

THE COMPOSITION OF THE GASES OF THE BLOOD  
IN CHLOROFORM-ANÆSTHESIA. BY G. A. BUCK-  
MASTER AND J. A. GARDNER.

(From the Physiological Laboratory, University of London.)

LITTLE attention has been paid to the changes in composition of the blood-gases in chloroform-anæsthesia, in spite of the well-known fact that, as the various stages of anæsthesia by chloroform which are clinically recognised succeed one another, the aspect of arterial blood to the naked eye becomes progressively venous in character. This change in colour must be due either to an altered ratio of oxy-hæmoglobin to reduced hæmoglobin, or to changes in form of the red corpuscles, which consequently reflect different amounts of light to the eye, as the observations of Harless in 1846 showed was possible when blood outside the body is saturated with oxygen or carbon-dioxide gas. The researches of Hamburger, G. N. Stewart and others have demonstrated that a many-sided exchange exists between the red corpuscles and plasma, which may be accompanied by an alteration in their volume and shape. When defibrinated blood is saturated with carbon-dioxide, some dissociated electrolytes pass from the corpuscles into the serum, and at the same time water enters the corpuscles, so that these individually become swollen, a phenomenon which is obvious by the alteration in the colour of the blood, which then becomes darker. Formanèk, Krüger and Edie have also shown that *in vitro* quantities of chloroform added to blood in amounts which produce no visible precipitation alter the colour.

Gangitano<sup>1</sup>, who employed a spectro-photometric method, showed by periodic examinations, extending over many days, of the blood of

<sup>1</sup> F. Gangitano. *Arch. Ital. de Biol.* LI. p. 66. 1909.

patients who had been anæsthetised by chloroform, that the power of their hæmoglobin to fix oxygen was at first diminished, and this did not again become normal for several days. This change is not apparent to the naked eye. Moreover we have never been able to satisfy ourselves that the red corpuscles alter their shape either during anæsthesia or after death by chloroform. It is therefore probable that the darkened aspect of arterial blood is entirely connected with an altered gas-content. Satisfactory information on this point we have been unable to find.

Analyses have been published by Paul Bert<sup>1</sup>, de St Martin<sup>2</sup>, J. Tissot<sup>3</sup> and others, and also by Oliver and Garrett<sup>4</sup> of the gas-content of arterial blood during chloroform narcosis. The results appear to be somewhat conflicting.

Paul Bert considered that as anæsthesia proceeded the arterial blood became progressively poorer in oxygen and richer in carbon dioxide, and we quote one of his experiments on the gas-content of arterial blood in the dog under chloroform narcosis. Before anæsthesia the oxygen was 22·0 c.c. and the carbon dioxide 31·2 c.c. Thirty minutes later the oxygen had fallen to 16·8 c.c. and the carbon dioxide risen to 41·2. One hour later, and ten minutes before death, the value for oxygen was 14 c.c. and for carbon dioxide 44 c.c. De St Martin's analyses confirmed the opinions advanced by Paul Bert, though in some experiments he could find no diminution of oxygen at all in the arterial blood of chloroformed dogs.

The results obtained by J. Tissot only show that when the respiration stops in asphyxia induced by prolonged anæsthetisation arterial blood may contain only ·78 c.c. or 2·83 c.c. of oxygen, while the blood-gases in samples taken at intervals during anæsthesia by chloroform showed only a slight fall in oxygen-content so long as the ventilation of the lungs remained normal. Tissot concluded that during narcosis the blood retains to the time of death the same power of taking up oxygen, and if the amount of this diminishes in the blood, the decrease is solely due to a slowing of the respiration.

The experiments of T. Oliver and F. C. Garrett<sup>4</sup> were carried out on one dog and several rabbits, which were completely narcotised. For

<sup>1</sup> P. Bert. *Étude analytique de l'Anesthésie*, p. 144.

<sup>2</sup> St Martin. *Recherches expér. sur la respiration*, p. 189.

<sup>3</sup> J. Tissot. *Report of the Special Chloroform Committee of Brit. Med. Assoc.*, 1901-1902. Paper V, July 12, 1902.

<sup>4</sup> *Lancet*, Sept. 9, p. 625. 1893.

dog's arterial blood the figures were; CO<sub>2</sub> 37·21 c.c.; Oxygen 17·09; Nitrogen 8·03 c.c.; CHCl<sub>3</sub> ·92 c.c. For rabbits' blood as follows:

	i.	ii.	iii.
CO <sub>2</sub>	6·46	19·33	24·85
O	20·96	16·88	13·14
N	—	38·33	13·7
CHCl <sub>3</sub> }	54·72	4·55	2·59

*Criticism of the foregoing experiments.* We have shown<sup>1</sup> that the presence of chloroform introduces serious errors into the analyses of the gases of the blood which may often contain as much as 10 % of chloroform by volume, and consequently that the method of reducing the nitrogen values to 1·2 %, and adjusting the oxygen accordingly is not justifiable<sup>2</sup>. The French observers make no mention of the presence of chloroform vapour and the analyses of Paul Bert give no figures for nitrogen at all. Thus, so far as can be judged, their results are necessarily unconvincing, and if so cannot be used as a basis for any views as to the gas-content of blood during chloroform anæsthesia. On the other hand, Oliver and Garrett were aware of the presence of chloroform vapour in the blood, and attempted to estimate its amount by combustion; but they made the mistake of combusting the residue *after* the absorption of the carbon dioxide by potash, and oxygen by ferrous tartrate. Some of the chloroform must have dissolved and been decomposed with the formation of carbon monoxide by the re-agents<sup>3</sup>. Their Pflüger pump obviously leaked considerably, and if the enormous nitrogen values are reduced to normal, and the oxygen values adjusted accordingly, the figures obtained are in general agreement with those which we have found in experiments that are described later in this paper.

