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SHORT-TERM INHALATION EXPOSURES OF RODENTS TO PENTABORANE-9

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TO PENTABORANE-9**

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FOREWORD

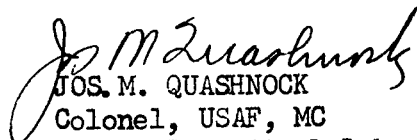
Investigations of short-term inhalation exposures of rodents to pentaborane-9 described herein were conducted by Francis W. Weir, Dale W. Bath, and Maurice H. Weeks of the Directorate of Medical Research, U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland. They were performed under Air Force Project No. 7165, "Health Hazards of Materials and Radiation," Task No. 716501, "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 December 1960 and completed September 1961.

Animal experimentation was performed in accordance with the Rules for Animal Care established by the American Medical Association.

ABSTRACT

Rats and mice were exposed to pentaborane to determine the concentration causing 50 per cent deaths for single 5-, 15-, 30-, and 60-minute exposure periods. The LC50 values for single 5-, 15-, 30-, and 60-minute exposure periods were: for rats, 66.6, 31.2, 15.2, and 10.4 ppm, respectively; for mice: 40.5, 18.6, 10.6, and 7.8 ppm, respectively. Information from these exposures is to be used in planning further studies which will aid in the estimation of safe levels for short human exposures to this compound.

PUBLICATION REVIEW


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SHORT-TERM INHALATION EXPOSURES OF RODENTS TO PENTABORANE-9

INTRODUCTION

During the past 10 years increasing interest has been shown in the use of boron hydride compounds as a source for more powerful fuels and propellants. Accidental exposures have indicated that this class of compounds is very toxic and presents a health hazard to personnel handling these materials (6).

Toxicity data from animal experimentation show that pentaborane is one of the more toxic compounds of this group. Feinsilver *et al.* report a 4-hour LC50 value of 5.8 ppm of pentaborane for rats and 3.4 ppm for mice (2). Exposures of rats and mice for 6 hours per day, 5 days a week, to 1.0 ppm pentaborane resulted in 9 of 12 rats dead and 8 of 11 mice dead after 12 exposures (5).

The American Conference of Governmental Industrial Hygienists (ACGIH) suggested a tentative threshold limit value of 0.005 ppm for pentaborane (9). Bases for this recommendation were toxicological observations on animals (4,5), and human exposures (6,7). Concern for the health of workers handling this highly toxic compound presents a need for animal data from single, short-term exposures to pentaborane.

The object of the present investigation was to determine the LC50's of pentaborane to rats and mice for single 5-, 15-, 30-, and 60-minute exposures. The results from this investigation will be used in planning further studies on animals. Information from these investigations will aid in the estimation of safe levels for short human exposures to this compound.

MATERIALS AND METHODS

The pentaborane (B_5H_9) used in these experiments was obtained from Callery Chemical Co., Callery, Pa. The material was dispersed into the chamber by a method similar to the one described by Svirebely (8). The only significant modification in the method of dispersion was that the temperature of the pentaborane cylinder was maintained at $2.0^\circ C (\pm 0.1^\circ C)$ with a refrigerated water bath.

The exposures were carried out in a 0.4 cu m dynamic-flow gassing chamber operated at a flow rate of 0.25 cu m/minute. Animals were introduced and withdrawn from the chamber by a sliding carriage assembly. Measured samples of chamber-air were drawn through Edgewood-type collection

bubblers containing 20 ml of purified Cellosolve* and analyzed for boron by a procedure based on the carmine method of Hatcher and Wilcox (3). The analytical results expressed in mg of boron per ml of sample were used to calculate the chamber concentration as ppm of pentaborane.

Young male white rats weighing 100 to 120 gm and female CF-1 mice weighing 20 to 24 gm were used in these experiments. Groups of 10 animals each, chosen at random, were exposed to various levels of pentaborane for single 5-, 15-, 30-, and 60-minute periods. Groups of control animals were observed for mortality along with the exposed animals.

All animals were observed for toxic signs and death during exposure and the survivors for 7 days post-exposure. The LC50's with 19/20 confidence limits and slopes of the dose response curves with their standard errors were calculated by the method of Bliss (1).

RESULTS

The 5-, 15-, 30-, and 60-minute LC50 values for rats exposed to pentaborane with 19/20 confidence limits and slopes of the dose-response curves with their standard errors are shown in table 1. The exposure concentrations and mortality from each experiment are detailed in table 2.

Toxic signs noted in the order of onset were tremors, ataxia, convulsions, a reddish exudate around the mouth and nose, and death. Most of the animals that died from exposure died within 4 hours after completion of the exposure. All deaths occurred within 24 hours after exposure.

DISCUSSION

The toxic signs seen in the present investigation are similar to those reported in previous investigations. In our experiments with rodents, only small differences were noted between the concentration producing no apparent toxic response and maximum response. However, a linear relationship is seen between the LC50 values and exposure times

*Cellosolve is a trade mark of the Union Carbide & Carbon Corporation for the monoethyl ether of ethylene glycol.

