TABLE 2

RELATIVE SUSCEPTIBILITY OF THREE HOUSEFLY STRAINS TO RESIDUAL DEPOSITS OF BENZENE HEXACHLORIDE

Housefly strain	No. of insects used		Percent kill in 24 hr	
	Male	Female	Male	Female
		5-min exposure		
Slaughterhouse	97	166	100	65
Laboratory	147	146	100	67
Quaranfil	71	96	6	4
		10-min exposure		
Slaughterhouse	93	133	98	90
Laboratory	207	101	99	74
Quaranfil	108	122	8	4
		30-min exposure		
Slaughterhouse	119	135	100	100
Laboratory	221	102	100	100
Quaranfil	110	105	15	12
		60-min exposure		
Slaughterhouse	136	93	100	100
Laboratory	199	88	100	100
Quaranfil	125	116	84	42
		120-min exposure		
Slaughterhouse	...	...	...	...
Laboratory	...	...	...	...
Quaranfil	163	108	86	62

There were no reversals in any of the comparisons.

Entomologists have hoped that benzene hexachloride would be one of the residual-type insecticides that could be used satisfactorily in situations where houseflies have developed resistance to DDT. The results obtained in Quaranfil indicate that any benefit derived from a change to this insecticide might be only temporary.

Acceleration of Carbon Monoxide Elimination in Man by High Pressure Oxygen[1]

Nello Pace, Enrique Strajman, and Elaine L. Walker

Division of Physiology, and The Donner Laboratory, University of California, Berkeley

Claude Bernard (*2*) was the first to point out that carbon monoxide produces hypoxia through its reversible combination with blood to form carboxyhemoglobin, and pure oxygen at normal barometric pressures has been used as an effective therapeutic aid in the treatment of CO poisoning ever since it was first tried by Linas and Limousin (*8*). The relative affinity relationship between CO and O_2 for hemoglobin has been enunciated by Douglas, Haldane, and Haldane (*5*) in the form $\frac{[COHb]}{[HbO_2]} = K\frac{[pCO]}{[pO_2]}$ where K, the relative affinity constant, has been measured to be 210 for man (*12*). The rationale for increasing the partial pressure of inspired O_2 in the treatment of CO poisoning, therefore, seems clear on the basis of mass action consideration alone, and a direct relationship between alveolar pO_2 and the rate of CO elimination from the body might be expected. Such a relationship has been demonstrated recently for man (*10*), and will be reported in detail later. The rate of CO elimination in man is increased approximately fivefold from a half-time of over 4 hr while breathing air to a half-time of about 45 min while breathing pure oxygen, corresponding to the fivefold increase in pO_2.

The most serious effect of CO inhalation was convincingly demonstrated by Haldane (*7*) to be the combination of the gas with the blood hemoglobin and the consequent reduction in O_2-carrying capacity of the blood. In his classic experiment, a mouse was exposed in a pressure chamber to one atmosphere of CO and two atmospheres of oxygen with no loss of consciousness or obvious ill effects, the mouse apparently having met its metabolic oxygen requirement by utilizing the greatly increased oxygen in physical solution in the blood plasma. There is implicit in this experiment the use of oxygen at pressures higher than normal barometric pressure for the treatment of CO poisoning, and End and Long (*6*) have shown the worth of high pressure oxygen in treating laboratory animals after exposure to CO. Reluctance to use high pressure oxygen in the treatment of persons suffering CO poisoning stems from the toxic nature of oxygen itself at pressures of one atmosphere and higher; however, as pointed out by Bean (*1*), there is a relationship between time and concentration in the development of oxygen poisoning. This makes it possible to select an optimal combination of exposure time and ambient oxygen partial pressure such that the rate of CO elimination may be materially increased without incurring the risk of oxygen poisoning.

Following mild, acute exposure to CO, ten volunteer subjects, comprising five men and five women, were placed in a recompression chamber[2] at 22 psi gage pressure. Measurements of the rate of CO elimination were carried out while the individuals seated at rest, breathed pure oxygen for 1 hr. In this way, the subjects were exposed to an ambient pO_2 of 2.5 atmospheres. The procedure consisted in allowing the subject to rebreathe a mixture of 250 ml of CO and 2 l of air from a rubber bag for 30 sec. The individual was then seated in the recompression chamber, and the ambient pressure was raised to 2.5 atm, absolute. Oxygen breathing was begun through an A-14 mask with free flow from a tank of medical oxygen, and the first blood sample was withdrawn from the antecubital vein after a few minutes. The initial blood levels of CO ranged from 20% to 30% COHb, and blood samples were withdrawn by venepuncture every 15 min during the hour of oxygen breathing. The samples were analyzed for CO content by the method of Scholander and Roughton (*11*), and the rate of elimination was determined as the slope of the line of least squares through a plot of the logarithm of blood concentration against time. As shown elsewhere (*10*), CO elim-

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[2] Thanks are due to the Commandant, San Francisco Naval Shipyard and to Lieutenant W. M. Minor, U. S. N., and the men of the Ship Salvage Unit for permission to use the recompression chamber and for its operation.