*Methods in which an attempt was made to eliminate the chloroform by absorption by neutral re-agents.*

A variety of re-agents were tried, such as olive oil, vacuum oil, higher alcohols such as octyl alcohol, but all proved unsatisfactory, as they absorbed other constituents of the gas mixture besides chloroform. Paraffin wax of high melting point, cut into small spheres of about the size of a pea and with a perfectly smooth polished surface, proved less

<sup>1</sup> *Proc. Roy. Soc. B*, LXXXI. p. 516. 1909.

<sup>2</sup> *This Journal*, XL. p. 373. 1910.

<sup>3</sup> *Proc. Roy. Soc. B*, LXXXI. p. 525. 1909.

objectionable than the other re-agents tried. Preliminary experiments, in which measured volumes of chloroform-air mixture were passed into a Hempel pipette filled with paraffin balls and the resultant gases tested for chloroform by passing in a moist condition through a red-hot platinum spiral tube into silver nitrate solution, showed that, provided a sufficient surface of paraffin was used and sufficient time allowed for absorption, all the chloroform in the mixture could be got rid of. Unfortunately, however, the other constituents of the blood-gas were not unaffected by paraffin, but the oxygen was absorbed to a considerably less extent than the carbon dioxide. In the case of oxygen, the gas was run into a Hempel pipette filled with balls of paraffin; in one hour 0.13% was absorbed, in 48 hours 2.4%, in 52 hours 2.8%, and in 76 hours 3.2%. In a similar experiment with carbon dioxide, in 2 hours 4.1% was absorbed, 10.3% after 26 hours. We attempted to minimise this absorption by previously soaking the paraffin balls in a mixture of carbon dioxide and oxygen, but with only moderate success. It was evident therefore that if the chloroform vapour was eliminated in this manner and the blood-gases analysed in the ordinary way, the carbon dioxide would be too low and the chloroform be too high. The oxygen value would be approximately correct. A number of analyses were made by this method, the results of which are given below for what these are worth. The gases were extracted in the Toepler-Barcroft pump and the analyses made with Haldane's apparatus.

The results of the gas analyses are given in the following table; the nitrogen values are adjusted to about 1% and the oxygen figures reduced accordingly, except in the case of Exp. I, which we give to show the figures actually obtained.

The volume of blood taken for a sample was 12.5 c.c. Strength of chloroform and air 2-3%. This was administered through a tracheal cannula provided with Chauveau's valves, 10 to 15 c.c. of hirudin injected (except in Exp. IV) into femoral vein. We give Exp. III in detail. Continuous respiratory tracings were taken throughout the experiments.

### III. Weight of cat 3.5 kilos.

45 mins.	Chloroform off.
47 "	Hirudin injected.
69 "	Reflexes all back.
	Chloroform on.
87 "	Reflexes all gone.
103 "	Sample A, 12.5 c.c.; blood very dark.
	Chloroform off.
	A sample taken at the same time was analysed by the method previously described by us <sup>(1)</sup> , and found to contain 8.9 c.c. of chloroform vapour per 100 grammes of blood.
116 "	Eye reflexes back.
230 "	Sample B, 12.8 c.c.; blood bright red.

## Volumes of gas per 100 c.c. of blood.

No. of Exp.	Mins. from starting chloroform.	Samples A					Reflexes well back, mins. after cessation of $\text{CHCl}_3$	Samples B				
		Total gas in c.c.	$\text{CHCl}_3$ vapour and $\text{CO}_2$ in c.c.		O. in c.c.	N. in c.c.		Total gas in c.c.	$\text{CHCl}_3$ vapour and $\text{CO}_2$ in c.c.		O. in c.c.	N. in c.c.
I	34	57.99	46.24	$\text{CO}_2$ 36.16 $\text{CHCl}_3$ 10.08	8.16	3.6	56	26.72	9.61	$\text{CO}_2$ 8.83 $\text{CHCl}_3$ 0.78	13.26	3.75
II	51	37.28	31.89	$\text{CO}_2$ 22.45 $\text{CHCl}_3$ 9.36	4.10	1.37	69	39.96	26.11	$\text{CO}_2$ 24.35 $\text{CHCl}_3$ 1.76	12.85	1.00
III	34	47.93	40.47	$\text{CO}_2$ 31.93 $\text{CHCl}_3$ 8.54	6.30	1.17	127	40.62	28.05	$\text{CO}_2$ 25.52 $\text{CHCl}_3$ 2.53	10.99	1.56
IV	34	49.34	42.11	$\text{CO}_2$ 33.67 $\text{CHCl}_3$ 8.44	6.24	1.00	89	36.68	21.57	$\text{CO}_2$ 19.68 $\text{CHCl}_3$ 1.87	14.11	1.01

This method of experiment was finally discarded, because a number of observations showed that on making comparative analyses of chloroform-air mixtures by Waller's method and absorption by paraffin, the latter method uniformly yielded lower values, and the discrepancy was greater the higher the percentage of chloroform.

