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AFAMRL-TR-84-046

CHAPTER IX

TOXICOLOGY OF MIXED DISTILLATE AND HIGH-ENERGY SYNTHETIC FUELS

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ABSTRACT

In joint research to assess the hazard of exposure to hydrocarbon aircraft and missile fuels, the United States Air Force (USAF) and United States Navy (USN) have performed long-term inhalation exposures to numerous military fuel vapors. From these studies, a general picture of the toxic response to the hydrocarbon fuels is evolving. Male rats sacrificed immediately after continuous 90-day exposures display renal proximal tubule degeneration and multifocal dilatation near the corticomedullary junction, caused by plugs of necrotic cell debris. At terminal sacrifice, 19 months postexposure, male rat kidneys exhibit marked medullary mineralized casts, multifocal and diffuse hyperplasia of pelvic urothelium, and advanced tubular degeneration compatible with "old-rat nephropathy." After one-year intermittent exposures, extensive proximal tubular degeneration is not observed; however, at terminal sacrifice, there are significant numbers of renal tumors in male rats. Neither toxic nephropathy nor renal tumors were found in female rats and other species examined. Female mice exposed to hydrocarbon fuels exhibited mild, reversible hepatocellular fatty changes immediately postexposure; however, these lesions were absent at the 24-month sacrifice. The mechanisms of dose-dependent, hydrocarbon-induced male rat nephropathy and renal tumors, and fatty vacuoles in female mice livers are not known.

INTRODUCTION

As one of the nation's largest users of aircraft turbine fuels and missile propellants, the USAF has interest in assuring the safe use of these hydrocarbons by its military and civilian workers. This concern stimulated research to define potential adverse health effects and to develop criteria for safe exposure limits for these unique military fuels.

The first inhalation exposure to JP-4, a fuel used exclusively by the USAF, was conducted in 1973. Since this initial subchronic study, the USAF and USN have conducted numerous subchronic and one-year oncogenic inhalation studies in a cooperative effort to establish health criteria for hydrocarbon fuels used in aircraft, ships, and missiles. JP-5 is the fire-safe turbine engine fuel used by the USN. In addition, the Navy is also investigating the use of shale oil-derived JP-5 as an alternative fuel. Although refined from different crudes, petroleum derived and shale oil derived JP-5 are produced to the same specifications. In the early 1970s, the USAF and USN began development of new cruise missile fuels with volumetric energies higher than those available in mixed distillate hydrocarbons. From a number of pure synthetic fuels, JP-10 was selected as the primary fuel for the Air Launched Cruise Missile and is proposed for the other sea and land-based cruise missiles. RJ-5 is also an active candidate for ramjet fuels because of its considerable volumetric energy content. During the early phases of fuel development research, there was a complete absence of toxicity data. To obtain the necessary data for accurate hazard assessments and safe exposure criteria, a comprehensive battery of toxicity tests was performed. These included mutagenic assays; acute, oncogenic, and teratologic studies; and experiments to describe the pharmacokinetics in mammalian systems.

This paper summarizes the status of studies to define the toxicity of hydrocarbon mixed distillate aircraft turbine engine and synthetic ramjet fuels and discusses the preliminary findings of toxic nephropathy and primary renal tumors observed in male Fischer 344 rats.

Military Unique Hydrocarbon Fuels

The properties of the different turbine engine fuels used in USAF and USN aircraft and the synthetic high-energy density fuels used in cruise missiles are shown in Table I. Turbine engine fuels used in USAF and USN aircraft are mixed distillate hydrocarbons varying in composition from JP-4, which has characteristics similar to gasoline, to JP-8, which is a kerosene-based fuel equivalent to the commercial aircraft turbine fuel, Jet A-1. JP-4 represents the greatest inhalation hazard to military personnel because of its vapor pressure of 13 kPa (2–3 PSI), compared with less than 0.7 kPa (0.1 PSI) for the other fuels, and because it constitutes 85% of turbine fuel used by the Department of Defense. JP-5, the fire-safe fuel used by USN aircraft, accounts for the majority of the remaining 15%. JP-8 is used primarily in NATO countries, and JP-7 and JP-TS are special high-altitude fuels restricted to a small number of SR-71 and U-2 reconnaissance aircraft.

