

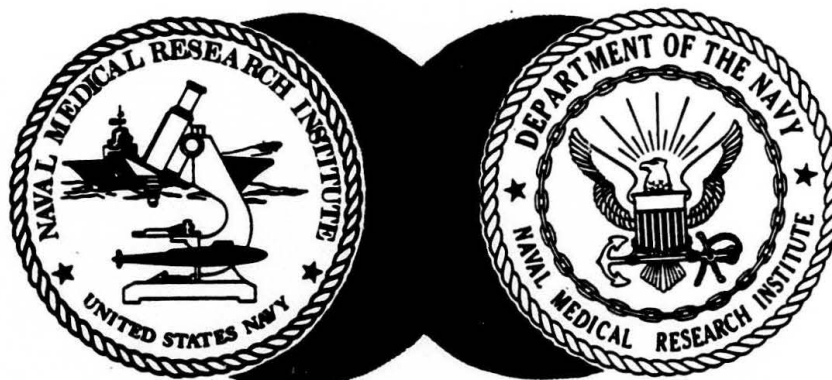
2

12

NAVAL MEDICAL RESEARCH INSTITUTE

BETHESDA, MARYLAND

AD A088427



79-0112

EFFECTS OF OXYGEN AND CARBON DIOXIDE ON CARBON MONOXIDE TOXICITY

F.L. Rodkey and H.A. Collison

W. F. Miner, CAPT, MC, USN

Commanding Officer

Naval Medical Research Institute

NAVAL MEDICAL RESEARCH AND DEVELOPMENT COMMAND

DDC FILE COPY

80 8 28 005

DTIC
ELECTE
AUG 28 1980

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER (14) NMRI-79-0112	2. GOVT ACCESSION NO. AD-A088427	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) (6) EFFECTS OF OXYGEN AND CARBON DIOXIDE ON CARBON MONOXIDE TOXICITY.	5. TYPE OF REPORT & PERIOD COVERED (9) Medical Research Progress Report.	6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) (10) F. Lee/Rodkey and Harold A./Collison	8. CONTRACT OR GRANT NUMBER(s) (11) 5 Mar 79	
9. PERFORMING ORGANIZATION NAME AND ADDRESS Naval Medical Research Institute Bethesda, Maryland 20014 PE 61158N	10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS (16) MR041.01.004.0002 Report No. 4	
11. CONTROLLING OFFICE NAME AND ADDRESS Naval Medical Research and Development Command Bethesda, Maryland 20014	12. REPORT DATE August, 1979	
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office) Bureau of Medicine and Surgery Department of the Navy Washington, D. C. 20372	13. NUMBER OF PAGES 5 (17) MR04101004	15. SECURITY CLASS. (of this report) UNCLASSIFIED
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited. and sale		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES Published in Journal of Combustion Toxicology, Vol. 6, 208-212, 1979		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Toxic effects of fire gases; oxygen; carbon dioxide; carbon monoxide; carboxyhemoglobin		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Mean survival time (MST) and fatal blood carboxyhemoglobin (COHb) have been measured in rats exposed to simulated fire atmospheres containing carbon monoxide. Addition of carbon dioxide to the atmosphere decreased MST but did not change the final COHb. Atmospheres with decreased oxygen caused markedly lower MST with an increase in COHb at death. The changes of MST and COHb observed are largely explained by the stimulation of pulmonary ventilation from three sources: 1) decreased inspired oxygen content, 2) the "cellular hypoxia" from increased COHb, and 3) an increased CO2 of the expired air.		

S/N 0102- LF- 014- 6601

F. LEE RODKEY AND HAROLD A. COLLISON

*Laboratory of Analytical Biochemistry
Naval Medical Research Institute
National Naval Medical Center
Bethesda, Maryland, 20014*

EFFECTS OF OXYGEN AND CARBON DIOXIDE ON CARBON MONOXIDE TOXICITY

Original manuscript received March 5, 1979

Revised manuscript received June 12, 1979

ABSTRACT: Mean survival time (MST) and fatal blood carboxyhemoglobin (COHb) have been measured in rats exposed to simulated fire atmospheres containing carbon monoxide. Addition of carbon dioxide to the atmosphere decreased MST but did not change the final COHb. Atmospheres with decreased oxygen caused markedly lower MST with an increase in COHb at death. The changes of MST and COHb observed are largely explained by the stimulation of pulmonary ventilation from three sources: 1) decreased inspired oxygen content, 2) the "cellular hypoxia" from increased COHb, and 3) an increased CO₂ of the inspired air.