In another series of experiments the oxygen was first absorbed by means of phosphorus; the residual gas, consisting of chloroform vapour, carbon dioxide and nitrogen, was heated with strong potash until no further absorption took place; then mixed with oxygen and electrolytic gas in the well-known proportions, and exploded. The excess of oxygen was then absorbed by alkaline pyrogallate, and the residual nitrogen determined, the chloroform vapour and  $\text{CO}_2$  being thus determined together by difference.

We give three experiments and the protocol of V when the animals were in the second stage of anæsthesia.

Tracings of the respiration were taken, both during and after the animal recovered from the anæsthetic. The results are given with the nitrogen values uncorrected.

V. Weight of cat, 3.3 kilos. Chloroformed in Bell-jar. Operation as in previous experiments.

35 mins. Hirudin injected into femoral vein.

53 ,, Sample taken, 12.5 c.c. blood very dark.

*Volumes of gas per 100 c.c. of blood.*

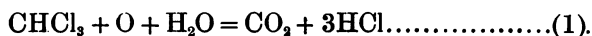
No. of Exp.	Hirudin	Total gases in c.c.	O in c.c.	CO <sub>2</sub> & COCl <sub>2</sub> in c.c.	N in c.c.	Corrected oxygen, c.c.
V	+	60.39	9.03	48.69	2.67	8.58
VI	0	61.20	7.48	50.13	3.6	6.79
VII	0	60.65	9.69	46.58	4.4	8.79

*Method in which the blood-gas was analysed after combustion of the chloroform with excess of oxygen.*

It did not seem feasible to explode with oxygen and electrolytic gas as, owing to the high percentage of chlorine in the chloroform, it was uncertain what the products would be; but it appeared likely that satisfactory results might be obtained by burning the chloroform with excess of oxygen in the presence of moisture by means of a red-hot platinum spiral in a manner similar to that used by Vernon Harcourt<sup>1</sup> for the estimation of chloroform. The apparatus used in the gas analyses was the well-known form of Frankland, as modified by W. A. Bone. For combusting the chloroform we used a pear-shaped glass bulb about 70 c.c. capacity, through the sides of which two stout platinum wires, connected by a spiral of fine platinum wire, were fused. The bulb was connected by a three-way tap with the measuring vessel of the gas analysis apparatus and with a small exit tube, through which water could be introduced. The bulb was also fitted with a separate mercury reservoir. The arrangement is shown in Fig. 1.

The gas to be analysed was measured, then mixed in the vessel *A* with a suitable quantity of oxygen, remeasured, and passed into the combustion bulb *B*, into which a few drops of water or copper sulphate solution had been previously introduced through the tube *C*. The chloroform was then combusted by heating the spiral to a bright red heat by means of an electric current for a period of from 40 to 60 minutes. After cooling and standing until all the hydrochloric acid produced had dissolved in the water, the diminution in volume was determined. The carbon dioxide was then absorbed by potash and the oxygen by alkaline pyrogallate in the usual manner.

We expected the burning of the chloroform to take place according to the equation given by Vernon Harcourt :



<sup>1</sup> *Trans. Chem. Soc.* p. 1065. 1899.

Had this been the case, and the hydrogen chloride all dissolved in the water present, the volume of the chloroform present in the original gas mixture and the volume of the carbon dioxide produced by its combustion should have been respectively double the diminution in volume on combustion.

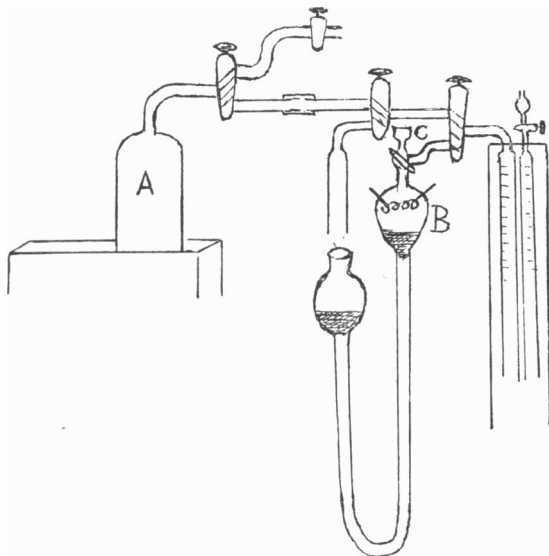
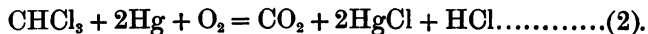


Fig. 1.

On carrying out the analysis as described above it was, however, noticed that a considerable quantity of calomel was deposited on the sides of the bulb, and the amount of the deposit did not appear to be affected by increasing the quantity of water. Mercury therefore appeared to enter into the reaction and the combustion appeared to be best represented by the equation



According to this equation the volumes of the chloroform and the carbon dioxide produced by its combustion should respectively equal the diminution in volume.

In order to test the validity of this equation a large number of combustions of different mixtures of air or oxygen and chloroform were made, and the diminution in volume and the quantities of carbon dioxide produced were determined. The results, expressed in terms of

10 c.c. of gas measured at 0° C. and 760 mm., are given in the following table.

