EFFECT OF ACUTE CARBON MONOXIDE POISONING ON WORK CAPACITY INFLUENCE OF 5% CO₂ ON RATE OF RECOVERY

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Donald and Paton in 1955 reviewed the theoretical and historical aspects of the administration of gases during artificial respiration. They paid particular attention to the treatment of severe carbon monoxide poisoning with respiratory depression, and emphasized the importance of immediate artificial respiration and the administration of oxygen. They condemned the use of 5% carbon dioxide in oxygen (carbogen) in such patients on the grounds that a patient with respiratory depression must already have excessive amounts of carbon dioxide in his blood, and further administration of carbon dioxide can do no good and might well do harm, 'since a very high carbon dioxide level in the blood depresses the respiratory centre and may cause death. Their arguments appear conclusive.

The arguments for and against the use of carbogen are not so clear-cut in cases of lesser severity in which respiratory depression has either not occurred or has improved after effective artificial respiration. It is obvious that the use of carbogen can be justified in such patients only if it can be shown that it significantly increases the rate at which carbon monoxide is eliminated from the body and if the rapid elimination of carbon monoxide is a factor in avoiding such sequelae as brain damage (Dutra, 1952), myocardial infarction (Hadley, 1952), or pneumonia.

The main purpose of this work was to compare the effect of carbogen and pure oxygen on the rate of elimination of carbon monoxide in four acutely poisoned

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normal subjects. The effect of carbon monoxide on respiration, pulse rate, and the ability to carry out steady work has also been studied.

Method

The experiments were performed by the four of us, all normal healthy subjects, on each other. Each walked at a steady 2½ miles (4 km.) an hour on a motor-driven treadmill. The carbon monoxide was administered by injecting slowly 100 ml. or 150 ml. of pure carbon monoxide into the inspiratory side of a simple open breathing circuit to which the subject was connected. Under these conditions about half of the carbon monoxide injected is absorbed (Bates, 1952). The mixed expired gas was continuously sampled and analysed by an infra-red carbon monoxide meter. Every 15 minutes the pulse and respiratory rates were noted, and when the circuit was shown to be clear of the injected carbon monoxide a sample of expired air was collected for two minutes. This was analysed for oxygen and carbon dioxide on a Haldane apparatus and for carbon monoxide by infra-red analysis. Simultaneously with the collection of expired gas, 10 ml. of venous blood was taken into a heparinized syringe and analysed for carbon monoxide by the method of Lawther and Apthorp (1955).

When the COHb saturation of the subject's blood was estimated to be between 30 and 50% the treadmill was stopped and the subject was assisted to a couch. Oxygen and carbogen (5% CO₂/95% O₂) were then administered for alternate 10-minute periods. The time was accurately measured by stopwatch, and 10-ml. venous blood samples were taken every 10 minutes at each change of inspired gas mixture.

Calculation

The volume of blood cleared of carbon monoxide per minute while breathing air during the exercise phase was calculated from the volume of carbon monoxide expired as follows:

$$\begin{aligned} & \text{Volume of blood cleared of carbon monoxide} \\ &= \frac{\text{Volume of CO expired in 1 minute}}{\text{Volume of CO in 1 ml. blood}} \quad \text{ml. cleared/min} \\ &= \frac{\text{Minute-volume (ml./min.)} \times \text{CO\% in mixed expired air}}{\text{Volumes \% CO in blood}} \quad \frac{\text{ml. cleared}}{\text{min.}} \end{aligned}$$

During the recovery phase the volume of blood cleared of carbon monoxide per minute was calculated from the decrease in blood carbon monoxide content over the 10-minute period, the blood volume being estimated according to the formula of Hicks *et al.* (1956).