TABLE I
Fuel Properties

Fuel	Mean MW	Boiling Range (°C)	Freeze Pt (°C)	Flash Pt (°C)
Synthetic				
JP-10	136	182	-90	53
RJ-5	188	260-285	-40	104
Mixed distillate				
JP-4	133	60-270	-72	-29
JP-5	168	205-290	-51	60
JP-7	141	182-288	-43	60
JP-8	167	205-300	-56	38
JP-TS	150	157-260	-53	43

In contrast to the multicomponent composition of turbine engine fuels, the high-energy density ramjet fuels used in cruise missiles are made from synthetic chemicals. The higher volumetric energy content of these fuels is due in large part to their high carbon/hydrogen ratios, increased density, and lack of carbon-carbon double bonds. JP-10 is a bicyclic, bridged compound, exo-tetrahydrodi (cyclopentadiene), with a vapor pressure of 0.18 kPa (0.027 PSI). RJ-5 consists of the hydrogenated dimers of norbornadiene with a vapor pressure of 1.3 kPa (0.2 PSI) at 103°C.

EXPERIMENTAL METHODS

Exposure Chambers

All inhalation exposures were conducted in the Thomas Domes, located in the Toxic Hazards Research Unit (THRU), Wright-Patterson AFB, Ohio. The Thomas Domes are unique exposure chambers designed to provide long-term, continuous exposure of animals or humans to gases or aerosols at atmospheric pressures as low as 34.5 kPa (5 PSIA), air flow rates of 0 to 2.8 m^3/min (0-100 CFM), and 0 to 100% oxygen atmospheres. For standard animal exposures, the 23.4 m^3 (828 ft^3) chambers are capable of housing 400 rodents, 6 dogs, or 6 primates, and are normally operated at 68 m^3/hr (40 CFM) air flow, 2.6 kPa (10.6 in. H_2O) negative pressure and 40-60% relative humidity. During continuous exposures, the animals are fed and the cages cleaned by technicians who enter the chambers through vertical air locks. The technicians are protected from exposure to the test chemical by impermeable suits and airline respirators. Continual observation of the experimental animals is possible through 20 2 x 4 ft windows ringing the Domes. For intermittent exposures, the removable Dome tops are lifted by an overhead crane and supported on struts for easy access to the animals.

Experimental Animals

The experimental animals used in these studies were randomized from the main groups after quality control procedures and quarantine periods were completed.

Each exposure chamber contained as few species as possible to minimize the risk of cross infection. The numbers of animals in each chamber and cage configuration were compatible with ILAR (Institute of Laboratory Animal Resources) standards for animal care. Enough rodents were used to permit a statistically valid number of each species to reach the required age for tumor induction with natural and toxicologic attrition. Purebred beagle dogs were selected from a baseline group on the basis of examination, general observation of good health, and several preexposure clinical laboratory determinations. Fischer 344 rats and Golden Syrian hamsters were obtained from the Charles River Breeding Laboratories. C57B1/6 mice were purchased from the Jackson Laboratory.

All animals were observed hourly during the exposure phase of the study. Daily observations were conducted during the postexposure phases until termination of the experiments. Rats, hamsters, and dogs were weighed individually at biweekly intervals during exposure and at monthly intervals during the postexposure period. Mice were weighed in groups and with group mean weights were followed on a monthly basis throughout the experimental period. Blood samples were drawn from all dogs at biweekly intervals for selected laboratory determinations.

Generation of Test Atmospheres

Because turbine engine fuels are a mixture of alkane, aromatic, and alkene compounds with a wide boiling range, it was necessary to operate the chambers from a single master generator to assure equivalent exposures at the desired concentrations. Concentrated fuel vapors were produced by passing fuel through dual constant temperature evaporator towers operated between 50° and 57° and mixed with air to establish the desired atmospheric concentrations in the respective chambers. Fuel not vaporized was collected in a waste drum for disposal. Vapor concentrations were measured continuously using a Beckman Model 400 Hydrocarbon Analyzer and compared with measured fuel consumption and air flows. The absence of aerosols was documented using a Royco Aerosol Particle Counter. Quality control on the test fuels and analysis of the chamber atmospheres were performed using gas chromatography and mass spectrometry.

