFR and respite might confuse the rats and preclude learning. Specifically, during respite periods, the paradigm did not provide for escape reinforcement whenever a rat entered the safer area nor was punishment administered whenever a rat left the safer area. The response to the argument was that the periodic respites might retard avoidance learning, but that escape learning is motivated primarily during the application of noxious stimulation, an argument validated by their results with faradic shock.

Another point considered by the authors was their use of faradic shock as a positive control rather than infrared radiation (IR). The response to this point was that the rats used for RFR exposure and faradic shock served as their own controls, and that the findings with the two forms of stimulation were independent, with no comparison intended; that the primary purpose of the use of faradic shock was to demonstrate that a simple escape task could be learned rapidly.

An important implication of the findings of this investigation is that humans who might be exposed to intense levels of RFR at frequencies that penetrate deeply may not sense the internal heat generated in time to avoid tissue damage. This could be true under some conditions. It is also interesting to note that Justesen et al. (1982) reported that the power-density threshold for detecting 2.45-GHz RFR in the human forearm was about 15 times larger than for IR.

Levinson et al. (1982) similarly studied 4 groups of 4 rats each. One group, designated M, was exposed to the RFR (60 W/kg) only; the second, designated L, was stimulated photically (350 lx) only; the third, ML, was concurrently stimulated with the RFR and photically; and the last, a positive-control group designated S, was given the faradic shock only.

As in Carroll et al. (1980), the cavity was equipped with either of two false floors of opaque white Plexiglas on which the boundary of a "safe" region about 25% of the total floor area was marked with black tape; the "unsafe" area of the floor for administering faradic shock was painted with 22 parallel equidistant stripes of conductive silver, and with the alternate stripes connected to form 2 poles, to which the shock source was fed. However, a similar grid of nonconductive paint was applied to the unsafe area of the floor used in the RFR sessions.

A thermally sheltered 40-W white incandescent lamp placed in an upper rear corner of the cavity provided continuous illumination except when it was used for photic cuing. Two 40-W red incandescent lamps in the top wall of the cavity operated continuously permitted observation of animal behavior when the white lamp was extinguished.

Daily sessions of 22-min duration were conducted with each group for consecutive days. Baseline data (without stimulation) were obtained for each group in session 1, during which the number of entries by each

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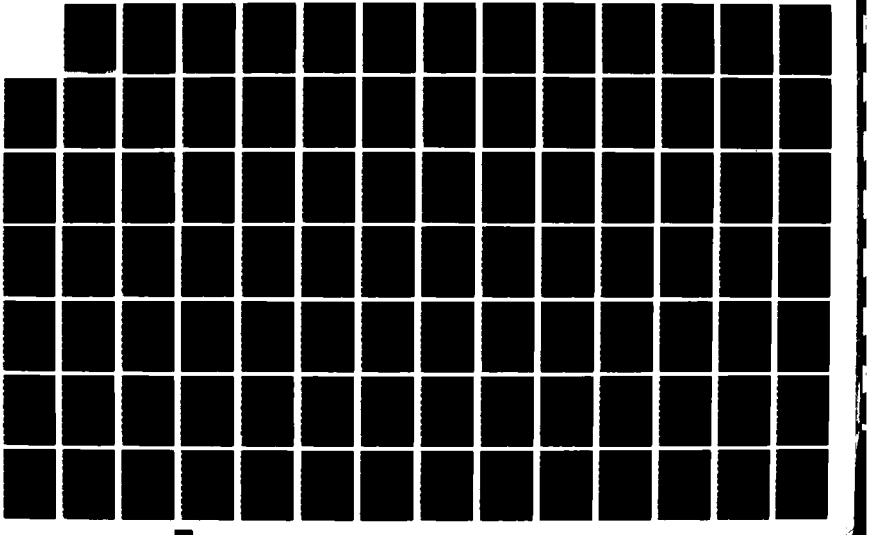

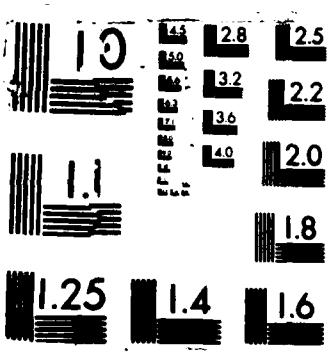
2.8
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1.6

into the safe area and the times spent therein were recorded. The criterion for entry into either area was traversal of the boundary by the entire head of the rat. Sessions 2-6 each comprised 11 serially numbered 2-min periods, with the respective stimuli available during the 5 even-numbered periods only. During stimulation-availability periods, the rats were continuously subjected to the stimuli except when they moved into the safe area. Rectal temperatures were taken just before the start of session 6 and immediately after completion of the last stimulation period.

To determine whether the rats did have adequate opportunity to associate entry into the safe area with cessation of stimulation, the numbers of entries by each rat during the even periods of each session (total time 10 min) were summed and the daily sums were averaged by group. The mean numbers of entries for session 1 (baseline) were about 4 for the S group, 6 each for the M and L groups, and 8 for the ML group. No SEs or SDs were given, but the authors stated that by analysis of variance, the differences among these baseline means were due to chance.

The S group showed a small initial rise for session 2; for sessions 3-6, the mean number of entries (during the 10 min of stimulation) decreased to a plateau of about 2 (half its baseline value 4). The M group showed successive rises for sessions 2 and 3, after which the mean for sessions 4-6 diminished to a plateau comparable to its baseline value. Results for the L and ML groups were similar to those for the M group, but with plateaus of 14 and 19, higher than their respective baseline values.

The mean times spent in the safe area by each group during the entire 22-min (1320-second) session of each day, i.e., irrespective of presence or absence of stimulation, were presented in Fig. 3 of the paper (with SE bars). The baseline values (session 1) for the 4 groups were all about 100 seconds or about 8% of the session time. For the L group, the mean times remained at baseline for sessions 2-6. The values for the M group also remained at baseline for sessions 2 and 3, but rose to about 300 seconds (23% of the session time) for sessions 4-6. By contrast, the mean times for the ML group rose linearly for sessions 2-3 to a plateau of about 650 seconds (49%) for sessions 4-6, and the values for the S group rose similarly to a plateau of about 1200 seconds (91%).

The mean times each group spent in the safe area during each of the five 2-min periods of stimulation and the six 2-min periods of nonstimulation each session were presented separately in Fig. 4. Photic stimulation only (L group) produced no significant differences among mean values for stimulation and nonstimulation periods either within each session or for all 6 sessions. RFR stimulation only (M group) yielded similar results for sessions 1-3, but the variations among period values progressively increased for sessions 4-6 with no clear differences between stimulation and nonstimulation, and a trend toward longer durations in the safe area was discernible, to a mean of 25% per period for session 6 as compared with 8% for session 1.

The combination of photic stimulation and RFR (ML group) produced no significant differences between stimulation and nonstimulation values, but the variations among period values were much larger, as was the trend toward longer durations in the safe area, 49% for session 6. By contrast with the other three groups, the faradic-shock (S) group spent about 75% of session 2 in the safe area (with no significant difference between mean values for stimulation and nonstimulation). In addition, after the first two 2-min periods, the rats spent 100% of the remainders of sessions 3-6 in the safe area.

The results of the rectal temperature measurements in session 6 showed significant ($p<0.05$) increases for the M and S groups and nonsignificant ($p>0.05$) increases and decreases for the L group. For the ML group, the difference between final and initial temperatures was not significant; however, the temperature of one of the four rats was initially above normal (40.6 deg C), presumably from excitation, and it did not change. The temperature increases of the other three rats were significant.

In this study, although the safe area of each false floor was about 25% of its total area, Fig. 3 indicated that even during baseline sessions, all four groups spent only about 8% of the session time there, which again suggests the possibility of some repellent factor associated with that region of the cavity (or conversely an attractive factor in the unsafe area). If so, there is no basis for assuming that such a factor would bias the results for each group equivalently so as to exclude the factor from consideration.

On the basis of their findings with rats, Levinson et al. (1982), with due regard for the species difference, argued against the conclusion of Monahan and coworkers that mice could detect 2.45-GHz RFR and endeavor to ameliorate their exposure by reorienting themselves in the waveguide to reduce their SARs. One point supporting this argument was that the SAR reductions were only about 30%, or too small to discriminate because of thermal inertia. This basis appears to be irrelevant because perhaps the 30% represented about the maximum reduction of SAR available to the mouse rather than a measure of its detection sensitivity. The other point argued was that the detection sensitivity increased (rather than decreased) with increasing ambient temperature in the waveguide, citing a reliable SAR decline from an initial value of only 0.06 W/kg at 35 deg C. [Note that Table 1 of Monahan and Ho (1977) did show a trend toward SAR decline with time for exposure at 0.06 W/kg but that those results were not labeled statistically significant; the SAR declines at 0.6 W/kg and higher at 35 deg C were significant.] This basis appears to ignore the lower thresholds for loss of thermoregulation at higher ambients.

Levinson et al. (1982) suggested that the SAR declines with exposure time observed by Monahan and coworkers were more likely due to heat prostration of the mice, resulting in lower energy-absorption profiles in the waveguide, rather than to behavioral reorientations. However, the SAR declines with time were gradual rather than sudden. (It should be noted that qualitatively similar SAR reductions were obtained in rats by Monahan and Henton, 1977b, as well as in mice.) There appears to be

common agreement, however, that under some exposure conditions, intense levels of deeply penetrating RFR may not be sensed in time to avoid tissue damage.

Bermant et al. (1979) subjected 12 Sprague-Dawley mature female rats to classical conditioning in which the conditional stimulus (CS) was a 30-second 525-Hz auditory signal presented for 30 habituation trials, 200 conditioning trials, and 100 extinction trials. The rats were randomly divided into four treatment groups. For any treatment, each rat was confined in a restrainer of Lexan mesh and placed in the center of a Plexiglas chamber within a modified microwave cavity (Justesen et al., 1971). Colonic temperature was measured continuously during treatment with a thermocouple.

The control group was given only the CS tone. The other three groups were presented an unconditional stimulus (US) during the conditioning phase, with the CS also given these groups starting 30 seconds prior to, and continuing to the end of, the US. For one of these three groups, the US was 2 seconds of electric shock (60 Hz, 300 V rms, 1 mA maximum) to the tail; for another, the US was exposure for 10 seconds to 2.45-GHz RFR at 420 W/kg; the US for the third group was exposure to the RFR for 30 seconds at 220 W/kg. These SARs were selected to produce a colonic-temperature increase (positive delta-T) of 1.5 deg C by the end of the respective durations. The SARs were determined calorimetrically with cylindrical water models. The authors noted that the fit between delta-Ts of animals and water models was excellent for 10-second but not 30-second exposures, indicating that metabolic contribution to the delta-T for the latter was substantial.

During habituation, each rat was given 10 daily sessions, each session consisting of three 30-second presentations of the tone at aperiodic intervals of 20-25 min. The conditioning phase for the experimental groups comprised 10 discrete trials in which the pairings of CS and US occurred during each of 10 sessions, with trials spaced aperiodically at intervals of 4-6 min. Since the rats of the three experimental groups exhibited conditioning before the tenth session of CS-US pairings, the extinction phase for all four groups consisted of 10 sessions of 10 trials each at the same intervals, in which only the CS was presented.

Baseline colonic temperatures, taken for each rat during each initial portion before presentation of the CS, were averaged for each session and compared with the mean and peak temperatures observed during each CS presentation for that session, to determine whether the formation of a conditioned response (CR) would elicit a delta-T. Of 800 trials sampled from sessions 8 through 17 of the conditioning phase, only 34 (about 4%) were associated with positive delta-Ts. These delta-Ts were scattered over trials, did not exceed 0.1 deg C, and appeared to be spurious.

The colonic temperatures for the three experimental groups tended to increase over the course of the 200 conditioning trials, whereas those for the control group tended to decline. Least-squares analyses for linear temperature trends indicated that the slopes for the four groups

differed only during the conditioning phase. In Tukey tests, the positive slopes for the three experimental groups did not differ from one another, but the negative slope for the control group differed significantly from the combined slope for the experimental groups.

The authors also compared mean baseline temperatures (and SEs) of each group measured just before the first and last trials in each phase. For the control group in the conditioning phase, the mean temperature change was -0.47 deg C; the changes for the tail-shock, 30-second-RFR, and 10-second-RFR groups were respectively 0.37, 0.50, and 0.70 deg C, the last three averaging to 0.52 deg C. In addition, the mean temperature of the control group remained stable during extinction, but the corresponding temperatures of the experimental groups did not decrease reliably during that phase. (The authors indicated that two of the rats had died from pathologically verified pulmonary infections before completion of the study, one rat each from the 30-second and 10-second RFR groups, during the conditioning and extinction phases, respectively, and that the data for these rats were excluded).

The authors considered whether the statistically discerned generalized hyperthermic results for the experimental groups were valid CRs elicited by the conditioning milieu or were equivocal. To resolve the validity question, they performed several ad hoc studies. In one study, two experienced handlers (not previously involved in the formal study), one called "Trainer" and the other "Stranger," removed each of the surviving rats of the formal study from its home cage in ignorance of its previous treatment and inserted a thermometer into its colon. (Trainer handled the rats after the formal study but prior to this ad hoc study.) The digitally displayed temperatures, not visible by the handlers, were read independently by two other individuals who were also ignorant of the rat's treatment. For each of the three experimental groups and to a lesser extent for the control group, the mean colonic temperature of the rats when handled by Trainer was significantly higher than when handled by Stranger.

To verify the apparent differences in results from the two handlers, three each of the RFR-exposed and sham-exposed (tone-only) rats were randomly selected along with six naive cage controls. Trainer and Stranger measured the colonic temperature of each rat in the vivarium once a day for five days. The mean temperatures of the cage controls were virtually the same for the two handlers, but Trainer's means for the RFR- and sham-exposed rats were reliably higher than those found by Stranger. The authors drew these inferences: (1) handling techniques of Trainer and Stranger did not differ; (2) Trainer was selectively acting as a CS with respect to the experimental rats; and (3) the tone-only controls also exhibited indications of conditioning. The authors found in another experiment with these 12 rats that immobilizing them in the restraining apparatus was a hyperthermal trigger that produced sharp increases in colonic temperature. In view of these non-RFR influences, any specific effects of the RFR per se are difficult to discern.

Gage (1979) trained each of 12 Long-Evans hooded male rats on a

random-interval schedule of reinforcement to insert its head into a cup for food pellets. A head-insertion response interrupted an infrared (IR) beam, permitting recording of the action. After the rats had achieved stable performances, they were matched and distributed into three groups of four each by response rates.

For exposure, each group was housed in a diamond array of ventilated acrylic boxes in a controlled-environment Styrofoam chamber maintained at a relative humidity of 50% within a larger anechoic chamber (Elder and Ali, 1975). One group was exposed from above to far-field 2.45-GHz CW RFR at 5 mW/sq cm for 15.5 hr per night (1630 to 0800) without food and water available, three nights each at ambient temperatures of 22 and 28 deg C and one night again at 22 deg C. The long axes of the boxes were parallel to the E-vector. By twin-well calorimetry, the spatial mean SAR at 5 mW/sq cm was 1.0 W/kg, with a range 0.7-1.3 W/kg.

The exposures were spaced at six-night intervals. During the night preceding each RFR-exposure, the group was sham-exposed in the anechoic chamber; during the four nights following each exposure night, the group was housed in acrylic boxes within a similar Styrofoam chamber placed outside the anechoic chamber, but which shared the environment of the latter. The second and third groups were respectively exposed at 10 and 15 mW/sq cm (2.0 and 3.0 W/kg) but otherwise similarly treated.

Behavioral test sessions, each lasting 30 min, were conducted daily, starting 15 min after removal from the treatment chambers; the rats were given free access to water during this 15-min period. Testing was done concurrently in four boxes equipped with pellet dispensers programmed as follows. An electric pulse sent at 10-second intervals to a gate was passed through the gate with a 25% probability, and every second pulse that passed through the gate allowed the next response by the rat in each of the four boxes to be reinforced. A reinforcement was missed if no response occurred before a subsequent opportunity for reinforcement was programmed. The authors stated that this program was theoretically comparable to a variable-interval 1.33 (VI-1.33-min) schedule, i.e., a rat could obtain a reinforcer on the average of every 1.33 min.

After initial training, control performances on the random-interval schedule consisted of responses at linear rates that ranged among the rats from about 0.25 to more than 2 responses per second. Some rats exhibited distinct short pauses following reinforcement, a consequence of the relatively long minimal time (20 seconds) between reinforcements. Also, several rats that initially exhibited consistent daily performance rates began to progressively increase their rates shortly before the start of the treatment sequence, behavior that persisted for the control sessions during the sequence.

Cumulative records following exposure to the three levels of RFR at 22 deg C or to 5 mW/sq cm (1.0 W/kg) at 28 deg C yielded few changes from corresponding control performances. The records following exposure to 10 or 15 mW/sq cm (2.0 or 3.0 W/kg) at 28 deg C, however, showed marked reductions in response rate, more frequent long pauses between bursts of

responding, and decreased numbers of reinforcers received.

Two of the four rats exposed to 15 mW/sq cm (3.0 W/kg) at 28 deg C died during exposure and were replaced with two others for the remainder of the sequence. The response rates of the replacement rats after exposure to these conditions were also below control values.

The rectal temperature of one rat of each group was measured in the afternoon, before the rat was placed in its box and again on the next morning immediately after removal from the treatment chamber. Overnight decreases of about 1 deg C were obtained for the rats sham-exposed at either ambient temperature. Comparable overnight decreases were also observed for other rats kept in their home cages. The decreases for those exposed to 5 mW/sq cm were smaller, 0.6 and 0.7 deg C respectively at 22 and 28 deg C. Exposure to 10 mW/sq cm at 22 and 28 deg C yielded respectively a 0.3-deg-C decrease and a 0.2-deg-C increase. For 15 mW/sq cm, the respective values were a 0.3-deg-C decrease and a 0.9-deg-C increase.

The author noted that "...there were occasions when rectal temperature changed but behavior did not, and also occasions when behavior changed but mean rectal temperature did not. A hypothesis that the behavioral effects are solely due to increments of rectal temperature is difficult to support." However, the small number of rats in each group and the large differences in response rates among them for control sessions renders it difficult to ascribe statistical validity to the findings of this study.

In a similar later study, Gage and Guyer (1982) trained 64 Long-Evans male rats to perform on a VI-1 schedule of reinforcement, in which the opportunity to obtain a food pellet occurred on the average of once each minute in a preplanned sequence of intervals without cueing. The rat forfeited a reinforcement opportunity if it did not respond before the next programmed reinforcement opportunity.

RFR- and sham-exposures of groups of four rats in individual acrylic boxes were conducted from above in the chambers, previously described in Gage (1979), in which the relative humidity was held constant at 50% to within 5% and the ambient temperature at 22, 26, or 30 deg C to within 1 deg C. Unlike in Gage (1979), the long axes of the boxes were parallel to the H-vector. From Durney et al. (1978), p. 95, however, the SARS at 2.45 GHz for the E- and H-polarizations are about the same.

Behavioral sessions were begun daily at 0800. The first response in each session yielded a pellet. Each session lasted until 30 additional reinforcement opportunities had been programmed on the VI-1 schedule, which required about 30 min. A week of daily sessions were conducted for the rats to achieve performance stability; during this week, they became adapted to being in the boxes overnight and to having rectal temperatures taken. For three sessions before RFR-exposure, the rats were tested after overnight sham-exposure at 22 deg C, to acclimate them to the housing conditions during exposure. The last of these comprised

the 0-mW/sq-cm exposure at 22 deg C.

Two groups were then exposed without access to food or water to 2.45-GHz RFR for 15.5 hr (1630-0800) under each of the following conditions: 8 or 14 mW/sq cm at 22 deg C; 0, 8, or 14 mW/sq cm at 26 deg C; and 0, 8, or 14 mW/sq cm at 30 deg C. Mean SARs (and spatial ranges) corresponding to 8 and 14 mW/sq cm were 1.6 (1.1-2.1) and 2.8 (2.0-3.6) W/kg. On the night following an RFR-exposure, each group was sham-exposed at the same temperature. Rectal temperature was measured in one rat of each group before and after each RFR- or sham-exposure. Test sessions were begun about 10 min after treatment; during this 10-min interval, the rats were given access to water and the post-treatment rectal temperatures were taken. Analysis of covariance was used on the data.

Mean rectal temperatures decreased after all treatments (including sham-exposure) except after exposure to 14 mW/sq cm (2.8 W/kg) at 26 and 30 deg C, at which they increased respectively by 0.1 and 2.7 deg C.

The response rates under control conditions differed among rats, so the data obtained for each rat before and after RFR-exposure were compared with its baseline data. The results were expressed as mean ratios (in percent) of the post-treatment response rate to the response rate for the previous session. For treatment at 22 deg C, the results were about 100%, 88%, and 78% respectively for 0, 8, and 14 mW/sq cm (0, 1.6, and 2.8 W/kg). The corresponding values for 26 deg C were 81%, 72%, and 56%; those for 30 deg C were 100%, 22%, and 20%. Thus, response-rate reductions directly dependent on RFR level were evident at each ambient temperature. However, the effects of ambient temperature per se were not consistent, notably the 81% and 100% sham-exposure results at 26 and 30 deg C, respectively.

Analysis of covariance confirmed that the effect of power density and the interaction of power density and temperature on response rate were both significant, as was the effect of temperature. The analysis showed that the response rate of each rat after RFR-exposure was dependent on its control rate. During sessions one day after RFR-exposure, many rats exhibited rates higher than those on the day before (overcompensation).

The total duration of post-treatment IR-beam interruptions was divided by the number of responses to obtain a mean response duration, which was expressed as the percentage of the value for the previous day. Results for the 22-deg-C groups were 100% for 0, 8, and 14 mW/sq cm (0, 1.6, and 2.8 W/kg). Results for the 26-deg-C groups at 0, 8, and 14 mW/sq cm (0, 1.6, and 2.8 W/kg) were 100%, 100%, and 140%, respectively, and those for the 30-deg-C groups were 100%, 170%, and 145%. Covariance analysis showed that the effect of ambient temperature on response duration was significant, but that the effects of power density and of interaction between power density and temperature were not significant.

Mitchell et al. (1977) randomly assigned and exposed 15 Sprague-Dawley female rats (mean weight 307 g), each rat restrained in a ventilated polystyrene cylinder, to 110 daily sessions of 5 hr each, 5 days/week

(550 hr total in 22 weeks), of 2.45-GHz CW RFR. The exposures were done concurrently at 15 of 30 possible locations within a large multimode, mode-stirred cavity at 24 deg C and 50% relative humidity (Bronaugh and Kerns, 1975), and the locations of the rats were varied daily. The mean SAR of each rat was 2.3 W/kg (by calorimetry on distilled-water models). Fourteen other rats were similarly sham-exposed in a dummy chamber.

The baseline locomotor activities of 5 rats in the RFR group and 5 rats in the sham group were recorded periodically for 60 min each at 15-min intervals during 14 pretreatment sessions. Immediately after each of the daily treatments, their locomotor activities were recorded again for 60 min at 15-min intervals. In the pretreatment sessions, the RFR- and sham-exposed rats showed progressive, significant declines in activity, to between 500 and 600 counts for the last pretreatment session, but no significant differences between groups, declines which were ascribed to simple habituation. However, starting with the second post-treatment session, the mean activities of the RFR-exposed rats rose to and stayed between 700 and 800 counts per session, whereas those for the sham-exposed rats declined slowly to less than 500 counts by week 22.

Five other rats each of the RFR and sham groups, maintained at 80% of normal body mass, were trained during 30-min sessions on a reinforced discriminative operant schedule, in which a food pellet was delivered for every fifth response (FR-5) to lighting of a cue lamp. Successive lamp-on and lamp-off durations averaged 15 seconds each. Responses when the lamp was off were recorded but not reinforced. To obtain baseline data, 25 pretreatment sessions were conducted with each rat; during the 22-week treatment period, 54 regularly spaced sessions were conducted immediately after treatment.

For the pretreatment data, the authors gave 676.0 and 787.9 as the mean numbers of responses per session respectively for the RFR- and sham-exposed rats during the lamp-on intervals, and 18.4 and 24.4 as the corresponding numbers during the lamp-off intervals. Statistical data were not provided but they indicated that analysis of variance yielded no significant differences between groups. They noted that the high ratios of lamp-on to lamp-off responses were indicative of reliable pretreatment discrimination by both groups and they used the inverse ratio (lamp-off/lamp- on responses of each rat) as the discrimination measure. The pretreatment mean ratios for the rats in the RFR and sham groups were respectively 0.026 and 0.034, a nonsignificant difference.

The mean numbers of responses per session by the sham group during lamp-on intervals of the 54 post-treatment sessions were between 700 and 800. For the RFR group, the values were less than 700 except for the last 18 post-treatment sessions for which they rose to above 700. The authors presented results of analysis of variance showing that the differences between the groups were not significant, but that the rise by the RFR group was significant. The mean numbers of responses per session by the RFR- and sham groups during the lamp-off intervals throughout the post-treatment sessions were respectively about 130 and 30, a significant difference. Thus, the corresponding discrimination

ratios were about 0.2 and 0.03. Also, comparison of the RFR-group ratios for their first and last post-treatment sessions confirmed the performance deterioration by this group.

The remaining 5 rats of the RFR group and 4 rats of the sham group were trained in 30-min sessions on the Sidman shock-avoidance test, in which a train of 2.0-mA, 0.3-second shock pulses was delivered to the feet via the bottom of the rat cage without prior cue every 15 seconds (response-shock interval), with the successive pulses in each train given every 0.5 second (shock-shock interval). A lever press by the rat would delay the next train. With training, the rat could avoid being shocked for most of or perhaps the entire session by pressing the lever at 15-second intervals. The last 25 pretreatment sessions yielded baseline data, and test sessions of 30 min were given immediately after each of 54 daily treatments. Data for each session were recorded in 6 blocks of 5 min each of interresponse times (IRTs), numbers of avoidance responses, numbers of shocks received, and numbers of shock trains entered.

For the pretreatment sessions, the differences between the groups were nonsignificant. For the post-treatment sessions, the overall mean IRTs for the RFR and sham groups were respectively 5.09 and 4.23 seconds, values stated to be comparable to those for the pretreatment sessions. By analysis of variance, there were no significant session-to-session differences in mean daily numbers of avoidance responses per session or mean values between the groups. During the 5-min blocks of each 30-min session, however, each group exhibited significant increases in numbers of avoidances, indicating intrasession learning, with those for the RFR group nonsignificantly higher than for the sham group at corresponding times. The block results also showed that both the numbers of shocks received and the numbers of shock trains entered decreased during each session and from session to session for both groups. Mitchell et al. (1977) concluded: "The analyses of post-irradiation Sidman avoidance data revealed no significant effects involving groups and thus provided no evidence of differential avoidance performance as a function of MW radiation."

Rectal temperatures were taken daily on randomly selected rats of the RFR group, about midway through each treatment, which required that the RFR be shut off for about 3 min. Temperatures of selected rats of the sham group were similarly taken. The respective mean values were 38.27 and 38.24 as compared with 38.0 +/- 0.5 deg C, the normal temperature for this rat strain. Reported, however, was the unexplained occurrence of conspicuous depilation of the backs of 4 of the 15 RFR-exposed rats, first observed about the tenth week of exposure and persisting for the remaining weeks, and the absence of depilation in any of the 14 sham-exposed rats. The authors stated (without giving data) that comparisons of the performance records of the four affected rats with those of the other RFR-exposed rats revealed no striking abnormalities in behavior.

Lin et al. (1977) deprived female Sprague-Dawley (200-g) rats of food to maintain them at 80% of their free-feeding body masses and sham-

exposed or exposed them individually in acrylic restraining holders in 30-min sessions to near-field 918-MHz CW RFR at 10, 20, and 40 mW/sq cm from a cavity-backed square-aperture applicator located 8 cm above the proximal surface of the rat's body and directed toward its longitudinal midpoint.

Energy absorption rates in rat carcasses were determined by computerized thermography. Isothermal plots of energy absorption in the midsagittal plane yielded ranges (per mW/sq cm) of 0.1-0.9 W/kg in the tail and 0.1-0.8 W/kg in the body, values that were sensitive to the position of the tail. Consequently, exposures were performed with the tail immobilized. Mean whole-body SARs were not measured, but theoretical calculations for mass-equivalent muscle spheres yielded spatially averaged SARs of 0.21 W/kg per mW/sq cm or 2.1, 4.2, and 8.4 W/kg at 10, 20, and 40 mW/sq cm.

The holder was a truncated cone of acrylic rods designed for adequate ventilation and to allow the rat to poke its head through the narrower end, thus permitting free movement of the rat's neck and head while restraining the rest of its body. The rats learned after a few sessions to run into the holder and extend their heads through the opening. The receiver for the holder and the exposure chamber were designed so that a small upward movement of the rat's head interrupted a horizontal light beam. The task required of the rat was to execute 30 such movements rapidly and regularly to receive a food pellet (fixed-ratio, or FR-30 schedule). A slight downward movement of the head permitted the rat access to the pellets delivered. After achieving stable performances, they typically responded about 2000 times during each 30-min session.

Typical records of baseline cumulative responses vs time for 3 rats indicated virtually uniform response rates of about 80/min. One of those rats was exposed for 30 min each at 10, 20, and 40 mW/sq cm on 5 consecutive days, another was exposed at the same levels on alternate days (Monday, Wednesday, and Friday), and the third rat was subjected to 30-min sessions of sham exposure. No significant changes of performance rates were evident for the third rat or for the other two rats at 10 or 20 mW/sq cm (2.1 or 4.2 W/kg).

At 40 mW/sq cm (8.4 W/kg), the performance rate of the first rat was unchanged for the first 5 min, at which time its rate dropped to almost zero; the second rat performed at approximately baseline rate for the first 5 min or so, then at slowly decreasing rate for the next 15 min, and it essentially ceased performing for the remaining 10 min. The rats exposed at this RFR level exhibited physiological signs of heat stress, including panting, fatigue, and foaming of the mouth.

Another rat was subjected to exposures in increments of 3 mW/sq cm (0.63 W/kg) up to 32 mW/sq cm (6.7 W/kg), at which the rat exhibited similar signs of heat stress. Its response rate remained at baseline through about the first 13-14 min, diminished slightly during the next 5-6 min, and then decreased significantly (but not to zero) for the remainder of the session.

The behavioral results of this study appear to be straightforward and indicate the existence of a threshold between 30 and 40 mW/sq cm (6.3 and 8.4 W/kg) at 918 MHz for the specific task studied. An important general finding is the large range of local SARs (peak-to-average ratio of about 4) found by thermography in the rat carcass exposed at constant incident power density and animal orientation. As noted by the authors, there may be high local SAR values ("hot spots") within animals exposed to RFR at seemingly thermally insignificant power densities.

Sanza and de Lorge (1977), in three daily practice sessions of 1-2 hr, trained four Sprague-Dawley male rats, each maintained at 80% of its free-feeding body mass, to press the lever to obtain a food pellet. The rats were then trained, in 3-day sequences of 1-hr-daily sessions, to respond on a fixed-interval 15-second (FI-15-s) schedule the first day, a FI-30-s schedule the second day, and a FI-50-s schedule the third day. After five such sessions per week for six weeks, the rats were able to respond on the FI-50-s schedule for at least 22 consecutive daily 1-hr sessions at the same time each day (between 0900 and 0930 for the first rat, followed by the others at about 90-min intervals). No water was provided during sessions.

After completion of training, the rats were exposed to 120-Hz-modulated 2.45-GHz RFR in a Styrofoam operant-conditioning chamber from above with a standard-gain horn within an enclosure lined with RFR absorber at an ambient temperature of 24 +/- 0.6 deg C, relative humidity of 70%, and air-flow rate of 1.52-3.44 m/min. The floor of the operant-conditioning chamber was a grid of polyethylene. With exhaust fans operating, the white-noise sound-pressure level within the closed chamber was 76 dB. Exposures were for 60 min at 8.8, 18.4, or 37.5 mW/sq cm. SARs were not determined, but based on 0.21 W/kg per mW/sq cm obtained by Lin et al. (1977), were about 1.8, 3.9, and 7.9 W/kg. To minimize possible carry-over effects, the sequence of exposure at each power density was varied from rat to rat and each value was used only once in each sequence. In addition, sham-exposure sessions were conducted after each day of RFR exposure and when necessary to restabilize training. Water was provided between sessions.

Throughout the baseline sessions, two of the rats responded with lever presses at relatively high rates and the other two at relatively low rates, performances that were generally maintained except at the highest power density. RFR exposure caused no obvious changes in distribution of responses within the FI or in the interresponse-time distributions. Also, the lever-response rate of none of the rats was significantly altered at 8.8 or 18.4 mW/sq cm (1.8 or 3.9 W/kg). The response rates of the high-performance rats, however, diminished greatly at 37.5 mW/sq cm (7.9 W/kg), and these rats exhibited signs of overheating on removal from the chamber. The low-performance rats did not show such changes or overheating.

For sham-exposures, the mean pause times were 40.7 and 30.6 seconds for the low- and high-rate rats, respectively. At 8.8 and 18.4 mW/sq cm (1.8 and 3.9 W/kg), none of the rats showed statistically significant

changes from these values. At 37.5 mW/sq cm (7.9 W/kg), the mean value for the low-rate rats was 45.4 seconds, a statistically nonsignificant increase; the mean value for the high-rate rats was 48.4 seconds, a highly significant increase.

Pause times for the high-rate rats became progressively longer across successive fixed intervals, and were related to the apparent preference for the one area (near the wall on the opposite side of the food cup) found to have a relative power-density depression in horizontal mapping of the chamber. The behavior of the low-rate rats was similar but less pronounced. During sham-exposure or exposure at 8.8 mW/sq cm (1.8 W/kg), all four rats spent only 3-4% of the session time in that area. At 18.4 and 37.5 mW/sq cm (3.9 and 7.9 W/kg), however, the low-rate rats spent respectively about 56% and 78% of the time there, whereas the corresponding values for the high-rate rats were 81% and 92%.

The authors ascribed their results to "workload-microwave interaction," and indicated that the pronounced effects at 37.5 mW/sq cm (7.9 W/kg) on the high-rate rats were due to the significant thermal burden added to their high metabolic rates. They also suggested that "well-practiced operant behaviors, such as we used, may be impervious to the influence of radiation at low power densities," but also that other behavioral measures may be more sensitive to low power densities.

Description of the exposure facility did not include details regarding how the ambient temperature within the operant-conditioning chamber was maintained at 24 +/- 0.6 deg C. Not clear was whether the temperature within the chamber was monitored during the RFR exposures and used for feedback control. If not, then the heat rising through the grid floor from the RFR-absorbent walls of the enclosure beneath the chamber may have markedly increased the temperature within the chamber, especially at the higher power densities.

As indicated by the results at the higher power densities, the rats endeavored to minimize their heat loads by spending more than 50% of the session periods in the region of minimum power density. Although such behavior is an indication of the thermal basis of the effects observed, the presence of such power-density minima may have artifactually altered the numerical response-rate and pause-duration values, a point implied by the investigators.

De Lorge and Ezell (1980), to determine the effects of RFR exposure on observing-behavior, sham-exposed or exposed each of 8 Long-Evans male rats in a Styrofoam operant-conditioning box to pulsed RFR at 1.28 GHz (3-microsecond pulses at 370 pps) and at 5.62 GHz (0.5- or 2-microsecond pulses at 662 pps) from a horizontally radiating horn in an anechoic chamber designed for each frequency. Exposure sessions were for 40 min, with the E-vector vertical and with the right side of the rat toward the horn while the rat was performing. About 78 dB of masking noise was present during exposures. The ambient temperature varied with building values in the range 23-26.5 deg C, with small increases within the box due to RFR-generated heat in the wall opposite the horn in each chamber.

The relative humidities were about 50%.

Power density measurements were made with no rat present. Whole-body SARs were measured for Styrofoam models in the shape of a standing rat and filled with saline. The mean values were 0.25 W/kg per mW/sq cm at 1.28 GHz and 0.19 W/kg per mW/sq cm at 5.62 GHz. Also, local SARs were measured in the head, shoulder, abdomen, and hip (12 locations) within the models filled with muscle-equivalent synthetic material. Results (per mW/sq cm) were relative maximum SARs of about 5.5 W/kg in the left side of the head (the side away from the source) at 1.28 GHz and about 7 W/kg in the right side of the head at 5.62 GHz.

The operant-conditioning box was equipped with two levers and a food hopper midway between them. Two speakers, a 100-W lamp for general illumination, and a video monitor were mounted on the wall behind the horn of each chamber. A 25-W stimulus lamp was mounted in each ceiling above the box.

The rats, maintained at well below their free-feeding body masses, were given 40-min training sessions daily for 5 days per week to achieve a behavioral response that required the rat to depress the right lever, thereby producing a 1-kHz tone for 0.7 s or a 1.25-kHz tone for 10 s. Right-lever responses that yielded the 1.25-kHz tone were reinforced on the average of once every 20 s (VI-20-s schedule); otherwise the 1-kHz tone was presented. Depression of the left lever during the 10 s of the higher tone resulted in its cessation and the delivery of a food pellet. Depression of the left lever in the absence of the higher tone yielded a 10-s period during which responses on the right lever produced only 0.7-s intervals of the lower tone. If the left lever were not pressed by the end of the 10-s periods of the higher tone, the VI-20-s schedule would recycle.

After completing training (90 sessions), the rats were exposed to the 5.62-GHz RFR at power densities of 7.5, 11.5, 16, 26, 31.5, 38.5, 42, and 48.5 mW/sq cm, comprising a total of 183 sessions. The mean of their body masses during this phase was 362 g or about 88% of the mean free-feeding mass. The whole-body SARs ranged from 1.4 to 9.2 W/kg.

About 90 days later, the rats were exposed to the 1.28-GHz RFR at power densities between 0.1 and 1 mW/sq cm (obtained by interposing a sheet of absorber between the horn and the box) and at 5.5, 9.5, 10, and 15 mW/sq cm, totaling 62 sessions. The mean of their body masses was 400 g or about 90% of the mean free-feeding mass. Whole-body SARs ranged from 0.025 to 3.75 W/kg.

No overt physiological signs of hyperthermia were evident for either RFR frequency. Sham-exposures were conducted on days before and after RFR-exposure sessions.

Results showed consistent disruption of the behavior pattern, manifested as overall reductions of right-lever response rates during RFR exposure, long pauses unrelated to pellet delivery, and cessation of

responding after 15-20 min of exposure. Behavior disruption was consistent in all 8 rats for 5.62 GHz at 38.5 mW/sq cm (whole-body SAR of 7.3 W/kg) and higher, and for 7 of the rats at 26 mW/sq cm (4.9 W/kg) and higher. For 1.28 GHz, consistent disruption was obtained in all rats at 15 mW/sq cm (3.8 W/kg), and a statistically significant drop in mean response rate to about 88% of the mean sham-exposure rate was evident at 10 mW/sq cm (2.5 W/kg). However, some of the rats showed habituation (i.e., less disruption) to successive RFR exposures at the same power density (with interposed sham-exposure sessions).

Incorrect left-lever or false-detection responses (made in the absence of the food-availability tone) were affected in similar fashion. For 1.28-GHz RFR, their frequencies decreased substantially at 10 mW/sq cm (2.5 W/kg) and higher, and similarly for 5.62-GHz RFR at 26 mW/sq cm (4.9 W/kg) and higher. However, the ratio of false detections to total observing-responses increased significantly with increasing RFR level.

The pause time for a correct left-lever response following a right-lever reinforced detection-response was also found to increase with increasing RFR level, with reliable differences at 10 mW/sq cm (2.5 W/kg) for 1.28 GHz and at 16 mW/sq cm (3.0 W/kg) for 5.62 GHz.

The authors concluded that the behavioral disruptions were "almost certainly related to the thermal consequences of such radiation" and suggested that the widely different thresholds for behavioral disruption at the two frequencies, i.e., 10 mW/sq cm (2.5 W/kg) for 1.28 GHz and 26 mW/sq cm (4.9 W/kg) for 5.62 GHz, may have been due to different spatial SAR variations within the rats. This point is well taken, because the SAR maxima in the head were 5.5 W/kg per mW/sq cm at 1.28 GHz and 7 W/kg per mW/sq cm at 5.62 GHz, and the ratio of the latter to the former was only about 1.3 compared with 2 for the corresponding whole-body SARs. In view of such spatial-SAR-distribution differences, however, frequency scaling of effects in a single species or comparisons of results in one species with those in another species on the basis of whole-body SARs seems to be unjustified.

The pulsed RFR used may have yielded the RFR-auditory effect. If so, however, the authors were probably correct in discounting this effect as a factor in their results, because the pulse repetition rates used (370 and 662 pps) were much lower than the 1-kHz and 1.25-kHz tones used in the behavioral regimen.

The findings of this investigation with 1.28-GHz and 5.62-GHz RFR were qualitatively similar to those of previous behavioral studies with 2.45-GHz RFR in this laboratory with rats on fixed-interval schedules (Sanza and de Lorge, 1977), and with primates on variable-interval schedules (de Lorge, 1976 and 1979), discussed in Section 3.7.1.2.

In one of two studies, D'Andrea et al. (1977) maintained 11 Long-Evans male rats at 85% of their free-feeding body mass and trained them, daily during 1-hr sessions, to respond for food-pellet reward on a variable-interval schedule of reinforcement. Training sessions were conducted

until stable performance was achieved, defined as when the total number of lever presses during a session differed by less than 15% from the total of a previous session. An average of 14 sessions was necessary to achieve stability. The rats were also given four to six retraining sessions after each RFR-exposure session.

After training, five of the rats were each exposed in a monopole-above-ground chamber while housed in Plexiglas holding cages to 400-, 500-, 600-, and 700-MHz CW RFR in random order at a constant power density of 20 mW/sq cm with the rat's long axis parallel to the electric field, starting on the fifth min of each 1-hr session. Water was not provided during exposures. The ambient temperature and relative humidity were maintained at 21-22 deg C and 27%. The rats were monitored by closed-circuit TV. Each exposure was continued until the end of the session or was terminated at the instant of work stoppage, defined as the end of the first min during which response rate fell below 33% of its normal rate. The primary behavioral measure was the time interval to such work stoppage. Colonic temperatures were measured just before and after RFR exposure and some training sessions.

The results for these five rats showed that the most rapid stoppage of work and the highest elevations of body temperature occurred at 600 MHz (14.4 W/kg). The mean duration to work stoppage at this frequency was about 23 min as compared with about 51 min at 400 MHz (6 W/kg), 37 min at 500 MHz (10 W/kg), and 33 min at 700 MHz (14 W/kg). By analysis of variance, the differences between the value at 600 MHz and the values at 500 and 700 MHz were significant ($p<0.05$), and all three values differed significantly ($p<0.01$) from the value at 400 MHz. Comparison of total numbers of responses in training sessions before and after RFR-exposure sessions showed no significant influence of RFR on post-RFR sessions.

At the end of RFR-exposure, all the rats were clearly stressed by heat. They were prone, immobile, and showed signs of vasodilation on removal, but recovered within minutes. Colonic-temperature rise during exposure was divided by exposure duration as a measure of energy delivered. The mean value of this measure (in deg-C/min) at 600 MHz was 0.088, compared with 0.024 at 400 MHz, 0.049 at 500 MHz, 0.063 at 700 MHz, and about 0.01 for training sessions. All the differences were statistically significant ($p<0.01$).

As noted by the authors, the results indicated that 600 MHz is close to the resonance-absorption frequency for rats weighing 380-400 g and 19-20 cm in length (exclusive of tail) exposed with their long axes parallel to the E-vector, thus confirming analytical calculations for a prolate-spheroidal model of a medium rat (Gandhi, 1974; Johnson et al., 1976; subsequently incorporated into Durney et al., 1978, p. 95).

In the other study, D'Andrea et al. (1977) exposed each of the other six trained rats to 600-MHz CW RFR in random order at 20, 10, 7.5, and 5 mW/sq cm (14.4, 7.2, 5.4, and 3.6 W/kg) and similarly evaluated them. Invariably, work stoppage occurred at 20 and 10 mW/sq cm (14.4 and 7.2 W/kg); the respective mean durations to work stoppage were 25 and 44

min. The corresponding rates of colonic-temperature rise were 0.066 and 0.043 deg-C/min. The mean durations to work stoppage at 7.5 and 5 mW/sq cm did not differ significantly from 55 min, and the corresponding rises in colonic temperature were 0.019 and 0.017 deg C. Again there was no significant influence of RFR exposure on post-exposure sessions. Thus, the SAR threshold at 600 MHz for this behavioral measure was probably between 6 and 8 W/kg.

Three of these six rats were also exposed to 600-MHz pulsed RFR at a peak power density of 170 mW/sq cm and similarly evaluated. Pulse durations of 3 and 30 microseconds at 1000 pps were used, which yielded average power densities of 0.51 and 5.10 mW/sq cm (0.37 and 3.7 W/kg). The rats responded at near normal rates, and the colonic-temperature rises were small (no data presented). One rat stopped responding near the end of a session of 3-microsecond pulses. The authors noted that the energy in each 30-microsecond pulse was about half that found by Guy et al. (1975b) as the energy threshold for the RFR-auditory effect.

In a subsequent study, D'Andrea et al. (1979) exposed Long-Evans male adult rats to 2.45-GHz CW RFR. Exposures were done in two halves of a chamber lined with RFR-absorption materials and partitioned vertically with aluminum-covered sheets that served as ground planes. A quarter-wavelength monopole was mounted horizontally on each ground plane, and an array of 10 rat-holding cages was supported along a vertical circle of 90-cm radius around each monopole, with long axes parallel to the monopole. The RFR source was a 2M53 magnetron. The power densities for the 10 locations in the left chamber ranged from 4.92 to 5.84 mW/sq cm, with a mean of 5.42 mW/sq cm. The range for the right chamber was 4.15 to 5.68 mW/sq cm, with a mean of 4.85 mW/sq cm. The mean SAR at 5 mW/sq cm, determined calorimetrically for 3 carcasses of representative body mass, was 1.23 W/kg.

Sham-exposures were done in a chamber of the same design and interior dimensions but lined with Styrofoam sheet and sprayed with gray acoustic material to match the lighting and sound conditions of the RFR chamber. RFR- and sham-exposures were from 0900 to 1700 (8 hr/day), 5 days/week for 16 weeks. No food or water was provided in either chamber.

The subjects, 30 rats (350 to 375 g), were adapted to handling and the chambers by placing each in a chamber from 0900 to 1700 (without food or water), 5 days/week for 4 weeks prior to exposure. At 1700, the rat was removed and usually placed in a Wahman rodent-activity cage with food and water ad libitum. Wheel revolutions, food and water consumption, and body mass were measured at 0800 the next day, prior to returning the rat to one of the chambers. The rats were then divided into two groups of 15 on a random basis and statistically assessed for equality of mean daily wheel revolutions during the last two weeks of adaptation. With nonsignificant differences in means for the two groups, one group was selected by chance to serve as controls and the other for RFR exposures.

RFR- and sham-exposures were done from 0900 to 1700 daily, 5 days/week for 16 weeks, and wheel revolutions, food and water consumption, and

body mass were measured as before. In addition, the rats were each placed on one of two BRS/LVE stabilimetric platforms from 1700 to 1800 once every 2 weeks, starting with the week preceding exposure. Each platform, which measured lateral movements of the rat, was placed in a sound-attenuating enclosure ventilated with an exhaust fan and lighted with a 10-W bulb. The tests of each rat were done on the same platform.

Under ether anesthesia, blood samples were taken from a tail vein at 4-week intervals. One sham-exposed and two RFR-exposed rats died under anesthesia at the first blood collection. For the blood samples from the remaining rats, hematocrit was assayed and counts of red blood cells (RBC), white blood cells (WBC), and differential WBC were made. Plasma- and whole-blood cholinesterase activities and total plasma sulfhydryls were determined. Also, 24-hr urine samples were collected at 4-week intervals on Saturdays and analyzed for 17-ketosteroid levels. At the end of 16 weeks of exposure, six RFR-exposed and seven sham-exposed rats were euthanized and examined for gross pathology. The adrenal glands, liver, and heart of each rat were weighed.

No statistically significant differences between RFR- and sham-exposed rats in body mass, food intake, or water intake were obtained. The mean number of wheel revolutions for each group decreased about linearly with time, at a rate somewhat faster for the sham group than the RFR group. The mean values for the RFR group were consistently but nonsignificantly higher ($p>0.05$) than for the sham group at corresponding times.

By contrast, the mean numbers of activity responses on the stabilimetric platform, expressed as percentages of mean baseline responses, did not vary significantly with time, but the values for the RFR group were consistently lower than for the sham group at corresponding biweekly times. The differences were statistically significant ($p<0.05$) for test sessions 1, 3, and 4, but not for the other 5 biweekly sessions.

The hematological results showed statistically significant differences between RFR and sham groups only for the samples taken at week 6. The mean RBC count for the RFR group at week 6 was significantly lower than at weeks 2 and 10, whereas the values for the sham group at these three times did not differ significantly from one another or from the week-2 and week-10 values for the RFR group. The RBC values for both groups at week 14 were significantly higher than corresponding values at week 10, but did not differ significantly from each other. By contrast, the mean WBC count at week 6 for the sham group decreased while the count for the RFR group increased; both changes were significant, and so was the difference between groups at week 6.

Hemoglobin values for both groups at week 6 were higher than at week 2, but only the increase for the RFR group was significant, thus yielding a significant difference between groups. Hematocrit decreased in the sham group from week 2 to week 6, but remained unchanged in the RFR group, also yielding a significant intergroup difference. The mean percentages of neutrophils or lymphocytes between groups or within each group with time did not differ significantly.

RBC cholinesterase activity increased with time in both groups but did not differ significantly between groups at corresponding times. Plasma cholinesterase varied nonmonotonically with time in both groups. The values for the RFR group were consistently lower than for the sham group at corresponding times, but the differences were significant initially (before exposure) and only at week 6. Sulfhydryl levels also varied nonmonotonically, with the values consistently higher for the RFR group, but only the difference at week 6 was significant.

Mean 17-ketosteroids level in urine, which also showed nonmonotonic variations, was significantly lower for the RFR group than the sham group only initially and at week 1.

The measurements of body mass and masses of liver, heart, and adrenal glands, with the latter three expressed both in grams and as ratios to body masses, showed nonsignificant differences between groups. No data on pathology were presented.

Describing the controls in this study as "sham-exposed" is not accurate in a strict sense, because the rats were not sham-exposed in the actual chamber used for RFR exposures. The authors endeavored to make the RFR and control chambers similar, but the two chambers did differ in some respects, notably in the shape and composition of the inner surfaces (which could affect the optical and acoustic characteristics of each chamber) and conceivably the odor-bearing emissions from the walls (which could influence behavior). However, the degree of influence (if any) of such differences on the results cannot be assessed.

The RFR used was characterized as CW. However, the means by which the output power of the 2M53 magnetron was adjusted to yield the desired 5 mW/sq-cm power density was not described. Often an unfiltered half-wave or full-wave rectifier is used to power magnetrons. Such power supplies yield, respectively, 1 or 2 sinusoidal voltage half-cycles of 1 polarity for each 60-Hz alternation. Each half-cycle activates the magnetron for only part of the half-cycle, and the average output power is frequently adjusted by varying the fraction of the half-cycle or the duration of magnetron operation per half-cycle. Consequently, the RFR is amplitude-modulated (at 60- or 120-Hz) and may have small duty cycles (ratios of average-to-peak output powers) at relatively low average powers, and could produce the RFR-auditory effect under appropriate conditions. It is not clear whether this consideration applies to this investigation.

The mean body masses of both groups increased substantially during the experiment, from 350-375 g to 570 g and 535 g respectively for the euthanized control- and RFR-exposed rats. However, based on prolate-spheroidal models, the whole-body SARs for 2.45 GHz at 5 mW/sq cm for the "medium" and "large" rat (320 and 520 g, respectively) are about 1.2 and 0.9 W/kg (Durney et al., 1978, pp. 95- 96). Therefore, the SARs of the rats used in this study must have decreased significantly with time.

The primary RFR-induced effect, i.e., the lower mean activities of the RFR-exposed rats on the stabilimetric platforms, is open to question.

Specifically, the curves of mean activity vs test session for the RFR- and control groups were nonmonotonic but surprisingly similar in shape (Fig. 4 of the paper), an indication that perhaps time-dependent factors other than exposure were affecting both groups in at least qualitatively similar fashion. Strong evidence for the existence of such factors is the significant decline with time of the mean wheel activity of both groups, probably reflecting the tendency of male rats to decrease their activity rates as their body masses increase with time.

In addition, the stabilimetric data (expressed only in percentages of baseline performances) showed that during the first four sessions, the control group performed at 125-150% of their baseline values for reasons that were not discussed, and that the differences between the groups were statistically significant only for sessions 1, 3, and 4 (out of a total of 8 sessions). Lacking were the baseline results for each group.

Another point to be noted about the stabilimetric results is that the converse effect was reported in a subsequent study by D'Andrea et al. (1980), discussed below, conducted with rats of the same strain and with essentially the same methodology but at 915 MHz. This apparent reversal of effect is difficult to explain, particularly since 915- and 2450 MHz are both above the whole-body resonance for the mature rat.

The findings that the significant differences between groups in the hematologic measures were mostly for the week-6 samples and that there were significant week-to-week (time-dependent) changes within each group may also be indications that non-RFR factors were involved.

As noted above, D'Andrea et al. (1980) similarly exposed Long-Evans male adult rats 8 hr/day, 5 days/week, for 16 weeks to 915-MHz CW RFR at 5 mW/sq cm (2.46 W/kg) while housed in Plexiglas cages within the two halves of a partitioned chamber, with a JC-300 magnetron as the RFR source. The subjects, 30 rats (350-375 g), were treated as in the previous study. Blood samples were taken under anesthesia from a tail vein at 4-week intervals and assayed as in the previous study. Two rats of each group died under ether anesthesia during blood collection, but at the eighth week of adaptation prior to the start of exposures.

In addition, 14 days after completion of the 16th week of exposure, six randomly selected rats of each group were euthanized; hypothalamic tissue sections were prepared for light- and electron-microscopy; and the adrenal glands, liver, and heart of each rat were weighed. The other seven rats of each group were surgically fitted with stainless-steel recording electrodes placed bilaterally in calvarium over the visual cortices. For reference and grounding, electrodes were also placed in calvarium over the cerebellum and frontal sinus. One week after surgery, EEG recordings were made for 10 min. The rats were then euthanized and treated in the same manner as the other rats. (Although not explicitly stated, the EEGs presumably were taken 7 weeks after cessation of exposures.)

The mean values of the serum-chemistry measures showed that only the

level of sulfhydryl in plasma at week 2 was significantly affected; the level for the control group decreased from a mean baseline value of 9.1 to 8.8 mM at week 2, while the level for the RFR group rose from 9.4 to 11.1 mM.

The mean number of wheel revolutions for the control group decreased approximately linearly with time, whereas that of the RFR group rose monotonically through the fourth week of exposure and subsequently diminished approximately linearly in a manner similar to that of the control group.

The results of the tests on the stabilimetric platforms showed that the mean activities of both groups at test-session 1 (week 4 of exposure) were 175% above their baseline values. However, the values for the RFR group rose to about 400% and 475% above baseline at sessions 2 (week 8) and 3 (week 12), respectively, whereas the corresponding values for the control group were about 225% and 175%. However, the authors stated that intergroup differences for both activity measures were of doubtful statistical significance because of the large intragroup variations.

The mean body masses of both groups rose with time, with the values for the RFR group slightly but nonsignificantly lower than the corresponding values for the control group. The food intake of both groups varied with time in nonmonotonic but similar fashion, but with nonsignificant differences between groups. The results for water intake indicated that the mean values for the RFR group were lower than for the control group for the last two months of the experiment, but the authors characterized the differences as unreliable.

The mean values of RBC, WBC, and hemoglobin, and the percentages of hematocrit, polymorphic neutrophils, and lymphocytes, exhibited no significant differences between corresponding values for the RFR and control groups. Similarly, the results for urinary 17-ketosteroids showed no significant intergroup differences.

The measurements of body mass and masses of liver, heart, and adrenal glands of the rats euthanized two and seven weeks after cessation of RFR exposure showed no significant differences between groups.

Spectral analyses of the 10-min EEG recordings were done by computer. The frequency range (in Hz) was divided into four bins (subranges): 0.6-10.5, 10.6-20.5, 20.6-30.5, and 30.6-40.5; each recording was scanned four times; and the spectral content in each bin was averaged for the four scans. The results showed no significant differences between the groups. The maximum spectral content for each group was in the 10.6-20.5 bin.

Examination, by light microscopy, of hypothalamic slices stained with methylene blue showed some abnormal vacuolization and chromatolysis in specimens from both groups but no significant differences between the groups. By electron microscopy, neuronal cells having such morphologic

changes exhibited a lack of endoplasmic reticulum, the presence of deep enfolding of nuclei, and a larger number of mitochondria in some cells. Counting of such cells yielded nonsignificant differences between the groups. (Such abnormal cells were found in 7 of 12 control rats and in 6 of 10 RFR-exposed rats.)

The reported elevation of serum sulfhydryl levels for the RFR group at week 2 and not for any other assay time is difficult to ascribe to RFR exposure, in view of the variations of mean levels with time for both groups. Specifically, the mean week-2 level for the RFR group increased nonsignificantly from its baseline whereas that for the control group decreased nonsignificantly from its baseline. A t-test of these levels yielded 1.97 ($p>0.05$).

The decline of wheel activity by the control group during the course of the experiment was a non-RFR effect probably ascribable to the tendency of male rats to reduce their activity rate as their body masses increase with time. Consequently, the rise in activity by the RFR group during the first month or so probably was RFR-induced. The subsequent decline by this group for the remainder of the experiment at a rate comparable to that of the control group may have been due to the decrease of whole-body SARs with time.

The stabilimetric-platform results, which showed significant rises of activities for the RFR group during the course of the experiment, were at variance with the corresponding results of the earlier investigation at 2.45 GHz (D'Andrea et al., 1979), which showed a decline for the RFR group. It is noteworthy that the newer data (presented, as before, only in percentages of baseline performances) also showed that both groups performed well above their baseline levels (175% at exposure week 4), an indication that non-RFR factors may have been involved. Again, baseline results for each group were not presented.

The description of the EEG results was rather obscure, particularly with regard to the number of rats in each group, why four scans per recording were taken, and why any changes ascribable to the RFR exposure would be expected to persist for so long after cessation of exposure. Moreover, the surgical procedure used to implant the electrodes could have had significant effects on the EEGs of both groups. Therefore, even though the results showed no apparent RFR-induced effects, the finding is of little value.

Schrot et. al. (1980) investigated the effects of 2.8-GHz pulsed RFR (2-microsecond pulses at 500 pps) at average power densities of 0.25, 0.5, 1, 5, and 10 mW/sq cm on the acquisition of behavior. Three male albino rats (Nmri:O[SD]CV) were trained by food reinforcement to acquire a different four-member chain of responses each session.

Immediately before behavior assessment, the rats were sham-exposed or exposed for 30 min at one of the RFR levels in an anechoic chamber at 21 deg C. Each rat was restrained in a sleeve holder of fine plastic mesh suspended from a Styrofoam frame located 68 cm (about 6.3 wavelengths)

in front of a standard-gain horn. The electric field was vertically polarized. The rats were exposed laterally with the H-vector parallel to the long body dimension. Mean whole-body SARs, calculated from core-temperature rises in rats exposed at 5 and 10 mW/sq cm in restraint harnesses, were respectively 0.7 and 1.7 W/kg.

The testing apparatus consisted of a standard two-lever rat chamber augmented with a third lever. The chamber was enclosed in a ventilated sound-attenuating enclosure. Each rat was trained to respond on each of the three levers individually, and responses were reinforced with food pellets. The rat then proceeded through a sequence of increasing chain lengths of responses on the levers, with auditory stimuli incorporated, until a predetermined sequence of four presses of the three levers was learned. The rats were thus required to perform sequences such as left (L), center (C), left (L), right (R), i.e., LCLR, or other combinations, with four auditory signals (900-Hz tone, 1-per-second clicks, 2000-Hz tone, and 10-per-second clicks) indicating the need for the next lever response in the chain.

The auditory stimuli were set at 72 dB, measured in the cage, and their ordering was the same from session to session. The ordering of lever responses was changed randomly from session to session. Correct lever responses to the auditory stimuli advanced the chain to the next member and ultimately produced food pellet reinforcement. Incorrect responses produced a 3-second timeout, heralded by extinguishing the houselight and current auditory stimulus and turning on a 2.8-Hz, 92-dB signal. Incorrect responses did not reset the sequence. Each auditory stimulus was presented until a correct response advanced the sequence to the next member of the chain, which thereby produced the next auditory stimulus. Sessions were conducted at daily scheduled times, five days a week, and were terminated after 150 reinforcements or 2 hr, whichever occurred first. Each rat was therefore tested once or twice a week.

Baseline response training took four months. After seven sessions of adaptation to the sleeve holder, a series of exposures was carried out. The rats were exposed to RFR for 30 min just before behavioral testing on one or two days a week. Each was exposed to 0.25, 0.5, 1, 5, and 10 mW/sq cm in mixed order, with each level presented at least three times (total of 15 or more exposure sessions for each rat). Sham-exposures were conducted throughout the exposure series. A normal baseline session was conducted after each sham- and RFR-exposure session.

For the three rats, a 30-min presession exposure at 10 mW/sq cm (1.7 W/kg) resulted in higher error-responding, lower sequence-completion rates, and alteration in the normal pattern of acquisition. These changes were termed "disruption of the daily acquisition curve generated by the repeated-acquisition procedure." Similar effects were seen at 5 mW/sq cm (0.7 W/kg) but to a lesser extent. Below 5 mW/sq cm, most of the data points fell within the control range, but a few were outside it. The significance of these few points is uncertain. Observation of rats during a session revealed that increase in error-responding was often associated with failure of the rat to switch response locations

after a single lever press, which could be interpreted as loss of stimulus control.

Similar RFR-induced disruptions of stimulus control in the context of multiple schedules of reinforcement were demonstrated by Thomas et al. (1975) and Mitchell et al. (1977). The mechanism of action of RFR in the present study is not clear. At 5 and 10 mW/sq cm, the peak power densities were 5 and 10 W/sq cm. With 2-microsecond pulses, these peak levels were sufficient to yield the RFR-auditory effect. Also, high local SARs may have caused selective brain heating. Such mechanisms were not investigated, but the authors noted: "any explanation will require effects that persist for 60 to 90 min postexposure."

In a later study, Thomas et al. (1982) similarly exposed four male rats of the same strain maintained at approximately 80% of their free-feeding weights to 2.8-GHz RFR, to compare the effects of CW RFR and pulsed RFR (2-microsecond pulses at 500 pps) at average power densities ranging from 1 to 15 mW/sq cm on their performance on a temporally defined schedule of positive reinforcement. Whole-body SARs were calculated from rises of rectal temperatures measured 5 min before and after 30 min of sham- and RFR-exposure at each power density. T$ mean temperature increases for 1, 5, 10, and 15 mW/sq cm were 0.1, 0.5, 1.1, and 1.5 deg C, yielding SARs of 0.2, 1.2, 2.5, and 3.6 W/kg, respectively.

The rats were initially trained on a lever-pressing schedule in which a food pellet was delivered only when the interval between two successive responses (interresponse time or IRT) was not less than 1 second and not more than 2 seconds. After about 20 sessions of reinforcement, a differential-reinforcement-of-low-rate (DRL) schedule was instituted, in which the required IRT (1-2 seconds) was reinforced only if the interval between successive correct IRT responses was more than 8 seconds but less than 12 seconds. A correct DRL response was reinforced by delivery of a pellet and the DRL interval was restarted. Incorrect IRT responses were not reinforced and had no effect on the timing of the 8-second DRL interval. A correct IRT response in less than 8 or more than 12 seconds after a correct IRT response was not reinforced and the DRL interval was restarted. Daily sessions were conducted 5 days per week. Each session was terminated after delivery of 150 pellets or 1 hr.

The rats were trained for 3 months to stabilize their baseline rates and to accustom them to the sleeve holder. After training completion, the rats were exposed once a week to either the CW or pulsed RFR at an average power density of 1, 5, 10, or 15 mW/sq cm for 30 min and tested following exposure. The levels were administered in mixed order, each rat was exposed at least three times at each level (except for 5 mW/sq cm), and the response rate (number of correct DRL responses per second) in each session was recorded. Comparison data were obtained by testing each rat for baseline performance between RFR-exposure sessions and for performance after sham-exposures, the results of which were averaged.

The response rates of the four rats to CW RFR were comparable to their respective mean control values and there was no consistent variation of

response rate with power density. The response rates to pulsed RFR, however, were significantly lower than for the corresponding levels of CW RFR, and a statistically significant downward trend of rate with increasing average power density was observed.

The records of cumulative number of correct DRL responses of one rat and its cumulative number of total responses were shown for a representative baseline session and for representative sessions involving exposure to pulsed RFR at 10 and 15 mW/sq cm and to CW RFR at 15 mW/sq cm. These records indicated that the rate of correct responses for pulsed RFR at 10 mW/sq cm (2.5 W/kg) was lower than the rate of correct baseline responses even though the RFR rate of total responses was higher than the baseline rate of total responses. For pulsed RFR at 15 mW/sq cm (3.6 W/kg), the rates of correct and total responses were both lower than the respective baseline rates and the corresponding rates at 10 mW/sq cm (2.5 W/kg). By contrast, for CW RFR at 15 mW/sq cm (3.6 W/kg), the correct-response and total-response rates were only slightly lower than the corresponding baseline rates.