No. of Exp.	Volume of gas taken	Diminution in volume	CO <sub>2</sub> produced
(1)	10	0·77	0·67
(2)	„	0·90	0·69
(3)	„	0·55	0·65
(4)	„	0·73	0·82
(5)	„	0·60	0·79
(6)	„	1·09	0·95
(7)	„	1·07	0·87
(8)	„	1·09	0·83
(9)	„	0·81	0·82
(10)	„	0·62	0·75
(11)	„	0·64	0·78
(12)	„	0·59	0·58
(13)	„	0·47	0·61
(14)	„	0·66	0·63
		10·59	10·44

The average value of the ratio of the diminution in volume to the carbon dioxide produced is therefore  $\frac{10\cdot59}{10\cdot44} = 1\cdot014$ . According to equation (1) this ratio should be 0·5, and according to equation (2) it should equal 1. Though the average ratio is very nearly 1, it will be noticed that the ratios in individual experiments show considerable variations in either direction. We have not determined finally the cause of this variation, but it is probably very largely due to the difficulty of getting a sharp separation of carbon dioxide and hydrogen chloride by means of the water.

The method of calculating the composition of a blood-gas from the analytical data will be best made clear by an example.

Pressure of gas at 0° C. and const. volume = 22·57 c.c., after addition of oxygen 32·31 cm., after combustion 30·53, after treatment with potash 15·98 cm., and after alkaline pyrogallate 0·57 cm. The oxygen added therefore measured 32·21 - 22·57 = 9·64 cm., the chloroform vapour 32·21 - 30·53 = 1·68 cm.; the carbon dioxide = 30·53 - 15·98 - 1·68 = 12·87 cm.; the oxygen = 15·98 - 0·57 - 9·64 + 1·68 = 7·45 cm.; the nitrogen = 0·57 cm.

As we have already pointed out, though the average ratio of the diminution in volume to the volume of CO<sub>2</sub> produced by combustion is practically 1, individual ratios often deviate from this very considerably in either direction. In any one experiment therefore the chloroform number given is liable to error, and can only be considered as approximately true, and this error also comes into the correction applied to the carbon dioxide and oxygen. As, however, the error in the correction



is small compared with the values corrected, it does not invalidate the result.

As it proved very difficult to keep the taps and joints of our Toepler pump in satisfactory order for a long series of experiments, we found it necessary to devise a special form of pump without taps or joints, the froth-chamber of which was continued downwards as a barometer tube, up which the blood was directly introduced. This pump has been fully described, together with its method of use<sup>1</sup>.

Cats were used in all the experiments. Great care was taken to keep the temperature of the animals normal, since, in deep anæsthesia produced by chloroform and ether, the metabolism of the body is markedly depressed, and the thermotaxis of an animal is interfered with, so that any possibility of a warm-blooded animal passing into the condition of a cold-blooded one was as far as possible obviated. The temperature of an anæsthetised animal may fall as low as 22° C. We were careful to carry out the necessary operations with a minimum amount of interference and with absence of any hæmorrhage. A tracing of the respiratory movements was generally taken throughout the experiment. In some cases the percentage of chloroform administered was regulated by the Woulff bottle which we used in our previous work; in other cases by Waller's chloroform balance. The tracheal cannula was connected with Chauveau's valves. The blood from the vessel was always taken from the carotid artery, the cannula being introduced immediately before taking the sample. In some cases the blood ran from the animal through a capillary tube directly up the barometer tube into the froth-chamber. In other experiments the blood was collected by displacement of mercury in a bulb of known volume and again displaced up the barometer tube without coming in contact with the air. The details of these methods were fully described in our former paper<sup>1</sup>.

In our experiments the main object was to compare the composition of the blood-gases of the normal animal with the composition on the one hand of the blood-gases at the stage when the reflexes vanished, and on the other hand the composition at a later stage of anæsthesia, when the animal was deeply anæsthetised, and in what we have previously described as the second stage of anæsthesia, when there is an equilibrium between the rate of absorption and the rate of elimination of chloroform by the blood<sup>2</sup>. It appeared to us that this informa-

<sup>1</sup> *This Journal*, XL. p. 373. 1910.

<sup>2</sup> *Proc. Roy. Soc. B*, LXXIX. p. 562. 1907.

tion would be obtained much more accurately by making a number of experiments on different animals at the different stages of anæsthesia, rather than by taking two samples at the different stages from each animal, because the withdrawal of the first amount of blood, sometimes a quarter of what the animal possesses, could not be without influence on the gas-content of the blood, since the absolute amount of hæmoglobin must be diminished, and the percentage of this would fall during a long experiment owing to the restoration of the blood-volume by an influx of lymph from the extra-vascular districts.

The results of our experiments as to the gas-content of the blood :

1. At the moment when the reflexes re-appeared,
2. When the reflexes disappeared,
3. During deep narcosis (second stage of anæsthesia),

are given in the following tables, and details of each experiment will be found at the end of this paper.

Experiments, in which the chloroform was administered for a very short time, just up to the moment of disappearance of the reflexes, and others in which these re-appeared during taking of the samples, are given in Table I. Respiratory tracings showed that the animals were breathing quietly and steadily.

TABLE I. *Composition of the blood-gases at 0° and 760 per 100 grammes of cat's blood at disappearance of reflexes.*

No. of Exp.	% of CHCl <sub>3</sub>	Time in mins. from commencement of CHCl <sub>3</sub>	Hirudin 10 c.c. injected	Amount of blood in c.c.	Colour	Total gas in c.c.	CHCl <sub>3</sub> in c.c. vapour	CO <sub>2</sub> in c.c.	O. in c.c.	N. in c.c.
A	2—3	3	+	29	Bright	43·65	3·32	27·76	9·52	3·05
B	—	5	+	29	Slightly	38·49	3·88	26·45	6·12	2·03
C	1—2	23	0	28·5	Fairly Bright	45·96	2·36	34·51	7·71	1·38

*Remarks:*—Exp. A. Reflexes re-appear during taking of sample. Oxygen used for combustion not quite free from nitrogen.

