UNCLASSIFIED

AD 273 490

Reproduced
by the

ARMED SERVICES TECHNICAL INFORMATION AGENCY
ARLINGTON HALL STATION
ARLINGTON 12, VIRGINIA

UNCLASSIFIED

NOTICE: When government or other drawings, specifications or other data are used for any purpose other than in connection with a definitely related government procurement operation, the U. S. Government thereby incurs no responsibility, nor any obligation whatsoever; and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data is not to be regarded by implication or otherwise as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use or sell any patented invention that may in any way be related thereto.

Best
Available
Copy

273 490

ASD TECHNICAL REPORT 61-526

# VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES

*MAURICE H. WEEKS*
*GEORGE C. MAXEY – SP-4, US ARMY*
*MARY E. SICKS – MAJOR, CmlC*
*EARLE A. GREENE*

*U. S. ARMY CHEMICAL AND DEVELOPMENT LABORATORIES*
*ARMY CHEMICAL CENTER, MARYLAND*

*OCTOBER 1961*

ASTIA
RECEIVED
MAR 29 1962
TISIA B

MIPR (33-616) 60-32

BIOMEDICAL LABORATORY
AEROSPACE MEDICAL LABORATORY
AERONAUTICAL SYSTEMS DIVISION
AIR FORCE SYSTEMS COMMAND
UNITED STATES AIR FORCE
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

## NOTICES

When Government drawings, specifications, or other data are used for any purpose other than in connection with a definitely related Government procurement operation, the United States Government thereby incurs no responsibility nor any obligation whatsoever; and the fact that the Government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data, is not to be regarded by implication or otherwise as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use, or sell any patented invention that may in any way be related thereto

☆

Qualified requesters may obtain copies of this report from the Armed Services Technical Information Agency, (ASTIA), Arlington Hall Station, Arlington 12, Virginia.

☆

This report has been released to the Office of Technical Services, U. S. Department of Commerce, Washington 25, D. C., for sale to the general public.

☆

Copies of WADD Technical Reports and Technical Notes should not be returned to the Wright Air Development Division unless return is required by security considerations, contractual obligations, or notice on a specific document.

ASD TECHNICAL REPORT 61-526

# VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES


*GEORGE C. MAXEY – SP-4, U.S. ARMY*
*MARY L. SICKS – MAJOR, CmlC*
*LABEL A. GREENE*

*U.S. ARMY CHEMICAL AND DEVELOPMENT LABORATORIES*
*ARMY CHEMICAL CENTER, MARYLAND*


*OCTOBER 1961*


CONTRACT MONITOR: KENNETH C. BACK, PH.D.
MIPR 33-616-60-32
PROJECT No. 7165
TASK No. 71836


**BIOMEDICAL LABORATORY**
**AEROSPACE MEDICAL LABORATORY**
**AERONAUTICAL SYSTEMS DIVISION**
**AIR FORCE SYSTEMS COMMAND**
**UNITED STATES AIR FORCE**
**WRIGHT-PATTERSON AIR FORCE BASE, OHIO**


[illegible] - January 1962 - 17-736 6-73

## FOREWORD

Investigations of the inhalation toxicity of UDMH described herein were conducted by Maurice H. Weeks, George C. Maxey, Mary E. Sicks, and Earle A. Greene of the Directorate of Medical Research, U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland. They were performed under Air Force Project No. 7165, "Health Hazards of Materials and Radiation," Task No. 71836, "Evaluation and Control of Toxic Chemical Materials." The contract monitor was Dr. Kenneth C. Back, Toxic Hazards Section, Physiology Branch, Biomedical Laboratory of the Aerospace Medical Laboratory. The experiments were started on April 1960 and completed on May 1961. The publication of this report does not constitute approval by the Air Force of the findings or conclusions contained herein.

## ABSTRACT

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five- to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures. No clinical abnormalities resulted from these single short-term exposures.

Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man

PUBLICATION REVIEW

JOSEPH M. QUASHNOCK
Colonel, USAF, MC
Chief, Biomedical Laboratory
Aerospace Medical Laboratory

## VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES

### INTRODUCTION

The use of 1,1-dimethylhydrazine (UDMH) as a storable liquid fuel in advanced type missile systems has resulted in the need for additional information on the health hazards from single, short exposures to this compound. It is indicated that the conditions of exposure most likely will involve large amounts of agent in confined areas for short periods of time.

The toxicology of UDMH shows it to be primarily a central nervous system stimulant causing convulsion and death irrespective of the route of administration (3). Inhalation of its vapors may also cause respiratory and gastrointestinal irritation, anorexia, and lethargy (4,6).