Experimental Protocols

Mixed hydrocarbon and high-energy fuels toxicity studies conducted by the THRU since 1973 are shown in Table II. Exposures were continued 24 hours per day, 7 days per week, during 90-day continuous studies. The exposure regimen for intermittent (occupational exposure schedule) studies was 6 hours per day, excluding weekends and holidays.

RESULTS

RJ-5 Toxicity

In acute studies of RJ-5 toxicity, the oral LD50 in rats was 16 g/kg, and the fuel was not irritating to the eyes or skin. The low volatility and low toxicity of RJ-5 prevented acute inhalation exposures at concentrations which would cause significant effects, so a six-month, intermittent exposure to the saturated vapor (150 mg/m^3) was performed. Reduced weight gain in rats and dogs was the only response observed during exposures, but this may have been caused by appetite suppression due to the disagreeable odor of the fuel. Acute inflammation of the lungs and some bronchopneumonia were found in rats and dogs sacrificed immediately postexposure (1). After a one-year holding period, a high incidence of alveolar carcinomas (25%) was observed in the exposed CF-1 mouse, a strain predisposed to this type of tumor (2). RJ-5, subjected to a matrix of in vitro assays employing microbial cells and mammalian cells in culture, and in vivo tests measuring germ cells effects in mice and rats, did not exhibit mutagenic activity in any of the cell cultures or in vivo assays. There was evidence for increased unscheduled DNA synthesis, which is not a measure of mutagenicity, but may indicate some DNA toxicity (3).

To assess the oncogenic potential of RJ-5, dogs, rats, hamsters, and C57B1/6 mice were exposed to 30 mg/m^3 and 150 mg/m^3 for one year and held post exposure for an additional year of observation. The body weights of exposed male rats and hamsters were depressed throughout the exposure period and for one year postexposure. The weights of the exposed female rats were higher than controls during the exposure; however, this trend was reversed during the postexposure observation. There was a minimally significant decrease in female rat kidney/body weight ratio ($p < 0.05$), but this difference was not significant in the male rats (4). Histopathologic examination of the male rat kidneys, however, revealed evidence of significant toxic nephropathy and a high incidence of renal tumors. Four (7%) renal cell adenomas and five (8%) renal cell carcinomas were found in the high-dose group, and one (2%) renal cell carcinoma was present in the low-dose group. No renal cell tumors were apparent in controls. In male rat kidneys, the incidence of medullary mineralization was 57/62 (92%) in the high-dose group, 2/59 (3%) in the low-dose group, and 0% in the control. Moderate pelvic urothelial hyperplasia (58%), hyaline droplets (18%), and cortical cysts (24%) were identified in the high-dose animals, as compared with 7%, 19%, and 2% in the low-dose animals and 2%, 2%, and none in the control group. These data indicate a dose-response relationship between long-term inhalation of RJ-5 and both renal cell tumor formation and toxic nephropathy in male rats.

JP-10 Toxicity

As with RJ-5, the synthetic fuel JP-10 was also found to be relatively nontoxic, with an oral LD50 of greater than 18.8 g/kg and an LC50 of 6840 mg/m^3 (5,6). Skin and eye irritation tests were negative with a moderate potential for some sensitization. JP-10 produced marginal clastogenic effects in the CHO/chromosome aberration assay but was negative in the other mutagenic assays (7). It was not embryotoxic in rats after inhalation of 600 ppm vapors or oral doses up to 1 g/kg (8).

Following these range-finding studies, a concentration of 562 mg/m^3 of JP-10 was selected as the level for a one-year intermittent study in dogs, rats, mice, and hamsters to assess oncogenic response. During the exposure, there was a slight weight depression in the exposed rats and hamsters, but no observable weight difference between exposed and control mice and dogs (9). Female mice displayed liver cell vacuolization in 50% of control and 75% of exposed animals. The most significant histopathologic finding in exposed male rats held for one year postexposure was the presence of nine renal cell carcinomas and one poorly differentiated malignant renal neoplasm, compared with only one renal cell carcinoma in the controls. Accentuated renal tubular degeneration was also more prevalent in the exposed male rats, with 43/49 (87%) exhibiting lesions compatible with old-rat nephropathy, as compared with 32/49 of the control animals. In addition to increased frequency of old-rat nephropathy, this degenerative lesion was judged to be more severe in exposed animals than in the controls.