INTRODUCTION

FIRES ABOARD SHIPS lead to the production and accumulation of a complex mixture of toxic components. Acute effects of the toxic environment on crew members in closed spaces of the ship may be rapid, incapacitating and lethal. The composition of the fire atmosphere is partially determined by the chemical composition of the burning material [1], the conditions under which the burning or pyrolysis occurs [2], and the amount of dilution of the fire atmosphere with normal air. Carbon monoxide is the major toxic gas produced by most fires. In confined spaces the decrease in O₂ content and increase in CO₂ associated with combustion contribute in a major way to the physiological response to the fire atmospheres though changes in O₂ and CO₂ do not appear as a serious problem in open fires [3,4].

The present study was done to determine how the toxicity of CO in normal air was changed by increasing the CO₂ content and/or lowering the O₂ of the simulated fire atmosphere. Mean survival time (MST) of rats and fatal blood COHb levels were chosen to measure the relative CO toxicity in the different atmospheres.

EXPERIMENTAL

The 250-300g female rats used were the outbred stock of the Naval Medical Research Institute, NMRI:O(SD)CV. They were maintained on a standard rat chow and water *ad libitum*. Exposures were conducted in groups of 6 rats in a 15-liter glass chamber [5]. The atmosphere in the glass chamber was continuously mixed with a

Reprinted from Journal of COMBUSTION TOXICOLOGY, Vol. 6 (August, 1979)

0362-1669/79/02 0208-05 \$04.50/0

© 1979 Technomic Publishing Co., Inc.

small (7 watt) fan. The temperature of the chamber was maintained between 23.5° and 27°C. Control MST [6] values in the absence of CO₂ were determined with mixtures of 0.6% CO in air or in a 14% O₂-86% N₂ mixture. Experimental MST values were determined with increasing amounts of CO₂ but maintaining a constant O₂ concentration at either 21 or 14% by appropriate reduction in the nitrogen content. Cessation of respiratory movements was taken as the end point and exposure was continued until all 6 rats died. Blood samples for measurement of fatal blood % COHb were obtained from the heart or inferior vena cava with disodium ethylenediamine tetraacetic acid as anticoagulant. Gas chromatograph procedures were used to measure the CO content of the exposure gas [7] and of the blood [8]. Total hemoglobin was determined as cyanmethemoglobin [9].

RESULTS

The subjective observations of the rats were similar in all exposures. Within two or three minutes after the animals were placed in the contaminated atmosphere there was agitation, and all animals moved about the cage. Most animals lost the ability to walk in about four minutes, and the rats tended to pile on one another rather than just falling on the cage bottom. Only respiratory movements were observed after this time; no muscular convulsions other than gasping were observed during any exposure.

The MST values together with the fatal levels of blood COHb are presented in Table 1. The fatal blood COHb was 85% when the atmosphere contained 21% O₂ and was unchanged in the presence of CO₂. A significantly higher level of COHb ($p < 0.01$) was observed in 14% O₂, but this value also was not changed at any CO₂ concentration studied.

Table 1. Mean Survival Time and Fatal Blood COHb of Rats Breathing 0.6% CO.

Atmosphere		N ^a	MST ^b Minutes	COHb ^c %
O ₂ %	CO ₂ %			
21	0	9	22.4 ± 0.8	83.4 ± 0.9
21	2.1	4	18.4 ± 1.1	86.4 ± 0.4
21	4.5	5	16.8 ± 0.6	84.3 ± 0.5
14	0	3	9.6 ± 0.3	89.4 ± 1.0
14	2.3	4	10.1 ± 0.8	90.6 ± 0.4
14	5.4	5	10.4 ± 0.6	90.2 ± 0.4

^aNumber of exposures of 6 rats each.

^bMean Survival Time ± Standard Error of the Mean.

^cMean % COHb ± Standard Error of the Mean.