The authors suggested that the behavioral changes seen after exposure to the pulsed RFR may be the result of alterations in the stimulus control of very precise temporal discriminations, but that the mechanism was unclear. Also mentioned was that the RFR-auditory effect might have been involved. However, the authors noted that because the behavioral tests were performed after the exposures were completed, persistence of the effect (whatever its nature) of the pulsed RFR for at least 1 hr after exposure is an important aspect to be considered.

Lebovitz (1981), concurrently sham-exposed and exposed groups of 15 Long-Evans female rats each to circularly polarized 1.3-GHz pulsed RFR (1-microsecond pulses at 600 pps) in individual circular-waveguides with the electric vector transverse to the propagation direction. The room was maintained at 21 deg C but with unregulated relative humidity, which varied mostly between 40% and 60%. The waveguides were similar to those designed by Guy and Chou (1976), but each waveguide had a vertical displacement bar (behavioral operandum), a means for illuminating the operandum as a cue (visual discriminative stimulus), and means for delivering a food pellet when appropriate. The rats, which were not restrained, were facing the RFR source during operant performance.

Prior to exposure, rats in groups of 46 were initially deprived of food for 2 days and were trained for 10 days to bar press for food pellets at increasing fixed-ratio (FR) schedules to FR-5 (requiring 5 successive lever presses to obtain a pellet). Thirty rats from each group, those that performed at the highest and most stable rates, were selected and trained on a multiple fixed-ratio, extinction schedule of reinforcement using visual discriminative stimuli, in which only the responses when an operandum was illuminated (SD) were reinforced by pellet delivery. Such responses were tabulated. The reinforcements were done on a fixed-ratio schedule that was gradually increased to FR-25 during several weeks of training. Rat responses when the operandum was not illuminated (Sd), which yielded no pellets, were tabulated

separately.

Each set of 30 rats that achieved high and steady performance at FR-25 was given a baseline period of sham exposures and testing, after which half were randomly assigned to the RFR group and half to the sham group, with the 2 groups matched by baseline FR-25 performance. RFR- and sham-exposures were for 3 hr at the same time each day for 5 days/week. The daily behavioral sessions were begun 15 min after the start of exposure and were terminated 15 min before the end of exposure, for a 150-min session duration. The rats were also tested during a 2-week recovery period after the exposure regimen. Each behavioral session was divided into 6 sequential blocks of 25 min, each block consisting of a 15-min SD interval (when the operandum was illuminated) followed by a 10-min Sd interval (when the operandum illumination was extinguished). Response rates of each rat for SD and Sd during baseline, exposure, and recovery periods were summed weekly by block number and the results for the rats in each group were averaged.

One group each was exposed at 1.5, 3.6, or 6.7 W/kg. The corresponding average power densities were 3.9, 9.2, and 17.2 mW/sq cm, determined by noting that the SAR for a 300-g rat at 1.3 GHz was 2.2 W/kg per W of forward power and by dividing 1 W by the cross-sectional area of the waveguide (177 sq cm). The corresponding peak power densities were 6.4, 15.4, and 28.7 W/sq cm. When not in their waveguides, the rats were kept in home cages with water available ad libitum. In addition, each rat was given 8 g of food daily irrespective of its operant performance, and was weighed three times per week. All rats maintained satisfactory growth curves.

The results for 8 weeks of sham-exposure and exposure at 1.5 W/kg (3.^{o} mW/sq cm) showed stable response rates and no statistically significant differences for SD between RFR and sham groups for corresponding blocks and weeks. Both groups showed a slight but significant rise in weekly SD response rate for blocks 1 and 3 and a slight decline for block 6. There were also modest declines in rates during sessions, i.e., over blocks 1-6. The response rates for Sd were more variable than for SD. A rise in the block-1 weekly rate and declines in the block-3 and block-6 weekly rates were found, but the changes were not significant. Also, the decline in Sd rates during sessions, which was also evident for the baseline and recovery weeks, was sharper than for SD. However, there were no significant differences between the RFR and sham groups.

There were also no significant differences between groups in SD response rates for 9 weeks of exposure at 3.6 W/kg (9.2 mW/sq cm). The changes in weekly rates for both groups were marginally significant and the intrasession decline in rate was significant. Regarding the Sd response rates (which again showed sharp intrasession declines for both groups during baseline, exposure, and recovery periods), analysis revealed an apparently transient difference between groups: the Sd response rate by the RFR group was significantly lower than for the sham group only for blocks 2 and 3 of the first exposure week. The author indicated that similar results were obtained with another group of rats

exposed at the same RFR level.

The results for 6 weeks of exposure at 6.7 W/kg (17.2 mW/sq cm) showed no statistically significant differences between groups in overall SD response rates, but there were significant block-dependent differences between the groups. Specifically, the SD rates of both groups during blocks 1 and 3 did not change significantly week by week and differences between groups for blocks 1, 3, and 6 during the baseline and recovery periods were not significant; however, the SD rate of the RFR group for block 6 was significantly lower than the block-6 rate of the sham group for exposure-week 2 and was marginally significantly lower for exposure-weeks 1, 3, and 4. These differences were ascribed to marked reductions in bar pressings near the end of behavioral sessions (blocks 4-6) during those weeks. An analysis by rat showed that the differences between SD rates during the last baseline week and the first exposure week were not significant, showing that the decline was gradual rather than immediate.

Regarding the Sd rates for the 6.7-W/kg (17.2-mW/sq-cm) regimen, there were significant intrasession declines (differences in successive rates for blocks 1, 3, and 6) for both groups during the baseline period, with nonsignificant intergroup differences. However, the Sd rates for blocks 1, 3, and 6 of the RFR group declined during the first week of exposure, whereas the corresponding rates for the sham group rose (for unknown reasons), yielding significant intergroup differences for corresponding weeks and blocks. After 3 weeks of exposure, the block-1 rate rose for the RFR group and declined for the sham group, so the two rates became comparable again by the fifth week of exposure. The block-3 rate of the sham group also rose at the beginning of the exposure regimen and later declined; the rate for the RFR group concurrently dropped to very low values but showed sharp recovery at the end of the exposure regimen. The block-6 rates of both groups were already low during the baseline period, but the Sd rate of the RFR group dropped to almost zero during exposures, with only slight increases seen during the recovery period.

Based on the negative results for SD and Sd at 1.5 W/kg (3.9 mW/sq cm) and the doubtfully significant decline in Sd rate at 3.6 W/kg (9.2 mW/sq cm), the investigator suggested that this SAR could be the approximate threshold for modifying the rate of operant responding in the absence of visual cue or food reinforcement. About the results at 6.7 W/kg (17.2 mW/sq cm), although there were no significant differences in overall SD response rates between the RFR and sham groups, the decline rate of the intrasession SD response rate of the RFR group was higher than for the sham group. By contrast, the decline of the weekly and intrasession Sd rates of the RFR group were pronounced during exposure, with recovery to control levels after exposure.

The author noted that 6.7 W/kg is close to the resting metabolic rate for a 240-g rat, so such RFR exposure represented a virtual doubling of the heat dissipation requirements of the animal, and he thus concluded that thermal factors were likely involved in the observed behavioral effects. He also calculated that the energy deposited in the rat during each pulse exceeded the threshold for the RFR-auditory effect. However,

he questioned whether the loudness perceived by the rat would constitute an adequate acoustic cue or how the presence of such a cue could account for the observation that the major decline in Sd responding was gradual rather than immediate with the onset of RFR exposure. He then indicated that other studies with CW RFR (manuscript then in preparation) yielded essentially the same findings as those reported for this investigation.

As noted, the operant data for each rat consisted of the number of bar presses during each of the 6 blocks or pairs of cued (SD) and uncued (Sd) response intervals sequentially numbered 1-6 daily. However, not clear was the rationale for summing the responses for correspondingly numbered blocks to obtain weekly block totals of SD and Sd responses as the "primary descriptive variables" for each rat, and why the time-dependent data for the successive blocks during daily sessions were not described or treated more explicitly, since even the baseline results indicated intrasession diminutions of both SD and Sd rates. Despite the extensive statistical treatment of the data, it is difficult to assess the contribution of this time-dependent non-RFR factor to the results of this investigation. However, this point does not gainsay the existence of the RFR-induced effects discussed.

In a later study, Lebovitz (1983) concurrently sham-exposed and exposed similarly trained groups of rats to CW as well as pulsed 1.3-GHz RFR, (1-microsecond pulses at 600 pps). Distinct groups of 15 rats each were used for exposures to the CW and pulsed RFR (and for their respective concurrent sham-exposures). Again, the rats were trained initially to bar press for pellets at increasing fixed-ratio schedules to FR-5, and then were trained daily on a multiple schedule that started with a 15-min interval (labeled S+ instead of SD) of bar illumination and pellet availability at FR-25, followed by a 10-min timeout interval (labeled S- instead of Sd) of no illumination or pellet availability. As in the previous study, each session consisted of 6 contiguous thus-paired 25-min periods, which were numbered 1-6 sequentially.

One group was exposed to CW RFR at 5.9 W/kg (15.2 mW/sq cm). The S+ results for the baseline week preceding exposure showed a trend toward decreasing response rates of about 10% from period 1 to period 6 for both the RFR- and concurrently-sham-exposed groups but no significant differences between the groups. The S+ rates of both groups for periods 1 and 2 were higher for the week of exposure than for the corresponding periods of the baseline week, and both groups showed a downward trend, but the RFR group's decline in response rate was significantly faster.

Breakdown of those results by operant days and period numbers showed no significant differences in daily period-1 response rates between groups for the entire 2-week (baseline and exposure) duration. However, the daily S+ response rates of the RFR group for periods 3 and 6 declined significantly during the first 3 days of exposure, with the decline for period 6 sharper. Recovery occurred during the last 2 days (to values comparable with those of the sham group).

During the baseline week, the S- response rates of this RFR group were

initially higher than for the sham group, but declined faster between period 4 and period 5, so the rates for the 2 groups were comparable for periods 5 and 6. During the week of exposure, the sham group exhibited higher rates for periods 1 and 2 than they did for the same periods of the baseline week, and approximately the same rate of decline. However, the rates of the RFR group dropped sharply for periods 1-3 to almost zero for periods 4-6.

Breakdown of the S- results by operant days and period numbers showed a significant decline of the period-1 response rates for the RFR group during the first 3 days of exposure, followed by recovery during the last 2 days. However, the response rates of this group for periods 3 and 6 dropped to, and remained at, extremely low values for the entire exposure week.

For a group exposed to pulsed RFR at 6.7 W/kg (17.2 mW/sq cm), the response rates during both S+ and S- were similar to those with CW RFR at 5.9 W/kg (15.2 mW/sq cm). (Equipment limitations did not readily permit closer match of SARs.) The author noted that the results with pulsed RFR at this level were similar to those obtained in the previous study with pulsed RFR at the same level (Lebovitz, 1981), and that the occurrence of similar changes in S+ rates with CW RFR at a comparable SAR showed that the effect was not ascribable to the pulsed character of the RFR.

For a group exposed to CW RFR at 3.6 W/kg (9.2 mW/sq cm), the S+ rates during the baseline week were consistently lower than those for the corresponding sham group, but the rates of decline for periods 1-6 were essentially the same. Also, similar results were obtained for the week of exposure except that the initial (period-1) response rates for both groups were higher than the initial rates for the baseline week. The S- rates of the RFR group were consistently higher than those of the sham group for the baseline week, but with comparable rates of decline, thus yielding no significant differences between the groups. The S- results for the week of exposure showed that the response rates of the RFR group were consistently higher than of the sham group; the response rates of both groups declined for periods 1-6, but the decline was significantly faster for the RFR group. These results were again consonant with those of the previous study.

Separate groups of 5 rats each were used to determine core-temperature rises due to RFR-exposure. Each rat was exposed in the waveguide for 1 or 3 hr and its rectal temperature was measured just before insertion and again within 10 min after its removal. Exposures to CW or pulsed RFR at about 3.5 W/kg (9.0 mW/sq cm), approximately the threshold for the behavioral effects above, yielded no significant differences in rectal-temperature changes as compared with rats sham-exposed for the same durations. However, exposures at about 6.3 W/kg (16.2 mW/sq cm), CW or pulsed, yielded increases of 0.5 to 1 deg C, with no significant duration-dependent differences.

As was true for the previous investigation, the engineering aspects

were excellent, and the statistical treatment of the data provided a sound basis for the conclusions reached. Moreover, the presentation of the data at 5.9 W/kg (CW) by operant days (a format lacking in the previous paper) provided greater insight into the time-dependent aspects of the results. Especially noteworthy was that the daily S+ response rates for period 1 were not significantly affected by the entire week of exposure to RFR and that the declines in these rates occurred progressively in the subsequent periods of each session. Also more clearly evident were the virtually immediate sharp declines in S- response rates for all periods at the onset of RFR exposure. In the absence of light cue and pellet rewards, it is possible that the rats were thoroughly confused by the presence of the RFR. Another possibility, suggested by the author, was that without such reinforcement, the rats endeavored to reorient themselves so as to redistribute the thermal burden added by the RFR.

As indicated by the author, the thermal basis for the behavioral changes observed is evident, with a threshold SAR of about 3.5 W/kg (9.0 mW/sq cm) irrespective of whether the RFR is CW or pulsed. Also, even though the pulse width (1 microsecond) and peak power density (estimated to be about 28.7 W/sq cm) were sufficient to produce the RFR-auditory effect, there was little doubt that perception of the pulses as sound (if it occurred) was not a factor in the results obtained.

REFERENCES:

Bermant, R.I., D.L. Reeves, D.M. Levinson, and D.R. Justesen
CLASSICAL CONDITIONING OF MICROWAVE-INDUCED HYPERTHERMIA IN RATS
Radio Sci., Vol. 14, No. 6S, pp. 201-207 (1979)

Bronaugh, E.L. and D.R. Kerns
CALIBRATION OF A MULTIMODE MICROWAVE EXPOSURE CHAMBER
1975 Electromagnetic Compatibility Symposium Record, IEEE No. 75CH1002-5 EMC, pp. 5BIIb1-5BIIb5 (1975)

Carroll, D.R., D.M. Levinson, D.R. Justesen, and R.L. Clarke
FAILURE OF RATS TO ESCAPE FROM A POTENTIALLY LETHAL MICROWAVE FIELD
Bioelectromagnetics, Vol. 1, No. 2, pp. 101-115 (1980)

Chernovetz, M.E., D.R. Justesen, N.W. King, and J.E. Wagner
TERATOLOGY, SURVIVAL, AND REVERSAL LEARNING AFTER FETAL IRRADIATION OF MICE BY 2450-MHZ MICROWAVE ENERGY
J. Microwave Power, Vol. 10, No. 4, pp. 391-409 (1975)

D'Andrea, J.A., O.P. Gandhi, and J.L. Lords
BEHAVIORAL AND THERMAL EFFECTS OF MICROWAVE RADIATION AT RESONANT AND NONRESONANT WAVELENGTHS
Radio Sci., Vol. 12, No. 6S, pp. 251-256 (1977)

D'Andrea, J.A., O.P. Gandhi, J.L. Lords, C.H. Durney, C.C. Johnson, and L. Astle
PHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF CHRONIC EXPOSURE TO 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 14, No. 4, pp. 351-362 (1979)

D'Andrea, J.A., O.P. Gandhi, J.L. Lords, C.H. Durney, L. Astle, L.J. Stensaas, and A.A. Schoenberg
PHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF PROLONGED EXPOSURE TO 915 MHZ MICROWAVES
J. Microwave Power, Vol. 15, No. 2, pp. 123-134 (1980)

de Lorge, J.O.
THE EFFECTS OF MICROWAVE RADIATION ON BEHAVIOR AND TEMPERATURE IN RHESUS MONKEYS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 158-174 (1976)

de Lorge, J.O.
OPERANT BEHAVIOR AND RECTAL TEMPERATURE OF SQUIRREL MONKEYS DURING 2.45-GHZ MICROWAVE IRRADIATION
Radio Sci., Vol. 14, No. 6S, pp. 217-225 (1979)

de Lorge, J.O. and C.S. Ezell
OBSERVING-RESPONSES OF RATS EXPOSED TO 1.28- and 5.62-GHZ MICROWAVES
Bioelectromagnetics, Vol. 1, No. 2, pp. 183-198 (1980)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Elder, J.A. and J.S. Ali
THE EFFECT OF MICROWAVES (2450 MHZ) ON ISOLATED RAT LIVER MITOCHONDRIA
Ann. N.Y. Acad. Sci., Vol. 247, pp. 251-262 (1975)

Frey, A.H. and S.R. Feld
AVOIDANCE BY RATS OF ILLUMINATION WITH LOW POWER NONIONIZING ELECTROMAGNETIC ENERGY
J. Compar. Physiol. Psychol., Vol. 89, No. 2, pp. 183-188 (1975)

Frey, A.H., S.R. Feld, and B. Frey
NEURAL FUNCTION AND BEHAVIOR: DEFINING THE RELATIONSHIP
Ann. N.Y. Acad. Sci., Vol. 247, pp. 433-439 (1975)

Gage, M.I.
MICROWAVE IRRADIATION AND AMBIENT TEMPERATURE INTERACT TO ALTER RAT BEHAVIOR FOLLOWING OVERNIGHT EXPOSURE
J. Microwave Power, Vol. 14, No. 4, pp. 389-398 (1979)

Gage, M.I., E. Berman, and J.B. Kinn
VIDEOTAPE OBSERVATIONS OF RATS AND MICE DURING AN EXPOSURE TO 2450-MHZ MICROWAVE RADIATION
Radio Sci., Vol. 14, No. 6S, pp. 227-232 (1979a)

Gage, M.I. and W.M. Guyer
INTERACTION OF AMBIENT TEMPERATURE AND MICROWAVE POWER DENSITY ON SCHEDULE-CONTROLLED BEHAVIOR IN THE RAT
Radio Sci., Vol. 17, No. 5S, pp. 179-184 (1982)

Gandhi, O.P.
POLARIZATION AND FREQUENCY EFFECTS ON WHOLE ANIMAL ABSORPTION OF RF ENERGY
Proc. IEEE, Vol. 62, No. 8, pp. 1171-1175 (1974)

Guy, A.W., C.-K. Chou, J.C. Lin, and D. Christensen
MICROWAVE-INDUCED ACOUSTIC EFFECTS IN MAMMALIAN AUDITORY SYSTEMS AND PHYSICAL MATERIALS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 194-218 (1975b)

Guy, A.W. and C.-K. Chou
SYSTEM FOR QUANTITATIVE CHRONIC EXPOSURE OF A POPULATION OF RODENTS TO UHF FIELDS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. II, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8011, pp. 389-410 (1976)

Ho, H.S., E.I. Ginns, and C.L. Christman
ENVIRONMENTALLY CONTROLLED WAVEGUIDE IRRADIATION FACILITY
IEEE Trans. Microwave Theory Tech., Vol. 21, No. 12, pp. 837-840 (1973)

Hunt, E.L., N.W. King, and R.D. Phillips
BEHAVIORAL EFFECTS OF PULSED MICROWAVE RADIATION
Ann. N.Y. Acad. Sci., Vol. 247, pp. 440-453 (1975)

Johnson, C.C., C.H. Durney, P.W. Barber, H. Massoudi, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-76-35, pp. 100-101, (1975)

Justesen, D.R. and N.W. King
BEHAVIORAL EFFECTS OF LOW LEVEL MICROWAVE IRRADIATION IN THE CLOSED SPACE SITUATION
In S.F. Cleary (ed.), BIOLOGICAL EFFECTS AND HEALTH IMPLICATIONS OF MICROWAVE RADIATION, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication BRH/DBE 70-2, pp. 154-179 (1970)

Justesen, D.R., D.M. Levinson, R.L. Clarke, and N.W. King
A MICROWAVE OVEN FOR BEHAVIOURAL AND BIOLOGICAL RESEARCH: ELECTRICAL AND STRUCTURAL MODIFICATIONS, CALORIMETRIC, DOSIMETRY, AND FUNCTIONAL EVALUATION
J. Microwave Power, Vol. 6, No. 3, pp. 237-258 (1971)

Justesen, D.R., E.R. Adair, J.C. Stevens, and V. Bruce-Wolfe
A COMPARATIVE STUDY OF HUMAN SENSORY THRESHOLDS: 2450-MHZ MICROWAVES VS FAR-INFRARED RADIATION
Bioelectromagnetics, Vol. 3, No. 1, pp. 117-125 (1982)

King, N.W., D.R. Justesen, and R.L. Clarke
BEHAVIORAL SENSITIVITY TO MICROWAVE IRRADIATION
Science, Vol. 172, No. 3982, pp. 398-401 (1971)

Lebovitz, R.M.
PROLONGED MICROWAVE IRRADIATION OF RATS: EFFECTS ON CONCURRENT OPERANT BEHAVIOR
Bioelectromagnetics, Vol. 2, No. 2, pp. 169-185 (1981)

Lebovitz, R.M.
PULSE MODULATED AND CONTINUOUS WAVE MICROWAVE RADIATION YIELD EQUIVALENT CHANGES IN OPERANT BEHAVIOR OF RODENTS
Physiology and Behavior, Vol. 30, No. 6, pp. 891-898 (1983)

Levinson, D.M., A.M. Grove, R.L. Clarke, and D.R. Justesen
PHOTIC CUING OF ESCAPE BY RATS FROM AN INTENSE MICROWAVE FIELD
Bioelectromagnetics, Vol. 3, No. 1, pp. 105-116 (1982)

Lin, J.C., A.W. Guy, and L.R. Caldwell
THERMOGRAPHIC AND BEHAVIORAL STUDIES OF RATS IN THE NEAR FIELD OF 918-MHZ RADIATIONS
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 10, pp. 833-836 (1977)

Lobanova, E.A.
THE USE OF CONDITIONED REFLEXES TO STUDY MICROWAVE EFFECTS ON THE CENTRAL NERVOUS SYSTEM
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 109-118 (1974)

Mitchell, D.S., W.G. Switzer, and E.L. Bronaugh
HYPERACTIVITY AND DISRUPTION OF OPERANT BEHAVIOR IN RATS AFTER MULTIPLE EXPOSURES TO MICROWAVE RADIATION
Radio Sci., Vol. 12, No. 6S, pp. 263-271 (1977)

Moe, K.E., R.H. Lovely, D.E. Myers, and A.W. Guy
PHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF CHRONIC LOW LEVEL MICROWAVE RADIATION IN RATS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 248-256 (1976)

Monahan, J.C. and H.S. Ho
MICROWAVE INDUCED AVOIDANCE BEHAVIOR IN THE MOUSE
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 274-283 (1976)

Monahan, J.C. and H.S. Ho
THE EFFECT OF AMBIENT TEMPERATURE ON THE REDUCTION OF MICROWAVE ENERGY ABSORPTION BY MICE
Radio Sci., Vol. 12, No. 6S, pp. 257-262 (1977)

Monahan, J.C. and W.W. Henton
FREE-OPERANT AVOIDANCE AND ESCAPE FROM MICROWAVE RADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 23-33 (1977a)

Monahan, J.C. and W.W. Henton
MICROWAVE ABSORPTION AND TASTE AVERSION AS A FUNCTION OF 915 MHZ RADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 34-40 (1977b)

Nealeigh, R.C., R.J. Garner, R.J. Morgan, H.A. Cross, and P.D. Lambert
THE EFFECT OF MICROWAVE ON Y-MAZE LEARNING IN THE WHITE RAT
J. Microwave Power, Vol. 6, No. 1, pp. 49-54 (1971)

Sanza, J.N. and J. de Lorge
FIXED INTERVAL BEHAVIOR OF RATS EXPOSED TO MICROWAVES AT LOW POWER DENSITIES
Radio Sci., Vol. 12, No. 6S, pp. 273-277 (1977)

Schrot, J., J.R. Thomas, and R.A. Banvard
MODIFICATION OF THE REPEATED ACQUISITION OF RESPONSE SEQUENCES IN RATS BY LOW-LEVEL MICROWAVE EXPOSURE
Bioelectromagnetics, Vol. 1, No. 1, pp. 89-99 (1980)

Thomas, J.R., E.D. Finch, D.W. Fulk, and L.S. Burch
EFFECTS OF LOW-LEVEL MICROWAVE RADIATION ON BEHAVIORAL BASELINES
Ann. N.Y. Acad. Sci., Vol. 247, pp. 425-432 (1975)

Thomas, J.R., S.S. Yeandle, and L.S. Burch
MODIFICATION OF INTERNAL DISCRIMINATIVE STIMULUS CONTROL OF BEHAVIOR BY LOW LEVELS OF PULSED MICROWAVE RADIATION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 201-214 (1976)

Thomas, J.R., J. Schrot, and R.A. Banvard
COMPARATIVE EFFECTS OF PULSED AND CONTINUOUS-WAVE 2.8-GHZ MICROWAVES ON TEMPORALLY DEFINED BEHAVIOR
Bioelectromagnetics, Vol. 3, No. 2, pp. 227-235 (1982)

3.7.1.2 NONHUMAN PRIMATES

Galloway (1975) studied the effects of 2.45-GHz CW RFR on the discriminative performance of four male rhesus monkeys (mean body weight 5 kg) trained to obtain food pellets by responding correctly to one or more of three horizontally-arrayed lever-equipped stimulus panels when the panels were selectively illuminated with light (white or specific color). Prior to the study, the monkeys were adapted to restraint and trained on several multiple variable-interval schedules of reinforcement and extinction. Galloway (1975) also studied the effects of the RFR on two other rhesus monkeys in a repeated-acquisition behavioral paradigm. The experimental sessions were conducted daily, each lasting until either 60 pellets were delivered or 120 min elapsed.

For RFR-exposure, an applicator was held close to each monkey's head by a copper-lined fitted plastic helmet. The author estimated the power absorbed by the head by subtracting reflected power from forward power. The integral dose rates used were 5, 10, 15, 20, and 25 W. Mean SARs for the head can be estimated roughly by dividing these dose rates by a representative head mass, 0.75 kg (15% of the body mass), which yielded 7, 13, 20, 27, and 33 W/kg.

In the discrimination study, the RFR was administered just before each behavioral session for 2 min but was terminated sooner if the monkey began to convulse. Convulsions occurred for each exposure at 25 W (33 W/kg) and frequently at 15 W (20 W/kg). During a 9-month period, each monkey was exposed at least twice at each level. In addition, three of the monkeys were exposed to the RFR at 10 W (13 W/kg) throughout five consecutive daily 1-hr behavioral sessions on a 2-min-on, 1-min-off schedule, totaling 40 min/day of exposure. No significant effects of either exposure regimen on discriminative behavior were evident.

In the repeated-acquisition study, all three panels were illuminated concurrently by one of four stimuli: green, red, or yellow light or a horizontal white line on a green background, in the following "fixed-ratio" (FR) procedure. To obtain a pellet, each monkey was required to press the correct lever for each stimulus (e.g., left lever for green light, right lever for yellow light, center lever for red light or horizontal white line) in a sequence of four presses for each trial. Each stimulus was changed only after a correct response was made. The press of an incorrect lever yielded a 15-second timeout, during which a vertical white line was superposed and any lever presses had no effect. Sessions consisting of 60 trials each were conducted daily for 39 days before exposure, with the correct sequence changed each day.

During a 100-day series, the monkeys were exposed at least twice at 10, 15, 20, and 25 W (13, 20, 27, and 33 W/kg) immediately before a session for 2 min or until convulsions began, which occurred for each exposure at 20 and 25 W. The results for each 60-trial session just preceded by RFR exposure were divided into 6 sequential blocks of 10 trials each, to elicit whether learning had occurred during the session, and the total number of errors per block was displayed for each power

level. The mean and range of performance per block for sessions on each day preceding exposure were presented for comparison. The results for the latter showed a slight learning trend (decreasing mean number of errors per successive block), but the differences were too small, relative to the block ranges, to ascribe statistical significance. This was also true for the results at all power levels except 25 W (33 W/kg), for which the number of errors in the first block was close to the top of the control range for that block. However, the mean numbers of errors for the next five blocks did not differ markedly from their respective control means. Thus, except possibly for the 25-W first-block result noted, the RFR had no effect on this FR paradigm.

In the FR procedure above, a monkey was always rewarded if it pressed the same fourth lever in the fixed correct sequence in the trials, e.g., the center lever if the correct sequence were left, right, left, center. Therefore, in the other series performed, the task was not changed, but a variable-ratio (VR) paradigm was used, in which the reinforcement was delivered at random points within the sequence. The two monkeys were trained on this procedure for 37 days, after which they were exposed to an RFR series similar to the previous one. The results were presented in time-sequential blocks as before. At 25 W (33 W/kg), the mean number of errors for the first block was well above the control range for that block, and was close to the top of the control ranges for the succeeding blocks, a clear indication that the RFR had caused a significant deficit in performance that was largely overcome by learning. The results for sequential blocks at each of the lower power levels were all within their respective control ranges. Since convulsions were caused by brief exposures at 25, 20, and less frequently at 15 W, it is surprising that the behavioral responses of the monkeys were not disrupted severely.

Cunitz et al. (1975) trained two male rhesus monkeys (body weights 3 and 5 kg) on a four-choice, forced-choice serial reaction program. The head of the subject was inserted through a hole in the bottom of a right-circular cylindrical cavity having a loaded resonant frequency of 383 MHz, with the subject facing a diamond array of light pipes mounted in the cavity sidewall. The subject was required to move a lever to the left, right, up, or down in response to lighting of the corresponding pipe. Criterion performance required 100 correct lever movements to obtain a food pellet. During criterion performance, the stimuli were presented in random order. Correct responses produced immediate changes in stimulus and presentation of a 1-kHz tone for 0.75 second. Incorrect responses produced 3-second timeouts during which all stimulus lights were$xtinguished and lever movements had no consequences.

For each session, the subject was placed in a restraining chair (with its head in the cavity) for 60 min prior to the start of the behavioral program, which also lasted for 60 min or was terminated sooner if the monkey obtained its entire daily food ration. Sessions without RFR were conducted until the number of errors per day was less than 2% of the total number of responses on five successive days (which required 285 days for one monkey and 255 days for the other). Each monkey was then successively exposed to the 383-MHz (CW) RFR at integral dose rates of

0.001, 0.01, 0.1, 1.0, 10.0, and 15.0 W. In addition, the heavier (5-kg) monkey was exposed at 17.5 W. Based on head masses of 0.45 and 0.75 kg (15% of the respective body masses), the authors estimated the mean head SARs to range from 0.0022 to 33 W/kg for the 3-kg monkey and 0.0013 to 23 W/kg for the 5-kg one. The monkeys were exposed during the entire session (including the 60 min prior to start of the behavioral program) for five successive days at each level, and were allowed 2-7 days for recovery of baseline performance, with interspersed sessions of sham-exposure, before the dose rate was increased.

Exposures at less than 10 W had no effect on the performance of either monkey. For the 3-kg monkey, the correct-response rate (the number of correct responses divided by the session duration in min) decreased sharply during the first three days at 10 W (22 W/kg) and recovered only partially on the fourth and fifth days and the subsequent sham-exposure sessions; the drop was very severe (almost to zero on the fifth day) at 15 W (33 W/kg), with recovery to about one-third of the baseline rates during the subsequent sham-exposure sessions. The performance of the 5-kg monkey was not affected significantly at 15 W (20 W/kg). At 17.5 W (23 W/kg), its performance dropped sharply, but recovered to baseline levels in the subsequent sham-exposure sessions, i.e., the effect was reversible. The authors noted that the lowest head SARs for diminished performance by the two monkeys were comparable: 22 and 23 W/kg.

Since the 3-kg monkey did not recover to baseline performance following exposure at 15 W, it was euthanized. No abnormalities were found in its brain under gross or light-microscopic examination.

Scholl and Allen (1979) trained three male rhesus monkeys (6.2, 7.9, and 6.4 kg) for 18-36 months in a visual-tracking task that required each monkey, while in a Plexiglas restraining chair, to move a lever so as to maintain a continuously moving spot within a predetermined clear area on the screen of a 10-cm-diameter cathode-ray-tube display monitor. The spot was electronically moved by three summed sinusoids of frequencies 0.05, 0.111, and 0.37 Hz at amplitude ratios 2:2:1, and lever responses by the monkey generated continuous difference signals (errors). The clear on-target area consisted of the center 15% of the screen, which was surrounded by a 35% area of light blue; the remaining 25% on each side was dark blue. For each 1 second accumulated outside the clear on-target area, the subject received a 0.1-second electric shock.

Following training, the monkeys were exposed to horizontally polarized, 1.2-GHz CW RFR at 10 and 20 mW/sq cm (at the center of the head in the absence of the monkey) for 2 hr per day at two-day intervals until each monkey was exposed for 120 min at each level. This polarization and frequency were chosen to provide half-wave resonant absorption in the monkey head. (Nonexposure runs were conducted on alternate days to test for 24-hr carryover, but none occurred). The corresponding SARs in the head were 0.8 and 1.6 W/kg. Each daily session consisted of 40 1.5-min work trials alternating with 40 1.5-min rest periods. Baseline runs were conducted for 26 consecutive days to ensure performance stability, and the results of the last six runs were used for statistical analysis.

The endpoint scored was the adjusted root mean square (ARMS) of the tracking error for each trial, expressed as a percentage of the total target area. The 95% simultaneous confidence limits were calculated for each monkey's baseline runs and the ARMS were plotted for each of the 40 trials in each 2-hr session during RFR exposure at each level. Of 720 data points collected during a total of 36 hr of RFR, only four points were outside the confidence limits, fewer than expected by chance.

De Lorge (1976) first trained five male rhesus monkeys to respond on an auditory vigilance task and then exposed each frontally in a Styrofoam restraining chair to vertically polarized, far-field 120-Hz-modulated 2.45-GHz RFR within an anechoic chamber at ambient temperature 21-24 deg C and relative humidity 55-70%. Superposed in some experiments were 0.1-second pulses at 1 Hz, but the peak power densities were not given.

Relative power-density measurements were made at the levels of the head, chest, and abdomen (with the monkey absent). The results indicated that the highest relative values were at head level, which were roughly 50% higher than at trunk levels. The mean power densities given below are for the head. Head- or whole-body SARs were not determined. However, the whole-body SAR for a prolate-spheroidal model of a sitting rhesus monkey at 2.45 GHz in the E-polarization (frontal exposure) is about 0.07 W/kg per mW/sq cm (Durney et al., 1978, p. 87). Using the 50% factor above would yield a head SAR of roughly 0.1 W/kg per mW/sq cm. The SARs shown below in parentheses are based on this assumption.

Prior to exposure, each monkey was food-deprived to maintain it at 90-100% of its free-feeding weight and was trained in a Plexiglas chair for 70 sessions to perform a vigilance or observing-response task. In this task, the monkey was to press a Teflon lever in front of its right arm, which produced either a 1070-Hz tone for 0.5 second to signal that no food pellet will be delivered, or a 2740-Hz tone that remained on until the monkey pressed a lever in front of its left arm, which produced a pellet and extinguished the 2740-Hz tone.

Food was available on a variable-interval 30-second (VI 30 s) schedule during 1-hr sessions and on a VI-60-s schedule during 2-hr sessions. In these schedules, the time intervals between availability of pellets were varied during the session but the intervals averaged 30 and 60 seconds, respectively. For example, under the VI-30-s schedule, presses of the right lever would produce the high tone once about every 30 seconds and the low tone at other times. A left-lever response while the high tone was present yielded a pellet. However, a left-lever response at other times caused a 10-s period during which right-lever presses only yielded the low tone, which inhibited extraneous left-lever responses.

After stable behavior was achieved and 122 subsequent sessions on the VI-30-s schedule were performed, 1-hr test sessions on the VI-30-s schedule were conducted on each of the 5 monkeys, during which it was exposed to the pulsed RFR at 4 or 16 mW/sq cm (0.4 or 1.6 W/kg) for 30 min. Similar sessions were conducted with the unpulsed RFR and with no RFR. No effect on the performances of the monkeys was obtained for the

unpulsed or pulsed RFR at either power density. These negative results led to use of only the unpulsed RFR and of the VI-60-s schedule during 2-hr test sessions for the remainder of the study. Only three of these monkeys were used for the 2-hr tests, during which they were exposed at 16, 32, 42, 52, 62, or 72 mW/sq cm for 60 min. In addition, one of them was exposed at 16 mW/sq cm for entire 2-hr test sessions. During some of the sessions, colonic temperatures were measured.

Exposures of the three monkeys at 16 mW/sq cm (1.6 W/kg) for 1 hr or the monkey for 2 hr had no differential effect on their behavior. Colonic temperatures at this power density were measured on only one monkey, and the mean value did not differ significantly from control values.

Colonic temperatures were measured on all three monkeys during 1-hr exposures at 32, 42, 52, 62, and 72 mW/sq cm. During exposure at 62 mW/sq cm (6.2 W/kg) or lower levels, increases of about 0.3- to 1.0 deg C to plateaus indicative of thermal equilibrium were obtained in all three monkeys. At the end of exposure at 72 mW/sq cm (7.2 W/kg), the increases were about 2 deg C, but the temperatures continued to rise, thus precluding studies at higher power densities.

The performances on the VI-60-s schedule, as measured by the right-lever response rate, showed no significant departures from control rates for all three monkeys up to 52 mW/sq cm (5.2 W/kg) and for two of them at 62 mW/sq cm (6.2 W/kg). The mean performance of the third monkey at the higher level was about 80% of its mean control performance. At 72 mW/sq cm (7.2 W/kg), all three monkeys performed at about 50% of their control values. Typically, a monkey at 72 mW/sq cm accelerated its movements in the chair after about 20 min of exposure, take short naps after about 30 min, and sometimes appear to be deep asleep, with resumption of activity about 10 min after cessation of exposure.

Latency time for a pellet-producing left-lever response (reinforcement reaction time) was not significantly increased in two of the monkeys up to 62 mW/sq cm (6.2 W/kg). For the third monkey, the latency time increased by about 20% at 52 and 62 mW/sq cm. At 72 mW/sq cm (7.2 W/kg), the mean latency time of this animal was about 800% of control values. The corresponding values for the other two were 200% and 130%.

These results suggest that the monkeys reacted to subtle body heating by the RFR at the higher power densities and that their performances were diminished because of such heat. Their behavior was further inhibited for about 10 min after cessation of the RFR, more so for the higher than the lower power densities. Such observations led the author to suggest that this postexposure behavior may have been related to the relatively larger colonic-temperature drops after removal of the higher RFR levels. He surmised: "When the microwave energy was removed and the heat could be more rapidly dissipated, it is as if a cooling stimulus appeared and behavior was further inhibited."

The monkeys were also given standard physical examinations, including

ophthalmoscopy before and after each series of exposures. No clinically detectable abnormalities in eye structure or blood chemistry (no data presented) were found in any of the five monkeys.

In another study, de Lorge (1979) maintained four male squirrel monkeys at 74-77% of free-feeding body mass. Each was initially trained, in 1-hr sessions, to press either the right or the left of 2 Teflon levers on top of the chair to obtain a food pellet. Red and blue incandescent lights in front of the monkey were turned on alternately with each lever press. After each animal pressed one or both levers consistently during at least 3 sessions, the contingencies were changed so that a left-lever press only during blue-light illumination was rewarded; depression of the right lever continued to alternate the red and blue lights.

Training progressed in stages, during subsequent sessions, each stage consisting of increasing the number of right-lever responses needed to turn on the blue light. The end result was performance on a schedule in which each right-lever response yielded either 0.5 second of red light or 10 seconds of blue light. Only a left-lever press during the latter yielded a pellet. The blue light occurred on an average of once per min (a variable interval of 1 min, or VI-1-min schedule) contingent on a right-lever response.

After stable behavior was achieved, each monkey was exposed from above in a Styrofoam restraining chair within an anechoic chamber at ambient temperature of 23 deg C to far-field, 120-Hz-modulated (100%), 2.45-GHz RFR at constant power density in the range 10-70 mW/sq cm in 10-mW/sq-cm increments. SARs were not determined, but are estimated from a prolate-spheroidal model in the K-polarization (Durney et al., 1978, p. 88) as about 0.05 W/kg per mW/sq cm.

The exposures were done daily during the middle 30 min of 1-hr testing sessions, with the other 15-min periods providing baseline data. Twenty such sessions were conducted without rectal-temperature measurements. Sham exposures were conducted between sessions at each power density. The next 21 RFR-exposure sessions were similar but included rectal-temperature measurements with a commercial probe. (Field perturbation of or by the probe was discounted because the RFR was incident from above the head.)

For the remaining 53 sessions, only three of the monkeys were tested, the session duration was 2 hr, and the exposures were for the middle 60 min. The number of sessions at each power density ranged from 2 to 5, with sham-exposures between sets. The order of exposure with respect to power density was varied, but most exposures at 60 and 70 mW/sq cm (3.0 and 3.5 W/kg) were done near the end of the sequence, and the last three sessions involved exposures at 75 mW/sq cm (3.75 W/kg). Neither of the RFR-exposure regimens caused any obvious permanent physical changes in any of the monkeys. Rectal temperatures were measured in all sessions.

Behavioral results for the 30-min exposures without rectal-temperature

probes were similar to those with such probes. Among the variety of performance measures on the observing-response task, only the right-lever-response rate indicated an RFR-induced change. This measure, expressed in percentage of mean control value, showed a slight trend toward lower rates with increasing power density to a minimum of about 90% at 60 mW/sq cm (3.0 W/kg) and a slightly higher value (92%) at 70 mW/sq cm (3.5 W/kg). However, the mean response rate (%) was never larger than one standard deviation from 100%.

A recurring effect on response rate was a cessation of responses within 30 seconds of commencement or termination of RFR exposure even though no mechanical vibrations or audible noises were detected by the author at such times. The "on-effect" was noticed first in one monkey at 40 mW/sq cm (2.0 W/kg) but was less evident at higher levels. The "off-effect" did not occur consistently in all animals except at 70 mW/sq cm (3.5 W/kg), where the pause was more pronounced than for the on-effect.

The preexposure mean rectal temperature was 38.8 +/- 0.3 deg C, or 0.8 deg C lower than the norm for the restrained squirrel monkey, presumably due to extensive chairing and handling. The mean rectal-temperature rise (difference between temperatures at termination and initiation of exposure) for the 30-min exposures showed a highly significant ($p<0.001$) linear trend from sham exposure to 70 mW/sq cm (3.5 W/kg). However, the differences between the mean for sham-exposure and the means for power densities to 30 mW/sq cm (1.5 W/kg) were not significant ($p>0.05$), but those for 50, 60, and 70 mW/sq cm (2.5, 3.0, and 3.5 W/kg) significantly differed from each other and from those below 40 mW/sq cm (2.0 W/kg).

Presumably but not explicitly stated, the temperatures at termination of RFR-exposure were plateau values reached before the end of the exposure period. However, sham-exposures yielded small temperature rises (0.36 +/- 0.13 deg C) with no indication of plateaus, which compounded the difficulty of removing the possible contributions of restraint to the results for RFR-exposure.

The mean rectal-temperature rises for the 1-hr exposures at 30 mW/sq cm (1.5 W/kg) or less (during the 2-hr test sessions) were lower than those for the 30-min exposures (during the 1-hr sessions) at the corresponding levels, an indication that the contributions from restraint per se were smaller during the longer than the shorter exposures.

The plots of mean rectal-temperature rise (on a logarithmic scale) vs power density (on a linear scale) for the three monkeys exposed for 1 hr showed qualitatively similar nonmonotonic increases for power densities up to about 40 mW/sq cm (2.0 W/kg), an abrupt shift upward between 40 and 50 mW/sq cm (2.5 W/kg), and monotonic increases for the higher power densities. The author surmised that the monkeys could equilibrate to the heat loads below 50 mW/sq cm but that the animals were not able to dissipate the heat loads at higher levels within the 60- min exposure periods. The temperature rises at 75 mW/sq cm (3.75 W/kg) were close to lethality, so exposure was terminated whenever a monkey's temperature

exceeded 42.5 deg C.

The general behavioral effects of 1-hr exposures were similar to those of 30-min exposures but were more pronounced. No consistent behavioral changes occurred below 50 mW/sq cm (2.5 W/kg); above that level, the effects increased with power density. The right-lever-response rate vs power density varied widely among the three animals, but at 60 mW/sq cm (3.0 W/kg), all showed decrements to about 60% of control values.

Two monkeys exhibited only the off-effect (pauses following RFR-exposure termination). The third monkey exhibited the on-effect (pauses on initiation of exposure) as well. Occasionally, this monkey would also respond by spuriously pressing both levers simultaneously, precluding reinforcement, but evidently such responses were not RFR-induced because they also occurred during control sessions. Pauses in the off-effect, which were longer than those for the on-effect, were ascribed to the larger differential rates of rectal-temperature change at the end than at the beginning of exposure. An effect similar to the off-effect was observed in the earlier study with the rhesus monkey exposed frontally (de Lorge, 1976).

Below 60 mW/sq cm (3.0 W/kg), there were no large differences from the control values of the time delay in food-lever response when food was available (reinforcement reaction time), but large increases were seen above that level, with wide differences among the animals.

One other effect, obvious in only one monkey, was a reliable increase in the number of incorrect left-lever responses with power density. Other behavioral indices, including post-reinforcement time and left-lever-response rate, showed no consistent RFR-induced changes.

The author concluded that the behavioral changes observed were temporary and obviously related to hyperthermia, with consistent results when the rise in rectal temperature exceeded 1 deg C, corresponding to a power-density threshold between 40 and 50 mW/sq cm (2.0 and 2.5 W/kg). He also obtained similar results with the rhesus monkey tested for the same behavioral task during exposure to 2.45-GHz RFR, but with a threshold 10 to 20 mW/sq cm higher (de Lorge, 1976), and suggested that RFR-induced behavioral changes in different species may be scaled on the basis of body mass. Regarding the on-effect and the off-effect, it is possible that the pauses by the monkeys were behavioral responses to sensory cues of sudden onset or removal of a heat source.

The findings of this study with the squirrel monkey, reinforced by the similar results with the rhesus monkey (de Lorge, 1976), are important because the performance measurements of a complex behavioral task during exposure to RFR were carried out with two species much closer to human physiology and intelligence than the laboratory animals more commonly used, and because reasonably accurate power-density thresholds for each species were determined.

In a more recent study, de Lorge (1984) similarly trained each of five

male rhesus monkeys, food-deprived to 92% of their normal body masses, to perform a task in which the monkey was to press a lever in front of its right hand (an observing response), which produced either a 0.7-second low tone (860-1000 Hz) to indicate that no food pellet will be delivered, or a high tone (1250-3703 Hz) lasting up to 1.2 seconds to signify the availability of a food pellet. If the monkey pressed a lever in front of its left hand while the high tone was on (a detection response), the tone would stop and a pellet would be delivered. A left-lever response at other times produced a 5-second interval during which right-lever presses yielded only the low tone. If the left lever were not pressed during 1.2 seconds of the high tone, the tone ceased and the reinforcement schedule would recycle. No tones were presented without a lever press, and right-lever presses during the presence of either tone had no consequences.

The low tone was sounded most frequently and the high tone was delivered randomly at an average of about once every 30 seconds. Reinforcement was at random intervals of about 1 min initially, and were shorter as the responses of the monkeys became more efficient.

After several sessions of stable performance on the task had occurred, each monkey, seated in a Styrofoam restraining chair, was frontally exposed, during 1-hr sessions, to vertically polarized 225-MHz CW RFR, 1.3-GHz pulsed RFR, or 5.8-GHz pulsed RFR, 225 MHz being near whole-body resonance and the other two above resonance. The exposures were done with horns in separate ventilated anechoic chambers designed for each frequency. Within each chamber was a 25-W incandescent lamp, a closed-circuit-TV camera, a speaker for acoustic stimuli, and another speaker for white noise. The noise level from all sources averaged about 74 dB on the C scale.

Normalized SAR estimates were derived from exposure of saline models to 225 MHz and 1.3 GHz and of flesh-simulating materials to 5.8 GHz. The results, in W/kg per mW/sq cm, were about 0.4 for 225 MHz, 0.13 for 1.3 GHz, and 0.03 for 5.8 GHz. Exposures to 225 MHz were at 5-11 mW/sq cm, with the center of the monkey's head at 0.78 of the conventional far-field distance from the horn, yielding SARs of 2.0-4.4 W/kg. For the other two frequencies, the distances were varied but were never less than half the respective far-field distances. The 1.3-GHz RFR consisted of 3-microsecond pulses, 370 pps, at 20-95 mW/sq cm Av (2.6-12.4 W/kg), and the 5.8-GHz RFR consisted of 0.5- or 2-microsecond pulses, 662 pps, at 11-150 mW/sq cm Av (0.34-4.7 W/kg). Rectal temperature was monitored continuously during each session with a nonperturbing probe.

Totals of 328 sessions were devoted to the 1.3-GHz study, 133 to the 5.8-GHz study, and 53 to the 225-MHz study in that order, with about 70 days between the studies. For each frequency, each monkey (with a few exceptions) was exposed three times at each power density, sequenced usually in ascending order. However, all RFR-exposure sessions were followed with sham-exposure sessions. Sham-exposures were also given after weekends if the behavior was not at baseline levels. About 100 sessions were necessary before all five monkeys responded consistently

within and between sessions. Four of the monkeys reduced their rates of incorrect detection responses (on the left lever) to low, stable levels. The fifth, subject 10, made excessive numbers of incorrect detection responses throughout the study, which were sometimes greater than its observing-response rate (on the right lever).

Reductions in observing-response rates occurred at above threshold power densities, illustrated by representative cumulative 1-hr records of one monkey, subject 13, during exposure to 1.3-GHz RFR at 26, 50, 70, and 90 mW/sq cm. Decreases in observing-response rates were seen at 50 mW/sq cm (6.5 W/kg) and higher and the rate reduction increased toward the latter part of each session as the RFR level was raised. The cumulative records of the monkeys also showed that the response patterns became increasingly erratic during sessions, an effect that was most pronounced at 225 MHz, at which the animals paused for as long as 15 min and often stopped responding completely for the last half of a session at 10 mW/sq cm (4 W/kg).

As more definitive indices of behavioral changes than the individual cumulative records, means and SEs of the ratio of observing-responses during RFR-exposure at each frequency to observing-responses during the previous sham-exposure session vs power density were presented. For 225 MHz, the mean ratio decreased monotonically from 1.02 at 5 mW/sq cm (2 W/kg) to 0.75 at 10 mW/sq cm (4 W/kg), with a large drop between 7.5 and 10 mW/sq cm; the departures from unity were significant at 7.5 and 10 mW/sq cm (3 and 4 W/kg).

For 1.3 GHz, the mean ratio was about unity up to 45 mW/sq cm (5.9 W/kg), at which it increased to 1.1, a significant change primarily associated with the behavior of subject 10. At 50 mW/sq cm (6.5 W/kg), the representative cumulative record of subject 13 showed diminution of the response rate, but the mean ratio for the monkeys was unity at this power density. At 63 mW/sq cm (8.2 W/kg), the mean ratio decreased to 0.86, a significant change, and it diminished only slightly more at 93 mW/sq cm (12.1 W/kg).

For 5.8 GHz, the mean ratio varied nonmonotonically above and below unity up to 140 mW/sq cm (4.3 W/kg), changes that were relatively small, but some were statistically significant because the SEs below this power density were much smaller than those at the other frequencies. Again, however, the increases in mean ratio were due to the behavior of one monkey. At 140 and 150 mW/sq cm (4.3 and 4.6 W/kg), the mean ratio was 0.92 and 0.90, respectively, both significant decreases. Also evident was the increase in threshold power density with frequency, i.e., about 7.5 mW/sq cm at 225 MHz, 63 mW/sq cm at 1.3 GHz, and 140 mW/sq cm at 5.8 GHz, but the corresponding threshold SARs were respectively 3, 8.2, and 4.3 W/kg.

Exposure to 5.8-GHz RFR at 150 mW/sq cm (4.6 W/kg), the highest level for this frequency, also produced minor burns on the faces of three of the five monkeys, the worst occurring between the eyes and along the orbitonasal area. The erythema generally disappeared within a few days,

except in one monkey that continually irritated the burned skin by removing scabious material. Burns did not occur at 140 mW/sq cm (4.3 W/kg), the behavioral threshold for this frequency, or at the highest power densities for the other frequencies. The small penetration depth for 5.8 GHz (about 0.8 cm) probably was an important factor.

The detection-response rate on the food lever was not consistently affected by exposure to RFR at any frequency. No effect was observed for 225 MHz or 5.8 GHz; for 1.3 GHz, a decreased response rate was occasionally observed, but only at 83 mW/sq cm (10.8 W/kg) or higher. However, plots of the mean ratio of detection-response latencies during RFR exposure to the latencies during sham exposure vs power density showed values slightly but significantly higher than unity at all frequencies and at most power densities. For each frequency, the mean ratio increased nonmonotonically with power density; the correlation coefficients were significant at the 5% level for 225 MHz and 1.3 GHz but not for 5.8 GHz. Also noteworthy were the successive decreases of the SEs for these ratios at 1.3 GHz, 5.8 GHz, and 225 MHz, the order in which these frequencies were used.

Postreinforcement pause (pause after a reinforced detection-response) was also affected. The mean ratio of postreinforcement pause during RFR-exposure to the pause during sham-exposure was plotted vs power density for each frequency. For 225 MHz, this ratio was about unity in the range 5-7.5 mW/sq cm (2-3 W/kg), but rose to about 1.5 at 10 mW/sq cm (4 W/kg), a significant change. For 1.3 GHz, the changes were both upward and downward and nonsignificant up to 63 mW/sq cm (8.2 W/kg), at which the mean ratio was 1.3; the ratios decreased above 63 mW/sq cm to about 1.1 at 93 mW/sq cm (12.1 W/kg), still a significant increase. For 5.8 GHz, the SEs were again much smaller than for the other frequencies; the only significant change was at 150 mW/sq cm (4.6 W/kg), to about 1.06, a smaller increase than for the other frequencies.

The mean colonic temperature at the start of the 1-hr sessions was 38.6 deg C and generally increased by an average of 0.15 deg C during the sham-exposure sessions. The mean increases in temperature vs power density for each frequency were exhibited on linear scales in Fig. 5 of the paper. No SEs were shown, but the author noted that they were typically 0.2 deg C or less. The results showed that for 225 MHz, the temperature increases rose linearly from about 0.8 deg C at 5 mW/sq cm (2 W/kg) to about 2.1 deg C at 10 mW/sq cm (4 W/kg). For 1.3 GHz, the temperature increases rose less than linearly, from about 0.4 deg C at 20 mW/sq cm (2.6 W/kg) to about 1.9 deg C at 93 mW/sq cm (12.1 W/kg). For 5.8 GHz, the increases rose more gradually, from about 0.2 deg C at 10 mW/sq cm (0.31 W/kg) to about 1.0 deg C at 150 mW/sq cm (4.6 W/kg).

The author also referred to the somewhat different 2.45-GHz temperature curves previously obtained for squirrel monkeys (de Lorge, 1979) and rhesus monkeys (de Lorge, 1976); these 2.45-GHz curves were relatively flat initially and then accelerated dramatically as the temperature increases reached 1 deg C.

Estimates of absolute thresholds for disruption of observing-response rates were made for each frequency on the basis of the following: The highest power density at which the SE bar overlapped the unity-ratio line was designated the "no-difference" estimate. The threshold power density for "obvious" difference in performance was defined as the value at which the SE bar did not overlap the unity-ratio line and for which a 10% or greater difference from the no-difference power density ratio was obtained. The resulting estimates were 8.1 mW/sq cm for 225 MHz, 57 mW/sq cm for 1.3 GHz, 67 mW/sq cm for 2.45 GHz (from de Lorge, 1976), and 140 mW/sq cm for 5.8 GHz, a monotonic increase with frequency. The corresponding SARs, however, were nonmonotonic with frequency, perhaps again reflecting differences in penetration. The values were 3.2, 7.4, 6.7, and 4.3 W/kg. (Note that for 2.45 GHz, the author used 0.07 from Durney et al., 1978, instead of 0.1 W/kg per mW/sq cm for the head, discussed above in de Lorge, 1976, but the difference does not affect this point.)

For each frequency, the author also calculated the minimal power density associated with colonic-temperature increments of 1 deg C. The values showed an almost linear relation between power density and frequency: 7.5, 40, 63, and 150 mW/sq cm respectively at 0.225-, 1.3-, 2.45, and 5.8 GHz. The corresponding SARs were 3.0, 5.2, 6.3, and 4.6 W/kg.

The author concluded: "Disruption of the observing-response, a behavior predicated on highly motivated performance, by microwave irradiation was closely related to increases in core temperature. The relationship is no doubt dependent upon various factors but, invariably, this behavior was not greatly disrupted unless body temperature increased by about 1 deg C, or unless an animal was suffering superficial burns or was bothered by facial skin irritation. Other aspects of operant behavior such as the detection-response rate and post-reinforcement pause failed to show this relationship." He also stated:

"The results of this study illustrate that predictions of biological effects based solely on power density are poor. Similarly, the information shown in Figure 6 reflecting the dependence of SAR on frequency demonstrates that predictions based on normalized whole-body energy absorption are not very useful." He noted that the ratio of highest-to-lowest threshold SAR, 2.6 (8.4/3.2), was much smaller than the ratio of the corresponding power densities, 17.5 (140/8), so SAR is a more efficient predictor than power density, but both are frequency-dependent. He concluded, however, that about a 1-deg-C increase in colonic temperature is a more reliable single index of behavioral disruption. His general conclusion was that the results of this study will allow predictions of possible behavioral alterations in other species, notably humans, during exposure to RFR at frequencies near and above resonance, especially if elevations of body temperature were used as indices, an idea that should be investigated further experimentally.

In the author's discussion, he speculated that the 225-MHz data reflect a resonance heating effect of the blood in the entire body, lead-

ing to extreme difficulty in thermoregulating because heated blood cannot be replaced with cooler blood. He also suggested that the results at 1.3 and 5.8 GHz illustrate normal thermoregulation, since limbs or skin are heated to a much greater extent than the interior of the head at these frequencies, citing Burr and Krupp (1980) and Olsen et al. (1980).

Absent was any discussion of the possible occurrence of the RFR-auditory effect with the 1.3-GHz and 5.8-GHz pulsed RFR. The author presumably discounted this effect as a factor in the results, because the pulse repetition rates used (370 and 662 pps) were lower than the tones used in the behavioral paradigm.

Because primates are better surrogates for humans than the usually used lower species of laboratory animals, results with the latter could be misleading with regard to setting safety standards for human exposure to RFR. For example, as discussed in Section 3.1.7.1, de Lorge and Ezell (1980) obtained changes in observing-response rates in rats exposed to 1.28 and 5.62 GHz, with power-density thresholds of 15 and 26 mW/sq cm, respectively. These values were considerably lower than those for the rhesus monkeys at comparable frequencies (57 mW/sq cm at 1.3 GHz and 140 mW/sq cm at 5.8 GHz). (In the rat study, rises in colonic temperature were not measured.)

Kaplan et al. (1982) exposed 33 unrestrained female squirrel monkeys near the beginning of the second trimester of pregnancy to 2.45-GHz RFR in 12 multimode, mode-stirred cavity modules. Each cavity contained a cage (of dielectric grille) opaquely partitioned to hold two adult monkeys and equipped with upper and lower perches (Heynick et al., 1977). Groups of 10, 12, and 11 females were exposed at respective whole-body SARs of 3.4, 0.34, or 0.034 W/kg for 3 hr/day, 5 days/week, until parturition. On completion of each daily exposure, the monkeys were returned to home cages, where they were housed in pairs. Eight pregnant monkeys were sham-exposed for the same periods in modules with RFR off. After parturition, 6 dams each of the 3 RFR groups and their offspring were exposed as dyads (one dam and neonate per partition in each module) to each RFR level for an additional 6 months; then the offspring were exposed (one per partition) without the dams for another 6 months.

The plane-wave equivalent power densities were determined by exposing a saline-filled rubber doll about the size of a squirrel monkey to far-field high-level RFR in an anechoic chamber and two such dolls in a module at various locations and orientations within each partition, and measuring the saline temperature increases. The results were used to adjust the power inputs to the modules to obtain the equivalents of 10, 1, and 0.1 mW/sq cm, which yielded the respective SARs above.

To obtain a measure of locomotor activity of the adult monkeys during RFR exposure, the frequency of movements between the upper and lower perches and lateral movements between front and back of the module cages were recorded for each monkey in ten 5-min sessions during three weeks of the third trimester. Because of large interanimal variability within

all groups and the small group sizes, scores were ranked and subjected to the nonparametric Kruskal-Wallis analysis of variance by ranks. The median activity scores combined for the 10 sessions each at 0, 0.034, 0.34, and 3.4 W/kg were respectively 16, 8, 46, and 12.5, statistically nonsignificant differences.

Each mother-and-infant pair was observed in the home cage for two to four 5-min periods each week for the first 24 weeks postpartum. The frequency and duration of maternal responses related to protection and rejection (e.g., retrieval, punishment) and of infant responses related to independence (e.g., departure from and return to mother, time spent off mother) were scored and evaluated in blocks of 4 weeks for each exposure group. There were no significant differences among groups in any of the measures of infant or maternal behavior at corresponding 4-week blocks.

To increase the number of subjects for statistical considerations, the results were analyzed by comparing the four exposure levels (including sham-exposure) regardless of when subjects were exposed (prenatally only vs prenatally and postnatally) and by comparing the two exposure periods irrespective of exposure level. Again no statistically significant differences were found.

Baseline EEGs and EEG changes with presentation of light flashes were obtained from mothers and offspring in a restraining chair (under light sedation to reduce movement) at weaning time (infant age 6 months) and from offspring of the prenatal and postnatal exposure groups at ages 9 and 12 months. The recordings were made (in the absence of RFR) with Beckman biominiature AgCl electrodes attached midline at the occiput and frontal regions. The frontal electrode was used for reference and an electrode near the vertex was grounded. Blocks of 20 trials at each of three light-flashing frequencies (6, 10, and 16 per second) were given to each subject in a single session, with each trial consisting of four seconds of baseline EEG recording followed by four seconds of visual stimulation. The interval between trials was 20-30 seconds. The order of presentation of the three frequencies was counterbalanced across the subjects for the separate recording sessions.

The EEG recordings were digitized by computer and subjected to spectral analysis in the bands 5-7, 9-11, and 15-17 Hz that straddled the three flicker rates, and in the bands for delta (0.5-4 Hz), alpha (8-13 Hz), and beta (15-23 Hz) activity. To determine the extent of photic driving at each flicker rate, flicker-to-baseline EEG ratios were calculated. By Kruskal-Wallis analysis of variance by ranks of the seven groups of mothers, there were no significant differences on any of the measures. Moreover, no significant differences were found after combining subjects from the three RFR levels into separate groups according to when they were exposed (during gestation only and gestation plus 6 months after parturition). Similarly, no significant differences were obtained in comparing either the prenatally exposed or prenatally and postnatally exposed groups of offspring (irrespective of exposure level) with the nonexposed group.

The major finding of this study was the death of 5 of the 6 infants exposed at 3.4 W/kg (10 mW/sq cm) both prenatally and postnatally vs no deaths in the corresponding 6 sham-exposed infants, but as discussed in Section 3.3.2.2, little confidence can be placed in this difference because of the smallness of these two groups. Also, a followup study with infant mortality as the major endpoint and sufficient numbers of animals for greater statistical validity did not confirm this finding.

REFERENCES:

Burr, J.G. and J.H. Krupp
REAL-TIME MEASUREMENT OF RFR ENERGY DISTRIBUTION IN THE MACACA MULATTA HEAD
Bioelectromagnetics, Vol. 1, No. 1, pp. 21-34 (1980)

Cunitz, R.J., W.D. Galloway, and C.M. Berman
BEHAVIORAL SUPPRESSION BY 383-MHZ RADIATION
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 3, pp. 313-316 (1975)

de Lorge, J.O.
THE EFFECTS OF MICROWAVE RADIATION ON BEHAVIOR AND TEMPERATURE IN RHESUS MONKEYS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 158-174 (1976)

de Lorge, J.O.
OPERANT BEHAVIOR AND RECTAL TEMPERATURE OF SQUIRREL MONKEYS DURING 2.45-GHZ MICROWAVE IRRADIATION
Radio Sci., Vol. 14, No. 6S, pp. 217-225 (1979)

de Lorge, J.O.
OPERANT BEHAVIOR AND COLONIC TEMPERATURE OF MACACA MULATTA EXPOSED TO RADIO FREQUENCY FIELDS AT AND ABOVE RESONANT FREQUENCIES
Bioelectromagnetics, Vol. 5, No. 2, pp. 233-246 (1984)

de Lorge, J.O. and C.S. Ezell
OBSERVING-RESPONSES OF RATS EXPOSED TO 1.28- and 5.62-GHZ MICROWAVES
Bioelectromagnetics, Vol. 1, No. 2, pp. 183-198 (1980)

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)

Galloway, W.D.
MICROWAVE DOSE-RESPONSE RELATIONSHIPS ON TWO BEHAVIORAL TASKS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 410-416 (1975)

Heynick, L.N., P. Polson, and A. Karp
A MICROWAVE EXPOSURE SYSTEM FOR PRIMATES
Radio Sci., Vol. 12, No. 6S, pp. 103-110 (1977)

Kaplan, J., P. Polson, C. Rebert, K. Lunan, and M. Gage
BIOLOGICAL AND BEHAVIORAL EFFECTS OF PRE- AND POSTNATAL EXPOSURE TO 2450 MHZ ELECTROMAGNETIC RADIATION IN THE SQUIRREL MONKEY
Radio Sci., Vol. 17, No. 5S, pp. 135-144 (1982)

Olsen, R.G., T.A. Griner, and G.D. Prettyman
FAR-FIELD MICROWAVE DOSIMETRY IN A RHESUS MONKEY MODEL
Bioelectromagnetics, Vol. 1, No. 2, pp. 149-160 (1980)

Scholl, D.M. and S.J. Allen
SKILLED VISUAL-MOTOR PERFORMANCE BY MONKEYS IN A 1.2-GHZ MICROWAVE FIELD
Radio Sci., Vol. 14, No. 6S, pp. 247-252 (1979)

3.7.2 RFR AND DRUGS

Various studies have been conducted on possible interactive effects of exposure to RFR and medications or other drugs taken or administered. Preparations studied have included excised turtle and rat hearts, and rabbits, rats, and mice.