Medullary mineral deposits were identified by light microscopy in all the exposed males but were entirely absent in the controls. These deposits appeared to be mineralized cell debris originating from toxic damage to the proximal tubular epithelium during exposure. Papillary hyperplasia of the renal pelvic epithelium was also noted in 26/49 (53%) of the exposed and 2/49 (4%) of the control animals. No significant lesions were noted in female mice. Male hamsters had an increased incidence of zona glomerulosa adenomas in the adrenal gland (14%), compared with controls (5%). Although the overall incidence of cortical cell adenomas/carcinomas were similar in both groups (27% control, 28% exposed), the finding of increased tumors of the outer zone of cortical cells, combined with an increased recorded hyperplasia of the zona glomerulosa (72% versus 45%), suggests that JP-10 may have primary or secondary effects on the mineralocorticoid secreting cells of the adrenal. There was a slight rise in parathyroid tumors (8%) in exposed hamsters with no tumors in controls. The percentage of male hamsters with testicular atrophy was elevated over control 35% to 14%. Although there was only one exposure concentration, toxic nephropathy and renal cell tumors in male rats appear to result from exposure to JP-10 for extended periods.

JP-4 Toxicity

Initial intermittent eight-month exposures to 2500 mg/m^3 and 5000 mg/m^3 JP-4 and 80 mg/m^3 benzene were conducted in 1974. An exposure concentration of

5000 mg/m^3 was chosen to produce a benzene vapor concentration of 80 mg/m^3, which was the TLV® (Threshold Limit Value) at that time. Benzene was selected as the critical vapor since there were concerns that it might be the most toxicologically significant fuel component. The only abnormalities observed in the high-dose animals were increases in weight and weight/body weight ratios for the male rat kidney, liver, lung, and spleen; a 27% incidence of rat murine bronchitis; and a transient increase in the female dog red blood cell (RBC) fragility between the 14th and 22nd week of exposure. This increase in fragility resulted in extension of the original six-month study to eight months when the values had returned to normal. There were no statistically significant differences between hematologic measurements and bone marrow analyses in JP-4 and benzene-exposed animals and controls. Histopathologic findings failed to show any treatment-related effects.

Ninety-day continuous exposures of dogs, mice, and rats to 500 mg/m^3 and 1000 mg/m^3 were begun in 1979. During these exposures, there was an increase in the serum globulin and total protein in both low- and high-dose dogs and a dose-related increase in blood urea nitrogen (BUN). The transient increase in RBC fragility found in female beagles during the previous eight-month intermittent study was not duplicated in this continuous exposure. Both concentrations of JP-4 caused reduced weight gain in male and female rats during the exposure; however, this difference disappeared during the 19-month postexposure observation period (10).

Histopathology of animals sacrificed immediately following exposure indicated there were significant exposure-related tissue lesions in both rodent species. The most significant finding in female mice was centrilobular hepatocellular fatty change in 88% of the low-dose and 89% of the high-dose animals. These lesions, consisting of multiple, discrete vacuoles of varying size within the hepatocytes, which were absent in controls, were thought to be the result of a mild, reversible toxic insult.

In male rats, 100% of the kidneys in the high- and low-dose groups exhibited hyaline droplet formation in the proximal tubular epithelium. Furthermore, in 96% and 100% of the low- and high-dose male rats, respectively, focal dilatation of the renal tubules was present near the corticomedullary junction, and these dilated segments were plugged with necrotic cell debris.

All lesions found in exposed and control dogs were common infectious/degenerative changes consistent with aging in all canine species.