A hygienic standard or maximal allowable concentration (MAC) of 0.5 ppm UDMH vapor has been recommended for industrial atmospheres (9). This suggested MAC established a value which should give adequate protection during a normal eight-hour workday, five days a week, for the life of the worker. However, brief exposures to much higher concentrations may occur in emergency situations, and our knowledge of UDMH poisoning is insufficient to predict adequately the levels of human tolerance from such exposure. The effects resulting from a few accidental exposures have been reported in the literature, but circumstances in such situations do not contribute to establishing well defined values for exposure times or for concentration levels (6).

The purpose of our study was to obtain data on the inhalation toxicity of UDMH in animals from single, short exposures. Results from these controlled experiments will help to establish more realistic short-term exposure standards for UDMH and provide information on toxicology and public health.

The present paper reports the effects of both single exposure of rats and dogs and of repeated exposure of dogs to UDMH vapor. The experiments with rats were designed to determine the range of concentrations producing severe toxic effects from single 5-, 15-, 30-, and 60-minute exposure periods. The objective of the experiments with dogs was to find the concentration of UDMH causing minimal or no toxic signs at short exposure periods.

### METHODS

#### A. Experimental Procedures

Exposures were carried out in a 370-liter dynamic flow gassing chamber operated at an airflow of 200 liters per minute. UDMH* was dispersed

*UDMH, trade name Dimazine, was obtained from Westvaco Chemical Div., Food Machinery & Chemical Corporation, New York, New York.

into the exposure chamber as a vapor by passing oil-pumped nitrogen through a dispersion bubbler containing the liquid agent. The bubbler was maintained in a constant temperature bath at 29°C in the 15-, 30-, and 60-minute studies and at 50°C in the 5-minute studies. Concentrations of UDMH were determined from measured air samples collected in bubblers containing dilute HCl solution and analyzed by a $KIO_3$ titration method (1).

B. Toxicity Studies with Rats

Young, male rats (100 to 120 gm) were exposed in groups of 10 to various concentration levels of UDMH for single 5-, 15-, 30-, and 60-minute periods. They were observed for toxic signs during exposure and for seven days after exposure. All were weighed before exposure and survivors for seven days thereafter and their growth rate compared with that of the controls. Histopathologic studies were conducted on groups of rats sacrificed immediately and one, three, and seven days after exposure to various concentrations of UDMH. Deaths resulting from inhalations of UDMH were recorded and the LC50 values for the exposure periods were computed by the method of Bliss as described by Finney (2).

A separate group of 20 male unexposed rats was observed for food and water consumption and for spontaneous activity as measured by means of voluntary rotary activity cages. Ten rats from this group were then exposed to 1000 ppm of UDMH for 60 minutes. Blood was taken from the tail before and after exposure and hematocrit and erythrocyte counts were determined. Measurements of food and water consumption and of activity were continued for three weeks after exposure and compared with the 10 control animals.

C. Toxicity Studies with Dogs

1. Single Exposures

Mongrel dogs in groups of three were exposed to various concentrations of UDMH vapor for single 5-, 15-, and 60-minute periods. A modified 400-liter chamber was used for these exposures. The dispersion, chamber operation, and analysis of UDMH vapor were similar to that described previously.

Lethal effects of UDMH at various concentration levels for each exposure time were determined, and the LC50 values were estimated. Toxic signs, weight changes, and deaths were recorded during a seven-day observation period. During these experiments extraneous noises and movements were kept to a minimum for three to five hours after the dogs had been exposed. Histopathologic studies were conducted on selected dogs from the various exposures which were sacrificed immediately, 7, 14, and 21 days after exposure.

The response of animals to concentrations of UDMH approximating 50, 25, and 12.5 percent of the previously estimated LC50 values was determined in groups of dogs exposed for single 5-, 15-, and 60-minute periods.

Fifteen minutes after each exposure and at one hour and two hours thereafter, these dogs were subjected to auditory, visual, and mild electrical stimuli and observed for toxic signs and for behavior.

In another series of experiments the retention of inhaled UDMH was determined in six anesthetized dogs* exposed by means of an endotracheal tube or an oronasal mask. Each animal was exposed to a known concentration for about one hour and the percent retention of the inhaled dose was determined. Respiratory volumes and rates were measured and EKGs were recorded during the exposures.

Multiple Exposures

Results obtained from acute exposures indicated that single exposures to 50, 200, and 600 ppm of UDMH for periods of 30, 15, and 5 minutes, respectively, probably [illegible] toxic signs in dogs. Experiments to support these estimates were conducted by exposing three groups of four mixed breed dogs twice weekly (Monday and Thursday) for six weeks to these concentrations and exposure times.