Lords et al. (1973) had found that exposure of excised turtle hearts in Ringer's solution to 960-MHz CW RFR caused bradycardia at SARs of 2-10 W/kg and tachycardia at 16-40 W/kg. They hypothesized that the RFR caused neurotransmitter release by excitation of the remnants of the autonomic (parasympathetic and sympathetic) nervous system. On this basis, Tinney et al. (1976) studied the effects on turtle hearts of adding the parasympathetic-system inhibitor atropine sulfate and the sympathetic-system inhibitor propranolol hydrochloride (beta-blocker) separately or in combination to the Ringer's solution prior to exposure, and Reed et al. (1977) performed a similar study on excised rat hearts. The results of these in-vitro studies are discussed in Section 3.6.3.

In an early in-vivo study, Baranski and Edelwejn (1968) determined the effects of luminal, strychnine, phenactil, and cardiasol in various combinations on the EEGs of rabbits, and how exposure to RFR altered these effects. Luminal is a trademark for phenobarbital, a sedative and anticonvulsant; strychnine, a poisonous alkaloid, is a convulsant, and has been used as a CNS stimulant; the other two drugs are not listed in the current Physicians Desk Reference, but phenactil was said to act directly on the reticular formation, and cardiasol on the cerebral cortex and the reticular formation.

In this study, EEG screw electrodes were implanted within the skulls (symmetrically over the motor, sensory, and optic regions) of 65 male (3-kg) rabbits and the rabbits were divided into two major groups. The effects of one 20-min exposure to pulsed RFR in the 10-cm band (3 GHz, pulse parameters not indicated) at 20 mW/sq cm (presumably average power density) were studied with one group (45 rabbits); the other group (20 rabbits) was used to study the effects of exposure to the RFR at 7 mW/sq cm 3 hr/day for a total of 70-80 hr. SAR estimates were not given, but the SAR for a prolate-spheroidal model of a 1-kg rabbit at 3 GHz is about 0.1 W/kg per mW/sq cm (Durney et al., 1978, p. 92), which yields about 2 and 0.7 W/kg for 20 and 7 mW/sq cm. The whole-body SARs for a 3-kg rabbit would be lower, but the presence of the presumably metallic EEG electrodes probably produced significantly higher SARs in the local regions within the head (Chou et al., 1982).

The first (acute) group was distributed into subgroups A, B, and C (15 each) and was treated as follows: Ten of subgroup A were intravenously injected with phenactil at 4 mg/kg; one hour later, these rabbits were exposed at 20 mW/sq cm once for 20 min; after exposure, the rabbits were injected with cardiasol at 3 mg/kg. The other five rabbits of subgroup A were given the drugs but not exposed to the RFR (controls). Ten of subgroup B were injected with luminal at 40 mg/kg one hour before RFR-exposure and, after 20 min of exposure, with cardiasol at 6 mg/kg (twice

the dose used for subgroup A), again with the remaining five not exposed to the RFR. The treatment of subgroup C was the same as for subgroup A, but strychnine at 0.1 mg/kg was given in the end phase.

The EEGs were taken with a 16-channel recorder: for testing before drug injection, 60 min after injection of phenactil or luminal, right after RFR-exposure, and right after injection of cardiasol or strychnine. The authors stated without elaboration that the following parameters were considered in evaluating the EEGs:

1) basic rhythm of bioelectric activity
2) reaction to rhythmic light stimuli
3) amplitude
4) hypersynchronic waves
5) focal or generalized changes

Various regional EEGs of one rabbit of acute subgroup A before and one hour after phenactil injection were presented as representative results for that subgroup. Distinct signs of synchronization could be seen in the EEGs after phenactil injection, and slow waves of high amplitude were clearly evident in the optic region. The EEGs of the same rabbit immediately after RFR-exposure and after cardiasol injection were also presented. The amplitudes of the regional post-exposure EEGs were smaller, and absent therefrom were signs of the synchronization after phenactil injection. Thus, phenactil injection 1 hr before exposure did not prevent RFR-induced desynchronization. The EEGs following cardiasol injection were similar to those following RFR-exposure except for the presence of a segment of waves, most prominent in the optic region, of frequency about 3-4 Hz and amplitude that increased slowly to a maximum and decreased at about the same rate (resembling a half-wave segment of 100% amplitude modulation), described as "a characteristic threshold reaction." The authors also noted that control animals exhibited no reaction to cardiasol injection.

Regarding acute subgroup B, injection of luminal yielded EEG changes "in the form of alternating rhythm of fast waves and bursts." RFR-exposure one hour later "only slightly modified the character of the EEG record; amplitude of the basic rhythm became lower, other parameters remaining unchanged." Administration of cardiasol (6 mg/kg) "failed to induce threshold reaction in bioelectric activity." "Control animals reacted in an identical way." These effects were illustrated by the EEGs of a rabbit after injection of luminal and immediately after RFR-exposure.

Illustrative of the results for acute subgroup C (treated with phenactil and then with strychnine) were the EEGs of a rabbit right after RFR-exposure and strychnine injection and of a control rabbit (not RFR-exposed but injected with strychnine). The EEGs of the control rabbits consisted almost entirely of spikes of amplitudes that varied among the regions, whereas the post-exposure-and-injection EEGs consisted mainly of slow waves in the optic region and irregular fast-wave rhythms in the motor region. The authors stated that: "EEG records showed tolerance to

strychnine to be much higher in irradiated than control animals. In the latter the spikes were found to occur for 3 to 14 seconds."

The second (chronic) group was divided into subgroups A, B, C, and D (5 rabbits each) that were respectively injected with phenactil at 4 mg/kg, cardiasol at 3 mg/kg, luminal at 40 mg/kg, and strychnine at 0.1 mg/kg. Not clear, however, were the experimental sequences of drug injections and multiple RFR-exposures (at 7 mW/sq cm) administered these subgroups. The authors stated: "In animals of the second [chronic] group, resting EEG records showed desynchronization with rather high amplitude of the recorder potentials. In subgroup A, intravenous administration of phenactil was followed by synchronization which was, however, less intense than in animals of the first [acute] group." One interpretation is that all daily RFR-exposures of each chronic subgroup were completed before any drug injection, that such cumulative exposure yielded the observed desynchronization, and that subsequent phenactil injection into the subgroup-A rabbits was not as effective for synchronization.

Regarding chronic subgroup B, cardiasol injection was reported to have induced severe convulsions within 8-10 seconds, indicating that these rabbits were much less tolerant of cardiasol than those exposed once. The EEGs of chronic-subgroup-C rabbits were reported to be unmodified by luminal injection except for a slight amplitude decrease. The reactions of chronic-subgroup-D rabbits to strychnine injection were not uniform: "Series of spikes were observed in 3 cases, and in other animals single spikes were only found. It should be stressed that tolerance to the drug was markedly lower than in animals of the first group. In 2 cases the animals died soon after the drug administration."

In the discussion of the acute-exposure results, the authors interpreted the desynchronization induced by RFR-exposure to stimulation of the ascending part of the reticular formation, as confirmed by the observed functional antagonism between the RFR and phenactil, since phenactil acts directly on the reticular formation. Cardiasol is known to excite the cerebral cortex and the reticular formation, and the results with this drug showed that the RFR potentiated the effects of cardiasol, an indication that RFR can affect structures sensitive to cardiasol. The lack of desynchronization in rabbits treated with luminal prior to RFR-exposure, taken in conjunction with the cardiasol results, suggest that RFR affects the thalamic part of the reticular formation. In the experiments with strychnine, the results indicated that the reactions to this drug by the RFR-exposed rabbits was much weaker than those of the controls, perhaps by the combined effect of phenactil and strychnine.

Lotz and Michaelson (1979) had found that exposure of rats to 2.45-GHz RFR stimulates the pituitary-adrenal axis and they studied whether such stimulation could be blocked by pretreatment with the glucocorticoid dexamethasone. The results of this study were given in Section 3.6.2.

Monahan and Henton (1977a) found that mice could be trained to escape from, or avoid exposure to, 2.45-GHz CW RFR at 45 W/kg by an operant

response, as discussed in Section 3.7.1.1. In a later study, Monahan and Henton (1979) used the same behavioral paradigm to determine the effects of the psychoactive drugs chlordiazepoxide, chlorpromazine, and dextroamphetamine (d-amphetamine) on such behavior, and whether RFR would alter the effects of these drugs on behavior. D-amphetamine is a stimulant for the central nervous system, whereas chlordiazepoxide and chlorpromazine are depressants (tranquilizers).

Five CD1 male mice were studied. As in the previous study, each mouse was housed in a ventilated opaque Plexiglas container (large enough to permit free movement) within a waveguide system held at 24 deg C and 50% relative humidity, with air flow at 38 l/min. Behavioral sessions were for 30 min; exposures were at 45 W/kg (estimated as 45 mW/sq cm) for durations determined by the responses of the mouse in each session.

A beam of light was shone through aligned holes in the side walls of the waveguide and the mouse container to a photosensor, and interruption of the beam constituted the basic response by the mouse. Paired with the RFR was a 2900-Hz tone. The procedure was to turn on the RFR (and tone) 12 seconds after the start of the session. These stimuli remained on as long as the mouse made no response. When the stimuli were on, a beam-interruption response terminated the stimuli and they remained off for 12 seconds in the absence of another response during the period. Such actions were characterized as escape responses. If the mouse responded again during the 12-second interval of no RFR and tone, the response would delay the onset of the stimuli for 12 seconds. These actions were characterized as avoidance responses.

Stable baseline data were obtained for each mouse after 10-15 sessions of 30-min RFR-plus-tone exposure conducted daily. The baseline pattern of each mouse was self-consistent, with only minor variability, but the patterns differed among the mice and could be classified as primarily escape response, primarily avoidance response, or mixed response.

After the baseline period, the mice were intraperitoneally administered chlordiazepoxide (1, 5, 10 mg/kg), chlorpromazine hydrochloride (0.25, 0.5, 10 mg/kg), d-amphetamine sulfate (0.5, 1, 2 mg/kg), or saline in random sequence once a week 15 min before a session. The results showed that saline injection reduced the total response rate of mouse 1 to 80% of its mean control value, increased the total response rate of mouse 3 to 120%, and did not substantially affect the total response rates of the other three mice.

Injection of 10 mg/kg of chlordiazepoxide into mouse 1 yielded the same reduction of response rate as saline (to about 80%), but doses of 1 and 5 mg/kg yielded higher rate reductions, respectively to about 60% and 40%. For mouse 2 (unaffected by saline), chlordiazepoxide reduced the rate to about 60% for doses of 1 and 5 mg/kg, and to about 40% for 10 mg/kg. For mouse 3 (rate increased to 120% by saline), 1 mg/kg yielded a rate comparable to its control value (i.e., 100%), but 5 and 10 mg/kg yielded reductions to about 80%. Mouse 4 (unaffected by saline), showed large rate reductions for all 3 doses, but the least

reduction (to about 60%) was for 5 mg/kg, with successively larger reductions (to about 50% and 30%) for 1 and 10 mg/kg. Mouse 5 (rate slightly lowered by saline) exhibited successively larger reductions with increasing dose, to about: 80% for 1 mg/kg, 40% at 5 mg/kg, and 10% at 10 mg/kg.

The responses of each mouse following injection of chlordiazepoxide or saline at each dose were classified into avoidance and escape responses and the numbers of each response were compared with their respective control values. For mouse 1, the saline reduced both the avoidance and escape responses, but only slightly. At 10 mg/kg, the drug had little effect on avoidance or escape responses, but at 1 and 5 mg/kg it reduced the avoidance rate and increased the percentage of escape responses, the latter effect being higher for 1 mg/kg than 5 mg/kg. The results for mice 2, 3, and 5 were qualitatively similar to those of 1. For mouse 4, the results were more consistent; rates of avoidance and escape response with saline were comparable to their respective control means, whereas 10 mg/kg of the drug produced maximum reduction in avoidance rate and maximum increase in percentage of escape responses. However, these response changes were smaller for 5 mg/kg than 1 mg/kg.

Less equivocal were the cumulative exposure durations per session. The mean baseline values ranged from about 8 seconds (mouse 4) to about 30 seconds (mouse 3), and saline did not significantly alter the value for each mouse. However, chlordiazepoxide doses of 5 and 10 mg/kg increased exposure durations of all five mice significantly, with clear dependence on dose.

Examination of the results showed that the baseline data were similar to those obtained previously (Monahan and Henton, 1977a), but description of many results with saline and chlordiazepoxide was obscure. Not clear is whether each mouse was treated with each dose of the drug (or saline) more than once. Error bars were absent in the figures, which could be taken to mean that each specific treatment was given prior to only one session. If this was so, the credence given to the quantitative aspects of the findings is diminished and it is more difficult to determine the dose-dependence involved, especially with so few mice having such large differences in baseline behavioral patterns.

Because of the high degree of variability of the results with the other drugs, the authors presented no detailed data. They did indicate that chlorpromazine appeared to lower the response rate without increasing the cumulative exposure duration and that d-amphetamine at the highest dose (2 mg/kg) increased the response rate in several mice and decreased the exposure duration.

Thomas et al. (1979) maintained four Long-Evans hooded male rats at 80% of their free-feeding weights of 325-375 g and trained them daily for 4 months to respond on a fixed-interval, 1-min (FI-1) schedule to press a bar for a food pellet reward. By this time, the rats achieved a stable baseline pattern consisting of accelerated rate of responding throughout each FI period until a food pellet was obtained. A dose-

effect function was then established for chlordiazepoxide (injected i.p. 30 min before a session) in the range 1-40 mg/kg, which indicated that responding rate increased up to about 10 mg/kg (by 2 to 3 times baseline), and then decreased at higher doses (to about zero at 40 mg/kg).

The rats were then exposed to 2.45-GHz pulsed RFR (2-microsecond pulses, 500 pps) at 1 mW/sq cm (average) during the 30 min preceding each bar-pressing session (i.e., starting immediately after drug injection). The SAR was not given, but is estimated to have been about 0.2 W/kg (Durney et al. 1978, p. 95). Appropriate control runs were conducted to ensure stable and repeatable performance of each rat under the various dosing situations. Exposure yielded the same general shape of the dose-effect functions, but the magnitudes were generally increased by a factor of about 2. By contrast, exposure to the RFR without injection of the drug produced no difference in the FI-1 responding rate.

The results of this study are unequivocal, but the mechanisms involved are obscure. For example, although the average power density and the whole-body SAR were low, local SARs in the regions of the brain that are target areas for chlordiazepoxide's central actions may have been high enough for a thermally potentiating effect. It is also conceivable that 2-microsecond pulses at a peak power density of 1 W/sq cm (based on the 0.001 duty cycle) produced the RFR-hearing effect during the pre-session 30-min period, but if so, it is not clear whether or how any influence of this effect would have carried over into the session, during which the RFR was no longer present.

Thomas and Maitland (1979) also conducted a study in which six male albino rats (Nmri:O[SD]CV), maintained at 80% of their free-feeding weights, were trained to depress a small lever to produce food pellets on a differential-reinforcement-of-low-rate (DRL) schedule. Only the responses that followed a preceding response by 18 seconds or more were rewarded with pellets. Responses that occurred within 18 seconds reset the timing period (DRL 18 s). With daily, 5-days-a-week training, the rats achieved stable baseline performances in 13 weeks.

The effects of RFR on the dose-response function were then determined. Exposures were to the 2.45-GHz pulsed RFR used previously (2-microsecond pulses, 500 pps, at 1 mW/sq cm average power density). In this study, however, the corresponding whole-body SAR (0.2 W/kg) was ascertained calorimetrically with a water model.

Three of the rats were each dosed with the drug once per week, exposed for 30 min, and observed immediately for operant behavior for 1 hr, to ascertain any direct drug-RFR interaction (single-exposure condition). To seek for possible cumulative action of the RFR, each of the other three rats was exposed for 30 min daily on 4 days per week except on days when the drug was injected (multiple-exposure condition). Operant behavior was observed 30 min after injection. Sessions were conducted for 13 weeks, and included sham-RFR exposures and control injections of saline for all six rats.

The baseline performance, in total responses per min, of the three rats studied under the single-exposure condition was a mean of about 3.3 with a standard deviation (SD) of about 0.5. (Most of these responses were correct relative to the DRL-18-s schedule.) The mean response rate of these rats was 3.0 after saline injection and sham-exposure and was 3.7 after saline injection and RFR-exposure (no SDs given), both of which were within the SD limits of the baseline value.

The mean response rate of these rats when dosed with the drug and sham-exposed rose from 3.3 (0.6 SD) for a dose of 0.25 mg/kg to a maximum of 8.9 (2.4 SD) for 2.0 mg/kg, with consequent reductions in frequency of correct responses yielding reinforcement, as discussed below. Although the SDs were larger at the higher doses in this range, the increases in total responses per min were monotonic with dose and the trend appeared to be statistically significant. For doses larger than 2.0 mg/kg, the mean response rate declined sharply (with large SDs) to 0 for 4.5 mg/kg.

By contrast, the mean total response rate of these rats dosed with the drug and RFR-exposed rose from 5.1 for 0.25 mg/kg to a maximum of 7.1 for 0.5 mg/kg, values that were significantly higher than those for the corresponding doses without RFR-exposure. Above 0.5 mg/kg, the mean total response rate declined sharply to 0.6 for 1.0 mg/kg and 0 for 1.5 mg/kg. These results indicate that RFR-exposure after injecting a given dose of d-amphetamine yielded behavior similar to that obtained with a larger dose without RFR-exposure.

For the three rats studied under the multiple-exposure condition, the mean baseline performance and the mean performances for saline injection followed by sham- or RFR-exposure were not significantly different from the values for the other saline-injected rats. Also, the dose-response functions with and without multiple RFR-exposures were qualitatively similar to those with and without single RFR-exposures even though the performances of the former group were determined 24 hr after the final exposure. With multiple sham-exposures, maximum responses were obtained for 2.0 mg/kg, with a sharp decline to 0 for 4.5 mg/kg. For 0.25 mg/kg, the total response rate with multiple RFR-exposures was significantly higher than with multiple sham-exposures; for 0.5 mg/kg, it rose to a maximum; and for 2.0 mg/kg, it declined sharply to 0.

Representative cumulative-response records for rats from both groups were displayed. The slope of such a record for any sub-interval of time indicated the mean rate of lever pressing during that period (including incorrect presses that did not yield a food pellet) and was a measure of the activity of the rat; the number of downward deflections during that period represented the number of correct (pellet-producing) responses. For example, a presumably typical record for one of the single-exposure rats showed that for a dose of 0.5 mg/kg, the slope during the first half-hour of the test period after RFR-exposure was about twice that for the same rat after sham-exposure, but the number of correct responses with RFR was only about a third of the number without RFR. For 1.0 mg/kg, this rat performed rapidly but poorly after sham-exposure, but

hardly at all after RFR-exposure.

In their discussion, the authors indicated that the modest average power density may have produced relatively high local SARs, particularly in the head by resonant absorption, which could have selectively heated the brain. In addition, head resonance could have yielded energy values above the threshold for the RFR-hearing effect. However, the authors discounted these possibilities because they would not account for the persistence of the behavioral effects for 1 hr after cessation of the single exposures and 25 hr after the last of the multiple exposures.

The effects of body restraint, which can synergize with low RFR levels and stressful events to produce sizable elevations of body temperature, were considered and discounted because restraint of the rats injected with saline and exposed to RFR produced no significant deviations from the baseline values and the dose-effect functions of unrestrained and restrained rats not exposed to RFR were the same.

Because d-amphetamine has been reported anecdotally to heighten human perception with the various senses, it could be hypothesized that rats can perceive lower levels of RFR under the influence of the drug than in its absence, and that such perception would alter their behavior. This hypothesis, however, would not account for the 24-hr persistence of the influence of RFR seen in the multiple-exposure group.

In a subsequent study, Thomas et al. (1980) extended their work on the interactions of RFR with chlordiazepoxide and d-amphetamine to include diazepam and chlorpromazine. Diazepam (Valium) is a widely prescribed minor tranquilizer and skeletal muscle relaxant. Chlorpromazine, used as a sedative and as an antiemetic, is a phenothiazine derivative and in a different class of drugs than chlordiazepoxide and diazepam which are benzodiazepine derivatives.

Four Long-Evans Hooded (LEH) male rats and four albino male rats served as subjects. All were maintained at 80% of their free-feeding weights of 360-380 g throughout the study and trained on a fixed-interval, 1-min (FI 1) schedule of reinforcement until stable baseline performance was obtained (about 3 months). Dose-effect functions were then obtained for chlorpromazine over the dose range 0.25-4 mg/kg with the LEH rats and for diazepam over the dose range 0.5-20 mg/kg with the albino rats. A single dose was given intraperitoneally 30 min before each session and doses were given in mixed order, with at least three replications for each dose.

Effects were evaluated by comparing the response rate and the response pattern within an FI interval with corresponding baseline performance. The response rate for each session was taken as the total number of responses divided by the session duration; the response pattern within intervals was evaluated by the index of curvature, calculated from the accumulated responses in each of the 12 successive 5-second periods of the FI.

Chlorpromazine lowered both the response rate and the index of curvature with increasing doses for all four LEH rats. The response rates stayed within baseline variability for doses out to about 1 mg/kg and declined thereafter. Diazepam produced little change or slight increases in the response rate by the albino rats at doses up to about 2.5 mg/kg, with a decline in the response rate thereafter. The index of curvature usually declined with increasing doses of diazepam.

Dose-effect functions for the two drugs were obtained, but the rats were exposed, during the 30 min before a session, to 2.8-GHz pulsed RFR (2-microsecond pulses at 500 Hz) at 1 mW/sq cm average power density (0.2 W/kg) right after administration of the drug. RFR-exposure did not seem to significantly alter the effects of diazepam or chlorpromazine on FI performance, in contrast to the positive results with chlordiazepoxide and d-amphetamine. Thus, although chlordiazepoxide and diazepam are in the same pharmacological activity or classification class, this point alone is not sufficient to predict synergistic or antagonistic effects with low-level RFR-exposure, and such apparently contradictory findings are difficult to reconcile.

Pappas et al. (1983) performed three experiments to study RFR-induced alterations of pentylenetetrazol-induced seizures and the effects of RFR on the efficacy of chlordiazepoxide for counteracting such seizures.

In experiment 1, rats in individual circular acrylic cages spaced about 3 wavelengths apart in an anechoic chamber were sham-exposed or exposed from above in pairs for 30 min to far-field, circularly polarized 2.7-GHz pulsed RFR (2-microsecond pulses at 500 pps) at 5, 10, 15, or 20 mW/sq cm (average). The SARs were determined by measuring the rectal-temperature increases for rats anesthetized with sodium pentobarbital (45 mg/kg) and singly exposed for 3 min at 144 mW/sq cm. With heat-loss corrections in rats sham-exposed for 3 min, the results yielded 1.5 W/kg for 10 mW/sq cm. Prior to exposure, each rat was weighed, its rectal temperature was recorded, and it was injected intraperitoneally with 1.0 ml/kg of saline. After exposure, the rectal temperatures of the rats were recorded again; the rats were injected with the seizure-inducing drug pentylenetetrazol (PTZ) at 0, 20, 40, 60, 70, or 80 mg/kg in 1.0 ml/kg of saline; and seizure activity was studied.

In experiment 2, the rectal temperature of each rat was measured and the rat was injected with chlordiazepoxide (CDZ) at 2.0, 7.5, or 15.0 mg/kg prior to exposure. Exposures were for 30 min at 0 (sham), 5, 10, or 15 mW/sq cm in factorial combination with the CDZ doses. After exposure, rectal temperatures were measured again, the rats were injected with 70 mg/kg of PTZ, and the strength of CDZ inhibition of seizure induction by PTZ was studied.

In experiment 3, part 1 was done to check some results of experiment 1; rats were injected with 60 mg/kg of PTZ after exposure at 0, 5, 10, 15, or 20 mW/sq cm. In part 2, designed to check some results of experiment 2, rats were injected with 7.5 mg/kg of CDZ prior to, and with 70 mg/kg of PTZ after, exposure at those power densities. The

effect of each treatment on seizure activity was determined.

In each experiment, the rats were watched for signs of seizure activity for 8 min after injection of PTZ. The latency interval to the onset of the first sign was recorded and seizure intensity was rated on a scale from 0 (no seizure, normal exploratory activity) to 4 (wild running and tonic-clonic convulsions with 99% mortality).

Average preexposure core temperature for all rats was 36.8 deg C. In experiment 1, the mean postexposure core-temperature increases were 0.5, 0.74, 0.75, and 1.35 deg C for respectively 0, 5, 10, and 15 mW/sq cm (0, 0.75, 1.5, and 2.25 W/kg). By analysis of variance with body weight as the covariate and temperature increase as the dependent variable, body weight accounted for a significant amount of the variability and RFR-exposure was the main effect; although sham-exposure yielded a rise of 0.5 deg C, the RFR-induced rises were significantly ($p<0.05$) larger.

In experiment 1, latency-to-seizure times after PTZ injection decreased with increasing PTZ dose for all power densities, reaching a plateau of about 50 seconds at 60 mg/kg. Analysis of variance with PTZ dose and RFR power density as independent variables showed a significant effect of dose: Post-hoc analysis with Tukey's test indicated that although the 60-, 70-, and 80-mg/kg groups did not differ from one another (plateau region), all other between-group comparisons were significant. Analysis of variance also showed a slight but significant ($p<0.032$) main effect of RFR. In post-hoc analysis (Tukey's test), the rats exposed at 15 mW/sq cm (2.25 W/kg) exhibited significantly shorter latencies than the sham-exposed rats; the latencies, averaged across PTZ doses, were 82.9 and 89.4 seconds, respectively. However, interaction between PTZ dose and RFR power density was not found.

In experiment 1, the mean seizure-intensity score vs PTZ dose ranged monotonically from 0 at 0 mg/kg to about 3.8 at 80 mg/kg, with no apparent effect of power density. Analysis of variance with PTZ dose and power density as independent variables showed a significant effect of dose, each dose yielding a significantly higher seizure intensity than all lower doses, and a significant main effect of power density. Post-hoc analysis (Tukey's test) showed that the mean seizure intensity was significantly greater for rats exposed at 15 mW/sq cm (2.25 W/kg) than at 5 mW/sq cm (0.75 W/kg), but that none of the values for the RFR groups differed significantly from those for the sham-exposed group. Again there was no interaction between PTZ dose and RFR power density.

The authors suggested that the significant changes in seizure latency and intensity at 15 mW/sq cm (2.25 W/kg) obtained in experiment 1 could have been due to local brain hyperthermia rather than to alteration of the effect of PTZ on brain neuronal activity.

For experiment 2, the CDZ doses used to inhibit PTZ-induced seizures were derived from the unpublished results of a pilot study by Pappas, Anisman, and Ings. They had found that 2.0, 7.5, and 15 mg/kg of CDZ respectively caused minimal, modest, and maximal attenuation of the

seizure-inducing effects of 70 mg/kg of PTZ.

Analysis of variance of the core-temperature changes in experiment 2 showed significant main effects for both CDZ dose and power density, with no interaction between them. Core temperature was progressively reduced from baseline (37.7 deg C) with increasing CDZ dose. After the data were collapsed over power density, the temperature reductions at 7.5 and 15.0 (but not at 2.0) mg/kg were significant relative to the mean core temperature of the saline-control group, and the reduction at 15.0 mg/kg was significantly larger than at 7.5 mg/kg, which, in turn, was significantly larger than at 2.0 mg/kg. Collapsing the data over CDZ dose indicated that only 15 mW/sq cm (2.25 W/kg) increased core temperature significantly relative to that of the sham-exposed group.

Analysis of variance of the seizure-onset latencies in experiment 2 showed that CDZ significantly increased the latency time in a clearly dose-dependent manner. The analysis also showed a main effect of power density and a significant CDZ-RFR interaction. By subsequent analysis, however, the effect of RFR could be ascribed to two observations: that rats given 7.5 mg/kg of CDZ had longer latencies after exposure at 15 mW/sq cm (2.25 W/kg) than at 0, 5, or 10 mW/sq cm (0, 0.75, or 1.5 W/kg) and that the latencies of rats given 15 mg/kg were shorter following exposure at 5 mW/sq cm (0.75 W/kg) than at 0, 10, or 15 mW/sq cm (0, 1.5, or 2.25 W/kg).

Analysis of variance of the seizure-intensity scores of experiment 2 indicated significant main effects of CDZ dose and power density, and a significant interaction between them. All CDZ doses except 2.0 mg/kg lowered seizure intensity significantly relative to saline controls at every power density. However, the RFR effect was entirely accounted for by only one difference: The group given 7.5 mg/kg of CDZ and exposed at 15 mW/sq cm exhibited a significantly lower seizure intensity than its corresponding sham-exposed group.

Thus, the only consistent effect of RFR on the two seizure parameters in experiment 2 was for rats given 7.5 mg/kg of CDZ; exposure at 15 mW/sq cm (2.25 W/kg) increased their latency-to-seizure times and reduced the intensity of their seizures. The authors noted that 7.5 mg/kg was close to the threshold dose for protection against seizure and they reasoned that RFR-exposure may be effective only near the dose threshold, since 15 mg/kg of CDZ already provided effective protection (without RFR) but 2.0 mg/kg offered virtually none. They also suggested the possibility that the apparent positive findings were ascribable to random (Type II) statistical error. Experiment 3 was performed to test these hypotheses.

In experiment 3, groups of rats were exposed for 30 min at 0, 5, 10, 15, or 20 mW/sq cm, following which they were given 60 mg/kg of PTZ; other groups of rats were given 7.5 mg/kg of CDZ, exposed at those levels of RFR, and subsequently given 70 mg/kg of PTZ. Temperatures and seizure data were obtained as before. The principal experimenter was unaware of the level of RFR administered to each rat. (Presumably this

was not the case in the previous experiments.)

Analysis of variance of the core-temperature data for the rats injected only with PTZ showed a significant effect of power density; by Tukey's test, temperature elevations of RFR-exposed rats relative to those of sham-exposed rats were significant for 10 mW/sq cm (1.5 W/kg) or higher. However, there was no significant relationship between power density and latency-to-seizure time or seizure-severity score. For the rats given CDZ before RFR-exposure, analysis of variance of the temperature data again showed a significant effect of power density, but by Tukey's test, the mean temperature of only the rats exposed at 20 mW/sq cm (3 W/kg) differed significantly from that of the sham-exposed rats.

Comparison of the temperature-vs-power-density curves of the CDZ/PTZ rats and PTZ-only rats indicated that the hyperthermic effects of RFR-exposure were attenuated by CDZ and/or that the hypothermic effects of CDZ were counteracted by RFR-exposure. However, analysis of variance of the seizure data for the CDZ/PTZ rats showed no significant effect of power density on either latency or severity. Thus, despite the thermal antagonism between CDZ and RFR, the latter did not alter the protective efficacy of this CDZ dose against PTZ-induced seizure.

About experiment 3, the authors stated: "This experiment, which employed a more rigorous (rater blind) seizure scoring procedure than our earlier experiments, failed to support the hints from those experiments that high (15 mW/sq cm) or even higher (20 mW/sq cm) pulsed microwave power densities enhance PTZ seizures and increase the antiseizure protection afforded by 7.5 mg/kg of CDZ. We conclude that these earlier hints which were restricted to only a few of the many possible comparisons represented spurious, Type II statistical errors although we cannot, of course, rule out the possibility of experimenter bias."

The authors also noted the following, with appropriate citations: "It is currently believed that PTZ induces seizures by blocking the inhibitory effects of the neurotransmitter GABA as well as by a direct effect on neuronal membranes. Conversely, chlordiazepoxide, which as shown here effectively blocks PTZ seizures, appears to facilitate GABA transmission through a postsynaptic action. From the present experiments in which microwaves reliably affected neither PTZ nor CDZ action, it would appear that brief, acute exposure to such radiation has no pharmacologically significant effect upon GABA neurons."

The experimental design of this study, the statistical treatment of the data, and the lucid presentation of the results are commendable. In particular, the inclusion of saline-injected controls and sham-exposed groups as well as adequate numbers of rats in all groups engenders much confidence in the findings.

Pappas et al. (1983) noted also that their negative results seem to be at variance with those of Thomas et al. (1979), who found that exposure of rats trained on a fixed-interval (FI) behavior schedule to 2.45-GHz pulsed RFR at 1 mW/sq cm (average) did not alter their behavior. Thomas

et al. (1979) also had established a dose-effect relationship for CDZ over the range 1-40 mg/kg on the FI behavior schedule. They then found that exposure to the RFR immediately after administering CDZ yielded a dose-effect curve of the same shape as that without the RFR but of about twice the magnitude. Possible reasons for the differences in findings of the two studies (besides the widely different biological endpoints) would be speculative.

Ashani et al. (1980) divided adult male rats (Tac:N[SD]fBR) of weights 250-388 g into three treatment groups. Those in Group A were injected with 0.05-0.12 ml of the anticholinesterase drug phospholine (iodide) at 0.030, 0.040, 0.045, 0.050 or 0.055 mg/kg and were sham-exposed. Those in Group B were given phospholine (same doses), followed 10 min later by exposure to 2.8-GHz pulsed RFR (2-microsecond pulses at 500 pps) at 10 mW/sq cm (average) in the anechoic chamber used by Thomas et al. (1979). The rats in Group C were given phospholine at the same doses 3 min after exposure to the RFR. The mean SAR was not determined, but is estimated to have been about 2 W/kg (Durney et al., 1978, p. 95). A thermistor or clinical thermometer was used to measure core temperatures before drug injection, just after exposure, and at various later intervals.

Before and after treatment, some rats of each group were housed two per cage in standard cages at 25-26 deg C, with food and water available ad libitum, and their core temperatures were measured at intervals of 40 min for 240 min after treatment. Other rats were similarly housed and measured, but the ambient temperature was decreased to 10 deg C during post-treatment time intervals 80-140 min and 260-320 min. (Such changes of ambient temperature were used to enhance any hypothermia induced by treatment.) The control rats for each treatment group were given saline instead of phospholine.

Mean core temperatures taken 90 min after treatment (without reduction of ambient temperature) were plotted vs dose for the three treatments. The means for Group A, estimated from the plotted points, were 38.5, 38.4, 38.0, 37.8, and 37.1 deg C respectively for the five doses in increasing order. The corresponding values for Group B were 38.5, 37.8, 37.3, 37.3, and 37.0 deg C. Thus, the largest core-temperature changes occurred for the intermediate doses of the drug, indicating the possible existence of a drug-dose "window" for most effective RFR interaction. The mean core temperatures for Group C were 38.3, 37.8, 38.1, 37.6, and 36.7 deg C, which were comparable to those for Group A.

T-test analysis of the dependence of core temperature on dose for Group A showed that the mean temperatures for 0.030-0.045 mg/kg did not differ significantly from one another, but that the differences for 0.045-0.055 mg/kg were significant. Group C yielded similar results. For Group B, however, the differences in mean temperatures for 0.030-0.045 mg/kg were significant, as well as those for 0.045-0.055. Thus, all three groups suffered progressive hypothermia with increasing dose, but the effect was more severe for Group B than either Group A or Group C, which did not differ significantly from each other.

Plots of mean core temperature vs time for sham-exposed, saline-control rats held at 25-26 deg C during the entire post-treatment test period showed a value of 38.8 deg C at 0 min (immediately after treatment), a drop to 38.3 at 40 min, and minor variations from the latter at later times. The temperature of the sham-exposed, saline-control rats held at the lower ambient temperature dropped to 38.1 deg C at 40 min, but the results were otherwise similar. Regarding comparative results with RFR, the authors stated (without presenting data): "The same profiles were recorded for irradiated and nonirradiated rats that did not receive the anticholinesterase drug." They also noted that all the rats (more than 200) in this study exhibited relatively high initial core temperatures, which they ascribed to the stress imposed during preliminary handling and temperature measurement.

To ascertain the origin of the hypothermia induced by phospholine, some unexposed rats were injected with 0.022 mmole/kg of atropine sulfate or atropine methyl nitrate (both antidotes for phospholine) or with saline 5 min before injection of 0.045 mg/kg of phospholine. The temperatures of the rats were measured for 3 hr at ambient temperature: 25-26 deg C during the first hr, 10 deg C for the next hr, and 25-26 deg C for the remaining hr. All the rats had an initial core temperature of 38.8 deg C. The mean temperatures of the saline controls at 1, 2, and 3 hr post-treatment were respectively 37.6, 36.9, and 37.5 deg C; corresponding temperatures for the rats given atropine sulfate were 38.4, 37.5, and 38.0 deg C; and those for the rats given atropine methyl nitrate were 37.1, 36.4, and 36.8 deg C. Thus, atropine sulfate reduced phospholine-induced hypothermia and atropine methyl nitrate enhanced it.

To determine the effects of the antidotes alone, other unexposed rats were injected with atropine sulfate or atropine methyl nitrate followed by saline instead of phospholine. The core temperatures obtained with the former were respectively 38.2, 38.0, and 37.6 deg C at 1, 2, and 3 hr. The corresponding temperatures for atropine methyl nitrate were 37.9, 37.7, and 37.6 deg C, and the differences at corresponding times were smaller than for those with phospholine present. Thus, both of the antidotes induced hypothermia.

Groups of rats were subcutaneously injected with 0.2 mg/kg of another anticholinesterase drug, paraoxon, followed 10 min lat$ by 10 min of RFR- or sham-exposure. The mean core temperature of both groups dropped from 39.0 to about 36 deg C at 80 min, the start of the first 60-min interval at 10 deg C. At interval end (140 min after treatment), the mean core temperature of the RFR-exposed rats dropped to 33.6 deg C as contrasted with 35.0 for the sham-exposed rats. The mean temperatures of both groups rose to 37.7 deg C at 260 min, the start of the second 60-min interval at 10 deg C, and decreased to 35.7 and 36.4 deg C for the RFR and sham groups, respectively, at the end of that interval. The difference in means at 140 min was significant. Thus, exposure to the RFR significantly enhanced the hypothermia induced by paraoxon, as was the case for phospholine.

Other groups of rats were injected with 50 mg/kg of 2-pyridine aldox-

ime methyl methanesulfonate (P2S), an antidote for paraoxon, and 10 min later were RFR- or sham-exposed for 10 min. The hypothermia shown by both groups was less pronounced than for paraoxon, but again the mean temperature for the RFR group at 140 min was significantly lower than for the sham group.

In the final set of experiments, temperature profiles were obtained for groups of rats given P2S, exposed to the RFR for 10 min, and injected 10 min later with paraoxon. At 0 min (after paraoxon injection), the mean core temperature was 38.9 deg C for both groups, but the values for the RFR group were lower than those for the sham group at all corresponding subsequent times. Specifically, at 80 and 160 min, the start and end of the 10-deg-C interval, the core temperatures for the RFR group were 35.4 and 33.7 deg C, respectively, and the corresponding values for the sham group were 36.3 and 35.2 deg C. The values for the RFR group at 260 and 320 min, spanning the second 10-deg-C interval, were respectively 35.7 and 34.8, and those for the sham group were 36.7 and 36.2 deg C. These differences were larger than those for injection with P2S that was not followed with paraoxon.

Ashani et al. (1980) stated: "Rats administered 0.045 mg/kg phospholine iodide developed slight poisoning symptoms such as fasciculations and tremors. Furthermore, peripheral inhibition of AChE induced possible changes in several physiological systems such as cardiovascular impairments. Therefore, it will be impossible to relate the observed combined effects on the hypothermia to a specific mechanism."

Since few people ingest anticholinesterase drugs or their antidotes, there appears to be no direct significance of the findings of this investigation with regard to possible effects of RFR on human health. On the other hand, the authors suggested that use of certain drugs in combination with RFR might enhance the effects of RFR, and therefore such use would serve as a tool for investigating possible effects of low-level RFR, by implication, in the absence of such drugs.

Most of the results of this study demonstrated the converse, that RFR enhanced the effects of the drugs used, but with no clear evidence that RFR would induce effects in the absence of the drugs. However, the authors noted that "P2S is a powerful reactivator of phosphorylated acetylcholinesterase and cannot penetrate the blood-brain barrier, presumably due to the presence of a positive charge on the aromatic quaternary nitrogen. We could show that low-level microwave irradiation of rats injected with 50 mg/kg P2S reduced significantly the body temperature compared to that of the nonirradiated control group that received the same dose of P2S." A possible interpretation of this finding is that the RFR increased the permeability of the BBB to P2S, but this interpretation would not apply to the positive findings with paraoxon because, as indicated by the authors, paraoxon readily passes through the BBB.

Lai et al. (1983) exposed male Sprague-Dawley rats (250-300 g) to 2.45-GHz circularly polarized, pulsed RFR (2-microsecond pulses, 500 pps) in a cylindrical-waveguide system (Guy et al., 1979) at a time-

averaged and spatially-averaged power density of 1 mW/sq cm for 45 min at an ambient temperature of 22.0 deg C. The SAR, determined calorimetrically, was 0.6 W/kg. (With linearly polarized plane-wave RFR, the corresponding average power density would be 3 to 6 mW/sq cm.) Right after exposure, one of several drugs was administered and their effects were studied. The control rats were sham-exposed concurrently and otherwise treated similarly. Each rat was given only one treatment. All drug experiments were performed in the blind (without knowing whether any given rat was RFR- or sham-exposed).

The first experiment was directed toward determining the effect of RFR-exposure on apomorphine-induced stereotypy. Apomorphine (hydrochloride, 1 mg/kg, with 1 mg/ml of l-ascorbic acid, in saline) was subcutaneously injected immediately after exposure. Following injection, each rat was placed in a plastic cage covered with a metal grid, and its stereotypic behavior was observed for 5 min and at subsequent 15-min intervals for 1 hr. The rating scale below was used, with the sum of the five ratings taken as the stereotypic behavior score for the rat:

1) awake but largely immobile
2) moving with short bursts of sniffing
3) moving over the area of the cage with continuous sniffing and rearing
4) some or no movement and continuous sniffing with head directed down
5) same as 4, but with licking, biting, or gnawing

Results of the first experiment were a mean score of 17.2 for 15 RFR-exposed rats and 14.5 for 9 sham-exposed rats (no standard errors or deviations given). The percentage of the mean score in each rating was displayed for each group. For ratings 1 through 5, the values for the RFR group were respectively 8%, 11%, 32%, 28%, and 21%. Corresponding values for the sham group were 20%, 11%, 38%, 24%, and 7%. Thus, the RFR group yielded lower percentages for ratings 1 and 3, and higher percentages for ratings 4 and 5 than the sham group. By 2-tailed Mann-Whitney U-test, the differences were significant. The authors stated: "Microwave exposure shifted the distribution towards the higher scores, ie, more intense stereotypy with biting and clawing being observed in the microwave-treated animals."

The effect of RFR-exposure on the hypothermia induced by apomorphine was studied in the next experiment. The colonic temperature of each rat was measured right after exposure, the rat was injected with apomorphine (1 mg/kg), and its colonic temperature was recorded again for 1 hr at 15-min intervals. The results were displayed as the mean change in colonic temperature vs time interval after injection for 15 RFR-exposed rats, and similarly for 12 sham-exposed rats. For the RFR group, the mean colonic temperature immediately after exposure was 38.3 deg C and for the sham group, 38.2 deg C.

Fifteen min after injection, the mean temperature of the RFR group had decreased by 0.95 deg C, whereas the decrease for the sham group was only 0.63 deg C. Progressive recovery from the hypothermia was evident for both groups at 30 min and 45 min after injection. By nonparametric

test (Krauth, 1980), the difference between the groups was significant, indicating that the RFR had enhanced apomorphine's hypothermic effect.

In the next experiment, the effect of RFR on the stereotypy syndrome induced by d-amphetamine was studied. Each rat was injected i.p. with d-amphetamine (sulphate, 10 mg/kg in saline) immediately after exposure, placed in a plastic cage, and observed for the presence of any of three normal behaviors (immobility, rearing, and forward walking) and three abnormal behaviors (backward walking, circling, and head swaying). The rats were observed for 1 min every 5 min during a 1-hr session, starting 4 min after injection. The occurrence of each behavior was recorded on an all-or-none basis and the total incidence of each was determined for each rat. By Mann-Whitney U-test, the difference between RFR- and sham-exposed groups in averaged score for each of the six behaviors was not significant.

The effect of RFR on amphetamine-induced hyperthermia was studied also. Colonic temperatures of rats were measured right after exposure and at 15-min intervals during the 90-min period after the rats were injected i.p. with d-amphetamine (5 mg/kg). The results were displayed as the change in mean colonic temperature for each group vs time interval after injection. The mean temperature at zero time was 38.3 deg C for the RFR group and 38.2 deg C for the sham group. The temperature of the sham group reached its maximum at 45 min, at which time it had increased by 1.4 deg C to a maximum of 39.6 deg C, and it diminished to about 39.3 deg C at the end of the 90-min period. By contrast, the temperature of the RFR group attained its maximum at 60 min, an increase of 1.2 deg C to 39.5 deg C, and then diminished to 39.2 deg C at 90 min. These differences between groups in time-dependent temperature increases were significant.

In the final experiment, morphine sulphate was injected i.p. into rats at doses of 1, 5, 10, 15, or 20 mg/kg immediately after exposure. The number of animals exhibiting catalepsy at 30 min after injection, i.e., general muscular rigidity and a certain posture for more than 1 min, was recorded. Also recorded was the number of rats that died within 2 hr after injection.

The percentages of RFR- and sham-exposed rats that exhibited catalepsy for each dose were displayed. The authors had indicated that by the chi-square test, the differences were significant. In an erratum (Lai et al., 1985), however, they stated that the statistical method used was inappropriate and that use of the "logistic regression" method (by J. Crowley, no reference cited) showed a positive dose-response in the sham group but no dose-response relationship in the RFR group. Therefore, the responses of the sham group at low morphine doses were lower than of the RFR group and were higher at high doses.

There were no deaths within 2 hr in either group for doses of 1 or 5 mg/kg, but the differences in percentages of deaths at 10, 15, and 20 mg/kg were reported to be significantly higher in the RFR group. In the erratum, however, the authors stated: "The probability of death caused

by morphine administration increased with dose in a similar way for both microwave- and sham-irradiated groups, with no significant effects of microwaves."

In the original paper, the authors stated: "It may also be important to point out that the effect of microwaves on drug action was not observed in all of the animals irradiated. About 70% of the irradiated rats showed positive responses. Therefore, large samples were required to achieve statistically significant differences in response between the microwave- and sham-irradiated animals. We are probably working at an intensity of microwave irradiation close to the threshold level. Furthermore, since in our experiments drug actions were studied after microwave irradiation, the effect of microwaves might have dissipated in some rats." Presumably the results for the animals that did not exhibit the effect were included in the statistical treatment of the data. The last sentence in the quotation suggests that perhaps exposure to RFR after drug administration would yield more definitive results.

It is interesting to note that the mean colonic temperatures of the apomorphine-injected and amphetamine-injected groups immediately after exposure to RFR were both 0.1 deg C higher than for their respective sham-exposed groups (38.3 vs 38.2 deg C in both cases). Presumably the temperatures of the RFR group were even higher during exposure, and the postexposure difference between the RFR and sham groups was due to the residual thermal response to the RFR. In the light of this point, not clear was the influence of thermoregulation on the results. For both drugs, the differences in mean colonic temperature between RFR and sham groups during the postinjection intervals were smaller than the changes per se. With apomorphine, for example, the sum of the mean colonic temperature of the RFR group before injection and its maximum change (15 min after injection) was 37.35 deg C, and the corresponding sum for the sham group was 37.57 deg C, a difference of only 0.22 deg C. Was this difference statistically significant? Would similar results be obtained if the preinjection colonic temperatures of rats were raised by an agent other than RFR?

The peak power density of the RFR pulses was at least 1 W/sq cm, within the range of perception of the pulses as sound. Thus, it is possible that the rats perceived the pulses and were influenced thereby, but as discussed above relative to Thomas et al. (1979), whether the influence persisted into the postexposure period is unknown.

The results on the effects of RFR on apomorphine-induced stereotypic behavior appear to be somewhat ambiguous because the percentage scores for the RFR group were lower than for the sham group for two of the responses (1 and 3) and higher for two of the other responses (4 and 5). Evidently the authors gave qualitatively greater weight to responses 4 and 5 than to 1 and 3, a reasonable point.

Regarding the stereotypic-behavioral results for d-amphetamine (in which all six behavioral responses were given equal weight), even though the differences between the RFR and sham groups were nonsignificant, it

is interesting that the sham group (as well as the RFR group) exhibited a high score for "head sway," one of the "abnormal" responses.

Lacking in this investigation were data on control animals administered saline instead of the drugs. Such data might have better delineated subtle non-RFR factors that may have influenced the results.

In a similar study, Lai et al. (1984a) examined the effects of the same RFR on the actions of pentobarbital in the rat. In the first of two series, 13 unanesthetized, unrestrained rats were exposed to the RFR. The colonic temperature of each rat was taken with a probe right after exposure, the probe was removed, and the rat was injected with sodium pentobarbital at a dose sufficient to induce surgical anesthesia. After loss of the righting reflex, the probe was reinserted, the temperature was recorded at 15-min intervals for 150 min, and the time interval to regain the righting reflex after injection was noted. Another group of 13 rats was sham-exposed and similarly treated.

In the second series, baseline colonic temperatures were measured and the rats were injected with pentobarbital. Fifteen min later, by which time all the rats had lost their righting reflex, 12 rats were exposed anteriorly (head toward source) and 10 rats posteriorly (rear toward source) for 45 min to the RFR concurrently with 10 rats sham-exposed in each orientation. Colonic temperatures were recorded for 90 min after exposure and the time interval to regain the righting reflex after exposure was noted.

Colonic-temperature-response curves were compared by a nonparametric statistical method (Krauth, 1980), in which the temperature-response curve of each rat was approximated by orthogonal polynomials and the zero-order orthogonal coefficients from the different treatment groups were compared by chi-square analysis. Student's two-tailed t-test was used to compare colonic temperatures at corresponding times and to compare time intervals for regaining the righting reflex.

In the first series, the (conscious) rats did not exhibit any preferred orientation during RFR exposure and there was no significant difference in mean colonic temperature between the RFR and sham groups immediately after exposure (37.8 deg C for both). Mean colonic-temperature changes for each group vs time after pentobarbital injection showed that both groups reached maximal hypothermia (about -3 deg C) at 75 min. The mean temperature depressions at corresponding times were larger for the sham group than for RFR group until 90 min after injection; at 90 min, the two plots intersected, but none of the differences between the groups up to 105 min was significant. At corresponding times from 105 to 150 min, the mean depressions for the RFR group were significantly larger than for the sham group, i.e., recovery of the RFR group from the hypothermia was slower. Also, the mean time to righting-reflex recovery for the RFR group was significantly longer than for the sham group (100 vs 90 min).

In the second series, baseline mean colonic temperatures of the

injected rats before RFR- or sham-exposure were 37.9 deg C. For the groups sham-exposed in the two orientations, there was no significant difference in mean temperatures immediately after sham-exposure so their results were pooled. Immediately after exposure, the mean colonic temperatures for anterior-exposure and posterior-exposure to the RFR and for the combined sham group were 34.6, 34.7, and 34.1 deg C, respectively. Those for the two RFR groups did not differ from one another significantly; however, the values for both were significantly higher than for the sham group.

Plots of mean change in colonic temperature (from the values preceding injection) vs time after exposure showed that all three groups attained maximal hypothermia 30 min after exposure (45 min after injection). The mean changes at that time for the posterior-RFR, anterior-RFR, and sham groups were respectively about -3.8, -4.2, and -4.5 deg C, but only the difference between the posterior-RFR and sham groups was significant.

From 30 to 90 min, all three groups exhibited recovery toward baseline temperatures, with no significant differences at corresponding times between the anterior-RFR and sham groups. However, the temperatures of the posterior-RFR group were significantly higher than those of the other groups at corresponding times during that interval, indicating that the posterior-RFR group recovered from the hypothermia earlier. Moreover, the rats in that group recovered their righting reflex more quickly (26, 45, and 50 min respectively for posterior-RFR, anterior-RFR, and sham groups, with the difference between the latter two groups not significant).

Lai et al. (1984a) stated: "In our [first] study, when the effect of pentobarbital was studied after exposure, we found that microwaves affected the recovery rate from pentobarbital-induced hypothermia without affecting the initial rate and the maximal fall in colonic temperature. The cause of this effect is not readily known. However, the fact that there is no effect on initial rate and extent of fall in colonic temperature between microwave- and sham-exposed animals indicates that microwaves do not affect drug absorption and distribution at least to the sites of action. However, effect on drug metabolism cannot be discounted. Even though no significant effect on colonic temperature was detected in our irradiated animals, focal heating of areas of the brain or body leading to altered drug metabolism cannot be ruled out."

Regarding their second series, they stated: "...we found that microwave exposure attenuated the fall in colonic temperature in pentobarbital-anesthetized animals. This is probably due to absorption of energy from the radiation. Both anterior- and posterior-exposed rats showed the same degree of attenuation, which is consistent with the dosimetry finding that similar amounts of radiation energy are absorbed by the whole body in both orientations of exposure. The fact that microwave irradiation affects the core temperature in anesthetized but not in conscious rats, suggests that in the conscious rats a compensatory thermoregulatory mechanism is functioning during the exposure to maintain a constant core temperature...by increasing heat loss or de-

creasing heat production... However, during pentobarbital anesthesia the rat is rendered poikilothermic and the thermal effect of microwaves is seen as an attenuation of the hypothermia... A similar phenomenon has also been reported in animals after treatments with other drugs that disturb thermoregulation."

The authors noted: "...the extents of pentobarbital-induced hypothermia in the sham-irradiated rats are different in the two experiments. In experiment 1, the average fall in colonic temperature for the sham-irradiated rats at 90 min after pentobarbital injection was -3.0 +/- 0.2 deg C (n=13), whereas the temperature change at the same time after injection (ie, 30 min after exposure) for the sham-irradiated animals in experiment 2 was -4.2 +/- 0.2 deg C (n=20) (significantly different at $P<.001$, two-tailed Student's t-test). This difference was probably due to differences in experimental procedures between the two experiments. In experiment 1, thermistor probes were left inserted into the rats after the drug treatment and during the course of the study, whereas in experiment 2, the animals were left undisturbed during the 45-min exposure period which started at 15 min after the drug treatment. Owing to this difference, caution should be taken in comparing the results of the two experiments."

Another finding commented on by the authors was the smaller maximal colonic-temperature depression and the earlier recovery time of the righting reflex for the posterior-RFR group relative to the values for the anterior-RFR and sham groups. They surmised that these orientation-dependent findings were due to differences in local energy depositions for the two orientations, which could yield differences in drug metabolism or kinetics.

As in the earlier investigation, the peak power density of the pulses was at least 1 W/sq cm, within the range of perception of the pulses as apparent sound. Thus, it is possible that conscious rats in experiment 1 perceived the pulses. However, it would be difficult to connect such perception with the RFR-related differences in the pentobarbital-induced hypothermia and analepsis therefrom reported.

The authors' remark above about the difference in hypothermia depth induced in the sham-exposed rats in the two experiments appears to be in error: the -3.0 deg C at 90 min after injection for experiment 1 is correct; however, the corresponding time in experiment 2 was not 30 but 75 min after exposure, at which time the mean temperature depression was also about 3 deg C. Moreover, in neither case did the 90-min point correspond to the time of maximal hypothermia, which occurred at 75 min in experiment 1 and 45 min in experiment 2 (both reckoned from injection time). The temperature depressions for the sham groups at these times were about 3.2 and 4.5 deg C, respectively. Thus, not only were the maximal depressions significantly different, but so were their times of occurrence. The reasons for these differences are not clear. Lacking were data on sham-exposed animals given saline instead of pentobarbital.

In another similar study, Lai et al. (1984b) determined the effects of

the same RFR on ethanol-induced hypothermia and on ethanol consumption. For the ethanol-hypothermia experiment, 15 rats were RFR-exposed and 14 rats were concurrently sham-exposed for 45 min. Each rat was removed from its waveguide immediately after exposure, its colonic temperature was measured, and it was injected intraperitoneally with ethanol (3 g/kg in a 25% v/v water solution). The rats were then housed 6 to a cage and their colonic temperatures were measured with a thermistor inserted and removed at 15-min intervals for 120 min.

In the ethanol-consumption study, 48 rats were given nine daily 90-min sessions in the waveguides. Drinking water was removed from the home cages 24 hr prior to the first session. On session days 1, 2, and 3, the rats were inserted in the waveguides for 45 min with the RFR source on "standby." At this time, a bottle containing a 10% sucrose solution (w/v) was inserted in each waveguide and the amount consumed during the remaining 45 min was measured. The day-4 procedure was the same except that half the rats (24) selected randomly (and blindly) were exposed to the RFR and the other half were sham-exposed for the full 90 min. The procedure on days 5-7 was the same as for days 1-3 except that a (w/v) solution of 10% sucrose + 15% ethanol was used (the latter to render the ethanol more palatable).

On day 8, half the rats (group I, randomly selected) were exposed to RFR and the remaining rats (group II) were sham-exposed for the 90 min, and the amounts of sucrose-ethanol solution consumed during this period were determined. On day 9, the group roles were reversed: group I was sham-exposed, group II was RFR-exposed, and fluid consumption was noted. The colonic-temperature-response curves were compared by the nonparametric statistical method of Krauth (1980) and the fluid-consumption data for the various sessions were compared by the two-tailed, paired t-test.

In the ethanol-hypothermia experiment, the mean colonic temperatures of the RFR- and sham-exposed rats immediately after exposure were 38.2 and 38.3 deg C, respectively, a nonsignificant difference. Ataxia developed within 5 min of ethanol injection, but righting reflex remained intact. The mean colonic temperature changes vs time after ethanol injection for the two groups indicated that hypothermia had occurred in the RFR group at a slower rate than in the sham group. For example, the temperature depressions at 15 min after injection were about 0.4 and 0.9 deg C for the RFR and sham groups, respectively, a significant difference; the corresponding depressions at 60 min were about 1.5 and 1.8 deg C, also a significant difference; at 90 min, the depressions were about 1.9 deg C for both groups and did not differ significantly from one another at subsequent times.

The mean sucrose consumptions for days 1, 2, and 3 (during which all 48 rats were sham-exposed and offered the sucrose solution) respectively were 29.0, 46.5, and 67.0 ml/kg, significant monotonic increases. On day 4 (when half were exposed to RFR and the remainder were sham-exposed for 90 min), the respective consumptions were 70.6 and 71.6 ml/kg, which did not differ significantly from each other or from the day-3 value. Thus, exposure to RFR had no apparent effect on sucrose consumption.

For days 5, 6, and 7 (during which all 48 rats were sham-exposed and offered the sucrose-ethanol solution), the mean consumption values were 26.2, 34.2, and 30.0 ml/kg; the changes were clearly nonmonotonic with time. For day 8 (when group I was RFR-exposed and group II was sham-exposed), the respective values were 37.6 and 30.5 ml/kg; the group-II value did not differ significantly from its day-7 value, but the group-I value was significantly higher (about 23%) than its day-7 value. For day 9 (when group II was RFR-exposed and group I was sham-exposed), the group-II value was 38.9 ml/kg and the group-I value was 30.4 ml/kg; so again, consumption increased (about 28%) for the group exposed to RFR on that day. However, consumption by group I under sham-exposure on day 9 returned to its day-7 value, so the increase in consumption associated with its RFR-exposure on day 8 was a temporary effect.

Regarding the ethanol-hypothermia experiment, the authors noted: "Our results show that acute microwave irradiation at 0.6 W/kg delays the effect of ethanol on body temperature. The mechanism of the effect is not known. Ethanol renders an animal poikilothermic, thus inducing hypothermia when the ambient temperature is lower than body temperature [Myers, 1981]. It is unlikely that microwaves retard the action of ethanol by affecting the entry of ethanol into the brain, since ethanol readily permeates the blood-brain barrier and is rapidly distributed in brain tissue. A possible explanation is that microwaves affect neural thermoregulatory mechanism(s), which in turn retards the heat-loss processes triggered by ethanol."

They also stated: "The results from the second experiment show that microwaves enhance consumption of a sucrose + ethanol solution without affecting consumption of a sucrose solution. Because sucrose is similar in caloric value to ethanol, and because its consumption was unaffected by microwave irradiation, it would appear that the microwave-induced increase in ethanol consumption was not due to a shift in caloric requirement of the rats." They offered several hypotheses about the apparent RFR-induced alterations of ethanol action, but concluded that further research would be necessary to elicit specific mechanisms.

The procedures used in the two experiments, the statistical treatment of the data, and the experimental findings reported appear sound. However, the relevance of the results of the ethanol-hypothermia experiment to possible hazards to humans of RFR-ethanol interactions may be questioned because of the high dose of ethanol used. On the basis of body weight, injection with 3 g/kg of ethanol in a 25% v/v water solution would be about equivalent to a 700-ml dose of 50-proof liquor for a 70-kg human, a clearly substantial "slug" of alcohol.

In the second experiment, the mean consumption of sucrose alone on day 3 was 67.0 ml/kg, whereas the day-3 consumption of sucrose-ethanol was 30.0 ml/kg, indicating that even when water-deprived, the rats still found the sucrose-ethanol solution sufficiently distasteful to restrict its consumption. On the other hand, their higher consumption of the sucrose-ethanol solution under RFR- than sham-exposure may indicate that the additional heat produced by the RFR induced the water-deprived rats

to drink more despite their aversion to ethanol. Support for this point is in the authors' following sentence: "In another experiment, we found that rats absorbed a considerable amount of microwave energy (about 0.16 J/g) when irradiated in the pulsed, 1-mW/sq-cm field for 45 min [Lai et al., 1984(a)]. However, the animals did not show any change in body temperature immediately after exposure; the implication is that they were actively dissipating the thermalized microwave energy." It should be noted that by calculation, the amount of energy absorbed in 45 min at a whole-body SAR of 0.6 W/kg is 1.6, not 0.16 J/g, which strengthens the point made. It is also interesting that 0.6 W/kg is about 10% of the basal metabolic rate for a medium rat (Durney et al., 1978, p. 47).

REFERENCES:

Ashani, Y., F.H. Henry, and G.N. Catravas
COMBINED EFFECTS OF ANTICHOLINESTERASE DRUGS AND LOW-LEVEL MICROWAVE RADIATION
Radiat. Res., Vol 84, pp. 496-503 (1980)

Baranski, S. and Z. Edelwejn
STUDIES ON THE COMBINED EFFECT OF MICROWAVES AND SOME DRUGS ON BIOELECTRIC ACTIVITY OF THE RABBIT CENTRAL NERVOUS SYSTEM
Acta Physiologica Polonica, Vol. 19, No. 1, pp. 31-41 (1968)

Chou, C.-K., A.W. Guy, J.B. McDougall, and L.-F. Han
EFFECTS OF CONTINUOUS AND PULSED CHRONIC MICROWAVE EXPOSURE ON RABBITS
Radio Sci., Vol. 17, No. 5S, pp. 185-193 (1982)

Guy, A.W., J. Wallace, and J.A. McDougall
CIRCULARLY POLARIZED 2450 MHZ WAVEGUIDE SYSTEM FOR CHRONIC EXPOSURE OF SMALL ANIMALS TO MICROWAVES
Radio Sci., Vol. 14, No. 6S, pp. 63-74 (1979)

Krauth, J.
NONPARAMETRIC ANALYSIS OF RESPONSE CURVE
J. Neurosci. Meth., Vol. 2, pp. 239-252 (1980)

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
PSYCHOACTIVE-DRUG RESPONSE IS AFFECTED BY ACUTE LOW-LEVEL MICROWAVE IRRADIATION
Bioelectromagnetics, Vol. 4, No. 3, pp. 205-214 (1983)

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
ERRATUM to Lai et al. (1983)
Bioelectromagnetics, Vol. 6, No. 2, p. 207 (1985)

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
EFFECTS OF ACUTE LOW-LEVEL MICROWAVES ON PENTOBARBITAL-INDUCED HYPOTHERMIA DEPEND ON EXPOSURE ORIENTATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 203-211 (1984a)

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
ETHANOL-INDUCED HYPOTHERMIA AND ETHANOL CONSUMPTION IN THE RAT ARE AFFECTED BY LOW-LEVEL MICROWAVE IRRADIATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 213-220 (1984b)

Lords, J.L., C.H. Durney, A.M. Borg, and C.E. Tinney
RATE EFFECTS IN ISOLATED HEARTS INDUCED BY MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 21, No. 12, pp. 834-836 (1973)

Lotz, W.G. and S.M. Michaelson
EFFECTS OF HYPOPHYSECTOMY AND DEXAMETHASONE ON RAT ADRENAL RESPONSE TO MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 47, No. 6, pp. 1284-1288 (1979)

Monahan, J.C. and W.W. Henton
FREE-OPERANT AVOIDANCE AND ESCAPE FROM MICROWAVE RADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 23-33 (1977a)

Monahan, J.C. and W.W. Henton
THE EFFECT OF PSYCHOACTIVE DRUGS ON OPERANT BEHAVIOR INDUCED BY MICROWAVE RADIATION
Radio Sci., Vol. 14, No. 6S, pp. 233-238 (1979)

Myers, R.D.
ALCOHOL'S EFFECT ON BODY TEMPERATURE: HYPOTHERMIA, HYPERTHERMIA, OR POIKILOTHERMIA?
Brain Res. Bull., Vol. 7, pp. 209-220 (1981)

Pappas, B.A., H. Anisman, R. Ings, and D.A. Hill
ACUTE EXPOSURE TO PULSED MICROWAVES AFFECTS NEITHER PENTYLENETETRAZOL SEIZURES IN THE RAT NOR CHLORDIAZEPOXIDE PROTECTION AGAINST SUCH SEIZURES
Radiat. Res., Vol. 96, No. 3, pp. 486-496 (1983)

Reed, J.R.III, J.L. Lords, and C.H. Durney
MICROWAVE IRRADIATION OF THE ISOLATED RAT HEART AFTER TREATMENT WITH ANS BLOCKING AGENTS
Radio Sci., Vol. 12, No. 6S, pp. 161-165 (1977)

Thomas, J.R. and G. Maitland
MICROWAVE RADIATION AND DEXTROAMPHETAMINE: EVIDENCE OF COMBINED EFFECTS ON BEHAVIOR OF RATS
Radio Sci., Vol. 14, No. 6S, pp. 253-258 (1979)

Thomas, J.R., L.S. Burch, and S.S. Yeandle
MICROWAVE RADIATION AND CHLORDIAZEPOXIDE: SYNERGISTIC EFFECTS ON FIXED-INTERVAL BEHAVIOR
Science, Vol. 203, pp. 1357-1358 (1979)

Thomas, J.R., J. Schrot, and R.A. Banvard
BEHAVIORAL EFFECTS OF CHLORPROMAZINE AND DIAZEPAM COMBINED WITH LOW-LEVEL MICROWAVES
Neurobehav. Toxicol., Vol. 2, pp. 131-135 (1980)

Tinney, C.E., J.L. Lords, and C.H. Durney
RATE EFFECTS IN ISOLATED TURTLE HEARTS INDUCED BY MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 24, No. 1, pp. 18-24 (1976)

3.7.3 CONCLUSIONS

Early studies in the U.S.A. on possible effects of RFR on behavior were engendered by the hypothesis held in the USSR that RFR can have direct effects on the central nervous system (CNS) and that such effects could occur at "nonthermal" levels of RFR and thereby alter behavior in the absence of measurable RFR-induced increases in body temperature. RFR pulses of appropriate characteristics that do not cause rises in core temperature can be perceived by humans and animals as sound, but as discussed in Section 3.1.4.2, perception is attributed to induction of thermoelastic waves in the head rather than direct CNS stimulation.