A one-year intermittent exposure to 500 mg/m^3 and 1000 mg/m^3 was begun in February 1980 to allow comparison of the tumorigenic potential of petroleum-derived JP-4 and JP-4 refined from shale oil as part of the USAF alternate fuels program. Examination of tissues collected for histopathologic evaluation from this study is incomplete. As in the previous JP-4 studies, the only effects documented during the exposure phase were decreased male rat body, kidney, and liver weights in high- and low-dose groups and decreased spleen and kidney weights in the low dose females (4).

JP-5 Toxicity

In contrast to the JP-4 inhalation studies, the low volatility of JP-5 prevented exposure of animals to a fuel concentration which would produce a TLV of benzene. The highest vapor concentration that could be generated without obtaining a significant number of aerosol levels was 750 mg/m^3, which contained only 0.3 to 0.6 ppm benzene. Purebred beagles, rats, and mice were continuously exposed to 150 mg/m^3 and 750 mg/m^3 of petroleum JP-5 and shale-derived JP-5 for 90 days. As in the other hydrocarbon fuel studies, exposure effects noted during the JP-5 exposures were decreased growth rate in male rats and a statistically significant increase in BUN and serum creatinine levels in high-dose male and female rats (11). In mice, mild diffuse fatty changes consisting of numerous small cytoplasmic vacuoles within the hepatocytes were seen in 3% of controls, 73% of low-dose, and 24% of high-dose animals. These lesions were positive for fat with special stains. Additionally, "foamy" hepatocellular cytoplasmic vacuoles were noted in 18% of controls, 15% of low-dose, and 44% of high-dose females; these irregular vacuoles were negative for fat and glycogen stains. The vacuolar changes were regarded as mild, reversible injury to subcellular organelles.

The most significant pathologic changes observed in male rats sacrificed immediately postexposure were dilated tubules near the corticomedullary junction, which were plugged with granular, necrotic debris. In both petroleum and shale JP-5 exposed males, these changes were present in almost all of the subjects. These lesions were not present in the controls of either JP-5 group. Markedly increased hyaline droplets were also observed in proximal tubular cells of exposed males and were not recorded in females or control males.

Final pathology of the animals after 19 months postexposure observation found tubular degeneration representative of old-rat nephropathy in 96% of the high-dose group, 96% of the low-dose group, and in 84% of controls. Although the incidence of tubular degeneration was equally high in the control and exposed male rats and could not be readily distinguished from progressive renal nephropathy, the severity of the lesions in the control rats was less than in the low-dose and high-dose male animals. In contrast to animals sacrificed immediately postexposure, there was an absence of cellular debris at the intersection of the proximal tubule and the descending loop of Henle.

The sloughed cellular material from the exposure-related necrosis of the proximal tubular epithelium appeared to have migrated to the hairpin turn separating the ascending and descending limb of the nephron where it became mineralized by calcium impregnation. Medullary tubular mineralization appeared to be dose-dependent, with 82% of high-dose, 59% of low-dose, and 0% of control male rats exhibiting this lesion. Dose-related focal hyperplasia of the renal pelvis was also detected in the exposed male rats; however, its pathogenesis remains obscure. As with the other fuels, the increased severity of progressive renal nephropathy and intratubular mineralized debris, not common in aged rats, suggests the fuel exposure as the etiologic factor in these kidney effects.

DISCUSSION

A general picture of the toxic response to long-term exposure to hydrocarbon vapors is beginning to evolve. In male rats, continuous exposure for 90 days reduces body weight gain and increases kidney body/weight ratios. Hyaline droplets in the proximal tubule epithelium and multifocal dilatation near the corticomedullary junction present in 80 to 90% of exposed male rats are absent in female and control animals. The dilated tubules are filled with necrotic cell debris. After 19 months postexposure, the tubular degeneration is present in exposed rats and is distinguishable from old-rat nephropathy only because it is more severe than the aging nephropathy observed in controls and is accompanied by marked medullary mineralization and pelvic urothelial hyperplasia.

