Ventilation of the Lung during Chloroform Narcosis.

By G. A. Buckmaster and J. A. Gardner.

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(From the Physiological Laboratory, South Kensington, University of London.)

In the report of the Chloroform Committee of the British Medical Association for 1910, the view is expressed that during chloroform narcosis the blood retains unimpaired up to the time of death its normal capacity of absorbing oxygen, and that if the amount of this gas diminishes in the blood, the decrease is solely due to the slowing of the respiration. This opinion is based on experiments made by J. Tissot. These indicate that when the respiration stops in an asphyxia induced by long anæsthetisation, 100 c.c. of the arterial blood of the dog may contain as little as 0·78 c.c. and 2·83 c.c. of oxygen, although samples taken at intervals during anæsthesia show only a slight fall in oxygen content, so long as the ventilation of the lung remained normal. In our experiments on the composition of the blood-gases during chloroform anæsthesia,* examination of the tracings of the respiratory movements during continuous inhalation of chloroform gave no indication that the progressive diminution in the amount of oxy-hæmoglobin as anæsthesia continued could be attributed to any slowing of the respiration, and none of our tracings showed any marked alteration in the frequency or amplitude of the respiratory movements. We were, therefore, unable to agree with the views expressed by Tissot. All our tracings were taken by means of a tambour applied to the chest wall in the usual way. Observations on the respiratory movements made by other observers were, as far as we can gather, made in a similar manner. It is obvious that such records afford no information which will enable an opinion to be formed with regard to the lung ventilation which is capable of precise interpretation. In order to ascertain more definitely whether the diminution in the amount of oxy-hæmoglobin in chloroform narcosis was due to changes in the type or depth of respiration, or whether it was due to the direct interference by the chloroform with the function of transporting oxygen which the red corpuscles possess, we determined to investigate the pulmonary ventilation during anæsthesia by means of a plethysmograph.

* 'Journ. Physiol.,' Nov. 9, 1910, vol. 41, p. 246.

Description of Plethysmograph.

The instrument consisted of a rectangular glass box, fitting into a groove channelled in a thick slate slab forming the floor of the chamber. The box was of such a size as to comfortably hold a cat. In order to make it airtight, the groove was filled up with a stiff mixture of vaseline and beeswax. The dimensions of the box were as follows: length 67 cm., breadth 32 cm., depth 17 cm. Four holes were bored through the slate bed near the corners of the box. These were fitted with rubber corks, through which passed glass tubes of wide bore. The two holes at one end were connected with one another by a Chauveau's valve apparatus. Through a third hole, a wide tube led to a recording gasometer, made of aluminium, similar to that used by Haldane and Priestley.* The drum of the gasometer was 8 cm. high, and 6·2 cm. diameter. The gasometer, carrying a light adjustable recording lever, rose and fell in a bath of paraffin oil, which appeared to possess advantages over water. The inertia of this part of the apparatus was inappreciable. The fourth hole was connected with a bottle into which a burette fitted for purposes of graduation, and this was carried out and tested in the manner described in the paper just quoted.

The dimensions of the gasometer given were found to be most suitable for cats. In investigating respiratory ventilation, it is obviously important to avoid as far as possible breathing through long tubes and systems of valves. To minimise these disadvantages, the mixture of chloroform and air was passed through the Chauveau's valves at a slight positive pressure, and the percentage composition kept constant by the use of Waller's chloroform balance.† The animal actually respired through a cannula connecting the trachea with the central tube of the Chauveau's valve apparatus. This tube was as wide and short as possible, the length in every case being less than the distance of the tracheal opening from the mouth. It was found that expansion of air, owing to rise of temperature, caused no trouble, as during the time taken to seal up the box the temperature had become constant.

The general mode of procedure was as follows:—The animal was anæsthetised with nitrous oxide, and a cannula quickly placed in the trachea. The cannula was fitted on to the Chauveau valves, the glass box placed on the slate slab, and the whole chamber made airtight. When the animal recovered from nitrous oxide, chloroform of known percentage was administered by Waller's balance. In those experiments where a knowledge of the gas-content of the blood was required, the animal received 3 c.c. of strong

* 'Journ. Physiol.,' 1905, vol. 32, p. 486.

† 'Journ. Physiol.,' Feb. 22, 1908, vol. 37.

hirudin solution in 1-per-cent. sodium sulphate through the femoral vein, and a cannula was tied into the carotid artery at the beginning of the experiment while it was under nitrous oxide. The animal was placed in the box, and its lung-ventilation determined for a few minutes. The glass box was rapidly lifted off the slate and a sample of blood taken. The box was then replaced and the respiration again recorded.