Many of the studies on avoidance behavior by animals appear to indicate that RFR is a noxious or unpleasant stimulus. There is much evidence, however, that the observed RFR-induced changes in behavioral patterns are responses by their thermoregulatory systems, either to minimize heat absorption in normal or warm ambient environments (including high levels of humidity) or to obtain warmth in relatively cold environments. Thus, other than auditory perception of RFR pulses, animals do not appear to directly sense RFR. Results of studies on RFR disruption of performance or learned behavior were variable; however, most of the findings showed that the behavioral changes were ascribable to the additional thermal burden imposed by the RFR, and specifically were significant at measured or estimated whole-body SARs well in excess of 1 W/kg.

The relatively few studies of possible synergism of RFR with various psychoactive drugs, such as diazepam, chlorpromazine, chlordiazepoxide, and dextroamphetamine, yielded unclear or inconsistent results. In some studies, the changes in drug dose-response relationship were subtle and not necessarily induced by the RFR. In most of the studies that yielded RFR-induced changes in drug response, average power densities of 1 mW/sq cm or higher coupled with relatively high drug dosages were necessary. Negative results were obtained in still others. Especially noteworthy were the negative findings of synergistic effects between consumption of alcohol and RFR except at very high doses of the former. In general, it is most unlikely that the effects of psychoactive drugs prescribed by physicians or the effects of recreationally taken alcohol would be altered by exposure to RFR at environmental levels.

3.8 CELLULAR AND SUBCELLULAR EFFECTS

Many of the studies on cellular and subcellular effects of RFR were discussed in previous sections under specific topics such as the blood-brain barrier, immunology, hematology, and calcium efflux. For the present section, therefore, studies were selected that describe other effects on cells and their constituents.

3.8.1 STRUCTURES AND CONSTITUENTS OF MICROORGANISMS AND OTHER SINGLE-CELL SYSTEMS

Takashima (1966) sought possible effects of in-vitro exposure to RFR of the enzyme alcohol dehydrogenase and of DNA. Buffered enzyme in 10-ml quantities were exposed within a cell to pulsed RFR at frequencies in the range 1-60 MHz for periods of 0.5 to 2 hr. Details of the exposure cell were not given, except that it was cooled by circulation of water at 4-5 deg C during exposure. The amplitude was 200 V peak-to-peak and the duty cycle was 0.01-0.4, 0.4 being the highest value that did not produce significant heating, as measured with a thermocouple during intermittent removal of the field. With a solution resistance of 200 ohms and a pulse duration and repetition frequency of 1 millisecond and 330 pps, the power applied to the solution was calculated to be 33.0 W. Control solutions were placed in the cell for the same durations without applying the RFR.

Right after exposure, enzyme activity was spectrophotometrically assayed at 340 nm by the increase in optical density vs time. Representative results were displayed as semilog plots of activity vs time for a sample exposed for 1 hr to 1 MHz (as stated in the text) or 10 MHz (as stated in the figure) and for a control sample. Both plots were linear, an indication that oxidation of alcohol by this enzyme follows first-order reaction kinetics, but there was no significant difference in their slopes. A plot of the ratio of the slope for samples exposed at each frequency to the slope for the corresponding control samples vs RFR frequency (1-60 MHz) showed values in the range 1 +/- 0.1.

Similar experiments were done with samples of calf-thymus DNA. Neutral solutions (15 mg/ml) of DNA were exposed to pulsed RFR at frequencies within two ranges: 10 Hz to 10 kHz and 100 kHz to 10 MHz. The amplitude was 300 V peak-to-peak and the pulse durations ranged from 0.5 to 5 ms at duty cycles up to 0.5. Following exposure, optical density at 260 nm and viscosity were measured. The optical density measurements showed no significant differences between exposed and control samples (data not presented); the author noted that this result excluded the possibility that the RFR exposure caused strand separation. Displayed was a plot of viscosity ratio of exposed samples to corresponding control samples vs frequency for the range 1-10 MHz. The ratios were also 1 +/- 0.1. The author stated that no change in optical density or viscosity could be detected after exposure to frequencies in the range 10 Hz to 100 kHz, but presented no data.

Various studies were devoted to possible effects on microorganisms of

RFR in the submillimeter-wave region. In a preliminary investigation, Webb and Dodds (1968) reported that growth of E. coli B bacteria was inhibited by exposure to 136-GHz RFR. Bacteria were grown in nutrient broth, collected by centrifugation, washed twice in 0.85% NaCl, and resuspended in fresh nutrient broth to 10,000 cells per ml; 0.2-ml aliquots were inserted in 1-cm-diameter flat-bottom vials and the vials were placed immediately (in lag growth phase) or after 90 min of incubation at 37 deg C (log phase) on the top of a microwave horn and exposed to the RFR for up to 4 hr. The forward power was stated to be about 7 microwatts. The vials were periodically shaken by hand and their temperature kept at ambient (about 25 deg C) with a cooling fan. Temperatures after specific exposure durations were determined with a small thermocouple inserted in a vial containing nutrient broth only.

On completion of each exposure, 0.8 ml of nutrient broth was added to each vial, serial tenfold dilutions were made, 0.2 ml of each dilution was plated on nutrient agar, and colony counts were made after 24 hr of incubation at 37 deg C. The results were tabulated as counts of viable cells from the bacteria exposed in lag phase (immediately) for 0 to 240 min (steps of 30 min) and counts from lag-phase control bacteria for the same durations, each averaged over three independent experiments. The results for log-phase bacteria (exposed after 90 min of incubation) and corresponding controls were similarly presented. Also shown were the respective temperatures after each exposure duration.

For the lag-phase control bacteria, the mean count (in units of 1000 cells per ml) rose nonmonotonically with duration from 125 at 0 min to 810 at 240 min; the mean count for the lag-phase RFR-exposed bacteria, however, fluctuated from 125 at 0 min to 129 at 240 min, with a maximum of 142 at 60 min and a minimum of 121 at 30 min. The mean count for the log-phase control bacteria increased monotonically from 126 at 0 min to 1960 at 240 min; for the log-phase RFR-exposed bacteria, the mean count rose more slowly from a minimum of 142 at 0 min to a maximum of 288 at 240 min.

The authors concluded that immediate exposure to the RFR inhibited cell division, but that the RFR was not lethal because the cell count did not decrease after 4 hr of exposure; that exposure to the RFR after 90 min of incubation did not inhibit cell division immediately, since the count after 4 hr of exposure was about double the initial value. They also noted that comparison of the lag-phase and log-phase results suggests that the RFR can slow down cell division and can inhibit some specific metabolic process occurring in the early part of the cell's life span.

No statistical treatment of the data was given. Noteworthy, however, is that the mean counts for the RFR-exposed and control log-phase bacteria at 0 min and for the control lag-phase bacteria at 90 min, which should have been about the same, were respectively 142, 126, and 138, probably indicating that uncontrolled non-RFR factors were present.

Mean vial temperature varied nonmonotonically from a minimum of 25.2

deg C for durations of 0 and 30 min to a maximum of 25.9 deg C for 210 min, an apparent trend toward temperature rise with exposure duration, even though a cooling fan was used. If this trend were actual, it could be interpreted as indicating that the forward power was much higher than 7 microwatts and that the fan was not very effective; on the other hand, it is unlikely that much heat was produced in the samples at the stated level. In any case, sample-temperature variability may have been one of the uncontrolled factors.

Webb and Booth (1969) reported that preparations of E. coli Br cells and protein, RNA, and DNA in such cells absorb RFR at specific frequencies within the range 65-75 GHz and they discussed effects of such absorption on cell metabolic processes. Cells were grown for 24 hr at 37 deg C in nutrient broth and either washed twice in 0.85% NaCl and deposited as a pellet by centrifugation or resuspended after washing to a concentration of 1 million cells per ml in a medium (GCT) consisting of 0.5% glucose, 0.5% casamino acids, and 0.05 mg/ml thymine in 0.1-M phosphate buffer at a pH of 6.9.

To determine the effects of RFR on cell growth, 0.5-ml aliquots of cells suspended in GCT were placed in flat-bottom 1.5-cm-diameter vials, and some vials were incubated at 25 deg C while being exposed to RFR at each frequency for unspecified power level or durations, and other vials were similarly incubated at 25 deg C without RFR. Following such treatment, vials were removed and cell counts were made by dilution and plating on nutrient agar.

To ascertain effects of RFR on metabolic processes, washed cells were resuspended to a concentration of 100 million cells per ml in a medium consisting of 1% glucose in 0.1-M phosphate buffer (pH 6.9), and 0.2-ml aliquots of the suspension were placed within vials. Added to each vial was 0.3 ml of a solution that contained thymine (a constituent of DNA), uracil-2 (a component of RNA), or algal protein hydrolysate, all labeled with C-14 (0.8 microcurie per ml), and two of these three substances not labeled with C-14. After incubation with or without RFR, the cells from each vial were deposited onto a Millipore filter and washed with 100 ml of 1-N HCl. The filter was then dried and radioactivity was determined by counting.

To determine the RFR-absorption spectra of cells, water, protein, RNA, and DNA, films of each material were made on a thin mica window and the films were dried at 80% relative humidity and covered with a second mica window. The absorption of each material at each RFR frequency was the difference between (ratio of?) the absorption by the window preparation and that of a blank sandwich. The apparatus used to measure absorption was not described. The absorption spectra were presented in Fig. 1 of the paper as graphs of attenuation (dB) vs frequency, with experimental points in the range 65-75 GHz at 1-GHz intervals and additional points at 71.5 and 73.7 GHz.

The water-film graph had relative absorption maxima at 69 GHz (5 dB), 71.5 GHz (4 dB), and 73.7 GHz (3 dB), but also higher absorption at 65

GHz (7 dB) than these maxima, a result not discussed. The spectrum for E. coli cells had relative maxima at 66 GHz (7 dB), 68 GHz (9 dB), 71 GHz (5 dB), and 73 GHz (14 dB). For protein, maxima were obtained at 67 and 73 GHz (13 dB) and smaller ones at 70 and 71.5 GHz (8 dB). At 68 GHz, however, the protein graph dipped below 0 dB to about -3 dB. The authors did not discuss this observation, a seeming 2:1 amplification, or its physical significance, if any. The DNA spectrum showed equal maxima (12 dB) at 66 and 69 GHz and a smaller one (7 dB) at about 72 GHz. RNA had maxima at 68 GHz (12 dB) and 71 GHz (10 dB). The authors endeavored to interpret the similarities and differences among the five RFR-absorption spectra, but their discussion was speculative at best.

Growth rate for E. coli, expressed as the ratio of the "mean generation time" for RFR-exposed preparations to the same parameter for unexposed preparations, was presented vs frequency in Fig. 2a of the paper, but that parameter was not defined. The graph showed that at 65 and 68 GHz, the growth rate thus defined was enhanced (respective ratios of 1.2 and 1.4), but was inhibited at all other frequencies, with relative minimum ratios at 66 GHz (0.4), 71 GHz (0.6), and 73 GHz (0.3).

Uptake vs frequency of the C-14-labeled metabolites thymine, uracil-2, and protein hydrolysate, each expressed as the ratio of counts for RFR-exposed preparations to counts for unexposed preparations, were shown in Fig. 2b. For thymine (DNA), deep minimum ratios were obtained at 66 GHz (0.48) and 73 GHz (0.45) and a lesser dip at 71.3 GHz (0.75). The graph for protein hydrolyslate was roughly similar to that for thymine, but its dips at 66, 73, and 71.3 GHz were smaller (respectively 0.75, 0.60, and 0.85). Uracil-2 (RNA) showed only one minimum, a relatively shallow one at 73 GHz (0.85), but enhanced uptake in the approximate frequency range from 65 to 69 GHz, with a maximum at 68 GHz (1.25).

Regarding the results above, the authors stated: "Three frequencies, 66, 71 and 73 GHz, were found to slow the growth of cells whereas 68 GHz microwaves stimulated it. Two of the frequencies able to slow cell growth matched the absorption maxima of DNA at 66 GHz and of protein at 73 GHz, while the third, 71 GHz, corresponded to one of the peaks in the absorption spectrum of RNA and a shoulder in that of DNA. The frequency which seemed to stimulate growth matched one of the absorption maxima at 68 GHz. All of the frequencies which had maximal effect on growth rate corresponded with absorption peaks in the spectrum of the cells."

They concluded that: "Bacterial cells clearly absorb microwaves of definite frequencies and the absorbed energy alters metabolic processes and cell growth. Temperature changes do not seem to play a part in these phenomena because, first, only a fraction of a degree rise was recorded during the experimental period, and second, the optimum growth temperature of E. coli is at 37 deg C; therefore, any increase above 25 deg C should have resulted in increased cell growth or metabolism, not decreases as we observed. Moreover, the cell counts showed that none of the frequencies killed the cells."

Evaluation of the findings of this study is problematical because of

the absence of adequate information on the methodology, instrumentation, and statistical treatment of the data.

Grundler et al. (1977), noting the study by Webb and Booth (1969) in which the growth of E. coli was reported to be depressed by exposure to RFR at 71 and 73 GHz, investigated the effects of RFR in the range 40-60 GHz on the growth of a diploid wild strain of Saccharomyces cerevisiae cells. After appropriate preparation, 2.5 ml of a suspension of the yeast in aqueous medium was placed and stirred in a standard rectangular glass receptacle. Cell growth in the suspension was monitored optically by transmission photometry. Extinction (decrease of light transmission through the suspension) was recorded vs time and was found to increase exponentially over about three generations (about four hours). The data were replotted semilogarithmically to obtain the growth rate (the slope of the new plot).

Growth curves were obtained with no RFR at suspension temperatures in the range 30.5-34 deg C. (The authors noted that during any experiment, suspension temperature never varied by more than +/- 0.5 deg C.) The resulting growth rates were plotted vs suspension temperature, which showed that without RFR, the growth rate decreased from 4.0% per deg C at 31 deg C to 1.3% at 33 deg C and also indicated that the results were reproducible to within +/- 3%.

A Siemens BWO-60 backward-wave oscillator operating in the range 40-60 GHz was the RFR source. The oscillator was controlled by a Micro-Now 702/703C power supply connected to an Alfred 650 sweep unit. Frequency stability and resettability respectively were +/- 1 MHz and 3 MHz (+/- 25 and 75 parts per million at 40 GHz). The oscillator output was fed through a metallic waveguide to a vertical horn terminated by a Teflon structure that was immersed in the aqueous suspension. For penetration depth into water of about 0.2 mm at 42 GHz, the RFR power emitted into the suspension ranged between 11 and 27 mW. The total emission area was stated to be 10 sq cm, so the power densities ranged between 1.1 and 2.7 mW/sq cm, which increased suspension temperature by roughly 0.4 deg C. The relative or normalized growth rate was then defined as the ratio of the growth rate in the presence of RFR to the rate in its absence at the corresponding suspension temperature.

Sixty-seven experiments were performed. The results of five experiments were discarded because the growth rates were very small in the sample studied and in a monitor beaker, probably due to bacterial infection or chemical poisoning. The results of the remaining 62 experiments were tabulated as normalized growth rate at specific frequencies, suspension temperatures, and absorbed RFR powers (which varied from 11 to 27 mW). Also, the normalized growth rate was plotted vs frequency. This figure exhibited several sharp maxima and minima that spanned unity growth rate ("a multiplet of biological resonances") in the frequency region between 41.83 and 41.96 GHz, with apparently little effect below or above this region. The largest increase in growth rate was 15% at 41682 +/- 3 MHz, 17 mW of power absorbed, and suspension temperature of 32.4 deg C. The largest decrease in growth rate was 29% at 41712 +/- 3

MHz, 23 mW of power absorbed, and suspension temperature of 31.7 deg C. (The figure showed one smaller minimum and maximum at intermediate frequencies.)

The authors noted that on an absolute frequency scale, a systematic offset of up to +/- 20 MHz was possible. They also stated: "The strong absorption of the radiation in water means that in our geometry only a small part of the total volume is subjected to the full intensity. We have not yet measured the dependence on intensity and thus would not know how to correct the results for the varying power. Inspection of the figure shows, however, that this can cause only minor alterations even if linear dependence on power is assumed."

The results of this study appear to indicate (implied in the abstract of the paper) that RFR in the resonant range either enhances or inhibits cell growth, depending on the specific frequency. However, the authors did not speculate on possible mechanisms for such effect reversals.

Some millimeter-wave studies were directed toward confirmation of the existence of resonances on theoretical grounds, predicted for example by Froehlich (1975), and therefore that nonthermal effects can occur. Webb and Stoneham (1977) reported that by laser-Raman spectroscopy, they had detected resonant frequencies in the range 70-5000 GHz in active cells of B. megatorium and E. coli. The cells of each species were grown for 6 hr at 30 deg C in nutrient broth, washed and resuspended in saline, held in an ice bath for 15 min to produce synchrony, and resuspended to 50 million cells/ml in growth medium or saline. After obtaining the same cell concentration in each suspension, determined by the intensity of the Rayleigh line in a laser-Raman spectrometer, the cells were incubated at 30 deg C for 15 min and Cary Raman cuvettes were filled with aliquots of the suspensions. Each consecutive scan of the Raman spectrum was done with fresh cells from the master culture.

A typical spectrum from active B. megatorium 30 min after resuspension in a Davis minimal medium showed three shift lines corresponding to resonance frequencies of 570, 3750, and 4300 GHz, and an apparent fourth one at 120 GHz. The spectra from E. coli showed five lines between 600 and 6600 GHz. The authors stated that these resonances were not present in resting cells, cell homogenates, or nutrient solutions, and were therefore associated with active metabolic processes.

Webb et al. (1977) also noted that the ratio R of the intensities of the Raman antiStokes-to-Stokes lines must be close to unity for coherent nonequilibrium excitations, as compared with 0.55 for an oscillating system in thermal equilibrium. They reported obtaining values of R very nearly one for active E. coli B treated as in Webb and Stoneham (1977).

Cooper and Amer (1983) disputed the findings of Webb and Stoneham (1977) and Webb et al. (1977), indicating that cell suspensions yield spurious Raman lines in the frequency range of interest under certain conditions, particularly by Mie scattering from settled cell clumps, and that they were able thereby to reproduce many of the spectra reported by

Webb and coworkers. They noted that Webb and coworkers had used an experimental procedure that greatly enhances the probability of artifacts due to Mie scattering. Specifically, Cooper and Amer (1983) stated, citing Webb and Stoneham (1977): "Having determined that spectra could only be produced for about 6 min when a cell suspension was placed in a laser beam, they adopted a technique by which they scanned a given sample for only 3 min, and then changed to a fresh sample of cells from a master culture. This procedure would systematically introduce settling and mixing artifacts for each scan."

Cooper and Amer (1983) presented an example of Mie scattering from a settling suspension of commercial yeast cells in deionized water, which displayed numerous intense lines as cell-density fluctuations occurred and for which the intensity declined with time as settling and mixing of the suspension proceeded. They noted that this pattern matches the temporal activity recorded from resuspended E. coli cells under similar optical conditions. They also took issue with the theoretical basis for predicting a higher cross section for Raman scattering by intracellular molecules in that frequency range, because the energies required could be sufficient to rupture molecular covalent bonds.

Gandhi et al. (1980) used a solid-state computer-controlled system to perform swept-frequency measurements of RFR absorption by a variety of biological specimens in the range 26.5-90.0 GHz. The subranges 26.5-40.0 GHz, 40.0-60.0 GHz, and 60.0-90.0 GHz were covered by three similar circuits, and the circuit for each subrange had three IMPATT oscillator diodes (nine total), covering the following further subdivided ranges: 26.5-30.0, 30.0-35.0, 35.0-40.0, 40.0-46.0, 45.0-51.0, 50.0-60.0, 60.0-70.0, 70.0-80.0, and 80.0-90.0 GHz. Oscillator output was controlled by a ferrite modulator and was fed by waveguide to a sample holder through appropriate instrumentation. As output frequency was stepped during each sweep, the incident, reflected, and absorbed powers were measured and stored on magnetic tape. The stability of the system in amplitude and frequency was measured several times. Extreme amplitude variations were +/- 0.06 dB (+/- 1.4%) in 1-hr tests and +/- 0.16 dB (+/- 3.8%) in 15-hr tests. Typical frequency shifts were 1-6 ppm/min.

The sample holders were custom-fabricated thin-wall rectangular glass tubes 20 mm long and of precisely specified wall thickness, inside width, and outside height for each frequency subrange. Each holder was permanently inserted transversely through nonradiating slots in the narrow walls of the respective waveguide, occupying the entire cross section of the waveguide. In each case, the wall thickness was less than 2% of the free-space guide wavelength at the center frequency of the subrange. The samples had total thicknesses of the order of a tenth of the guide wavelength.

In recognition that biological material of high permittivity within the holder could increase the effective electrical width of the slots and thereby cause significant RFR leakage, reflected and transmitted powers were measured both with material extending 1 cm or more beyond either side of the waveguide and with material extending only to the

waveguide boundaries. This filling difference caused variations in reflectance and transmittance of no more than +/- 0.3 dB, so the extended fill was used subsequently.

Some measurements were also made with frozen samples. For this purpose, the sample holder consisted of a U-shaped section of waveguide filled with biological material for a total path length of 24 cm. The U-shaped section was immersed in a thermos of either liquid nitrogen or a mixture of dry ice and acetone. Short sections of thin-wall waveguide and heat sinks provided thermal isolation of the holder from the remainder of the measurement system.

Observation that absolute measurements of insertion loss and reflectance of biological specimens were largely dominated by the strong absorbance of the water in all samples (10-30 dB) led to measurements of relative insertion loss and reflectance, made by direct comparison with those of the solutions in which the specimens were either dissolved or suspended. A substitution method was used that allowed determining differences in relative insertion loss and reflectance of much less than 1 dB. This method involved the following steps. First, the digitized outputs of the diodes used to measure reflected and transmitted power were recorded during a frequency sweep with the sample in place. Then the comparison medium was substituted in the tube and the outputs were recorded during frequency sweeps for several settings of a variable attenuator in the circuit. Interpolation was then used to determine the difference in attenuation necessary to obtain the same diode outputs of transmitted and reflected power as with the sample in place, thus yielding relative insertion loss and relative reflectance. The authors indicated that the accuracy of the substitution procedure depended on the accuracy of the variable attenuator and width of the interpolation intervals, amplitude and frequency stability of the measurement system, and flatness of the oscillator power with frequency.

A solution of DNA from salmon sperm was prepared at 20 mg/ml in 0.1-M phosphate buffer. Solutions of RNA from whole yeast were prepared at 120, 36, and 12 mg/ml in 0.1-M NH4OH. The yeast-like organisms Candida albicans and C. krusei were grown overnight at room temperature; cells were washed from agar slants and suspended in dextrose broth; viability of some suspensions was assayed by standard plate-counting techniques. Suspensions of E. coli B were prepared from aerated broth cultures grown overnight; cells concentrated from nutrient broth by centrifugation were resuspended in the same medium and enumerated by standard plate-counting methods. Low-passage-level baby-hamster-kidney cells transformed with mouse sarcoma virus (BHK-21/C13) were grown in minimal essential medium (MEM) that contained 0.1% tryptose and 10% sterile calf serum; for the majority of studies, the cells were grown in plastic tissue culture flasks under a 5%-CO2 and 95%-air atmosphere; by standard cell-culture techniques, confluent cell populations were passaged or prepared for experiments by use of a 0.25% trypsin solution; whole-cell counts were made by hemocytometer.

The measurements of relative insertion loss and relative reflectance

were summarized in Table 47 (adapted from Table 2 of the paper). The comparison medium in each test was the solvent or suspending medium required for that sample. Five frequency sweeps were made over the specified frequency range for each sample, with a dwell time of 50 ms at each frequency. One-hundred frequencies were sampled in each of the nine frequency ranges corresponding to the nine IMPATT diodes; because the diodes differed in frequency range, the steps varied from extremes of 35 MHz in the band 26.5-30.0 GHz to 100 MHz in the band 80.0-90.0 GHz. The results of tests of water vs water, included in Table 47, demonstrated the relatively small degree of variation in these measurements.

TABLE 47: RELATIVE INSERTION LOSS AND REFLECTANCE FOR VARIOUS SAMPLES

Bio. sample	Comparison medium	Frequency range (GHz)	Mean	Min.	Max.
Relative insertion loss (dB)					
H2O	H2O	26.5-90.0	-0.024	-0.20	+0.16
MEM	H2O	26.5-90.0	-0.13	-0.38	+0.033
12.0% RNA	1-M NH4OH	26.5-90.0	-0.71	-1.16	+0.22
3.6% RNA	1-M NH4OH	26.5-90.0	-0.26	-1.37	+0.42
0.5% RNA	1-M NH4OH	26.5-90.0	+0.020	-0.76	+0.67
BHK-21/C13	MEM	26.5-60.0	-0.14	-0.47	+0.19
C. albicans	broth	26.5-60.0	-0.21	-0.52	0.00
C. albicans	broth	70.0-90.0	-0.12	-0.24	+0.032
C. krusei	broth	70.0-90.0	-0.13	-0.30	-0.002
E. coli	broth	70.0-90.0	-0.12	-0.21	-0.023
Relative reflectance (dB)					
H2O	H2O	26.5-90.0	-0.018	-0.39	+0.18
MEM	H2O	26.5-90.0	-0.020	-0.48	+0.29
12.0% RNA	1-M NH4OH	26.5-90.0	+0.11	-0.55	+0.69
3.6% RNA	1-M NH4OH	26.5-90.0	+0.0052	-0.18	+0.32
0.5% RNA	1-M NH4OH	26.5-90.0	-0.12	-1.64	+0.75
BHK-21/C13	MEM	26.5-60.0	+0.024	-0.32	+0.50
C. albicans	broth	26.5-60.0	+0.013	-0.38	+0.17

The authors noted that the results above strongly suggest that none of the biological materials examined absorb a significant amount of energy in the range 26.5-90.0 GHz. First, all means of relative insertion loss exceeding 0.02 dB were negative, as exemplified by those for 3.6% and 12.0% solutions of RNA, -0.26 dB and -0.71 dB, respectively. Since the decrease in this case was directly proportional to the amount of RNA in solution, it seems most probable that such decreases were ascribable to replacement of part of the water by one or more solutes that absorbed little or no RFR energy. Second, peak values of relative insertion loss and relative reflectance were very small. Since the values in Table 47 summarized the data from large numbers of different frequencies (200 for 70.0-90.0 GHz, 600 for 26.5-60.0 GHz, and 900 for 26.5-90.0 GHz), these results indicate that substantial resonance peaks were not observed at any of the frequencies sampled.

The authors noted that possible absorption peaks of moderate size (<= 2 dB) were sometimes observed at specific frequencies in a single scan, but were never replicated in subsequent scans of identical preparations. In addition, similar apparent peaks of moderate size were occasionally observed in control experiments in which a sample of medium was compared with itself (data not shown).

Representative scans of relative insertion loss and relative reflectance for C. albicans with the six IMPATT oscillators covering the range 26.5-60 GHz were presented to show that the departures from 0 db were due to system noise and were not significant.

More extensive tests were performed on C. krusei using only 6-MHz steps in the frequency range 41.2-41.8 GHz, within which range Grundler et al. (1977) had reported resonances in S. cerevisiae. The results were given in Table 48 (adapted from Table 3 of the paper), with N representing the number of samples tested:

TABLE 48: TESTS OF C. KRUSEI VS BROTH AT 41.2-41.8 GHZ

Concentration (million/ml)	Dwell time (ms)	Power (microwatts)	N	Mean	Min.	Max.
Relative insertion loss (dB)						
200	50	60.0	2	-0.054	-0.087	-0.012
200	5	60.0	1	-0.054	-0.091	-0.021
200	50	60.0	5	-0.068	-0.110	-0.038
200	50	10.0	5	-0.100	-0.170	-0.047
200	50	2.0	5	+0.025	-0.064	+0.150
20	50	60.0	1	-0.037	-0.089	+0.025
Relative reflectance (dB)						
200	50	60.0	2	-0.010	-0.076	+0.053
200	5	60.0	1	-0.037	-0.120	+0.069
200	50	60.0	5	+0.013	-0.017	+0.048
200	50	10.0	5	+0.012	-0.071	+0.100
200	50	2.0	5	+0.015	-0.210	+0.31
20	50	60.0	1	-0.012	-0.10	+0.091

The authors stated: "Although the frequency interval of 6 MHz should have been adequate to resolve the reported biological spectra, no significant differences were seen in experiments comparing yeast with its nutrient broth at any combination of cell concentration, dwell time, and incident power level (Table 3)." A representative plot of relative insertion loss vs frequency for one set of conditions was presented.

Similar experiments in the range 70.0-73.5 GHz were performed on BHK-21/C13 tumor cells on the basis that Webb and Booth (1971) had reported that tumor cells absorb 69-GHz, 72-GHz, and 75-GHz RFR more strongly, and absorb 66-GHz, 68-GHz, and 70-GHz RFR less strongly, than normal baby hamster kidney cells. Steps of 35 MHz were used. No significant

differences were seen when the cells were compared with their medium at any combination of cell concentration, dwell time, and incident power.

Additional experiments were also done in which relative insertion loss of a suspension of E. coli was compared with that of nutrient broth when a water jacket was used to maintain the sample holder at 37 deg C to ensure cell viability. In three sets of experiments, the power levels used were in the ranges 8.0-24.0, 0.18-0.35, and 1.0-4.0 microwatts. The results, presented graphically, showed no evidence of resonances.

Spectra were also obtained over the range 26.5-40.0 GHz for suspensions of BHK-21/C13 cells frozen in liquid nitrogen or dry ice, based on the point that RFR-absorption by solid water is much smaller than for liquid water and is not strongly temperature-dependent. The average insertion losses of solid and liquid water in this range were respectively 0.2 and 130.0 dB/cm. The mean absolute insertion loss and SD measured at each frequency in the range 26.5-40.0 GHz were displayed graphically for five samples each of frozen water, MEM, and suspension of BHK cells in medium containing 10% glycerol as a cryoprotectant.

The authors stated: "Such plots exhibited a very jagged appearance which was replicable with repeated frequency sweeps of the same frozen sample. However, each successive thawing and refreezing of the same sample changed the location of the peaks and troughs but not the jagged nature of the curves. It is felt, therefore, that the pattern of peaks and troughs results from interference phenomena associated with reflection from flaws in the frozen samples and not from some inherent property of the cells themselves. In all experiments carried out with frozen BHK cells, no evidence of frequency-specific absorption peaks was found, even though the sensitivity to absorption by the cells was markedly increased by this experimental manipulation."

However, they also concluded that: "In spite of the negative spectral measurements and the absence of effects on the BHK-21/C13 cells studied so far, the possibility of frequency-specific biological effects on other media cannot be ruled out. It is necessary to use great care in the design of both the microwave and biological aspects of experiments in this region of the electromagnetic spectrum where it is difficult to consistently generate and accurately measure microwave fields."

In Partlow et al. (1981), the first of three concurrent papers published subsequently, a novel in-vitro method for investigating cellular effects of millimeter waves was described, in which temperature-sensitive liquid crystals coated on mylar sheets were used to determine temperatures of cell monolayers. The speed of the method permits assessment of effects at many RFR power densities and frequencies on a single monolayer. In this study, the method was used to determine the effects of RFR at 41.8 or 74.0 GHz on both RNA and protein synthesis by monolayer cultures of BHK-21/C13 cells both during and right after exposure.

Approximate frequency ranges 37-42, 42-48, and 65-75 GHz were covered by three klystrons. The output of each klystron was fed to an open-

ended waveguide section appropriate for the specific frequency range, through an attenuator, a directional coupler and associated instrumentation for monitoring the incident power and frequency, a directional coupler and associated instrumentation for measuring reflected power, and an E-H tuner to minimize reflected power and optimize output-power coupling. The waveguide from the E-H tuner was passed through the wall of a walk-in incubator to the open-ended section via a 90-deg bend, to direct the RFR upward.

The authors stated: "Following a 30-minute warm-up period, power fluctuations were less than a few percent. Furthermore, frequency shifts were less than 0.05 GHz even after several hours of operation." The sample holder, described below, was placed on the open end of the waveguide. The intensities incident at specimen center were determined with thermistors in temperature-compensated mounts placed at the holder location and used in conjunction with a power meter. The intensity calculations accounted for both the frequency-dependent correction factor of the mounts and their effective areas.

Low-passage-level BHK-21/C13 cells certified as mycoplasma-free were obtained and were experimentally verified to be free of mycoplasma contamination. Each cell monolayer was cultured in a well 20 mm in diameter and 1 mm deep, fashioned by drilling a hole in the bottom of a standard 35-mm Falcon tissue culture dish. The bottom of each hole was covered with a polystyrene coverslip (25 mm in diameter; treated for tissue culture) held in place by paraffin. A template was used to mark the undersurface of each coverslip to permit positioning it precisely on the waveguide. Exposures were done in the aforementioned walk-in incubator. The klystrons were operated at maximum output, yielding spatially averaged power densities for 41.8 and 74.0 GHz of 320 and 450 mW/sq cm, respectively, at the undersurface. The cultures were exposed for 1 hr. Control cultures were sham-exposed.

The temperature of the culture medium at the level of the cell monolayer was estimated by use of mylar sheets coated with two types of liquid crystals that exhibited color changes in the ranges 35-40 and 40-45 deg C. The sheets were calibrated in a water bath containing a precision thermometer and a spectrophotometer that provided reference colors of known wavelengths. The results of calibration of the sheet for 35-40 deg C were displayed as a graph of color wavelength vs temperature. Readily discernible were differences of +/- 0.1 deg C in the subrange 36.5-38.5 deg C; above and below this subrange, the colors did not correspond to single wavelengths. The calibration curve for the range 40-45 deg C was not displayed, but was said to be similar.

The heating patterns produced by the RFR were determined by replacing the polystyrene coverslips in holders with discs cut from the liquid-crystal sheets. The authors noted that direct measurements of the RFR absorption in the two frequency bands had shown that the mylar substrate and the polystyrene coverslips are both essentially transparent to the RFR (dielectric constant 2.4). As a consequence, exposure of a disc of dry liquid-crystal material in the range 42-48 GHz at 320 mW/sq cm did

not change its color, and exposure in the range 65-75 GHz at 450 mW/sq cm yielded a color change in a small region just above the center of the waveguide aperture that corresponded to a rise less than 0.5 deg C.

By contrast, exposure to 41.8 GHz or 74.0 at these levels after addition of water to the wells resulted in distinct, complex color patterns. The corresponding temperature rises were displayed as contours vs transverse distance from the center of the waveguide aperture. Displayed also were graphs of temperature variation along the transverse central axis of each waveguide parallel to its long dimension. The curves were best-fitted with a cosine-square relation. They showed that the maximum power density at the center of the aperture was twice the spatially averaged value, i.e., for the 320- and 450-mW/sq-cm means, the central maxima were about 640 and 900 mW/sq cm.

In some experiments, a peristaltic pump was used to circulate 15 ml of culture medium at 650 ml/hr during RFR-exposure at maximum levels, which maintained the temperature of the cell monolayer constant at 37.2 deg C, as evidenced by the uniform color of the liquid crystals; recirculation was not used in other experiments, to assess the thermal effects of RFR.

The radiotracers used for protein and RNA were respectively tritiated methyl-methionine and uridine (final concentrations of 0.015 and 0.020 mCi/ml). Each labeled substrate was added to the RFR- and sham-exposed cultures and incubated for 1 hr either during or just after exposure. Following the incorporation period, the monolayer-bearing coverslips were removed, subjected to appropriate washing procedures to prevent the nonspecific binding of unincorporated label, and fixed.

Radioactivity in washed cell monolayers was shown to result from either incorporation of labeled methionine into protein or of labeled uridine into RNA in the following manner. An inhibitor of protein synthesis (cyclohexamide) or RNA synthesis (actinomycin D) was added to cultures 1 hr before addition of the appropriate labeled substrate, and the radioactivities of the cultures were compared with those for cultures without the inhibitor. To determine the absolute level of radiotracer incorporation per unit area in each cell monolayer, a rectangular portion of the monolayer was cut from each coverslip and its area was measured; after autoradiography (see below), the cell-bearing segment was dissolved in scintillation cocktail and counted, using an external-standards ratio to convert CPM to DPM.

Autoradiography of cell monolayers was done using a tritium-sensitive single-coated film. A plot of relative radioactivity (scale 0-1) vs relative optical density at 540 nm (scale 0-1) was displayed; regression analysis was used to obtain the curve of best fit, which was slightly nonlinear. Exposure times were then chosen to obtain a mean relative optical density of about 0.5. The radioactivity values corresponding to actual optical densities were corrected for the film nonlinearity.

In view of the previously noted spatial variation of temperature along the long dimension of the waveguide (in the absence of recirculation),

an optical microscope equipped with a narrow slit was used to measure the optical densities of contiguous 0.1-mm-wide regions along that axis, in expectation that different degrees of effect might be found. Optical densities were also determined for both the adjacent unexposed areas of each RFR-exposed culture and for sham-exposed cultures, to express the results in percentages of control values. All values were presented as means and SDs.

As expected, macromolecular synthesis of protein or RNA in BHK-21/C13 cell monolayers, evidenced by incorporation of tritiated methionine or uridine, was found to be unaffected by sham-exposure, either with or without recirculation. Displayed was a micrograph and autoradiograph of a cell monolayer labeled with methionine and exposed to 74.0-GHz RFR at 450 mW/sq cm with no medium recirculation and stained with toluide blue after being autoradiographed; the micrograph showed massive destruction; the autoradiograph showed that no methionine incorporation had occurred in the central region. A similar micrograph of a monolayer exposed to 41.8-GHz RFR at 320 mW/sq cm exhibited no discernible damage, but the autoradiograph indicated that incorporation of methionine into protein was greatly depressed in the central region. The authors noted that results similar to those for 41.8-GHz RFR at 320 mW/sq cm were obtained with 74.0 GHz at the same level (no data given), and they surmised that the damage observed with 74.0-GHz RFR at 450 mW/sq cm was related to RFR-level and not to RFR-frequency.

In the previous experiments, monolayer incubation was done in 0.4 ml of medium. In the next experiment, to extend the range of usable power densities without killing the cells, incubation was done with 2 ml of labeled-methionine medium (a larger heat sink) during exposure without recirculation to 41.8-GHz RFR at 400, 800, 1200, 1600, or 2000 mW/sq cm at waveguide center. The 2000-mW/sq-cm level resulted in destruction of the central region of the monolayer (data not shown). For each of the other RFR levels, the spatial variation of relative optical density fitted a cosine-square curve, with the highest percentage inhibition of methionine incorporation into protein (relative to control) at waveguide center. Replotting the data for the four power densities revealed a linear relationship between percentage inhibition and power density.

Monolayers (incubated in 0.4 ml of medium)) cooled by recirculation during exposure to 41.8-GHz RFR at 320 mW/sq cm or to 74.0-GHz RFR at 450 mW/sq cm exhibited no inhibition of protein or RNA synthesis, from which the authors concluded that the alterations of synthesis observed for cultures not maintained at 37.2 deg C must have been due entirely to RFR-induced heating of the cells.

The authors concluded: "Our results demonstrate that synthesis of RNA and protein by BHK-21/C13 cells was unaffected by exposure to 41.8 or 74.0 GHz radiation for 1 hour under conditions that prevented microwave-induced heating. The high levels of radiation incident on the cells make it unlikely that we failed to observe a biological effect because of inadequate intensity. Since macromolecular synthesis was examined both during and after acute exposure, both transient and persistent

biological effects were excluded. Our results further demonstrate that microwave-induced heating profoundly affected synthesis of both RNA and protein. Thus, the absence of an observed effect in cultures maintained at normal temperature during irradiation was not due to the inability of our measuring system to detect such a change."

In Stensaas et al. (1981), the second of the two papers, the method for exposing monolayers of BHK-21/C13 cells to 41.8-GHz at 320 mW/sq cm (640 mW/sq cm in the central area) or 74.0-GHz RFR at 450 mW/sq cm (900 mW/sq cm in the central area) was the same (with or without recirculating the medium), but no radiotracers were added to the culture medium. Instead, cell ultrastructures were examined by scanning and transmission electron microscopy after 1-hr exposure or sham-exposure.

A scanning electron micrograph of the central cell area of a specimen exposed to 74.0-GHz RFR at 900 mW/sq cm while being maintained at 37.2 deg C by recirculation and one for a sham-exposed specimen were shown. The two micrographs were very similar; frequency of fiber projections, appearance of cell-cell interfaces, nature of attachment to substrate, particle density on upper cell surfaces, and extent of confluency were essentially the same in both. Transmission electron micrographs from a pair of specimens treated in the same manner exhibited ultrastructural characteristics that were similar in both the nucleus (heterochromatin distribution and number of nucleoli) and cytoplasm (rough and smooth endoplasmic reticulum, mitochondria, cytoplasmic filaments, and free ribosomes). In addition, no differences were observed in the appearance of the plasma membrane or in the incidence and distribution of filopodia or of coated vesicles on or near the upper cell surface. Non-central regions of such specimens, where the power densities were lower, were likewise unaffected by the RFR. Similar results were obtained for the central regions of cell monolayers exposed to 41.8 GHz at 640 mW/sq cm while being maintained at 37.2 deg C by recirculation.

For cell monolayers exposed to RFR at either frequency and corresponding mean power density without cooling by medium recirculation, the central-region temperature reached approximately 42 deg C. The authors stated: "Nevertheless, no ultrastructural effects were seen by either scanning ot transmission electron microscopy at any point along the longer axis of the waveguide aperture, even though the cell monolayer was substantially heated for a period of 1 hour."

For an uncooled cell monolayer exposed to 41.8-GHz RFR at a mean power density of 1000 mW/sq cm (2000 mW/sq cm in the central region), scanning electron microscopy revealed profound morphological changes. Regions of the exposed monolayer midway between waveguide center and edge exhibited decreased cellular attachment to the substrate, increased space between neighboring cells, increased rounding of the cells, and an increased number of broken cell processes, relative to those for the unexposed peripheral regions of the same monolayer. Cells in the central region were damaged more severely; they appeared to have been heat-killed and all were almost completely detached from the substrate.

Transmission electron microscopy was used to examine the central region of an uncooled monolayer exposed for 1 hr to 41.8-GHz RFR at mean power densities of 600, 800, and 1000 mW/sq cm (1200, 1600, and 2000 mW/sq cm in the central region) and that of a sham-exposed monolayer. Cellular damage in the RFR-exposed monolayer was proportional to power density; increased clumpings of heterochromatin in the nuclei and appearance of large vesicles in the cytoplasm were the most obvious effects. If culture fixation was delayed for 1 hr after exposure, the central cells exposed at 1600 mW/sq cm or higher always became detached.

The temperature in the central region of the monolayer rose to about 44 deg C within seconds after initiation of exposure at 600 mW/sq cm (1200 mW/sq cm in the center); for exposure at 800 or 1000 mW/sq cm (1600 or 2000 mW/sq cm in the center), the temperature in the central region rose to 45 deg C or higher. Therefore, the authors surmised that threshold temperature for RFR-induced damage detectable by electron microscopy was between 44 and 45 deg C. They also showed micrographs indicating that similar results were obtained for uncooled cell monolayers exposed to 74.0-GHz RFR at 450 mW/sq cm (900 mW/sq cm in the central region), the highest available level, provided that the ambient temperature in the walk-in incubator was raised to 38.5 deg C. Under these conditions, the temperature in the central region rose to about 44.5 deg C.

The authors of this study concluded that the RFR-induced ultrastructural changes seen in BHK-21/C13 cells were due exclusively to heating.

In the third paper, Bush et al. (1981) used the same method for exposing monolayers of BHK-21/C13 cells to RFR. However, the endpoints sought were frequency-specific effects and existence of amplitude windows for protein synthesis as determined by incorporation of tritiated methionine (with autoradiography). For these purposes, monolayers of cells were exposed to RFR in the ranges 38-48 GHz and 65-75 GHz in 0.1-GHz steps, a total of 202 frequencies, for 15 min each, during which the incubation with tritiated methionine was done and the monolayers were maintained at 37.2 deg C by medium recirculation. The mean power densities in the two ranges were 292 and 177 mW/sq cm, respectively, the available maxima.

Relative optical densities in 31 contiguous regions (0.1-mm wide) along the longer central axis of the waveguide aperture were measured for the autoradiographs obtained of the monolayers exposed in the range 38-48 GHz, and similarly for 48 contiguous regions of those exposed in the range 65-75 GHz. In each case, the results for four exposed monolayers were averaged. Scintillation counting was used to determine absolute levels of methionine incorporation (in DPM/sq mm).

For the monolayers exposed in the range 38-48 GHz, the distributions of relative optical density along the longer central waveguide axis were displayed for each frequency. The maxima and minima in each spatial sweep were all within +/- 10% of control level and the differences were said to be statistically nonsignificant.

Statistical techniques designed to test for the presence of biological effects not discernible because of their small amplitude were used. The central-axial distribution of relative optical density for each exposed monolayer was divided into sequential 4% increments, the results within each increment for all exposed monolayers were pooled, and a histogram of the frequency of each relative optical density was constructed. This process was also used for all of the sham-exposed monolayers and the two histograms were compared. The two distributions were almost identical; the means and SEs for the control and exposed distributions were 100.16 +/- 0.21 (n=1008) and 100.28 +/- 0.05 (n=18,816), respectively; variance comparison yielded an F statistic of 1.046. Evidently, the two data sets were from a common population.

Similar results and conclusions were obtained for the monolayers exposed in the range 65-75 GHz. The means and SEs for the control and exposure histograms were 100.27 +/- 0.26 (n=837) and 100.27 +/- 0.07 (n=12,152), respectively, and the F statistic was 1.035.

In their discussion, the authors noted that protein synthesis was chosen as an indicator of possible biological effects of millimeter waves because it is "exquisitely sensitive" to changes in many aspects of cell metabolism, and that great care was taken to avoid possible artifactual effects such as RFR-induced heating. Yet, no evidence was found for the existence of any athermal frequency-selective effect on the synthesis of protein by BKK-21/C13 cells.

For studies of interactions between cellular constituents and RFR at frequencies below as well as within the submillimeter range, Swicord and Davis (1983) described a new method for measuring RFR absorption by an optically transparent liquid. A single-frequency (He-Ne) laser beam is split into two beams in a Mach-Zehnder interferometer; after traversing approximately equal path lengths, the two beams are rendered collinear again with another splitter for photodetection. The sample (in a 1-cm-pathlength cell) is inserted in one of the two paths; a piezoelectric (PZT) transducer mounted on the back side of the mirror in the other path is used for alignment and for adjustment to obtain phase quadrature between the two beams.

The novel feature of the method is injection of a short RFR pulse into the sample. The temperature rise thus caused in the sample produces a density (refractive-index) variation observable as a phase fluctuation in the signal detected. In this study, injection of the RFR was done with a special section of waveguide vertically immersed in the sample. The waveguide's upper end was shorted and was fed by coax-to-waveguide adapter. The section was filled with solid dielectric for a distance of 5 cm downward (partially immersed) and was open for the remainder of its length (totally immersed in the sample). Slots cut in the centers of the broad walls, about 0.8 mm wide and 2 cm long from the dielectric-liquid interface to the open end, permitted movement of the transverse laser beam (parallel to the maximum E-field) along the propagation direction and therefore measurements of absorption as a function of distance from the dielectric-liquid interface.

Phase-change-detection sensitivity is enhanced by applying a small sinusoidal voltage to the piezoelectric transducer, which produces mirror vibrations of a few nanometers and a sinusoidal heterodyne signal. The method is called "phase-fluctuation-optical-heterodyne (PFLOH) spectroscopy." To maintain the sensitivity constant against changes in ambient temperature and pressure, the dc component of the heterodyne signal is used via a servo system to apply a correction to the piezoelectric transducer.

Using the PFLOH system, the absorption properties of aqueous solutions of DNA extracted from E. coli were measured in the frequency range 8-12 GHz. A plot of attenuation coefficient for DNA vs frequency exhibited no resonances but the values were found to increase linearly from about 0.4 per mm at 8 GHz to about 0.6 per mm at 12 GHz, all of which were considerably higher than for Ringer's solution or for deionized water at corresponding frequencies. The ratio of the attenuation coefficient for DNA to that of deionized water was linear with frequency and of negative slope, with values of about 1.4 at 8 GHz and about 1.1 at 12 GHz.

Edwards et al. (1985) subsequently reported that biochemical analysis of the samples of E. coli DNA in aqueous solution used in previous studies showed the presence of significant amounts of RNA and protein impurities and that the DNA had been extensively sheared by improper handling. In addition, the enhanced broadband absorption observed for such samples in the range 8-12 GHz was absent for carefully prepared DNA samples of high molecular weight (exceeding 200,000 base pairs) and free of protein and RNA.

In the present study, the authors examined theories of acoustic modes in long molecules that predicted length-dependent resonances in DNA and endeavored to experimentally demonstrate the existence of such modes. Accordingly, they prepared solutions of cloned DNA of uniform length and known sequence from E. coli by standard plasmid extraction and isolation procedures, and used standard dielectrometry to determine the absorption characteristics of such samples in the frequency range 2-9 GHz. (Some of the same information was also presented in Edwards et al., 1984.)

Based on acoustic velocity data in DNA (Hakim et al., 1984), samples of DNA were prepared that had lengths in the range up to a few wavelengths of sound waves on the double helix Among the experimental results was a plot of relative absorption vs RFR frequency (2-9 GHz) for a solution of supercoiled circular DNA molecules having 2,740 bp; the plot showed sharp resonant absorption peaks at 2.55, 4.00, 6.60, and 8.75 GHz. A plot for a solution of 2,740-bp linearized DNA showed resonances at 2.75, 4.15, and 5.60 GHz and a plot for an equimolar solution of 948-bp and 1,792-bp linear DNA fragments had resonances at 2.65 and 4.10 GHz. The authors, noting that the occurrence of such resonances is not in accord with recent models that include damping of normal modes by the solvent (Dorfman and Van Zandt, 1983, 1984), stated: "It is surprising to observe such sharp microwave resonances in dense solutions at room temperature. It has generally been believed that such resonances should be overdamped. If not overdamped, the resonances were

expected to be heavily damped, and thus very broad."

The authors observed that the three resonant frequencies for the 2,740-bp linearized DNA were in approximate ratio 3:5:7 and they associated these resonances with those predicted from an acoustic model to have a fundamental and odd harmonics (1:3:5:7). However, they noted that the expected fundamental resonance near 0.9 GHz was conspicuously absent and offered possible reasons for its absence.

Among other investigations on effects of RFR on bacterial growth was that of Hamrick and Butler (1973). They exposed four strains of E. coli and one strain of Pseudomonas aeruginosa to 2.45-GHz far-field CW RFR for 12 hr at 60 mW/sq cm in an RFR-absorber-lined horn system (McRee and Walsh, 1971) and compared the resulting growth curves with those for unexposed but otherwise similarly treated control cultures of each strain.

Following overnight incubation of an appropriately diluted culture of each strain at 37 deg C, 0.1 ml therefrom was used to inoculate 30 ml of nutrient broth in two plastic tissue culture flasks, one for exposure and the other for control. As determined by colony counts, the initial concentrations in the flasks were 100 to 1000 cells per ml and the final titers after 12 hr of exposure were 10 million to 100 million cells per ml. The RFR power density was adjusted to maintain sample temperature at 37 +/- 0.5 deg C, as measured with a shielded thermistor placed in the center of the flask.

The authors noted that temperature was fairly uniform over the entire flask (+/- 0.6 deg C) and that RFR had little effect on thermistor readings (+/- 0.2 deg C), determined by switching the RFR on and off. Moreover, RFR exposure in the presence and absence of the thermocouple also yielded small temperature differences (+/- 0.2 deg C). The RFR-absorption rate by the medium in a flask was determined by heating the medium with RFR to 44 deg C, recording the temperature vs time as the medium cooled, and using the slope of the resulting cooling curve at 37 deg C in the heat-loss equation. At an incident power density of 60 mW/sq cm (measured with a Narda probe), for example, the absorbed power per unit surface area (determined from the slope of the cooling curve) was about 41 mW/sq cm, and the absorbed power per unit volume was 29.2 mW/cu cm [i.e., the SAR was about 29 W/kg]. The control flasks were treated in an incubator at 37 deg C.

After each 2 hr of treatment, 0.5-ml samples were taken and serially diluted in phosphate buffer, and 0.1-ml or 1-ml aliquots thereof were moved by pipette into sterile petri plates, 20 ml of melted nutrient agar at 50 deg C was poured into each plate, the plates were swirled to distribute the bacteria uniformly, and colony counts were made after incubation of the plates for 24 hr at 37 deg C. Results were expressed as semilog plots of colony counts vs time.

The curve of growth for E. coli strain 9637 exposed to RFR at 60 mW/sq cm (29 W/kg) and that for the same strain heated in the incubator at 37 deg C were S-shaped (slow initial growth rate followed by rapid growth,

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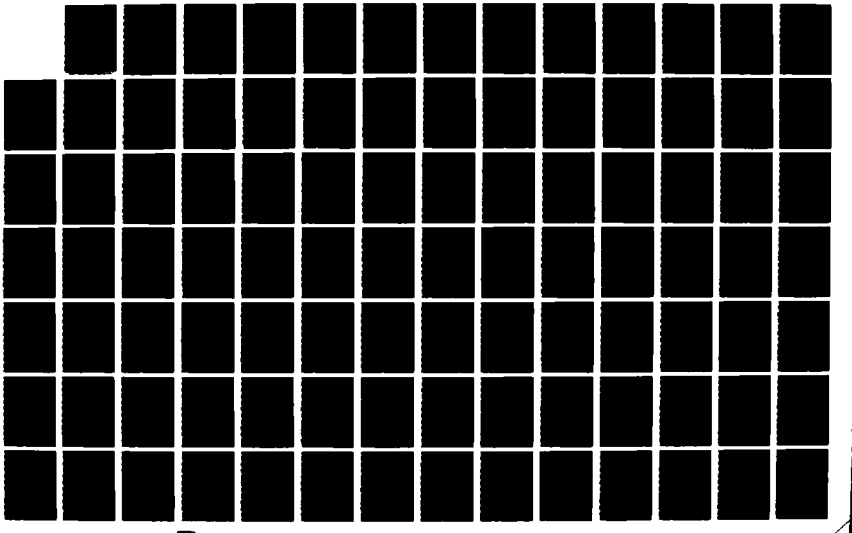

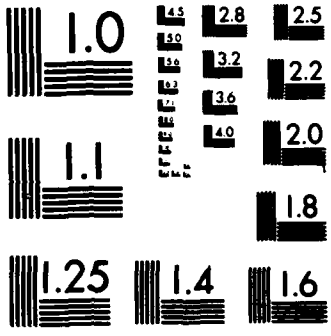

reaching a plateau at about the last 2 hr) covering a range more than five orders of magnitude. The RFR curve was slightly higher than the incubator curve, but the authors noted that the difference was within the limits of experimental error. Similar pairs of curves were obtained for E. coli strains 23224, 11303, and 12407, but the initial and plateau counts differed from strain to strain. The RFR and incubator curves for P. aeruginosa strain 25327 at 37 deg C were also virtually coincident, but exhibited only about four orders of magnitude of growth during the 12 hr without attaining a plateau.

A flask of E. coli strain 23224 was exposed for 12 hr at an absorbed dose rate of 259 mW/sq cm (SAR about 185 W/kg). To maintain the culture at 37 deg C during exposure, the flask was wrapped in wet gauze and air was blown over the surface. Again, the difference between the RFR and incubator curves was negligible. To permit a still higher RFR exposure level, growth was determined at 44 deg C for flasks of E. coli strain 9637 heated by RFR and incubator. The absorbed RFR level was about 450 mW/sq cm (SAR about 320 W/kg). Once more, there was no appreciable difference between the curves.

To show the dependence of growth on temperature, curves for E. coli strain 9637 grown in flasks for 24 hr in an incubator at 34, 37, and 40 deg C were displayed. As expected, the growth rates at 34 and 40 deg C were less than at 37 deg C. The data also showed that a 3-deg-C change is readily detectable in the growth curves.

Szmigielski et al. (1975b) sought possible effects of RFR on continuous cell lines growing in vitro, including alterations of cell function and virus replication in such cells. The cell system used was a monolayer of WISH cells on a glass surface, reputed to comprise a very homogeneous cell population. Used for infecting WISH cells was parainfluenza-3, a myxovirus (characterized by an RNA nucleocapsid in a loose membrane and the ability to agglutinate erythrocytes).

WISH cells passaged once every three days of growth on a medium composed of 15% Hanks' balanced salt solution, 75% Parker's solution, 10% fetal calf serum, and kanamycin were exposed, 24 hr after passage, to 3-GHz CW RFR from a horizontally radiating conical horn 30 cm in diameter within an anechoic chamber. For exposure, a monolayer of cells was deposited on the vertical internal surface facing the horn of a plaque or Legroux flask at a distance of 230 cm from the horn's mouth (far field). The source was a 500-W magnetron, but its type was not stated.

A 1-cm elementary dipole was used as a miniprobe to measure the power densities at several locations within and outside an empty flask and one that held a monolayer of cells. For an empty flask with 20 mW/sq cm at the outside front surface (toward the source), the value at the inside front surface was 14.5 mW/sq cm, from which the power-density decrease in the glass was stated to be 1.35 dB. (By calculation, the decrease was 1.40 dB, but the difference is inconsequential.) Also given was the power density at the posterior surface of the empty flask, 7.5 mW/sq cm, for a total decrease of 4.24 dB. For a monolayer-bearing flask with 20

mW/sq cm at its outside front surface, the corresponding values at the inside front and posterior surfaces were respectively 12.5 and 6.5 mW/sq cm, for a total decrease of 4.88 dB. The authors gave no interpretation of these decreases in terms of specific absorption rate by the cells.

WISH cultures were exposed for 30 min at 5 or 20 mW/sq cm [presumably levels at the outside front surface], and cells (treated with various vital stains) were given morphologic examination by microscope and cytochemical evaluations 1, 24, and 48 hr after exposure. Control cultures were similarly treated.

Other WISH cultures were infected with parainfluenza-3 virus 1 or 24 hr after exposure to RFR, with control cultures similarly treated; 48 hr after infection, cells were examined morphologically and assessed for virus multiplication. In other experiments, cultures were infected with the virus first, then exposed for 30 min to the RFR 2, 8, or 16 hr after infection, and assessed for virus multiplication 48 hr after infection.

Morphologic examination of control WISH cultures that were not infected with the virus yielded the following results: Only small percentages of cells were stained with nigrosine, viable cells without any symptoms of degeneration were noted, and no diffuse absorption of Janus green B or neutral red was evident. Cytochemical tests for nitro blue tetrazolium reduction revealed three distinguishable classes of cells: those having large granules and blue-stained formazin deposits, cells having small distinct granules without diffuse staining, and cells that were not stained. Staining with succinic dehydrogenase yielded the same three classes of reactivity.

By contrast, 1 hr after 30-min exposure of uninfected WISH cultures at 20 mW/sq cm, 30-38% of the cells were stained with nigrosine, and the majority of the cells had numerous small round vacuoles; the nitro blue tetrazolium reduction rate was markedly lower; and only 10-15% of the cells showed large granules, deposits of formazin, and diffuse staining, as compared with 50-70% for the control cultures. Also, the percentage of cells with succinic dehydrogenase activity was much lower than for control cultures. Cell function partially returned to normal 24 hr after exposure: the percentage of nigrosine-stained cells decreased to nearly control value; vacuoles stained with Janus green B were still evident in most cells, but diffuse staining with the same dye or with neutral red was seen in only a few cells. The succinic dehydrogenase activity was lower than for control cultures, but was higher than for cells 1 hr postexposure.

Uninfected WISH cultures exposed for 30 min at 5 mW/sq cm exhibited no differences in the percentage of cells stained with nigrosine relative to controls. The only deviation from normal was the presence, in 30% of the cells, of large granules stained with Janus green B. The exposed cultures yielded slightly higher percentages of cells than the control cultures for succinic dehydrogenase activity.

Virus multiplications were given as numbers of infectious particles

per ml, and the results for the cultures inoculated with the virus after and before RFR exposure and for the corresponding controls were displayed in Table 49 (Table 4 of the paper). For convenience, the table was adapted below to express virus concentration as log (base 10) of the number of infectious particles per ml (LVC):

TABLE 49: LOG VIRUS CONCENTRATION (LVC)

	Control LVC	5 mW/sq cm LVC	20 mW/sq cm LVC
Post-exposure interval before inoculation (hr)			
1	5.00	5.77	3.67
24	3.67	3.67	4.50
Post-inoculation interval before exposure (hr)			
2	4.53	5.33	
8	4.53	5.50	
16	4.53	5.50	

As seen above, the LVC values for 1-hr post-exposure inoculation were 5.00 (100,000 particles per ml) for controls, 5.77 (roughly 600,000 particles per ml) for 5 mW/sq cm, but only 3.67 (about 4700 particles per ml) for 20 mW/sq cm, thus showing no clear dependence on dose-rate. The authors noted that the dominant feature of the 20 mW/sq-cm culture was the presence of large multinuclear cells, with very few syncytia (multinucleate masses of protoplasm produced by the merging of cells) visible. The 24-hr post-exposure inoculation value for 5 mW/sq cm was the same as for controls (3.67), but was higher for 20 mW/sq cm (4.50). These 24-hr changes were accompanied by the appearance of large numbers of nigrosine-stained cells, decreases in nitro blue tetrazolium, and increased percentages of cells showing succinic dehydrogenase activity in the form of large granules and formazin deposits. Also, multiple syncytia were formed.

In the experiments involving inoculation of cultures at the indicated intervals before exposure at 5 mW/sq cm, the LVCs for both the exposed and control cultures appeared to be independent of the time interval, (4.53 at 2, 8, and 16 hr for the controls, and respectively 5.33, 5.50, and 5.50 for the exposed cultures) but the latter were larger than the former. (Similar data were not presented for exposure at 20 mW/sq cm.)

The authors summarized their findings as follows: "Continuous cell cultures, WISH cells, manifested temporal functional disturbances, observed with morphologic and virologic techniques, after a 30-min irradiation with 3 GHz microwaves at 5 or 20 mW/sq cm power densities, as measured on culture flask surfaces. The rise in both nitro blue tetrazolium reduction and myxovirus multiplication rates in cultures exposed to 5 mW/sq cm suggests that this radiation dose stimulated cell metabolism, especially since no changes in supravital staining and phase-contrast observations were found.

"Conversely, a 30-min irradiation at 20 mW/sq cm resulted in increased membrane permeability (staining with nigrosine, diffuse staining with Janus green B and neutral red), decreased nitro blue tetrazolium reduction rate and succinic dehydrogenase activity, and the appearance of widespread cellular vacuolization. These findings were accompanied by inhibition of myxovirus replication. The above phenomena all suggest severe cellular injury, with a possible disturbing effect on the mitochondrial system. Surprisingly enough, 24 and 48 hr after irradiation at 20 mW/sq cm, partial regeneration of the cultures was observed; the virus replication rate also returned to normal.

"Because staining with nigrosine and cytoplasmic vacuolization are believed to be the symptoms of irreversible cellular injury, it is possible that only certain cells were injured at 20 mW/sq cm and that regeneration is possible by proliferation of the unaffected cells.