All animals were observed for general health, characteristic behavioral signs, coordination, and reflex reactions (5) for two months prior to and during exposure. Base line values were also obtained for red and white blood cell, reticulocyte counts, hematocrit, nonprotein nitrogen, glucose, bilirubin, and cholinesterase** levels. The clinical determinations and physical examinations were made at weekly intervals during the active stages of exposure.

Two dogs from each group were trained to perform a conditioned avoidance test in a traumatic avoidance apparatus (7). In this test dogs were trained to jump over a barrier within five seconds after a conditioned stimulus (flashing light and pulsating buzzer) was presented. Electric shock, given through a grid floor, five seconds after the conditioned stimulus was presented, was used to train the animal. Each session on the apparatus consisted of 20 jump trials. The dogs were considered trained when they were able to complete five sessions (100 trials) given over a five-day period, without error. During the exposure period each trained dog's behavior, average response time, and number of mistakes (jumping before signal) were recorded. These trials of 20 jumps each were conducted on each nonexposure day and on each exposure day once before and once 15 minutes after they had been exposed.

---

*Anesthetic - Pentosin, J. S. Buch & Son, Baltimore, Maryland. Each - contains 64 mg sodium pentobarbital, 32 mg mephenesin in aqueous solution of 10% alcohol and 20% propylene glycol. (The iv dose was 0.1 ml/kg of body weight.)

**Groff, W. A.: Modification of Serum Cholinesterase Method of Wetstone and Bowers (in preparation).

After six weeks of exposure the three groups of dogs were then exposed twice weekly for two weeks to double the previous concentrations, i.e. to 100, 400, and 1200 ppm of UDMH for 60, 15, and 5 minutes, respectively. The previously described clinical determinations, physical examinations, and other observations were continued during this period.

Results from these exposures were compared with a range-finding test in which two groups of two mongrel dogs each, previously non-exposed, were subjected twice weekly (Monday and Thursday) to 100 and 1200 ppm of UDMH for exposure periods of 60 and 5 minutes, respectively. Exposures were discontinued during the second week because of the appearance of severe toxic signs. Values were obtained prior to and through at the exposure period for red and white blood cell counts, reticulocyte counts, hematocrit, and nonprotein nitrogen levels. All animals were examined to determine their health and behavioral characteristics before and during the exposure period.

## RESULTS

Comparison of the vapor concentrations of UDMH determined by chemical analyses to the weight of agent used during an exposure showed that 80 percent or better of the amount dispersed into the chamber remained airborne.

### A. Toxicity Studies with Rats

Rats exposed to UDMH showed signs of irritation during exposure as demonstrated by face washing, sneezing, closing of eyes, and restless agitation. The pelt appeared rough and unkempt for one to two days after exposure, but thereafter looked normal. All deaths occurred within 24 hours after exposure. Surviving animals showed no weight changes consistently different from the control animals.

The sequence of events preceding death was a quiet period of one to two hours after exposure followed by a short period of wild running about the cage, stopping for a few seconds, and then an intermittent clonic-tonic convulsive seizure of about 15 to 30 seconds duration. Several series of these seizures interspersed with periods of quiet preceded death.

The 5-, 15-, 30-, and 60-minute LC50 values for rats exposed to UDMH with 19/20 confidence limits and slopes of the dose-response curves with their standard errors are shown in Table 1. The four-hour values as determined by Jacobson et al. (4) are included for comparison. These results are shown graphically in figure 1. Statistical analysis of the slopes of the 15-, 30-, and 60-minute exposure curves, as well as the Jacobson four-hour slope, showed that they were not significantly different at the 95 percent confidence level.

TABLE 1

LC50 VALUES FOR RATS EXPOSED TO UDMH

| Exposure Time | LC50 | 95/20 Confidence Limits | Slope | Standard Error of Slope |
|---|---|---|---|---|
| min | ppm | ppm | | |
| 240 | 252 | 219-290 | 8.65 | 2.8 |
| 60 | 1411 | 1301-1531 | 9.70 | 2.4 |
| [illegible] | [illegible] | [illegible] | [illegible] | [illegible] |
| 15 | 8230 | 6930-9778 | 5.90 | 1.7 |
| 5 | 24457 | 23400-25500 | 25.80 | 9.6 |

The LC50s of UDMH for rats versus exposure times were plotted on log-log coordinates as shown in figure 2. The solid line drawn represents the concentration exposure time relationship for a single exposure above which at least 50 percent mortality may be expected among the exposed animals. In Table 2 are given the calculated response levels of 1, 50, and 84 percent death for each of these exposures.