TABLE 1

LC50 VALUES FOR RATS AND MICE EXPOSED TO PENTABORANE

<u>Species</u>	<u>Exposure Period</u> min	<u>LC50</u> ppm	<u>19/20 Confidence Limits</u> ppm	<u>Slope</u>	<u>Standard Error of Slope</u>
Rats	5	66.6	65.1 - 68.1	44.9	± 13.6
Rats	15	31.2	30.3 - 32.2	31.8	± 9.1
Rats	30	15.2	14.1 - 16.4	12.2	± 3.7
Rats	60	10.4	9.7 - 11.1	16.8	± 4.7
Mice	5	40.5	38.4 - 42.6	17.9	± 5.3
Mice	15	18.6	17.8 - 19.4	20.1	± 5.2
Mice	30	10.6	8.2 - 13.9	5.8	± 2.5
Mice	60	7.8	7.4 - 8.1	22.5	± 13.2

TABLE 2

MORTALITY IN RODENTS EXPOSED TO PENTABORANE

RATS				MICE			
Exposure Period min	Concentration ppm	Mortality Fraction (No Dead/No Exposed)	Exposure Period min	Concentration ppm	Mortality Fraction (No Dead/No Exposed)		
5	62.2	0/10	5	28.7	0/10		
	66.5	4/10		33.5	1/10		
	65.3	6/10		36.4	1/10		
	70.2	8/10		36.4	2/10		
15	84.7	10/10	15	38.8	2/10		
	29.0	0/10		37.5	5/10		
	32.5	7/10		43.5	7/10		
	32.8	7/10		15.4	1/10		
30	34.3	8/10	30	18.4	2/10		
	31.4	9/10		18.8	5/10		
	13.0	2/10		20.4	7/10		
	14.7	4/10		18.9	8/10		
60	15.5	6/10	60	21.9	10/10		
	17.1	7/10		10.5	2/10		
	19.3	9/10		13.0	5/10		
	7.5	0/10		13.2	6/10		
60	9.8	3/10	60	9.6	7/10		
	10.7	7/10		12.7	8/10		
	12.9	9/10		15.8	10/10		
	15.1	10/10		6.9	0/10		
					7.3	1/10	
					6.9	3/10	
					7.4	3/10	
					7.5	5/10	
					11.6	10/10	

when the logs of the LC50's are plotted against the logs of the exposure times. Since linearity exists between these levels of response, perhaps estimates of other time-effect factors may be calculated at lower levels of pentaborane exposures. However, our present knowledge on the effects from short, single exposures to pentaborane is not sufficient to permit such estimates due to the lack of a clear definition of the toxic action of this compound.

The most critical need at the present is some sensitive, measurable change as an index of exposure. With this measurement of effect, estimates of the maximum intensities of single exposure without detectable adverse physiological changes should be possible.

SUMMARY

The concentrations of pentaborane causing 50% deaths of rats and mice for single 5-, 15-, 30-, and 60-minute exposures were determined. Toxic signs were tremors, ataxia, convulsions, and death. The LC50 values for single 5-, 15-, 30-, and 60-minute exposure periods were: for rats, 66.6, 31.2, 15.2, and 10.4 ppm, respectively; for mice, 40.5, 18.6, 10.6, and 7.8 ppm, respectively. Small differences were noted between the concentration producing no apparent toxic response and maximum response.

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<p>ASD TR 61-663</p> <p>U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland</p> <p>SHORT-TERM INHALATION EXPOSURES OF RODENTS TO PENTABORANE-9, by F. W. Weir, D. W. Bath, and M. H. Weeks. December 1961. 12p. incl. tables. 9 refs. (Proj. 7165; Task 716501) Unclassified report</p> <p>Rats and mice were exposed to pentaborane to determine the concentration causing 50 per cent deaths for single 5-, 15-, 30-, and 60-minute exposure periods. The LC50 values for single 5-, 15-, 30-, and 60-minute exposure periods were: for rats, 66.6, 31.2, 15.2, and 10.4 ppm, respectively; (over)</p>	<p>UNCLASSIFIED</p> <p>I. Weir, F. W. II. Bath, D. W. III. Weeks, M. H. IV. Aeronautical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio</p> <p>V. MIPR No. (33-616) 60-41</p> <p>UNCLASSIFIED</p>	<p>ASD TR 61-663</p> <p>U. S. Army Chemical Research and Development Laboratories, Army Chemical Center, Maryland</p> <p>SHORT-TERM INHALATION EXPOSURES OF RODENTS TO PENTABORANE-9, by F. W. Weir, D. W. Bath, and M. H. Weeks. December 1961. 12p. incl. tables. 9 refs. (Proj. 7165; Task 716501) Unclassified report</p> <p>Rats and mice were exposed to pentaborane to determine the concentration causing 50 per cent deaths for single 5-, 15-, 30-, and 60-minute exposure periods. The LC50 values for single 5-, 15-, 30-, and 60-minute exposure periods were: for rats, 66.6, 31.2, 15.2, and 10.4 ppm, respectively; (over)</p>	<p>UNCLASSIFIED</p> <p>I. Weir, F. W. II. Bath, D. W. III. Weeks, M. H. IV. Aeronautical Systems Division, Aerospace Medical Laboratory, Wright-Patterson Air Force Base, Ohio</p> <p>V. MIPR No. (33-616) 60-41</p> <p>UNCLASSIFIED</p>
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