CARBOGEN IN EXPERIMENTAL CARBON-MONOXIDE POISONING

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The use of carbon dioxide with oxygen (carbogen) for the treatment of carbon-monoxide poisoning was first suggested by Henderson and Haggard (1920) after a series of experiments on dogs in which they used 10% carbon dioxide and 90% oxygen. Later they recommended the use of a mixture of 95% oxygen and 5% carbon dioxide (Haggard and Henderson, 1922). Nicloux, Nerson, Stahl, and Weill (1925) and Walton, Eldridge, Allen, and Witherspoon (1926) were unable to confirm the great increase in the speed of carbon-monoxide elimination which Haggard and Henderson claimed to be due to the presence of carbon dioxide. They therefore advocated the use of pure oxygen only as the treatment of choice. Carbogen mixtures, however, were almost universally adopted throughout the world.

The Medical Research Council Committee for Research on Breathing Apparatus for Protection against Dangerous Fumes and Gases condemned the use of mixtures of oxygen and carbon dioxide in resuscitation (Donald and Paton, 1955). This was done on the hypothesis that a patient in severe respiratory depression was inevitably already suffering from the effects of an excess of carbon dioxide in his tissues and was in urgent need of oxygen alone. In this country carbogen was therefore replaced by oxygen in the first-aid treatment of carbon-monoxide poisoning by ambulance men, by mine-rescue teams, and by other first-aid groups. This change provoked vigorous criticism by certain experienced clinicians, among whom was Marriott (1955a, 1955b), who had successfully treated large numbers of cases of carbon-monoxide poisoning with 7% carbogen. Marriott agreed that the use of carbon dioxide in the treatment of respiratory depression from most causes was illogical, but he urged that carbon-monoxide poisoning was a special case where it was vital that the body should be rid of carbon monoxide by the most rapid and effective means possible, and that was by the use of carbogen.

The work of Killick and Marchant (1959) on dogs clearly demonstrated that 5% carbogen cleared the blood of carbon monoxide significantly faster than did oxygen alone: carbogen produced no dangerous side-actions. The use of 5% carbogen was then given official sanction by the Medical Research Council (1958). The Council also stated that they did not consider that there was anything to be gained by the use of a higher percentage of carbon dioxide in oxygen.

Marriott (1958) still maintained, however, that the best results could only be obtained by the use of 7% carbogen rather than 5%. He emphasized his point by quoting the percentage of deaths from carbon-monoxide poisoning in New York over a period of eight years. During the first three years 5% carbogen was used: in this period there was a higher percentage of deaths than during the succeeding five years when 7% carbogen was used.

In view of all this it seemed desirable to compare experimentally the relative efficiencies of 5% and of 7% carbogen in the treatment of carbon-monoxide poisoning. This was done by gassing a dog under standard conditions until the blood level of carboxy-haemoglobin was 70%. The dog was then given 5% carbogen to breathe and the time required for the gas to be excreted was noted. Several weeks later, under identical conditions, the experiment was repeated in the same dog using 7% carbogen.

Method

The animals were anaesthetized by the intravenous route with minimal doses of pentobarbitone sodium to allow the insertion of a cuffed Magill endotracheal tube: a "polythene" catheter was passed down the external jugular vein to the right atrium to permit sampling of mixed venous blood. Two groups, A and B, each of 10 dogs, were used.

Group A

The circuit shown in Fig. 1 was attached to the endotracheal tube. A T-junction was applied close behind the Heidbrink valve, and through one limb of this passed a supply of oxygen to replace that used by the animal. The carbon dioxide produced by the dog was removed by a to-and-fro soda-lime absorber of the Waters type. Through the other limb of the T-junction measured amounts of pure carbon monoxide were admitted to the circuit. After the addition of each increment of carbon monoxide the concentration of carboxyhaemoglobin in

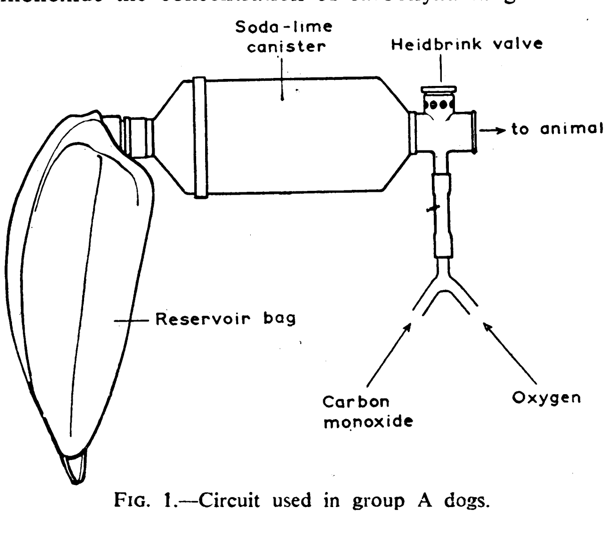

FIG. 1.—Circuit used in group A dogs.

the blood was estimated. The level rose in a stepwise fashion until 70% saturation was reached, taking an average of 45 minutes to do so. At this point gassing was stopped and the resuscitating mixture was applied direct to the inspiratory side of the Heidbrink valve. This latter was now set with the minimal amount of tension on the spring which retains the valve disk in its seating. The soda-lime canister was removed, retaining the bag, which was allowed to fill with the resuscitating mixture and was emptied frequently during the process of resuscitation.