Volume of blood cleared of carbon monoxide

$$= \frac{\text{COHb}^1 - \text{COHb}^2}{\text{COHb}^2 \times 10} \times \text{B.V. ml. cleared/min.},$$

where COHb¹ = Vols. CO per 100 ml. of blood at beginning of 10-minute period;

Table of Results

	Gas Breathed	Subject G.H.A.			Subject D.M.			Subject D.V.B.			Subject R.M.		
		COHb%	Min. Vol. l./min.	ml. Blood Cleared min.	COHb%	Min. Vol. l./min.	ml. Blood Cleared min.	COHb%	Min. Vol. l./min.	ml. Blood Cleared min.	COHb%	Min. Vol. l./min.	ml. Blood Cleared min.
Exercise 2½ m.p.h.	Air	20.0	15.5	23.2	15.6	15.8	25.5	11.7	21.9	33.3	6.3	18.8	36.0
	"	25.5	17.0	32.5	28.6	15.2	26.8	15.6	22.8	36.4	14.0	17.5	32.3
	"	30.2	13.6	28.4	33.0	17.8	31.6	23.2	22.7	37.0	19.0	17.5	29.7
	"	38.5	13.9	26.2	37.5	16.0	29.0	26.4	19.6	36.2	28.5	16.3	32.6
	"	43.5	15.5	26.4									
	"	51.3											
Recovery phase	Oxygen	32.5	14.5*	104	33.3	7.5	89	23.0	7.25	89	29.3	9.0	78
	CO ₂ /O ₂	28.0	9.3†	73	29.0	12.7	97	18.7	21.6	139	24.3	15.1	114
	Oxygen	24.0	18.0*	102	24.9	9.1	95	14.9	7.7	97	20.4	7.7	80
	CO ₂ /O ₂	20.7	7.5†	52	21.3	11.1	106	12.1	22.4	130	17.0	19.3	108
	Oxygen	17.3	18.25*	136	18.5	9.0	89	10.0	7.9	77	14.3	7.7	65
	CO ₂ /O ₂	15.0	11.8†	69	16.2	13.8	104	8.5	20.1	107	12.1	23.7	112
Mean values	Oxygen	13.2	15.85*	132									
	Air												
Mean values	Air		15.1	27.3		16.1	28.2		21.7	35.7		17.7	32.6
	Oxygen		16.6*	119		8.5	93		7.6	88		8.1	74
	CO ₂ /O ₂		9.5†	64		12.5	102		21.4	125		19.3	111

The first column indicates the gas breathed—air, 100% oxygen, or 5% CO₂/95% O₂. COHb% = Blood level of carbon monoxide in terms of % saturation. Min. vol. l./min. = Minute-volume in litres per minute. ml. blood cleared/min. = Volume of blood cleared of carbon monoxide per minute in millilitres. Subject G.H.A. voluntarily hypoventilated while breathing CO₂/O₂† and hyperventilated while breathing oxygen*.

COHb²=vols. CO per 100 ml. of blood at end of 10-minute period;
COHb³=mean value at mid-point of period in ml. per 100 ml. blood;
B.V. =blood volume in ml.

The results are shown in full in the Table. In Fig. 1 the effect of the increasing blood COHb% on the minute volume, oxygen uptake, and pulse rate is shown for each experimental subject. Only the pulse rate shows any consistent change, and there is no evidence of respiratory depression.

FIG. 1.—All subjects exercising continuously at 2½ miles (4 km.) an hour on the flat. The scale is identical in all figures. Each arrow indicates an injection into the circuit of pure carbon monoxide, 100 ml. in subjects R. M. and D. V. B., and 150 ml. in subjects G. H. A. and D. M. Pulse/min.=Radial pulse rate per minute. Vent. l./min.=Volume breathed out per minute. Blood COHb%=Blood carbon monoxide level in terms of % of haemoglobin saturated with carbon monoxide.

Fig. 2 shows the results of observations made during the recovery period, when each subject breathed oxygen and carbogen for alternating 10-minute periods. All breathed normally except subject G. H. A., who voluntarily hyperventilated while breathing oxygen and hypoventilated as best he could while breathing carbogen. Although there is considerable scatter, the results show an increase in the volume of blood cleared as the minute-volume of ventilation increases. Doubling the minute-volume during oxygen-breathing from 8 to 16 l./min. increases the volume of blood cleared per minute from about 75 to 100 ml. This increased clearance is independent of whether pure oxygen or carbogen is administered and appears to be solely related to the hyperventilation, which was voluntary in the case of subject G. H. A. and due to the carbogen in the other three subjects. The doubling of the ventilation therefore causes about a 30% increase in the rate of excretion of carbon monoxide. In a subject whose blood volume is 5 litres, ignoring the carbon monoxide bound to myohaemoglobin, the time to halve the blood carbon monoxide content would be reduced from about 41 minutes to about 25 minutes by doubling the minute ventilation.