Exp. B. Eye-reflexes and patellar back during taking of sample. Oxygen used contained a trace of nitrogen.

Exp. C. Chloroformed very slowly. Eye and patellar tendon just gone, not tail reflex.

In Table II we give the results in which the animal received chloroform in a bell-jar for a considerable length of time, and when fully anæsthetised was removed for the necessary operation; the administration continued for a variable length of time, and the sample was taken when the reflexes re-appeared after cessation of the

anæsthetic. Although a considerable quantity of blood was abstracted, the colour showed that it was bright red arterial blood. The animals were respiring somewhat faster than when fully under the anæsthetic.

TABLE II. *Composition of the blood-gases at 0° and 760 per 100 grammes of blood at reappearance of reflexes.*

No. of Exp.	% of CHCl <sub>3</sub>	Time in mins. from commencement of CHCl <sub>3</sub>	Hirudin 10 c.c. injected	Amount of blood in c.c.	Colour	Total gas in c.c.	CHCl <sub>3</sub> in c.c. vapour	CO <sub>2</sub> in c.c.	O in c.c.	N in c.c.
D	—	20	+	48·6 gr. =46·11 c.c.	—	46·67	3·47	26·62	15·41	1·18
E	1—2	45	+	76·65 gr. =72·72 c.c.	Somewhat dark	40·54	0·89	26·31	12·14	1·19
F	2	Intermittent for a long time		10·8	Bright red	42·00	4·19	30·31	5·82	1·68
G	—	35	+	47	Bright red	49·96	3·27	32·83	12·58	1·28

Remarks:—Exp. D. Sample on re-appearance of reflexes.

Exp. E. Sample just before re-appearance of reflexes.

Exp. F. Chloroform repeatedly on and off; occasionally artificial respiration. Reflexes back when sample taken.

Exp. G. Eye, patellar and tail back.

In Table III the composition of the blood-gases in arterial blood, in that condition of narcosis which we have called the second stage of anæsthesia, is given.

TABLE III. *Composition of the blood-gases at 0° and 760 per 100 grammes of blood in the second stage of anæsthesia.*

No. of Exp.	% of CHCl <sub>3</sub>	Time in mins., CHCl <sub>3</sub>	Hirudin	Amount of sample, c.c.	Colour	Total gas	CHCl <sub>3</sub> in c.c. of vapour	CO <sub>2</sub>	O	N
H	1·5—2	56	+	29	Dark	44·52	1·38	36·73	4·06	2·35
I	2	33	0	22	Dark	57·37	3·55	48·38	3·51	1·84
J	2	45	0	51·23	Fairly dark	33·67	2·89	16·98	11·63	1·17
K	2	60	+	95·83	Very dark	53·99	5·95	36·79	9·90	1·34
L	2	55	0	47	Very dark	56·69	5·27	41·66	8·58	1·16
M	2	100	+	47	Very dark	58·48	6·51	39·73	10·83	1·38
N	2	63	+	47	Very dark	46·21	6·92	29·91	8·12	1·26
O	2	76	+	47	Very dark	53·37	5·68	37·78	8·50	1·40

Remarks:—Exp. H. Respiration regular and steady. Animal very slowly anæsthetised with a low percentage of CHCl<sub>3</sub>.

Exp. J. Animal not far beyond reflex point.

Exp. N. Not far from asphyxial point.

In Table IV the composition of normal cat's blood is compared with that of the same species of animal :

1. When the reflexes re-appear after anæsthesia.
2. When the reflexes just disappear.
3. In the second stage of anæsthesia.

TABLE IV.

	Average volume in c.c. per 100 c.c. of blood			Average composition % of gas			Ratio of O to CO <sub>2</sub>
	CO <sub>2</sub>	O	N	CO <sub>2</sub>	O	N	
Normal cats <sup>1</sup> ... ..	25·07	13·60	1·00	63·2	34·28	2·52	1 : 1·84
Reflexes just re-appear	29·02	11·49	1·33	65·06	25·44	2·87	1 : 2·55
Reflexes just disappear	29·57	7·78	2·15	69·14	18·17	5·09	1 : 3·8
2nd stage of anæsthesia	36·00	8·14	1·49	71·27	16·12	2·95	1 : 4·42

## DISCUSSION OF RESULTS.

The total gases found in the blood of normal cats, as was pointed out by Pflüger, is low compared with that of dogs. A hundred grams of arterial blood, we found in six experiments, yielded an average amount of 39·68 c.c. of mixed gases<sup>2</sup>. In animals slightly anæsthetised with chloroform the average amount of gas in six experiments was 43·74 c.c., and in cats completely anæsthetised it was 50·5 c.c.; an increase per cent. of 10·2 and 26·2 respectively. It is evident from the tables that the increase is chiefly due to an augmented amount of carbon dioxide gas.