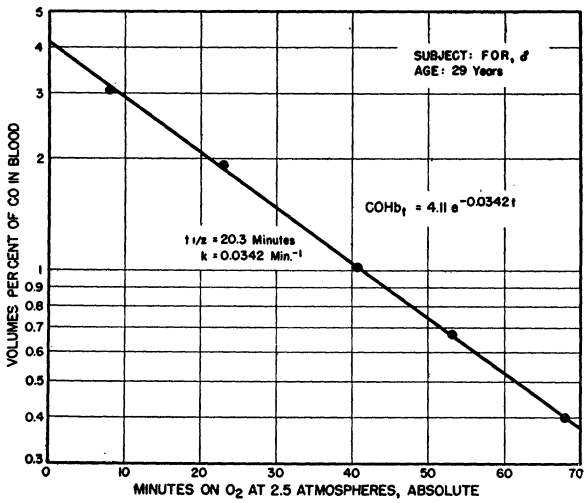

FIG. 1. CO elimination curve from the venous blood of a man breathing pure oxygen at an ambient pressure of 2.5 atm, absolute, following mild, acute exposure to CO. The line and equation parameters were obtained by the method of least squares. Each point is the mean of a triplicate blood analysis.

ination under standard conditions of activity follows a simple exponential rate expression of the type: $COHb_t = COHb_0 e^{-kt}$ where $COHb_t$ is the blood concentration of CO at time t, $COHb_0$ is the concentration at zero time, and k is the rate constant measured as the slope of the line described previously. The rate constant, k, represents the fraction of blood CO eliminated per unit time, and may be expressed as a half-time of elimination by the relationship: $t_{\frac{1}{2}} = \frac{\ln 2}{k}$. The results of a typical experiment are shown in Fig. 1, and it is to be noted that the slope of the time, i.e., the rate constant, is determined on the basis of five points, each of which is the mean of a triplicate analysis on the blood samples they represent.

The CO elimination rate data obtained on the ten subjects are seen in Table 1. Care was taken to select individuals in a comparable age group so as to control the effect of age on CO elimination (*9*).

TABLE 1

RATE OF CO ELIMINATION BY MEN AND WOMEN BREATHING PURE OXYGEN AT 2.5 ATMOSPHERES, ABSOLUTE

Male subjects	Age (yr)	k (min^{-1})	$t_{1/2}$ (min)	Female subjects	Age (yr)	k (min^{-1})	$t_{1/2}$ (min)
STR	34	0.0363	19.1	WAL	25	0.0447	15.5
GLA	24	0.0262	26.5	JOH	28	0.0465	14.9
KAW	30	0.0318	21.8	THI	27	0.0444	15.6
PAC	33	0.0289	24.0	POW	27	0.0495	14.0
FOR	29	0.0342	20.3	SYR	27	0.0447	15.5
Mean	30.0	0.0315	22.3	Mean	26.8	0.0460	15.1

As discussed elsewhere (*10*), a significant sex difference in the rate of CO elimination is apparent in these data. It may also be noted that the half-time of elimination is of the order of 20 min, so that 1 hr of oxygen breathing in the recompression chamber at 2.5 atm, absolute, will result in reduction of blood carboxyhemoglobin level to 10% or 15% of whatever the starting level might have been. It follows, then, that 1 hr is the maximum exposure to a pO_2 of 2.5 atm necessary for lowering blood CO to safe limits, i.e., below three volumes percent. One hour is a completely tolerable exposure to this pO_2 in regard to oxygen-poisoning symptoms (*1*).

For purposes of comparison, mean rates of CO elimination by men and women breathing ordinary air and pure oxygen at normal barometric pressure are given in Table 2. The alveolar pO_2, as calculated from the equation of Brink (*3*), is included because blood is in equilibrium with alveolar rather than ambient pO_2, and hence the alveolar pO_2 is more meaningful in considering relative O_2 and CO affinities for hemoglobin.

Again, the pronounced sex difference is seen in the rate of elimination, women losing CO about 30% more rapidly than do men under comparable conditions; for present purposes it suffices merely to point out this finding. It may also be seen from Table 2 that although there is a great increase in CO elimination rate when pure oxygen is breathed at normal barometric pressure, the half-time of elimination is still long in terms of the

TABLE 2

COMPARISON OF MEAN RATE OF CO ELIMINATION BY MEN AND WOMEN BREATHING OXYGEN AT VARIOUS PARTIAL PRESSURES

Ambient pO_2 (atm)	Calculated alveolar pO_2 (atm)	Male				Female			
		No. of subjects	Mean age (yr)	Mean k (min^{-1})	Mean $t_{1/2}$ (min)	No. of subjects	Mean age (yr)	Mean k (min^{-1})	Mean $t_{1/2}$ (min)
0.2	0.14	5	30.0	0.0028	249	5	26.2	0.0039	179
1.0	0.89	10	27.1	0.0150	47	5	26.6	0.0199	36
2.5	2.37	5	30.0	0.0315	22	5	26.8	0.0460	15

rapidity with which the deleterious effects of hypoxia set in. Hence, in treatment of CO poisoning, where not only resuscitation of the victim but avoidance of serious and permanent after effects of prolonged hypoxia is also important, the further increase in CO elimination rate by administration of O_2 under high pressure seems of considerable practical value.