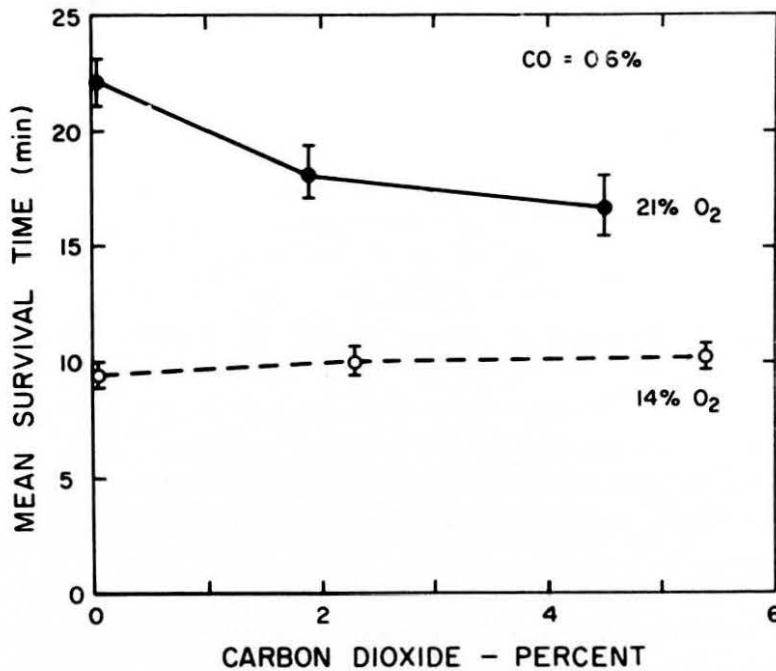


Figure 1. Effects of carbon dioxide on the Mean Survival Time of rats breathing 0.6% carbon monoxide in 21% oxygen (●) and in 14% oxygen (○). The standard error of the mean is indicated by the vertical lines at each concentration of CO₂.

The data in Figure 1 graphically show the significant decrease in MST caused by decreased O₂ in the absence ($p \ll 0.01$) and in the presence of CO₂ ($p < 0.01$). The addition of 2% CO₂ in the presence of 21% O₂ caused a significant decrease in MST ($p < 0.02$) which was not changed by further addition of CO₂ ($p > 0.2$). Addition of either level of CO₂ in the presence of 14% O₂ did not change ($p > 0.3$) the MST.

DISCUSSION

A concentration of CO, 0.6%, was chosen to exceed the rat LD₅₀ for 60-minute exposure [10] and to insure that all animals would die within an hour. The extreme range of individual survival time observed was 6 to 36 minutes. The decreased survival time and increased fatal COHb concentration caused by the 14% O₂ results from two effects. First, due to the extreme hypoxia the hemoglobin in the pulmonary capillary is more highly deoxygenated leading to an increased rate of removal of CO from the alveolar gas. Second, the hypoxic stimulation of pulmonary ventilation brings in a greater volume of contaminated air from which the CO is more effectively absorbed. Low O₂ is expected to increase the rate of COHb change by both effects [11]. These data indicate that hypoxia leads to a marked decrease in MST whether or not there is a simultaneous increase in CO₂. There was, indeed, no effect of CO₂ over that of hypoxia alone in 14% O₂.

The experiments in 21% oxygen demonstrate the decrease in MST caused by CO₂ alone. Carbon dioxide is known to stimulate the rate of pulmonary ventilation. Though the extent of such stimulation for rats has not been completely determined, it may reasonably be assumed to be similar to that for man [12]. Carbon dioxide stimulates both the rate and depth of respiration such that there is reproducible increase in pulmonary ventilation with CO₂ concentration. The data of Comroe [12] show that control pulmonary ventilation is increased 1.4 times in 2% CO₂ and 4.9 times in 5% CO₂. The fall in MST of rats observed here reflects this stimulation of respiration and the extraction of CO from a greater volume of inspired contaminated air. The combined effect in 21% O₂ by 2% CO₂ and the "cellular hypoxia" from the accumulated COHb caused a significant decrease in the measured MST. Physiological limits on this effect are shown by the fact that no further significant decrease in MST was observed by increasing the CO₂ to 5%, though at least a 3-fold increase in pulmonary ventilation [12] would be expected. It was quite clear that respiratory stimulation from "cellular hypoxia" due to the accumulating COHb was important. Even in the absence of CO₂ at 21% O₂ we observed an increased depth of respiration to the degree of "gasping" after 3 to 5 minutes of exposure.