"Inasmuch as WISH cells react differently to 5 or 20 mW/sq cm power densities, quantitation of the energy absorbed becomes a problem. Power density measurements from free field conditions, empty flasks placed in the field, and flasks with WISH cell monolayers only yielded part of the answer. At the 20 mW/sq cm power density, as measured on the flask surface, values of 7.5 and 6.5 mW/sq cm were found on the other side of the empty and cell monolayer flasks, respectively. This difference may partially be due to increased wave reflection and to their absorption in the monolayer; more precise measurement techniques are needed to distinguish the effects of both components."

The response to a question following oral presentation of this paper on whether temperatures were measured was: "We made some measurements of culture media temperatures, and elevations of about 3 or 4 deg C were seen in the cells. These cells normally live at 37 deg C. At the beginning of the experiment the culture was at 25 deg C, and after irradiation, the temperature had increased to 29-30 deg C, which is still below normal for the cells. It is well known that cell cultures tolerate temperature decreases of as much as 4 deg C very well, whereas they tolerate temperatures above 39 deg C very poorly."

As is evident, the results of this study were not definitive. Control over experimental conditions appears to have been inadequate, rendering any possible dependence of findings on power density and/or temperature obscure at best. In addition, the numbers of cultures studied under each set of conditions was not stated and no statistical treatment of the results was given.

Paulsson et al. (1977) investigated whether the chemical and functional properties of cellular microtubules (a structural component of cells that is composed primarily of the polymerized protein tubulin) would be affected by exposure to RFR in vitro. The authors noted that tubulin can be extracted from microtubule-rich tissues (e.g., the brain) and can be polymerized to microtubules in vitro, and that the antimitotic drug colchicine binds specifically to tubulin and inhibits its polymerization to microtubules. They also noted that colchicine has a blocking effect

on axonal transport of intracellular materials within nerve fibers. Thus, they investigated the following:

1) Colchicine-binding properties of RFR-exposed brain extracts.
2) Assembly of microtubules in brain extracts during RFR-exposure.
3) Effect of RFR-exposure on protein transport in nerve axons in vitro.

The RFR source was a magnetron that emitted 1.4-microsecond pulses of 3.1-GHz RFR at a peak power of 250 kW and pulse repetition frequencies in the range 100-300 pps. The magnetron was coupled to a rectangular horn of face dimensions 15.7 x 13.5 cm. For exposure, a sample within the container described below was placed 40 cm from the horn (about 0.8 of the conventional far-field distance).

The biological materials studied were obtained from euthanized albino rabbits. For the colchicine-binding aspect, the brain was excised, chilled on ice, and homogenized at 0 deg C in sodium phosphate buffer containing appropriate concentrations of sucrose, guanosine triphosphate (GTP), and magnesium chloride. After the homogenate was centrifuged for 1 hr at 4 deg C, 1.2-ml quantities of supernatant were transferred into a pair of reentrant polytetrafluorethylene (PTFE) containers that had inner rectangular dimensions 2.4 x 2.1 cm transverse to, and 0.3 cm along, the RFR-propagation direction, and were heated to 34 deg C. The containers were thermally insulated in styrenefoam [sic], and one of each pair was exposed to pulsed RFR (200 pps) at a mean power density (MPD) of 24 mW/sq cm for 300 or 480 seconds, or at 52 mW/sq cm for 600 or 900 seconds, while the other one of each pair was kept as a control.

The normalized SAR was determined from thermocouple measurements of the temperature vs time of a 1.5-ml sample in such a container (of known geometry and dielectric properties) following exposure for 1 min at 145 mW/sq cm. The result was 4.6 W/l (about 4.6 W/kg) per mW/sq cm, from which the SARs for MPDs of 24 and 52 mW/sq cm were 110 and 240 W/l. The authors noted that at 52 mW/sq cm, sample temperature increased by 4 deg C during a 900-second exposure, so the starting temperature (34 deg C) was chosen to ensure that the final temperature would not exceed body temperature of the normal rabbit.

Colchicine binding after exposure was assayed by adding 5 microliters of a mixture of tritiated colchicine (2 Ci/mmole) and vinblastine to 0.2-ml aliquots of exposed sample to attain final colchicine and vinblastine concentrations of 2.5 and 10 micromoles, respectively. These solutions were then incubated for 60 min at 37 deg C, after which they were put on ice to stop the binding reaction. After the latter step, the solutions were passed through a Millipore microanalysis apparatus, free colchicine was removed, the filter discs were placed in vials that contained 10 ml of Butler's scintillation fluid, and the radioactivities were measured by liquid scintillation counting. Aliquots of the control samples were similarly treated. The results, each expressed as the mean ratio of the difference in bound colchicine between control and exposed samples to control bound colchicine (in percent), [denoted R], were displayed in Table 50 (adapted from Table 1 of the paper):

TABLE 50: RFR EFFECTS ON COLCHICINE BINDING ACTIVITY IN RABBIT BRAIN

MPD (mW/sq cm)	SAR (W/l)	Duration (seconds)	No. of samples	R (%)	SE
24	112	300	4 + 4	1	10
24	112	480	4 + 4	-12	6
52	243	600	5 + 5	9	7
52	243	600	5 + 5	-4	13
52	243	900	5 + 5	-8	13

The authors concluded that the RFR in the range of levels used had no significant effect on colchicine binding activity.

Viscometry was used to measure polymerization of tubulin to microtubules in appropriately prepared extracts of rabbit brains excised, chilled on ice, and homogenized at 0 deg C. Just before the extracts were put into the 34-deg-C PTFE containers, GTP was added to a concentration of 1 mM. The pulsed-RFR-exposures (200 pps) were for 10 min at an MPD of 90 mW/sq cm (430 W/l), which increased the temperature by 7 deg C. At exposure end, the specific viscosity of each sample, defined as the ratio of the difference in running times of the sample and buffer in the viscometer to the running time of the buffer was measured at 37 deg C at intervals of 2 min for about 30 min, and the specific viscosities (%) were plotted vs time. The authors noted that a few points more than 10% larger than their respective preceding points were ascribable to nonspecific protein aggregation and were discarded. A representative graph was given, which showed a mean specific viscosity of about 5% before exposure, rapid rise to about 38% at exposure end, and post-exposure viscosity measurements that yielded a plateau of slightly negative slope.

Control samples were similarly treated and the percentage differences between the specific viscosity of each control sample and its paired exposed sample at each point in the plateau region were tabulated and averaged. The differences ranged from -23.8% to +20.0%, with a mean (for 16 such differences) of -4.2% +/- 2.7% (SE), a statistically nonsignificant result.

To investigate whether RFR-exposure affects protein transport in nerve axons in vitro, 10 rabbit vagus nerves and nodose ganglia were incubated for 24 hr in two PTFE blocks, each block containing five two-compartment chambers (a two-compartment chamber for each nerve trunk and ganglion). The volume of medium in each nerve-trunk compartment was 0.8 ml and that in each ganglion compartment was 0.04 ml. The proteins were labeled by adding 5 microcuries of tritiated leucine (58 Ci/mmole) to the medium in the ganglion compartment; the labeled proteins flowed along the nerve to be accumulated at a ligature on the nerve.

One block was exposed to the pulsed RFR (100 pps) at 30 mW/sq cm for the entire 24-hr incubation period, with the other as control. Circula-

ting oil was used to hold the two blocks at about 38.5 deg C; the temperature difference between them was less than 1 deg C. At the end of the 24-hr incubation period, each nerve was cut into 0.5-cm segments and each was assayed for radioactive protein. The radioactivity of each segment was normalized to the total radioactivity of a 4-cm length, to obtain the protein profile along that length. The value in the segment just before the ligature was taken as a measure of the protein-transport capability of the nerve, and the percentage differences between control and exposed samples were averaged.

In one of two experiments, the E-vector of the RFR was aligned parallel to the nerves, which yielded a mean difference of 11.1% +/- 17.4% (SE). In the other experiment, the E-vector was aligned perpendicular to the nerves; the resulting protein profile was similar to that of the first experiment, but with about half the protein accumulation. The mean difference was 12.5% +/- 18.3%. The SARs of the samples were estimated by calculation of RFR-absorption in a 1.5-mm-thick water slab to be in the range 10-100 W/1.

The authors concluded that..."3.1 GHz pulsed microwave radiation has no strong effect on rabbit brain microtubules in vitro at power levels where other biological effects have been reported."

Ortner et al. (1983) indicated that in a previous study (Ortner et al., 1981b), they had found that 2.45-GHz RFR at 600 W/kg affected the secondary structure of human erythrocyte spectrin, a reversible effect, but they were unable to correlate the effect with any change in spectrin function. Therefore, they sought to determine whether such reversible changes comprised a generalized effect of RFR on large macromolecular assemblies, exemplified by microtubules.

The authors noted that tubulin, the major component of the microtubular wall is a 6S, 110,000-dalton protein, and that under proper in-vitro conditions (37 deg C in the presence of guanosine 5'-triphosphate), purified tubulin and accessory proteins assemble or polymerize into microtubules that are morphologically identical with those studied in vivo. Cooling to 4 deg C or the addition of Ca++ causes the assembled microtubules to depolymerize back into 6S tubulin and oligomers.

Microtubular protein was purified from fresh calf brains by successive cycles of polymerization and depolymerization and stored at -20 deg C in buffer. The protein was determined by the Biuret method with bovine serum albumin as a standard. Tubulin was separated from the accessory proteins by chromatography. The purities of the microtubular-protein and purified-tubulin preparations were determined by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE).

Exposures were to 2.45-GHz CW RFR at 20 or 200 W/kg. The sample chamber was a quartz cylinder inserted in a direction of maximum E field of a fluid-filled waveguide section. The waveguide impedance was matched to that of air by a quarter-wave dielectric slab. During exposure, sample temperature could be held at 37 deg C by circulating a

mixture of water and glycerol through a jacket around the chamber from an external bath kept constant at 38.5 deg C. For exposure at 200 W/kg, the temperature of the external bath was set to 35 deg C to offset sample heating by the RFR. Sample temperature could also be lowered to 4 deg C within 1-2 min by circulating water-glycerol mixture from a bath held at -4 deg C, and the cooling process could be reversed. During exposure, samples were stirred magnetically (with a stirrer in one end of the cylinder outside the waveguide) and their temperatures were monitored continuously with a nonperturbing Vitek probe. SARs were determined as described in Ortner et al. (1981b) from time-temperature profiles measured under the same conditions without temperature control.

To determine the effects of RFR on each of the three critical stages of the intracellular polymerization cycle, experiments were performed on scattering of light from microtubular protein during exposure. Light at about 380 nm from a monochrometer was conveyed to the sample by a quartz fiber-optic nonfluorescent cable passed through the waveguide wall and fastened to the sample compartment with a Plexiglas holder. The light scattered by the sample was directed via a similar fiber-optic cable to a photomultiplier and amplifier through a 520-nm filter, the latter to attenuate the scattered light sufficiently to remain within the maximum sensitivity range of the instrument. To raise the signal-to-noise ratio of the scattered light, the amplifier signal was also fed to a polygraph and averaged by setting the high-frequency response to 0.08 Hz.

In the light-scattering experiments, samples of depolymerized cycle-purified microtubular protein were incubated and exposed at 200, 20, or 0 W/kg for 10 min, during which sample temperature was maintained at 37 +/- 0.3 deg C and the turbidity was monitored with the photomultiplier instrumentation. After exposure, polymerization was initiated by adding ethylene glycol-bis (B-amino ethyl ether) tetraacetic acid (EGTA) and guanosine 5'-triphosphate (GTP), and turbidity from polymerization was determined for 12-15 min after initiation. At this time, the samples were cooled to depolymerize them, by circulating water-glycerol mixture at -4 deg C through the jacket, and turbidity was monitored.

The results of a typical experiment with a sample exposed at 20 W/kg were presented graphically in terms of the light scattered by the sample (in arbitrary units) vs time. The baseline turbidity (zero) did not change during the 10 min of RFR-exposure. Turbidity rose essentially linearly during the 12-15 min after polymerization initiation and fell to baseline in about 2 min after cooling was instituted. All subsequent turbidity measurements were normalized to the maximum value attained.

The results of the scattering experiments at 200, 20, and 0 W/kg (7-10 runs at each level) were exhibited graphically as the mean normalized percentages of light scatter (with SE bars) vs time. For all three levels, a relatively steep rise in percentage occurred during the first 2 min after the addition of EGTA and GTP, followed by a basically linear rise at a slower rate to maximum (100%) at 12-15 min. The authors stated: "The data show that microwave radiation at power levels up to 200 mW/g SAR had no observable effect on the nucleation or elongation of

microtubules in vitro." However, the part of the 200-W/kg curve for the 2-12 min of slower rise was slightly above the corresponding part of the 20-W/kg curve, and the latter was slightly above that for the 0-W/kg curve, but presumably the differences among the three at corresponding times were not statistically significant.

Data on the effect of exposure at 200, 20, and 0 W/kg on temperature-induced depolymerization were presented graphically as mean normalized percentage turbidities (with SE bars) vs progressively lower cooling temperature. All three curves were "reverse-S" shaped, showing slight turbidity diminution from 100% in the temperature range from about 30 to 20 deg C followed by steep drop to 0% at about 4 deg C. The differences among the curves were minor and were ascribed to a difference in cooling rate for the samples exposed at 200 W/kg.

Circular-dichroism spectroscopy was used to determine the effect of RFR on the secondary structure of purified tubulin polypeptides. For such measurements of purified tubulin, a spectropolarimeter was modified to accept a similar sample-exposure system. No significant differences in optical activity were found between purified tubulin exposed at 200 and 0 W/kg. Moreover, high-resolution measurements of optical activity in the region of aromatic amino acid absorption showed no RFR effects.

The authors noted that their findings extended those of Paulsson et al. (1977), in which no effect on the final development of the microtubule elongation process was observed from exposure to 3.1-GHz pulsed RFR. They noted that the instrumentation used by Paulsson et al. (1977) did not permit measurements of the effect of RFR on the critical nucleation phase of polymerization, depolymerization, or elongation rate.

Citing appropriate references, the authors stated: "In vivo, microtubule assembly and disassembly occur at precise times in the cellular reproductive cycle, and it has been suggested that the dynamic exchange of subunits on and off microtubules may influence the movement of chromosomes during mitosis. Microtubule-tubulin dynamics are also important in axonal transport, and the extremely high concentration of microtubular protein in the brain strongly implicates microtubules in nervous-system function. Microwave radiation has been shown in vivo to affect many biological functions that may involve microtubule dynamics as outlined above." However, they then stated:

"The entire process [of polymerization and depolymerization] appears to be unaffected by microwave field intensities high enough to increase the ambient temperature (from 34 to 37 deg C). This would indicate that the energy deposited within the sample chamber was sufficient to affect the solvent water and possibly protein-bound water molecules. Since the association of tubulin molecules to form the microtubule wall involves a loss of 'bound' water, it might be expected that microwave radiation could influence polymerization or perhaps the critical protein concentration required to support polymerization. However, we also found that the critical protein concentration needed for polymerization was unchanged by irradiation." They then concluded that: "A molecular basis

for the reported effects of microwave radiation on biological systems will probably, therefore, be found in some other aspect of cellular physiology."

The negative results of this investigation and the conclusions of the authors appear to be correct. However, this in-vitro study was done on extracted microtubule samples in the absence of cell membranes and their interactions with intracellular and extracellular components, so the relevance of the findings (though negative) to effects of RFR on intact cells is open to question. Moreover, others (notably Adey, 1981, cited in this paper) have reported that direct effects of RFR fields on cells can and does occur at the membrane level. If feasible, it would be interesting to seek possible effects of RFR exposure on microtubules in intact cells suspended in appropriate media.

Seaman and Wachtel (1978) determined the SARs necessary to alter the firing rates of individual pacemaker neurons in the abdominal ganglion of Aplysia californica. After removal from an Aplysia, each ganglion was placed in artificial seawater at room temperature (21-26 deg C) within a small acrylic chamber having a wax base. Cactus needles were used to attach the ganglion to the center of the base. The chamber was then placed between the center conductor and outer ground conductor of a rectangular stripline transmission section, which was inserted in a coaxial cable terminated with a shorted stub. A bidirectional coupler between the source and stripline section was used to measure forward and reflected average powers. Small holes in the narrow (ground) walls of the stripline section permitted transillumination and viewing of the specimen and insertion of glass microelectrodes (filled with 2.5 molar KCl) transverse to the electric field for intracellular recordings. For altering specimen temperatures in the absence of RFR, warm or cold water was drawn through an enclosed volume surrounding the specimen.

Both CW and pulsed-wave (PW) RFR at 1.5 or 2.45 GHz were used. Pulse durations ranged from 0.5 to 10 microseconds, at repetition rates from 1000 to 5000 pps, respectively. The pulse rise times were less than 0.1 microsecond. A coaxial switch permitted application of the RFR (and removal) within a few milliseconds. The determination of SARs in such preparations at each frequency was described in Wachtel et al. (1975), in which the authors noted that the volume occupied by the ganglion and seawater in different chambers ranged from 0.3 to 0.8 cc. The net RFR power absorbed by the volume was calculated from the stripline geometry, the input power, and the reflection and attenuation characteristics of the volume. The results were verified (within a factor of about 2) by measurement of temperature rises in specimens.

The beating-pacemaker neuron in the abdominal ganglion of Aplysia was selected for study because it produces action potentials at very regular rates with little or no synaptic input and because the effects on single neurons could be studied. The firing rate was measured in terms of the interspike interval (ISI) recorded on a strip chart together with the transmembrane potential. After stability in transmembrane potential and ISI was achieved in each preparation, successively higher levels of RFR

were applied for 2-3 min at each level, but the RFR was removed earlier if the neuron stopped firing.

In the lower range of SARs that yielded effects, firing rates changed after the onset of the RFR and attained new stable rates with a time constant of about 1 min. At higher SARs, the changes occurred earlier during the exposure period. For 46% of the neurons studied, RFR at effective SARs reduced the firing rate consistently (for 100% of the exposures). For the other 54% of the neurons, effective SARs reduced the rate for 79% of the exposures, but increased the rate for others. For the entire population of beating-pacemaker neurons, 87% of responses were firing-rate reductions. No obvious correspondence was seen between the direction of change and SAR, frequency, or modulation for any single neuron or for the population in general. For all the beating-pacemaker neurons, post-RFR firing rates returned to pre-RFR rates after 1-2 min.

A representative example was presented in Fig. 1 of the paper for a beating-pacemaker neuron exposed to 1.5-GHz CW RFR at SARs of 5.7, 7.1, and 25.5 W/kg. No change in peak spike potential was evident at each SAR or with change in SAR. At 5.7 W/kg, there were also no discernible changes in ISI. At 7.1 W/kg, however, a rise in ISI was evident shortly after the onset of the RFR; at 25.5 W/kg, the rise was much faster and higher. The authors noted that the firing-rate decreases of this neuron occurred in 10 of 11 responses to the RFR.

The dose-dependence of the effect on this neuron was shown for SARs up to about 69 W/kg. At each SAR, the average firing rate in the interval 10 to 20 seconds after the onset of RFR was normalized to the average for the four action potentials just before exposure and the ratio was plotted vs SAR. At low SARs, the normalized firing rates were basically unity. A least-squares linear-regression fit to the data for the seven largest SARs was drawn. This procedure was also used for the interval 20 to 30 seconds after RFR onset. For the interval 10-20 seconds, the regression value at 69 W/kg was about 0.6. For the interval 20-30 seconds, the decrease in normalized rate was much steeper: to about 0.5 at 40 W/kg and to 0 at 69 W/kg.

The lowest SARs that caused changes in slow firing rate were determined for 39 neurons from 29 ganglia. The result for the neuron discussed above was 7 W/kg; no other values were given.

In addition to the slow ISI changes, rapid changes were observed in 8 neurons from 8 different ganglia. A rapid ISI change was defined as a firing-rate increase within one ISI of RFR onset, i.e., the occurrence of an ISI during or just after the onset of RFR that was shorter than the pre-RFR ISI. Within 25 seconds of the firing-rate increase in these neurons, the rate gradually decreased until it attained nearly the pre-RFR value. The largest rapid change was for a neuron that responded uniquely with two separate rate increases when it was exposed to 0.5-microsecond pulses, 5000 pps, of 1.5-GHz RFR at peak and average SARs of 400 and 1 W/kg. The recording presented for this neuron showed a step decrease in ISI to a plateau for the first few seconds after RFR onset,

at which time a sudden additional ISI decrease occurred, followed by a gradual return toward pre-RFR level. The mean SAR, 1 W/kg, was smaller than any of the threshold values for the slow firing-rate changes and was also the lowest value for all rapid changes.

The authors stated: "Rapid changes in firing rate were seen for 2.45 GHz CW and PW and for 1.5 GHz PW. Although the sparse data on this response prevented a systematic analysis, it seemed that the rapid change was better defined for PW than for CW radiation. The rapid changes also tended to occur at smaller averaged SARs for PW radiation." They also noted that two neurons showed a decrease in firing rate at termination of RFR. A recording for one of these neurons exhibited the firing-rate decrease on cessation of 1.5-GHz CW RFR at 8.4 W/kg.

The authors suggested that a possible mechanism for firing-rate changes in beating pacemakers during RFR exposure is the consequent temperature increase of the preparation. This hypothesis was tested by comparing the responses of 29 neurons to heating by RFR and by convection. The temperature time courses and increments were matched. The firing-rate changes with heating (presumably by either method) were slow, requiring 30 to 60 seconds to reach steady state. In this neuron subpopulation, 94% of the changes were reductions in firing rate and 62% of the cells responded similarly to RFR- and convection heating. The authors noted, however, that in the preliminary study (Wachtel et al., 1975), "the slow responses of some cells to microwave radiation did not always duplicate those to conventional heating. No rapid changes in firing rate were seen when cells were warmed or cooled by convection."

They also suggested that direct interaction of RFR with the neurons is another possible mechanism, and displayed a representative example of the firing rates of a neuron during successive intervals of injection of 2, 3, and 2 nA of depolarizing current. The record exhibited a higher firing rate during the 3-nA interval than the preceding or subsequent 2-nA interval, but no significant change in spike amplitude. They stated: "These rapid changes, each of which adapts to an intermediate value, resemble those seen at the onset and termination of irradiations. Microwave radiation produced the same effect as an increase in depolarizing current."

The other type of neuron selected for study was the bursting-pacemaker cell in the abdominal ganglion of Aplysia. These neurons produce action potentials in bursts coincident with an endogenous, depolarizing slow-wave potential. Their otherwise highly regular interburst intervals (IBIs) can be modulated by synaptic input from other neurons in the ganglion. Only bursting pacemakers without synaptic potentials were studied, to help ensure that observed effects were occurring in single neurons. Also, the bursting pacemakers were required to exhibit regular IBIs, either spontaneously or when injected with a small depolarizing current, criteria that were met by about 20% of the neurons tested. Bursting and beating pacemakers were often studied in the same ganglion.

The exposure procedure used was similar to that for beating pace-

makers, and smallest effective SARs were determined. Representative responses of a bursting pacemaker to 7.3, 16.0 and 21.6 W/kg were exhibited in Fig. 4 of the paper, a low-resolution reproduction that displayed bursts as thick spikes. At each level, there were minor variations (increases and decreases) of IBI apparently not associated with the RFR. Exposure at 7.3 W/kg had no apparent effect; the IBIs, which ranged from 10.4 to 12.3 seconds during the entire pre-RFR and exposure time interval shown (about 2 min), exhibited no discernible RFR-induced differences. The bursts at 16.0 W/kg were of longer duration (thicker) than those before exposure (which were comparable to those at 7.3 W/kg), and the mean IBI after onset of RFR was smaller than before onset. The pre-RFR range of IBIs was 8.2-8.7 seconds, but the IBI range during exposure could not be discerned from the figure because of the longer durations of the bursts. At 21.6 W/kg, the burst durations before and during exposure were like those at 7.3 W/kg; however, the pre-RFR IBIs ranged from 11.0 to 12.1 seconds, whereas the range during exposure was 7.2 to 11.2 seconds, a clear reduction of mean IBI.

The smallest effective SARs were determined for 16 bursting pacemakers from 12 ganglia. The authors noted that the post-RFR IBI did not always return to the pre-RFR value after 2-3 min of exposure. They also stated that all these pacemakers exhibited a slow, graded response (exemplified in Fig. 4), but that the direction of change was not the same for all cells; 7 cells showed decreased IBIs, 3 cells showed increased IBIs, and the IBIs of the other 6 showed changes in both directions. For cells exhibiting increased IBIs, the cells would stop firing at sufficient SAR and duration, as evidenced by steady hyperpolarized membrane potentials. As noted in the previous study (Wachtel et al., 1975), the responses of a given cell to convective warming were not always in the same direction as the RFR responses of that cell, again suggesting more than a simple heating effect.

Some bursting pacemakers exhibited phasic responses at the onset or termination of RFR. For 3 cells that yielded a smaller IBI-steady-state response to RFR, the IBI at the onset of RFR was longer than the IBI just before or after, a type of response that was seen occasionally with convection heating. For 2 cells, the IBI at RFR termination was shorter than the IBIs immediately preceding and following termination, a type of response not seen wi h convection cooling. Phasic responses occurred during exposure to 1.5- and 2.45-GHz CW RFR at SARs from 7 to 291 W/kg.

Bursting-pacemaker IBIs also were sensitive to injected currents: "The change in IBI as a result of an increase in injected hyperpolarizing current resembled the phasic increase of IBI that occurred at the onset of irradiation. Also, a decrease in hyperpolarizing current caused a phasic decrease of IBI similar to that which occurred at the termination of irradiation. Thus, microwave energy seemed to act in the same way as an injected hyperpolarizing current."

The results for the 39 beating-pacemaker and 16 bursting-pacemaker neurons were summarized in the form of histograms of the frequency distributions of the smallest SARs that caused slow changes in firing

patterns. The data for CW and pulsed RFR at both RFR frequencies were merged, since no difference in effectiveness was seen among them. The combined histogram for both kinds of neurons showed a rough resemblance to a normal distribution. The histogram values were then plotted as the percentage of neurons that responded at a given or smaller value of SAR (cumulative percent responses) on a probability scale vs the smallest effective SARs on a logarithmic scale. The data fitted a straight line with only small deviations. The lower and upper ends of the line showed that 1% of the 55 neurons responded to about 2 W/kg and 99% of the neurons responded to about 100 W/kg; the median SAR (50%) was 14.5 W/kg. The authors stated: "The proximity of the data points to a straight line indicated that the distribution of smallest effective SARs can be represented by a log-normal distribution."

The authors noted that spontaneous firing rates of nonpacemaker neurons in the abdominal ganglion were affected (increased slightly) only for SARs greater than about 50 W/kg, but over 90% of the pacemaker neurons were affected at this SAR, an indication of the higher sensitivity of pacemaker neurons to RFR.

In considering their findings, the authors suggested that the slow responses of pacemaker neurons to RFR were largely thermally induced because the responses had followed time courses similar to those due to specimen-temperature rises and that the responses depended on average SAR (with a thermal sensitivity of 0.02 deg C per W/kg) and not on the RFR frequency or modulation. However, they stated: "On the other hand, that a slow response was not always duplicated by identical irradiations and that irradiation did not always elicit the same response that was elicited by thermal stimulation weaken the argument for a purely thermal interaction." This point is open to question, because unlike convective heating, in which heat is transferred into the specimen-seawater volume via the surface of the volume, RFR penetration into the volume at the two frequencies used would yield significant internal heating, and the heating patterns by the two modes would not be similar. In addition, although presumably the ambient temperature (ranging from 21 to 26 deg C) remained basically constant during each RFR exposure, it is not clear that it had the same value for all the RFR exposures (during which no convective fluid was used).

The authors also stated: "The rapid changes seen in beating pacemakers and some of the phasic responses seen in bursting pacemakers cannot be readily attributed to a thermal mechanism. These responses took place much faster than the increase in temperature of the preparation. This was more obvious for beating pacemakers, probably because the ISI provided finer resolution of time than did the IBI. Both the rapid and phasic changes were in a direction opposite to the majority of slow changes, which followed temperature. In addition, no rapid responses were observed when temperature was similarly increased by convective means. One mechanism that could explain the rapid changes is a direct action of the electromagnetic field on the neuron...There also exists the possibility that the pacemakers were sensitive in some way to the mechanical energy created by the absorbed microwave energy...In our

study, rapid on- and off-incident energy occurred during PW radiation and for the onsets and terminations of irradiations, all being occurrences for which rapid changes seemed to be enhanced. However, it still remains to be determined whether pacemakers of Aplysia can detect small shock waves." These points were logical, but require experimental verification.

Also considered was that the rapid responses resulted from RFR-induced currents in the neuron. However, they noted that their experimental results were in conflict with this hypothesis: "In their rapid responses, beating pacemakers always responded as if to a depolarizing current; the bursting pacemakers, always as if to a hyperpolarizing current. We cannot easily explain these opposite effects in terms of induced currents since we would expect that induced current would flow in one direction (equivalent DC) so that the responses of all cells would mimic the responses to one polarity of injected current."

Perhaps insufficiently considered were the response variations among specimens due to uncontrolled non-RFR factors and those by individual specimens at various times. Exemplifying the latter point were the results for the bursting pacemaker exposed at 7.3, 16.0, and 21.6 W/kg (discussed above); the pre-RFR IBIs for the intermediate SAR (range 8.2-8.7 seconds) were much shorter than the IBIs for 7.3 W/kg (range 10.4-12.3 seconds) and the pre-RFR IBIs for 21.6 W/kg (11.0-12.1 seconds).

In tests by the authors, use of glass microelectrodes filled with 2.5-M KCl yielded less than 0.01 nA on RFR-exposure, lower than that required to cause measurable changes in the firing rates of pacemaker neurons. Nevertheless, possible electrode artifact may not be ruled out entirely, because Yee et al. (1984) demonstrated that 3-M KCl electrodes produced artifactual responses in the beating rate of the isolated frog heart during exposure to 2.45-GHz RFR at 8.55 W/kg.

In various studies, Pickard and coworkers sought effects of RFR on giant cells (about 10 mm long) isolated from Characean algae. In one study, Pickard and Barsoum (1981) investigated electrophysiological responses to RFR of such cells. In that paper, the theory underlying the approach used and the experimental results obtained with a specially devised RF microstrip exposure apparatus were discussed.

In brief, the theory indicates that for a cell exposed to RFR, the electric component of the RFR normal to the plasma membrane produces an RF voltage gradient that modifies the current flow across the membrane, and that the effect would be especially prominent for a long cylindrical cell with its axis normal to the electric vector. Also, if the current-vs-voltage relationship of the membrane is nonlinear (rectifying), the modified flow of current should alter the quantity of charge on the membrane capacitance and thus shift the cell's resting potential. The steady-state limits of this resting-potential offset (for cases where the transit time of the charge carriers across the membrane is much smaller than the oscillation period of the RFR) were quantitatively predicted by Barnes and Hu (1977) and by Pickard and Rosenbaum (1978),

who characterized such direct rectification as a nonthermal effect.

The theory also covers conditions for which transit time is comparable to the oscillation period of the RFR. In particular, the rectification efficiency should decrease with increasing RFR frequency, and Pickard and Rosenbaum (1978) indicated that estimated membrane transit times of about 50 nanoseconds or longer would yield an upper frequency limit for rectification near 10 MHz.

Accordingly, Pickard and Barsoum (1981) exposed single Characean cells (Chara braumii and Nitella flexilis) to rectangular pulses of RFR having carrier frequencies in the range 0.25-50 MHz. Pulse duration was varied from roughly 10 microseconds to more than 10 seconds but was typically 250 ms. Pulse delivery was one every 6.3 seconds in synchrony with the 60-Hz power-line frequency to reduce interference from that source.

For exposure, the cell was mounted within the microstrip in a channel through which flowed electrogenic artificial pond water (EAPW) held at constant temperature. The upstream end of the cell was placed under the center conductor of the microstrip; its other end was either impaled by a pipette (agar-KCl) 2-4 mm downstream (beyond the center conductor) for recording intracellular potential or in light contact with the pipette shank for recording extracellular potential. The reference pipette was placed upstream from the center conductor at about the same distance as the signal pipette, and recordings were taken differentially from the two pipettes to reduce 60-Hz interference. Other provisions were also made to minimize 60-Hz pickup and to maximize the signal-to-noise ratio.

Sought first were possible sources of artifact that mimic cell-potential offsets. Slight frequency-dependent nonlinearities were found in two of the amplifiers, which caused weak rectification of the RF and yielded artifactual offsets; this problem was resolved by addition of a filter. Also found was that the microstrip silver electrodes rectify weakly if they become corroded. Therefore, they were kept scrupulously clean.

The authors noted that only part of the cell is exposed to the RF field in their apparatus, yielding a rectified current injected only across that part of the cell membrane. Thus, the closed loop of current flow crosses the cell membrane in the exposure region, flows intracellularly out of the exposure region, crosses the cell membrane again outside the exposure region, and flows extracellularly back to the starting region. With an extracellular medium of low electrical conductivity, the current flow should produce detectable extracellular voltage offsets. Theory predicts that the voltage offsets should be directly proportional to the square of the applied microstrip voltage and inversely proportional to the square of the frequency.

Such behavior was verified experimentally: A log-log plot of normalized extracellular offset vs microstrip voltage (at 1 MHz) was linear, with a mean slope of +2.00 for Chara and 1.94 for Nitella. In addition, a log-log plot of normalized extracellular offset vs frequency over the

range 0.1-1 MHz (at a microstrip voltage of 10 V rms) for Chara was linear with a mean slope of -1.95, also consonant with the theory; however, the mean slope of a similar plot for Nitella was -1.54, which was noted by the authors as an unexplained anomaly. No variations of time constant with voltage or frequency were found.

In discussing intracellular results, the authors divided Characean cells into two categories: those that have resting potentials more negative than -125 mV, indicative of a significant active-transport component and therefore designated by them "electrogenic," and those having resting potentials less negative than -90 mV, denoted as "nonelectrogenic." The results presented were primarily on nonelectrogenic cells.

Log-log plots of normalized intracellular offset vs microstrip voltage were also linear, with mean slopes of 1.99 and 1.95 respectively for Chara and Nitella. The frequency plots over the range up to about 4 MHz yielded slopes of about -2; in the approximate range 4-10 MHz, the data scatter was much larger, with the mean slope gradually becoming more negative; at 10 MHz, the relative offset had diminished to about 0.002, and no offset was detected in the range 15-50 MHz, in consonance with the theory.

Also displayed were representative intracellular-offset responses of a Chara cell (of resting potential - 82 mV) to 250-ms pulses of 1, 2, and 20 MHz at a microstrip voltage of 10 V rms. At 1 MHz, the negative-going intracellular offset voltage attained a maximum of about -0.9 mV within about 40 ms and diminished slowly (small positive slope) during the rest of the pulse. At 2 MHz, the maximum was about -0.3 mV, reached within about 150 ms, but the offset did not change during the rest of the pulse (zero slope). At 20 MHz, however, to which no response should have been obtained, a very small and gradual change in offset during the pulse to a maximum of about -0.02 mV (negative slope) was evident.

The ramp of negative slope was characterized by the authors as a thermal effect on the basis that if the effect is thermal, the slope should be proportional to the square of the microstrip voltage; this conjecture was confirmed experimentally by a log-log plot of slope (normalized at 10 MHz) vs microstrip voltage that was linear with a slope of 2. The authors then suggested that the offset response of the cell is a linear combination of a hyperpolarizing step and a hyperpolarizing ramp, with the former dominating the latter in the lower frequency range (less than about 10 MHz) and conversely for higher frequencies.

The connection between extracellular and intracellular responses was investigated by clipping the end off the cell during recording of the extracellular offset. Elimination of the voltage drop across the cell membrane in this manner immediately raised the extracellular offset toward the intracellular level, but the offset decayed to zero within a few minutes, presumably indicating membrane death and disorganization.

In one of two subsequent studies, Barsoum and Pickard (1982a) exposed single Chara and Nitella cells to RFR pulses in the frequency range 20-

300 MHz at electric field strengths up to 6250 V/m and reported that the only effect observed was the thermally induced hyperpolarization ramp and that the slope of the ramp increased with increasing frequency. In the other study, Barsoum and Pickard (1982b) used the frequency range 200-8200 MHz at a nominal power density of 10 mW/sq cm, determined by dividing the forward power in the channel region of the microstrip by the area of the microstrip. At this power level, no offsets were seen. At much higher power levels, the hyperpolarization ramp could be seen but not measured accurately. The ramp appeared to decay beyond 500 MHz and to be absent at about 950 MHz and higher.

Brunkard and Pickard (1984), prompted by the studies of the calcium-efflux phenomenon (Section 3.4.4), sought effects of amplitude-modulated 147-MHz RFR on the electrophysiological responses of Chara and Nitella cells. They noted that because there was no obvious way of predicting what combinations of power level and modulation frequency would yield a response, they undertook a blind search in a pattern of exposures to 147-MHz RFR consisting of discrete power densities in the range 0.2-100 mW/sq cm amplitude-modulated (90%) at 16 Hz and a fixed power density of 10 mW/sq cm amplitude-modulated at discrete frequencies in the range 4-64 Hz. Modulation-synchronized components of vacuolar resting potential were sought by phase-sensitive detection. The authors noted that the resolution of their system was about 1 part in a million and that since the resting potential is of the order of 100 mV, responses at the 100 nV level should have been obvious.

The results were displayed as plots of synchronized displacement vs power density and vs modulation frequency (showing the discrete values of each used). Each data point was the mean for 3-5 cells. For each combination of conditions, there were both positive and negative mean displacements. No statistical treatment of the data was presented, but presumably the scatter of points about the zero displacement line in each plot yielded a mean that did not differ significantly from zero, representing no membrane-potential changes. The authors qualified their results with the following: "Although no response to amplitude modulated 147-MHz radiation was detected in this study, it cannot be concluded definitely that there is no effect in Characean cells analogous to the effects observed in other tissues."

3.8.2 CONCLUSIONS

Many of the early studies on microorganisms, notably those of Webb and coworkers, yielded results that were taken as evidence of nonthermal effects of RFR, and therefore created considerable controversy. The existence of resonances in the submillimeter-wave region was postulated on theoretical grounds, and a number of studies were performed that apparently confirmed that hypothesis. Later studies, however, in which subsequently developed more sophisticated techniques were used in both the engineering and biological aspects and the presence of artifacts was reduced significantly, yielded results that did not confirm the earlier findings of resonances or other indications of nonthermal effects. In addition, the effects of RFR on giant algal cells found by Pickard and

coworkers were thermally induced. On the other hand, the resonances in the range 2-9 GHz reported recently for DNA molecules of substantially uniform length in aqueous solution, derived from E. coli, are indicative of direct action of RFR with such molecules, but the effect is evidently damped out for intact DNA within cells.

The effects of exposure of mammalian cells and constituents thereof to RFR in vitro were also studied, mostly at SARs higher than 4 W/kg (the basis of the 1982 ANSI exposure standard). As would be expected at such SARs, the effects reported were associated with temperature changes.

In general, research on possible effects of RFR on microorganisms or of in-vitro exposure to RFR of cells derived from macroorganisms appears to be useful toward eliciting possible mechanisms of direct interaction of RFR with such biological entities or their constituents at levels that can be characterized as nonthermal. Open to question, however, is the relevance of extrapolating such findings to possible effects of exposure of intact animals to RFR and ultimately their significance with regard to possible hazards of RFR to humans.

REFERENCES:

Adey, W.R.
TISSUE INTERACTIONS WITH NONIONIZING ELECTROMAGNETIC FIELDS
Physiol. Rev., Vol. 61, pp.435-514 (1981)

Barnes, F.S. and C.-L.J. Hu
MODEL FOR SOME NONTHERMAL EFFECTS OF RADIO AND MICROWAVE FIELDS ON BIOLOGICAL MEMBRANES
IEEE Trans. Microwave Theory Tech., Vol. 25, No.9, pp. 742-746 (1977)

Barsoum, Y.H. and W.F. Pickard
EFFECTS OF ELECTROMAGNETIC RADIATION IN THE RANGE 20-300 MHZ ON THE VACUOLAR POTENTIAL OF CHARACEAN CELLS
Bioelectromagnetics, Vol. 3, No. 2, pp. 193-201 (1982a)

Barsoum, Y.H. and W.F. Pickard
THE VACUOLAR POTENTIAL OF CHARACEAN CELLS SUBJECTED TO ELECTROMAGNETIC RADIATION IN THE RANGE 200-8,200 MHZ
Bioelectromagnetics, Vol. 3, No. 4, pp. 393-400 (1982b)

Brunkard, K.M. and W.F. Pickard
THE MEMBRANE POTENTIAL OF CHARACEAN CELLS EXPOSED TO AMPLITUDE-MODULATED, LOW-POWER 147-MHZ RADIATION
Bioelectromagnetics, Vol. 5, No. 3, pp. 353-356 (1984)

Bush, L.G., D.W. Hill, A. Riazi, L.J. Stensaas, L.M. Partlow, and O.P. Gandhi
EFFECTS OF MILLIMETER-WAVE RADIATION ON MONOLAYER CELL CULTURES. III. A SEARCH FOR FREQUENCY-SPECIFIC ATHERMAL BIOLOGICAL EFFECTS ON PROTEIN SYNTHESIS
Bioelectromagnetics, Vol. 2, No. 2, pp. 151-159 (1981)

Cooper, M.S. and N.M. Amer
THE ABSENCE OF COHERENT VIBRATIONS IN THE RAMAN SPECTRA OF LIVING CELLS
Phys. Lett., Vol. 98A, No. 3, pp. 138-142 (1983)

Dorfman, B.H. and L.L. Van Zandt
VIBRATION OF DNA POLYMER IN VISCOUS SOLVENT
Biopolymers, Vol. 22, pp. 2639-2665 (1983)

Dorfman, B.H. and L.L. Van Zandt
EFFECTS OF VISCOUS SOLVENT ON DNA POLYMER IN A FIBER
Biopolymers, Vol. 23, pp. 913-922 (1984)

Edwards, G.S., C.C. Davis, J.D. Saffer, and M.L. Swicord
RESONANT MICROWAVE ABSORPTION OF SELECTED DNA MOLECULES
Phys. Rev. Lett., Vol. 53, No. 13, pp. 1284-1287 (1984)

Edwards, G.S., C.C. Davis, J.D. Saffer, and M.L. Swicord
MICROWAVE-FIELD-DRIVEN ACOUSTIC MODES IN DNA
Biophys. J., Vol. 47, pp. 799-807 (1985)

Froehlich, H.
EVIDENCE FOR BOSE CONDENSATION-LIKE EXCITATION OF COHERENT MODES IN BIOLOGICAL SYSTEMS
Phys. Lett., Vol. 51A, No. 1, pp. 21-22 (1975)

Gandhi, O.P., M.J. Hagmann, D.W. Hill, L.M. Partlow, and L. Bush
MILLIMETER WAVE ABSORPTION SPECTRA OF BIOLOGICAL SAMPLES
Bioelectromagnetics, Vol. 1, No. 3, pp. 285-298 (1980)

Grundler, W., F. Keilmann, and H. Froehlich
RESONANT GROWTH RATE RESPONSE OF YEAST CELLS IRRADIATED BY WEAK MICROWAVES
Phys. Lett., Vol. 62A, No. 6, pp. 463-466 (1977)

Hakim, H.B., S.M. Lindsay, and J. Powell
THE SPEED OF SOUND IN DNA
Biopolymers, Vol. 23, pp. 1185-1192 (1984)

Hamrick, P.E. and B.T. Butler
EXPOSURE OF BACTERIA TO 2450 MHZ MICROWAVE RADIATION
J. Microwave Power, Vol. 8, No. 3, pp. 227-233 (1973)

McRee, D. and P. Walsh
MICROWAVE EXPOSURE SYSTEM FOR BIOLOGICAL SPECIMENS
Rev. Sci. Instr., Vol. 42, pp. 1860-1864 (1971)

Ortner, M.J., M.J. Galvin, C.F. Chignell, and D.I. McRee
A CIRCULAR DICHROISM STUDY OF HUMAN ERYTHROCYTE GHOST PROTEINS DURING EXPOSURE TO 2450 MHZ MICROWAVE RADIATION
Cell Biophys., Vol. 3, pp. 335-347 (1981b)

Ortner, M.J., M.J. Galvin, and R.D. Irwin
THE EFFECT OF 2450-MHZ MICROWAVE RADIATION DURING MICROTUBULAR POLYMERIZATION IN VITRO
Radiat. Res., Vol. 93, pp. 353-363 (1983)

Partlow, L.M., L.G. Bush, L.J. Stensaas, D.W. Hill, A. Riazi, and O.P. Gandhi
EFFECTS OF MILLIMETER-WAVE RADIATION ON MONOLAYER CELL CULTURES. I. DESIGN AND VALIDATION OF A NOVEL EXPOSURE SYSTEM
Bioelectromagnetics, Vol. 2, No. 2, pp. 123-140 (1981)

Paulsson, L.-E., Y. Hamnerius, and W.G. McLean
THE EFFECTS OF MICROWAVE RADIATION ON MICROTUBULES AND AXONAL TRANSPORT
Radiat. Res., Vol. 70, pp. 212-223 (1977)

Pickard, W.F. and F.J. Rosenbaum
BIOLOGICAL EFFECTS OF MICROWAVES AT THE MEMBRANE LEVEL: TWO POSSIBLE ATHERMAL ELECTROPHYSIOLOGICAL MECHANISMS AND A PROPOSED EXPERIMENTAL TEST
Math. Biosci., Vol. 39, pp. 235-253 (1978)

Pickard, W.F. and Y.H. Barsoum
RADIO-FREQUENCY BIOEFFECTS AT THE MEMBRANE LEVEL: SEPARATION OF THERMAL AND ATHERMAL CONTRIBUTIONS IN THE CHARACEAE
J. Membrane Biol., Vol. 61, pp. 39-54 (1981)

Seaman, R.L. and H. Wachtel
SLOW AND RAPID RESPONSES TO CW AND PULSED MICROWAVE RADIATION BY INDIVIDUAL APLYSIA PACEMAKERS
J. Microwave Power, Vol. 13, No. 1, pp. 77-86 (1978)

Stensaas, L.J., L.M. Partlow, L.G. Bush, P.L. Iverson, D.W. Hill, M.J. Hagmann, and O.P. Gandhi
EFFECTS OF MILLIMETER-WAVE RADIATION ON MONOLAYER CELL CULTURES. II. SCANNING AND TRANSMISSION ELECTRON MICROSCOPY
Bioelectromagnetics, Vol. 2, No. 2, pp. 141-150 (1981)

Swicord, M.L. and C.C. Davis
AN OPTICAL METHOD FOR INVESTIGATING THE MICROWAVE ABSORPTION CHARACTERISTICS OF DNA AND OTHER BIOMOLECULES IN SOLUTION
Bioelectromagnetics, Vol. 4, No. 1, pp. 21-42 (1983)

Szmigielski, S., M. Luczak, and M. Wiranowska
EFFECT OF MICROWAVES ON CELL FUNCTION AND VIRUS REPLICATION IN CELL CULTURES IRRADIATED IN VITRO
Ann. N.Y. Acad. Sci., Vol. 247, pp. 263-281 (1975b)

Takashima, S.
STUDIES ON THE EFFECT OF RADIO-FREQUENCY WAVES ON BIOLOGICAL MACROMOLECULES
IEEE Trans. Biomed. Eng., Vol. 13, No. 1, pp. 28-31 (1966)

Wachtel, H., R. Seaman, and W. Joines
EFFECTS OF LOW-INTENSITY MICROWAVES ON ISOLATED NEURONS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 46-62 (1975)

Webb, S.J. and D.D. Dodds
INHIBITION OF BACTERIAL CELL GROWTH BY 136 GC MICROWAVES
Nature, Vol. 218, pp. 374-375 (27 April 1968)

Webb, S.J. and A.D. Booth
ABSORPTION OF MICROWAVES BY MICROORGANISMS
Nature, Vol. 222, pp. 1199-1200 (21 June 1969)

Webb, S.J. and A.D. Booth
MICROWAVE ABSORPTION BY NORMAL AND TUMOR CELLS
Science, Vol. 174, pp. 72-74 (1 October 1971)

Webb, S.J. and M.E. Stoneham
RESONANCES BETWEEN 100 AND 1000 GHZ IN ACTIVE BACTERIAL CELLS AS SEEN BY LASER RAMAN SPECTROSCOPY
Phys. Lett., Vol. 60A, No. 3, pp. 267-268 (1977)

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EVIDENCE FOR NON-THERMAL EXCITATION OF ENERGY LEVELS IN ACTIVE BIOLOGICAL SYSTEMS
Phys. Lett., Vol. 63A, No. 3, pp. 407-408 (1977)

Yee, K.C., C.-K. Chou, and A.W. Guy
EFFECT OF MICROWAVE RADIATION ON THE BEATING RATE OF ISOLATED FROG HEARTS
Bioelectromagnetics, Vol. 5, No. 2, pp. 263-270 (1984)

4 UNRESOLVED ISSUES

The potential biological effects of RFR at frequencies up to 300 GHz have been assessed from representative peer-reviewed studies published in the scientific literature. The preponderance of reliable evidence in the studies evaluated indicates that chronic exposure to RFR at average power densities generally found in the environment is not hazardous to human health, even with due recognition that a few of the negative findings reported might have been obtained because the experiments had been poorly conducted. Nevertheless, the following uncertainties in the body of knowledge regarding the biological effects of RFR are worthy of mention. Such uncertainties may be reduced but are not likely to be eliminated entirely in the foreseeable future.

(1) Many of the epidemiologic studies on RFR bioeffects performed to date were extensive and reasonably well done, but they contain defects in varying degrees, such as imprecise assignment of individuals to the exposure and control groups; classification of the individuals in the exposure groups with regard to the frequencies, levels, and durations of RFR exposure; and difficulties in obtaining complete or accurate medical records, death certificates, or responses to health questionnaires for the individuals in both groups. With the recent advent and continual upgrading of computer-archival health-data bases, it is likely that considerable improvements can be obtained in the latter aspects for possible future epidemiologic studies.

(2) As noted in the Introduction (Section 1.4), application of results on laboratory animals to humans by extrapolation or otherwise, though essential, is a resort containing fundamental problems and uncertainties due to basic interspecies differences. Studies with nonhuman primates as surrogates for humans considerably narrow the interspecies gaps, but at costs that are often prohibitive. Thus, major reductions in such kinds of uncertainties seem unlikely, at least in the near future.

(3) The results of many investigations indicate the existence of RFR threshold levels for various bioeffects, thus providing confidence that exposure to levels that are appreciably below the thresholds are most unlikely to be deleterious. However, most experimental data indicating the existence of thresholds were obtained by use of single or repetitive exposures of relatively short durations. Although it is difficult to conceive of mechanisms whereby RFR exposures at well below threshold values over a long time could result in cumulative effects deleterious to health, there have been very few investigations involving essentially continuous exposure of animals to low-level RFR during most (if not all) of their lifetimes. The high costs of such investigations are the major impediment to their pursuit.

(4) Regarding basic mechanisms of interaction between RFR and various biological entities, many important discoveries have been made recently, notably by exposure of cells and subcellular structures and constituents in vitro to relatively low levels of RFR. The effects on such entities

can be characterized as nonthermal, but the gap between such effects and possibly hazardous effects on intact humans or animals from exposure to such RFR levels is enormous. Because such factors as large body masses, penetration depth and internal field distributions, and body-orientation changes in exposures to RFR in vivo vastly moderate such interactions or remove them entirely, as well as because of the complexities of various life processes per se, this gap is not likely to be reduced to any great extent.

Based on the foregoing, it is most unlikely that new information would reveal a significant hazard from chronic exposure to low levels of RFR (i.e., levels below those that can cause significant heating). Whether such exposure could be hazardous nevertheless will remain an unresolved issue, at least in the near term. On the other hand, it is noteworthy that to date, although EPA has been able to characterize a large number of chemical and physical agents as toxic (including ionizing radiation) and regulate them, it has been unable to similarly characterize chronic exposure to environmental RFR levels on the basis of any mortality or morbidity data in the general population.

5 MISCONCEPTIONS

Several misconceptions regarding the bioeffects of RFR continue to be expressed in popular and other accounts outside peer-reviewed scientific publications on the subject. Those accounts tend to be sources of some confusion for the nonspecialist. The following are typical examples.

Often, the distinction between nonionizing radiation (RFR) and ionizing radiation is not made; consequently, the well known hazards of ionizing radiation are linked--by implication--with exposure to RFR. In essence, ionizing radiation (which includes ultraviolet light, X-rays, and the emissions from nuclear and other radioactive materials) has sufficient quantum energy (see Section 2.2) to expel an electron from a molecule, leaving the molecule positively charged and thereby strongly affecting its interactions with neighboring molecules. Ionization can alter the functions of biological molecules fundamentally and often irreversibly.

By contrast, the quantum energies of RFR are so much smaller that their primary effect is to agitate rather than ionize molecules; absorption of RFR quanta at high rates (in large numbers per unit time) produces heat. (Nonthermal quantum interactions are not excluded, but as noted above in Section 4, their occurrence in humans or live animals is not likely to yield harmful effects.)

In addition, RFR-induced molecular agitation virtually ceases as soon as exposure to RFR is halted. At relatively low RFR intensities (depending on the animal species), the heat that such agitation represents is well accommodated by the normal thermoregulatory capabilities of the species, and therefore any effects produced are generally reversible. At higher RFR intensities, the thermoregulatory capabilities of any given species may be exceeded, so inadequate compensation for such effects may occur; thus, exposure at such intensities may lead to thermal distress or even irreversible thermal damage. In short, a single quantum of ionizing radiation that is absorbed by a molecule alters the properties of that molecule, and exposure to such radiation may thereby profoundly affect the function of the biological constituent involved. By contrast, in exposure to RFR in vivo, the concurrent absorption of many quanta is necessary to produce effects of clinical or biological importance.

Even if an effect is produced by RFR, that effect may not necessarily be deleterious to the entity involved. As an example of a nonhazardous effect, absorption of visible light (a form of electromagnetic radiation having quantum energies above those of RFR but below those of ionizing radiations mentioned previously) in the eyes is necessary for vision. Visible light and infrared radiation are also absorbed by the skin and at normal levels are converted into harmless heat. On the other hand, ultraviolet light can cause skin cancer.

Concerned people frequently ask whether guarantees can be offered that chronic exposure to low levels of an agent such as RFR will have no

deleterious effects many years in the future. As noted in Section 1.4, to obtain data on which a guarantee of absolute safety can be based is scientifically impossible. However, the large body of experimental data on the bioeffects of RFR indicates that, unlike the ingestion of certain substances in small quantities that can accumulate into a potentially harmful total dose, the RFR energy that is continually absorbed at low incident power densities (dose rates) is readily dissipated and does not accumulate in the body toward a total dose equivalent to the RFR energy absorbed in short exposures at high incident power densities. This is a basic reason for the existence of RFR-bioeffects threshold levels.

6 GENERAL SUMMARY AND CONCLUSIONS

6.1 ACTUAL OR PRESUMED EXPOSURE OF HUMANS

It is believed that considerable weight should be accorded findings of well performed studies involving actual or presumed human exposure to RFR despite the previously stated limitations of such studies because of the problems and uncertainties in animal studies related to interspecies differences. Summarized below are the findings of various epidemiologic studies on the effects of exposure to RFR, either occupationally or due to residence in the neighborhood of RFR emitters, and those of several studies with human volunteers. Analyses of such studies produced no unequivocal evidence that chronic exposure to RFR at levels within the previous or current U.S. exposure guidelines was implicated in reported detrimental health effects.

Especially noteworthy among the various epidemiologic studies on the effects of exposure to RFR, because of the large numbers of records amassed (about 20,000 each in the exposed and control groups), is that by Robinette and Silverman of former Naval personnel. This study did not yield significant correlations between exposure to RFR and long-term mortality or between exposure and various clinical manifestations that required hospitalization. Also noteworthy is the epidemiologic study by Lilienfeld and coworkers of personnel who resided in the U.S. embassy in Moscow during periods when the Embassy was irradiated with low levels of RFR, a subject that created considerable alarm. They were not able to find any statistically significant differences associated with RFR in total mortality or mortality from specific causes or in other illnesses (including cancer) between personnel in the Moscow embassy and controls comprised of personnel in other Eastern European U.S. embassies.

Lester and Moore had postulated higher cancer incidence for populations in the vicinity of Air Force bases and presented a statistical treatment purporting to demonstrate the validity of the hypothesis. However, a reanalysis by Polson and Merritt of the data showed that the differences in mortality from cancer incidence among the counties that included Air Force bases and those that did not were statistically non-significant. Polson and Merritt ascribed the findings of Lester and Moore to a data base that was incorrectly assembled. In another study, Lester and Moore reported a neighborhood pattern of higher cancer incidence in Wichita, Kansas, associated with the locations of radar transmitters at airports. Analysis indicated that this study was replete with flaws.

Milham had analyzed decedent information on 429,926 males and 25,066 females in Washington State to search for relationships between causes of death and various occupations, and reported an increase in leukemia in workers exposed to electric and magnetic fields. However, this finding should be treated with caution, because the author apparently did not assume any hypotheses a priori, and used a method that did not meet normal criteria for statistical testing of hypotheses. Moreover, the commentaries of the author on patterns of mortality underlying the

different occupations seemed to show personal bias.

Hamburger and coworkers hypothesized that physical therapists might be subject to adverse health effects from frequent use of various diathermy modalities ("microwave, shortwave, infrared, and ultrasound"). They therefore analyzed responses from male members of the American Physical Therapy Association to a questionnaire about their occupational history of diathermy use. The final sample consisted of 3004 respondents from 5187 therapists solicited. The responses were divided in various ways into subgroups for statistical analyses, and 3x3 contingency tables of condition versus modality were formed for each of 10 medical conditions.

The only medical condition with a statistically significant association with the microwave and shortwave modalities was heart disease. However, of the 90 contingency tables, only four showed statistical significance at the 5% level, a finding no better than chance. None of the tables for the other nine medical conditions, including incidence of neoplasms, was statistically significant. This study also illustrates the problems with using responses to a mailed, self-administered questionnaire, such as the relatively low response rate (58%) and possible self-selection by respondents because they had medical conditions.

Results of early studies by Sigler and coworkers showed a significantly higher incidence of Down's syndrome of case mothers exposed to ionizing radiation in Baltimore, Maryland, but also an association between the occurrence of Down's syndrome and presumed exposure of the fathers to RFR from radars during military service. In a more extensive study that embodied additional case-control pairs, Cohen and coworkers were unable to confirm a significant relationship between case fathers and incidence of Down's syndrome.

Peacock and coworkers examined the birth certificates in an Alabama statewide file by counties of 31,700 white males, 29,400 white females, 14,900 black males, and 14,900 black females, and found 932 infants with 968 birth defects of various types, corresponding to an overall rate of 10.3 newborns with anomalies per thousand births, a rate comparable with those of similar registries elsewhere. However, they also reported that in comparison with statewide averages, the incidences of certain birth defects significantly exceeded chance in six counties, and associated this finding with the radars at Fort Rucker, which is within Coffee and Dale counties (two of the six).

In a later paper, Peacock and coworkers adjusted the data to account for "non-radar" factors and compared the anomaly rates at Lyster Hospital (at Fort Rucker) with the rates for three military hospitals at bases with minimal radar networks. Those results confirmed that the total anomaly rate and the rates for anomalies of the heart, genital organs, and musculoskeletal categories were abnormally high at Lyster Hospital, and also that fetal death rates at Lyster and at the hospital at Eglin Air Force Base were almost the same and may be associated with radar. However, Burdeshaw and Schaffer subsequently compared the Coffee and Dale county data used by Peacock and coworkers with those of the

other 65 counties in Alabama instead of with the statewide averages and were unable to confirm the findings of Peacock and coworkers.

More recently, Kallen and coworkers, hypothesizing that physiotherapists were more likely to have been occupationally exposed to various agents (chemicals, drugs, x-rays, RFR) than the general population, conducted a cohort study of 2,043 infants (including 25 pairs of twins) born in Sweden to 2,018 registered female physiotherapists. Analysis of the infant data for the entire cohort yielded results comparable to or more favorable than those for the general population, which led the authors to suggest that the outcome may be an indication of a "healthy worker" effect. They therefore performed a case-control study within the cohort and found a borderline statistically significant ($p=0.03$) association of perinatal deaths with therapists in the "often/daily" category of use of shortwave equipment (for 11 case mothers), but with no obvious pattern of specific malformations. However, sensitivity analysis of their data, which were derived from responses to a questionnaire, showed that the outcome depended critically on accurate recollection; if, for example, one mother had responded "seldom" instead of "often" use, the difference between perinatal deaths in case and control infants would have been nonsignificant ($p=0.056$).

Individual cases of eye damage from occupational exposure to RFR have been reported at various times since the end of World War II; some of those cases may have resulted from exposure at average power densities substantially higher than the threshold found in animal studies (about 150 mW/sq cm). In addition, several epidemiologic studies were done to determine whether ocular damage could be statistically associated with occupational exposure to RFR.

Cleary and coworkers found 2,946 cataract cases in Army and Air Force veterans of World War II and the Korean War in records of Veterans Administration hospitals, and used a random sample of 2,164 veterans hospitalized for other causes during the same period for comparison. The authors classified each individual in both groups on the basis of military occupational specialties as a radar worker, a nonradar worker, or not classifiable by specialty as either. Of those placed in the radar group, they found 19 individuals with cataracts and 2,625 without cataracts; of those in the nonradar group, 21 had cataracts and 1,935 did not, a nonsignificant difference. (The remaining 510 individuals with and without cataracts could not be classified.)

In another study, Cleary and Pasternack obtained occupational histories from personnel then employed at 16 microwave installations and used the histories to differentiate controls from exposure cases. By this means, they selected 736 workers as being occupationally exposed to RFR and 559 workers from the same locations and occupational environments (other than RFR) as controls.

Exposed and control groups were given slit-lamp examinations and each person was graded for subcataractous lens changes, classified as minute defects, opacification, relucency, sutural defects, and posterior polar

defects on a scale of 0 ("insignificant") to 3 ("large numbers or major degree of change, short of clinically recognized cataract"). The "eye score" was the unweighted sum of scores for each type of defect, and a linear regression of mean eye scores versus age was used for each group. The slope of the regression line for the exposed group was significantly higher that for the control group, but a significant difference in age distribution between the two groups as well as the subjective scoring method and arbitrary scale rendered the results questionable.

Appleton and coworkers performed a survey consisting of examinations of the eyes of personnel at Army posts where various types of electronic communication, detection, guidance, and weather equipment were under development, test, and use. Ophthalmologists without prior knowledge of the occupational histories of the individuals examined their eyes for visual acuity and the presence of vacuoles, and the fundus with special attention to the posterior pole. Opacities, vacuoles, and posterior subcapsular iridescence were each scored on a binary basis (presence or absence). By occupation, each person was deemed to be either in the experimental group or control group and the scores for each group were tabulated by age (in decade increments). The authors concluded that the results do not support the contention that cataracts occurring in those performing duties in the vicinity of equipment that generates RFR are a result of RFR exposure except in documented cases of severe exposure. A similar conclusion was reached in a later survey that included personnel at other military bases, but no statistical treatment of the results was given for either study.

Hollows and Douglas more recently examined the lenses of 53 radiolinemen occupationally exposed to RFR by erecting and maintaining radio, TV, and repeater towers throughout Australia. The group included workers who had maximal cumulative RFR exposure but excluded persons known to have cataracts or who had cataracts removed. The frequencies ranged from 558 kHz to 527 MHz. Measurements of power density in and around work areas yielded values varying from 0.08 to 3956 mW/sq cm. The results of these examinations were statistically compared with those for 39 age-matched non-radiolinemen controls from the same Australian states.

The primary ocular finding was of "posterior subcapsular cataract (PSC)" in one or both eyes of 21% (11/53) of the radiolinemen and in 8% (3/39) of the controls, a difference at the 8.6% significance level; or in 18% (19/106) of both eyes of the radiolinemen and 8% (6/78) of the control eyes, a difference at the 4.3% significance level. The authors also reported that nuclear sclerosis (a type of lens opacity possibly due to exposure to solar irrradiation) was present in 50 (47%) of the eyes of radiolinemen and in 34 (44%) of the eyes of controls, a nonsignificant difference. Lens capsule pseudoexfoliation was not found in either group. Not indicated, however, was the degree of vision degradation due to the presence of postcapsular cataract (and/or of nuclear sclerosis).

In summary, most of the findings of ocular effects in humans were due

more to age rather than exposure to RFR, except for cases of possible occupational exposure of individuals at levels and durations likely to have been sufficient to heat the eye to temperatures well in excess of those found damaging in animal experiments.

The RFR-auditory effect is a well recognized phenomenon experienced by persons in the main beam of pulsed-RFR emitters within short distances from the antenna. Although extensive studies have not been performed that involved exposures of humans to pulsed RFR directed specifically toward determining whether the effect can cause harm, no cases are known of health impairment related to perception of RFR pulses as sound. It is especially noteworthy that no apparent ill effects were experienced by volunteers from exposure to pulse power densities as high as 2,000 mW/sq cm.

Perception of 2.45-GHz CW RFR via the skin by human volunteers (for exposure durations of the order of 10 seconds) was found to have a threshold of about 30 mW/sq cm. Therefore, persons who inadvertently enter a region in which the incident power densities are below this threshold but above present exposure standards may not perceive the RFR cutaneously and thus not be warned thereby that such levels are present. By contrast, the threshold for human perception of infrared radiation was found to be about 2 mW/sq cm.

Several studies have been performed indicating that shocks and burns of varying degrees of severity could occur for persons making electrical contact with large metallic objects in the vicinity of emitters of RFR in the VLF-MF range (10 kHz to 3 MHz), a problem that was not explicitly addressed in the prevailing RFR-exposure standards. However, exposure standards currently being developed, and specifically the 1987 ANSI standard, are expected to include maximum permissible levels to avoid such hazards.