In one-year intermittent exposures, there is only a slight weight depression in exposed rats, hyaline droplet formation in the proximal tubules, and a slight increase in mineralization in the loop of Henle. The most significant finding is the presence of renal carcinomas in the animals sacrificed at 24 months. Renal tumors were found in 15% of male rats exposed to 150 mg/m^3 RJ-5 and 18% exposed to 562 mg/m^3 JP-10. In addition to progressive aged-rat nephropathy, dose-dependent medullary mineralization and hyperplasia of the renal pelvis is present in the exposed animals and almost entirely absent in controls. There is a slight nonsignificant increase in BUN and serum creatinine in high-dose male rats in most exposures; however, these increases are insufficient to indicate decreased renal function.

Because the etiology of toxic nephropathy and renal tumors is unknown, the question remains as to whether these effects of exposure to hydrocarbon vapors are significant in humans. As indicated in Table II, results for many of the long-term inhalation studies on hydrocarbon fuels conducted in the THRU will not be available for a number of years. Histopathologic examination of the animals in these studies should provide additional data on the renal lesions and provide evidence to evaluate whether they are a generic effect of many hydrocarbons. There is a critical need for further definitive research to elucidate the mechanism of the observed hydrocarbon-induced renal lesions and to understand why this nephrotoxicity is specific to male rats. Research on the metabolism of JP-10 has identified the ketone, 5-keto-JP-10, in the kidney of the male rat but not in other tissues or in the female rat (12,13). Further studies are underway to determine whether this ketone is associated with renal damage. Research is currently in progress in the Toxic Hazards Division to identify the urinary metabolites in urine from male rats exposed to different fractions of the mixed distillate fuels and to assess the role of a male rat specific protein, alpha-2 globulin, in the initial formation of hyaline droplets and tubular degeneration. The Navy Toxicology Detachment is also evaluating the sex-related differences observed in the rat and the steric effects of branched alkanes (14).

In female mice, the most significant finding was a reversible centrilobular

TABLE II
Description of Fuel Inhalation Exposures

Fuel	Exposure Duration (months)	Concentration (mg/m^3)	Species	End Date
Synthetic				
JP-10	12, int[b]	560	D,R,Mi,H	Completed
RJ-5	6, int	155	D,R,Mi,M	Completed
RJ-5	12, int	30, 150	D,R,Mi,H	Completed
Mixed distillate				
JP-4	8, int[e]	2500, 5000	D,R,M,Mi	Completed
JP-4	3, cont[c]	500, 1000	D,R,Mi	Completed
JP-4	12, int	500, 1000	R,Mi	Jul 84
JP-5	3, cont	150, 750	D,R,Mi	Completed
JP-5(S)[d]	3, cont	150, 750	D,R,Mi	Completed
JP-7	12, int	150, 750	R,Mi	Dec 85
JP-8	3, cont	500, 1000	R,Mi	Jul 85
JP-TS	12, int	200, 1000	R,Mi	Dec 85
DFM	3, cont	50, 300	R,Mi	Completed
DFM(S)	3, cont	50, 300	R,Mi	Completed

[a] D = dogs, R = rats, M = monkeys, Mi = mice (female), H = hamsters.
[b] Intermittent (6 hours/day, 5 days/week, one = year postexposure hold).
[c] Continuous (24 hours/days, 7 days/week, 19 = Month postexposure hold).
[d] Shale.
[e] One = year postexposure hold.

hepatocellular fatty change in over 80% of the exposed animals. This probably represents a mild hydrocarbon effect on the subcellular organelles, which disappears at the end of exposure. The mechanism of this lesion is unclear but could be due to interferences with the enzymes involved in protein and fat metabolism.

No consistent response was observed in exposed male beagles; however, there were two instances of transient increased RBC fragility in the females.

SUMMARY

As part of their biotechnology research programs, the USAF and USN have ongoing hazard assessment programs for the unique fuels used in military aircraft and missiles. In the several completed subchronic and oncogenic inhalation studies on the synthetic cruise missile fuels and mixed distillate hydrocarbons used in turbine engine aircraft, the only significant exposure-related responses observed are dose-dependent toxic nephropathy and renal tumors in male rats and a reversible hepatocellular fatty change in female mice. The etiology of these effects and the relevant hazards to workers exposed to concentrations of hydrocarbon vapors found in the occupational environment are presently unknown.