Symptoms

Only one subject (D. V. B.) complained of headache, which started when his blood was 20% saturated. He had no other symptoms. Subject D. M. had no symptoms, but was unsteady when the treadmill was stopped. Subject R. M. had no symptoms at all. In subject G. H. A. a greater quantity of carbon monoxide was administered. He complained of feeling "muzzy" between 30 and 40% saturation and became ataxic between 40 and 50% saturation, being unable to stand without support. There was no loss of consciousness, but further administration of carbon monoxide was thought unwise. These symptoms are similar to those observed by Haldane in his classical experiments upon himself (Haldane and Priestley, 1935).

Discussion

During the whole of the exercise and intake period no change occurred in respiratory rate or minute-volume breathed. This finding is in agreement with the work of Asmussen and Chiodi (1941). They showed that ventilation was increased and dyspnoea caused only when the oxygen content of both the plasma and the haemoglobin was reduced by 20-30% by breathing a gas mixture low in oxygen; but no change occurred when 20-30% of the haemoglobin was bound to carbon monoxide. In the latter case, although the haemoglobin bound to carbon monoxide is unable to transport oxygen, the remaining haemoglobin and the plasma are fully saturated with oxygen after passing through the lung capillaries, and consequently the oxygen tension of the blood is little changed. Dyspnoea is not, therefore, a symptom of carbon monoxide poisoning. A rise in pulse rate occurred in all subjects when the blood became 30% saturated with carbon monoxide, and in one subject rose significantly before this level was reached.

Asmussen and Chiodi also noticed a tachycardia in their three subjects when the blood was about 30% saturated with carbon monoxide. They suggested that this increase in heart rate might be due to anoxic dilatation of peripheral

FIG. 2.—Volume of blood cleared of carbon monoxide per minute is plotted against ventilation (volume breathed out per minute) in l./min. ●=Breathing air during steady exercise. ○=Breathing 100% oxygen during recovery. ×=Breathing 5% CO₂/95% O₂ during recovery. □=Breathing 100% oxygen but voluntarily hyperventilating. +=Breathing 5% CO₂/95% O₂ but voluntarily hypoventilating.

capillaries causing a decreased venous return to the heart. This in turn would lower the stroke output of the heart and cause a compensatory tachycardia to maintain cardiac output. But since heart muscle has a large blood supply and high extraction of oxygen it seems likely that it will be one of the first organs in the body to be affected by carbon monoxide poisoning. In addition, the myohaemoglobin in the heart muscle will take up some carbon monoxide and there may be interference with the intracellular transport of oxygen. It seems possible, therefore, that the tachycardia may be due to the direct effect of carbon monoxide on the myocardium.

The lack of symptoms during the early stages was most noticeable. Headache occurred in only one subject, and the tiredness and dyspnoea on moderate exercise described as occurring at these levels of saturation (Claudy, 1955) were not noticed. The ability to carry out moderate exercise was unimpaired until ataxia developed. The oxygen consumption remained unchanged. This is in marked contrast to the situation found in cases of severe and prolonged carbon monoxide poisoning. A patient recently admitted to this hospital was in coma two hours after removal from the source of carbon monoxide, although at that time the blood was only 20% saturated with COHb. Three hours after removal she was still semicomatose, the blood level then being only 11.8% saturated. These observations can be contrasted with those in this experiment in which all four subjects were symptom-free at the 20% saturation level, and subject G. H. A., who is a heavy smoker, was 9% saturated before the start of the experiment.