TABLE 2

DOSE-RESPONSE LEVELS FROM RATS EXPOSED TO UDMH

| Exposure Time | LC1 | LC50 | LC84 |
|---|---|---|---|
| min | | | |
| 240 | 136 | 252 | 529 |
| 60 | 613 | 1411 | [illegible] |
| 30 | 2638 | 4008 | 4792 |
| 15 | 3345 | 8230 | 12099 |
| 5 | 19004 | 24457 | 26730 |

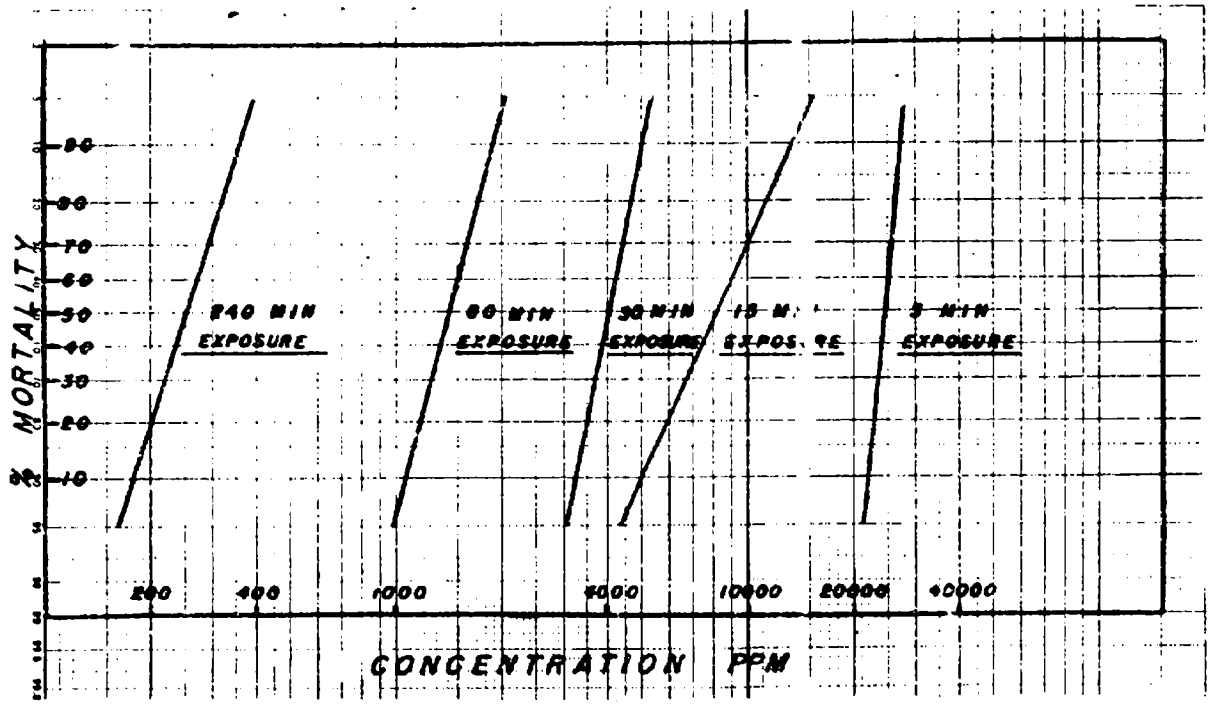


Figure 1. Mortality in Rats Exposed to UDMH

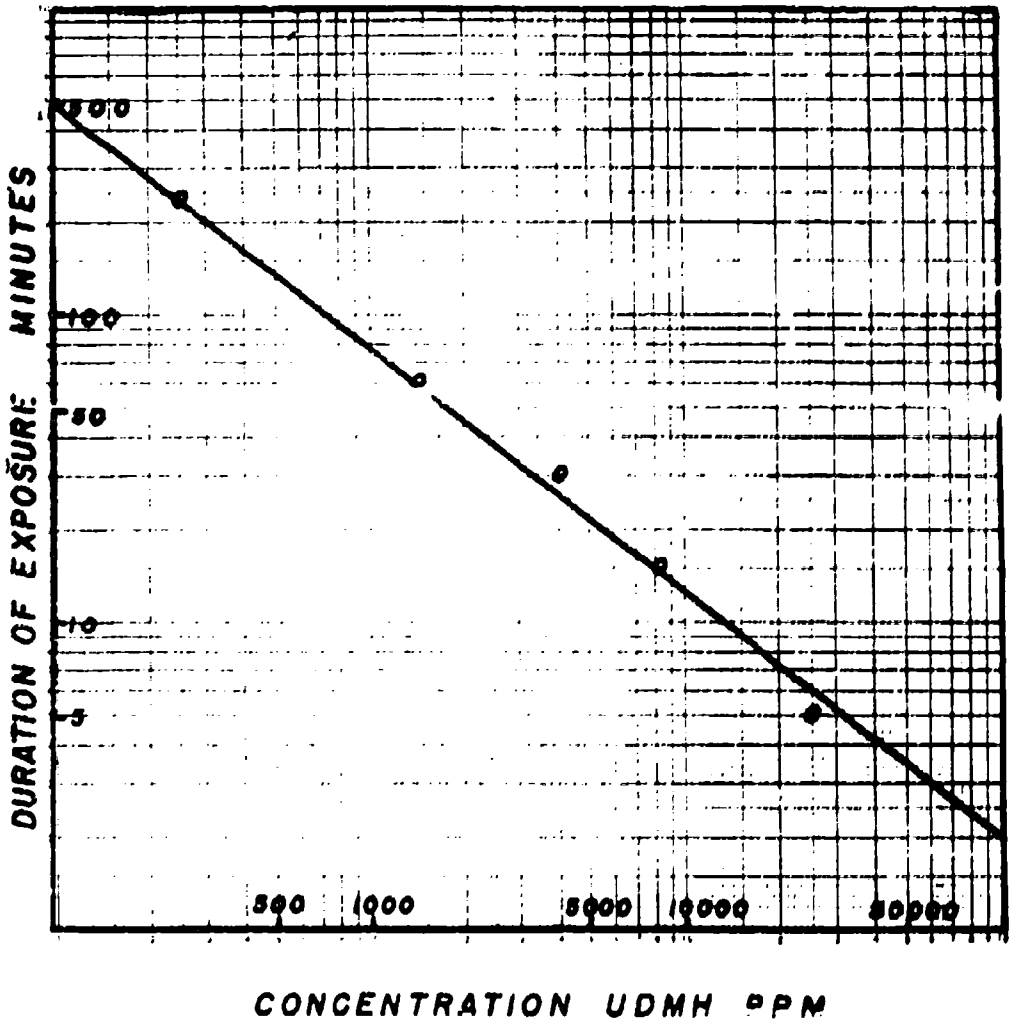


Figure 2. LC50 of UDMH for Rats

In other experiments no differences were found between exposed and control rats in food and water consumption, in food utilization, and in weight gain. However, the voluntary activity of exposed rats was markedly reduced by exposure to UDMH and remained lower than the controls throughout the three-week observation period.

Hematocrit and erythrocyte counts on rats exposed to 1000 ppm UDMH for one hour were not different from pre-exposure control values.

Histopathologic studies of organs and tissues from the exposed animals showed no lesions that could be attributable to UDMH poisoning.

B. Toxicity Studies with Dogs

1. Human Exposures

Dogs showed few toxic signs during exposure, some licked their noses and lips during the 5- and 15-minute runs; a few vomited during the 60-minute runs. After exposure all animals seemed dazed, depressed, or in a state of shock. Sharp noises made them shiver and cower. Intermittent clonic and tonic convulsive seizures of 2 to 15 minutes duration were seen in dogs that died and in some of the survivors. Surviving dogs seemed completely recovered 48 hours after exposure.