Blood samples were removed at 1, 3, 5, 7, 9, 12, and 15 minutes, and thereafter at five-minute intervals from the beginning of resuscitation until carboxyhaemoglobin could be no longer detected. Thereafter the animals breathed air.

In three dogs of this group the procedure was repeated after several weeks, substituting a Ruben non-return valve for the Heidbrink valve. Again 5% and 7% carbogen were tested. This was done because there is reason to believe that the Heidbrink valve, even with the minimum spring-loading possible, allows a degree of rebreathing while the Ruben valve does not.

Group B

In this series coal-gas and air were withdrawn from cylinders of these gases and passed through a system of flowmeters. The gas mixture then passed into a large reservoir bag and finally on to the dog through a Ruben non-return valve (Fig. 2).

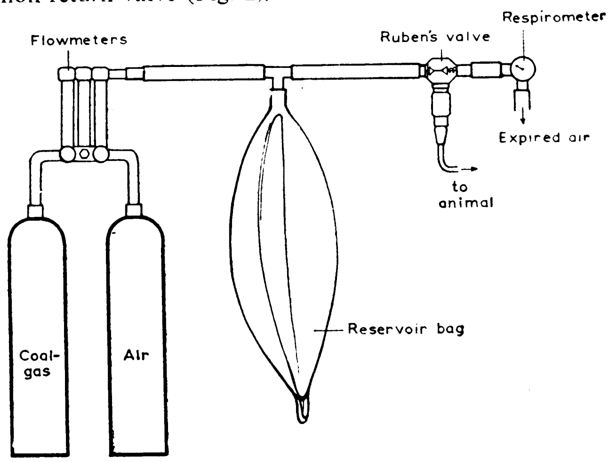

FIG. 2.—Circuit used in group B dogs.

Since the coal-gas in the cylinder contained 18.8% carbon monoxide and the gases were delivered at rates of 100 ml. gas/min. and 5 l. air/min., the gas delivered to the dog contained 0.37% carbon monoxide. The use of the Ruben valve ensured that the gas mixture delivered to the animal was of known composition and prevented rebreathing.

The rising carboxyhaemoglobin levels were again recorded during the period of gassing, and when the 70% level was reached, after an average period of two hours, the carbogen mixture under test was fed into a 20-litre rubber bag which was connected to the inspiratory side of the Ruben valve. The carboxyhaemoglobin levels were followed in the same manner as in group A until the carbon-monoxide content of the blood was negligible.

Estimation of Carboxyhaemoglobin

All estimations of carboxyhaemoglobin levels were performed by Harrison's (1957) quantitative method, using a Hartridge reversion spectroscope. In each group all the observations were made by one observer using his own calibration curve, constructed from the mean values obtained from measurements made on the blood of six dogs.

This method had the advantage of speed and simplicity, but in order to confirm the results obtained by it two other methods of determining carboxyhaemoglobin were carried out in certain cases. They were: (1) the spectrophotometric method of Heilmeyer and Krebs as described by Heilmeyer (1943), using a Unicam SP. 600 spectrophotometer; and (2) the manometric method of Van Slyke and Neill (1924) as modified by Horvath and Roughton (1942).

Table I shows the results obtained when the three methods were applied to the same samples of blood. It will be seen that there is good agreement among the methods down to a level of 35% as recorded by the reversion spectroscope.

TABLE I.—*Estimations of Carboxyhaemoglobin Percentage on the Same Blood Samples by Three Methods*

Reversion Spectroscope	Manometric Method	Spectrophotometric Method
72	80	81
69	78	80
62	64	74
61	58	58
53	53	59
45	49	57
44	43	50
37	41	44
22	38	39
20	29	33
19	27	30
3	23	25

It was therefore decided to take the time for the carboxyhaemoglobin percentage to fall from 70% to 35%—that is, the half-clearance time (T/2)—as a parameter with which to compare the efficiency of treatment of one group with another.

Results

Table II shows the half-clearance times obtained in animals of group A when resuscitated with 5% and 7% carbogen on the circuit utilizing the Heidbrink valve.

TABLE II.—*Half-clearance Times of 10 Dogs Resuscitated with 5% and 7% Carbogen, Using a Heidbrink Valve in the Circuit*

Dog	5% Carbogen. T/2 (min.)	7% Carbogen. T/2 (min.)
1	17	14
2	21	17
3	18	11
4	21	18·5
5	19	19
6	13	12
7	21	13
8	27	15·5
9	30	27
10	18·5	16
Mean	20·55 (S.D.=4·9)	16·3 (S.D.=4·6)

The difference between the means of the half-clearance times suggests that 7% carbogen clears the blood of carbon monoxide faster than does 5%—in 16.3 minutes as compared with 20.6 minutes—although the difference is not statistically significant.