In order to ascertain the precise effect of the inhalation of chloroform and ether on the pulmonary ventilation, it would have been desirable to determine the normal respiratory ventilation during rest. This obviously could not be determined by means of our apparatus, as an operation on the unanæsthetised animal would have been necessary; further, it was impossible to use the apparatus in the way described for human beings in Haldane and Priestley's paper, for such an animal as a cat. We thought that comparisons of the ventilation under chloroform with that during recovery from a low percentage of some anæsthetic such as nitrous oxide, the effect of which rapidly passes off and which is rapidly eliminated, would give data sufficiently reliable for our purpose. Another factor which we are unable to take into account is the question of the dead-space. This will no doubt vary in different animals, and, *cæteris paribus*, the larger the dead-space in any particular animal, the more air must it breathe in order to maintain a given alveolar ventilation. We can find no data as to the dead-space in cats, and the only satisfactory way of determining the volume of the dead-space would have been by preparing a number of plaster casts of the trachea and bronchi, such as Loewy* made when estimating the dead-space of the respiratory passages in man. We attempted to get over this difficulty by using as far as possible animals of similar size. In this paper we give the results of the effect of inhalation of chloroform and ether on the apparent total ventilation of the lung, regarded as the product of the average depth of respiration measured in cubic centimetres at 37° C., moist, and the average frequency per minute.

From a large number of records taken with varying percentages of chloroform and varying respiratory states of the animal prior to the anæsthetic, we give a selected number to illustrate the more important points which have been noticed during our experiments.

Effect of Different Percentages of Chloroform on the Lung Ventilation.

In former papers we have shown that a definite danger point in chloroform anæsthesia may occur during the first few minutes, and this danger point depends essentially on two factors: firstly, the percentage of chloroform which is being inhaled, and, secondly, upon the rate and depth of the respiration

* 'Pflüger's Archiv,' 1894, vol. 58, p. 416.

prior to anæsthetisation. When the hyperpnœa is marked, or the percentage of chloroform inhaled is high, the percentage of chloroform in the blood rises with great rapidity to a maximum value, and the activity of the respiratory centre is depressed; this may occur to such an extent that the animal ceases to respire with the diaphragm always in the state of rest. This is illustrated by the following tracings of six experiments selected from a greater number (figs. 1 to 6):—

Experiment 1.—Effect of 1·5 per cent. chloroform after deep respirations (fig. 1):—