The fatal levels of COHb suggest that the blood was nearly in equilibrium with the inspired air before respiration ceased. An equilibrium maximum COHb of 87.4% and 93.3% breathing 21% or 14% O₂, respectively, was calculated [13]. Data in Table 1 provide evidence that the COHb reached to within about 3% saturation of the calculated equilibrium values with a high degree of certainty. This is true in all cases even though the MST varied in the extreme from 6 to nearly 40 minutes. These experiments demonstrate that the fatal level of COHb depends upon the inhaled oxygen concentration. Above a certain level of COHb, however, respiration will continue for a shorter time at the more elevated COHb levels.

Fire gas atmospheres, especially in closed spaces, contain lower oxygen with higher carbon dioxide and carbon monoxide than normal air. Data on MST in rats cannot be directly transposed to human reactions. It is clear, however, that hypoxia alone as well as elevated CO₂ cause a decrease in MST. It was also observed that the period of purposeful movements in the rats followed, in a qualitative way, the change in MST. Thus one can expect that the time during which a human could respond to or escape from a fire will be lowered in a similar manner even when fatal levels of COHb are not reached.

FOOTNOTES

1. From the Naval Medical Research and Development Command, NNMCM, Department of the Navy, Research Task No. MR041.01.1004-0002. The opinions and assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

2. The experiments recorded herein were conducted according to the principles set forth in the "Guide for the Care and Use of Laboratory Animals", Institute of Laboratory Resources, National Research Council, DHEW Pub. No. (NIH) 74-23.

REFERENCES

1. R.E. Reinke and C.F. Reinhardt, Fires, Toxicity and Plastics. *Modern Plastics*, 50:94-98 (1973).
2. A. Fish, N.H. Franklin and R.T. Pollard, Analysis of Toxic Gaseous Combustion Products, *J. Appl. Chem.*, 13:506-509 (1963).
3. W.A. Burgess, R. Sidor, J.J. Lynch, P. Buchanan and E.V. Clougherty, Minimum Protection Factors for Respiratory Protective Devices for Fire Fighters, *Am. Ind. Hyg. Assoc. J.*, 38:18-23 (1977).
4. A. Gold, W.A. Burgess and E.V. Clougherty, Exposure of Fire Fighters to Toxic Air Contaminants, *Am. Ind. Hyg. Assoc. J.* 39:534-539 (1978).
5. L.J. Leach, A Laboratory Test Chamber for Studying Airborn Material, AEC Research and Development Report UR-629:1-12 (1963).
6. L.J. Jenkins, Jr., R.A. Jones and M.E. Anderson, The Use of Mean Survival Time Analysis to Determine Comparative Toxicity of Fire Atmospheres, *J. Combust. Toxicol.*, 4:87-96 (1977).
7. F.L. Rodkey, Carbon Monoxide Estimation in Gases and Blood by Gas Chromatography, *Ann. N.Y. Acad. Sci.*, 174, Art. 1:261-267 (1970).
8. H.A. Collison, F.L. Rodkey and J.D. O'Neal, Determination of Carbon Monoxide in Blood by Gas Chromatography, *Clin. Chem.*, 14:162-171 (1968).
9. E.J. Van Kampen and W.G. Zijlstra, Standardization of Hemoglobinometry II. The Hemiglobincyanide Method, *Clin. Chim. Acta*, 6:538-544 (1961).
10. G. Kimmerle, Apparatus and Methodology for the Evaluation of Toxicological Parameters During Fire Exposure, *J. Combust. Toxicol.*, 1:4-51 (1974).
11. R.F. Coburn, R.E. Forster and P.B. Kane, Consideration of the Physiological Variables that Determine the Blood Carboxyhemoglobin Concentration in Man, *J. Clin. Invest.*, 44:1899-1910 (1965).
12. J.H. Comroe, *Physiology of Respiration* Yearbook Medical Publishers, Inc., 1965, p. 59-69.
13. F.L. Rodkey, H.A. Collison and J.D. O'Neal, Carbon Monoxide and Methane Production in Rats, Guinea Pigs, and Germ-free Rats, *J. Appl. Physiol.*, 33:256-260 (1972).

Accession For	
NO. 1001	☒
NO. 100	
Unpublished	
JANUARY 1978	
By _____	
Distribution/	
Classification Code	
Author/	Editor/
Dist	Rel
A 20	