In a former paper<sup>3</sup>, we showed that the chloroform-content of the blood rises in the initial stages of anæsthesia with great rapidity to a value which approaches the maximum. During this period the amount of chloroform in the blood appears to chiefly affect the respiratory centres, so that the breathing becomes slower and sometimes stops altogether. If the animal passes this stage naturally, or recovers on cessation of the administration of chloroform, or by means of artificial respiration, then, on continuing the anæsthetic the amount of chloroform in the blood quickly rises again towards a maximal value and an equilibrium between the factors which determine the amount of chloroform in the blood appears to be established, the processes of intake and output at the pulmonary surface going on side by side.

<sup>1</sup> Buckmaster and Gardner, *This Journal*, xli. p. 60. 1910.

<sup>2</sup> *Ibid.*

<sup>3</sup> *Proc. Roy. Soc. B*, lxxix. p. 535. 1907.

The following curve is constructed from data given in the paper we have quoted.

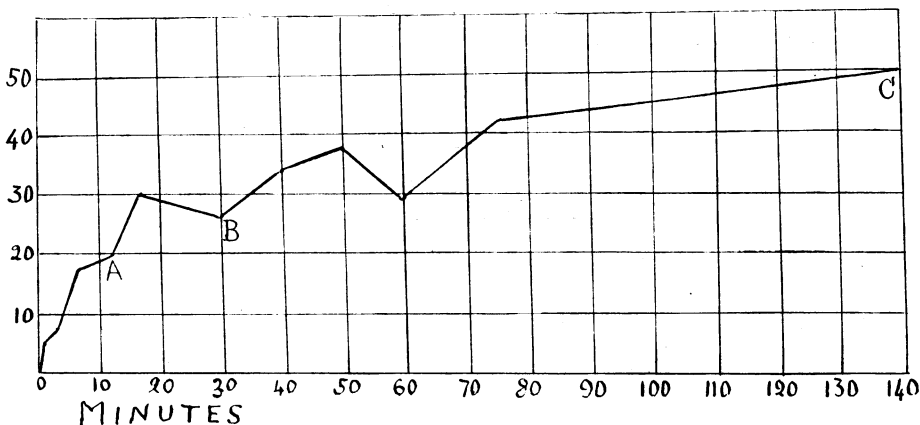


Fig. 2. Curve showing the chloroform-content of arterial blood of the cat during anæsthesia.

A, points at which the eye-reflexes vanish.

B to C, complete anæsthesia, second stage.

The vertical row of figures expresses the content of the blood in milligrams of chloroform in 100 grams of blood.

In Tables I and II the average amount of chloroform in milligrams per 100 grams of blood is 16—17. In Table III the amount is 26. The stages of anæsthesia at which the samples of blood were taken for gas-analysis will therefore be clear from the above curve.

It is obvious that the darkened colour of blood in chloroform narcosis is due to a diminution in the amount of oxy-hæmoglobin. In normal cats the amount of hæmoglobin by Gowers-Haldane hæmoglobinometer lies between 70 and 80, which, in terms of the percentage oxygen capacity, would give a value slightly higher than 13·6, which is the average volume of oxygen found by gas-analysis. The fall in oxygen-content during narcosis is well marked, even when the reflexes disappear; while, in the second stage of anæsthesia, the reduction is 40%. The hæmoglobin is therefore only partially saturated with oxygen during narcosis, indeed to the extent of 60%. The blood of the normal cat, on the assumption that the alveolar air contains 14% of oxygen, should, when allowance is made for the tension of aqueous vapour at 38° C., = 49·3 mm., with 40 mm. CO<sub>2</sub> tension in blood, be saturated to the extent of 90%, the oxygen tension being equal to

99.49 mm. But during narcosis the hæmoglobin is in the same state of partial saturation that it would be with a carbon dioxide tension of 40 mm. and an oxygen tension of only 45.5 mm. For it is probable since the salts in the red corpuscles in both the blood of dogs and cats are alike in containing chiefly salts of sodium, that the curve of dissociation of dogs' blood given by Barcroft and Camis<sup>1</sup> is applicable to the blood of cats.

Tracings of the respiratory movements taken during each of the experiments give no indication that this is to be attributed to slowing of the respiration. It is not necessary to reproduce these tracings in this paper, they all conform to those we have already published at full length<sup>2</sup>. An examination of these curves shows that in no case, during the second stage of anæsthesia, is there any marked alteration in the frequency or character of the respiration; certainly *there is not any slowing of the rate or depth* of the respiratory movements. We may therefore infer that the lung-ventilation is not interfered with, and are consequently quite unable to agree with the view expressed by J. Tissot,<sup>3</sup> from the results of three experiments and adopted in the Report of the Chloroform Committee of the British Medical Association<sup>4</sup> 1910, "that during narcosis, the blood retains up to the time of death the same power of taking up oxygen, and that if the amount of this gas diminishes in the blood, the decrease is solely due to a slowing of the respiration."

It is known that chloroform is associated with the red corpuscles, and outside the body aggregations of hæmoglobin and chloroform have been described<sup>5</sup>, which are said to possess distinctive spectra<sup>6</sup>. It is therefore probable that the fall in oxygen-content of the blood in chloroform narcosis, is due to direct interference with the single function of transporting oxygen from the lungs, which the red corpuscles possess.

<sup>1</sup> J. Barcroft and M. Camis. *This Journal*, xxxix. p. 132. 1909.

<sup>2</sup> G. A. Buckmaster and J. A. Gardner. *Proc. Roy. Soc. B*, xxix. p. 577. 1907.