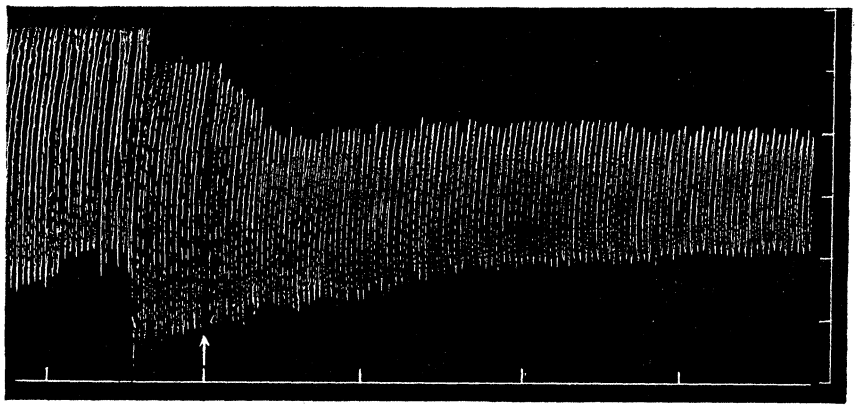


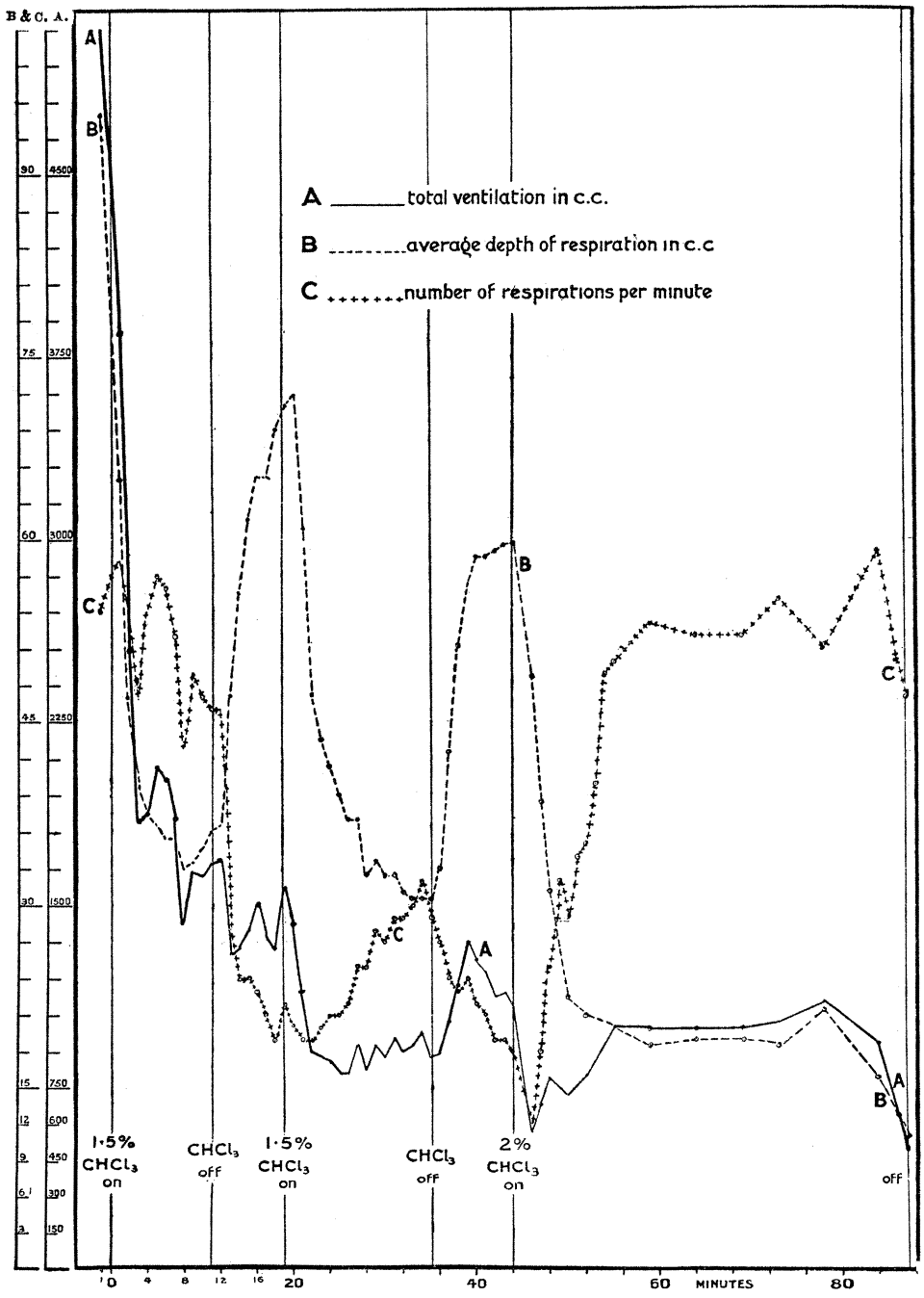
Fig. 1.

Depth of respiration, 1 division = 21·74 c.c.; time intervals, 30 secs; ↑, chloroform on.

Table I.—Measurements of Tracing in Fig. 1.

Intervals of time, in minutes.	Anæsthetic.	No. of respirations per minute.	Average depth of respiration, in c.c.	Lung ventilation, in c.c.	
1	0	54	94·79	5119	
0·5	1·5 per cent. $CHCl_3$	32	75·67	2421	3851
0·5	„	26	55·0	1430	
1	„	54	47·19	2548	

The remaining data of this experiment are given in Curve I, which shows the effect of chloroform (1·5 per cent.) for 11 minutes, recovery for 8 minutes, re-chloroforming with 1·5 per cent. for 16 minutes, recovery for 9 minutes, and, finally, re-chloroforming again with 2 per cent., death resulting in 43 minutes, in the 87th minute after the commencement of the experiment.


B & C. A.
A
B
C
A _____ total ventilation in c.c.
B ---------- average depth of respiration in c.c
C +++++++ number of respirations per minute
90
75
60
45
30
15
12
9
6.1
3.
4500
3750
3000
2250
1500
750
600
450
300
150
1·5% CHCl3 on
CHCl3 off
1·5% CHCl3 on
CHCl3 off
2% CHCl3 on
off
0
4
8
12
16
20
40
60
MINUTES
80

CURVE I.