ACKNOWLEDGEMENTS

The inhalation studies were performed in the THRU operated for the Air Force Aerospace Medical Research Laboratory by the University of California under contract F33615-80-C-0512. The conduct of these studies by the University of California was under the direction of Dr. J.D. MacEwen, THRU Laboratory Director. The Navy studies were supported by work unit MF58524001-002 of the Naval Medical Research and Development Command. Pathology was performed by the Pathology Branch, Toxic Hazards Division, under the supervision of Lt. Col. R.H. Bruner. The opinions expressed herein are the opinions of the authors and are not to be construed as official or reflecting those of the USAF or USN.

REFERENCES

1. MacEwen, J.D. and Vernot, E.H.: *Toxic Hazards Research Unit Annual Technical Report: 1975*, AMRL-TR-75-57 (AD A019 456), Aerospace Medical Research Laboratory, Wright-PattersonAir Force Base, Ohio (1975).
2. MacEwen, J.D. and Vernot, E.H.: *Toxic Hazards Research Unit Annual Technical Report: 1976*, AMRL-TR-76-57 (AD A019 860), Aerospace Medical Research Laboratory, Wright-PattersonAir Force Base, Ohio (1976).
3. Bruswick, D.J. and Matheson, D.W.: *Mutagen and Oncogen Study on RJ-5*, AMRL-TR-78-23 (AD A064 951), Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio (1978).
4. MacEwen, J.D. and Vernot, E.H.: *Toxic Hazards Research Unit Annual Technical Report: 1982*, AFAMRL-TR-82-62 (AD A121 717), Air Force Aerospace Medical Research Laboratory, Wright-PattersonAir Force Base, Ohio (1982).
5. MacEwen, J.D. and Vernot, E.H.: *Toxic Hazards Research Unit Annual Technical Report: 1979*, AFAMRL-TR-79-56 (AD A075 976), Aerospace Medical Research Laboratory, Wright-PattersonAir Force Base, Ohio (1979).
6. MacNaughton, M.G.: *Toxicology of High Energy Fuels*, AFAMRL-TR-81-136 (AD A111 686), Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio (1981).
7. Sivak, A.: *Evaluation of Dimethyl Methylphosphonate and Exo-Tetrahydrodi-(Cyclopentadiene) in a Battery of in vitro Short Term Assays*, AFAMRL-TR-82-95 (AD A124 785), Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio (1983).
8. Keller, W.C., Inman, R.C., Yu, K.O., and Back, K.C.: Evaluation of the Embryotoxicity of JP-10 in the Rat. *Drug Chem Toxocol* 6(2):181–190 (1983).
9. MacEwen, J.D. and Vernot, F.H.: *Toxic Hazards Research Unit Annual Technical Report: 1981*, AFAMRL-TR-81-126 (AD A110 587), Air Force Aerospace Medical Research Laboratory, Wright-PattersonAir Force Base, Ohio (1981).

10. MacEwen, J.D. and Vernot, E.H.: *Toxic Hazards Research Unit Annual Technical Report: 1980*, AFAMRL-TR-80-79 (AD A091 617), Air Force Aerospace Medical Research Laboratory, Wright-PattersonAir Force Base, Ohio (1980).
11. MacEwen, J.D. and Vernot, E.H.: *Toxic Hazards Research Unit Annual Technical Report: 1978*, AMRL-TR-78-55 (AD A062 138), Aerospace Medical Research Laboratory, Wright-PattersonAir Force Base, Ohio (1978).
12. Inman, R.C., Yu, K.O., and Serve, M.P.: *Identification of Cruise Missile Fuel Metabolites from Rat Organs by GC/MS*. Poster session, 31st Annual Conference on Mass Spectrometry and Allied Topics, Boston, MA (1983).
13. Inman, R.C., Yu, K.O., and Keller, W.C.: *Cruise Missile Fuel Inhalation Kinetics and Metabolite Identification by GC/MS*. Abstract, 30th Annual Conference on Mass Spectrometry and Allied Topics, Honolulu, HI (1982).
14. Pitts, L.L., Bruner, R.H., D'Addario, A.P., and Uddin, D.E.: Induction of Renal Lesions Following Oral Dosing with Hydrocarbon Fuels. *The Toxicologist* 3:70 (1983).