It seems certain that the patient was suffering from the results of cerebral anoxia. The condition of such a patient may be compared to that which follows prolonged hypoglycaemia, when consciousness is not fully regained until some hours after the sugar content of the blood has been returned to normal. It seems likely that in a patient suffering from prolonged exposure to carbon monoxide the speed of recovery once he has reached hospital will be mainly influenced by the length of time anoxia has been present and the degree of cerebral damage present. Clearly the rate of elimination of carbon monoxide during resuscitation is only one factor involved in the prognosis.

The rate of elimination of carbon monoxide during steady exercise while breathing air corresponds to a halving of blood level in 160 minutes. This is a somewhat faster rate of elimination than Roughton and Root (1945) observed at rest while breathing air. They found that the saturation was halved in 240 minutes. This difference is due to the increased cardiac output and ventilation during exercise.

During the recovery phase the rate of elimination of carbon monoxide was related to the minute-volume, so that doubling of the minute-volume caused a 30% increase in the rate of elimination. This increase was unrelated to the presence of carbon dioxide as such, as it occurred when the subject voluntarily hyperventilated pure oxygen. On theoretical grounds the rate of elimination of carbon monoxide is directly proportional to the alveolar oxygen tension, so that a sixfold increase in alveolar oxygen tension causes a sixfold increase in the rate of elimination of carbon monoxide. This has been confirmed experimentally by Lilienthal (1950). If 5% carbon dioxide is added to the inspired oxygen the rate of elimination will be further increased by an amount dependent on the hyperventilation caused by the CO₂.

A further action of carbon dioxide, unrelated to any effect it may have on the rate of elimination of carbon monoxide from the body, is the marked increase in cerebral blood flow which follows the administration of this gas (Kety and Schmidt, 1948). This increased blood flow may be of benefit to patients suffering from anoxic cerebral damage. Conversely, it should be remembered that manual or mechanical hyperventilation on pure oxygen will lower substantially the carbon dioxide content of the blood and correspondingly decrease cerebral blood flow.

These considerations suggest that the resuscitation of patients suffering from carbon monoxide poisoning must be based on recognition of the following principles:

1. Immediate administration of oxygen to combat anoxia. It is important that masks should be very carefully fitted and continually supervised, since it is essential that inspired oxygen be at the highest possible concentration. B.L.B. or plastic masks, while adequate for most clinical situations, are not likely to be the best possible appliances for this purpose. An anaesthetic mask and apparatus with a skilled administrator should provide the necessary high oxygen concentration.

2. Adequate ventilation to ensure that the alveolar oxygen tension is at the highest possible level. If respiration is depressed, intubation and manual ventilation might be used by an anaesthetist, or a respirator might be employed for this purpose. The administration of carbon dioxide would be indicated only if it could be observed to be producing hyperventilation.

3. Such hyperventilation would no longer be indicated when the COHb saturation had returned to a very low level, but if severe cerebral damage has occurred the patient may still be deeply comatose and care must be taken that the level of ventilation is adequate.

Summary

During steady state exercise four normal subjects were given pure carbon monoxide to raise their blood carbon monoxide levels to between 30 and 50% saturated. No change occurred in respiratory rate, minute-volume breathed, or in oxygen consumption. Tachycardia occurred in all subjects, and the cause of this is discussed.

The rate of elimination of carbon monoxide was compared during the breathing of oxygen to that during the breathing of carbogen (5% carbon dioxide in oxygen). It was found that carbogen caused an increase in the rate of elimination of carbon monoxide due to the increase in minute-volume it produced. The doubling of the minute-volume caused a 30% increase in the rate of elimination of carbon monoxide. The implications of this finding are discussed in relation to the problem of treatment of carbon monoxide poisoning.

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According to the *Annual Report of the Ministry of Labour and National Service for 1957* (H.M.S.O., 8s.), a special attack has been made on the problem of fires in factories. Investigations into future fires are to be co-ordinated so that the various Government departments concerned with their prevention can co-operate more closely in the task. The *Report* stresses the importance of factories having escape routes in case of fire and of the workers being led along them from time to time so that they shall know where they are. The Ministry has also carried out an investigation with the object of improving the standard of first aid in factories.