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# TIME HISTORY OF BIOLOGICAL RESPONSE TO IONIZING RADIATION

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ABSTRACT

Exposure of personnel to initial ionizing radiation from a nuclear air or surface burst can cause both prompt and delayed casualties. Their percentages and times to incapacitation (or combat ineffectiveness, in a military sense) after exposure can be of major significance in military operations. Although adequate data are lacking for the determination of dose-effect relationships vs time after exposure, quantitative estimates are needed nevertheless for guidance in battlefield predictions and decision-making. Available nuclear-accident data and other data on human exposures are used to obtain curves to represent the estimated time history of the acute radiation syndrome as a function of dose received in a very short time. The sources of data are clinical records of nuclear-accident casualties from 1945 to 1958, followup records of radiotherapy patients, and casualty studies on the atomic explosions at Hiroshima and Nagasaki. Emphasis is put on the time after exposure of the onset of the initial stage of radiation sickness (nausea, vomiting, malaise, etc.), duration of the initial stage, start and duration of the following asymptomatic latent period, time of onset of the second (or manifest illness) stage, and time of eventual recuperation or death. The estimated time history is depicted graphically with two other time histories for comparison. Analytical expressions are derived for the three time histories for use in estimating any of these syndrome times or periods.

## SUMMARY PAGE


### The Problem

Exposure of personnel to initial ionizing radiation from a nuclear air or surface burst can cause both prompt and delayed casualties. Their percentages and times to incapacitation (or combat ineffectiveness in a military sense) after exposure can be of major significance in military operations. Although adequate data are lacking for determination of dose-effect relationships vs time after exposure, quantitative estimates are needed for guidance in battlefield predictions and decision-making.

### Findings

Based on available nuclear-accident data and other data, curves were derived to represent the estimated time history of the acute radiation syndrome as a function of dose received in a very short time. The curves show the time after exposure of the onset of the initial stage of radiation sickness (nausea, vomiting, etc.), duration of the initial stage, start and duration of the following symptom-free latent period, time of onset of the second (or manifest illness) stage, and time of eventual recuperation or death. Analytical expressions have been derived from the curves to enable one to make approximate predictions. Comparison of the curves with curves developed by other investigators point to differences that could be militarily significant.

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# SECTION 1

# INTRODUCTION

## 1.1 PROBLEM

The initial phenomena of nuclear explosions that are capable of damaging material and personnel can cause either immediate or delayed effects. Thus, structural damage from air blast is immediate, whereas that from mass fires is delayed. The onset of sickness from exposure to initial ionizing radiation (gamma rays and neutrons) is a delayed effect. A person sufficiently exposed that he will eventually die can, nonetheless, remain operational for a period of time after exposure. For this reason, the knowledge of the relationship between dose (exposure) and the onset of nausea and incapacitation, however the latter may be defined operationally, would facilitate operational planning.

In a combat operation, the time to onset of sickness could be critical. Changes in the plan or concept of operations would depend on an evaluation of immediate casualties, an estimate of additional delayed casualties, and an estimate of the delay time. Or, in general terms, what is required are quantitative estimates of the percent of forces remaining operational (or, conversely, the percent attrition) as a function of time to the extent that such estimates affect decision-making during the conduct of operations, in operational planning, or in the design and development of support systems.

A thorough analysis of human radiation responses would be of considerable value since from such an analysis it might be possible to extract information which would be both radiobiologically and operationally of interest. Considerable uncertainties exist, however, as to individual human response to whole-body irradiation because of an

obvious lack of controlled experimental data. Whether or not these uncertainties result in a spread of estimates of force-operability vs time that is or is not acceptable, can in turn affect decisions in the planning of research and exploratory development programs. It is for this reason that the following analytical treatment of the available experimental data, admittedly meager and clinically unevaluated, has been attempted. Justification for the development of algebraic expressions to fit such data rests solely, therefore, on the extent to which the use of such expressions can assist in the definition of alternative courses of action in military decision-making. The reader is, therefore, cautioned against interpreting the following analytical development to represent precise, definitive characterizations of biological response in absolute terms.

Applications of the results of this study to situations of military interest will be reported separately.

## 1.2 OBJECTIVE OF STUDY

This study was conducted to:

a. Summarize the available experimental data on human response to whole-body irradiation, with particular emphasis on the time to incapacitation resulting from doses delivered in a very short time;

b. Present and compare results of previously derived dose-effect relationships vs time;

c. Derive empirical relationships that could be used analytically in attack-response studies in military contexts.

The type of biological responses that are associated with combat ineffectiveness include nausea, vomiting, diarrhea, malaise, and death.

## 1.3 BACKGROUND INFORMATION

Different dose-effect relationships have been estimated by several investigators,[1,2,3*] [**] but the factual evidence is not yet sufficient to establish their reliability. Most relationships are based on extrapolation and interpolation either from limited clinical acute-dose data or fromexperimental laboratory data and intuition. The sources of data on human response are:

1. Nuclear-accident reports compiled from 1945 to 1958.
2. Long-time followups of radiotherapy patients.
3. Results of studies of casualties from the atomic explosions over Hiroshima and Nagasaki.

The available data indicate a wide range of doses causing acute radiation syndrones[***] from which man can survive.

Estimates of initial-radiation exposure vs range from ground zero for a person or a group of persons can be made either by measurement or calculation. For such exposure doses in a given situation, the number or percentage of radiation casualties as a function of time after burst needs to be predicted. However, because of the various conflicting casualty criteria and data, prediction of the percentage of combat ineffectives vs time after exposure cannot be made with confidence.

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* Ref. 3 presents the biological response curve from E. L. Alpen, USNRDL (private communication).

** Teresi, J. D., Status of Biological Effects of Radiation on Importance to Military and Civil Defense, USNRDL-TR in preparation (UNCL).

*** The complex of symptoms characterizing the disease known as radiation injury, resulting from excessive exposure of the whole (or a large part) of the body to ionizing radiation. The earliest of these symptoms are nausea, vomiting, and diarrhea, which may be followed by loss of hair, hemorrhage, etc. In severe cases, where the radiation exposure has been relatively large, death may occur within 2 to 4 weeks. Those who survive 6 weeks after receiving a single dose of radiation may generally be expected to recover.

## 1.4 GENERAL APPROACH AND SCOPE

Radiation injury is generally characterized by two stages separated in time. The initial stage (prodrome) exhibits symptoms of nausea, vomiting, diarrhea, and malaise. After these symptoms disappear, there is a remission or latent period, characterized by a period of relative well-being. Subsequently, there is a return of symptoms, marking the onset of the second or manifest-illness stage which finally ends in recuperation or death.

Data from Refs. 1 and 2 were used to estimate the times of onset and remission of the initial stage and also the times of onset and recuperation or death of the manifest-illness stage. These times were compared graphically with curves previously derived by Alpen[3] and by Teresi*.

Four equations were then derived, expressing each of the above times as a function of dose received, and for each of the three sets of curves. These equations are intended to be used in a subsequent overall analysis of combined casualties from all three initial weapon effects: nuclear radiation, thermal radiation, and blast.

The dose range selected is from 200 to 2000 rads because it is highly unlikely that a dose of 200 rads will cause combat ineffectiveness, and a dose of 2000 rads or greater is highly likely to cause almost immediate and continuous combat ineffectiveness and ultimately death. The time range selected is from the time of exposure to the time of recuperation or death.

Finally, because of individual susceptibility and some other minor factors, probability ranges were determined and replotted to get %CE (combat effectives)** and %CI (combat ineffectives) vs time after burst for selected biological doses from 200 to 2000 rads. This probability effect is further accounted for with an analytical expression to be applied to the above-mentioned sets of curves.

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*Op. Cit.

**Mission-performing capability is discussed in terms of combat effectiveness. A combat ineffective (CI) is defined as a personnel combat casualty who has been injured to the degree that he cannot effectively perform his combat duties.

## 1.5 LIMITATIONS OF RESULTS

Biological response of man to ionizing radiation must be considered as being more than a complex process that can, to a certain degree, be studied and determined. For this reason, caution was necessarily exercised in handling the limited available data for the derivation of analytical dose-effect equations. The major limitations are:

1. Limited data on acute nuclear-radiation injury to man. These data can be grouped in two main categories: (a) nuclear-accident data reported in Ref. 1, and (b) fallout-exposure and clinical-therapy data reported in Ref. 2.
2. Consideration has to be given to the following question: Are the nuclear-accident data applicable to the military tactical situations involving the exposure of combat forces to (a) initial radiation and (b) fallout and/or induced-activity radiation? It will be assumed, for the intended use of the results of this study, that nuclear accident data are applicable to military tactical situations.
3. Military personnel can be considered as young and healthy in contrast to a random sample of the persons who were exposed to radiation, as reported in Refs. 1 and 2. It is expected that the variation in individual susceptibility to ionizing radiation may be smaller for military personnel, and will therefore provide a more reliable radiation syndrome for quantitative analysis.

Despite these limitations, an attempt has been made to utilize the data as a basis for establishing a relationship for biological response as a function of acute dose and time after exposure. Source data for the individual accidental-exposure cases were not analyzed. Conclusions drawn, therefore, are based on the interpretations of Refs. 1 and 2, but can probably be accepted with a reasonable degree of confidence.

## SECTION 2

## DOSE-EFFECT RELATIONSHIPS VS TIME

### 2.1 GENERAL

Nuclear-accident case histories of the past two decades describe the radiological injuries to humans who have received various single-exposure or "one shot" acute doses. These histories have been published in Refs. 1 and 2 and have been used in certain dose-effect studies.* When sufficient doses were received to cause radiation-sickness symptoms, a typical sequence of biological responses vs time after exposure was observed by medical doctors. The basic sequence of observable responses as a function of dose and time can be classified on the time scale as follows:

1. Length of time to onset of first symptoms, or initial reaction time.
2. Duration of initial reaction period (or prodrome) and the severity of the symptoms.
3. Length of the latent period, which starts with the remission of these symptoms.
4. Onset of the second reaction (radiation sickness) period and the severity of sickness.
5. Time of recovery or death.

In general, the onset and duration of these sequences (the acute radiation syndrome) can be generalized on the time scale for moderate whole-body doses from 200 to 600 rads as follows: The first symptoms will appear in about 1 to 2 hours after exposure. The general symptoms (nausea, vomiting, etc.) advance rapidly, culminate about 8 hours after

*For example, Op. Cit.

exposure,[1,2] and then subside (remission) rather quickly in a day or two. During the following latent period (lasting from 1 or 2 days to about 2 weeks, depending inversely on dose), the patient appears to be free of symptoms and his general condition is markedly improved; in a combat situation, he will be able to perform his normal duties.