6.2 STUDIES WITH ANIMALS

RFR-induced teratogenesis was sought in various organisms, including several species each of insects, birds, rodents, and nonhuman primates. In most studies with the darkling beetle (tenebrio molitor), the levels of RFR used were usually high enough to significantly heat the subjects. Nevertheless, the data of some early investigators led them to conclude that the terata they found were not due entirely to the heat produced by the RFR. Subsequent investigators, however, were unable to confirm such findings; they suggested instead that the earlier findings were probably ascribable to the presence of uncontrolled non-RFR factors. Thus, there is no valid evidence for the occurrence of teratogenic effects in the darkling beetle at RFR levels that are not thermogenic.

A similar conclusion can be reached about the teratogenesis studies with Japanese-quail eggs and about RFR-induced developmental abnormalities in hatched quail. On the other hand, retardation of development in embryos of domestic chickens was ascribed by others to exposure of eggs to RFR at relatively low power densities (about 3.5 mW/sq cm average).

In the latter studies, the ambient temperatures were selected to compensate for rises in mean internal egg temperature. However, other investigators showed that the temperature gradients within RFR-exposed eggs are much higher than in sham-exposed eggs, so even though the mean temperatures of RFR- and sham-exposed eggs were rendered approximately the same, the temperatures at various internal locations in the RFR-exposed eggs most likely significantly exceeded the highest local temperatures within the sham-exposed eggs. Thus, the purported nonthermal basis for RFR-induced teratogenesis in the chicken is questionable.

The results of studies of RFR-induced teratogenesis and developmental abnormalities in rodents were mixed. With mice, both positive and negative findings were reported. One effect, however, a statistically significant retardation in postnatal growth due to exposure in utero to RFR at levels exceeding 10 mW/sq cm, was reported in several of the more recent studies (an effect found with hamsters as well). On the other hand, all of the investigations with rats yielded negative results and indications that the RFR levels necessary to cause significant prenatal terata or postnatal growth or development retardation are close to, or above, the lethal level for rat dams.

The findings above led Berman and coworkers to conclude that the mouse may be more suitable than the rat as an animal model for investigations of possible teratogenic effects of RFR in humans, a conclusion that appears to be specious because of the large physiological differences between any species of rodent and humans, and among the three rodent species studied themselves. Investigations with nonhuman primates would yield much more definitive findings. In squirrel-monkey study primarily on possible behavioral effects, Kaplan and coworkers reported several unexpected infant deaths of borderline statistical significance for the RFR-exposure groups (at whole-body SARs up to 3.4 W/kg), a finding that could not be confirmed in a followup study specifically directed toward infant mortality. However, an independent replication of the latter study has not been undertaken.

Overall, the findings of investigations performed thus far on possible RFR-induced teratogenesis and developmental abnormalities support the conclusion that such effects can occur from temperature increases caused by the RFR rather than from any special teratogenic properties of RFR, and that the likelihood that such effects would occur in humans from nonoccupational exposure to RFR is negligible.

In the many studies of possible mutagenic effects of RFR on bacteria, yeasts, or fruit flies, the findings indicated that mutations do not occur except under conditions in which the RFR produces significant temperature rises in the specimens. Regarding mutagenesis in mammals, several studies showed that exposure of male rodents to levels of RFR that produce frank heating of the testes tends to reduce fertility, but that such RFR levels were not mutagenic. No valid evidence was found that chronic exposure to RFR at levels within prior or current standards induces or promotes any form of cancer in mammals. (However, note also the discussion below of the chronic study by Guy and coworkers.)

About possible effects of RFR on the nervous system, many early studies of the blood-brain barrier are now believed to have suffered from the presence of significant artifact in the biological methodology used. In other studies, results interpreted by the investigators as RFR-induced alterations of the BBB were most likely ascribable instead to changes in the relative sizes of vascular and extravascular volumes in the brain. In recent studies, however, in which artifact was reduced substantially and perhaps rendered negligible, the results indicated that hyperthermic levels of RFR are necessary to alter the BBB.

In studies on RFR-induced histopathological and histochemical changes in the nervous system, most of the positive findings were thermally based. A notable exception was the recent work by Sanders and co-workers, which showed that inhibition of respiratory chain function can be induced by RFR at levels that do not produce measurable tissue hyperthermia, an effect worthy of further investigation.

Problems associated with the use of metallic electrodes to record EEGs and evoked responses during exposure led to discounting of the positive findings in studies involving such use. Such problems were essentially eliminated by the development of high-resistance, carbon-loaded-Teflon electrodes that were tissue-compatible and thus chronically-implantable. When such electrodes were used to measure EEGs and/or evoked responses of conscious (unanesthetized) animals during RFR-exposure, differences between responses of RFR- and sham-exposed animals were nonsignificant. It is noteworthy that for rabbits, used frequently for such studies, the EEGs and evoked responses were found to vary widely among unanesthetized control animals, as well as with time for individual rabbits, thereby reducing confidence in any findings (positive or negative) with rabbits.

The controversy regarding the calcium-efflux phenomenon in its various manifestations (and apparent contradictions) seems rather unlikely to be resolved in the near future. Nevertheless, there appears to be common agreement among researchers on RFR bioeffects that the phenomenon is not one of concern as a possible RFR hazard to humans.

Possible effects of RFR on the immune system were sought in a variety of investigations. In many early studies, suspensions of various classes of leukocytes were exposed to RFR in vitro, but such studies suffered from lack of adequate control of cell temperature during exposure. In later studies, therefore, considerable effort was devoted to developing exposure systems that permitted maintenance of cell temperature constant at optimum value during exposure or that provided means for deliberate temperature increases to predetermined values for comparison. Many of the studies with such systems were devoted to determining the effects of RFR on lymphocyte proliferation (without and with stimulation by various mitogens) or on functional characteristics of lymphocytes as components of the immune system. In those studies where exposed cultures were held at the same temperature during exposure as control cultures, negative findings (nonsignificant differences in results between exposed and control cultures) were obtained, and where the findings were positive, the effects on the exposed cultures were

clearly of thermal origin.

Also sought in early studies were effects of exposure of erythrocytes to RFR in vitro. Among the findings reported were significant hemolysis and potassium-ion (K+) efflux for rabbit erythrocytes exposed to RFR at average power densities as low as 1 mW/sq cm. In subsequent studies, however, hemoglobin and K+ losses from rabbit erythrocytes by heating with RFR from room temperature to 37 deg C did not differ significantly from losses due to conventional heating; the threshold SAR for effect was found to exceed 46 W/kg. Significant hemolysis and K+ loss were not found for human erythrocytes heated by either means to 37 deg C, thus indicating that RFR may not induce similar changes in rabbit and human blood.

It is noteworthy that the temperatures used in all of those erythrocyte studies were well above the region where a phase transition occurs in the cell membrane. (Such a phase transition is observed as a sharp change in slope of an Arrhenius plot.) In other studies, in which temperatures were used that spanned the transition region, RFR was found to cause significant effects on erythrocyte hemolysis and K+ losses, but only at temperatures within the transition region. Possible mechanisms for such effects were suggested. However, the significance of such effects with regard to hazards of RFR to human health is unclear.

Exposure of animals to RFR in vivo to ascertain possible immunological effects yielded mixed results. Some studies showed apparent diminution of immune responses to RFR, but with no clear dependence on RFR level; results of other studies appeared to indicate that survival was extended by exposure to RFR. In investigations with Japanese quail, RFR-related differences in antigenic responses were not found, except when elevated temperature was implicated. Some investigators reported that exposure of mammals to RFR increased proliferation of leukocytes or production of antibodies (relative to controls), but with few exceptions, measured or estimated SARs were well in excess of 1 W/kg. In more recent studies, subtle effects on the mammalian immune system were sought with the use of advances in assay methods, with some investigations directed toward the effects of RFR on the activity of natural killer (NK) cells and with attention to the possible effects of non-RFR stress. The results showed that SARs much higher than 1 W/kg were necessary for such effects.

More directly relevant to possible effects of RFR-exposure on the human immune system would be studies in which animals are chronically exposed to RFR (preferably over virtually their entire lifetimes), to determine whether such exposure adversely affects their health, longevity, and resistance to natural disease or experimental challenge with various microorganisms or toxins therefrom. Because of limitations in funding, however, relatively few such studies have been done and even fewer have been repeated by other laboratories.

In the most comprehensive chronic study to date (by Guy and coworkers), which involved exposure of 100 rats to RFR and concurrent sham-exposure of 100 rats for virtually their full lifetimes (except those

withdrawn for interim tests and those that died before the end of the exposure regimen). Tests of 10 rats withdrawn from each group after 13 months of exposure (interim kill) showed that the RFR subgroup had significantly higher splenic T- and B-lymphocyte counts than the sham subgroup; these higher counts were ascribed to stimulation of the lymphoid system by the RFR. This effect, however, was not seen in similar tests conducted on completion of the exposure regimen, and its absence was provisionally ascribed to immunosenescence. Longevity was not affected by the RFR at corresponding times during the regimen.

No primary malignancies were found at the interim kill (in rats younger than one year). However, probably the most controversial finding of the entire study was that for the rats older than one year, a total of 18 of those RFR-exposed and only 5 of those sham-exposed had various kinds of primary malignant lesions. Several cogent arguments were advanced to discount the biological significance of this finding; these included the points that the difference between the numbers of RFR- and sham-exposed rats afflicted with each specific type of malignancy was nonsignificant, and that because the numbers of rats with each type of malignancy were small, statistical significance was attained only by combining them, an oncologically dubious procedure. Nevertheless, it appears that the issue can be resolved only by further studies.

Concerning other possible physiological and biochemical effects of RFR, various studies have shown that the thermoregulatory systems of nonhuman primates can readily compensate for high RFR levels, a finding that is most significant relative to possible hazards of human exposure because of the closer anatomical and physiological similarities among human and nonhuman primates than between those of humans and any other mammals.

Most of the studies of possible RFR-induced effects on the endocrine system were conducted on rodents. Those that yielded positive findings indicated that the effects were largely due to increases in the thermal burdens of the animals. In many of the studies, the observed changes in endocrine function may have been influenced significantly by stresses in the animals. For this reason, the studies by Michaelson and coworkers are notable for the efforts toward reducing stress by acclimating the animals to handling and to the experimental situation. Nevertheless, some of the reported subtle effects of RFR on the endocrine system are worthy of further study.

Regarding effects of RFR on the heart, some early studies were conducted in which excised hearts were exposed to RFR, and others in which the whole animal was exposed in vivo The positive findings reported in most of those studies (bradycardia, tachycardia, or both) were suspect because of the use of attached or indwelling electrodes that probably introduced significant artifact in the results. Later studies involving the use of electrodes that were not perturbed by, or did not perturb, the RFR yielded results indicating that heart rates were altered only at RFR levels that caused significant body-temperature rises or otherwise added to the thermal burden of the animal.

Also investigated, both in excised animal hearts and in vivo, was the possibility that pulsed RFR at repetition rates synchronous with various periodic characteristics of the EKG could alter heart rate. Frey and coworkers reported that tachycardia was induced in excised frog hearts by RFR pulses in synchrony with the EKG, but this finding with isolated hearts or in intact animals could not be confirmed by other researchers.

Other investigators showed that for CW RFR, levels well in excess of 1 mW/sq cm or 1 W/kg were necessary for significant alterations of heart rate. Results of another important study indicated that the functioning of hearts already damaged from other causes is not affected by exposure to CW RFR at levels of 10 mW/sq cm or lower.

Early studies in the U.S.A. on possible effects of RFR on behavior were engendered by the hypothesis held in the USSR that RFR can have direct effects on the central nervous system (CNS) and that such effects could occur at "nonthermal" levels of RFR and thereby alter behavior in the absence of measurable RFR-induced increases in body temperature.

Many studies of avoidance behavior by animals appeared to indicate that RFR is a noxious or unpleasant stimulus. However, there is considerable evidence that the RFR-induced changes in behavioral patterns observed in animals are the responses by their thermoregulatory systems, to minimize heat absorption in normal or warm ambient environments (including high levels of humidity) or to obtain warmth in relatively cold environments. Thus, other than auditory perception of RFR pulses, animals apparently do not directly sense RFR (other than as heat). The results of studies on RFR disruption of animal performance or learned behavior were quite variable; however, most of the findings showed that the observed changes in behavior were ascribable to the additional thermal burden imposed by the RFR, and specifically were significant at measured or estimated whole-body SARs well in excess of 1 W/kg.

The relatively few studies of possible synergism of RFR with various psychoactive drugs, such as diazepam, chlorpromazine, chlordiazepoxide, and dextroamphetamine, yielded unclear or inconsistent results. In some studies, the changes in drug dose-response relationship were subtle and not necessarily induced by the RFR. In most studies that yielded RFR-induced changes in drug response, average power densities of 1 mW/sq cm or higher coupled with relatively high drug dosages were necessary. The results of still other studies showed no RFR-induced response changes. The absence of synergistic effects between consumption of alcohol and RFR except at very high doses of the former were especially noteworthy. In general, it is most unlikely that the effects of psychoactive drugs prescribed by physicians or the effects of recreationally taken alcohol would be altered by exposure to RFR at environmental levels.

Results of early studies with microorganisms, notably those of Webb and coworkers, were regarded as evidence of nonthermal effects of RFR, and therefore created considerable controversy. Existence of resonances in the submillimeter-wave region was postulated on theoretical grounds, and a number of studies were performed that apparently confirmed that

hypothesis. However, results of later studies involving use of more sophisticated engineering and biological techniques to reduce artifact did not confirm the earlier findings of resonances or other indications of nonthermal effects. In addition, the effects of RFR on giant algal cells found by Pickard and coworkers were thermally induced. On the other hand, resonances in the range 2-9 GHz were reported recently for DNA from E. coli in specially prepared aqueous solutions to obtain DNA molecules having substantially uniform length. These resonances appear indicative of direct action of RFR with such molecules, but the effect is evidently damped out for intact DNA within cells.

The effects of exposure of mammalian cells and constituents thereof to RFR in vitro were also studied, mostly at SARs higher than 4 W/kg. As would be expected at such SARs, the effects reported were associated with temperature changes.

Thus far, several thousand investigations have been conducted on the biological effects of RFR, including virtually every aspect of possible interest or concern. In overall conclusion, most of the experimentally confirmed findings derived from the studies examined in this document (believed representative of that large body of literature) indicate that RFR at environmental levels is a benign agent with respect to possible deleterious effects on the health of humans, including those people most susceptible to risk of harm.

7 MASTER LIST OF REFERENCES

The references in each section are combined below alphabetically and chronologically by first author. In square brackets after each citation are the page numbers in which the citation appears in the printed version and the sections or subsections in which the citation appears in the computer-stored version.

Abhold, R.H., M.J. Ortner, M.J. Galvin, and D.I. McRee
STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHZ MICROWAVE RADIATION: II. EFFECTS ON THYROID AND ADRENAL AXES HORMONES
Radiat. Res., Vol. 88, No. 3, pp. 448-455 (1981)
[384, 440]

ACGIH
THRESHOLD LIMIT VALUES (TLV) FOR CHEMICAL SUBSTANCES AND PHYSICAL AGENTS IN THE WORK ENVIRONMENT WITH INTENDED CHANGES FOR 1983-84
Ann. American Conference of Governmental Industrial Hygienists, Vol. 8, pp. 190-191 (1984)
[7-9]

Adair, E.R. and B.W. Adams
MICROWAVES MODIFY THERMOREGULATORY BEHAVIOR IN SQUIRREL MONKEY
Bioelectromagnetics, Vol. 1, No. 1, pp. 1-20 (1980a)
[410]

Adair, E.R. and B.W. Adams
MICROWAVES INDUCE PERIPHERAL VASODILATION IN SQUIRREL MONKEY
Science, Vol. 207, pp. 1381-1383 (21 March 1980b)
[410]

Adair, E.R.
MICROWAVES AND THERMOREGULATION
In J.C. Mitchell (ed.), AEROMEDICAL REVIEW: USAF RADIOFREQUENCY RADIATION BIOEFFECTS RESEARCH PROGRAM--A REVIEW., USAF School of Aerospace Medicine, Brooks Air Force Base, TX, Review 4-81, Report No. SAM-TR-81-30, pp. 145-158 (1981)
[411]

Adair, E.R. and B.W. Adams
ADJUSTMENTS IN METABOLIC HEAT PRODUCTION BY SQUIRREL MONKEYS EXPOSED TO MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiology, Vol. 50, No. 4, pp. 1049-1058 (1982)
[411]

Adair, E.R. and B.W. Adams
BEHAVIORAL THERMOREGULATION IN THE SQUIRREL MONKEY: ADAPTATION PROCESSES DURING PROLONGED MICROWAVE EXPOSURE
Behav. Neurosci., Vol. 97, No. 1, pp. 49-61 (1983)
[411]

Adair, E.R., D.E. Spiers, J.A.J. Stolwijk, and C.B. Wenger
TECHNICAL NOTE: ON CHANGES IN EVAPORATIVE HEAT LOSS THAT RESULT FROM EXPOSURE TO NONIONIZING ELECTROMAGNETIC RADIATION
J. Microwave Power, Vol. 18, No. 2, pp. 209-211 (1983)
[417]

Adair, E.R., B.W. Adams, and G.M. Akel
MINIMAL CHANGES IN HYPOTHALAMIC TEMPERATURE ACCOMPANY MICROWAVE-INDUCED ALTERATION OF THERMOREGULATORY BEHAVIOR
Bioelectromagnetics, Vol. 5, No. 1, pp. 13-30 (1984a)
[412]

Adair, E.R., C.B. Wenger, and D.E. Spiers
TECHNICAL NOTE: BEYOND ALLOMETRY
J. Microwave Power, Vol. 19, No. 2, pp. 145-148 (1984b)
[417]

Adey, W.R.
TISSUE INTERACTIONS WITH NONIONIZING ELECTROMAGNETIC FIELDS
Physiol. Rev., Vol. 61, pp.435-514 (1981)
[26, 587]

Adey, W.R., S.M. Bawin, B.F. Burge, H.I. Bassen, and K.E. Franke,
ELECTRIC FIELDS IN CAT BRAIN EXPOSED TO 450 MHZ CW FIELDS IN SEMI-FAR FIELDS
In Abstracts of Bioelectromagnetics Symposium, Washington, D. C., p. 35 (August 1981)
[337]

Adey, W.R., S.M. Bawin, and A.F. Lawrence
EFFECTS OF WEAK AMPLITUDE-MODULATED MICROWAVE FIELDS ON CALCIUM EFFLUX FROM AWAKE CAT CEREBRAL CORTEX
Bioelectromagnetics, Vol. 3, No. 3, pp. 295-307 (1982)
[336, 338]

Adey, W.R. and A.F. Lawrence (eds.)
NONLINEAR ELECTRODYNAMICS IN BIOLOGICAL SYSTEMS
(Proceedings of the International Conference on Nonlinear Electrodynamics in Biological Systems, held at Pettis Memorial Veterans Hospital under sponsorship of the Veterans Administration, Loma Linda, CA, during 5-9 June 1983), Plenum Press, New York (1984)
[26]

AFOSH STANDARD 161-9
EXPOSURE TO RADIOFREQUENCY RADIATION
Headquarters, U.S. Air Force, Washington, DC 20330-5000 (1984)
[8-9, 77-78]

Air Force Magazine
GUIDE TO AIR FORCE BASES
Air Force/Space Digest, pp. 221-239 (September 1969)
[48]

Albert, E.N. and M. DeSantis
DO MICROWAVES ALTER NERVOUS SYSTEM STRUCTURE?
Ann. N.Y. Acad. Sci., Vol. 247, pp. 87-108 (1975)
[271, 273]

Albert, E.N. and M. DeSantis
HISTOLOGICAL OBSERVATIONS ON CENTRAL NERVOUS SYSTEM
In C.C. Johnson and M.L. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8010, pp. 299-310 (1976)
[272]

Albert, E.N.
LIGHT AND ELECTRON MICROSCOPIC OBSERVATIONS ON THE BLOOD-BRAIN BARRIER AFTER MICROWAVE IRRADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 294-304 (1977)
[234, 236, 246]

Albert, E.N.
REVERSIBILITY OF MICROWAVE-INDUCED BLOOD-BRAIN BARRIER PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 323-327 (1979)
[234-236]

Albert, E.N. and J.M. Kerns
REVERSIBLE MICROWAVE EFFECTS ON THE BLOOD-BRAIN BARRIER
Brain Res. Vol. 230, pp. 153-164 (1981)
[234]

Albert, E.N., M.F. Sherif, N.J. Papadopoulos, F.J. Slaby, and J. Monahan
EFFECT OF NONIONIZING RADIATION ON THE PURKINJE CELLS OF THE RAT CEREBELLUM
Bioelectromagnetics, Vol. 2, No. 3, pp. 247-257 (1981a)
[273, 277]

Albert, E.N., M.F. Sherif, and N.J. Papadopoulos
EFFECT OF NONIONIZING RADIATION ON THE PURKINJE CELLS OF THE UVULA IN SQUIRREL MONKEY CEREBELLUM
Bioelectromagnetics, Vol. 2, No. 3, pp. 241-246 (1981b)
[276-277]

Allen, J.W. and S.A. Latt
IN VIVO BrD U-33258 HOECHST ANALYSIS OF DNA REPLICATION KINETICS AND SISTER CHROMATID EXCHANGE FORMATION IN MOUSE SOMATIC AND MEIOTIC CELLS
Chromosoma, Vol. 58, pp. 325-340 (1976)
[182]

Allen, S. and W. Hurt
CALORIMETRIC MEASUREMENTS OF MICROWAVE ENERGY ABSORPTION BY MICE AFTER SIMULTANEOUS EXPOSURE OF 18 ANIMALS
Radio Sci., Vol. 14, No. 6S, pp. 1-4 (1979)
[25, 334]

Allis, J.W., C.M. Weil, and D.E. Janes, Jr.
A CROSSED-BEAM APPARATUS FOR SIMULTANEOUS SPECTROPHOTOMETRIC OBSERVATION AND MICROWAVE EXPOSURE OF BIOCHEMICAL SAMPLES
Rev. Sci. Instrum., Vol. 46, pp. 1344-1349 (1975)
[320]

Allis, J.W., C.F. Blackman, M.L. Fromme, and S.G. Benane
MEASUREMENT OF MICROWAVE RADIATION ABSORBED BY BIOLOGICAL SYSTEMS, 1, ANALYSIS OF HEATING AND COOLING DATA
Radio Sci., Vol. 12, No. 6S, pp. 1-8 (1977)
[156, 160, 320, 323]

Allis, J.W. and M.L. Fromme
ACTIVITY OF MEMBRANE-BOUND ENZYMES EXPOSED TO SINUSOIDALLY MODULATED 2450-MHZ MICROWAVE RADIATION
Radio Sci., Vol. 14, No. 6S, pp. 85-91 (1979)
[320-321]

Allis, J.W. and B.L. Sinha
FLUORESCENCE DEPOLARIZATION STUDIES OF RED CELL MEMBRANE FLUIDITY. THE EFFECT OF EXPOSURE TO 1.0-GHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 2, No. 1, pp. 13-22 (1981)
[353, 356-358]

Allis, J.W. and B.L. Sinha
FLUORESCENCE DEPOLARIZATION STUDIES OF THE PHASE TRANSITION IN MULTILAMELLAR PHOSPHOLIPID VESICLES EXPOSED TO 1.0-GHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 3, No. 3, pp. 323-332 (1982)
[356]

Ames, B.N., J. McCann, and E. Yamasaki
METHODS FOR DETECTING CARCINOGENS AND MUTAGENS WITH THE SALMONELLA/MAMMALIAN-MICROSOME MUTAGENICITY TEST
Mutation Res., Vol. 31, No. 6, pp. 347-364 (1975)
[15, 167]

Ames, B.N.
IDENTIFYING ENVIRONMENTAL CHEMICALS CAUSING MUTATIONS AND CANCER
Science, Vol. 204, pp. 587-592 (11 May 1979)
[155]

Anderstam, B., Y Hamnerius, S. Hussain, and L. Ehrenberg
STUDIES OF POSSIBLE GENETIC EFFECTS IN BACTERIA OF HIGH FREQUENCY ELECTROMAGNETIC FIELDS
Hereditas, Vol. 98, pp. 11-32 (1983)
[162, 166]

ANSI, C95.1-1974
SAFETY LEVEL OF ELECTROMAGNETIC RADIATION WITH RESPECT TO PERSONNEL
Published by the Institute of Electrical and Electronics Engineers, New York (1974)
[5-6, 9, 12, 148, 211]

ANSI, C95.1-1982
SAFETY LEVELS WITH RESPECT TO HUMAN EXPOSURE TO RADIO FREQUENCY ELECTROMAGNETIC FIELDS, 300 KHZ TO 100 GHZ
Published by the Institute of Electrical and Electronics Engineers, New York (1982)
[5-11, 13-14, 21-22, 25, 147, 149-151, 153, 211, 346, 351, 398]

Appleton, B. and G.C. McCrossan
MICROWAVE LENS EFFECTS IN HUMANS
Arch. Ophthal., Vol. 88, pp. 259-262 (1972)
[100-101, 104-106]

Appleton, B.
RESULTS OF CLINICAL SURVEYS FOR MICROWAVE OCULAR EFFECTS
U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 73-8031 (1973)
[102]

Appleton, B., S.E. Hirsh, and P.V.K. Brown
INVESTIGATION OF SINGLE-EXPOSURE MICROWAVE OCULAR EFFECTS AT 3000 MHZ
Ann. N.Y. Acad. Sci., Vol. 247, pp. 125-134 (1975a)
[90]

Appleton, B., S.E. Hirsh, and P.V.K. Brown
MICROWAVE LENS EFFECTS: II. RESULTS OF FIVE-YEAR SURVEY
Acta Ophthal., Vol. 93, pp. 257-258 (1975b)
[102, 104-106]

Ashani, Y., F.H. Henry, and G.N. Catravas
COMBINED EFFECTS OF ANTICHOLINESTERASE DRUGS AND LOW-LEVEL MICROWAVE RADIATION
Radiat. Res., Vol 84, pp. 496-503 (1980)
[543, 545]

Athey, T.W.
COMPARISON OF RF-INDUCED CALCIUM EFFLUX FROM CHICK BRAIN TISSUE AT DIFFERENT FREQUENCIES: DO THE SCALED POWER DENSITY WINDOWS ALIGN?
Bioelectromagnetics, Vol. 2, No. 4, pp. 407-409 (1981)
[326]

Aurell, E. and B. Tengroth
LENTICULAR AND RETINAL CHANGES SECONDARY TO MICROWAVE EXPOSURE
Acta Ophthal., Vol. 51, No. 6, pp. 764-771 (1973)
[99]

Baranski, S. and Z. Edelwejn
STUDIES ON THE COMBINED EFFECT OF MICROWAVES AND SOME DRUGS ON BIOELECTRIC ACTIVITY OF THE RABBIT CENTRAL NERVOUS SYSTEM
Acta Physiologica Polonica, Vol. 19, No. 1, pp. 31-41 (1968)
[531]

Baranski, S., H. Ludwicka, and S. Szmigielski
THE EFFECT OF MICROWAVES ON RABBIT ERYTHROCYTE PERMEABILITY
Medycyna Latnicza Z., Vol. 39, pp. 75-79 (1971)
[352]

Baranski, S., S. Szmigielski, and J. Moneta
EFFECTS OF MICROWAVE IRRADIATION IN VITRO ON CELL MEMBRANE PERMEABILITY
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 173-177 (1974)
[352]

Baranski, S. and Z. Edelwejn
EXPERIMENTAL MORPHOLOGIC AND ELECTROENCEPHALOGRAPHIC STUDIES OF MICROWAVE EFFECTS ON THE NERVOUS SYSTEM
Ann. N.Y. Acad. Sci., Vol. 247, pp. 109-116 (1975)
[300, 308]

Baranski, S. and P. Czerski
BIOLOGICAL EFFECTS OF MICROWAVES
Dowden, Hutchinson & Ross, Inc., Stroudsburg, Pennsylvania (1976)
[344]

Barnes, F.S. and C.-L.J. Hu
MODEL FOR SOME NONTHERMAL EFFECTS OF RADIO AND MICROWAVE FIELDS ON BIOLOGICAL MEMBRANES
IEEE Trans. Microwave Theory Tech., Vol. 25, No.9, pp. 742-746 (1977)
[592]

Barsoum, Y.H. and W.F. Pickard
EFFECTS OF ELECTROMAGNETIC RADIATION IN THE RANGE 20-300 MHZ ON THE VACUOLAR POTENTIAL OF CHARACEAN CELLS
Bioelectromagnetics, Vol. 3, No. 2, pp. 193-201 (1982a)
[594]

Barsoum, Y.H. and W.F. Pickard
THE VACUOLAR POTENTIAL OF CHARACEAN CELLS SUBJECTED TO ELECTROMAGNETIC RADIATION IN THE RANGE 200-8,200 MHZ
Bioelectromagnetics, Vol. 3, No. 4, pp. 393-400 (1982b)
[595]

Baum, S.J., M.E. Ekstrom, W.D. Skidmore, D.E. Wyant, and J.L. Atkinson
BIOLOGICAL MEASUREMENTS IN RODENTS EXPOSED CONTINUOUSLY THROUGHOUT THEIR ADULT LIFE TO PULSED ELECTROMAGNETIC RADIATION
Health Phys., Vol. 30, No. 2, pp. 161-166 (1976)
[175-176]

Bawin, S.M., L.K. Kaczmarek, and W.R. Adey
EFFECTS OF MODULATED VHF FIELDS ON THE CENTRAL NERVOUS SYSTEM
Ann. N.Y. Acad. Sci., Vol. 247, pp. 74-81 (1975)
[313, 317-319, 321-317, 332]

Bawin, S.M. and W.R. Adey
INTERACTIONS BETWEEN NERVOUS TISSUES AND WEAK ENVIRONMENTAL ELECTRIC FIELDS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 323-330 (1976a)
[315, 323]

Bawin, S.M. and W.R. Adey
SENSITIVITY OF CALCIUM BINDING IN CEREBRAL TISSUE TO WEAK ENVIRONMENTAL ELECTRIC FIELDS OSCILLATING AT LOW FREQUENCIES
Proc. Nat. Acad. Sci., Vol. 73, No. 6, pp. 1999-2003 (1976b)
[315-316, 323, 326, 328, 330]

Bawin, S.M., A. Sheppard, and W.R. Adey
POSSIBLE MECHANISMS OF WEAK ELECTROMAGNETIC FIELD COUPLING IN BRAIN TISSUE
Biochemistry and Bioenergetics, Vol. 5, pp. 67-76 (1978)
[319, 325]

Berman, E., J.B. Kinn, and H.B. Carter
OBSERVATIONS OF MOUSE FETUSES AFTER IRRADIATION WITH 2.45 GHZ MICROWAVES
Health Phys., Vol. 35, pp. 791-801 (1978)
[199-201]

Berman, E., H.B. Carter, and D. House
TESTS OF MUTAGENESIS AND REPRODUCTION IN MALE RATS EXPOSED TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 1, No. 2, pp. 65-76 (1980)
[175]

Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF RAT FETUSES AFTER IRRADIATION WITH 2450-MHZ (CW) MICROWAVES
J. Microwave Power, Vol. 16, No. 1, pp. 9-13 (1981)
[207, 212, 218]

Berman, E., H.B. Carter, and D. House
REDUCED WEIGHT IN MICE OFFSPRING AFTER IN UTERO EXPOSURE TO 2450-MHZ (CW) MICROWAVES
Bioelectromagnetics, Vol. 3, No. 2, pp. 285-291 (1982a)
[200-201, 213, 219]

Berman, E., H.B. Carter, and D. House
OBSERVATIONS OF SYRIAN HAMSTER FETUSES AFTER EXPOSURE TO 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 17, No. 2, pp. 107-112 (1982b)
[201, 219]

Bermant, R.I., D.L. Reeves, D.M. Levinson, and D.R. Justesen
CLASSICAL CONDITIONING OF MICROWAVE-INDUCED HYPERTHERMIA IN RATS
Radio Sci., Vol. 14, No. 6S, pp. 201-207 (1979)
[482]

Bianco, B., G.P. Drago, M. Marchesi, C. Martini, G.S. Mela, and S. Ridell
MEASUREMENTS OF COMPLEX DIELECTRIC CONSTANT OF HUMAN SERA AND ERYTHROCYTES
IEEE Trans. Instr. & Meas., Vol. 28, No. 4, pp. 290-295 (1979)
[19]

Birenbaum, L., G.M. Grosof, S.W. Rosenthal, and M.M. Zaret
EFFECT OF MICROWAVES ON THE EYE
IEEE Trans. Biomed. Eng., Vol.16, pp. 7-14 (1969a)
[85]

Birenbaum, L., I.T. Kaplan, W. Metlay, S.W. Rosenthal, H. Schmidt, and M.M. Zaret
EFFECT OF MICROWAVES ON THE RABBIT EYE
J. Microwave Power, Vol. 4, No. 4, pp. 232-243 (1969b)
[85-86]

Birenbaum. L., I.T. Kaplan, W. Metlay, S.W. Rosenthal, and M.M. Zaret
MICROWAVE AND INFRA-RED EFFECTS ON HEART RATE, RESPIRATION RATE AND SUBCUTANEOUS TEMPERATURE OF THE RABBIT
J. Microwave Power, Vol. 10, No. 1, pp. 3-18 (1975)
[450]

Blackman, C.F., S.G. Benane, C.M. Weil, and J.S. Ali
EFFECTS OF NONIONIZING ELECTROMAGNETIC RADIATION ON SINGLE-CELL BIOLOGIC SYSTEMS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 352-366 (1975)
[156, 170, 179-180]

Blackman, C.F., M.C. Surles, and S.G. Benane
THE EFFECT OF MICROWAVE EXPOSURE ON BACTERIA: MUTATION INDUCTION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 406-413 (1976)
[155]

Blackman, C.F. and J.A. Black
MEASUREMENT OF MICROWAVE RADIATION ABSORBED BY BIOLOGICAL SYSTEMS: II. ANALYSIS BY DEWAR-FLASK CALORIMETRY
Radio Sci., Vol 12, No. 6S, pp. 9-14 (1977)
[323]

Blackman, C.F., J.A. Elder, C.M. Weil, S.G. Benane, D.C. Eichinger, and D.E. House
INDUCTION OF CALCIUM-ION EFFLUX FROM BRAIN TISSUE BY RADIO-FREQUENCY RADIATION: EFFECTS OF MODULATION FREQUENCY AND FIELD STRENGTH
Radio Sci., Vol. 14, No. 6S, pp. 93-98 (1979)
[321, 323]

Blackman, C.F., S.G. Benane, J.A. Elder, D.E. House, J.A. Lampe, and J.M. Faulk
INDUCTION OF CALCIUM-ION EFFLUX FROM BRAIN TISSUE BY RADIO-FREQUENCY RADIATION: EFFECT OF SAMPLE NUMBER AND MODULATION FREQUENCY ON THE POWER-DENSITY WINDOW
Bioelectromagnetics, Vol. 1, No. 1, pp. 35-43 (1980a)
[323, 325]

Blackman, C.F., S.G. Benane, W.T. Joines, M.A. Hollis, and D.E. House
CALCIUM-ION EFFLUX FROM BRAIN TISSUE: POWER DENSITY VERSUS INTERNAL FIELD-INTENSITY DEPENDENCIES AT 50-MHZ RF RADIATION
Bioelectromagnetics, Vol. 1, No. 3, pp. 277-283 (1980b)
[324-325, 327]

Blackman, C.F., S.G. Benane, D.E. House, and W.T. Joines
EFFECTS OF ELF (1-120 HZ) AND MODULATED (50 HZ) RF FIELDS ON THE EFFLUX OF CALCIUM IONS FROM BRAIN TISSUE
Bioelectromagnetics, Vol. 6, No. 1, pp. 1-11 (1985a)
[326]

Blackman, C.F., S.G. Benane, J.R. Rabinowitz, D.E. House, and W.T. Joines
A ROLE FOR THE MAGNETIC FIELD IN THE RADIATION-INDUCED EFFLUX OF CALCIUM IONS FROM BRAIN TISSUE IN VITRO
Bioelectromagnetics, Vol. 6, No. 4, pp. 327-337 (1985b)
[326]

Blasberg, R.G.
PROBLEMS OF QUANTIFYING EFFECTS OF MICROWAVE IRRADIATION ON THE BLOOD-BRAIN BARRIER
Radio Sci., Vol. 14, No. 6S, pp. 335-344 (1979)
[246]

Bollinger, J.N.
DETECTION AND EVALUATION OF RADIOFREQUENCY ELECTROMAGNETIC RADIATION-INDUCED BIOLOGICAL DAMAGE IN MACACA MULATTA
Final report submitted by Southwest Research Institute, San Antonio, Texas, to the USAF School of Aerospace Medicine, Brooks AFB, Texas (February 1971)
[409]

Bollinger, J.N., R.L. Lawson, and W.C. Dolle
RESEARCH ON BIOLOGICAL EFFECTS OF VLF BAND ELECTROMAGNETIC RADIATION
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report SAM-TR-74-52 on Contract F41609-73-C-0035, submitted by Southwest Research Institute, San Antonio, Texas (1974)
[197]

Bowman, R.R.
A PROBE FOR MEASURING TEMPERATURE IN RADIO-FREQUENCY HEATED MATERIAL
IEEE Trans. Microwave Theory Tech., Vol. 24, No. 1, pp. 43-45 (1976)
[25, 305]

Bracken, T.D.
FIELD MEASUREMENTS AND CALCULATIONS OF ELECTROSTATIC EFFECTS OF OVERHEAD TRANSMISSION LINES
IEEE Trans. Power App. Syst., Vol. 95, pp. 494-504 (1976)
[148]

Bronaugh, E.L. and D.R. Kerns
CALIBRATION OF A MULTIMODE MICROWAVE EXPOSURE CHAMBER
1975 Electromagnetic Compatibility Symposium Record, IEEE No. 75CH1002-5 EMC, pp. 5BIIb1-5BIIb5 (1975)
[487]

Bruce, W.R., R. Furrer, and A.J. Wyrobek
ABNORMALITIES IN THE SHAPE OF MURINE SPERM AFTER ACUTE TESTICULAR X-IRRADIATION
Mutat. Res., Vol. 23, pp. 381-386 (1974)
[428]

Bruce-Wolfe, V. and D.R. Justesen
MICROWAVE-INDUCED HYPERTHERMIA AND THE VISUALLY EVOKED ELECTROCORTICAL RESPONSE OF THE GUINEA PIG
Radio Sci., Vol. 14, No. 6S, pp. 187-191 (1979)
[301]

Brunkard, K.M. and W.F. Pickard
THE MEMBRANE POTENTIAL OF CHARACEAN CELLS EXPOSED TO AMPLITUDE-MODULATED, LOW-POWER 147-MHZ RADIATION
Bioelectromagnetics, Vol. 5, No. 3, pp. 353-356 (1984)
[595]

Burdette, E.C., F.L. Cain, and J. Seals
IN VIVO PROBE MEASUREMENT TECHNIQUE FOR DETERMINING DIELECTRIC PROPERTIES OF VHF THROUGH MICROWAVE FREQUENCIES
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 4, pp. 414-427 (1980)
[19]

Burdeshaw, J.A. and S. Schaffer
FACTORS ASSOCIATED WITH THE INCIDENCE OF CONGENITAL ANOMALIES: A LOCALIZED INVESTIGATION
Final Report, Report No. XXIII, 24 May 1973-31 March 1976, Contract No. 68-02-0791, EPA 600/1-77-016 (March 1977)
[71-72, 220]

Burr, J.G. and J.H. Krupp
REAL-TIME MEASUREMENT OF RFR ENERGY DISTRIBUTION IN THE MACACA MULATTA HEAD
Bioelectromagnetics, Vol. 1, No. 1, pp. 21-34 (1980)
[25, 527]

Bush, L.G., D.W. Hill, A. Riazi, L.J. Stensaas, L.M. Partlow, and O.P. Gandhi
EFFECTS OF MILLIMETER-WAVE RADIATION ON MONOLAYER CELL CULTURES. III. A SEARCH FOR FREQUENCY-SPECIFIC ATHERMAL BIOLOGICAL EFFECTS ON PROTEIN SYNTHESIS
Bioelectromagnetics, Vol. 2, No. 2, pp. 151-159 (1981)
[574]

Cain, C.A. and W.J. Rissman
MAMMALIAN AUDITORY RESPONSES TO 3.0 GHz MICROWAVE PULSES
IEEE Trans. Biomed. Eng., Vol. 25, No. 3, pp. 288-293 (1978)
[114, 121, 127]

Cain, C.A., G.V. Rama Rau, and W.A.F. Tompkins
ENHANCEMENT OF ANTIBODY-COMPLEMENT CYTOTOXICITY AGAINST VIRUS-TRANSFORMED HAMSTER PARA-7 CELLS TREATED WITH HEAT AND MICROWAVE RADIATION
Radiat. Res., Vol. 88, No. 1, pp. 96-107 (1981)
[348]

Cairnie, A.B. and K.E. Leach
QUANTITATIVE STUDIES OF CYTOLOGICAL DAMAGE IN MOUSE TESTIS PRODUCED BY EXPOSURE TO HEAT
Can. J. Genet. Cytol., Vol. 22, pp. 93-102 (1980)
[427-428]

Cairnie, A.B., D.A. Hill, and H.M. Assenheim
DOSIMETRY FOR A STUDY OF EFFECTS OF 2.45-GHZ MICROWAVES ON MOUSE TESTIS
Bioelectromagnetics, Vol. 1, No. 3, pp. 325-336 (1980)
[427]

Cairnie, A.B. and R.K. Harding
CYTOLOGICAL STUDIES IN MOUSE TESTIS IRRADIATED WITH 2.45-GHZ CONTINUOUS-WAVE MICROWAVES
Radiat. Res., Vol. 87, pp. 100-108 (1981)
[427]

Candas, V., E.R. Adair, and B.W. Adams
THERMOREGULATORY ADJUSTMENTS IN SQUIRREL MONKEYS EXPOSED TO MICROWAVES AT HIGH POWER DENSITIES
Bioelectromagnetics, Vol. 6, No. 3, pp. 221-234 (1985)
[413]

Carpenter, R.L., D.K. Biddle, and C.A. Van Ummersen
OPACITIES IN THE LENS OF THE EYE EXPERIMENTALLY INDUCED BY EXPOSURE TO MICROWAVE RADIATION
IRE Trans. Med. Electronics, Vol. 7, pp. 152-157 (1960)
[82-84]

Carpenter, R.L. and C.A. Van Ummersen
THE ACTION OF MICROWAVE RADIATION ON THE EYE
J. Microwave Power, Vol. 3, No. 1, pp. 3-19 (1968)
[83, 85, 89]

Carpenter, R.L. and E.M. Livstone
EVIDENCE FOR NONTHERMAL EFFECTS OF MICROWAVE RADIATION: ABNORMAL DEVELOPMENT OF IRRADIATED INSECT PUPAE
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 173-178 (1971)
[185, 187]

Carroll, D.R., D.M. Levinson, D.R. Justesen, and R.L. Clarke
FAILURE OF RATS TO ESCAPE FROM A POTENTIALLY LETHAL MICROWAVE FIELD
Bioelectromagnetics, Vol. 1, No. 2, pp. 101-115 (1980)
[476, 479]

CENSUS
U.S. Bureau of the Census
COUNTY AND CITY DATA BOOK, 1967 (A STATISTICAL ABSTRACT SUPPLEMENT)
U.S. Government Printing Office, Washington, D.C. (1967)
[48, 50]

Chang, B.K., A.T. Huang, W.T. Joines, and R.S. Kramer
THE EFFECT OF MICROWAVE RADIATION (1.0 GHZ) ON THE BLOOD-BRAIN BARRIER IN DOGS
Radio Sci., Vol. 17, No. 5S, pp. 165-168 (1982)
[237]

Chatterjee, I., M.J. Hagmann, and O.P. Gandhi
ELECTROMAGNETIC-ENERGY DEPOSITION IN AN INHOMOGENEOUS BLOCK MODEL OF MAN FOR NEAR-FIELD IRRADIATION CONDITIONS
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 12, pp. 1452-1459 (1980)
[22, 26]

Chatterjee, I., M.J. Hagmann, and O.P. Gandhi
AN EMPIRICAL RELATIONSHIP FOR ELECTROMAGNETIC ENERGY ABSORPTION IN MAN FOR NEAR-FIELD EXPOSURE CONDITIONS
IEEE Trans. Microwave Theory Tech., Vol. 29, No. 11, pp. 1235-1238 (1981)
[26]

Chatterjee, I., O.P. Gandhi, and M.J. Hagmann
NUMERICAL AND EXPERIMENTAL RESULTS FOR NEAR-FIELD ELECTROMAGNETIC ABSORPTION IN MAN
IEEE Trans. Microwave Theory Tech., Vol. 30, No. 11, pp. 2000-2005 (1982)
[26]

Chatterjee I., D. Wu, and O.P. Gandhi
HUMAN BODY IMPEDANCE AND THRESHOLD CURRENTS FOR PERCEPTION AND PAIN FOR CONTACT HAZARD ANALYSIS IN THE VLF-MF BAND
IEEE Trans. Biomed. Eng., Vol. 33, No. 5, pp. 486-494 (1986)
[149]

Chen, K.-M. and B.S. Guru
INTERNAL EM FIELD AND ABSORBED POWER DENSITY IN HUMAN TORSOS INDUCED BY 1-500-MHZ EM WAVES
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 9, pp. 746-756 (1977)
[22]

Chernovetz, M.E., D.R. Justesen, N.W. King, and J.E. Wagner
TERATOLOGY, SURVIVAL, AND REVERSAL LEARNING AFTER FETAL IRRADIATION OF MICE BY 2450-MHZ MICROWAVE ENERGY
J. Microwave Power, Vol. 10, No. 4, pp. 391-409 (1975)
[198-199, 469]

Chernovetz, M.E., D.R. Justesen, and A.F. Oke
A TERATOLOGICAL STUDY OF THE RAT: MICROWAVE AND INFRARED RADIATIONS COMPARED
Radio Sci., Vol. 12, No. 6S, pp. 191-197 (1977)
[205, 207, 212]

Chou, C.-K., R. Galambos, A.W. Guy, and R.H. Lovely
COCHLEAR MICROPHONICS GENERATED BY MICROWAVE PULSES
J. Microwave Power, Vol. 10, No. 4, pp. 361-367 (1975)
[119-120, 123]

Chou, C.-K., A.W. Guy, and R. Galambos
CHARACTERISTICS OF MICROWAVE-INDUCED COCHLEAR MICROPHONICS
Radio Sci., Vol. 12, No. 6S, pp. 221-227 (1977)
[120]

Chou, C.-K. and A.W. Guy
EFFECTS OF ELECTROMAGNETIC FIELDS ON ISOLATED NERVE AND MUSCLE PREPARATIONS
IEEE Trans. Microwave Theory Tech., Vol. 26, No. 3, pp. 141-147 (1978)
[250, 254, 256-258, 265]

Chou, C.-K. and R. Galambos
MIDDLE-EAR STRUCTURES CONTRIBUTE LITTLE TO AUDITORY PERCEPTION OF MICROWAVES
J. Microwave Power, Vol. 14, No. 4, pp. 321-326 (1979)
[123, 125]

Chou, C.-K., and A.W. Guy
CARBON-LOADED TEFLON ELECTRODES FOR CHRONIC EEG RECORDINGS IN MICROWAVE RESEARCH
J. Microwave Power, Vol. 14, No. 4, pp. 399-404 (1979a)
[123, 301, 451]

Chou, C.-K., and A.W. Guy
MICROWAVE-INDUCED AUDITORY RESPONSES IN GUINEA PIGS: RELATIONSHIP OF THRESHOLD AND MICROWAVE-PULSE DURATION
Radio Sci., Vol. 14, No. 6S, pp. 193-197 (1979b)
[124]

Chou, C.-K., A.W. Guy, K.R. Foster, R. Galambos, and D.R. Justesen
HOLOGRAPHIC ASSESSMENT OF MICROWAVE HEARING
Science, Vol. 209, pp. 1143-1144 (5 Sept 1980a)
[129]

Chou, C.-K., L.F. Han, and A.W. Guy
MICROWAVE RADIATION AND HEART-BEAT RATE OF RABBITS
J. Microwave Power, Vol. 15, No. 2, pp. 87-93 (1980b)
[450]

Chou, C.-K., A.W. Guy, J.B. McDougall, and L.-F. Han
EFFECTS OF CONTINUOUS AND PULSED CHRONIC MICROWAVE EXPOSURE ON RABBITS
Radio Sci., Vol. 17, No. 5S, pp. 185-193 (1982)
[303, 527]

Chou, C.-K., A.W. Guy, and R.B. Johnson
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 3. SAR IN RATS EXPOSED IN 2450-MHZ CIRCULARLY POLARIZED WAVEGUIDE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-19 (1983b)
[397-399]

Chou, C.-K., K.-C. Yee, and A.W. Guy
AUDITORY RESPONSE IN RATS EXPOSED TO 2,450 MHZ ELECTROMAGNETIC WAVES IN A CIRCULARLY POLARIZED WAVEGUIDE
Bioelectromagnetics, Vol. 6, No. 3, pp. 323-326 (1985a)
[124]

Clapman, R.M. and C.A. Cain
ABSENCE OF HEART-RATE EFFECTS IN ISOLATED FROG HEART IRRADIATED WITH PULSE MODULATED MICROWAVE ENERGY
J. Microwave Power, Vol. 10, No. 4, pp. 411-419 (1975)
[452]

Clarke, R.L. and D.R. Justesen
TEMPERATURE GRADIENTS IN THE MICROWAVE-IRRADIATED EGG: IMPLICATIONS FOR AVIAN TERATOGENESIS
J. Microwave Power, Vol. 18, No. 2, pp. 169-180 (1983)
[194]

Cleary, S.F., B.S. Pasternack, and G.W. Beebe
CATARACT INCIDENCE IN RADAR WORKERS
Arch. Environ. Health, Vol. 11, pp. 179-182 (1965)
[97]

Cleary, S.F. and B.S. Pasternack
LENTICULAR CHANGES IN MICROWAVE WORKERS
Arch. Environ. Health, Vol. 12, pp. 23-29 (1966)
[98]

Cleary, S.F.
UNCERTAINTIES IN THE EVALUATION OF THE BIOLOGICAL EFFECTS OF MICROWAVE AND RADIOFREQUENCY RADIATION
Health Phys., Vol. 25, pp. 387-404 (1973)
[17, 26]

Cleary, S.F.
BIOLOGICAL EFFECTS OF MICROWAVE AND RADIOFREQUENCY RADIATION
CRC Critical Reviews in Environmental Control, Vol. 8, pp. 121-166 (1977)
[26]

Cleary, S.F.
RECAPITULATION: BIOMEDICAL EFFECTS
Bull. N.Y. Acad. Med., Vol. 55, No. 11, pp. 1119-1125 (1979)
[26]

Cleary, S.F., L.-M. Liu, and F. Garber
VIABILITY AND PHAGOCYTOSIS OF NEUTROPHILS EXPOSED IN VITRO TO 100-MHZ RADIOFREQUENCY RADIATION
Bioelectromagnetics, Vol. 6, No. 1, pp. 53-60 (1985)
[351]

Cogan, D.G., S.J. Fricker, M. Lubin, D.D. Donaldson, and H. Hardy
CATARACTS AND ULTRA-HIGH-FREQUENCY RADIATION
A.M.A. Arch. Ind. Health, Vol. 18, pp. 299-302 (1958)
[81]

Cockcroft, D.L. and D.A.T. New
EFFECTS OF HYPERTHERMIA ON RAT EMBRYOS IN CULTURE
Nature, Vol. 258, pp. 604-606 (1975)
[211]

Cohen, B.H., A.M. Lilienfeld, S. Kramer, and L.C. Hyman
PARENTAL FACTORS IN DOWN'S SYNDROME-RESULTS OF THE SECOND BALTIMORE CASE-CONTROL STUDY
In E.G. Hook and I.H. Porter (eds.), POPULATION GENETICS-STUDIES IN HUMANS, Academic Press, New York, pp. 301-352 (1977)
[67-68]

Conover, D.L., W.E. Murray, Jr., E.D. Foley, J.M. Lary, and W.H. Parr
MEASUREMENT OF ELECTRIC- AND MAGNETIC-FIELD STRENGTHS FROM INDUSTRIAL RADIO-FREQUENCY (6-38 MHZ) PLASTIC SEALERS
Proc. IEEE, Vol. 68, No. 1, pp. 17-20 (1980)
[211]

Cook, H.F.
DIELECTRIC BEHAVIOR OF SOME TYPES OF HUMAN TISSUES AT MICROWAVE FREQUENCIES
Brit. J. Appl. Phys., Vol. 2, pp. 295-300 (1951)
[18]

Cook, H.F.
A COMPARISON OF DIELECTRIC BEHAVIOR OF PURE WATER AND HUMAN BLOOD AT MICROWAVE FREQUENCIES
Brit. J. Appl. Phys., Vol. 3, pp. 249-255 (1952)
[18]

Cooper, M.S. and N.M. Amer
THE ABSENCE OF COHERENT VIBRATIONS IN THE RAMAN SPECTRA OF LIVING CELLS
Phys. Lett., Vol. 98A, No. 3, pp. 138-142 (1983)
[564-565]

Cornsweet, T.N.
THE STAIRCASE METHOD IN PSYCHOPHYSICS
Amer. J. Psych., Vol. 75, pp. 485-491 (1962)
[144]

Courtney, K.R., J.C. Lin, A.W. Guy, and C.-K. Chou
MICROWAVE EFFECT ON RABBIT SUPERIOR CERVICAL GANGLION
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 10, pp. 809-813 (1975)
[251]

Crawford, M.L.
GENERATION OF STANDARD EM FIELDS USING TEM TRANSMISSION CELLS
IEEE Trans. Electromagn. Compat., Vol. 16, No. 4, pp. 189-195 (1974)
[321]

Cunitz, R.J., W.D. Galloway, and C.M. Berman
BEHAVIORAL SUPPRESSION BY 383-MHZ RADIATION
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 3, pp. 313-316 (1975)
[516]

Czerski, P., M. Siekierzynski, and A. Gidynski
HEALTH SURVEILLANCE OF PERSONNEL OCCUPATIONALLY EXPOSED TO MICROWAVES. I. THEORETICAL CONSIDERATIONS AND PRACTICAL ASPECTS
Aerospace Med., pp. 1137-1142 (October 1974)
[43]

Czerski, P.
MICROWAVE EFFECTS ON THE BLOOD-FORMING SYSTEM WITH PARTICULAR REFERENCE TO THE LYMPHOCYTE
Ann. N.Y. Acad. Sci., Vol. 247, pp. 232-242 (1975)
[344, 368, 372]

Czerski, P.
RADIOFREQUENCY RADIATION EXPOSURE LIMITS IN EASTERN EUROPE
J. Microwave Power, Vol. 20, No. 4, pp. 233-239 (1985)
[10-11]

Dalziel, C.F. and T.H. Mansfield
EFFECT OF FREQUENCY ON PERCEPTION CURRENTS
Trans. AIEE, Vol. 69, Pt. II, pp. 1162-1168 (1950)
[148]

Dalziel, C.F. and W.R. Lee
LETHAL ELECTRIC CURRENTS
IEEE Spectrum, Vol. 6, pp. 44-50 (1969)
[148]

D'Andrea, J.A., O.P. Gandhi, and J.L. Lords
BEHAVIORAL AND THERMAL EFFECTS OF MICROWAVE RADIATION AT RESONANT AND NONRESONANT WAVELENGTHS
Radio Sci., Vol. 12, No. 6S, pp. 251-256 (1977)
[493-494]

D'Andrea, J.A., O.P. Gandhi, J.L. Lords, C.H. Durney, C.C. Johnson, and L. Astle
PHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF CHRONIC EXPOSURE TO 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 14, No. 4, pp. 351-362 (1979)
[495, 500]

D'Andrea, J.A., O.P. Gandhi, J.L. Lords, C.H. Durney, L. Astle, L.J. Stensaas, and A.A. Schoenberg
PHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF PROLONGED EXPOSURE TO 915 MHZ MICROWAVES
J. Microwave Power, Vol. 15, No. 2, pp. 123-134 (1980)
[498]

Dardalhon, M., D. Averbeck, and A.J. Bertaud
DETERMINATION OF A THERMAL EQUIVALENT OF MILLIMETER MICROWAVES IN LIVING CELLS
J. Microwave Power, Vol. 14, No. 4, pp. 307-312 (1979)
[158, 160]

Dardalhon, M., D. Averbeck, and A.J. Bertaud
STUDIES ON POSSIBLE GENETIC EFFECTS OF MICROWAVES IN PROCARYOTIC AND EUCARYOTIC CELLS
Radiat. Environ. Biophys., Vol. 20, pp. 37-51 (1981)
[160]

de Lorge, J.O.
THE EFFECTS OF MICROWAVE RADIATION ON BEHAVIOR AND TEMPERATURE IN RHESUS MONKEYS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 158-174 (1976)
[444, 493, 518, 522, 525-526]

de Lorge, J.O.
OPERANT BEHAVIOR AND RECTAL TEMPERATURE OF SQUIRREL MONKEYS DURING 2.45-GHZ MICROWAVE IRRADIATION
Radio Sci., Vol. 14, No. 6S, pp. 217-225 (1979)
[493, 520, 525]

de Lorge, J.O. and C.S. Ezell
OBSERVING-RESPONSES OF RATS EXPOSED TO 1.28- and 5.62-GHZ MICROWAVES
Bioelectromagnetics, Vol. 1, No. 2, pp. 183-198 (1980)
[491, 527]

de Lorge, J.O.
OPERANT BEHAVIOR AND COLONIC TEMPERATURE OF MACACA MULATTA EXPOSED TO RADIO FREQUENCY FIELDS AT AND ABOVE RESONANT FREQUENCIES
Bioelectromagnetics, Vol. 5, No. 2, pp. 233-246 (1984)
[522]

Deno, D.W.
CALCULATING ELECTROSTATIC EFFECTS OF OVERHEAD TRANSMISSION LINES
IEEE Trans. Power App. Syst., Vol. 93, pp. 1458-1471 (1974)
[148]

Descheux, P., T. Douss, R. Santini, P. Binder, and R. Fontanges
EFFECT OF MICROWAVE IRRADIATION (2450 MHZ) ON MURINE CYTOTOXIC LYMPHOCYTE AND NATURAL KILLER (NK) CELLS
J. Microwave Power, Vol. 19, No. 2, pp. 107-110 (1984)
[379]

Dietzel, F.
EFFECTS OF ELECTROMAGNETIC RADIATION ON IMPLANTATION AND INTRAUTERINE DEVELOPMENT OF THE RAT
Ann. N.Y. Acad. Sci., Vol. 247, pp. 367-376 (1975)
[207-208, 211]

Dixon, W.J.
RATIOS INVOLVING EXTREME VALUES
Ann. Math. Stat., Vol. 22, pp. 68-78 (1951)
[316]

Dorfman, B.H. and L.L. Van Zandt
VIBRATION OF DNA POLYMER IN VISCOUS SOLVENT
Biopolymers, Vol. 22, pp. 2639-2665 (1983)
[576]

Dorfman, B.H. and L.L. Van Zandt
EFFECTS OF VISCOUS SOLVENT ON DNA POLYMER IN A FIBER
Biopolymers, Vol. 23, pp. 913-922 (1984)
[576]

Dumanskij, J.D. and M.G. Shandala
THE BIOLOGIC ACTION AND HYGIENIC SIGNIFICANCE OF ELECTROMAGNETIC FIELDS OF SUPERHIGH AND ULTRAHIGH FREQUENCIES IN DENSELY POPULATED AREAS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 289-293 (1974)
[297, 300]

Durney, C.H., C.C. Johnson, P.W. Barber, H.W. Massoudi, M.F. Iskander, J.L. Lords, D.K. Ryser, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [SECOND EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-78-22 (1978)
[20-22, 93, 140, 173, 180, 184, 213-214, 227-230, 234, 270, 274, 282, 292, 296, 298, 300, 368, 393-395, 397, 409, 427, 432, 434, 461-465, 485, 494, 497, 518, 520, 526, 531, 536, 543, 554]

Durney, C.H., M.F. Iskander, H. Massoudi, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK [THIRD EDITION]
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-80-32 (1980)
[20, 218, 385]

Dutta, S.K., W.H. Nelson, C.F. Blackman, and D.J. Brusick
LACK OF MICROBIAL GENETIC RESPONSE TO 2.45-GHZ CW AND 8.5- TO 9.6-GHZ PULSED MICROWAVES
J. Microwave Power, Vol. 14, No. 3, pp. 275-280 (1979)
[156, 167]

Dutta, S.K., J. Choppalla, M.A. Hossain, T.N. Bhar, and H.S. Ho
DOSIMETRIC MEASUREMENT AND BIOEFFECT STUDIES OF LOW LEVEL 915 MHZ CW MICROWAVES USING TEM CRAWFORD CELL
J. Basic Appl. Sci., Vol. 2, pp. 43-52 (1982)
[330]

Dutta, S.K., A. Subramoniam, B. Ghosh, and R. Parshad
MICROWAVE RADIATION-INDUCED CALCIUM ION EFFLUX FROM HUMAN NEUROBLASTOMA CELLS IN CULTURE
Bioelectromagnetics, Vol. 5, No.1, pp. 71-78 (1984)
[330, 338]

Edwards, M.J.
CONGENITAL DEFECTS IN GUINEA PIGS: PRENATAL RETARDATION OF BRAIN GROWTH OF GUINEA PIGS FOLLOWING HYPERTHERMIA DURING GESTATION
Teratology, Vol. 2, pp. 329-336 (1969)
[219]

Edwards, M.J.
CONGENITAL DEFECTS DUE TO HYPERTHERMIA
Adv. Vet. Sci. Comp. Med., Vol. 22, pp. 29-52 (1978)
[210]

Edwards, G.S., C.C. Davis, J.D. Saffer, and M.L. Swicord
RESONANT MICROWAVE ABSORPTION OF SELECTED DNA MOLECULES
Phys. Rev. Lett., Vol. 53, No. 13, pp. 1284-1287 (1984)
[576]

Edwards, G.S., C.C. Davis, J.D. Saffer, and M.L. Swicord
MICROWAVE-FIELD-DRIVEN ACOUSTIC MODES IN DNA
Biophys. J., Vol. 47, pp. 799-807 (1985)
[576]

Ehrenberg, L., b. Anderstam, S. Hussain, and Y. Hamnerius
STATISTICAL ASPECTS OF THE DESIGN OF BIOLOGICAL TESTS FOR THE DETECTION OF LOW GENOTOXIC ACTIVITY
Hereditas, Vol. 98, pp. 33-41 (1983)
[163]

Elder, J.A. and J.S. Ali
THE EFFECT OF MICROWAVES (2450 MHZ) ON ISOLATED RAT LIVER MITOCHONDRIA
Ann. N.Y. Acad. Sci., Vol. 247, pp. 251-262 (1975)
[155-156, 180, 484]

Elder, J.A. and D.F. Cahill (eds.)
BIOLOGICAL EFFECTS OF RADIOFREQUENCY RADIATION
Final Report EPA-600/8-83-026F, Environmental Protection Agency, NC 27711 (September 1984)
[10]

EPA
FEDERAL RADIATION PROTECTION GUIDANCE; PROPOSED ALTERNATIVES FOR CONTROLLING PUBLIC EXPOSURE TO RADIOFREQUENCY RADIATION; NOTICE OF PROPOSED RECOMMENDATIONS
Federal Register (Part II), Vol. 51, No. 146, pp. 27318-27339 (30 July 1986)
[9-10, 12]

Fisher, P.D., J.K. Lauber, and W.A.G. Voss
THE EFFECT OF LOW-LEVEL 2450 MHZ CW MICROWAVE IRRADIATION AND BODY TEMPERATURE ON EARLY EMBRYONAL DEVELOPMENT IN CHICKENS
Radio Sci., Vol. 14, No. 6S, pp. 159-163 (1979)
[193]

Fleiss, J.L.
STATISTICAL METHODS FOR RATES AND PROPORTIONS
Wiley, NY (1973)
[105]

Fleiss, J.L.
STATISTICAL METHODS FOR RATES AND PROPORTIONS
2nd Edition, John Wiley and Sons, New York (1981)
[51]

Foster, K.R. and E.D. Finch
MICROWAVE HEARING: EVIDENCE FOR THERMOACOUSTIC AUDITORY STIMULATION BY PULSED MICROWAVES
Science, Vol. 185, pp. 256-258 (19 July 1974)
[110]

Foster, K.R. and J.L. Schepps
DIELECTRIC PROPERTIES OF TUMOR AND NORMAL TISSUES AT RADIO THROUGH MICROWAVE FREQUENCIES
J. Microwave Power, Vol. 16, No. 2, pp. 107-119 (1981)
[19]

Foster, K.R., J.L. Schepps, and B.R. Epstein
MICROWAVE DIELECTRIC STUDIES ON PROTEINS, TISSUES, AND HETEROGENEOUS SUSPENSIONS
Bioelectromagnetics, Vol. 3, No. 1, pp. 29-43 (1982)
[19]

Frazer, J.W., J.H. Merritt, S.J. Allen, R.H. Hartzell, J.A. Ratliff, A.F. Chamness, R.E. Detwiler, and T. McLellan
THERMAL RESPONSES TO HIGH-FREQUENCY ELECTROMAGNETIC RADIATION FIELDS
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-76-20 (September 1976)
[409]

Frey, A.H.
AUDITORY SYSTEM RESPONSE TO RADIO-FREQUENCY ENERGY
Aerospace Med., Vol. 32, pp. 1140-1142 (1961)
[111-112]