Another point to consider is the increase in oxygen carried in physical solution by the blood plasma. Under normal conditions of air breathing, the amount of dissolved oxygen is insignificant in comparison with the metabolic requirements of the body. The dissolved oxygen accounts for 1% of the normal arterial blood oxygen content, and is approximately 0.2 vol % (*13*). The arteriovenous oxygen difference for man at rest as measured between arterial blood and mixed venous blood by right auricle catheterization is found to be about 4.5 vol % (*4*). If, however, pure oxygen is breathed at 2.5 atm ambient pressure, the dissolved oxygen may be calculated to increase to just 4.5 vol %. Direct measurement of the dissolved oxygen under these conditions was not made

in the present study, but it was noted that venous blood samples withdrawn for CO analysis were consistently a bright red color in the high pressure experiments, in contrast to those drawn under other conditions, indicating a high degree of oxygen saturation of venous blood. In any case, it is apparent that the resting metabolic oxygen needs may be met almost completely by the dissolved oxygen when pure oxygen is breathed at 2.5 atm pressure. Thus, in addition to a significant acceleration in CO elimination rate, administration of oxygen at high pressure would also seem to relieve hypoxia immediately in victims of CO poisoning.

Clinical trial of high pressure oxygen as a means of therapeusis in CO poisoning therefore appears warranted, and is recommended where suitable pressure chamber facilities are available. There is no evident reason why its use cannot be coupled with a number of standard mechanical resuscitative devices, thereby extending its application to cases where respiration has stopped. In general, to go beyond CO poisoning, high pressure oxygen might be used profitably in many situations where the hemoglobin oxygen transport mechanism has been rendered inoperative, and may be regarded as a valuable adjunct to the already well-established technique of oxygen therapy.

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Further Investigation of the Reducibility of Lyophilized Catalase

Alexander L. Dounce and Robert R. Schwalenberg

Department of Biochemistry, School of Medicine and Dentistry, University of Rochester, Rochester, New York

It was reported by Dounce and Howland (*1*) that crystalline beef liver catalase became completely reducible with sodium hydrosulfite after lyophilization, as shown by the change in the visible absorption spectrum, although activity of the material per dry weight was reduced only to about one-third of the value obtained before lyophilization. Keilin (*2*) subsequently denied that these experimental results had been interpreted correctly, stating that a mixture of denatured and undenatured catalase must have been obtained, in which only the undenatured catalase was active and only the denatured catalase was reducible. No experimental work was offered to support these statements, however.

Our previous work was handicapped by the lack of a modern spectrophotometer. We have recently repeated the experiments using the Beckman spectrophotometer, and have completely confirmed our previous results, as indicated by the accompanying figures.

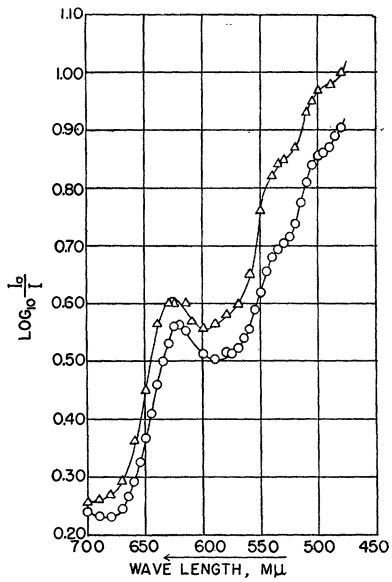

FIG. 1. Absorption spectra of lyophilized and nonlyophilized catalase. △ = 26.4 mg lyophilized catalase, Kat. f. = 14,000 in 4 ml of M/10 phosphate buffer, pH 8.0. ○ = 26.4 ml nonlyophilized catalase, Kat. f. = 25,000 in 4 ml of M/10 phosphate buffer, pH 8.0, containing 10% NaCl.

Fig. 1 shows the spectrum of a sample of recrystallized catalase which had not been lyophilized, with a Kat. f. value[1] of 25,000, together with the spectrum of a different sample of lyophilized material of Kat. f. about 14,000 which had been prepared from a sample of recrystallized catalase of Kat. f. about 23,000. The location of the three principal absorption bands is the same, but contrary to previous results (*1*) the spectra do not superimpose exactly. This might be partly ascribable to a difference in ionic strengths of the solutions, since M/10 phosphate buffer of pH 8.0 made up to contain 10% NaCl was used as the solvent for the material which

[1] The term *Kat. f.* is an abbreviation for *Katalase Fähigkeit.* It was introduced by von Euler and Josephson (*4*), and means

$$\frac{K \times \text{dilution}}{\text{g enzyme}}.$$

Here *K* is the so-called monomolecular reaction velocity constant extrapolated to zero time (*3*); *g enzyme* refers to the dry weight of enzyme per millimeter of the stock solution; and *dilution* means the number of times the stock solution is diluted before carrying out the determination.