According to Refs. 1 and 2, the onset of the second period or phase of radiation sickness occurs from several days to 2 or 3 weeks after exposure. The time of onset and the severity of radiation sickness will depend mainly on the total dose received. The condition progresses rapidly and culminates about the fourth week. If death hasn't occurred, the condition will improve, starting from the fifth to sixth week after exposure. This sequence is mainly a function of two parameters: (1) total dose received, and (2) different individual susceptibility to radiation.

## 2.2 ANALYSIS OF DATA IN REFS. 1 AND 2

Some data given in Ref. 1 are duplicated in Ref. 2. This duplication has been avoided in the analysis of data. A summary of nuclear-accident data given in Ref. 1 is reproduced in Table 1. The table also includes some additional data obtained in Ref. 2. The data in Table 1 are plotted in Fig. 1 for visual observation. To illustrate the complete time sequence of the acute radiation syndrome given in Refs. 1 and 2, a logarithmic time scale* has been selected. The data in Table 1 are approximate, and include some cases for which there were uncertainties in onset time and in others in termination time. Such cases are indicated in Figure 1 by dashed lines.

It can be observed that the most documented range of exposure doses in the nuclear-accident histories is from 150 to 650 rads. Doses less than 150 rads were clinically insignificant.[1,2] Only three cases are reported of a person who received more than a 650-rad acute dose (LA3, 1350 rads; LA11, 4850 rads** and from Ref. 4, 8800 rads). Although the

*Note that the logaristhmic scale for the exposure dose has been enlarged for data-plotting purposes.

**Recalculated to be 4850 rads according to Gordon C. Bell, CAPT., MSC, USN(Private Communication) .

Table 1

Time of Onset and Duration of Clinical Signs and Symptoms
Initial Stage and Manifest Illness Stage (MIS) After Exposure

(Based on Refs. 1,2, and 4)

| Ref. Code Ident | Accident | Calc. Total* Rad.Dose | Stage After Exposure: Initial Time of Onset | Initial Duration Time | Manif. Illness Time of Onset | Manif. Illness Duration Time | Remarks |
|---|---|---|---|---|---|---|---|
| LA11 | Los Alamos III | 9200** | 15 min | | | 35 hr | Patient died |
| LA 3 | Los Alamos II | 1350 | 1 hr | <1 d | 6 d | 4 d | Patient died |
| Y1 | Yugoslavia | 640 | 1 hr | ~2 d | 22 d | 11 d | Patient died |
| Y4 | Yugoslavia | 600 | 1 hr | ~2 d | 30 d | 6 d | |
| Y3 | Yugoslavia | 580 | 1 hr | ~2 d | 24 d | 6 d | |
| Y2 | Yugoslavia | 500 | 1 hr | ~2 d | 30 d | 6 d | |
| LA1 | Los Alamos I | 465 | 1 hr | 2 d | 10 d | 9 d | Not healthy person - died |
| R1 | USSR | 450 | 1 hr | 3 d | 19 d | 22 d | Other clinical symptoms |
| Y5 | Yugoslavia | 420 | 1 hr | ~2 d | 32 d | 7 d | Nausea & other clini.sym. |
| OR1 | Oak Ridge | 365 | 2 hr | 5 d | ~30 d | ~56 d | Fatigue and weakness only |
| Y6 | Yugoslavia | 350 | 1 hr | 1 d | 1 d | <4 wk | Other clinical symptoms |
| OR2 | Oak Ridge | 340 | 2 days | <1 hr | ~10 d | ~56 d | See Ref. 1 for symptoms |
| OR3 | Oak Ridge | 327 | 2 hr | 4 d | ~ 6 d | ~42 d | Other clinical symptoms |
| R2 | USSR | 300 | 1 hr | 4 d | 24 d | 20 d | Other clinical symptoms |
| OR4 | Oak Ridge | 270 | 4 hr | 2-3 d | 10-44 d | 1-42 d | Other clinical symptoms |
| LA4 | Los Alamos II | 242 | 6 hr | 12 hr | 5-18 d | 2-70 d | Other clinical symptoms |
| OR55 | Oak Ridge | 236 | 2 hr | 2 d | 3-44 d | 2-24 d | Other clinical symptoms |
| A1 | Argonne | 157 | 6 hr | 1 d | - | - | No manif. illness stage |
| HN1 | Hirosh.-Nagas. | 500 | *** | 2 d | 21 d | *** | Group data (GD) |
| JF | Japan. Fisherm. | 200-400 | *** | 4 d | 28 d | *** | Exposed to fallout, (GD) |
| HN2 | Hirosh.-Nagas. | 200 | *** | 3 d | 21-42 d | *** | Group data |
| MDA | Clinical Group | 151-200 | *** | 3 d | 21 d | 2-3 mo | Group data |
| M14 | Rongelap | 151-200 | *** | 3 d | - | - | Group data (fallout) |
| — | Providence, R.I.[4] | 8800 | 2-3 min | | | 49 hr | Patient died |

*Total calculated rad dose includes neutrons plus gamma; doses less than 150 rads from Ref 1 not included.

**Recalculated to be 4850 rads according to Gordon C. Bell, CAPT., MSC, USN (Private Communication).

***Not Known.

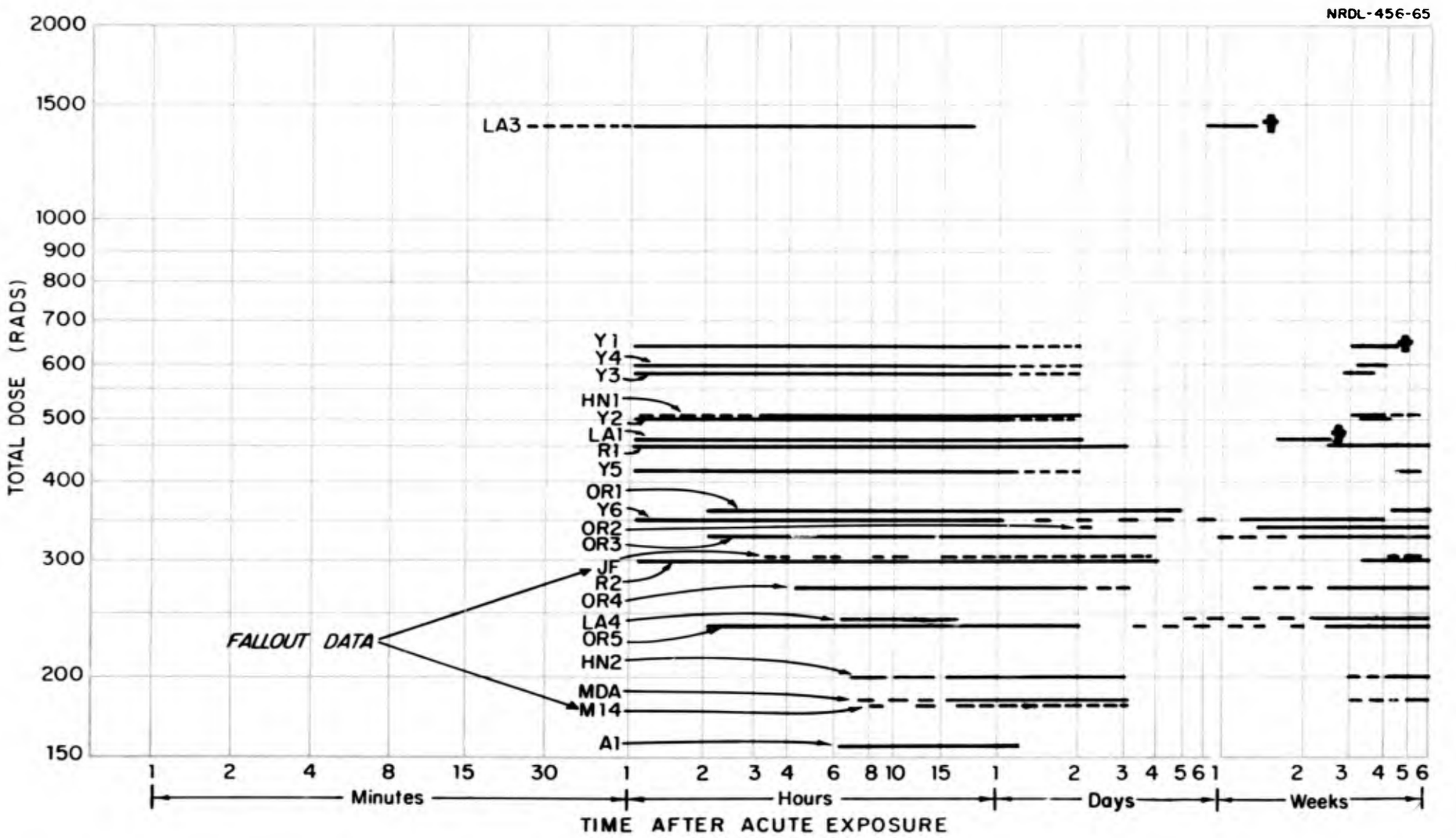


Fig. 1 Time of Onset and Duration of Clinical Signs and Symptoms for Initial Stage and Manifest Illness Stage After Exposure.[1,2]

person eventually died in each case, all the stages of the radiation-sickness syndrome (including the latent period) occurred.

From the limited data plotted in Fig. 1, it is difficult to reliably determine time of prodrome onset as a function of acute dose. The same difficulty also applies to teh duration of the prodrome. It is highly possible that individual susceptibility plays an important role here; however, that possibility cannot be proved with these available data, particularly because of uncertainties regarding the conditions and magnitudes of the exposures. All the accident-involved persons received almost prompt medical care, which may or may not have influenced their radiation-sickness history.

The data of Refs. 1 and 2 have to be carefully interpreted to provide a basis for decision in nuclear-warfare operations because (1) the degree and nature of exposure (whole body or partial, gamma rays and neutrons) is not clear cut; (2) in several cases, radiation injuries from alpha and/or beta radiation is included; (3) in some cases the data were gathered from persons who were not healthy at the time of exposure; and (4) the patients were given hospital treatment during the syndrome.