Frey, A.H.
HUMAN AUDITORY SYSTEM RESPONSE TO MODULATED ELECTROMAGNETIC ENERGY
J. Appl. Physiol., Vol. 17, No. 4, pp. 689-692 (1962)
[112]

Frey, A.H.
MAIN STEM EVOKED RESPONSES ASSOCIATED WITH LOW-INTENSITY PULSED UHF ENERGY
J. Appl. Physiol., Vol. 23, No. 6, pp. 984-988 (1967)
[112]

Frey, A.H. and E. Seifert
PULSE MODULATED UHF ENERGY ILLUMINATION OF THE HEART ASSOCIATED WITH CHANGE IN HEART RATE
Life Sci., Vol. 7, No. 10, Part II, pp. 505-512 (1968)
[254, 452-453]

Frey, A.H., A. Fraser, E. Siefert, and T. Brish
A COAXIAL PATHWAY FOR RECORDING FROM THE CAT BRAIN DURING ILLUMINATION WITH UHF ENERGY
Physiol. and Behav., Vol. 3, pp. 363-364 (1968)
[291]

Frey, A.H.
BIOLOGICAL FUNCTION AS INFLUENCED BY LOW-POWER MODULATED RF ENERGY
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 153-163 (1971)
[257]

Frey, A.H. and R. Messenger, Jr.
HUMAN PERCEPTION OF ILLUMINATION WITH PULSED ULTRAHIGH-FREQUENCY ELECTROMAGNETIC ENERGY
Science, Vol. 181, pp. 356-358 (27 July 1973)
[113-115]

Frey, A.H. and S.R. Feld
AVOIDANCE BY RATS OF ILLUMINATION WITH LOW POWER NONIONIZING ELECTROMAGNETIC ENERGY
J. Compar. Physiol. Psychol., Vol. 89, No. 2, pp. 183-188 (1975)
[465]

Frey, A.H., S.R. Feld, and B. Frey
NEURAL FUNCTION AND BEHAVIOR: DEFINING THE RELATIONSHIP
Ann. N.Y. Acad. Sci., Vol. 247, pp. 433-439 (1975)
[227, 229, 246, 464, 466]

Frey, A.H. and E. Coren
HOLOGRAPHIC ASSESSMENT OF A HYPOTHESIZED MICROWAVE HEARING MECHANISM
Science, Vol. 206, pp. 232-234 (12 Oct 1979)
[128]

Frey, A.H. and E. Coren
HOLOGRAPHIC ASSESSMENT OF MICROWAVE HEARING [A response]
Science, Vol. 209, pp. 1144-1145 (5 Sept 1980)
[129]

Frey. A.H.
DATA ANALYSIS REVEALS SIGNIFICANT MICROWAVE-INDUCED EYE DAMAGE IN HUMANS
J. Microwave Power, Vol. 20., No. 1, pp. 53-55 (1985)
[104-105]

Froehlich, H.
EVIDENCE FOR BOSE CONDENSATION-LIKE EXCITATION OF COHERENT MODES IN BIOLOGICAL SYSTEMS
Phys. Lett., Vol. 51A, No. 1, pp. 21-22 (1975)
[564]

Froehlich, H.
THE BIOLOGICAL EFFECTS OF MICROWAVES AND RELATED QUESTIONS
In L. and C. Marton (eds.), ADVANCES IN ELECTRONICS AND ELECTRON PHYSICS, Vol. 53, Academic Press, pp. 85-152 (1980)
[26]

Froehlich, H.
WHAT ARE NON-THERMAL ELECTRIC BIOLOGICAL EFFECTS?
Bioelectromagnetics, Vol. 3, No. 1, pp. 45-46 (1982)
[26]

Gage, M.I.
MICROWAVE IRRADIATION AND AMBIENT TEMPERATURE INTERACT TO ALTER RAT BEHAVIOR FOLLOWING OVERNIGHT EXPOSURE
J. Microwave Power, Vol. 14, No. 4, pp. 389-398 (1979)
[483, 485]

Gage, M.I., E. Berman, and J.B. Kinn
VIDEOTAPE OBSERVATIONS OF RATS AND MICE DURING AN EXPOSURE TO 2450-MHZ MICROWAVE RADIATION
Radio Sci., Vol. 14, No. 6S, pp. 227-232 (1979a)
[472, 474]

Gage, M.I. and W.M. Guyer
INTERACTION OF AMBIENT TEMPERATURE AND MICROWAVE POWER DENSITY ON SCHEDULE-CONTROLLED BEHAVIOR IN THE RAT
Radio Sci., Vol. 17, No. 5S, pp. 179-184 (1982)
[485]

Galloway, W.D.
MICROWAVE DOSE-RESPONSE RELATIONSHIPS ON TWO BEHAVIORAL TASKS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 410-416 (1975)
[515]

Galvin, M.J., D.I. McRee, and M. Lieberman
EFFECTS OF 2.45-GHZ MICROWAVE RADIATION ON EMBRYONIC QUAIL HEARTS
Bioelectromagnetics, Vol. 1, No. 4, pp. 389-396 (1980a)
[193, 452]

Galvin, M.J. and D.I. McRee
INFLUENCE OF ACUTE MICROWAVE RADIATION ON CARDIAC FUNCTION IN NORMAL AND MYOCARDIAL ISCHEMIC CATS
J. Appl. Physiol: Respiratory, Environmental, and Exercise Physiol., Vol. 50, No. 5, pp. 931-935 (1981a)
[451, 454]

Galvin, M.J., D.I. McRee, C.A. Hall, J.P. Thaxton, and C.R. Parkhurst
HUMORAL AND CELL-MEDIATED IMMUNE FUNCTION IN ADULT JAPANESE QUAIL FOLLOWING EXPOSURE TO 2.45-GHZ MICROWAVE RADIATION DURING EMBRYOGENY
Bioelectromagnetics, Vol. 2, No. 3, pp. 269-278 (1981a)
[367]

Galvin, M.J., C.A. Hall, and D.I. McRee
MICROWAVE RADIATION EFFECTS ON CARDIAC MUSCLE CELLS IN VITRO
Radiat. Res., Vol. 86, pp. 358-367 (1981b)
[194, 453]

Galvin, M.J., D.L. Parks, and D.I. McRee
INFLUENCE OF 2.45 GHZ MICROWAVE RADIATION ON ENZYME ACTIVITY
Radiat. Environ. Biophys., Vol 19, pp. 149-156 (1981c)
[266]

Galvin, M.J., M.S. Dutton, and D.I. McRee
INFLUENCE OF 2.45-GHZ CW MICROWAVE RADIATION ON SPONTANEOUSLY BEATING RAT ATRIA
Bioelectromagnetics, Vol. 3, No. 2, pp. 219-226 (1982a)
[454]

Galvin, M.J., M.J. Ortner, and D.I. McRee
STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHZ MICROWAVE RADIATION--III. BIOCHEMICAL AND HEMATOLOGIC EFFECTS
Radiat. Res., Vol. 90, pp. 558-563 (1982b)
[384]

Galvin, M.J., G.L. MacNichols, and D.I. McRee
EFFECT OF 2450 MHZ MICROWAVE RADIATION ON HEMATOPOIESIS OF PREGNANT MICE
Radiat. Res., Vol. 100, pp. 412-417 (1984)
[376]

Gandhi, O.P.
POLARIZATION AND FREQUENCY EFFECTS ON WHOLE ANIMAL ABSORPTION OF RF ENERGY
Proc. IEEE, Vol. 62, No. 8, pp. 1171-1175 (1974)
[494]

Gandhi, O.P.
CONDITIONS OF STRONGEST ELECTROMAGNETIC POWER DEPOSITION IN MAN AND ANIMALS
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 12, pp. 1021-1029 (1975)
[22]

Gandhi, O.P., E.L. Hunt, and J.A. D'Andrea
DEPOSITION OF ELECTROMAGNETIC ENERGY IN ANIMALS AND IN MODELS OF MAN WITH AND WITHOUT GROUNDING AND REFLECTOR EFFECTS
Radio Sci., Vol. 12, No. 6S, pp. 39-47 (1977)
[22]

Gandhi, O.P., M.J. Hagmann, D.W. Hill, L.M. Partlow, and L. Bush
MILLIMETER WAVE ABSORPTION SPECTRA OF BIOLOGICAL SAMPLES
Bioelectromagnetics, Vol. 1, No. 3, pp. 285-298 (1980)
[565]

Gandhi, O.P. and I. Chatterjee
RADIO-FREQUENCY HAZARDS IN THE VLF TO MF BAND
Proc. IEEE, Vol. 70, No. 12, pp. 1462-1464 (1982)
[148]

Gandhi, O.P., I. Chatterjee, D. Wu, J.A. D'Andrea, and K. Sakamoto
VERY LOW FREQUENCY (VLF) HAZARD STUDY
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report on Contract F33615-83-R-0613, submitted by University of Utah, Salt Lake City, UT (31 January 1985a)
[151, 153]

Gandhi, O.P., I. Chatterjee, D. Wu, and Y.-G. Gu
LIKELIHOOD OF HIGH RATES OF ENERGY DEPOSITION IN THE HUMAN LEGS AT THE ANSI RECOMMENDED 3-30-MHZ RF SAFETY LEVELS
Proc. IEEE, Vol. 73, No. 6, pp. 1145-1147 (1985b)
[151]

Glaser, Z.R. and G.M. Heimer
DETERMINATION AND ELIMINATION OF HAZARDOUS MICROWAVE FIELDS ABOARD NAVAL SHIPS
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 232-238 (1971)
[44]

Goldman, H., J.C. Lin, S. Murphy, and M.F. Lin
CEREBROVASCULAR PERMEABILITY TO Rb-86 IN THE RAT AFTER EXPOSURE TO PULSED MICROWAVES
Bioelectromagnetics, Vol. 5, No. 3, pp. 323-330 (1984)
[237]

Goldmann, N.
THE ROLE OF "OCCUPATIONAL HAZARD" DEFINITIONS IN THE ESTABLISHMENT OF MICROWAVE STANDARDS
Abstracts of Bioelectromagnetics Symposium, Los Angeles, CA, p. 2 (June-July 1982)
[11]

Goldstein, L. and Z. Cisko
A QUANTITATIVE ELECTROENCEPHALOGRAPHIC STUDY OF THE ACUTE EFFECTS OF X-BAND MICROWAVES IN RABBITS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 128-133 (1974)
[296]

Gordon, C.J.
EFFECTS OF AMBIENT TEMPERATURE AND EXPOSURE TO 2450-MHZ MICROWAVE RADIATION ON EVAPORATIVE HEAT LOSS IN THE MOUSE
J. Microwave Power, Vol. 17, No. 2, pp. 145-150 (1982)
[416]

Gordon, C.J.
NOTE: FURTHER EVIDENCE OF AN INVERSE RELATION BETWEEN MAMMALIAN BODY MASS AND SENSITIVITY TO RADIO-FREQUENCY ELECTROMAGNETIC RADIATION
J. Microwave Power, Vol. 18, No. 4, pp. 377-383 (1983)
[417]

Graham, R.B.
THE MEDICAL RESULTS OF HUMAN EXPOSURES TO RADIO FREQUENCY RADIATION
Advisory Group for Aerospace Research and Development (AGARD) Lecture Series No. 138, THE IMPACT OF PROPOSED RADIO FREQUENCY RADIATION STANDARDS ON MILITARY OPERATIONS, pp. 6-1 to 6-8 (1985)
[77]

Green, D.R., F.J. Rosenbaum, and W.F. Pickard
INTENSITY OF MICROWAVE IRRADIATION AND THE TERATOGENIC RESPONSE OF TENEBRIO MOLITOR
Radio Sci., Vol. 14, No. 6S, pp. 165-171 (1979)
[190]

Greene, F.M.
DEVELOPMENT AND CONSTRUCTION OF AN ELECTROMAGNETIC NEAR-FIELD SYNTHESIZER
U.S. Department of Commerce, National Bureau of Standards, NBS Technical Note 652 (1974)
[204, 208, 277]

Greene, F.M.
DEVELOPMENT OF ELECTRIC AND MAGNETIC NEAR-FIELD PROBES
U.S. Department of Commerce, National Bureau of Standards, NBS Technical Note 658 (1975)
[277]

Gruenau, S.P., K.J. Oscar, M.T. Folker, and S.I. Rapoport
ABSENCE OF MICROWAVE EFFECT ON BLOOD-BRAIN BARRIER PERMEABILITY TO C-14-SUCROSE IN THE CONSCIOUS RAT
Exper. Neurobiol., Vol. 75, pp. 299-307 (1982)
[232, 244]

Grundler, W., F. Keilmann, and H. Froehlich
RESONANT GROWTH RATE RESPONSE OF YEAST CELLS IRRADIATED BY WEAK MICROWAVES
Phys. Lett., Vol. 62A, No. 6, pp. 463-466 (1977)
[563, 568]

Guillet, R. and S.M. Michaelson
THE EFFECT OF REPEATED MICROWAVE EXPOSURE ON NEONATAL RATS
Radio Sci., Vol. 12, No. 6S, pp. 125-129 (1977)
[435]

Guy, A.W.
ANALYSIS OF ELECTROMAGNETIC FIELDS INDUCED IN BIOLOGICAL TISSUES BY THERMOGRAPHIC STUDIES ON EQUIVALENT PHANTOM MODELS
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 205-214 (1971)
[130]

Guy, A.W., J.C. Lin, P.O. Kramar, and A.F. Emery
EFFECT OF 2450-MHz RADIATION ON THE RABBIT EYE
IEEE Trans. Microwave Theory Techniques, Vol. 23, No. 6, pp. 492-498 (1975a)
[88-91]

Guy, A.W., C.-K. Chou, J.C. Lin, and D. Christensen
MICROWAVE-INDUCED ACOUSTIC EFFECTS IN MAMMALIAN AUDITORY SYSTEMS AND PHYSICAL MATERIALS
Ann. N.Y. Acad. Sci., Vol 247, pp. 194-218 (1975b)
[116, 118-120, 495]

Guy, A.W. and C.-K. Chou
SYSTEM FOR QUANTITATIVE CHRONIC EXPOSURE OF A POPULATION OF RODENTS TO UHF FIELDS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. II, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8011, pp. 389-410 (1976)
[397, 469, 503]

Guy, A.W., M.D. Webb, and C.C. Sorensen
DETERMINATION OF POWER ABSORPTION IN MAN EXPOSED TO HIGH FREQUENCY ELECTROMAGNETIC FIELDS BY THERMOGRAPHIC MEASUREMENTS ON SCALE MODELS
IEEE Trans. Biomed. Eng., Vol. 23, pp. 361-371 (1976)
[24]

Guy, A.W.
A METHOD FOR EXPOSING CELL CULTURES TO ELECTROMAGNETIC FIELDS UNDER CONTROLLED CONDITIONS OF TEMPERATURE AND FIELD STRENGTH
Radio Sci., Vol. 12, No. 6S, pp. 87-96 (1977)
[351]

Guy, A.W., M.D. Webb, and J.A. McDougall
RF RADIATION ABSORPTION PATTERNS: HUMAN AND ANIMAL MODELING DATA
U.S. Dept. of Health, Education, and Welfare, National Institute for Occupational Safety and Health (NIOSH), Cincinnati, Ohio, Publication PB-274 749 (1977)
[24]

Guy, A.W.
MINIATURE ANECHOIC CHAMBER FOR CHRONIC EXPOSURE OF SMALL ANIMALS TO PLANE-WAVE MICROWAVE FIELDS
J. Microwave Power, Vol. 14, No. 4, pp. 327-338 (1979)
[307]

Guy, A.W., J. Wallace, and J. McDougall
CIRCULARLY POLARIZED 2450 MHZ WAVEGUIDE SYSTEM FOR CHRONIC EXPOSURE OF SMALL ANIMALS TO MICROWAVES
Radio Sci., Vol. 14, No. 6S, pp. 63-74 (1979)
[124, 218, 397, 545]

Guy, A.W., P.O. Kramar, C.A. Harris, and C.-K. Chou
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: METHODOLOGY AND EVALUATION OF OCULAR AND PHYSIOLOGIC EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 37-44 (1980b)
[93, 375]

Guy, A.W., C.-K. Chou, R.B. Johnson, and L.L. Kunz
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 1. DESIGN, FACILITIES, AND PROCEDURES
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-17 (1983a)
[398]

Guy, A.W., C.-K. Chou, and B. Neuhaus
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 2. AVERAGE SAR AND SAR DISTRIBUTION IN MAN EXPOSED TO 450-MHZ RFR
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-18 (1983b)
[398]

Guy, A.W.
HAZARDS OF VLF ELECTROMAGNETIC FIELDS
Advisory Group for Aerospace Research and Development (AGARD) Lecture Series No. 138, THE IMPACT OF PROPOSED RADIO FREQUENCY RADIATION STANDARDS ON MILITARY OPERATIONS, pp. 9-1 to 9-20 (1985)
[147, 153]

Guy, A.W. and C.-K. Chou
VERY LOW FREQUENCY HAZARD STUDY
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report on Contract F33615-83-C-0625, submitted by University of Washington, Seattle WA (May 1985)
[151, 153]

Guy, A.W., C.-K. Chou, L.L. Kunz, J. Crowley, and J. Krupp
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 9. SUMMARY
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-85-64 (1985)
[398, 403]

GWEN
GENERIC ENVIRONMENTAL ASSESSMENT FOR THE GROUND WAVE EMERGENCY NETWORK
Office of Public Affairs, Electronic Systems Division, Hanscom AFB, MA 01731 (April 1985)
[9]

Hagmann, M.J. and O.P. Gandhi
NUMERICAL CALCULATIONS OF ELECTROMAGNETIC ENERGY DEPOSITION IN MODELS OF MAN WITH GROUNDING AND REFLECTOR EFFECTS
Radio Sci., Vol. 14, No. 6S, pp. 23-29 (1979)
[22]

Hagmann, M.J., O.P. Gandhi, and C.H. Durney
NUMERICAL CALCULATIONS OF ELECTROMAGNETIC ENERGY DEPOSITION FOR A REALISTIC MODEL OF MAN
IEEE Trans. Microwave Theory Tech., Vol. 27, No. 9, pp. 804-809 (1979a)
[22]

Hagmann, M.J., O.P. Gandhi, J.A. D'Andrea, and I. Chatterjee
HEAD RESONANCE: NUMERICAL SOLUTION AND EXPERIMENTAL RESULTS
IEEE Trans. Microwave Theory Tech., Vol. 27, No. 9, pp. 809-813 (1979b)
[22-25]

Hagmann, M.J., I. Chatterjee, and O.P. Gandhi
DEPENDENCE OF ELECTROMAGNETIC ENERGY DEPOSITION UPON ANGLE OF INCIDENCE FOR AN INHOMOGENEOUS BLOCK MODEL OF MAN UNDER PLANE-WAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 29, No. 3, pp. 252-255 (1981)
[22]

Hakim, H.B., S.M. Lindsay, and J. Powell
THE SPEED OF SOUND IN DNA
Biopolymers, Vol. 23, pp. 1185-1192 (1984)
[576]

Hall, C.A., D.I. McRee, M.J. Galvin, N.B. White, J.P. Thaxton, and V.L. Christensen
INFLUENCE OF IN VITRO MICROWAVE RADIATION ON THE FERTILIZING CAPACITY OF TURKEY SPERM
Bioelectromagnetics, Vol. 4, No. 1, pp. 43-54 (1983)
[194]

Hamburger, S., J.N. Logue, and P.M. Silverman
OCCUPATIONAL EXPOSURE TO NON-IONIZING RADIATION AND AN ASSOCIATION WITH HEART DISEASE: AN EXPLORATORY STUDY
J. Chron. Dis., Vol. 36, No. 11, pp. 791-802 (1983)
[57, 449]

Hamnerius, Y., H. Olofsson, A. Rasmuson, and B. Rasmuson
A NEGATIVE TEST FOR MUTAGENIC ACTION OF MICROWAVE RADIATION IN DROSOPHILA MELANOGASTER
Mutation Res., Vol. 68, No. 2, pp. 217-223 (1979)
[165-166, 170]

Hamnerius, Y.
EXPOSURE SYSTEMS FOR STUDIES OF THE EFFECTS OF ELECTROMAGNETIC FIELDS ON BIOLOGICAL SYSTEMS
Hereditas, Vol. 98, pp. 43-59 (1983)
[162, 166]

Hamnerius, Y., A. Rasmuson, and B. Rasmuson
BIOLOGICAL EFFECTS OF HIGH-FREQUENCY ELECTROMAGNETIC FIELDS ON SALMONELLA TYPHIMURIUM AND DROSOPHILA MELANOGASTER
Bioelectromagnetics, Vol. 6, No. 4, pp. 405- 414 (1985)
[166-167]

Hamrick, P.E. and B.T. Butler
EXPOSURE OF BACTERIA TO 2450 MHZ MICROWAVE RADIATION
J. Microwave Power, Vol. 8, No. 3, pp. 227-233 (1973)
[577]

Hamrick, P.E. and D.I. McRee
EXPOSURE OF THE JAPANESE QUAIL EMBRYO TO 2.45 GHZ MICROWAVE RADIATION DURING THE SECOND DAY OF DEVELOPMENT
J. Microwave Power, Vol. 10, No. 2, pp. 211-220 (1975)
[192]

Hamrick, P.E. and J.G. Zinkl
EXPOSURE OF RABBIT ERYTHROCYTES TO MICROWAVE IRRADIATION
Radiat. Res., Vol. 62, pp. 164-168 (1975)
[352]

Hamrick, P.E. and S.S. Fox
RAT LYMPHOCYTES IN CELL CULTURE EXPOSED TO 2450 MHZ (CW) MICROWAVE RADIATION
J. Microwave Power, Vol. 12, No. 2, pp. 125-132 (1977)
[345]

Hamrick, P.E., D.I. McRee, P. Thaxton, and C.R. Parkhurst
HUMORAL IMMUNITY OF JAPANESE QUAIL SUBJECTED TO MICROWAVE RADIATION DURING EMBRYOGENY
Health Phys., Vol. 33, pp. 23-33 (1977)
[193, 367-368]

Hamrick, P.E. and D.I. McRee
THE EFFECT OF 2450 MHZ MICROWAVE IRRADIATION ON THE HEART RATE OF EMBRYONIC QUAIL
Health Phys., Vol. 38, pp. 261-268 (1980)
[193, 452]

Hankin, N.N.
THE RADIOFREQUENCY RADIATION ENVIRONMENT: ENVIRONMENTAL EXPOSURE LEVELS AND RF RADIATION EMITTING SOURCES
U.S. EPA Technical Report EPA 520/1-85-014 (1985)
[12]

Harris, L.E., L.A. Stayura, P.F. Ramirez-Talavera, and J.F. Annegers
CONGENITAL AND ACQUIRED ABNORMALITIES OBSERVED IN LIVE-BORN AND STILLBORN NEONATES
Mayo Clinic Proc., Vol. 50, (1975)
[71]

Harrison, G.H., J.E. Robinson, D. McCulloch, and A.Y. Cheung
COMPARISON OF HYPERTHERMAL CELLULAR SURVIVAL IN THE PRESENCE OR ABSENCE OF 2.45 GHZ MICROWAVE RADIATION
Proc. URSI Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 41-45 (June-July 1980)
[347]

Heller, J.H.
CELLULAR EFFECTS OF MICROWAVE RADIATION
In S.F. Cleary (ed.), BIOLOGICAL EFFECTS AND HEALTH IMPLICATIONS OF MICROWAVE RADIATION, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication BRH/DBE 70-2, pp. 116-121 (1970)
[171]

Hendler, E. and J.D. Hardy
INFRARED AND MICROWAVE EFFECTS ON SKIN HEATING AND TEMPERATURE SENSATION
IRE Trans. Med. Electronics, Vol. 7, pp. 143-152 (1960)
[139]

Hendler, E., J.D. Hardy, and D. Murgatroyd
SKIN HEATING AND TEMPERATURE SENSATION PRODUCED BY INFRARED AND MICROWAVE IRRADIATION
In C.M. Herzfeld (ed.), TEMPERATURE. ITS MEASUREMENT AND CONTROL IN SCIENCE AND INDUSTRY, Vol. 3, Part 3, J.D. Hardy (ed.), BIOLOGY AND MEDICINE, Reinhold Pub. Corp., New York, pp. 211-230 (1963)
[139, 145-146]

Hendler, E.
CUTANEOUS RECEPTOR RESPONSE TO MICROWAVE IRRADIATION
In J.D. Hardy (ed.), THERMAL PROBLEMS IN AEROSPACE MEDICINE, Unwin Bros. Ltd., Surrey, U.K., pp. 149-161 (1968)
[139-140, 143, 145]

HEW
U.S. Department of Health, Education, and Welfare
ATLAS OF CANCER MORTALITY FOR U.S. COUNTIES: 1950-1969
DHEW Publication (NIH) 75-780, National Cancer Institute, Washington, D.C. (1975)
[48, 50]

Heynick, L.N., P. Polson, and A. Karp
A MICROWAVE EXPOSURE SYSTEM FOR PRIMATES
Radio Sci., Vol. 12, No. 6S, pp. 103-110 (1977)
[527]

Heynick, L.N. and J.S. Krebs
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-81-24 (November 1981)
[1]

Heynick, L.N.
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: SECOND REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-82-16 (May 1982)
[1]

Heynick, L.N. and P. Polson
BIOEFFECTS OF RADIOFREQUENCY RADIATION: A REVIEW PERTINENT TO AIR FORCE OPERATIONS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-1 (March 1983)
[1]

Heynick, L.N. and P. Polson
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: THIRD REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-84-6 (March 1984a)
[1]

Heynick, L.N. and P. Polson
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: FOURTH REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-84-17 (May 1984b)
[1]

Heynick, L.N. and P. Polson
USAFSAM REVIEW AND ANALYSIS OF RADIOFREQUENCY RADIATION BIOEFFECTS LITERATURE: FIFTH REPORT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-85-7 (March 1985)
[1]

Hill, D.A.
THE EFFECT OF FREQUENCY AND GROUNDING ON WHOLE-BODY ABSORPTION OF HUMANS IN E-POLARIZED RADIOFREQUENCY FIELDS
Bioelectromagnetics, Vol. 5, No. 2, pp. 131-146 (1984a)
[25]

Hill, D.A.
EFFECT OF SEPARATION FROM GROUND ON HUMAN WHOLE-BODY RF ABSORPTION RATES
IEEE Trans. Microwave Theory Tech., Vol. 32, No. 3, pp. 772-778 (1984b)
[25]

Hirsh, F.G. and J.T. Parker
BILATERAL LENTICULAR OPACITIES OCCURRING IN A TECHNICIAN OPERATING A MICROWAVE GENERATOR
AMA Arch. Ind. Hyg. Occup. Med., Vol. 6, pp. 512-517 (1952)
[97]

Ho, H.S., E.I. Ginns, and C.L. Christman
ENVIRONMENTALLY CONTROLLED WAVEGUIDE IRRADIATION FACILITY
IEEE Trans. Microwave Theory Tech., Vol. 21, No. 12, pp. 837-840 (1973)
[25, 415, 470]

Ho, H.S. and W.P. Edwards
THE EFFECT OF ENVIRONMENTAL TEMPERATURE AND AVERAGE DOSE RATE OF MICROWAVE RADIATION ON THE OXYGEN-CONSUMPTION RATE OF MICE
Radiat. Environ. Biophys., Vol. 16, pp. 325-338 (1979)
[415]

Hollows, F.C. and J.B. Douglas
MICROWAVE CATARACT IN RADIOLINEMEN AND CONTROLS
Lancet, No. 8399, pp. 406-407, Vol. 2 (18 August 1984)
[103]

Horne, R.A.
BIOLOGICAL EFFECTS OF CHEMICAL AGENTS
Science, Vol. 177, pp. 1152-1153 (1972)
[5]

Huang, A.T., M.E. Engle, J.A. Elder, J.B. Kinn, and T.R. Ward
THE EFFECT OF MICROWAVE RADIATION (2450 MHZ) ON THE MORPHOLOGY AND CHROMOSOMES OF LYMPHOCYTES
Radio Sci., Vol. 12, No. 6S, pp. 173-177 (1977)
[369]

Huang, A.T. and N.G. Mold
IMMUNOLOGIC AND HEMATOPOIETIC ALTERATIONS BY 2,450-MHZ ELECTROMAGNETIC RADIATION
Bioelectromagnetics, Vol. 1, No. 1, pp. 77-87 (1980)
[370]

Hunt, E.L. and R.D. Phillips
ABSOLUTE PHYSICAL DOSIMETRY FOR WHOLE ANIMAL EXPERIMENTS
Digest of Papers of the Microwave Density Workshop, Atlanta, Georgia, Department of Microwave Research, Walter Reed Army Institute of Research (1972)
[25]

Hunt, E.L., N.W. King, and R.D. Phillips
BEHAVIORAL EFFECTS OF PULSED MICROWAVE RADIATION
Ann. N.Y. Acad. Sci., Vol. 247, pp. 440-453 (1975)
[466-467]

Illinger, K.H. (ed.)
EFFECTS OF NONIONIZING RADIATION
American Chem. Soc. Series ACS 157 (1981)
[26]

Inouye, M., N. Matsumoto, M.J. Galvin, and D.I. McRee
LACK OF EFFECT OF 2.45-GHZ MICROWAVE RADIATION ON THE DEVELOPMENT OF PREIMPLANTATION EMBRYOS OF MICE
Bioelectromagnetics, Vol. 3, No. 2, pp. 275-283 (1982)
[202-203, 219]

IRPA
INTERIM GUIDELINES ON LIMITS OF EXPOSURE TO RADIOFREQUENCY ELECTROMAGNETIC FIELDS IN THE FREQUENCY RANGE FROM 100 KHZ TO 300 GHZ
Health Phys. J., Vol. 46, No. 4, pp. 975-984 (1984)
[10]

Iskander, M.F., P.W. Barber, C.H. Durney, and H. Massoudi
IRRADIATION OF PROLATE SPHEROIDAL MODELS OF HUMANS IN THE NEAR FIELD OF A SHORT ELECTRIC DIPOLE
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 7, pp. 801-807 (1980)
[26]

Ismailov, E.S.
MECHANISM OF THE EFFECT OF MICROWAVES ON THE PERMEABILITY OF ERYTHROCYTES FOR POTASSIUM AND SODIUM IONS
Biol. Nauki (Engl. Trans.), Vol. 3, pp. 58-60 (1971)
[352]

Issel, I. and P. Emmerlich
LENS CLOUDING AS A RESULT OF THE EFFECTS OF MICROWAVES
(Engl. Trans. of LINSENTRUEBUNG INFOLGE MIKROWELLENEINWIRKUNG)
Deutsche Gesundheitswesen, Vol. 36, No. 18, pp. 17-19 (1981)
[97]

Janes, D.E., R.A. Tell, T.W. Athey, and N.N. Hankin
RADIOFREQUENCY RADIATION LEVELS IN URBAN AREAS
Radio Sci., Vol. 12, No. 6S, pp. 49-56 (1977)
[12]

Janes, D.E., Jr.
RADIATION SURVEYS--MEASUREMENT OF LEAKAGE EMISSIONS AND POTENTIAL EXPOSURE FIELDS
Bull. N.Y. Acad. Med., Vol. 55, No. 11, pp. 1021-1041 (1979)
[12, 53]

Janna, W.S., E.P. Russo, R. McAfee, and R.M. Davoudi
A COMPUTER MODEL OF TEMPERATURE DISTRIBUTION INSIDE A LOSSY SPHERE AFTER MICROWAVE RADIATION
Bioelectromagnetics, Vol. 1, No. 3, pp. 337-343 (1980)
[22]

Jensh, R.P., A. Magaziner, and W.H. Vogel
EFFECTS OF MATERNAL ENVIRONMENT AND POSTNATAL MULTIPLE TESTING ON ADULT RAT OFFSPRING
J. Toxicol. Environ. Health, Vol. 7, Nos. 3-4, pp. 655-663 (1981)
[218]

Jensh, R.P., I. Weinberg, and R.L. Brent
TERATOLOGIC STUDIES OF PRENATAL EXPOSURE OF RATS TO 915-MHZ MICROWAVE RADIATION
Radiat. Res., Vol. 92, pp. 160-171 (1982a)
[211]

Jensh, R.P., W.H. Vogel, and R.L. Brent
POSTNATAL FUNCTIONAL ANALYSIS OF PRENATAL EXPOSURE OF RATS TO 915 MHZ MICROWAVE RADIATION
J. Am. Coll. Toxicol., Vol. 1, No. 3, pp. 73-90 (1982b)
[212]

Jensh, R.P., I. Weinberg, and R.L. Brent
AN EVALUATION OF THE TERATOGENIC POTENTIAL OF PROTRACTED EXPOSURE OF PREGNANT RATS TO 2450-MHZ MICROWAVE RADIATION: I. MORPHOLOGIC ANALYSIS AT TERM
J. Toxicol. Environ. Health, Vol. 11, pp. 23-35 (1983a)
[213]

Jensh, R.P., W.H. Vogel, and R.L. Brent
AN EVALUATION OF THE TERATOGENIC POTENTIAL OF PROTRACTED EXPOSURE OF PREGNANT RATS TO 2450-MHZ MICROWAVE RADIATION: II. POSTNATAL PSYCHOPHYSIOLOGIC ANALYSIS
J. Toxicol. Environ. Health, Vol. 11, pp. 37-59 (1983b)
[213]

Jensh, R.P.
STUDIES OF THE TERATOGENIC POTENTIAL OF EXPOSURE OF RATS TO 6000-MHZ MICROWAVE RADIATION--I. MORPHOLOGIC ANALYSIS AT TERM
Radiat. Res., Vol. 97, No. 2, pp. 272-281 (1984a)
[214]

Jensh, R.P.
STUDIES OF THE TERATOGENIC POTENTIAL OF EXPOSURE OF RATS TO 6000-MHZ MICROWAVE RADIATION--II. POSTNATAL PSYCHOPHYSIOLOGIC EVALUATIONS
Radiat. Res., Vol. 97, No. 2, pp. 282-301 (1984b)
[214]

Johnson, C.C. and A.W. Guy
NONIONIZING ELECTROMAGNETIC WAVE EFFECTS IN BIOLOGICAL MATERIALS AND SYSTEMS
Proc. IEEE, Vol. 60, No. 6, pp. 692-718 (1972)
[117, 291]

Johnson, C.C., C.H. Durney, P.W. Barber, H. Massoudi, S.J. Allen, and J.C. Mitchell
RADIOFREQUENCY RADIATION DOSIMETRY HANDBOOK
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-76-35, pp. 100-101 (1976)
[20, 494]

Johnson, R.B., D. Spackman, J. Crowley, D. Thompson, C.-K. Chou, L.L. Kunz, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 4. OPEN-FIELD BEHAVIOR AND CORTICOSTERONE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-42 (1983)
[398-399]

Johnson, R.B., L.L. Kunz, D. Thompson, J. Crowley, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 7. METABOLISM, GROWTH, AND DEVELOPMENT
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-84-31 (1984)
[398, 401-402]

Joines, W.T. and R.J. Spiegel
RESONANCE ABSORPTION OF MICROWAVES BY HUMAN SKULL
IEEE Trans. Biomed. Eng., Vol. 21, pp.46-48 (1974)
[22]

Joines, W.T. and C.F. Blackman
POWER DENSITY, FIELD INTENSITY, AND CARRIER FREQUENCY DETERMINANTS OF RF-ENERGY-INDUCED CALCIUM-ION EFFLUX FROM BRAIN TISSUE
Bioelectromagnetics, Vol. 1, No. 3, pp. 271-275 (1980)
[325]

Joines, W.T. and C.F. Blackman
EQUALIZING THE ELECTRIC FIELD INTENSITY WITHIN CHICK BRAIN IMMERSED IN BUFFER SOLUTION AT DIFFERENT CARRIER FREQUENCIES
Bioelectromagnetics, Vol. 2, No. 4, pp. 411-413 (1981)
[326]

Justesen, D.R. and N.W. King
BEHAVIORAL EFFECTS OF LOW LEVEL MICROWAVE IRRADIATION IN THE CLOSED SPACE SITUATION
In S.F. Cleary (ed.), BIOLOGICAL EFFECTS AND HEALTH IMPLICATIONS OF MICROWAVE RADIATION, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication BRH/DBE 70-2, pp. 154-179 (1970)
[459]

Justesen, D.R., D.M. Levinson, R.L. Clarke, and N.W. King
A MICROWAVE OVEN FOR BEHAVIOURAL AND BIOLOGICAL RESEARCH: ELECTRICAL AND STRUCTURAL MODIFICATIONS, CALORIMETRIC, DOSIMETRY, AND FUNCTIONAL EVALUATION
J. Microwave Power, Vol. 6, No. 3, pp. 237-258 (1971)
[301, 418, 459, 466, 482]

Justesen, D.R., E.R. Adair, J.C. Stevens, and V. Bruce-Wolfe
A COMPARATIVE STUDY OF HUMAN SENSORY THRESHOLDS: 2450-MHZ MICROWAVES VS FAR-INFRARED RADIATION
Bioelectromagnetics, Vol. 3, No. 1, pp. 117-125 (1982)
[143, 146, 479]

Kallen, B., G. Malmquist, and U. Moritz
DELIVERY OUTCOME AMONG PHYSIOTHERAPISTS IN SWEDEN: IS NON-IONIZING RADIATION A FETAL HAZARD?
Arch. Environ. Health, Vol. 37, No. 2, pp. 81-85 (1982)
[72]

Kalyada, T.V., P.P. Fukalova, and N.N. Goncharova
BIOLOGIC EFFECTS OF RADIATION IN THE 30-300 MHZ RANGE
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 52-57 (1974)
[40]

Kamenskii, Yu.I.
THE EFFECT OF MICROWAVES ON THE FUNCTIONAL STATE OF THE NERVE
Biophys., Vol. 9, No. 6, pp. 758-764 (1964)
[257]

Kamenskii, Yu.I.
EFFECT OF MICROWAVES ON THE KINETICS OF ELECTRIC PARAMETERS OF A NERVE IMPULSE
In SOCIETY OF NATURALISTS, Moscow, Vol. 28, pp. 164-172 (Engl. Trans., 1968)
[257]

Kaplan, I.T., W. Metlay, M.M. Zaret, L. Birenbaum, and S.W. Rosenthal
ABSENCE OF HEART-RATE EFFECTS IN RABBITS DURING LOW-LEVEL MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 19, No. 2, pp. 168-173 (1971)
[296, 449-450]

Kaplan, J., P. Polson, C. Rebert, K. Lunan, and M. Gage
BIOLOGICAL AND BEHAVIORAL EFFECTS OF PRENATAL AND POSTNATAL EXPOSURE TO 2450-MHZ ELECTROMAGNETIC RADIATION IN THE SQUIRREL MONKEY
Radio Sci., Vol. 17, No. 5S, pp. 135-144 (1982)
[219-220, 276, 309, 527]

Karimullah, K., K.-M. Chen, and D.P. Nyquist
ELECTROMAGNETIC COUPLING BETWEEN A THIN-WIRE ANTENNA AND A NEIGHBORING BIOLOGICAL BODY: THEORY AND EXPERIMENT
IEEE Trans. Microwave Theory Tech., Vol. 28, No. 11, pp. 1218-1225 (1980)
[26]

Kety, S.S.
METHODS MED. RES., Vol. 8, pp. 228 (1960)
[232]

Kim, Y.A., B.S. Fomenko, T.A. Agafonova, and I.G. Akoev
EFFECTS OF MICROWAVE RADIATION (340 AND 900 MHZ) ON DIFFERENT STRUCTURAL LEVELS OF ERYTHROCYTE MEMBRANES
Bioelectromagnetics, Vol. 6, No. 3, pp. 305-312 (1985)
[358, 361]

King, N.W., D.R. Justesen, and R.L. Clarke
BEHAVIORAL SENSITIVITY TO MICROWAVE IRRADIATION
Science, Vol. 172, No. 3982, pp. 398-401 (1971)
[460]

Kinn, J.F.
WHOLE BODY DOSIMETRY OF SMALL ANIMALS: THE EFFECT OF WEIGHT AND EXPOSURE GEOMETRY
Radio Sci., Vol 12, No. 6S, pp. 61-64 (1977)
[25, 323]

Klimkova-Deutschova, E.
NEUROLOGIC FINDINGS IN PERSONS EXPOSED TO MICROWAVES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 268-272 (1974)
[38]

Kramar, P.O., A.F. Emery, A.W. Guy, and J.C. Lin
THE OCULAR EFFECTS OF MICROWAVES ON HYPERTHERMIC RABBITS: A STUDY OF MICROWAVE CATARACTOGENIC MECHANISMS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 155-163 (1975)
[89]

Kramar, P.O., C. Harris, A.F. Emery, and A.W. Guy
ACUTE MICROWAVE IRRADIATION AND CATARACT FORMATION IN RABBITS AND MONKEYS
J. Microwave Power, Vol. 13, No. 3, pp. 239-249 (1978)
[90]

Krauth, J.
NONPARAMETRIC ANALYSIS OF RESPONSE CURVE
J. Neurosci. Meth., Vol. 2, pp. 239-252 (1980)
[547, 549, 552]

Kritikos, H.N. and H.P. Schwan
THE DISTRIBUTION OF HEATING POTENTIAL INSIDE LOSSY SPHERES
IEEE Trans. Biomed. Eng., Vol. 22, No. 6, pp. 457-463 (1975)
[22-23]

Kritikos, H.N. and H.P. Schwan
FORMATION OF HOT SPOTS IN MULTILAYER SPHERES
IEEE Trans. Biomed. Eng., Vol. 23, pp. 168-172 (1976)
[22-23]

Kritikos, H.N., K.R. Foster, and H.P. Schwan
TEMPERATURE PROFILES IN SPHERES DUE TO ELECTROMAGNETIC HEATING
J. Microwave Power, Vol. 16, Nos. 3 and 4, pp. 327-344 (1981)
[22]

Krupp, J.H.
THERMAL RESPONSE IN MACACA MULATTA EXPOSED TO 15- AND 20-MHZ RADIOFREQUENCY RADIATION
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-77-16 (September 1977)
[410]

Krupp, J.H.
LONG-TERM FOLLOWUP OF MACACA MULATTA EXPOSED TO HIGH LEVELS OF 15-, 20-, AND 26-MHZ RADIOFREQUENCY RADIATION
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-78-3 (January 1978)
[410]

Kues, H.A., L.W. Hirst, G.A. Lutty, S.A. D'Anna, and G.R. Dunkelberger
EFFECTS OF 2.45-GHZ MICROWAVES ON PRIMATE CORNEAL ENDOTHELIUM
Bioelectromagnetics, Vol. 6, No. 2, pp. 177-188 (1985)
[93, 96]

Kunz, L.L., K.E. Hellstrom, I. Hellstrom, H.J. Garriques, R.B. Johnson, J. Crowley, D. Thompson, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 5. EVALUATION OF THE IMMUNE SYSTEM'S RESPONSE
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-83-50 (1983)
[398-401]

Kunz, L.L., R.B. Johnson, D. Thompson, J. Crowley, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 6. HEMATOLOGICAL, SERUM CHEMISTRY, THYROXINE, AND PROTEIN ELECTROPHORESIS EVALUATIONS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-84-2 (1984)
[398, 400]

Kunz, L.L., R.B. Johnson, D. Thompson, J. Crowley, C.-K. Chou, and A.W. Guy
EFFECTS OF LONG-TERM LOW-LEVEL RADIOFREQUENCY RADIATION EXPOSURE ON RATS: VOLUME 8. EVALUATION OF LONGEVITY, CAUSE OF DEATH, AND HISTOPATHOLOGICAL FINDINGS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report USAFSAM-TR-85-11 (1985)
[398, 402-403]

Kurz, G.H. and R.B. Einaugler
CATARACT SECONDARY TO MICROWAVE RADIATION
Am. J. Ophthal., Vol. 66, No. 5, pp. 866-869 (1968)
[97]

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
PSYCHOACTIVE-DRUG RESPONSE IS AFFECTED BY ACUTE LOW-LEVEL MICROWAVE IRRADIATION
Bioelectromagnetics, Vol. 4, No. 3, pp. 205-214 (1983)
[419, 545]

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
EFFECTS OF ACUTE LOW-LEVEL MICROWAVES ON PENTOBARBITAL-INDUCED HYPOTHERMIA DEPEND ON EXPOSURE ORIENTATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 203-211 (1984a)
[420, 549-550, 554]

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
ETHANOL-INDUCED HYPOTHERMIA AND ETHANOL CONSUMPTION IN THE RAT ARE AFFECTED BY LOW-LEVEL MICROWAVE IRRADIATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 213-220 (1984b)
[420, 551]

Lai, H., A. Horita, C.-K. Chou, and A.W. Guy
ERRATUM to Lai et al. (1983)
Bioelectromagnetics, Vol. 6, No. 2, p. 207 (1985)
[547]

Lambert, P.D., R.C. Nealeigh, and M. Wilson
EFFECTS OF MICROWAVE EXPOSURES ON THE CENTRAL NERVOUS SYSTEM OF BEAGLES
J. Microwave Power, Vol. 7, No. 4, pp. 367-380 (1972)
[292]

Lancranjan, I., M. Maicanescu, E. Rafaila, I. Klepsch, and H.I. Popescu
GONADIC FUNCTION IN WORKMEN WITH LONG-TERM EXPOSURE TO MICROWAVES
Health Phys., Vol. 29, pp. 381-383 (1975)
[425]

Lary, J.M., D.L. Conover, E.D. Foley, and P.L. Hanser
TERATOGENIC EFFECTS OF 27.12 MHZ RADIOFREQUENCY RADIATION IN RATS
Teratology, Vol. 26, No. 3, pp. 299-309 (1982)
[208, 210-212]

Lary, J.M., D.L. Conover, P.H. Johnson, and J.R. Burg
TERATOGENICITY OF 27.12-MHZ RADIATION IN RATS IS RELATED TO DURATION OF HYPERTHERMIC EXPOSURE
Bioelectromagnetics, Vol. 4, No. 3, pp. 249-255 (1983)
[210-211]

Lawrence, A.F. and W.R. Adey
NONLINEAR WAVE MECHANISMS IN INTERACTIONS BETWEEN EXCITABLE TISSUE AND ELECTROMAGNETIC FIELDS
Neurolog. Res., Vol. 4, No. 1/2, pp. 115-153 (1982)
[26]

Lebovitz, R.M. and R.L. Seaman
MICROWAVE HEARING: THE RESPONSE OF SINGLE AUDITORY NEURONS IN THE CAT TO PULSED MICROWAVE RADIATION
Radio Sci., Vol. 12, No. 6S, pp. 229-236 (1977)
[122]

Lebovitz, R.M.
PROLONGED MICROWAVE IRRADIATION OF RATS: EFFECTS ON CONCURRENT OPERANT BEHAVIOR
Bioelectromagnetics, Vol. 2, No. 2, pp. 169-185 (1981)
[431, 503, 507]

Lebovitz, R.M.
PULSE MODULATED AND CONTINUOUS WAVE MICROWAVE RADIATION YIELD EQUIVALENT CHANGES IN OPERANT BEHAVIOR OF RODENTS
Physiology and Behavior, Vol. 30, No. 6, pp. 891-898 (1983)
[506]

Lebovitz, R.M. and L. Johnson
TESTICULAR FUNCTION OF RATS FOLLOWING EXPOSURE TO MICROWAVE RADIATION
Bioelectromagnetics, Vol. 4, No. 2, pp. 107-114 (1983)
[430]

Levinson, D.M., A.M. Grove, R.L. Clarke, and D.R. Justesen
PHOTIC CUING OF ESCAPE BY RATS FROM AN INTENSE MICROWAVE FIELD
Bioelectromagnetics, Vol. 3, No. 1, pp. 105-116 (1982)
[478-479, 481]

Lester, J.R. and D.F. Moore
CANCER MORTALITY AND AIR FORCE BASES
J. Bioelectricity, Vol. 1, No. 1, pp. 77-82 (1982a)
[48-51]

Lester, J.R. and D.F. Moore
CANCER INCIDENCE AND ELECTROMAGNETIC RADIATION
J. Bioelectricity, Vol. 1, No. 1, pp. 59-76 (1982b)
[52]

Lester, J.R.
REPLY TO "CANCER MORTALITY AND AIR FORCE BASES: A REEVALUATION"
J. Bioelectricity, Vol. 4, No. 1, pp. 129-131 (1985)
[52]

Liburdy, R.P.
EFFECTS OF RADIO-FREQUENCY RADIATION ON INFLAMMATION
Radio Sci., Vol. 12, No. 6S, pp. 179-183 (1977)
[369, 373]

Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: MODULATION OF T- AND B-LYMPHYOCYTE LEVELS AND CELL-MEDIATED IMMUNOCOMPETENCE BY HYPERTHERMIC RADIATION
Radiat. Res., Vol. 77, pp. 34-46 (1979)
[374, 381, 440]

Liburdy, R.P.
RADIOFREQUENCY RADIATION ALTERS THE IMMUNE SYSTEM: II. MODULATION OF IN VIVO LYMPHOCYTE CIRCULATION
Radiat. Res., Vol. 83, pp. 66-73 (1980)
[375]

Liburdy, R.P.
CARCINOGENESIS AND EXPOSURE TO ELECTRICAL AND MAGNETIC FIELDS
New England J. Med., Vol. 307, No. 22, p. 1402 (1982)
[57]

Liburdy, R.P. and A. Penn
MICROWAVE BIOEFFECTS IN THE ERYTHROCYTE ARE TEMPERATURE AND pO2 DEPENDENT: CATION PERMEABILITY AND PROTEIN SHEDDING OCCUR AT THE MEMBRANE PHASE TRANSITION
Bioelectromagnetics, Vol. 5, No. 2, pp. 283-291 (1984)
[357]

Liburdy, R.P. and A. Wyant
RADIOFREQUENCY RADIATION AND THE IMMUNE SYSTEM. PART 3. IN VITRO EFFECTS ON HUMAN IMMUNOGLOBULIN AND ON MURINE T- AND B-LYMPHOCYTES
Int. J. Radiat. Biol., Vol. 46, No. 1, pp. 67-81 (1984)
[350]

Liburdy, R.P. and P.F. Vanek, Jr.
MICROWAVES AND THE CELL MEMBRANE II. TEMPERATURE, PLASMA, AND OXYGEN MEDIATE MICROWAVE-INDUCED MEMBRANE PERMEABILITY IN THE ERYTHROCYTE
Radiat. Res., Vol. 102, pp. 190-205 (1985)
[357]

Liddle, C.G., J.P. Putnam, J.S. Ali, J.Y. Lewis, B. Bell, M.W. West, and O.H. Lewter
ALTERATION OF CIRCULATING ANTIBODY RESPONSE OF MICE EXPOSED TO 9-GHZ PULSED MICROWAVES
Bioelectromagnetics, Vol. 1, No. 4, pp. 397-404 (1980)
[397]

Lilienfeld, A.M., J. Tonascia, S. Tonascia, C.H. Libauer, G.M. Cauthen, J.A. Markowitz, and S. Weida
FOREIGN SERVICE HEALTH STATUS STUDY: EVALUATION OF STATUS OF FOREIGN SERVICE AND OTHER EMPLOYEES FROM SELECTED EASTERN EUROPEAN POSTS
Final Report, July 31, 1978, Contract No. 6025-619073, Dept. of Epidemiology, School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, MD (1978)
[46, 48]

Lilienfeld, A.M. and D.E. Lilienfeld
FOUNDATIONS OF EPIDEMIOLOGY
2nd edition, Oxford University Press, New York and Oxford (1980)
[4, 54]

Lin, J.C.
A CAVITY-BACKED SLOT RADIATOR FOR MICROWAVE BIOLOGICAL EFFECT RESEARCH
J. Microwave Power, Vol. 9, No. 2, pp. 63-67 (1974)
[90]

Lin, J.C.
MICROWAVE PROPERTIES OF FRESH MAMMALIAN BRAIN TISSUES AT BODY TEMPERATURE
IEEE Trans. Biomed. Eng., Vol. 22, pp. 74-76 (1975)
[19]

Lin, J.C.
MICROWAVE AUDITORY EFFECT--A COMPARISON OF SOME POSSIBLE TRANSDUCTION MECHANISMS
J. Microwave Power, Vol. 11, No. 1, pp. 77-81 (1976a)
[120]

Lin, J.C.
MICROWAVE-INDUCED HEARING: SOME PRELIMINARY THEORETICAL OBSERVATIONS
J. Microwave Power, Vol. 11, No. 3, pp. 295-298 (1976b)
[120]

Lin, J.C.
A NEW SYSTEM FOR INVESTIGATING NONTHERMAL EFFECT OF MICROWAVES ON CELLS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. II, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8011, pp. 350-353 (1976c)
[346-347]

Lin, J.C.
ON MICROWAVE-INDUCED HEARING SENSATION
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 7, pp. 605-613 (1977a)
[120]

Lin, J.C.
FURTHER STUDIES ON THE MICROWAVE AUDITORY EFFECT
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 7, pp. 938-943 (1977b)
[120]

Lin, J.C.
THEORETICAL CALCULATION OF FREQUENCIES AND THRESHOLDS OF MICROWAVE-INDUCED AUDITORY SIGNALS
Radio Sci., Vol. 12, No. 6S, pp. 237-242 (1977c)
[120]

Lin, J.C. and W.D. Peterson, Jr.
CYTOLOGICAL EFFECTS OF 2450 MHZ CW MICROWAVE RADIATION
J. Bioeng., Vol. 1, pp. 471-478 (1977)
[346]

Lin, J.C., A.W. Guy, and L.R. Caldwell
THERMOGRAPHIC AND BEHAVIORAL STUDIES OF RATS IN THE NEAR FIELD OF 918-MHZ RADIATIONS
IEEE Trans. Microwave Theory Tech., Vol. 25, No. 10, pp. 833-836 (1977)
[488, 490]

Lin, J.C.
MICROWAVE AUDITORY EFFECTS AND APPLICATIONS
Charles C. Thomas, Springfield, IL, p. 108 (1978)
[131]

Lin, J.C., M.J. Ottenbreit, S.-L. Wang, S. Inoue, R.O. Bollinger, and M. Fracassa
MICROWAVE EFFECTS ON GRANULOCYTE AND MACROPHAGE PRECURSOR CELLS OF MICE IN VITRO
Radiat. Res., Vol. 80, No. 2, pp. 292-302 (1979a)
[347]

Lin, J.C., R.J. Meltzer, and F.K. Redding
MICROWAVE-EVOKED BRAINSTEM POTENTIALS IN CATS
J. Microwave Power, Vol. 14, No. 3, pp. 291-296 (1979b)
[125]

Lin, J.C., J.C. Nelson, and M.E. Ekstrom
EFFECTS OF REPEATED EXPOSURE TO 148-MHZ RADIO WAVES ON GROWTH AND HEMATOLOGY OF MICE
Radio Sci., Vol. 14, No. 6S, pp. 173-179 (1979c)
[371]

Lin, J.C. and M.F. Lin
STUDIES ON MICROWAVE AND BLOOD-BRAIN BARRIER INTERACTION
Bioelectromagnetics, Vol. 1, No. 3, pp. 313-323 (1980)
[237]

Lin, J.C. and M.F. Lin
MICROWAVE HYPERTHERMIA-INDUCED BLOOD-BRAIN BARRIER ALTERATIONS
Radiat. Res., Vol. 89, pp. [illegible] (1982)
[237]

Lindauer, G.A., L.M. Liu, G.W. Skewes, and F.J. Rosenbaum
FURTHER EXPERIMENTS SEEKING EVIDENCE OF NONTHERMAL BIOLOGICAL EFFECTS OF MICROWAVE RADIATION
IEEE Trans. Microwave Theory Tech., Vol. 22, No. 8, pp. 790-793 (1974)
[189]

Liu, L.M., F.J. Rosenbaum, and W.F. Pickard
THE RELATION OF TERATOGENESIS IN TENEBRIO MOLITOR TO THE INCIDENCE OF LOW-LEVEL MICROWAVES
IEEE Trans. Microwave Theory Tech., Vol. 23, No. 11, pp. 929-931 (1975)
[189, 19]

Liu, L.M., F.J. Rosenbaum, and W.F. Pickard
THE INSENSITIVITY OF FROG HEART RATE TO PULSE MODULATED MICROWAVE ENERGY
J. Microwave Power, Vol. 11, No. 3, pp. 225-232 (1976)
[453]

Liu, L.M., F.G. Nickless, and S.F. Cleary
EFFECTS OF MICROWAVE RADIATION ON ERYTHROCYTE MEMBRANES
Radio Sci., Vol. 14, No. 6S, pp. 109-115 (1979)
[352]

Lobanova, E.A.
THE USE OF CONDITIONED REFLEXES TO STUDY MICROWAVE EFFECTS ON THE CENTRAL NERVOUS SYSTEM
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 109-118 (1974)
[461]

Lords, J.L., C.H. Durney, A.M. Borg, and C.E. Tinney
RATE EFFECTS IN ISOLATED HEARTS INDUCED BY MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 21, No. 12, pp. 834-836 (1973)
[453, 531]

Lotz, W.G. and S.M. Michaelson
TEMPERATURE AND CORTICOSTERONE RELATIONSHIPS IN MICROWAVE-EXPOSED RATS
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 44, No. 3, pp. 438-445 (1978)
[436]

Lotz, W.G. and S.M. Michaelson
EFFECTS OF HYPOPHYSECTOMY AND DEXAMETHASONE ON RAT ADRENAL RESPONSE TO MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 47, No. 6, pp. 1284-1288 (1979)
[437, 533]

Lotz, W.G. and R.P. Podgorski
TEMPERATURE AND ADRENOCORTICAL RESPONSES IN RHESUS MONKEYS EXPOSED TO MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 53, No. 6, pp. 1565-1571 (1982)
[443]

Lotz, W.G.
HYPERTHERMIA IN RADIOFREQUENCY-EXPOSED RHESUS MONKEYS: A COMPARISON OF FREQUENCY AND ORIENTATION EFFECTS
Radiat. Res., Vol. 102, pp. 59-70 (1985)
[414]

Lu, S.-T., N. Lebda, S.M. Michaelson, S. Pettit, and D. Rivera
THERMAL AND ENDOCRINOLOGICAL EFFECTS OF PROTRACTED IRRADIATION OF RATS BY 2450-MHZ MICROWAVES
Radio Sci., Vol. 12, No. 6S, pp. 147-156 (1977)
[438, 440]

Lu, S.-T., N. Lebda, S. Pettit, and S.M. Michaelson
DELINEATING ACUTE NEUROENDOCRINE RESPONSES IN MICROWAVE-EXPOSED RATS
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 48, No. 6, pp. 927-932 (1980b)
[439-441]

Lu, S.-T., N.J. Roberts, Jr., and S.M. Michaelson
A MODIFIED WAVEGUIDE EXPOSURE FACILITY FOR EXAMINING EFFECTS OF MICROWAVES ON IMMUNOCOMPETENT AND HEMATOPOIETIC CELLS
In J.C. Mitchell (ed.), AEROMEDICAL REVIEW: USAF RADIOFREQUENCY RADIATION BIOEFFECTS RESEARCH PROGRAM--A REVIEW, USAF School of Aerospace Medicine, Brooks Air Force Base, TX, Review 4-81, pp. 159-181 (1981a)
[346]

Lu, S.-T., N. Lebda, S. Pettit, and S.M. Michaelson
MICROWAVE-INDUCED TEMPERATURE, CORTICOSTERONE, AND THYROTROPIN INTERRELATIONSHIPS
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 50, No. 2, pp. 399-405 (1981b)
[439, 442]

Lu, S.-T., N. Lebda, S.M. Michaelson, and S. Pettit
SERUM-THYROXINE LEVELS IN MICROWAVE-EXPOSED RATS
Radiat. Res., Vol. 101, pp. 413-423 (1985)
[441]

Lyle, D.B., P. Schechter, W.R. Adey, and R.L. Lundak
SUPPRESSION OF T-LYMPHOCYTE CYTOTOXICITY FOLLOWING EXPOSURE TO SINUSOIDALLY AMPLITUDE-MODULATED FIELDS
Bioelectromagnetics, Vol. 4, No. 3, pp. 281-292 (1983)
[349]

Magin, R.L., S.-T. Lu, and S.M. Michaelson
MICROWAVE HEATING EFFECT ON THE DOG THYROID GLAND
IEEE Trans. Biomed. Eng., Vol. 24, No. 6, pp. 522-529 (1977a)
[435]

Magin, R.L., S.-T. Lu, and S.M. Michaelson
STIMULATION OF DOG THYROID BY LOCAL APPLICATION OF HIGH INTENSITY MICROWAVES
Am. J. Physiol., Vol. 233, No. 5, pp. E363-E368 (1977b)
[435]

Massoudi, H., C.H. Durney, and C.C. Johnson
A GEOMETRIC-OPTICS AND AN EXACT SOLUTION FOR INTERNAL FIELDS IN AND ENERGY ABSORPTION BY A CYLINDRICAL MODEL OF MAN IRRADIATED BY AN ELECTROMAGNETIC PLANE WAVE
Radio Sci., Vol. 14, No. 6S, pp. 35-42 (1979)
[22]

Mayers, C.P. and J.A. Habeshaw
DEPRESSION OF PHAGOCYTOSIS: A NON-THERMAL EFFECT OF MICROWAVE RADIATION AS A POTENTIAL HAZARD TO HEALTH
Int. J. Radiat. Biol., Vol. 24, No. 5, pp. 449-461 (1973)
[345]

McAfee, R.D., A Longacre, Jr., R.R. Bishop., S.T. Elder, J.G. May, M.G. Holland, and R. Gordon
ABSENCE OF OCULAR PATHOLOGY AFTER REPEATED EXPOSURE OF UNANESTHETIZED MONKEYS TO 9.3-GHZ MICROWAVES
J. Microwave Power, Vol. 14, No. 1, pp. 41-44 (1979b)
[92]

McRee, D and P. Walsh
MICROWAVE EXPOSURE SYSTEM FOR BIOLOGICAL SPECIMENS
Rev. Sci. Instr., Vol. 42, pp. 1860-1864 (1971)
[577]

McRee, D.I.
DETERMINATION OF ENERGY ABSORPTION OF MICROWAVE RADIATION USING THE COOLING CURVE TECHNIQUE
J. Microwave Power, Vol. 9, No. 3, pp. 263-270 (1974)
[182]

McRee, D.I., P.E. Hamrick, and J. Zinkl
SOME EFFECTS OF EXPOSURE OF THE JAPANESE QUAIL EMBRYO TO 2.45-GHZ MICROWAVE RADIATION
Ann. N.Y. Acad. Sci., Vol. 247, pp. 377-390 (1975)
[191]

McRee, D.I. and P.E. Hamrick
EXPOSURE OF JAPANESE QUAIL EMBRYOS TO 2.45-GHZ MICROWAVE RADIATION DURING DEVELOPMENT
Radiat. Res., Vol. 71, No. 2, pp. 355-366 (1977)
[192, 367]

McRee, D.I., R. Faith, E.E. McConnell, and A.W. Guy
LONG-TERM 2450-MHZ CW MICROWAVE IRRADIATION OF RABBITS: EVALUATION OF HEMATOLOGICAL AND IMMUNOLOGICAL EFFECTS
J. Microwave Power, Vol. 15, No. 1, pp. 45-52 (1980)
[375]

McRee, D.I., G. MacNichols, and G.K. Livingston
INCIDENCE OF SISTER CHROMATID EXCHANGE IN BONE MARROW CELLS OF THE MOUSE FOLLOWING MICROWAVE EXPOSURE
Radiat. Res., Vol. 85, pp. 340-348 (1981)
[181]

McRee, D.I. and H. Wachtel
THE EFFECTS OF MICROWAVE RADIATION ON THE VITALITY OF ISOLATED FROG SCIATIC NERVES
Radiat. Res., Vol. 82, pp. 536-546 (1980)
[257, 262, 264-265]

McRee, D.I. and H. Wachtel
PULSE MICROWAVE EFFECTS ON NERVE VITALITY
Radiat. Res., Vol. 91, pp. 212-218 (1982)
[262, 265]

Meddis, R.
STATISTICAL HANDBOOK FOR NON-STATISTICIANS
McGraw-Hill, Berkshire, England (1975)
[74]

Merritt, J.H. and J.W. Frazer
EFFECT OF 19 MHZ RF RADIATION ON NEUROTRANSMITTERS IN MOUSE BRAIN
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-75-28 (August 1975)
[277]

Merritt, J.H., R.H. Hartzell, and J.W. Frazer
THE EFFECTS OF 1.6 GHZ RADIATION ON NEUROTRANSMITTERS IN DISCRETE AREAS OF THE RAT BRAIN
USAF School of Aerospace Medicine, Brooks AFB, Texas, Report SAM-TR-76-3 (February 1976)
[278]

Merritt, J.H., A.F. Chamness, and S.J. Allen
STUDIES ON BLOOD-BRAIN BARRIER PERMEABILITY AFTER MICROWAVE-RADIATION
Rad. and Environm. Biophys., Vol. 15, pp. 367-377 (1978)
[229]

Merritt, J.H., W.W. Shelton, and A.F. Chamness
ATTEMPTS TO ALTER 45-CA++ BINDING TO BRAIN TISSUE WITH PULSE-MODULATED MICROWAVE ENERGY
Bioelectromagnetics, Vol. 3, No. 4, pp. 475-478 (1982)
[334, 338]

Merritt, J.H., K.A. Hardy, and A.F. Chamness
IN UTERO EXPOSURE TO MICROWAVE RADIATION AND RAT BRAIN DEVELOPMENT
Bioelectromagnetics, Vol. 5, No. 3, pp. 315-322 (1984)
[218]

