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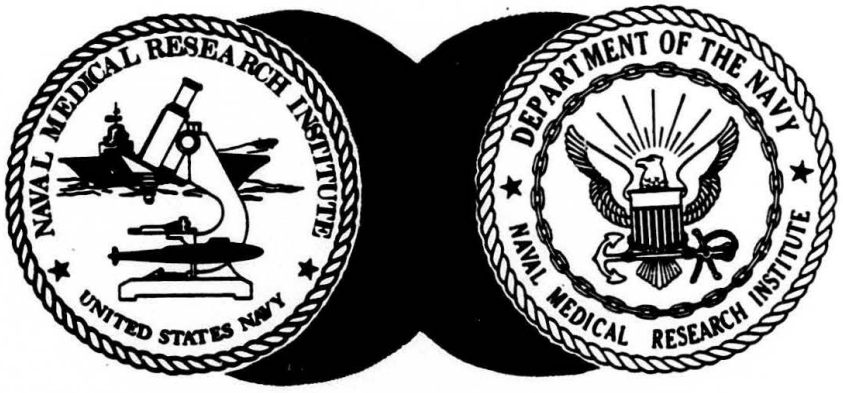

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EFFECTS OF OXYGEN AND CARBON DIOXIDE ON CARBON MONOXIDE TOXICITY

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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 inspirated oxygen content, 2) the "cellular hypoxia" from increased COHb, and 3) an increased CO_2 of the expired air.

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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 inspirated oxygen content, 2) the "cellular hypoxia" from increased COHb, and 3) an increased CO_2 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 O_2 content and increase in CO_2 associated with combustion contribute in a major way to the physiological response to the fire atmospheres though changes in O_2 and CO_2 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 CO_2 content and/or lowering the O_2 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

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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 CO_2 were determined with mixtures of 0.6% CO in air or in a 14% O_2-86% N_2 mixture. Experimental MST values were determined with increasing amounts of CO_2 but maintaining a constant O_2 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% O_2 and was unchanged in the presence of CO_2. A significantly higher level of COHb ($p < 0.01$) was observed in 14% O_2, but this value also was not changed at any CO_2 concentration studied.

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

Atmosphere				
O_2 %	CO_2 %	N[a]	MST[b] Minutes	COHb[c] %
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

[a] *Number of exposures of 6 rats each.*
[b] *Mean Survival Time* ± Standard Error of the Mean.
[c] Mean % COHb ± Standard Error of the Mean.

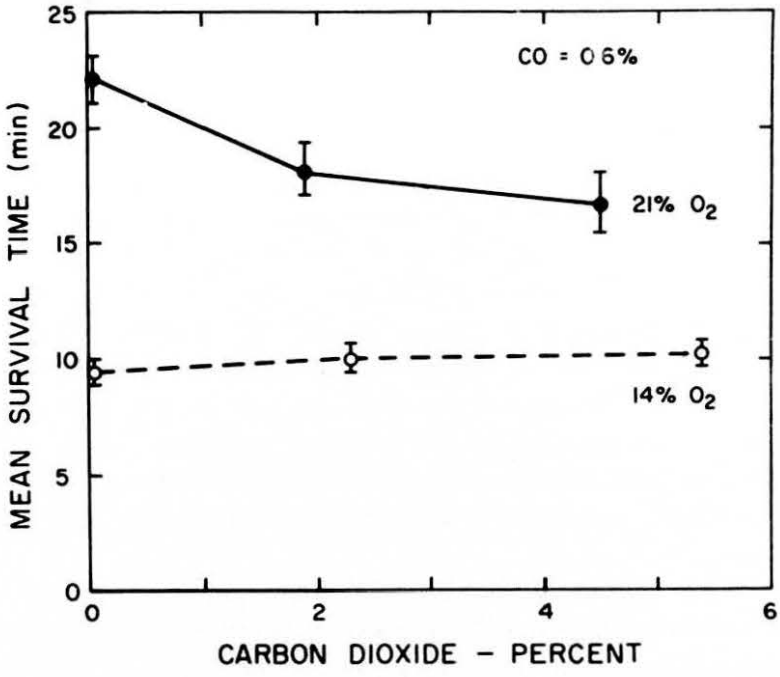

Figure 1. Effects of carbon dioxide on the Mean Survival Time of rats breathing 0.6% carbon monoxide in 21% oxygen (●) and in 14% oxygen (O). The standard error of the mean is indicated by the vertical lines at each concentration of CO_2.

The data in Figure 1 graphically show the significant decrease in MST caused by decreased O_2 in the absence ($p \ll 0.01$) and in the presence of CO_2 ($p < 0.01$). The addition of 2% CO_2 in the presence of 21% O_2 caused a significant decrease in MST ($p < 0.02$) which was not changed by further addition of CO_2 ($p > 0.2$). Addition of either level of CO_2 in the presence of 14% O_2 did not change ($p > 0.3$) the MST.

DISCUSSION

A concentration of CO, 0.6%, was chosen to exceed the rat LD_{50} 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% O_2 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 O_2 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 CO_2. There was, indeed, no effect of CO_2 over that of hypoxia alone in 14% O_2.

The experiments in 21% oxygen demonstrate the decrease in MST caused by CO_2 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 CO_2 concentration. The data of Comroe [12] show that control pulmonary ventilation is increased 1.4 times in 2% CO_2 and 4.9 times in 5% CO_2. 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% O_2 by 2% CO_2 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 CO_2 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 CO_2 at 21% O_2 we observed an icnreased 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 eqiuilibrium maximum COHb of 87.4% and 93.3% breathing 21% or 14% O_2, 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 CO_2 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, NNMC, 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.

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