From the two cases above 4000 rads, it can be inferred that doses above some value, say 2000 to 5000 rads, should be considered as early-time (about 15 min) incapacitating doses in tactical situations. Although some persons may recover from the prodrome for a short time, they will subsequently be practically unfit for future combat duty. In contrast to the higher limit, it can be seen that a single acute dose of less than 200 rads would result in no militarily significant radiation sickness. For these reasons, the doses of interest for combat ineffectiveness are ordinarily in the range from about 200 to 2000 rads.

## 2.3 COMPARISON OF REFS. 1 AND 2 DATA WITH OTHER DOSE-EFFECT CASUALTY CRITERIA

Figure 2 gives curves for the severity of radiation sickness due to an acute whole-body dose *vs* time after acute exposure as estimated by Teresi*. It also shows the percent combat-effective and percent

*Op. Cit.

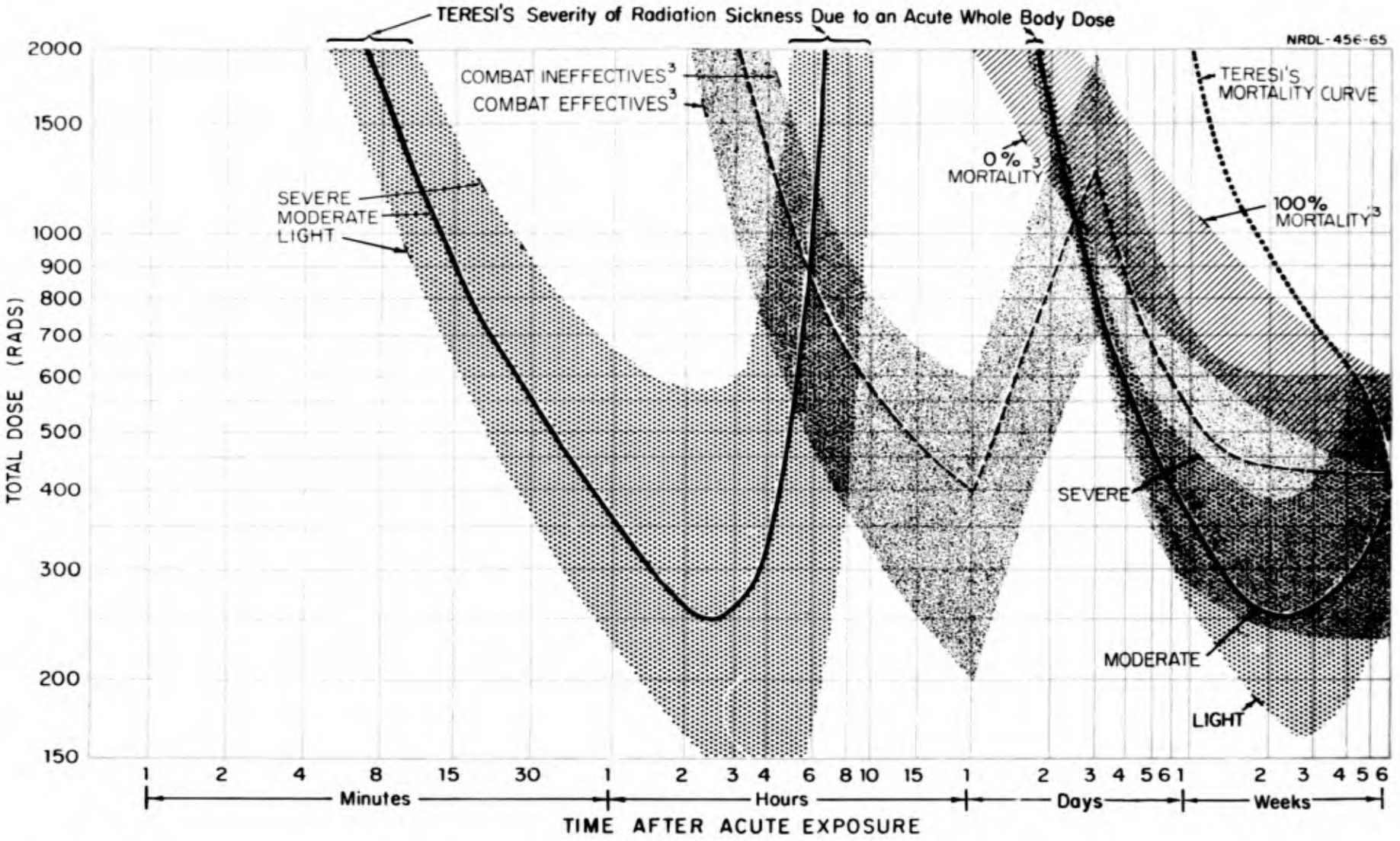


Fig. 2 The Acute Radiation Syndrome of Ref. 3 and Teresi*

*Op. Cit.

combat-ineffective curve band of Ref. 3 for acute and protracted doses vs time after exposure. (Doses received within 24 hr are called acute doses. Doses received over a longer time are called protracted doses.) In Ref. 3, the time for persons to become combat ineffective depends primarily on the total dose received and the exposure period. Reference 3 states that acute doses result from exposure to initial nuclear radiation and base-surge and fallout transit radiations; protracted doses, from exposure to fallout deposit radiation.

The observed values given in Table 1 and Fig. 1 and the curves of Fig. 2 are superimposed in Fig. 3. One may note in Fig. 3 the actual differences between the radiation-accident data of Refs. 1 and 2 and Teresi's and Alpen's plotted curves. The difference for the onset time of the initial stage of radiation sickness (or prodrome) is most noticeable between Teresi's and Alpen's curves -- numerically, approximately a factor of 10. The difference may be due to the following:

1. Different definitions and criteria used.
2. Teresi's exposure dose and the clinical accident doses in Fig. 1[1,2] can be considered as "one shot" exposures, whereas Alpen's dose-time band curves may also include exposure time, although the graph specifically states "time after exposure" on the time scale.

In general, the agreement improves considerably for the onset of the manifest illness stage, including the mortality curves.

The onset times of the initial stage of radiation sickness from Refs. 1 and 2 for 200- to 2000-rad doses agree reasonably well with those given by Teresi's curves; however the duration of the initial stage is somewhat longer according to Refs. 1 and 2 data.

There are insufficient data in Refs. 1 and 2 on the details of the treatment and clinical progress of the various patients to permit a valid explanation for the differences. It is possible that most of

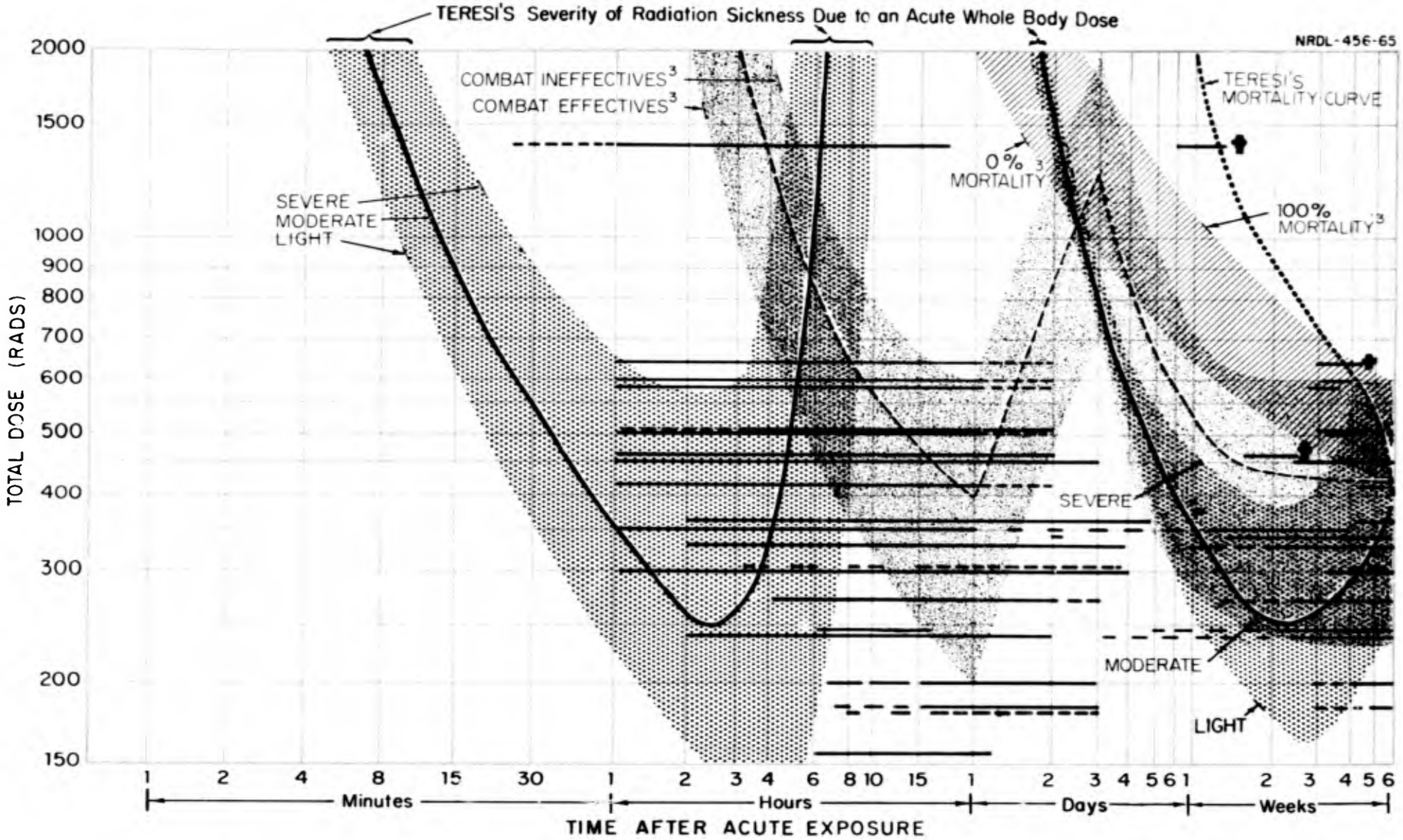


Fig. 3 The Acute Radiation Syndrome of Refs. 1, 2, and 3 and Teresi*

*Op. Cit.

these patients were kept in a hospital just for observational purposes, which enabled medical personnel to record any significant changes in condition.