Mikolajczyk, H.J.
MICROWAVE-INDUCED SHIFTS OF GONADOTROPIC ACTIVITY IN ANTERIOR PITUITARY GLAND OF RATS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 7-8010, pp. 377-382 (1976)
[434]

Milham, S., Jr.
MORTALITY FROM LEUKEMIA IN WORKERS EXPOSED TO ELECTRICAL AND MAGNETIC FIELDS (Correspondence)
New England J. Med., Vol. 307, No. 4, p. 249 (1982)
[57]

Milham, S., Jr.
OCCUPATIONAL MORTALITY IN WASHINGTON STATE: 1950-1979
DHHS (NIOSH) Publication No. 83-116, Contract No. 210-80-0088, U.S. Department of Health and Human Services, National Institute for Occupational Safety and Health, Cincinnati, Ohio (October 1983)
[53-54]

Millar, D.B., J.P. Christopher, J. Hunter, and S.S. Yeandle
THE EFFECT OF EXPOSURE OF ACETYLCHOLINESTERASE TO 2,450-MHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 5, No. 2, pp. 165-172 (1984)
[267]

Miller, D.A., A.R. Valentino, and M. Benedick
Tech. Memorandum No. 2, Project No. IIT RIE-6249, U. S. Naval Electronic Systems Command, Washington, D. C. (1974)
[318]

Milroy, W.C. and S.M. Michaelson
THYROID PATHOPHYSIOLOGY OF MICROWAVE RADIATION
Aerospace Med., Vol 43, No. 10, pp. 1126-1131 (1972)
[432, 442]

Mitchell, J.C.
A RADIOFREQUENCY RADIATION EXPOSURE APPARATUS
USAF School of Aerospace Medicine, Brooks AFB, TX, Report SAM-TR-70-43 (1970)
[204, 384, 409]

Mitchell, D.S., W.G. Switzer, and E.L. Bronaugh
HYPERACTIVITY AND DISRUPTION OF OPERANT BEHAVIOR IN RATS AFTER MULTIPLE EXPOSURES TO MICROWAVE RADIATION
Radio Sci., Vol. 12, No. 6S, pp. 263-271 (1977)
[486, 488, 502]

Moe, K.E., R.H. Lovely, D.E. Myers, and A.W. Guy
PHYSIOLOGICAL AND BEHAVIORAL EFFECTS OF CHRONIC LOW LEVEL MICROWAVE RADIATION IN RATS
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 248-256 (1976)
[469]

Monahan, J.C. and H.S. Ho
MICROWAVE INDUCED AVOIDANCE BEHAVIOR IN THE MOUSE
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 274-283 (1976)
[470, 474, 476]

Monahan, J.C. and H.S. Ho
THE EFFECT OF AMBIENT TEMPERATURE ON THE REDUCTION OF MICROWAVE ENERGY ABSORPTION BY MICE
Radio Sci., Vol. 12, No. 6S, pp. 257-262 (1977)
[471-472, 474, 476, 481]

Monahan, J.C. and W.W. Henton
FREE-OPERANT AVOIDANCE AND ESCAPE FROM MICROWAVE RADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 23-33 (1977a)
[474, 533, 535]

Monahan, J.C. and W.W. Henton
MICROWAVE ABSORPTION AND TASTE AVERSION AS A FUNCTION OF 915 MHZ RADIATION
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 34-40 (1977b)
[475, 481]

Monahan, J.C. and W.W. Henton
THE EFFECT OF PSYCHOACTIVE DRUGS ON OPERANT BEHAVIOR INDUCED BY MICROWAVE RADIATION
Radio Sci., Vol. 14, No. 6S, pp. 233-238 (1979)
[534]

Morton, W.E.
RE: "EFFECTS UPON HEALTH OF OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR)"
Am. J. Epidemiol., Vol. 113, p. 201 (1981)
[46]

Muraca, G.J., Jr., E.S. Ferri, and F.L. Buchta
A STUDY OF THE EFFECTS OF MICROWAVE IRRADIATION OF THE RAT TESTES
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 7-8010, pp. 484-494 (1976)
[426]

Myers, R.D.
ALCOHOL'S EFFECT ON BODY TEMPERATURE: HYPOTHERMIA, HYPERTHERMIA, OR POIKILOTHERMIA?
Brain Res. Bull., Vol. 7, pp. 209-220 (1981)
[553]

Myers, R.D. and D.H. Ross
RADIATION AND BRAIN CALCIUM: A REVIEW AND CRITIQUE
Neurosci. Biobehav. Rev., Vol. 5, No. 4, pp. 503-543 (1981)
[338]

NAS (National Academy of Sciences)
ANALYSIS OF THE EXPOSURE LEVELS AND POTENTIAL BIOLOGIC EFFECTS OF THE PAVE PAWS RADAR SYSTEM (1979)
[291, 297]

Nawrot, P.S., D.I. McRee, and R.E. Staples
EFFECTS OF 2.45 GHZ CW MICROWAVE RADIATION ON EMBRYOFETAL DEVELOPMENT IN MICE
Teratology, Vol. 24, No. 3, pp. 303-314 (1981)
[201, 203-204, 219]

Nawrot P.S., D.I. McRee, and M.J. Galvin
TERATOGENIC, BIOCHEMICAL, AND HISTOLOGICAL STUDIES WITH MICE PRENATALLY EXPOSED TO 2.45-GHZ MICROWAVE RADIATION
Radiat. Res., Vol. 102, No. 1, pp. 35-45 (1985)
[203]

NCRP
BIOLOGICAL EFFECTS AND EXPOSURE CRITERIA FOR RADIOFREQUENCY ELECTROMAGNETIC FIELDS
Report No. 86, NCRP Publications, Bethesda, MD 20814 (1986)
[9]

Nealeigh, R.C., R.J. Garner, R.J. Morgan, H.A. Cross, and P.D. Lambert
THE EFFECT OF MICROWAVE ON Y-MAZE LEARNING IN THE WHITE RAT
J. Microwave Power, Vol. 6, No. 1, pp. 49-54 (1971)
[461]

Neuder, S.M., R.B. Kellogg, and D.H. Hill
MICROWAVE POWER DENSITY ABSORPTION IN A SPHERICAL MULTILAYERED MODEL OF THE HEAD
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. II, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8011, pp. 199-210 (1976)
[22]

NIOSH
RADIOFREQUENCY/MICROWAVE OCCUPATIONAL EXPOSURE STANDARD AND RATIONALE, EXTERNAL REVIEW DRAFT
National Institute for Occupational Safety and Health, U.S. Department of Health and Human Services (1985)
[9]

NTIA
MICROWAVE RADIATION OF THE U.S. EMBASSY IN MOSCOW AND ITS BIOLOGICAL IMPLICATIONS: AN ASSESSMENT
Report NTIA-SP-81-12, National Telecommunications and Information Administration, Department of Commerce (March 1981)
[46]

Odland, L.T.
OBSERVATIONS, OPINIONS AND RECOMMENDATION; U.S. MEDICAL SERVICE PROGRAM FOR CONTROL OF RADIOFREQUENCY HAZARDS
USAF Radiological Health Laboratory, Report 72W-25 (1972)
[77]

Odland, L., V. Penikas, and R. Graham
RESULTS OF OPHTHALMOLOGICAL STUDIES ON SELECTED GROUPS OF USAF PERSONNEL WHOSE OCCUPATIONS PRESENTED A POTENTIAL FOR EXPOSURE TO MICROWAVES
USAF Radiological Health Laboratory, Report 72W-124 (1972)
[77]

Ogur, H., R. St. John, and S. Nagai
TETRAZOLIUM OVERLAY TECHNIQUE FOR POPULATION STUDIES OF RESPIRATION DEFICIENCY IN YEAST
Science, Vol. 25, pp. 928-929 (1957)
[158]

Olcerst, R.B. and J.R. Rabinowitz
STUDIES ON THE INTERACTION OF MICROWAVE RADIATION WITH CHOLINESTERASE
Radiat. Environ. Biophys., Vol 15, pp. 289-295 (1978)
[265]

Olcerst, R.B., S. Belman, M. Eisenbud, W.W. Mumford, and J.R. Rabinowitz
THE INCREASED PASSIVE EFFLUX OF SODIUM AND RUBIDIUM FROM RABBIT ERYTHROCYTES BY MICROWAVE RADIATION
Radiat. Res., Vol. 82, No. 2, pp. 244-256 (1980)
[352, 355, 357]

Oldendorf, W.H.
MEASUREMENT OF BRAIN UPTAKE OF RADIOLABELED SUBSTANCES USING A TRITIATED WATER INTERNAL STANDARD
Brain Res., Vol. 24, pp. 372-376 (1970)
[228-229]

Oldendorf, W.H.
BRAIN UPTAKE OF RADIOLABELED AMINO ACIDS, AMINES, AND HEXOSES AFTER ARTERIAL INJECTION
Am. J. Physiol., Vol. 221, pp. 1629-1639 (1971)
[228-229]

Olsen, R.G. and W.C. Hammer
MICROWAVE-INDUCED PRESSURE WAVES IN A MODEL OF MUSCLE TISSUE
Bioelectromagnetics, Vol. 1, No. 1, pp. 45-54 (1980)
[130]

Olsen, R.G., T.A. Griner, and G.D. Prettyman
FAR-FIELD MICROWAVE DOSIMETRY IN A RHESUS MONKEY MODEL
Bioelectromagnetics, Vol. 1, No. 2, pp. 149-160 (1980)
[25, 443, 527]

Olsen, R.G. and W.C. Hammer
EVIDENCE FOR MICROWAVE-INDUCED ACOUSTICAL RESONANCES IN BIOLOGICAL MATERIAL
J. Microwave Power, Vol. 16, Nos. 3 & 4, pp. 263-269 (1981)
[131-132]

Olsen, R.G. and J.C. Lin
MICROWAVE PULSE-INDUCED ACOUSTIC RESONANCES IN SPHERICAL HEAD MODELS
IEEE Trans. Microwave Theory Tech., Vol. 29, No. 10, pp. 1114-1117 (1981)
[131-132]

Olsen, R.G.
CONSTANT-DOSE MICROWAVE IRRADIATION OF INSECT PUPAE
Radio Sci., Vol. 17, No. 5S, pp. 145-148 (1982)
[191]

Olsen, R.G. and W.C. Hammer
THERMOGRAPHIC ANALYSIS OF WAVEGUIDE-IRRADIATED INSECT PUPAE
Radio Sci., Vol. 17, No. 5S, pp. 95-104 (1982)
[191]

Olsen, R.G. and J.C. Lin
MICROWAVE-INDUCED PRESSURE WAVES IN MAMMALIAN BRAINS
IEEE Trans. Biomed. Eng., Vol. 30, No. 5, pp. 289-294 (1983)
[132]

Olsen, R.G.
FAR-FIELD DOSIMETRIC MEASUREMENTS IN A FULL-SIZED MAN MODEL AT 2.0 GHZ
Bioelectromagnetics, Vol. 3, No. 4, pp. 433-441 (1984)
[25]

Ortner, M.J. and M.J. Galvin
THE EFFECT OF 2450 MHZ MICROWAVE RADIATION ON RAT PERITONEAL MAST CELLS
Cell Biophys., Vol. 2, pp. 127-138 (1980)
[383]

Ortner, M.J., M.J. Galvin, and D.I. McRee
STUDIES ON ACUTE IN VIVO EXPOSURE OF RATS TO 2450-MHZ MICROWAVE RADIATION--I. MAST CELLS AND BASOPHILS
Radiat. Res., Vol. 86, pp. 580-588 (1981a)
[383]

Ortner, M.J., M.J. Galvin, C.F. Chignell, and D.I. McRee
A CIRCULAR DICHROISM STUDY OF HUMAN ERYTHROCYTE GHOST PROTEINS DURING EXPOSURE TO 2450 MHZ MICROWAVE RADIATION
Cell Biophys., Vol. 3, pp. 335-347 (1981b)
[584-585]

Ortner, M.J., M.J. Galvin, and R.D. Irwin
THE EFFECT OF 2450-MHZ MICROWAVE RADIATION DURING MICROTUBULAR POLYMERIZATION IN VITRO
Radiat. Res., Vol. 93, pp. 353-363 (1983)
[584]

Oscar, K.J. and T.D. Hawkins
MICROWAVE ALTERATION OF THE BLOOD-BRAIN BARRIER SYSTEM OF RATS
Brain Res., Vol. 126, pp. 281-293 (1977)
[228-230, 232-233, 246]

Oscar, K.J., S.P. Gruenau, M.T. Folker, and S.I. Rapoport
LOCAL CEREBRAL BLOOD FLOW AFTER MICROWAVE EXPOSURE
Brain Res., Vol. 204, No. 1, pp. 220-225 (1981)
[231, 246]

Ottenbreit, M.J., J.C. Lin, S. Inoue, and W.D. Peterson, Jr.
IN VITRO MICROWAVE EFFECTS ON HUMAN NEUTROPHIL PRECURSOR CELLS (CFU-C)
Bioelectromagnetics, Vol. 2, No. 3, pp. 203-215 (1981)
[347]

Pappas, B.A., H. Anisman, R. Ings, and D.A. Hill
ACUTE EXPOSURE TO PULSED MICROWAVES AFFECTS NEITHER PENTYLENETETRAZOL SEIZURES IN THE RAT NOR CHLORDIAZEPOXIDE PROTECTION AGAINST SUCH SEIZURES
Radiat. Res., Vol. 96, No. 3, pp. 486-496 (1983)
[539, 542]

Parker, L.N.
THYROID SUPPRESSION AND ADENOMEDULLARY ACTIVATION BY LOW-INTENSITY MICROWAVE RADIATION
Am. J. Physiol., Vol. 224, No. 6, pp. 1388-1390 (1973)
[433]

Partlow, L.M., L.G. Bush, L.J. Stensaas, D.W. Hill, A. Riazi, and O.P. Gandhi
EFFECTS OF MILLIMETER-WAVE RADIATION ON MONOLAYER CELL CULTURES. I. DESIGN AND VALIDATION OF A NOVEL EXPOSURE SYSTEM
Bioelectromagnetics, Vol. 2, No. 2, pp. 123-140 (1981)
[569]

Paulsson, L.-E., Y. Hamnerius, and W.G. McLean
THE EFFECTS OF MICROWAVE RADIATION ON MICROTUBULES AND AXONAL TRANSPORT
Radiat. Res., Vol. 70, pp. 212-223 (1977)
[581, 586]

Pautrizel, R., A. Priore, P. Mattern, and A.N. Pautrizel
STIMULATION OF THE DEFENSES OF MICE WITH TRYPANOSOMIASIS BY EXPOSURE TO RADIATION ASSOCIATED WITH A MAGNETIC FIELD AND ELECTROMAGNETIC WAVES
Compt. Rend. D., Vol. 280, No. 16, pp. 1915-1918 (1975)
[390, 393]

Pay, T.L., E.C. Beyer, and C.F. Reichelderfer
MICROWAVE EFFECTS ON REPRODUCTIVE CAPACITY AND GENETIC TRANSMISSION IN DROSOPHILA MELANOGASTER
J. Microwave Power, Vol. 7, No. 2, pp. 75-82 (1972)
[164]

Pazderova, J.
WORKERS' STATE OF HEALTH UNDER LONG-TERM EXPOSURE TO ELECTROMAGNETIC RADIATION IN THE VHF BAND (30-300 MHz)
Pracovni Lekarstvi (in Czech), Vol. 23, No. 8, pp. 265-271 (1971)
English translation: JPRS No. UDC 616-001.228.1-057-07 (1971)
[35]

Pazderova, J., J. Pickova, and V. Bryndova
BLOOD PROTEINS IN PERSONNEL OF TELEVISION AND RADIO TRANSMITTING STATIONS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 281-288 (1974)
[37]

Peacock, P.B., J.W. Simpson, C.A. Alford, Jr., and F. Saunders
CONGENITAL ANOMALIES IN ALABAMA
J. Med. Assoc. Ala., Vol. 41, No. 1, pp. 42-50 (1971)
[69-71, 220]

Peacock, P.B., S.R. Williams, and E. Nash
RELATIONSHIP BETWEEN THE INCIDENCE OF CONGENITAL ANOMALIES AND THE USE OF RADAR IN MILITARY BASES
Final Report, Report No. III, Project No. 3118, Contract No. 68-02-0791 submitted by Southern Research Institute to EPA (Nov. 1973) (unpublished)
[70]

Penikas, V., R. Graham, H. Piltingsrud, and J. Stencel
SURVEY OF RADIATION LEVELS GENERATED BY EQUIPMENT USED ON EC-121 AIRCRAFT, AND CLINICAL EVALUATION OF SELECTED CREW MEMBERS
USAF Radiological Health Laboratory, Reports 70W-109 (1970) and 73W-26 (1973)
[77]

Peterson, D.J., L.M. Partlow, and O.P. Gandhi
AN INVESTIGATION OF THE THERMAL AND ATHERMAL EFFECTS OF MICROWAVE IRRADIATION ON ERYTHROCYTES
IEEE Trans. Biomed. Eng., Vol. 26, No. 7, pp. 428-436 (1979)
[351-352]

Phillips, R.D., E.L. Hunt, R.D. Castro, and N.W. King
THERMOREGULATORY, METABOLIC, AND CARDIOVASCULAR RESPONSE OF RATS TO MICROWAVES
J. Appl. Physiol., Vol. 38, No. 4, pp. 630-635 (1975)
[414-416, 451]

Pickard, W.F. and F.J. Rosenbaum
BIOLOGICAL EFFECTS OF MICROWAVES AT THE MEMBRANE LEVEL: TWO POSSIBLE ATHERMAL ELECTROPHYSIOLOGICAL MECHANISMS AND A PROPOSED EXPERIMENTAL TEST
Math. Biosci., Vol. 39, pp. 235-253 (1978)
[592-593]

Pickard, W.F. and R.G. Olsen
DEVELOPMENTAL EFFECTS OF MICROWAVES ON TENEBRIO: INFLUENCES OF CULTURING PROTOCOL AND OF CARRIER FREQUENCY
Radio Sci., Vol. 14, No. 6S, pp. 181-185 (1979)
[190-191]

Pickard, W.F. and Y.H. Barsoum
RADIO-FREQUENCY BIOEFFECTS AT THE MEMBRANE LEVEL: SEPARATION OF THERMAL AND ATHERMAL CONTRIBUTIONS IN THE CHARACEAE
J. Membrane Biol., Vol. 61, pp. 39-54 (1981)
[592-593]

Pollack, H.
EPIDEMIOLOGIC DATA ON AMERICAN PERSONNEL IN THE MOSCOW EMBASSY
Bull. N.Y. Acad. Med., Vol. 55, No. 11, pp. 1182-1186 (1979)
[46]

Polson, P. and J.H. Merritt
CANCER MORTALITY AND AIR FORCE BASES: A REEVALUATION
J. Bioelectricity, Vol. 4, No. 1, pp. 121-127 (1985)
[52]

Portela, A., et al.
TRANSIENT EFFECTS OF LOW-LEVEL MICROWAVE IRRADIATION ON BIOELECTRIC MUSCLE CELL PROPERTIES AND ON WATER PERMEABILITY AND ITS DISTRIBUTION
In FUNDAMENTAL AND APPLIED ASPECTS OF NONIONIZING RADIATION Plenum Press, N.Y., pp. 93-127 (1975)
[257]

Prausnitz, S. and C. Susskind
EFFECTS OF CHRONIC MICROWAVE IRRADIATION ON MICE
IRE Trans. Bio-Med. Electron., pp. 104-108 (1962)
[184, 386, 393-394, 397, 425]

Presman, A.S. and N.A. Levitina
NONTHERMAL ACTION OF MICROWAVES ON CARDIAC RHYTHM (COMM.): A STUDY OF THE ACTION OF CONTINUOUS MICROWAVES
Bull. Exp. Biol. Med., Vol. 53, No. 1, pp. 36-39 (1961a) Eng. Trans. of pp. 41-44 of 1962a Russ. publ.)
[449-450]

Presman, A.S. and N.A. Levitina
NONTHERMAL ACTION OF MICROWAVES ON THE RHYTHM OF CARDIAC CONTRACTIONS IN ANIMALS--REP. II: INVESTIGATION OF THE ACTION OF IMPULSE MICROWAVES
Bull. Exp. Biol. Med., Vol. 53, No. 2, pp. 154-157 (1961b)
(Engl. Transl. of pp. 39-43 of 1962b Russ. publ.)
[449]

Preston, E., E.J. Vavasour, and H.M. Assenheim
PERMEABILITY OF THE BLOOD-BRAIN BARRIER TO MANNITOL IN THE RAT FOLLOWING 2450 MHZ MICROWAVE IRRADIATION
Brain Res., Vol. 174, pp. 109-117 (1979)
[230]

Preston, E. and G. Prefontaine
CEREBROVASCULAR PERMEABILITY TO SUCROSE IN THE RAT EXPOSED TO 2,450-MHZ MICROWAVES
J. Appl. Physiol.: Respiratory, Environmental, and Exercise Physiol., Vol. 49, No. 2, pp. 218-223 (1980)
[231]

Preston, E.
FAILURE OF HYPERTHERMIA TO OPEN RAT BLOOD-BRAIN BARRIER: REDUCED PERMEATION OF SUCROSE
Acta Neuropathol. (Berl.), Vol. 57, pp. 255-262 (1982)
[244]

Putthoff, D.L., D.R. Justesen, L.B. Ward, and D.M. Levinson
DRUG-INDUCED ECTOTHERMIA IN SMALL MAMMMALS: THE QUEST FOR A BIOLOGICAL MICROWAVE DOSIMETER
Radio Sci., Vol. 12, No. 6S, pp. 73-80 (1977)
[e.?-e18]

Rabinowitz, J.R., R.B. Olcerst, and W.W. Mumford
THE DESCRIPTION OF A SYSTEM TO IRRADIATE CELLS IN CULTURE WITH MICROWAVES
In P.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIO FREQUENCY/MICROWAVES, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8026, pp. 216-229 (1977)
[352]

Ragan, H.A., R.D. Phillips, R.L. Buschbom, R.H. Busch, and J.E. Morris
HEMATOLOGIC AND IMMUNOLOGIC EFFECTS OF PULSED MICROWAVES IN MICE
Bioelectromagnetics, Vol. 4, No. 4, pp. 383-396 (1983)
[370-371]

Rama Rao, G., C.A. Cain, J. Lockwood, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. II. PERITONEAL MACROPHAGE FUNCTION
Bioelectromagnetics, Vol. 4, No. 2, pp. 141-155 (1983)
[381-382]

Rama Rao, G., C.A. Cain, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. III. MACROPHAGE RESISTANCE TO VESICULAR STOMATITIS VIRUS INFECTION
Bioelectromagnetics, Vol. 5, No. 4, pp. 377-388 (1984)
[382]

Rama Rao, G.V., C.A. Cain, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. IV. SPLEEN CELL IgM HEMOLYTIC PLAQUE FORMATION
Bioelectromagnetics, Vol. 6, No. 1, pp. 41-52 (1985)
[382]

Rand McNally and Company
1982 COMMERCIAL ATLAS AND MARKETING GUIDE
113th Edition (No. 113 07949), Chicago, New York, San Francisco (1982)
[50]

Rapoport, S.I., K. Ohno, W.R. Fredericks, and K.D. Pettigrew
A QUANTITATIVE METHOD FOR MEASURING ALTERED CEREBROVASCULAR PERMEABILITY
Radio Sci., Vol. 14, No. 6S, pp. 345-348 (1979)
[231-232, 246]

Reed, J.R.III, J.L. Lords, and C.H. Durney
MICROWAVE IRRADIATION OF THE ISOLATED RAT HEART AFTER TREATMENT WITH AN BLOCKING AGENTS
Radio Sci., Vol. 12, No. 6S, pp. 161-165 (1977)
[453, 531]

AD-A183 672 CRITIQUE OF THE LITERATURE ON BIOEFFECTS OF RADIOFREQUENCY RADIATION A CO (U) SRI INTERNATIONAL MENLO PARK CA L W HEYNICK JUN 87 USAFSAM-TR-87-3

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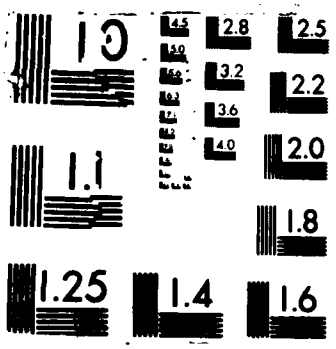
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2.2
2.5
2.8
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3.6
4.0
4.5

Roberts, N.J.Jr. and S.M. Michaelson
MICROWAVES AND NEOPLASIA IN MICE: ANALYSIS OF A REPORTED RISK
Health Phys., Vol. 44, No. 4, pp. 430-433 (1983)
[184, 394]

Roberts, N.J.Jr., S.-T. Lu, and S.M. Michaelson
HUMAN LEUKOCYTE FUNCTIONS AND THE U. S. SAFETY STANDARD FOR EXPOSURE TO RADIO-FREQUENCY RADIATION
Science, Vol. 220, pp. 318-320 (15 April 1983)
[346]

Robinette, C.D. and C. Silverman
CAUSES OF DEATH FOLLOWING OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR) 1950-1974
In D.G. Hazzard (ed.), SYMPOSIUM ON BIOLOGICAL EFFECTS AND MEASUREMENT OF RADIOFREQUENCY/MICROWAVES, Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication No. (FDA) 77-8026 (1977)
[43]

Robinette, C.D., C. Silverman, and S. Jablon
EFFECTS UPON HEALTH OF OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR)
Am. J. Epidemiol., Vol. 112, No. 1, pp. 39-53 (1980)
[45]

Robinette, C.D.
Response to Morton, W.E.
RE: "EFFECTS UPON HEALTH OF OCCUPATIONAL EXPOSURE TO MICROWAVE RADIATION (RADAR)"
Am. J. Epidemiol., Vol. 113, pp. 201-202 (1981)
[46]

Rodzilsky, B. and J. Olszewski
PERMEABILITY OF CEREBRAL BLOOD VESSELS STUDIED BY RADIOACTIVE IODINATED BOVINE ALBUMIN
Neurology, Vol. 7, pp. 270-279 (1957)
[227]

Rogers, S.J.
RADIOFREQUENCY BURN HAZARDS IN THE MF/HF BAND
In J.C. Mitchell (ed.), USAFSAM AEROMEDICAL REVIEW 3-81, PROCEEDINGS OF A WORKSHOP ON THE PROTECTION OF PERSONNEL AGAINST RFEM, pp. 76-89 (1981)
[147-148]

Roszkowski, W., J.K. Wremble, K. Roszkowski, M. Janiak, and S. Szmigielski
DOES WHOLE-BODY HYPERTHERMIA THERAPY INVOLVE PARTICIPATION OF THE IMMUNE SYSTEM?
Int. J. Cancer, Vol. 25, p. 289 (1980a)
[396]

Roszkowski, W., J.K. Wremble, M. Janiak, and S. Szmigielski
THE SEARCH FOR AN INFLUENCE OF WHOLE BODY MICROWAVE HYPERTHERMIA ON ANTITUMOR IMMUNITY
Clin. Exp. Oncol., in press (1980b)
[396]

Roszkowski, W., J.K. Wremble, M. Janiak, and S. Szmigielski
EFFECT OF WHOLE BODY HYPERTHERMIA AND DELAYED CUTANEOUS HYPERSENSITIVITY TO OXAZOLONE
Clin. Exp. Immunol., in press (1980c)
[396]

Roszkowski, W., S. Szmigielski, M. Janiak, J.K. Wremble, and W. Hryniewicz
EFFECT OF HYPERTHERMIA ON RABBIT MACROPHAGES
Zbl. Bakt. Hyg. Infekt., Vol. 1, No. 1 (1980d)
[396]

Rothmeier, J.
EFFECT OF MICROWAVE RADIATION ON THE FROG SCIATIC NERVE
In THE NERVOUS SYSTEM AND ELECTRIC CURRENTS, Plenum Press, N.Y., Vol. 1, pp. 57-69 (1970)
[257]

Rotkovska, D. and A. Vacek
THE EFFECT OF ELECTROMAGNETIC RADIATION ON THE HEMATOPOIETIC STEM CELLS OF MICE
Ann. N.Y. Acad. Sci., Vol. 247, pp. 243-250 (1975)
[368]

Ruch, T.C. and H.D. Patton
PHYSIOLOGY AND BIOPHYSICS
Vol. III, W.B. Saunders Co., Philadelphia, Pennsylvania (1973)
[21]

Ruggera, P.S.
MEASUREMENTS OF EMISSION LEVELS DURING MICROWAVE AND SHORTWAVE DIATHERMY TREATMENTS
Dept. of Health and Human Services, Bureau of Radiological Health, Rockville, MD, Publication No. (FDA) 90-8119 (1980)
[57]

Rugh, R., E.I. Ginns, H.S. Ho, and W.M. Leach
ARE MICROWAVES TERATOGENIC?
In P. Czerski et al. (eds.), BIOLOGICAL EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 98-107 (1974)
[197, 199]

Rugh, R., E.I. Ginns, H.S. Ho, and W.M. Leach
RESPONSES OF THE MOUSE TO MICROWAVE RADIATION DURING ESTROUS CYCLE AND PREGNANCY
Radiat. Res., Vol. 62, pp. 225-241 (1975)
[197, 199]

Rukspollmuang, S. and K.-M. Chen
HEATING OF SPHERICAL VERSUS REALISTIC MODELS OF HUMAN AND INFRAHUMAN HEADS BY ELECTROMAGNETIC WAVES
Radio Sci., Vol. 14, No. 6S, pp. 51-62 (1979)
[22-23]

Sadchikova, M.N.
CLINICAL MANIFESTATIONS OF REACTIONS TO MICROWAVE IRRADIATION IN VARIOUS OCCUPATIONAL GROUPS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 261-267 (1974)
[41]

Sanders, A.P., D.J. Schaefer, and W.T. Joines
MICROWAVE EFFECTS ON ENERGY METABOLISM OF RAT BRAIN
Bioelectromagnetics, Vol. 1, No. 2, pp. 171-181 (1980)
[279, 283, 285]

Sanders, A.P. and W.T. Joines
THE EFFECTS OF HYPERTHERMIA AND HYPERTHERMIA PLUS MICROWAVES ON RAT BRAIN ENERGY METABOLISM
Bioelectromagnetics, Vol. 5, No. 1, pp. 63-70 (1984)
[282, 284]

Sanders, A.P., W.T. Joines, and J.W. Allis
THE DIFFERENTIAL EFFECTS OF 200, 591, AND 2,450 MHZ RADIATION ON RAT BRAIN ENERGY METABOLISM
Bioelectromagnetics, Vol. 5, No. 4, pp. 419-433 (1984)
[284, 286]

Sanders, A.P., W.T. Joines, and J.W. Allis
EFFECTS OF CONTINUOUS-WAVE, PULSED, AND SINUSOIDAL-AMPLITUDE-MODULATED MICROWAVES ON BRAIN ENERGY METABOLISM
Bioelectromagnetics, Vol. 6, No. 1, pp. 89-97 (1985)
[286]

Sanza, J.N. and J. de Lorge
FIXED INTERVAL BEHAVIOR OF RATS EXPOSED TO MICROWAVES AT LOW POWER DENSITIES
Radio Sci., Vol. 12, No. 6S, pp. 273-277 (1977)
[490, 493]

Sapirstein, L.L.
REGIONAL BLOOD FLOW BY FRACTIONAL DISTRIBUTION OF INDICATORS
Am. J. Physiol., Vol. 193, pp. 161-168 (1958)
[237]

Saunders, R.D. and C.I. Kowalczuk
EFFECTS OF 2.45 GHZ MICROWAVE RADIATION AND HEAT ON MOUSE SPERMATOGENIC EPITHELIUM
Int. J. Radiat. Biol., Vol. 40, No. 6, pp. 623-632 (1981)
[183, 430]

Saunders, R.D., S.C. Darby, and C.I. Kowakczuk
DOMINANT LETHAL STUDIES IN MALE MICE AFTER EXPOSURE TO 2.45 GHZ MICROWAVE RADIATION
Mutation Research, Vol. 117, pp. 345-356 (1983)
[183]

Savin, V.M., K.V. Nikonova, and E.A. Lobanowa
NEW TENDENCIES IN STANDARDIZATION OF MICROWAVE ELECTROMAGNETIC RADIATION
Gigiena Truda i Prof. Zabolevaniya (in Russian), No. 3, pp. 1-3 (1983)
[11]

Sawicki, N. and K. Ostrowski
NON-THERMAL EFFECT OF MICROWAVE RADIATION IN VITRO ON PERITONEAL MAST CELLS OF THE RAT
Amer. J. Phys. Med., Vol. 17, pp. 225-234 (1968)
[383]

Schlagel, C.J., K. Sulek, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE. II. STUDIES ON THE MECHANISMS CONTROLLING SUSCEPTIBILITY TO MICROWAVE-INDUCED INCREASES IN COMPLEMENT RECEPTOR-POSITIVE SPLEEN CELLS
Bioelectromagnetics, Vol. 1, No. 4, pp. 405-414 (1980)
[372]

Scholl, D.M. and S.J. Allen
SKILLED VISUAL-MOTOR PERFORMANCE BY MONKEYS IN A 1.2-GHZ MICROWAVE FIELD
Radio Sci., Vol. 14, No. 6S, pp. 247-252 (1979)
[517]

Schramm, M.
SECRETION OF ENZYMES AND OTHER MACROMOLECULES
Ann. Rev. Biochem., Vol. 36, pp. 307-320 (1967)
[338]

Schrot, J., J.R. Thomas, and R.A. Banvard
MODIFICATION OF THE REPEATED ACQUISITION OF RESPONSE SEQUENCES IN RATS BY LOW-LEVEL MICROWAVE EXPOSURE
Bioelectromagnetics, Vol. 1, No. 1, pp. 89-99 (1980)
[500]

Schwan, H.P. and K. Li
CAPACITY AND CONDUCTIVITY OF BODY TISSUES AT ULTRAHIGH FREQUENCIES
Proc. IRE, Vol. 41, pp. 1,735-1,740 (1953)
[18]

Schwan, H.P. and G.M. Piersol
THE ABSORPTION OF ELECTROMAGNETIC ENERGY IN BODY TISSUE, PART II
Amer. J. Phys. Med., Vol. 34, pp. 425-448 (1955)
[18]

Schwan, H.P.
ELECTRICAL PROPERTIES OF TISSUE AND CELL SUSPENSION
In ADVANCES IN BIOLOGICAL AND MEDICAL PHYSICS, Vol. 5, Academic Press, New York, pp. 147-209 (1957)
[18]

Schwan, H.P.
ELECTRICAL CHARACTERISTICS OF TISSUES: A SURVEY
Biophysik, Vol. 1, pp. 198-208 (1963)
[18]

Schwan, H.P. and K.R. Foster
RF-FIELD INTERACTIONS WITH BIOLOGICAL SYSTEMS: ELECTRICAL PROPERTIES AND BIOPHYSICAL MECHANISMS
Proc. IEEE, Vol. 68, No. 1, pp. 104-113 (1980)
[19]

Seaman, R.L. and H. Wachtel
SLOW AND RAPID RESPONSES TO CW AND PULSED MICROWAVE RADIATION BY INDIVIDUAL APLYSIA PACEMAKERS
J. Microwave Power, Vol. 13, No. 1, pp. 77-86 (1978)
[587]

Seth, H.S. and S.M. Michaelson
MICROWAVE CATARACTOGENESIS
J. Occup. Med., Vol. 7, No. 9 (1965)
[86]

Shandala, M.G., U.D. Dumanskii, M.I. Rudnev, L.K. Ershova, and I.P. Los
STUDY OF NONIONIZING MICROWAVE RADIATION EFFECTS UPON THE CENTRAL NERVOUS SYSTEM AND BEHAVIOR REACTIONS
Environ. Health Perspectives, Vol. 30, pp. 115-121 (1979)
[298, 300]

Sharp, J.C., H.M. Grove, and O.P. Gandhi
GENERATION OF ACOUSTIC SIGNALS BY PULSED MICROWAVE ENERGY
IEEE Trans. Microwave Theory Tech., Vol. 22, No. 5, pp. 583-584 (1974)
[115]

Shelton, W.W., Jr. and J.H. Merritt
IN VITRO STUDY OF MICROWAVE EFFECTS ON CALCIUM EFFLUX IN RAT BRAIN TISSUE
Bioelectromagnetics, Vol. 2, No. 2, pp. 161-167 (1981)
[332, 334]

Sheppard, A.R., S.M. Bawin, and W.R. Adey
MODELS OF LONG-RANGE ORDER IN CEREBRAL MACROMOLECULES: EFFECTS OF SUB-ELF AND OF MODULATED VHF AND UHF FIELDS
Radio Sci., Vol. 14, No. 6S, pp. 141-145 (1979)
[319, 323, 325]

Shimkovich, I.S. and V.G. Shilyaev
CATARACT OF BOTH EYES WHICH DEVELOPED AS A RESULT OF REPEATED SHORT EXPOSURES TO AN ELECTROMAGNETIC FIELD OF HIGH DENSITY
Vestn. Oftal., Vol. 72, pp. 12-16 (1959)
[97]

Shnyrov, V.L., G.G. Zhadan, and I.G. Akoev
CALORIMETRIC MEASUREMENTS OF THE EFFECT OF 330-MHZ RADIOFREQUENCY RADIATION ON HUMAN ERYTHROCYTE GHOSTS
Bioelectromagnetics, Vol. 5, No. 4, pp. 411-418 (1984)
[357]

Shtverak, I., K. Marha, and G. Pafkova
SOME EFFECTS OF VARIOUS PULSED FIELDS ON ANIMALS WITH AUDIOGENIC EPILEPSY
In P. Czerski et al. (eds.), BIOLOGIC FFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 141-144 (1974)
[270]

Siekierzynski, M.
A STUDY OF THE HEALTH STATUS OF MICROWAVE WORKERS
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 273-280 (1974)
[42]

Siekierzynski, M., P. Czerski, H. Milczarek, A. Gidynski, C. Czarnecki, E. Dziuk, and W. Jedrzejczak
HEALTH SURVEILLANCE OF PERSONNEL OCCUPATIONALLY EXPOSED TO MICROWAVES. II. FUNCTIONAL DISTURBANCES
Aerospace Med., pp. 1143-1145 (October 1974a)
[43]

Siekierzynski, M., P. Czerski, A. Gidynski, S. Zydecki, C. Czarnecki, E. Dziuk, and W. Jedrzejczak
HEALTH SURVEILLANCE OF PERSONNEL OCCUPATIONALLY EXPOSED TO MICROWAVES. III. LENS TRANSLUCENCY
Aerospace Med., pp. 1146-1148 (October 1974b)
[43]

Siesjo, B.K.
BRAIN ENERGY METABOLISM
John Wiley and Sons, New York (1978)
[285]

Sigler, A.T., A.M. Lilienfeld, B.H. Cohen, and J.E. Westlake
RADIATION EXPOSURE IN PARENTS OF CHILDREN WITH MONGOLISM (DOWN'S SYNDROME)
Bull. Johns Hopkins Hosp., Vol. 117, pp. 374-395 (1965)
[67-68]

Silverman, C.
EPIDEMIOLOGIC APPROACH TO THE STUDY OF MICROWAVE EFFECTS
Bull. N.Y. Acad. Sci., Vol. 55, No. 11, pp. 1166-1181 (1979)
[44-45]

Skidmore, W.D. and S.J. Baum
BIOLOGICAL EFFECTS IN RODENTS EXPOSED TO 10 MILLION PULSES OF ELECTROMAGNETIC RADIATION
Health Phys., Vol. 26, No. 5, pp. 391-398 (1974)
[174-175, 184]

Smialowicz, R.J.
THE EFFECT OF MICROWAVES ON LYMPHOCYTE BLAST TRANSFORMATION IN VITRO
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8010, pp. 472-483 (1976)
[345]

Smialowicz, R.J., J.B. Kinn, and J.A. Elder
PERINATAL EXPOSURE OF RATS TO 2450-MHZ CW MICROWAVE RADIATION: EFFECTS ON LYMPHOCYTES
Radio Sci., Vol. 14, No. 6S, pp. 147-153 (1979a)
[179, 206, 376]

Smialowicz, R.J., K.L. Compton, M.M. Riddle, R.R. Rogers, and P.L. Brugnolotti
MICROWAVE RADIATION (2450 MHZ) ALTERS THE ENDOTOXIN-INDUCED HYPOTHERMIC RESPONSE OF RATS
Bioelectromagnetics, Vol. 1, No. 4, pp. 353-361 (1980)
[418]

Smialowicz, R.J., M.M. Riddle, P.L. Brugnolotti, R.R. Rogers, and K.L. Compton
DETECTION OF MICROWAVE HEATING IN 5-HYDROXYTRYPTAMINE-INDUCED HYPOTHERMIC MICE
Radiat. Res., Vol. 88, No. 1, pp. 108-117 (1981a)
[419]

Smialowicz, R.J., J.S. Ali, E. Berman, S.J. Bursian, J.B. Kinn, C.G. Liddle, L.W. Reiter, and C.M. Weil
CHRONIC EXPOSURE OF RATS TO 100-MHZ (CW) RADIOFREQUENCY RADIATION: ASSESSMENT OF BIOLOGICAL EFFECTS
Radiat. Res., Vol. 86, pp. 488-505 (1981b)
[274, 377]

Smialowicz, R.J., P.L. Brugnolotti, and M.M. Riddle
COMPLEMENT RECEPTOR POSITIVE SPLEEN CELLS IN MICROWAVE (2450-MHZ)-IRRADIATED MICE
J. Microwave Power, Vol. 16, No. 1, pp. 73-77 (1981c)
[373]

Smialowicz, R.J., C.M. Weil, P. Marsh, M.M. Riddle, R.R. Rogers, and B.F. Rehnberg
BIOLOGICAL EFFECTS OF LONG-TERM EXPOSURE OF RATS TO 970-MHZ RADIOFREQUENCY RADIATION
Bioelectromagnetics, Vol. 2, No. 3, pp. 279-284 (1981d)
[378]

Smialowicz, R.J., C.M. Weil, J.B. Kinn, and J.A. Elder
EXPOSURE OF RATS TO 425-MHZ (CW) RADIOFREQUENCY RADIATION: EFFECTS ON LYMPHOCYTES
J. Microwave Power, Vol. 17, No. 3, pp. 211-221 (1982a)
[378]

Smialowicz, R.J., M.M. Riddle, R.R. Rogers, and G.A. Stott
ASSESSMENT OF IMMUNE FUNCTION DEVELOPMENT IN MICE IRRADIATED IN UTERO WITH 2450-MHZ MICROWAVES
J. Microwave Power, Vol. 17, No. 2, pp. 121-126 (1982b)
[379, 381]

Smialowicz, R.J., M.M. Riddle, C.M. Weil, P.L. Brugnolotti, and J.B. Kinn
ASSESSMENT OF THE IMMUNE RESPONSIVENESS OF MICE IRRADIATED WITH CONTINUOUS WAVE OR PULSE-MODULATED 425-MHZ RADIO FREQUENCY RADIATION
Bioelectromagnetics, Vol. 3, No. 4, pp. 467-470 (1982c)
[379]

Smialowicz, R.J., R.R. Rogers, R.J. Garner, M.M. Riddle, R.W. Luebke, and D.G. Rowe
MICROWAVES (2,450 MHZ) SUPPRESS MURINE NATURAL KILLER CELL ACTIVITY
Bioelectromagnetics, Vol. 4, No. 4, pp. 371-381 (1983)
[379]

Spalding, J.F., R.W. Freyman, and L.M. Holland
EFFECTS OF 800 MHZ ELECTROMAGNETIC RADIATION ON BODY WEIGHT, ACTIVITY, HEMATOPOIESIS, AND LIFE SPAN IN MICE
Health Phys., Vol. 20, No. 4, pp. 421-424 (1971)
[173]

Spiegel, R.J., D.M. Deffenbaugh, and J.E. Mann
A THERMAL MODEL OF THE HUMAN BODY EXPOSED TO AN ELECTROMAGNETIC FIELD
Bioelectromagnetics, Vol. 1, No. 3, pp. 253-270 (1980)
[22]

Spiegel, R.J.
THE THERMAL RESPONSE OF A HUMAN IN THE NEAR-ZONE OF A RESONANT THIN-WIRE ANTENNA
IEEE Trans. Microwave Theory Tech., Vol. 30, No. 2, pp. 177-185 (1982)
[26]

Stavinoha, W.B., A. Modak, M.A. Medina, and A.E. Gass
GROWTH AND DEVELOPMENT OF NEONATAL MICE EXPOSED TO HIGH-FREQUENCY ELECTROMAGNETIC WAVES
USAF School of Aerospace Medicine, Brooks AFB, Texas; Final Report SAM-TR-75-51 on Contract F41609-74-C-0018, submitted by University of Texas Health Science Center, San Antonio, Texas (1975)
[204]

Stavinoha, W.B., M.A. Medina, J. Frazer, S.T. Weintraub, D.H. Ross, A.T. Modak, and D.J. Jones
THE EFFECTS OF 19 MEGACYCLE IRRADIATION ON MICE AND RATS
In C. C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 77-8010, pp. 431-448 (1976)
[205]

Stensaas, L.J., L.M. Partlow, L.G. Bush, P.L. Iverson, D.W. Hill, M.J. Hagmann, and O.P. Gandhi
EFFECTS OF MILLIMETER-WAVE RADIATION ON MONOLAYER CELL CULTURES. II. SCANNING AND TRANSMISSION ELECTRON MICROSCOPY
Bioelectromagnetics, Vol. 2, No. 2, pp. 141-150 (1981)
[573]

Stern, S., L. Margolin, B. Weiss, S.-T. Lu, and S.M. Michaelson
MICROWAVES: EFFECT ON THERMOREGULATORY BEHAVIOR IN RATS
Science, Vol. 206, pp. 1198-1201 (7 December 1979)
[420]

Stodolnik-Baranska, W.
LYMPHOBLASTOID TRANSFORMATION OF LYMPHOCYTES IN VITRO AFTER MICROWAVE IRRADIATION
Nature, Vol. 214, pp. 102-103 (1967)
[343, 372]

Stodolnik-Baranska, W.
THE EFFECTS OF MICROWAVES ON HUMAN LYMPHOCYTE CULTURES
In P. Czerski et al. (eds.), BIOLOGIC EFFECTS AND HEALTH HAZARDS OF MICROWAVE RADIATION, Polish Medical Publishers, Warsaw, pp. 189-195 (1974)
[171, 343-344, 372]

Stuchly, M.A. and S.S. Stuchly
DIELECTRIC PROPERTIES OF BIOLOGICAL SUBSTANCES--TABULATED
J. Microwave Power, Vol. 15, No. 1, pp. 19-26 (1980)
[19]

Stuchly, M.A., T.W. Athey, S.S. Stuchly, G.M. Samaras, and G. Taylor
DIELECTRIC PROPERTIES OF ANIMAL TISSUES IN VIVO AT FREQUENCIES 10 MHZ-1 GHZ
Bioelectromagnetics, Vol. 2, No. 2, pp. 93-103 (1981)
[19]

Stuchly, S.S., A. Kraszewski, M.A. Stuchly, G. Hartsgrove, and D. Adamski
ENERGY DEPOSITION IN A MODEL OF MAN IN THE NEAR FIELD
Bioelectromagnetics, Vol. 6, No. 2, pp. 115-129 (1985a)
[26]

Stuchly, M.A., A. Kraszewski, and S.S. Stuchly
EXPOSURE OF HUMAN MODELS IN THE NEAR AND FAR FIELD--A COMPARISON
IEEE Trans. Biomed. Eng., Vol. 32, nO. 8, pp. 609-616 (1985b)
[26]

Sulek, K., C.J. Schlagel, W. Wiktor-Jedrzejczak, H.S. Ho, W.M. Leach, A. Ahmed, and J.N. Woody
BIOLOGIC EFFECTS OF MICROWAVE EXPOSURE: I. THRESHOLD CONDITIONS FOR THE INDUCTION OF THE INCREASE IN COMPLEMENT RECEPTOR POSITIVE (CR+) MOUSE SPLEEN CELLS FOLLOWING EXPOSURE TO 2450-MHZ MICROWAVES
Radiat. Res., Vol. 83, pp. 127-137 (1980)
[372]

Sultan, M.F., C.A. Cain, and W.A.F. Tompkins
EFFECTS OF MICROWAVES AND HYPERTHERMIA ON CAPPING OF ANTIGEN-ANTIBODY COMPLEXES ON THE SURFACE OF NORMAL MOUSE B LYMPHOCYTES
Bioelectromagnetics, Vol. 4, No. 2, pp. 115-122 (1983a)
[349]

Sultan, M.F., C.A. Cain, and W.A.F. Tompkins
IMMUNOLOGICAL EFFECTS OF AMPLITUDE-MODULATED RADIO FREQUENCY RADIATION: B LYMPHOCYTE CAPPING
Bioelectromagnetics, Vol. 4, No. 2, pp. 157-165 (1983b)
[349]

Sutton, C.H. and F.B. Carroll
EFFECTS OF MICROWAVE-INDUCED HYPERTHERMIA ON THE BLOOD-BRAIN BARRIER OF THE RAT
Radio Sci., Vol. 14, No. 6S, pp. 329-334 (1979)
[235-237]

Swicord, M.L. and C.C. Davis
AN OPTICAL METHOD FOR INVESTIGATING THE MICROWAVE ABSORPTION CHARACTERISTICS OF DNA AND OTHER BIOMOLECULES IN SOLUTION
Bioelectromagnetics, Vol. 4, No. 1, pp. 21-42 (1983)
[575]

Szmigielski, S.
EFFECT OF 10-CM (3 GHZ) ELECTROMAGNETIC RADIATION (MICROWAVES) ON GRANULOCYTES IN VITRO
Ann. N.Y. Acad. Sci., Vol. 247, pp. 275-281 (1975)
[344, 394]

Szmigielski, S., J. Jeljazewicz, and M. Wiranowska
ACUTE STAPHYLOCOCCAL INFECTIONS IN RABBITS IRRADIATED WITH 3-GHz MICROWAVES
Ann. N.Y. Acad. Sci., Vol. 247, pp. 305-311 (1975a)
[345, 394]

Szmigielski, S., M. Luczak, and M. Wiranowska
EFFECT OF MICROWAVES ON CELL FUNCTION AND VIRUS REPLICATION IN CELL CULTURES IRRADIATED IN VITRO
Ann. N.Y. Acad. Sci., Vol. 247, pp. 263-281 (1975b)
[578]

Szmigielski, S., W. Roszkowski, M. Kobus, and J. Jeljaszewicz
MODIFICATION OF EXPERIMENTAL ACUTE STAPHYLOCOCCAL INFECTIONS BY LONG-TERM EXPOSURE TO NON-THERMAL MICROWAVE FIELDS OR WHOLE BODY HYPERTHERMIA
Proc. URSI Int. Symposium on Electromagnetic Waves and Biology, Paris, France, pp. 127-132 (June-July 1980)
[395]

Takashima, S.
STUDIES ON THE EFFECT OF RADIO-FREQUENCY WAVES ON BIOLOGICAL MACROMOLECULES
IEEE Trans. Biomed. Eng., Vol. 13, No. 1, pp. 28-31 (1966)
[559]

Takashima, S., B. Onaral, and H.P. Schwan
EFFECTS OF MODULATED RF ENERGY ON THE EEG OF MAMMALIAN BRAINS
Rad. and Environm. Biophys., Vol. 16, pp. 15-27 (1979)
[303]

Taylor, E.M. and B.T. Ashleman
ANALYSIS OF CENTRAL NERVOUS SYSTEM INVOLVEMENT IN THE MICROWAVE AUDITORY EFFECT
Brain Res., Vol. 74, pp. 201-208 (1974)
[115, 118]

Taylor, L.S. and A.Y. Cheung (eds.)
THE PHYSICAL BASIS OF ELECTROMAGNETIC INTERACTIONS WITH BIOLOGICAL SYSTEMS
U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 78-8055 (1978)
[26]

Taylor, L.S. and A.Y. Cheung (eds.)
THE MECHANISMS OF MICROWAVE BIOLOGICAL EFFECTS
Report of Workshop Held at University of Maryland, College Park, Maryland (May 14-16, 1979)
[26]

Taylor, L.S.
THE MECHANISMS OF ATHERMAL MICROWAVE BIOLOGICAL EFFECTS
Bioelectromagnetics, Vol. 2, No. 3, pp. 259-267 (1981)
[26]

Tell, R.A. and P.J. O'Brien
AN INVESTIGATION OF BROADCAST RADIATION INTENSITIES AT MT. WILSON, CALIFORNIA
Tech. Note ORP/EAD 77-2, U.S. Environmental Protection Agency (1977)
[13]

Tell, R.A. and E.D. Mantiply
POPULATION EXPOSURE TO VHF AND UHF BROADCAST RADIATION IN THE UNITED STATES
Proc. IEEE, Vol. 68, No. 1, pp. 6-12 (1980)
[12, 53]

Thomas, J.R., E.D. Finch, D.W. Fulk, and L.S. Burch
EFFECTS OF LOW-LEVEL MICROWAVE RADIATION ON BEHAVIORAL BASELINES
Ann. N.Y. Acad. Sci., Vol. 247, pp. 425-432 (1975)
[462, 502]

Thomas, J.R., S.S. Yeandle, and L.S. Burch
MODIFICATION OF INTERNAL DISCRIMINATIVE STIMULUS CONTROL OF BEHAVIOR BY LOW LEVELS OF PULSED MICROWAVE RADIATION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, Vol. I, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 201-214 (1976)
[463]

Thomas, J.R. and G. Maitland
MICROWAVE RADIATION AND DEXTROAMPHETAMINE: EVIDENCE OF COMBINED EFFECTS ON BEHAVIOR OF RATS
Radio Sci., Vol. 14, No. 6S, pp. 253-258 (1979)
[536]

Thomas, J.R., L.S. Burch, and S.S. Yeandle
MICROWAVE RADIATION AND CHLORDIAZEPOXIDE: SYNERGISTIC EFFECTS ON FIXED-INTERVAL BEHAVIOR
Science, Vol. 203, pp. 1357-1358 (1979)
[535, 542-543, 548]

Thomas, J.R., J. Schrot, and R.A. Banvard
BEHAVIORAL EFFECTS OF CHLORPROMAZINE AND DIAZEPAM COMBINED WITH LOW-LEVEL MICROWAVES
Neurobehav. Toxicol., Vol. 2, pp. 131-135 (1980)
[538]

Thomas, J.R., J. Schrot, and R.A. Banvard
COMPARATIVE EFFECTS OF PULSED AND CONTINUOUS-WAVE 2.8-GHZ MICROWAVES ON TEMPORALLY DEFINED BEHAVIOR
Bioelectromagnetics, Vol. 3, No. 2, pp. 227-235 (1982)
[502]

Tinney, C.E., J.L. Lords, and C.H. Durney
RATE EFFECTS IN ISOLATED TURTLE HEARTS INDUCED BY MICROWAVE IRRADIATION
IEEE Trans. Microwave Theory Tech., Vol. 24, No. 1, pp. 18-24 (1976)
[257, 453, 531]

Todorovich, P., R. Gensi, and M. Kosanovich
ON THE INFLUENCE OF MICROWAVES ON RAT ADRENALS
Arkhiv. Bioloshkih Nauka, Vol. 17, No. #, pp. 121-128 (1965)
[431]

Tolgskaya, M.S. and Z.V. Gordon
PATHOLOGICAL EFFECTS OF RADIO WAVES
(Translated from the original Russian text published by Meditsina Press, Moscow, 1971), Consultants Bureau, New York-London (1973)
[269]

Tyazhelov, V.V., R.E. Tigranian, and E.P. Khizhniak
NEW ARTIFACT-FREE ELECTRODES FOR RECORDING OF BIOLOGICAL POTENTIALS IN STRONG ELECTROMAGNETIC FIELDS
Radio Sci., Vol. 12, No. 6S, pp. 121-123 (1977)
[291-292]

Tyazhelov, V.V., R.E. Tigranian, E.O. Khizhniak, and I.G. Akoev
SOME PECULIARITIES OF AUDITORY SENSATIONS EVOKED BY PULSED MICROWAVE FIELDS
Radio Sci., Vol. 14, No. 6S, pp. 259-263 (1979)
[127]

Valtonen, E.J.
GIANT MAST CELLS--A SPECIAL DEGENERATIVE FORM PRODUCED BY MICROWAVE RADIATION
Exp. Cell Res., Vol. 43, pp. 221-224 (1966a)
[383]

Valtonen, E.J.
THE EFFECTS OF MICROWAVE RADIATION ON THE CELLULAR ELEMENTS IN THE PERITONEAL FLUID AND PERIPHERAL BLOOD OF THE RAT
Acta Rheumatol. Scand., Vol. 12, pp. 291-299 (1966b)
[383]

Van Ummersen, C.A. and F.C. Cogan
EFFECTS OF MICROWAVE RADIATION ON THE LENS EPITHELIUM IN THE RABBIT EYE
Arch. Ophthal., Vol. 94, pp. 828-834 (1976)
[84]

Varma, M.M. and E.A. Traboulay, Jr.
EVALUATION OF DOMINANT LETHAL TEST AND DNA STUDIES IN MEASURING MUTAGENICITY CAUSED BY NON-IONIZING RADIATION
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW publication (FDA) 77-8010, pp. 386-396 (1976)
[176-177, 179]

Varma, M.M., E.L. Dage, and S.R. Joshi
MUTAGENICITY INDUCED BY NON-IONIZING RADIATION IN SWISS MALE MICE
In C.C. Johnson and M. Shore (eds.), BIOLOGICAL EFFECTS OF ELECTROMAGNETIC WAVES, U.S. Dept. of Health, Education, and Welfare, Washington, D.C., HEW Publication (FDA) 77-8010, pp. 397-405 (1976)
[178-179]

Wachtel, H., R. Seaman, and W. Joines
EFFECTS OF LOW-INTENSITY MICROWAVES ON ISOLATED NEURONS
Ann. N.Y. Acad. Sci., Vol. 247, pp. 46-62 (1975)
[252, 587, 589-590]

Ward, T.R., J.A. Elder, M.D. Long, and D. Svendsgaard
MEASUREMENT OF BLOOD-BRAIN BARRIER PERMEATION IN RATS DURING EXPOSURE TO 2450-MHZ MICROWAVES
Bioelectromagnetics, Vol. 3, No. 3, pp. 371-383 (1982)
[232-233]

Ward, T.R. and J.S. Ali
BLOOD-BRAIN BARRIER PERMEATION IN THE RAT DURING EXPOSURE TO LOW-POWER 1.7-GHZ MICROWAVE RADIATION
Bioelectromagnetics, Vol. 6, No. 2, pp. 131-143 (1985)
[233]

Webb, S.J. and D.D. Dodds
INHIBITION OF BACTERIAL CELL GROWTH BY 136 GC MICROWAVES
Nature, Vol. 218, pp. 374-375 (27 April 1968)
[560]

Webb, S.J. and A.D. Booth
ABSORPTION OF MICROWAVES BY MICROORGANISMS
Nature, Vol. 222, pp. 1199-1200 (21 June 1969)
[561, 563]

Webb, S.J. and A.D. Booth
MICROWAVE ABSORPTION BY NORMAL AND TUMOR CELLS
Science, Vol. 174, pp. 72-74 (1 October 1971)
[564, 568]

Webb, S.J. and M.E. Stoneham
RESONANCES BETWEEN 100 AND 1000 GHZ IN ACTIVE BACTERIAL CELLS AS SEEN BY LASER RAMAN SPECTROSCOPY
Phys. Lett., Vol. 60A, No. 3, pp. 267-268 (1977)
[564-565]

Webb, S.J., M.E. Stoneham, and H. Froehlich
EVIDENCE FOR NON-THERMAL EXCITATION OF ENERGY LEVELS IN ACTIVE BIOLOGICAL SYSTEMS
Phys. Lett., Vol. 63A, No. 3, pp. 407-408 (1977)
[564]

Weil C.M.
ABSORPTION CHARACTERISTICS OF MULTILAYERED SPHERE MODELS EXPOSED TO UHF/MICROWAVE RADIATION
IEEE Trans. Biomed. Eng., Vol. 22, No. 6, pp. 468-476 (1975)
[22-23, 397]

Weil, C.M.
THE CHARACTERISTIC IMPEDANCE OF RECTANGULAR TRANSMISSION LINES WITH THIN CENTER CONDUCTOR AND AIR DIELECTRIC
IEEE Trans. Microwave Theory Tech., Vol. 26, pp. 238-242 (1978)
[321]

Weiter, J.J., E.D. Finch, W. Schultz, and V. Frattali
ASCORBIC ACID CHANGES IN CULTURED RABBIT LENSES AFTER MICROWAVE IRRADIATION
Ann. N.Y. Acad. Sci., Vol. 247, pp. 175-181 (1975)
[92]

White, R.M.
GENERATION OF ELASTIC WAVES BY TRANSIENT SURFACE HEATING
J. Appl. Phys., Vol. 34, No. 12, pp. 3559-3567 (1963)
[114]

WHO
ENVIRONMENTAL HEALTH CRITERIA 16, RADIOFREQUENCY AND MICROWAVES
World Health Organization, Geneva, Switzerland (1981)
[10]

Wike, E.L. and E.J. Martin
COMMENTS ON FREY'S "DATA ANALYSIS REVEALS SIGNIFICANT MICROWAVE-INDUCED EYE DAMAGE IN HUMANS"
J. Microwave Power, Vol. 20, No. 3, pp. 181-184 (1985)
[105]

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
IMMUNE RESPONSE OF MICE TO 2450-MHZ MICROWAVE RADIATION: OVERVIEW OF IMMUNOLOGY AND EMPIRICAL STUDIES OF LYMPHOID SPLENIC CELLS
Radio Sci., Vol. 12, No. 6S, pp. 209-219 (1977)
[371-372]

Wiktor-Jedrzejczak, W., A. Ahmed, P. Czerski, W.M. Leach, and K.W. Sell
EFFECT OF MICROWAVES (2450-MHZ) ON THE IMMUNE SYSTEM IN MICE: STUDIES OF NUCLEIC ACID AND PROTEIN SYNTHESIS
Bioelectromagnetics, Vol. 1, No. 2, pp. 161-170 (1980)
[372]

Wiktor-Jedrzejczak, W., C.J. Schlagel, A. Ahmed, W.M. Leach, and J.N. Woody
POSSIBLE HUMORAL MECHANISM OF 2450-MHZ MICROWAVE-INDUCED INCREASE IN COMPLEMENT RECEPTOR POSITIVE CELLS
Bioelectromagnetics, Vol. 2, No. 1, pp. 81-84 (1981)
[372]

Williams, W.M., W. Hoss, M. Formaniak, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. A. EFFECT ON THE PERMEABILITY TO SODIUM FLUORESCEIN
Brain Res. Rev., Vol. 7, pp. 165-170 (1984a)
[238, 245-246]

Williams, W.M., M. del Cerro, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. B. EFFECT ON THE PERMEABILITY TO HRP
Brain Res. Rev., Vol. 7, pp. 171-181 (1984b)
[240, 245-246]

Williams, W.M., J. Platner, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. C. EFFECT ON THE PERMEABILITY TO C-14 SUCROSE
Brain Res. Rev., Vol. 7, pp. 183-190 (1984c)
[241-242, 246]

Williams, W.M., S.-T. Lu, M. del Cerro, and S.M. Michaelson
EFFECT OF 2450 MHZ MICROWAVE ENERGY ON THE BLOOD-BRAIN BARRIER TO HYDROPHILIC MOLECULES. D. BRAIN TEMPERATURE AND BLOOD-BRAIN BARRIER PERMEABILITY TO HYDROPHILIC TRACERS
Brain Res. Rev., Vol. 7, pp. 191-212 (1984d)
[244, 246]

Wilson, B.S., J.M. Zook, W.T. Joines, and J.H. Casseday
ALTERATIONS IN ACTIVITY AT AUDITORY NUCLEI OF THE RAT INDUCED BY EXPOSURE TO MICROWAVE RADIATION: AUTORADIOGRAPHIC EVIDENCE USING [C-14] 2-DEOXY-D-GLUCOSE
Brain Res., Vol. 187, pp. 291-306 (1980)
[133-134]

Wong, L.S., J.H. Merritt, and J.L. Kiel
EFFECTS OF 20-MHZ RADIOFREQUENCY RADIATION ON RAT HEMATOLOGY, SPLENIC FUNCTION, AND SERUM CHEMISTRY
Radiat. Res., Vol. 103, No. 2, pp. 186-195 (1985)
[384]

Wu, C.L. and J.C. Lin
ABSORPTION AND SCATTERING OF ELECTROMAGNETIC WAVES BY PROLATE SPHEROIDAL MODELS OF BIOLOGICAL STRUCTURES
IEEE Antenna & Propagation Society Int. Symp. Digest, pp. 142-145 (1977)
[22]

Yang, H.K., C.A. Cain, J. Lockwood, and W.A.F. Tompkins
EFFECTS OF MICROWAVE EXPOSURE ON THE HAMSTER IMMUNE SYSTEM. I. NATURAL KILLER CELL ACTIVITY
Bioelectromagnetics, Vol. 4, No. 2, pp. 123-139 (1983)
[380-381]

Yee, K.C., C.K. Chou, and A.W. Guy
EFFECT OF MICROWAVE RADIATION ON THE BEATING RATE OF ISOLATED FROG HEARTS
Bioelectromagnetics, Vol. 5, No. 2, pp. 263-270 (1984)
[454, 592]

Zaret, M.
OPHTHALMIC HAZARD OF MICROWAVE AND LASER ENVIRONMENTS
39th Ann. Sci. Meeting Aerospace Med. Assoc., San Francisco, CA (1969)
[97]

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