All deaths occurred within 24 hours after exposure. Surviving animals were weighed during the seven-day observation period. The ranges of concentrations producing lethal effects in dogs were somewhat lower than those found with the rat. The LC50s with 19/20 confidence limits and the slope with standard error of the dose-response curves as calculated by the method of Bliss are shown in Table 3. Macro- and microscopic examination of tissues and organs from these dogs showed no changes that could be attributable to UDMH exposure.

TABLE 3

LC50 VALUES FOR DOGS EXPOSED TO UDMH

| Exposure Time | LC50 | 19/20 Confidence Limits | Slope | Standard Error of Slope |
|---|---|---|---|---|
| min | ppm | ppm | | |
| 60 | 981 | 862-1117 | 14.7 | 7.5 |
| 15 | 3570 | 2327-5503 | 3.9 | 2.2 |
| 5 | 22300 | 22050-22550 | 221.0 | 207.0 |

In the experiments in which animals were subjected to stress conditions and in which concentrations of UDMH were progressively lowered, groups of dogs were exposed for single 5-, 15-, and 60-minute periods until minimal or no toxic effects were seen.

The external stimuli and added stress seemed to magnify and perhaps hasten the development of toxic signs from UDMH poisoning at these lower dose levels. Toxic signs were produced which were previously seen only in dogs exposed to much higher concentrations of UDMH, but where the environment after exposure was less disturbing.

These studies showed that minimal toxic responses were produced by exposures to about 1200, 400, and 100 ppm of UDMH from single 5-, 15-, and 60-minute exposures, respectively. The results are shown in detail in Tables [illegible], [illegible] and [illegible].