The differences in the onset of the manifest illness stage, which is much later for the Refs. 1 and 2 clinical cases, could be credited to the fact that the patients received medical care during their assumed prodromal period which included some fraction of the actual latent period during which they could have been considered combat effectives. Lushbaugh and Cronkite* state that hospitalization of Kelly (LA-11) and Peabody [4] dit little to alter their terminal progression because of their very high doses.

From Fig. 3, it can be noted that there is agreement among the observed mortality data of Refs. 1 and 2, Teresi's mortality curve, and Alpen's[3] 100% mortality curve. Therefore, in predicting time of death vs acute dose, Teresi's and Alpen's mortality curves could be used as guidance.

* Private Communication

## SECTION 3

## DERIVATION OF EMPIRICAL EXPRESSIONS

### 3.1 GENERAL

The purpose of this section is to derive empirical expressions for biological response based on each of the three sets of dose-effect-time data illustrated in Fig. 3 of Sec. 2. These expressions can be utilized to write programs for performing any kind of multivariate analysis of nuclear-weapon effects with an electronic computer. Generally, in the application of a computer to solve a particular problem, it is preferable to use algebraic expressions instead of tabulated data to save storage space, search time, etc.

In military tactical situations, certain nuclear-weapon effects may be dominant: initial ionizing radiation, thermal radiation, airblast, and fallout radiation. These effects can be expressed analytically as functions of such parameters as weapon yield, weapon type, burst height, slant or horizontal range, and time after burst. Analytical expressions are also needed for calculating biological response as a function of acute dose of initial radiation and time after exposure for use in computerized analyses involving all the weapon effects and parameters of interest.

Since there are some militarily significant differences in the three sets of dose-time relationships given in Sec. 2 and in the biological-effect criteria used, the sets are treated separately, but consistently, for comparative purposes. For each set, four times and time periods in the radiation syndrome are of interest:

1. Time of onset of the initial stage of radiation sickness.
2. Duration of the initial stage.

3. Time of onset of the second, or manifest, illness stage.
4. Duration of the manifest illness stage (which ends with recuperation or death).

The latent period, which may be of military importance in certain situations, is implied by the end of the initial stage and the onset of the manifest illness stage. An analytical expression was derived for each stage.

In the derivations described in the next subsections, the three sets of data are treated in the following order:

1. Data from Refs. 1 and 2 -- given in Table 1 and illustrated in Figs. 1 and 3.
2. Data from Teresi's analysis -- illustrated in Figs. 2 and 3.
3. Data from Ref. 3 -- illustrated in Figs. 2 and 3.

Along with the derivations, an attempt has been made to introduce an expression for percent combat effectives (and combat ineffectives) vs dose and time for each set of data. This approach can be improved when more conclusive data become available.

## 3.2 DERIVATION OF ANALYTICAL EXPRESSIONS FROM REFS. 1 AND 2 DATA

The procedure used to derive the analytical expressions from the data of Refs. 1 and 2 is as follows:

1. From the initial stage, a curve was drawn through the starting points of time of onset vs dose in Fig. 1 and illustrated in Fig. 4 so that approximately 50% of the points are above the curve and 50% are below it. It is assumed that this curve represents the most reasonable approximation of time of onset vs total acute dose. A curve was similarly drawn through the points indicating the end of the initial stage (See Fig. 4.)*.

*The termination times for fixing the curve were reduced somewhat under the assumption that, for the data cited, the patients were hospitalized for a period longer than would be the case in judging combat personnel fit for duty.

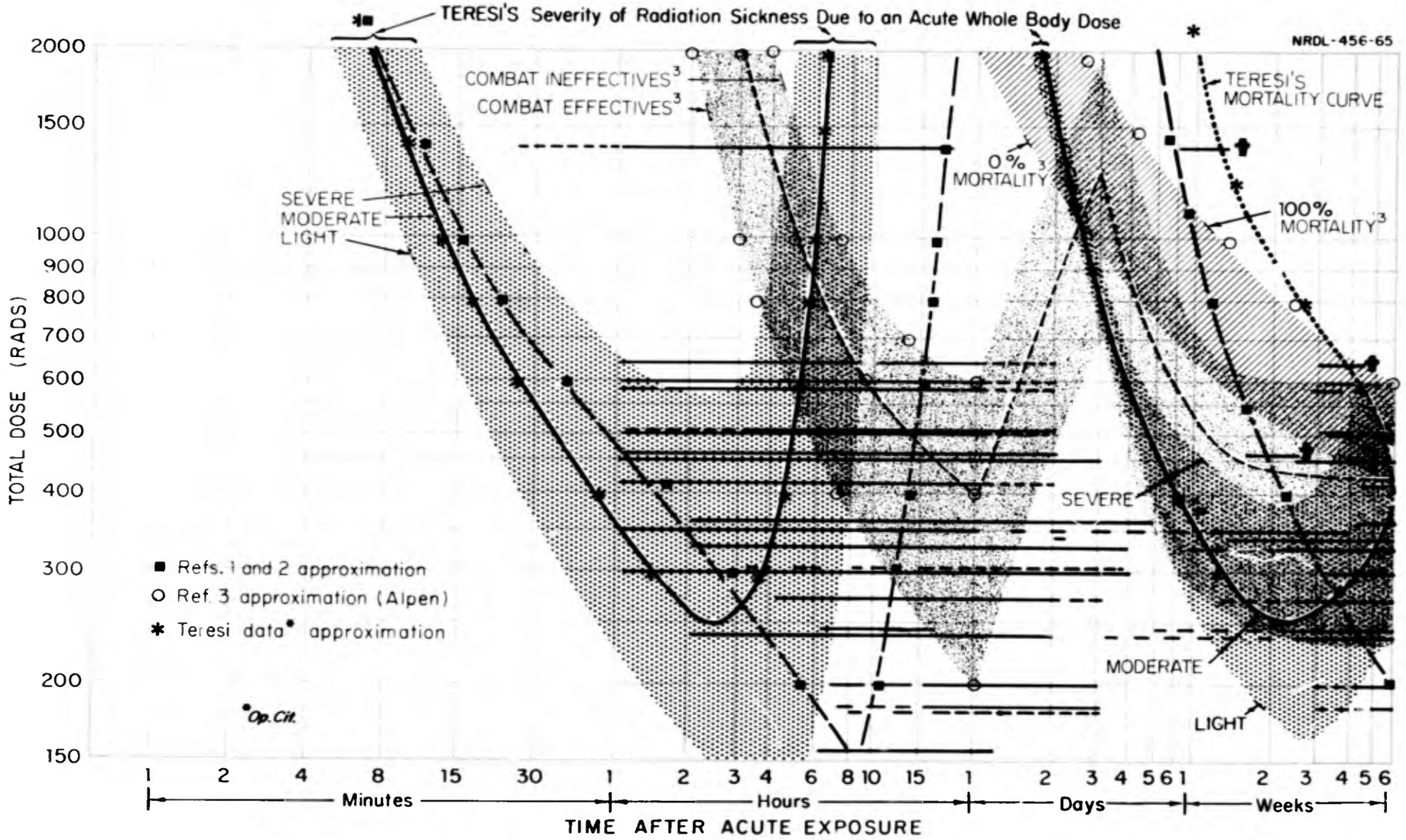


**Fig. 4** **The Acute Radiation Syndrome of Refs. 1, 2, 3 and Teresi and Comparison of the Fit of Data with Empirical Equations**

(Note that the curves were drawn approximately parallel to Teresi's curves for the initial stage because Teresi's are based on almost the same data. Although the slope of the curve for time of onset of the initial stage appears to be arbitrary, it is largely dependent on the two cases of exposures greater than 2000 rad, not shown in Fig. 4, and on the assumption that the time of onset does in fact increase in a reasonably continuous manner with decreasing exposure dose over the entire range of exposures). Note that the difference between the onset time of the initial stage and the end time of the initial stage indicates the duration time for the initial stage. An analytical expression was then derived for the time of onset of the initial stage and the duration of the initial stage.

2. Step 1 was repeated for the manifest illness stage. For the same reason, the curves were drawn approximately parallel to Teresi's curves for the second stage.

The same procedure was used in treating Teresi's* and Alpen's[3] curves. From Teresi's curves, a moderate-radiation-sickness curve due to acute whole-body exposure was arbitrarily chosen, and the average value between combat ineffectives and combat effectives in Ref. 3 was arbitrarily chosen as a criteria for estimated 50% CI's. For Alpen's[3] curve, however, only the onset of the initial stage as a function of dose and time was considered because the band for manifest illness stage includes protracted doses.

The rest of this subsection illustrates the derivation procedure using Fig. 4 values for the time of onset of nausea and vomiting as a function of total acute dose of initial radiation. (Figure 4 also illustrates the fit of the curves drawn with the equations derived, including Teresi's curves in 3.3 and Alpen's curves in 3.4). A sharp-edge or single curve is used here for analytical purposes. In 3.5 the spread of the data is indicated by a band whose boundaries are based

*Op. Cit.