In the three animals on which the experiment was repeated, substituting the Ruben for the Heidbrink valve, the increased efficiency of the 7% carbogen mixture disappears: 5% and 7% carbogen appear to be about equal in their effect as judged by the time taken to lower the concentration of carboxyhaemoglobin from 70% to 35%. This is shown in Table III.

In the animals of group B (Table IV) where only the Ruben valve was used, the difference between the means of the half-clearance times for animals resuscitated by 5% and by 7% carbogen again no longer exists—13.8 and 13.4 minutes.

TABLE III.—*Half-clearance Times from Three Dogs when Resuscitated with 5% Carbogen and Then with 7%, Using a Heidbrink Valve and Then a Ruben Valve in the Circuit*

Dog	Heidbrink Valve		Ruben Valve	
	5% Carbogen T 2 (min.)	7% Carbogen T/2 (min.)	5% Carbogen T/2 (min.)	7% Carbogen T 2 (min.)
4	21	18·5	10	8
5	19	19	15	12
8	27	15·5	17	24
Mean	22·3	17·7	14	14·7

TABLE IV.—*Half-clearance Times of 10 Dogs Resuscitated with 5% and 7% Carbogen with the Ruben Non-return Valve in the Circuit*

Dog	5% Carbogen. T 2 (min.)	7% Carbogen. T/2 (min.)
A	9	9
B	17	12·5
C	10	15
D	10	12
E	15	15
F	11	6
G	16	15
H	13	14·5
I	21·5	19
J	15	16
Mean	13·75 (S.D. = 3·9)	13·40 (S.D. = 3·7)

Discussion

Although the results of the first series of experiments (Table II) demonstrate that 7% carbogen clears the blood of carbon monoxide more rapidly than does 5% on the same animals, the second series (Tables III and IV) shows no such difference. The only alteration in the technique of resuscitation is the use of the Heidbrink valve for the first group and the Ruben valve for the second. Further, the difference in mean half-clearance time shown in Table II when 5% and 7% carbogen are used with the Heidbrink valve disappears when the Ruben valve is used. This clearly demonstrates that the difference is a function of the respiratory valve used in the circuit and indicates the importance of using a respiratory valve which does not permit rebreathing when resuscitation is undertaken.

There seems to be little point in using 7% carbogen in preference to 5%, since 5% carbogen will clear the blood of monoxide as efficiently as 7% if a respiratory valve which does not allow rebreathing is placed in the circuit by which the mixture is applied.

None of the dogs in either series died during gassing or resuscitation, though many were gassed to apnoea—an event which occurs shortly after the 70% level of carboxyhaemoglobin is recorded by the reversion spectroscope. Respiratory failure always occurred before cardiac arrest. When respiration ceased, artificial respiration was undertaken by rhythmically squeezing the rebreathing bag filled with the appropriate carbogen mixture for the experiment. All the dogs recovered uneventfully and seemed perfectly well by the following day. Up to three months later there was no evidence of neurological or other damage.

Summary

Two groups of 10 dogs were gassed with carbon monoxide until the level of carboxyhaemoglobin was 70%. The animals were then resuscitated using 5% and 7% carbogen in turn. In group A a Heidbrink valve was placed in the resuscitating circuit and there was a difference in efficiency of resuscitation in favour of 7% carbogen. In group B a Ruben non-return valve was placed in the resuscitating circuit and no difference between the efficiency of 5% and 7% carbogen was demonstrated. The choice of a respiratory valve which prevents rebreathing when resuscitation is undertaken in carbon monoxide poisoning is thus more important than the choice of a 5% or a 7% carbogen mixture.

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A NEW STERNAL REFLEX IN CASES OF SEVERE CEREBRAL DAMAGE

BY

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In man the sternal region has a specific sensitivity that can be explained in terms of ontogenetic and phylogenetic evolution. Sherrington (1898, 1911, 1915) observed that stimulation of the sternal area in male frogs evokes reflex movements of the fore-limbs, and that these movements are enhanced by decapitation. This, then, is purely a spinal phenomenon suppressed by higher levels of the central nervous system. Many physiological reflexes are suppressed as cerebral evolution progresses, especially if they have no significant value in normal states. But these reflexes become evident in pathological conditions. Minkowski (1921, 1928) insisted that abnormal responses in adults reflect ontogenetic evolution. Moro (1918, 1920) has described a sternal reflex in infants resembling that of Sherrington. After four months of life Moro's reflex becomes inhibited, though persisting much longer in mentally deficient infants. These observations are of great value in understanding the sternal reflex which can be elicited in the presence of cerebral damage. Such lesions abolish the physiological suppression and reveal responses which are found in the early stages of ontogenetic and phylogenetic evolution. Even in physiological states, when subcortical centres are preponderant—that is, during sound sleep—reflexes similar to those described by Sherrington can be obtained by stimulating the skin