TABLE 4

RESPONSE OF DOGS UNDER STRESS ENVIRONMENTS AFTER 5-MINUTE EXPOSURE TO UDMH VAPOR

| Exposure Concn ppm | No of Animals | Response After Exposure |
|---|---|---|
| 12300 | 2 | 1/2 died overnight, 2/2 convulsed |
| 9600 | 2 | 1/2 died after 5 hr, 2/2 convulsed |
| 6900 | 2 | 2/2 vomited, 1/2 convulsed |
| 4230 | 2 | 1/2 died after 3 hr, 2/2 convulsed, tremors |
| 1550 | 2 | 1/2 slightly timid, dull 1/2 no toxic signs |
| 1200 | 2 | 2/2 no toxic signs |
| 860 | 3 | 3/3 no toxic signs |
| 630 | 2 | 2/2 no toxic signs |

TABLE 5

RESPONSE OF DOGS UNDER STRESS ENVIRONMENTS
AFTER 15-MINUTE EXPOSURE TO UDMH VAPOR

| Exposure Concn | No of Animals | Response After Exposure |
|---|---|---|
| ppm | | |
| 1530 | 2 | 2/2 tremors, vomiting, convulsions, depressed, recovered 24 hr |
| 980 | 2 | 2/2 depressed, tremors<br>1/2 vomiting, convulsions, [illegible] |
| 610 | 4 | 2/4 tremors<br>2/4 vomiting, convulsions<br>2/4 depressed, tremors, salivating, recovered 24 hr |
| 400 | 4 | 2/4 no toxic signs<br>1/4 slightly more sensitive to shock<br>1/4 apprehensive |
| 360 | 3 | 2/3 no toxic signs<br>1/3 slight muscle fasciculations |

Results from studies determining the retention of inhaled UDMH in six anesthetized dogs exposed by means of an endotracheal tube or an oronasal mask are given in Table 7. Dog No. 2 died within 24 hours and Dog No. 5 vomited and went into tonic-clonic convulsive seizures after exposures. No other toxic signs could be seen due to the masking effects of the anesthesia. No changes attributable to inhalation of UDMH were seen in the respiratory rate, heart rate, or EKG. The data in Table 7 shows that at least 80 percent of the amount of UDMH inhaled is retained in the respiratory tract of the dog.

2. Multiple Exposures

Groups of 4 dogs each exposed twice a week for six weeks to 50, 200, and 600 ppm of UDMH for 60-, 15-, and 5-minute periods, respectively, showed no significant changes in red blood cell, white blood cell, and reticulocyte counts, hematocrit, nonprotein nitrogen, glucose, bilirubin, or in

## TABLE 6

### RESPONSE OF DOGS UNDER STRESS ENVIRONMENTS AFTER 60-MINUTE EXPOSURE

| Exposure Concn ppm | No of Animals | Response After Exposure |
|---|---|---|
| 400 to 500 | 3 | 2/3 convulsed and died<br>1/3 tremors, vomiting, recovered within 24 hr |
| 200 to 250 | 3 | 1/3 convulsed and died<br>1/3 slight tremors to [illegible] within 3 hr<br>1/3 no toxic signs |
| 80 to 120 | 4 | 3/4 no toxic signs<br>1/4 slight tremors, recovered within 1 hr |
| 96 | 5 | 5/5 no toxic signs |

serum, whole blood and red blood cell cholinesterase determinations. A very gradual decrease in glucose values was noted during the course of the experiment although the total decrease was not significantly below pre-exposure control levels.

No significant changes from normality were noted in the conditioned avoidance tests. Neurological examination during this period showed no change in the patellar, extensor thrust, and hopping reflexes. Heart sounds remained within normal limits throughout this period. The lungs remained clear in all dogs, except four which suffered from bronchial congestion which was suspected to be "kennel cough"; however, their condition responded to Furadantin® therapy. The mucous membranes of all but one animal appeared clinically to be "muddy" or pale at irregular intervals during the period of experimentation. However, in view of the results from the serological work this observation may be of questionable clinical significance.