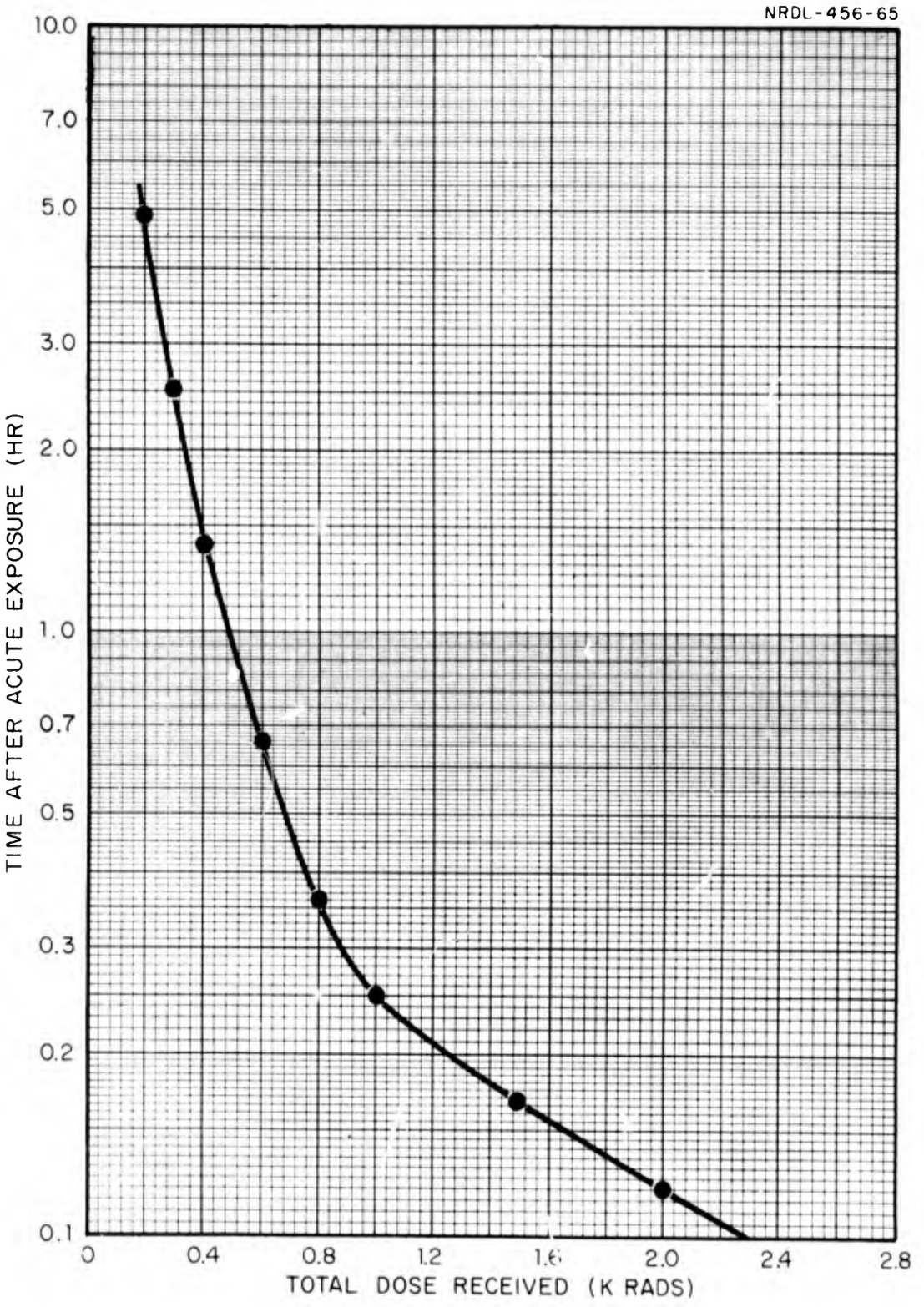


**Fig. 5 Initial-Stage Onset Time Vs Total Acute Dose**

on extreme data points[1,2]. Note that a 0.5 probability is assumed for the single curve (or midline). Onset times[1,2] for discrete doses (in kilorads) in the range from 200 to 2000 rads are given in Table 2. These values are plotted in Fig. 5 on semilog paper because it provides the most reasonable approximations.

TABLE 2

Onset Time for Nausea and Vomiting Vs Acute Dose[1,2]

| Time After Acute Exposure (Hr) | 4.8 | 1.3 | 0.66 | 0.36 | 0.26 | 0.17 | 0.12 |
|---|---|---|---|---|---|---|---|
| Total Dose From Fig. 4 (K-Rads) | 0.2 | 0.4 | 0.6 | 0.8 | 1.0 | 1.5 | 2.0 |

It can be shown that an analytical expression of the form:

$$T = ae^{-br} + ce^{-dr} \qquad (1)$$

where T (Time) is in hours or days (see Table 3), and r (dose) is in kilorads, provides a good fit to the data in Table 2. The derivation of the particular analytical expression is straightforward and involves only finding the appropriate constants a, b, c, and d.

For the data in Table 2, the following constant values provide the best fit:

$$a = 16.0 \quad c = 0.41$$
$$b = 6.27 \quad d = 0.6$$

Equations were also derived for the duration of the initial stage, which, when added to the onset time of the initial stage, will give the time for the end of the initial stage. Similarly, equations were derived for the onset time and the duration of the manifest illness stage. The appropriate constants for the equations of the data of Refs. 1 and 2 are given in Table 3. Note that the exposure dose range is from 0.2 to 2.0 kilorads.

Table 3

Constants to the Dose-Effect Equation
Based on Refs. 1 and 2 Data

| Acute Radiation Syndrome | $T = ae^{-br} + ce^{-dr}$ | | | |
|---|---|---|---|---|
| | a | b | c | d |
| Time of Onset of Initial Stage (Hr) | 16.0 | 6.27 | 0.41 | 0.6 |
| Duration of Initial Stage (Hr) | 15.5 | -0.123 | -22.0 | 4.012 |
| Onset Time of Manifest Illness Stage (Days) | 185.0 | 9.0 | 15.0 | 0.7 |
| Duration of Manifest Illness Stage (Days) | 107.0 | 5.17 | 4.3 | 0.315 |

3.3 DERIVATION OF DOSE-EFFECT EQUATIONS BASED ON TERESI'S CURVES*

Procedure for the derivation of analytical expressions for Teresi's curves in Figs. 2 and 3 is similar to that described in 3.2. The necessary constants to the appropriate equations are given in Table 4.

Table 4

Constants for the Dose-Effect Equations
Based on Teresi's Curves

| Acute Radiation Syndrome | $T = ae^{-br} + ce^{-dr}$ | | | |
|---|---|---|---|---|
| | a | b | c | d |
| Time of Onset of Initial Stage (Hr) | 7.2 | 6.27 | 0.36 | 0.6 |
| Duration of Initial Stage (Hr) | 5.0 | -0.123 | -13.8 | 5.3 |
| Onset Time of Manifest Illness Stage (Days) | 35.0 | 6.1 | 3.7 | 0.36 |
| Duration of Manifest Illness Stage (Days) | 300.0 | 5.17 | 12.0 | 0.315 |

*Op. Cit.

## 3.4 DERIVATION OF DOSE-EFFECT EQUATIONS BASED ON ALPEN'S CURVES[3]

Only the data of Ref. 3 on the onset of the initial illness stage is considered because times after 1 day of exposure include protracted doses only (see Fig. 10 in Appendix). The procedure used to derive the dose-effect equations for that stage is similar to that described in 3.2, and the appropriate constants are given in Table 5.

Table 5

Constants to the Time of Onset of Initial Stage Equations Based on Alpen's Curves[3]

| Time of Onset of Initial Stage (Hr) | $T = ae^{-br} + ce^{-dr}$ | | | | Notes* |
|---|---|---|---|---|---|
| | a | b | c | d | |
| CI Threshold | 130 | 9.54 | 5.0 | 0.482 | 200<r<2000 |
| Estimated 50% CI's | 500 | 8.32 | 7.5 | 0.476 | 400<r<2000 |
| Estimated 100% CI's | 1000 | 6.87 | 10.0 | 0.470 | 600<r<2000 |

Table 6

Constants to Alpen's 100% Mortality Curve Equation[3] Based on Fig. 2 Data

| Onset Time (Weeks) | $T = ae^{-br} + ce^{-dr}$ | | | | Notes* |
|---|---|---|---|---|---|
| | a | b | c | d | |
| Estimated 100% Mortality | 100 | 5.02 | 1.5 | 0.679 | 500<r<2000 |

*Note the applicable dose limits for each case.

## 3.5 DERIVATION OF EMPIRICAL EQUATIONS FOR THE FRACTION OF COMBAT INEFFECTIVES VS TIME AFTER ACUTE EXPOSURE BASED ON REF. 1 DATA

Variation of the biological response of man to whole-body radiation dose depends mainly on individual susceptibility to ionizing radiation. Persons in a group receiving the same dose from acute whole body exposure under the same conditions do not exhibit the same radiation syndrome. Therefore, it is customary to indicate this variation in the dose-effect relationship by a curve band.

In military tactical situations involving the exposure of troops to initial radiation, individual susceptibility may be important for decision-making purposes; therefore, its significance has to be analyzed. A multivariate analysis of combined nuclear weapon effects may give some indications on when and how to consider the differences in the syndromes and thereby provide the commander in the field with an improved decision-making procedure.

Figure 6 demonstrates the variation in individual susceptibility of man to ionizing radiation based on Ref. 1 data. Only the onset and the end of initial-stage radiation sickness is given, because the manifest-illness stage can be treated similarly. The exposure dose limits are the same ones used in Ref. 1 for the reasons mentioned in that report.

The data in Fig. 6 are replotted in Fig. 7. Note that the 0%- and 100%-CI points for the various doses are connected with straight lines. A question might arise: How good is this probability distribution? At the present time, this question cannot be answered with any confidence--the straight-line approach is used only for simplified computation. Once a better probability distribution is established, empirical equations can be corrected to fit the improved data.

Since the dose lines in Fig. 6 for 0% and 100% CI's are parallel, the slopes of the dose lines for fraction CI's vs time after acute exposure are also parallel. It should be pointed out that Alpen's and Teresi's bands also comprise parallel lines.