<sup>3</sup> *Report of Special Chloroform Committee of the Brit. Med. Assoc.* Paper V. 1901-2.

<sup>4</sup> *Final Report of Special Chloroform Committee of the Brit. Med. Assoc.* p. 52, July 9. 1910.

<sup>5</sup> B. Moore and Roaf. *Proc. Roy. Soc. LXXIII*. 1904, and *LXXVII*. 1905. Eadie, *Reports of Thompson Yates and Johnston Laboratories, Liverpool*, vi. 1905.

<sup>6</sup> F. Krüger. *Hofmeister's Beiträge*, III. p. 67. 1903.

*Protocols.*

A. Cat, weight 2.2 kilos. Animal killed by a blow on the head.

- 5th min. 10 c.c. hirudin in femoral vein.  
 12th ,,  $\text{CHCl}_3$  2% on (Woulff's bottle).  
 15th ,, Eye-reflexes gone, also patellar tendon.  $\text{CHCl}_3$  off.  
 Sample taken 29 c.c. medium dark colour.  
 Reflexes returned during taking of sample.

Pressure of gas at constant volume (72.48 c.c.) = 13.8 cm. at 10.8° C.: after addition of O. = 40.35 cm. at 10.8° C.: after combustion = 39.55 cm. at 12.6° C.: after potash 29.65 cm. at 12.5° C.: after alkaline pyrogallate 1.90 cm. at 11.8° C. The oxygen used contained 3.5% of nitrogen.

B. Cat, weight 3.2 kilos. As Exp. A.

- 7th min. Hirudin 11 c.c. into femoral vein.  
 11 ,,  $\text{CHCl}_3$  on.  
 14 ,, Eye-reflexes gone, then patellar tendon.  
 14.5 ,,  $\text{CHCl}_3$  off. Sample taken. Eye-reflexes back during taking of sample.  
 Blood slightly dark.

Pressure of gas at constant volume (72.48 c.c.) = 12.35 cm. at 15.1° C.: after addition of O. = 35.20 cm. at 15.4° C.: after combustion = 33.80 cm. at 14.1° C.: after potash 14.10 cm. at 14.1° C.: after pyrogallate 0.65 cm. at 14.1° C.

C. Exp. as A and B. No hirudin.

- 6th min. Reflexes present,  $\text{CHCl}_3$  on.  
 6.5 ,,  $\text{CHCl}_3$  off.  
 7 ,,  $\text{CHCl}_3$  on very weak (1%).  
 28 ,, Sample taken. Eye and patellar reflexes gone, but not tail. Vol. of blood 28.5 c.c.

Pressure of gas at constant volume (72.48 c.c.) = 14.4 cm. at 13.2° C.: after addition of O. 25.15 cm. at 13.1° C.: after combustion 24.30 cm. at 11.8° C.: after potash 12.80 cm. at 11.7° C.: after pyrogallate 0.43 cm. at 12° C.

D. Cat, weight 2.5 kilos.  $\text{CHCl}_3$  in bell-jar.

- 15th min. Hirudin 10 c.c. in femoral vein.  
 20 ,, Sample. Reflexes just gone. Weight of blood 48.6 grammes = 46.11 c.c.  
 Hb = 93% (Gowers-Haldane).

Pressure of gas at constant volume (72.48 c.c.) = 23.6 cm. at 12.5° C.: after addition of O. = 33.7 cm. at 12.6° C.: after combustion 31.9 cm. at 12.3° C.: after potash 16.75 cm. at 13.2° C.: after pyrogallate 0.60 cm. at 12.7° C.

E. Cat, weight 3.2 kilos.  $\text{CHCl}_3$  in bell-jar.

- 25th min. Hirudin 15 c.c. injected into femoral vein.  
 55 ,, Sample taken 76.65 grammes = 72.72 c.c. just before reflexes re-appeared, but these appeared during withdrawal of blood, which was somewhat dark.  
 Hb = 77% (Gowers-Haldane).

Pressure of gas at constant volume (72.48 c.c.) = 32.15 cm. at 10.9° C.: after addition of oxygen = 42.35 cm. at 11.3° C.: after combustion = 41.85 cm. at 12.8° C.: after potash 20.05 cm. at 11.5° C.: after pyrogallate 0.95 cm. at 12.3° C.

F. Cat, weight 4 kilos.  $\text{CHCl}_3$  in bell-jar.

$\text{CHCl}_3$  2 % on and off intermittently, and artificial respiration at times. No hirudin.

Sample bright red, when reflexes back, 10.8 c.c. Hb=71 % (Gowers-Haldane).

Pressure of gas at constant volume (72.48 c.c.)=5.0 cm. at 14° C.: after oxygen =30.7 cm. at 14.1° C.: after combustion 30.2 cm. at 14.1° C.: after potash 26.1 cm. at 14.2° C.: after pyrogallate 0.2 cm. at 14.8° C.

G. Cat, weight 2.9 kilos.  $\text{CHCl}_3$  in bell-jar.

22nd min. Tracheal cannula in,  $\text{CHCl}_3$  on.

35th ,, Hirudin 10 c.c. into femoral vein.

45 ,, Sample for pump 47 c.c. Blood bright red. Eye, patellar tendon and tail reflexes present.

Pressure of gas at constant volume (72.48 c.c.)=25.68 cm. at 11.7° C.: after addition of oxygen=44.24 cm. at 11.4° C.: after combustion=42.52 cm. at 11.1° C.: after potash =24.01 cm. at 11.1° C.: after pyrogallate=0.66 cm. at 11.1° C.