The only toxic signs seen in any of the dogs during these [illegible] were seen after the third exposure. On this day two dogs in the [illegible] run (50 ppm) were inadvertently exposed to 100 ppm of UDMH. About 15 minutes after exposure one dog vomited and one convulsed. However, both appeared

TABLE 7

RETENTION OF UDMH IN DOGS FOLLOWING INHALATION OF THE VAPOR

| Method of Delivery | Dog No. | Exposure Time | Av Minute Volume | Exposure Concn | Amount Retained | Per Cent Retention |
|---|---|---|---|---|---|---|
| | | min | l | mg UDMH/l | mg UDMH/kg | |
| Endotracheal tube | 1 | 64 | 1.6 | 6.43 | 67.3 | 71 |
| Endotracheal tube | 2 | 52 | 1.3 | 19.60 | 144.4 | 83 |
| Endotracheal tube | 3 | 60 | 1.6 | 3.17 | 40.0 | 83 |
| Oronasal mask | 4 | 60 | 0.9 | 2.96 | 22.7 | 79 |
| Oronasal mask | 5 | 55 | 3.7 | 2.90 | 108.2 | 93 |
| Oronasal mask | 6 | 51 | 1.2 | 2.97 | 26.2 | 91 |

normal the next day at which time no change in jump time or in reflex tests was noted. These dogs showed no toxic signs throughout the remaining experimental period.

Doubling the exposure concentrations of the three groups of dogs for two weeks had no effect on the responses of these dogs in the conditioned avoidance tests, and no changes were noted in the neurological and physical examinations. The clinical and serological values reflected no significant changes resulting from these exposures. However, the appearance of toxic signs immediately increased after the exposure concentrations had been doubled. All dogs vomited the first week and appeared dazed. Tonic-clonic convulsive seizures were seen in two dogs in the five-minute run during the second week. No deaths resulted from these exposures.

In the range-finding study in which two groups, each consisting of two previously non-exposed dogs, were exposed to 100 and 1200 ppm of UDMH the exposures were discontinued during the second week because of the appearance of severe toxic signs. All dogs vomited and convulsed and one dog from each group died. Both surviving dogs appeared normal the week following cessation of exposures. Clinically a slight drop in red blood cell count and hematocrit was noted during the first week of exposure while during the second week the surviving dogs showed nonprotein nitrogen values that were slightly increased but which returned to normal when exposures were discontinued.

## DISCUSSION

It is clearly apparent that single brief exposures to high concentrations of UDMH produced toxic signs generally quite similar to those seen at longer inhalation exposures but lower concentrations and in animals poisoned by other

routes of administration. The similarity in the toxic effects at both long- and short-term exposures suggests a common mechanism of action of UDMH dependent upon the dose. This is further demonstrated in figure 2 where the solid straight line connecting the LC50s for rats indicates a linearity wherein some common relationship exists for the production of lethal effects over the various short exposure times.

The ranges of concentration causing lethal effects in dogs from single 5-, 15-, and 60-minute exposures were somewhat lower than those obtained with rats. This reflects the known greater sensitivity of the dog over the rat to UDMH [illegible],10). The toxic signs in order of appearance and severity in the dogs at these levels were usually as follows: a dazed appearance, vomiting, tremors, convulsions, and death.

Due to the lack of [illegible] of the mechanism of action of UDMH and of some measurable change as an index of exposure, the criterion of toxicity in the minimal toxic response studies was limited to the observation of toxic signs. However, the observation of toxic signs produced as a result of UDMH exposure was aided by our finding that UDMH causes a hypersensitivity in exposed dogs to sharp noises and quick unexpected movements. These added stresses or stimuli seemed to magnify or perhaps hasten the development of toxic signs from UDMH poisoning. Progressively lowering the exposure concentrations showed that minimal toxic responses were produced by exposure to about 1200, 400, and 100 ppm of UDMH from single 5-, 15-, and 60-minute exposures, respectively.

Dogs receiving multiple exposures to 50, 200, and 600 ppm of UDMH for six weeks at 60-, 15-, and 5-minute periods, respectively, showed no changes from normal in clinical and hematological values and no toxic responses. These results indicate that the concentrations of UDMH at the various short-term exposures were nontoxic for dogs. These data also show that biweekly doses of UDMH are probably not additive for the production of toxic responses. Comparison of the results from the two experiments at exposure levels of 100 and 1200 ppm of UDMH for 60- and 5-minute periods, respectively, indicates that no increase in sensitivity developed in dogs exposed six weeks at the lower dose levels.

The absence of clinical abnormalities from the short-term exposures indicates that at present there is no measurable change produced as a result of exposure to UDMH and which will serve as a reliable index of exposure. Therefore, it would seem to be imperative that in cases of accidental poisoning of men the subjective responses of individuals be carefully analyzed. Further the absence of toxic responses in dogs exposed to 50, 200, and 600 ppm for single 60-, 15-, and 5-minute periods, respectively, provides levels of [illegible] from which hygienic standards for short-term exposures to UDMH may be derived for man.

## SUMMARY

Single 5- to 60-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures and in animals poisoned by other routes of administration.

The absence of clinical abnormalities from the single short-term exposures indicates that at present there is no measurable change produced as a result of exposure to UDMH which will serve as a reliable index of exposure.

Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

## BIBLIOGRAPHY


1. Audrieth, L. F., and B. A. Ogg, The Chemistry of Hydrazine, John Wiley & Sons, New York, N. Y., 1951.

2. Finney, D. J., Probit Analysis, Second Edition, Cambridge University Press, London, 1952.

3. Jacobson, K. H., Transactions of the Symposium on Health Hazards of Military Chemicals, CWL Special Publication 2-10, U. S. Army Chemical Warfare Laboratories, Army Chemical Center, Md., August 1958.

4. Jacobson, K. H., J. H. Clem, H. J. Wheelwright, Jr., W. E. Rinehart, and N. Mayer, "The [illegible] Toxicity of the Vapors of Some Methylated Hydrazine Derivatives", A.M.A. Archives of Industrial Health, Vol 12, pp 609-616, 1955.

5. McGrath, J. T., Neurologic Examination of the Dog, Lea and Febiger, Philadelphia, Pa., 1956.

6. Rinehart, W. E., E. Donati, and E. A. Greene, "The Sub-Acute and Chronic Toxicity of 1,1-Dimethylhydrazine Vapor", American Industrial Hygiene Association Journal, Vol 21, pp 207-210, 1960.

7. Saloman, R. L., and L. C. Wynne, "Traumatic Avoidance Learning Acquisition in Normal Dogs", Psychological Monographs: General and Applied, Vol 67, No. 4, 1953.

8. Shook, B. S., Sr., and O. H. Cowart, "Health Hazards Associated with Unsymmetrical Dimethylhydrazine", Industrial Medicine and Surgery, Vol 26, pp 333-336, 1957.

9. "Threshold Limit Values for 1960", Archives of Environmental Health, Vol 1, pp 140-144, 1960.

10. Witkin, L. B., "Acute Toxicity of Hydrazine and Some of Its Methylated Derivatives", A.M.A. Archives of Industrial Health, Vol 13, pp 34-36, 1956.

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M.H. Weeks, G.C. Maxey, Mary E. Sicks, and E.A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165; Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures. No clinical abnormalities

( over )

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromautical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M.H. Weeks, G.C. Maxey, Mary E. Sicks, and E.A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165; Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures. No clinical abnormalities

( over )

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromautical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

resulted from these single short-term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

UNCLASSIFIED

ASD TR 61-526

resulted from these single short-term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

UNCLASSIFIED

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M.H. Weeks, G.C. Maxey, Mary E. Sicks, and E.A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165, Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures. No clinical abnormalities

(over)

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromedical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

resulted from these single short-term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

UNCLASSIFIED

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M.H. Weeks, G.C. Maxey, Mary E. Sicks, and E.A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165, Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures. No clinical abnormalities

(over)

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromedical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

resulted from these single short-term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

UNCLASSIFIED

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M. H. Weeks, G. C. Maxey, Mary E. Sicks, and E. A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165; Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five- to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures. No clinical abnormalities

( over )

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromedical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

resulted from these single short term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5 minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M. H. Weeks, G. C. Maxey, Mary E. Sicks, and E. A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165; Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five- to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at longer inhalation exposures. No clinical abnormalities

( over )

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromedical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

resulted from these single short term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5 minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M. H. Weeks, G. C. Maxey, Mary E. Sicks, and E. A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165; Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five- to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at lower inhalation exposures. No clinical abnormalities

(over)

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromedical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland

VAPOR TOXICITY OF UDMH IN RATS AND DOGS FROM SHORT EXPOSURES, by M. H. Weeks, G. C. Maxey, Mary E. Sicks, and E. A. Greene. October 1961. 22p. incl. illus., tables. 10 refs. (Proj. 7165; Task 71836)

Unclassified report

A study was made of the inhalation toxicity of UDMH in animals from single short exposures. Five- to sixty-minute exposure of dogs and rats to high concentrations of UDMH produce toxic signs similar to those seen at lower inhalation exposures. No clinical abnormalities

(over)

UNCLASSIFIED

I. Weeks, M. H.
II. Maxey, G. C.
III. Sicks, Mary E.
IV. Greene, E. A.
V. Aeromedical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio
VI. MIPR (33-616) 60-32

UNCLASSIFIED

ASD TR 61-526

resulted from these single short-term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

UNCLASSIFIED

ASD TR 61-526

resulted from these single short-term exposures. Dogs exposed to 50, 200, and 600 ppm of UDMH for single or multiple 60-, 15-, and 5-minute periods, respectively, showed no adverse physiological effects. These levels of UDMH should serve as a basis from which short-term exposure standards may be estimated for man.

UNCLASSIFIED

UNCLASSIFIED