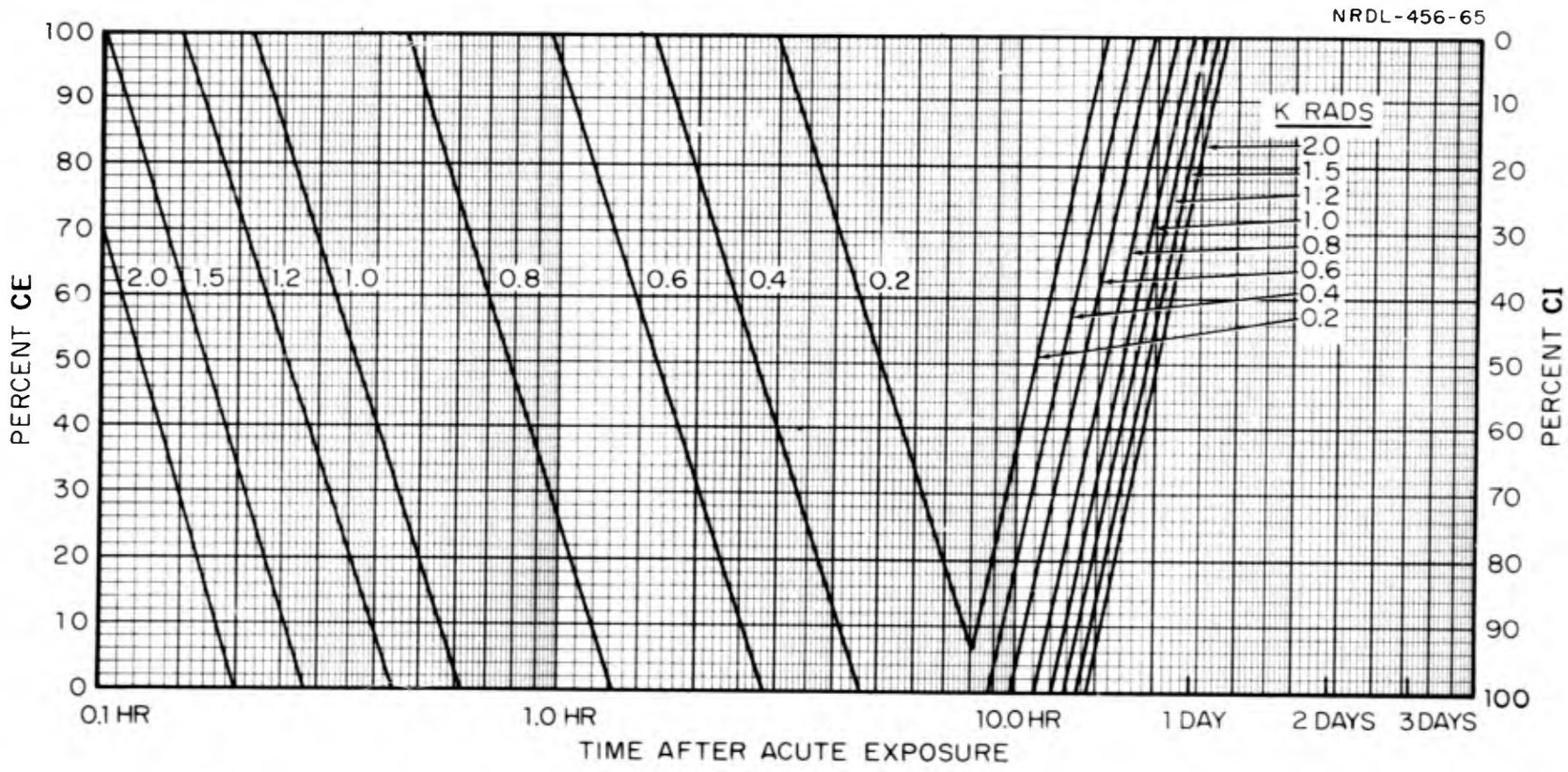


**Fig. 7 Percent of Prodrome CE's or CI's Vs Time After Various Acute Exposure and for Various Doses**

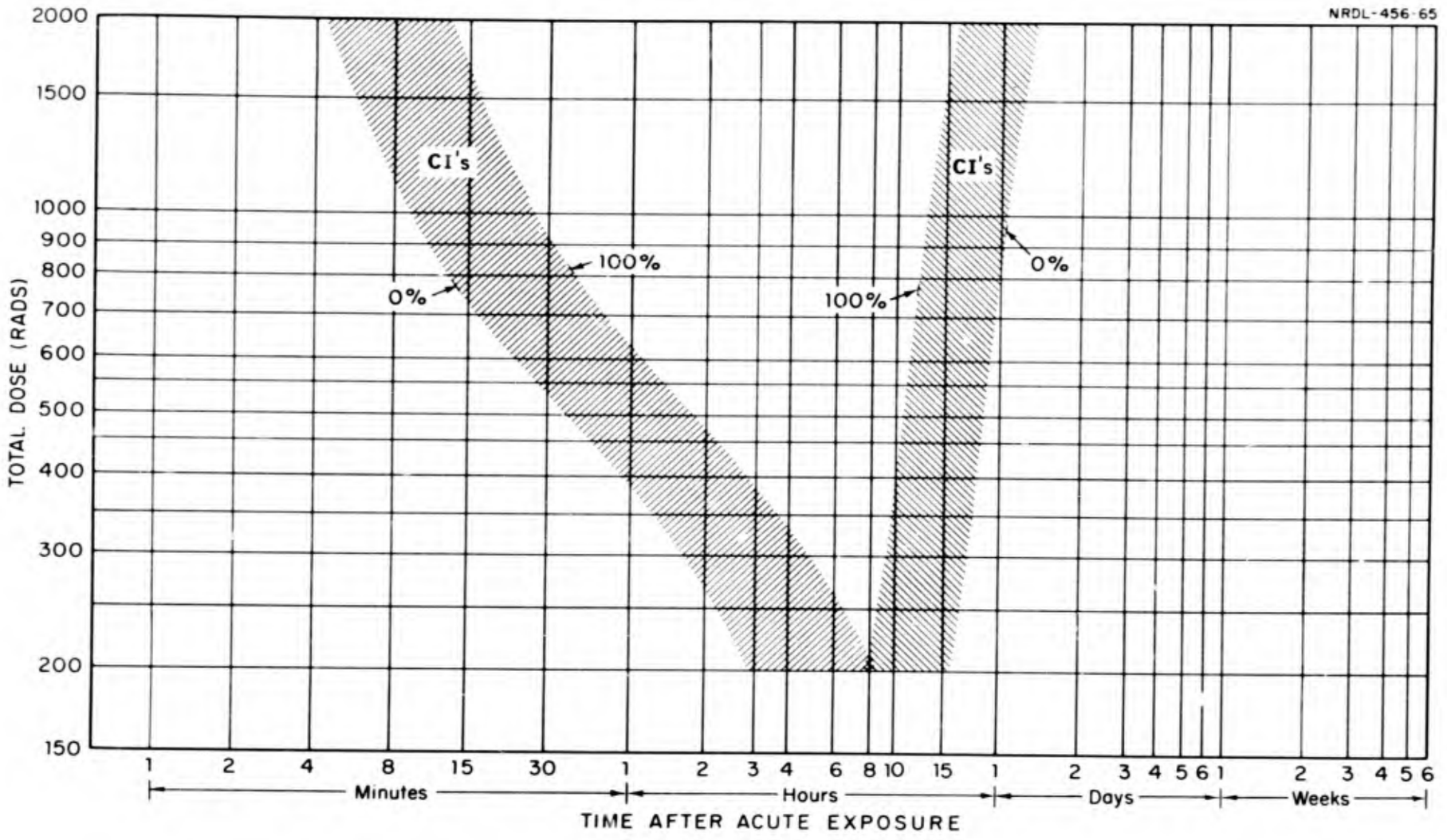


Fig. 6 **Variation in Initial-Stage Combat Ineffectives for Various Doses Vs Time**

Time after acute exposure (T) in Fig. 7 can be expressed analytically as follows:

$$T = ae^{bF} \tag{2}$$

where

a is a constant and is a function of dose.

b is the slope of the family of dose lines. Note that the b value determines the extent of individual susceptibility variation.

F is the fraction of CI's for dose vs time (%CI = F x 100)

Equation 2 can be written as follows:

$$F = \frac{1}{b} \ln(T/a) \tag{3}$$

The numerical values for b can be determined from Fig. 7. For the times of onset and end of the initial stage, the b values are correspondingly:

$$b_{onset} = 1.1 \qquad b_{end} = -0.692$$

Constant a is a function of dose (r) and can be expressed analytically as follows:

$$a_{onset} = 9.25\ e^{-6.27r} + 0.237\ e^{-0.6r} \tag{4}$$

$$a_{end} = 19.4\ e^{0.261r} - 14.1\ e^{-5.3r} \tag{5}$$

Substitution of the appropriate constants in Eq. 2 gives the following analytical expressions for fraction of CI:

$$F_{onset} = 0.91 \ln \left( \frac{T}{9.25e^{-6.27r} + 0.237e^{-0.6r}} \right) \quad (6)$$

$$F_{end} = -1.445 \ln \left( \frac{T}{19.4e^{0.261r} - 14.1e^{-5.3r}} \right) \quad (7)$$

Note:

$F \leq 0$ means 0% CI's, $F \geq 1.0$ means 100% CI's

Similar equations can be derived for Alpen's and Teresi's bands.

## SECTION 4

## RESULTS AND CONCLUSIONS

Empirical equations have been derived from the dose-effect-time data of Refs. 1 and 2 and for the curves given by Ref. 3 and Teresi* that relate time of onset of incapacitation (combat ineffectiveness) and duration of incapacitation following acute exposure to ionizing radiation. Figure 4 in 3.2 shows how the equations fit the data and curves plotted in Fig. 3. Figure 8 shows that the curves are somewhat different for early times after exposure. The dose-effect relationships are in some agreement for later times, and are therefore not plotted. The differences may be due to the different casualty criteria used, the apparent imprecise definition of acute dose in terms of exposure period (24 hr or less, as used in Ref. 3), and the availability in some cases of initial-stage (prodrome) hospital treatment (see 2.3 for discussion).

Since the equations derived from the clinical data of Refs. 1 and 2 are for "one-shot" gamma-neutron exposures, the results calculated with those equations would closely approximate the dose-effect-time relationships for "one-shot" initial-radiation exposures.

The curves fitted to Refs. 1 and 2 data and the curves of Teresi* indicate that, following the initial stage, a latent period (combat effectiveness) will occur regardless of the acute dose received. Teresi's curves, however, show the latent period occurring earlier than that indicated by the Refs. 1 and 2 data, which were taken from patients given initial-stage hospital treatment. In actual combat situations, such treatment will probably not be available.

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*Op. Cit.