H. Weight of Cat 2.7 kilos.  $\text{CHCl}_3$  in bell-jar.

25th min. Table. Eye reflexes present.  $\text{CHCl}_3$  on, weak 1.5 %—2 %.

38 ,, Eye reflexes still present.

42nd ,, Eye reflexes gone. Respiration regular and steady.

50th ,, Hirudin injected.

56 ,, Sample taken. Blood dark, 29 c.c. Hb=80 % (Gowers-Haldane).

Pressure of gas at constant volume (72.48 c.c.)=14.3 cm. at 15.4° C.: after oxygen 24.95 cm. at 15.1° C.: after combustion 24.25 cm. at 12.1° C.: after potash 12.2 cm. at 13.2° C.: after pyrogallate 0.75 cm. at 13.6.

I. Cat, weight 3.9 kilos.  $\text{CHCl}_3$  in bell-jar.

12th min. Tracheal cannula in,  $\text{CHCl}_3$  on 2 %.

30 ,, Cannula in carotid artery.

33rd ,, Sample. 22 c.c. Dark coloured blood.

Pressure of gas at constant volume (72.48 c.c.)=14.0 cm. at 15.8° C.: after oxygen =25.4 cm. at 15.8° C.: after combustion 24.6 cm. at 16.6° C.: after potash 11.9 cm. at 16.8° C.: after pyrogallate 0.45 cm. at 16.7° C.

J. Cat, weight 3.5 kilos.  $\text{CHCl}_3$  in bell-jar.

15th min. Hirudin injected.

45 ,, Blood sample fairly dark. 54 grammes=51.23 c.c. Hb=75 % (Gowers-Haldane).

Pressure of gas at constant volume (72.48 c.c.)=18.3 cm. at 11.7° C.: after oxygen =27.65 cm. at 10.1° C.: after combustion 25.95 cm. at 9.1° C.: after potash=14.90 cm. at 8.7° C.: after pyrogallate=0.65 cm. at 8.5° C.

K. Cat. Hirudin.  $\text{CHCl}_3$  in bell-jar.

15th min. Tracheal cannula in,  $\text{CHCl}_3$  on from Woulff's bottle.

60 ,, Sample very dark. 101 grams=95.83 c.c. Hb=68 % (Gowers-Haldane).

Pressure of gas at constant volume (72.48 c.c.)=56.2 cm. at 9.8° C.: after oxygen =70.9 cm. at 9.5° C.: after combustion=65.2 cm. at 11.6° C.: after potash 20.4 cm. at 11.3° C.: after pyrogallate 1.4 cm. at 9.1° C.



L. Cat, weight 2·8 kilos.  $\text{CHCl}_3$  in bell-jar. No hirudin.

20th min. Tracheal cannula in,  $\text{CHCl}_3$  on.

55 ,, Sample. Blood very dark. 47 c.c.

Pressure of gas at constant volume (72·48 c.c.)=28·99 cm. at 10·3° C. : after oxygen =43·79 cm. at 10·3° C. : after combustion=41·09 cm. at 10·3° C. : after potash=17·09 cm. at 10·3° C. : after pyrogallate=0·60 cm. at 10·3° C.

M. Cat, weight 3·3 kilos.  $\text{CHCl}_3$  in bell-jar, hirudin.

20th min. Tracheal cannula in,  $\text{CHCl}_3$  on.

100 ,, Sample taken 47 c.c. Blood very dark.

Samples taken for estimation of  $\text{CHCl}_3$  by Nicloux' method=59 mmgrs. of  $\text{CHCl}_3$  per 100 grams of blood.

Pressure of gas at constant volume (72·48 c.c.)=30·03 cm. at 11·5° C. : after addition of oxygen=39·15 cm. at 10·6° C. : after combustion=35·72 cm. at 9·8° C. : after potash =12·09 cm. at 9·3° C. : after pyrogallate=0·71 cm. at 11·3° C.

N. Cat.  $\text{CHCl}_3$  in bell-jar, hirudin.

12th min. Tracheal cannula in,  $\text{CHCl}_3$  on.

63 ,, Sample taken. Very dark not far from asphyxial point, 47 c.c.

Sample before and after gave by Nicloux' method ·45 and ·33 mmgrs. of  $\text{CHCl}_3$  per 100 grams of blood.

Pressure of gas at constant volume (72·48 c.c.)=23·81 cm. at 12·4° C. : after addition of oxygen=43·48 cm. at 12·1° C. : after combustion=39·96 cm. at 12·4° C. : after potash =21·08 cm. at 13·8° C. : after pyrogallate=0·65 cm. at 13·8° C.

O. Cat.  $\text{CHCl}_3$  in bell-jar. Hirudin.

10th min. Tracheal cannula in,  $\text{CHCl}_3$  on.

76 ,, Sample, very dark in colour, 47 c.c.

Pressure of gas at constant volume (72·48 c.c.)=27·31 cm. at 10·5° C. : after addition of oxygen=46·00 cm. at 9·7° C. : after combustion=43·30 cm. at 11·0° C. : after potash =20·97 cm. at 10·4° C. : after pyrogallate=0·72 cm. at 11·6° C.

We take this opportunity of expressing our thanks to the Government Grant Committee of the Royal Society for help in carrying out this work.