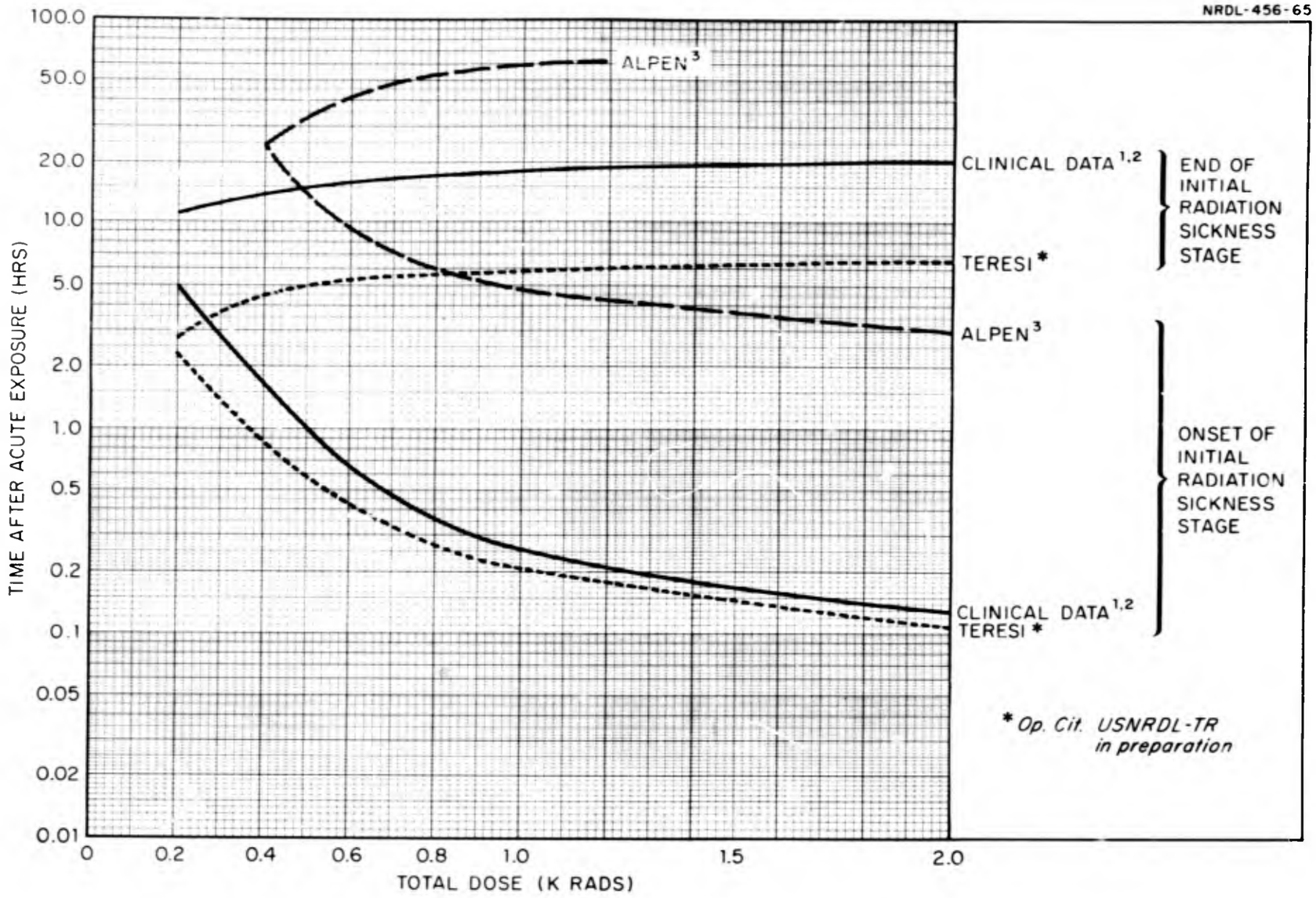


Fig. 8 Comparison of the Onset and End of Initial Radiation Sickness Stage

*Op. Cit. USNRDL-TR in preparation

The curves fitted to Refs. 1 and 2 data and the casualty criteria used by Teresi appear to be more realistic than those of Alpen[3] for estimating percent combat ineffectives. Figure 9 gives some guidance (taken from Ref. 1) on percent early-time combat ineffectives to expect according to the symptoms that radiation-sickness troops may exhibit as a function of time after exposure.

The equations have been put in a form that is easily applicable for computer programing of tactical problems. It is proposed that programs for the different sets of equations be run on a computer to check the significance of differences in dose-effect-time results within the context of various types of combat situations.

The curves and equations derived in this study have simply been fitted to previously derived dose-effect relationships vs time and to summaries of accidental-exposure data that may be subject to individual interpretation. Furthermore, the terms combat ineffectiveness, incapacitation, and casualties are loosely defined in terms of the complex of symptoms characterizing radiation injury. A more thorough analysis of human radiation-dose responses, together with their correlation with types of individual tasks to be performed in various combat situations, should result in a considerably improved technique for predicting combat ineffectiveness as a function of time after radiation exposure.

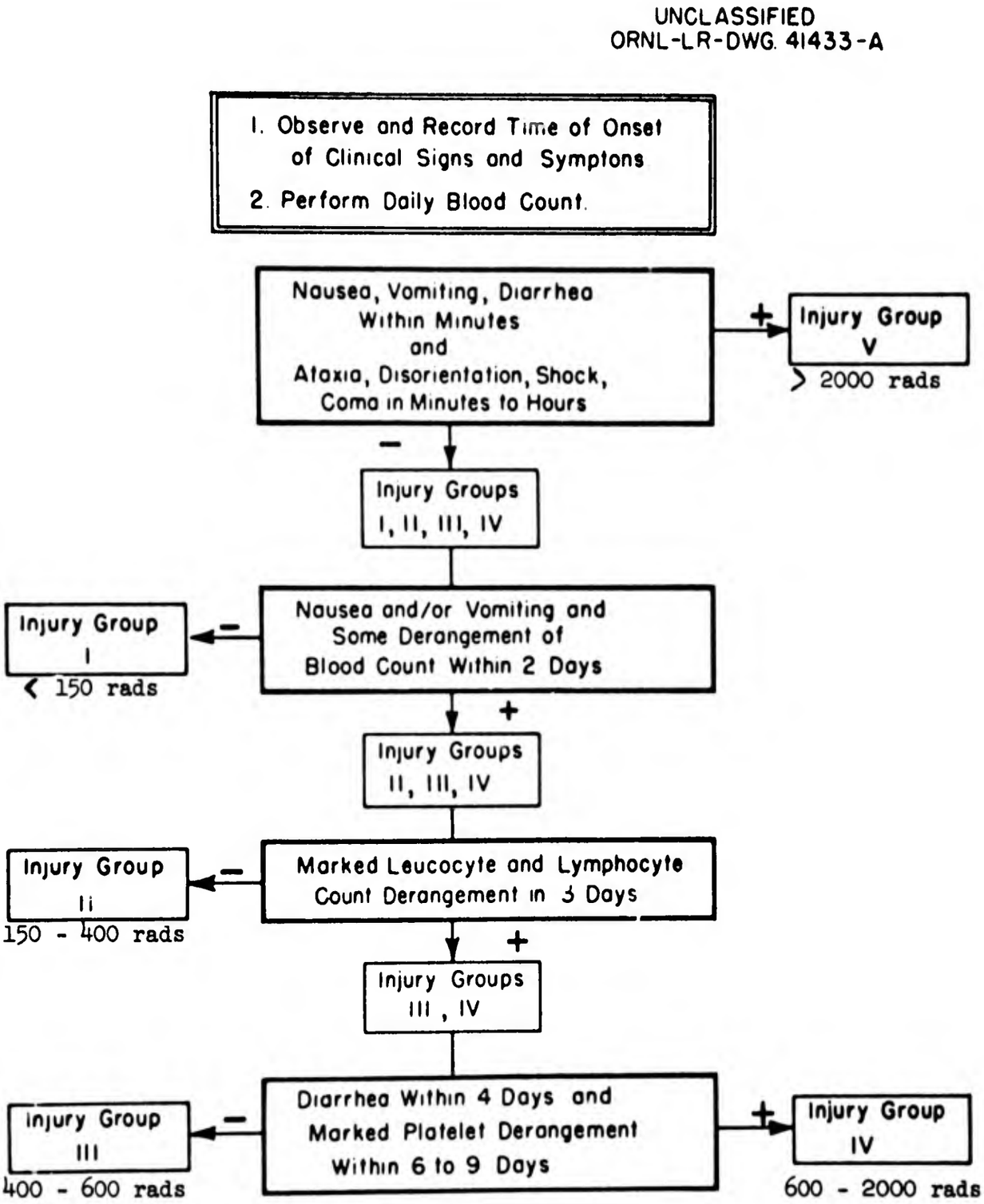


Fig. 9 Preliminary Evaluation of Radiation Injury (From Ref.1)

## APPENDIX

This Appendix presents Alpen's[3] and Teresi's* curves that were used for plotting and comparison purposes in this report. Figure 10 gives the expected times of onset and duration of combat ineffectiveness for whole-body acute and protracted doses (no medical treatment) from Alpen. Figure 11 gives the expected times of death for whole-body doses received in 4 weeks or less from Alpen. Figure 12 gives the severity of radiation sickness due to various acute whole-body doses vs time after acute exposure from Teresi.

*Op. Cit.

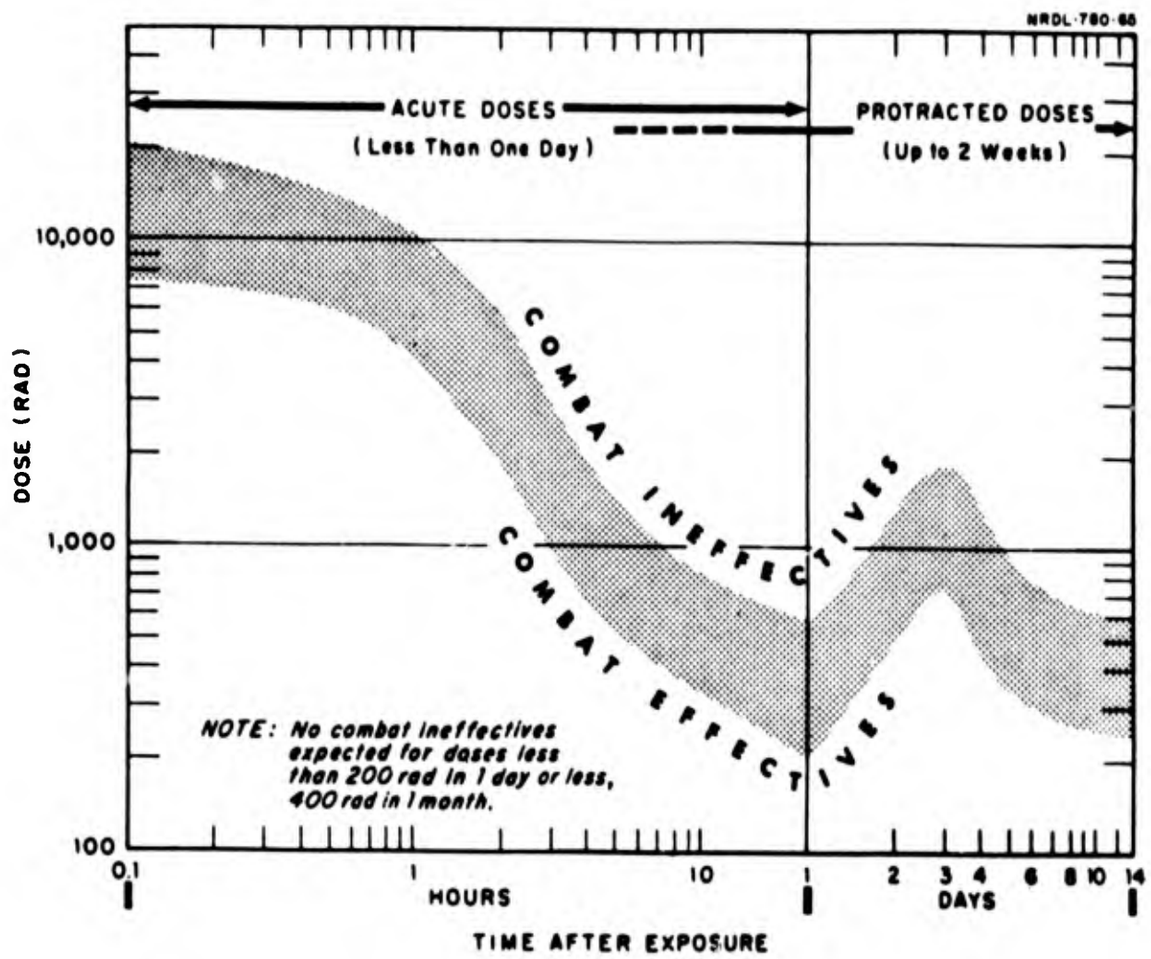


Fig. 10 Expected Times of Onset and Duration of Combat Ineffectiveness for Whole-Body Acute and Protracted doses (no medical treatment)

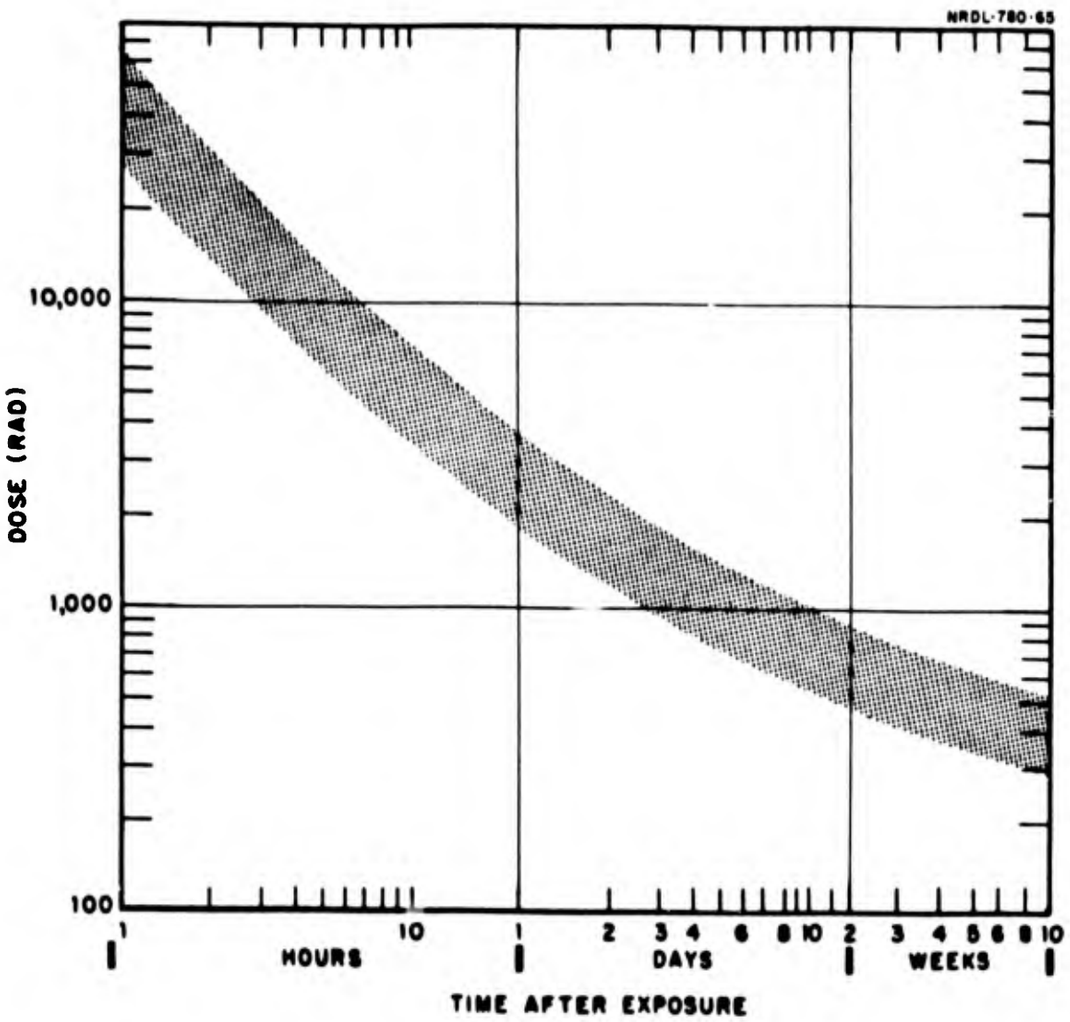


Fig. 11 Expected Times of Death for Whole-Body Doses Received in 10 Weeks or Less

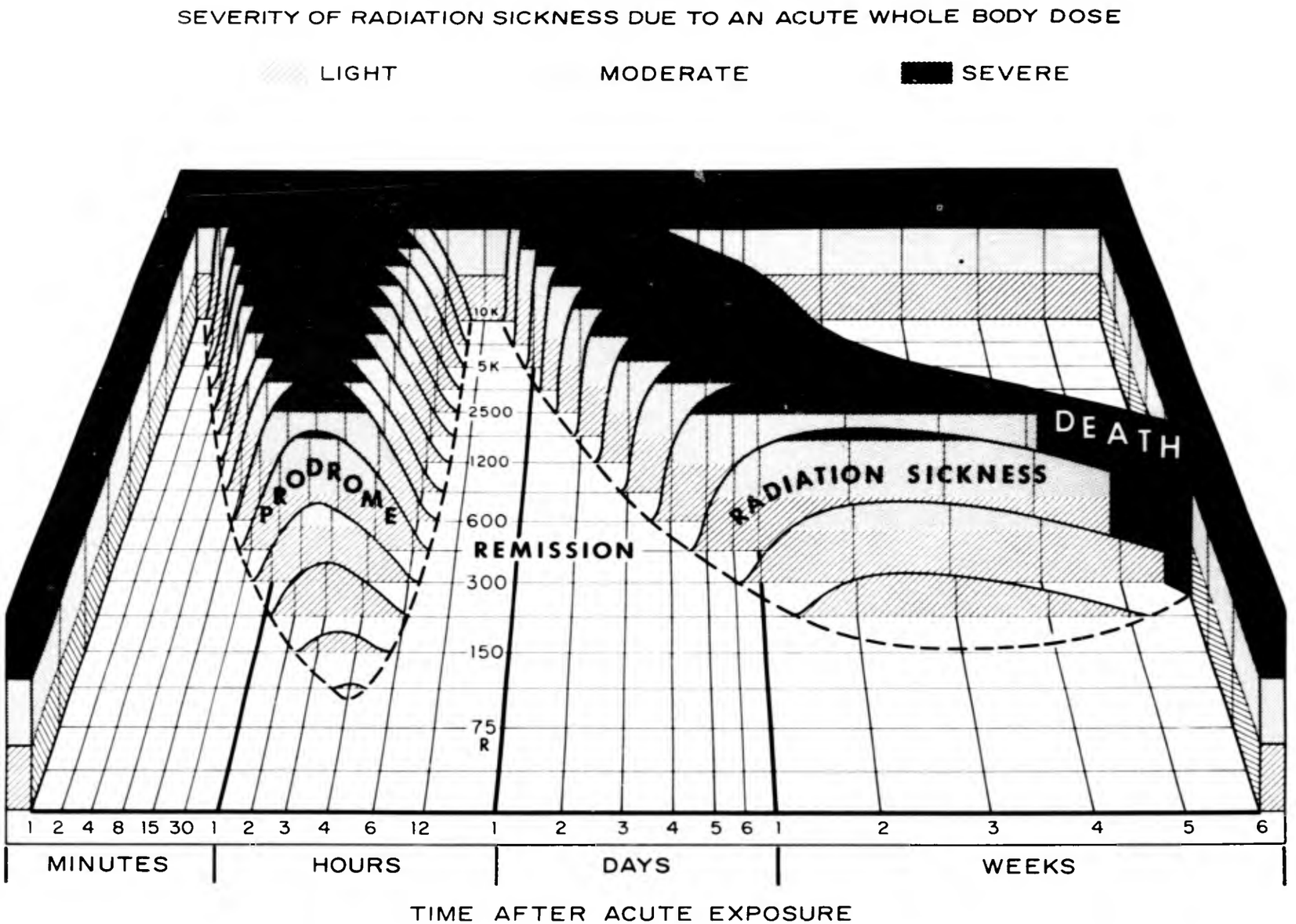


Fig. 12 The Acute Radiation Syndrome From Teresi*
*Op. Cit.

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13 ABSTRACT

Exposure of personnel to initial ionizing radiation from a nuclear air or surface burst can cause both prompt and delayed casualties. Their percentages and times to incapacitation (or combat ineffectiveness, in a military sense) after exposure can be of major significance in military operations. Although adequate data are lacking for the determination of dose-effect relationships vs time after exposure, quantitative estimates are needed nevertheless for guidance in battlefield predictions and decision-making. Available nuclear-accident data and other data on human exposures are used to obtain curves to represent the estimated time history of the acute radiation syndrome as a function of dose received in a very short time. The sources of data are clinical records of nuclear-accident casualties from 1945 to 1958, followup records of radiotherapy patients, and casualty studies on the atomic explosions at Hiroshima and Nagasaki. Emphasis is put on the time after exposure of the onset of the initial stage of radiation sickness (nausea, vomiting, malaise, etc.), duration of the initial stage, start and duration of the following asymptomatic latent period, time of onset of the second (or manifest illness) stage, and time of eventual recuperation or death. The estimated time history is depicted graphically with two other time histories for comparison. Analytical expressions are derived for the three time histories for use in estimating any of these syndrome times or periods.

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