Experiment 2.—Effect of moderate ventilation of the lung prior to the administration of 2 per cent. chloroform (fig. 2):—

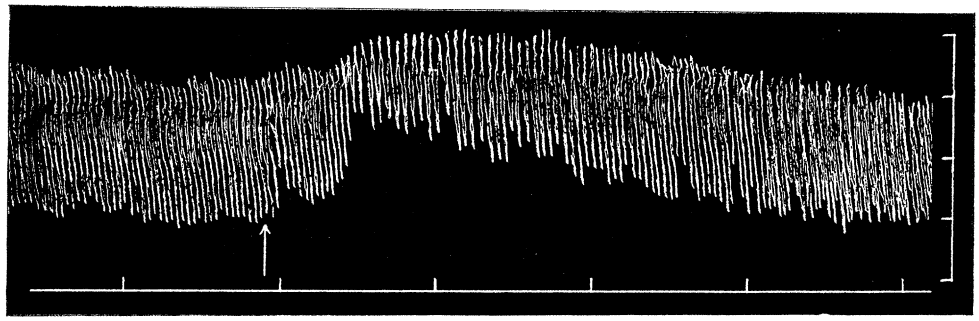


FIG. 2.

Depth of respiration, 1 division = 14·29 c.c.; time interval, 30 secs.; ↑, 2 per cent. chloroform on.

Table II.—Measurements of Tracing in Fig. 2.

Intervals of time, in minutes.	Anæsthetic.	No. of respirations per minute.	Average depth of respiration.	Lung ventilation, in c.c.	
1	0	55	48·28	2656	
0·5	2 per cent. $CHCl_3$	24	26·86	645	1161
0·5	,,	19	27·14	516	
0·5	,,	26	30·71	798	1755
0·5	,,	33	29·0	957	
1	,,	64	26·14	1699	

Experiment 3.—This shows the initial danger-point in chloroform anæsthesia, an effect of moderate rate with deep respiration prior to the administration of 2 per cent. chloroform (fig. 3):—

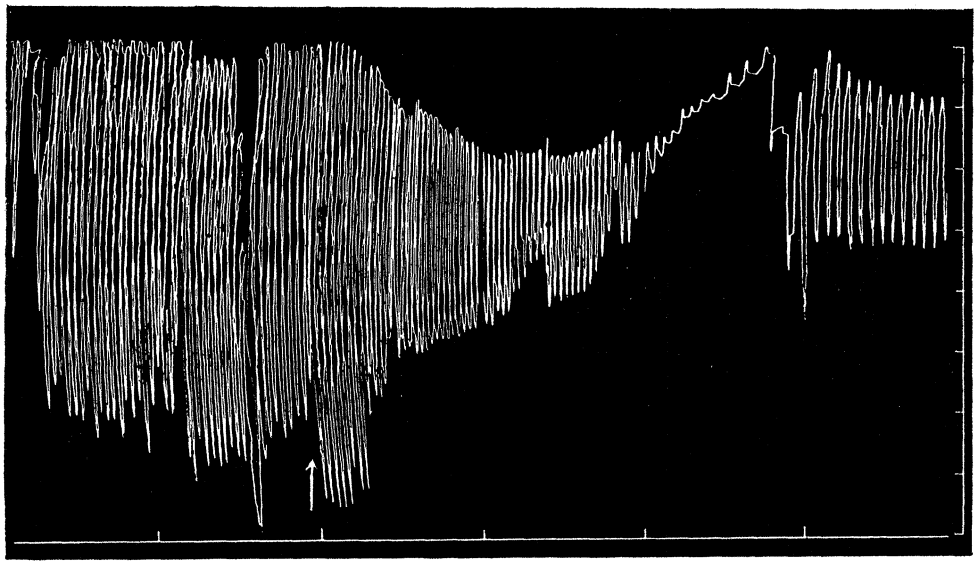


FIG. 3.

Depth of respiration, 1 division = 13·7 c.c.; time intervals, 30 secs.; ↑, 2 per cent. chloroform on.

The whole data of this experiment are given in Table III.

Table III.

Intervals of time during which respiration was counted, in minutes.	Anæsthetic.	Frequency of respiration.	Average depth of respiration.	Total ventilation, in c.c.	Remarks.
0·5	Interval before $CHCl_3$, recovery from N_2O	22	85·35	1878	
0·5	$CHCl_3$ on, 2 per cent., at beginning of this period	29	66·44	1927	
0·5	$CHCl_3$ 2 per cent.	27	28·08	758	
0·5	,,	13	8·22	107	
0·5	,,	15	37·26	559	
0·5	,,	8	17·95	144	
0·5	,,	11	52·61	579	
0·5	,,	13	31·1	404	
0·5	,,	15	28·5	427	
0·5	,,	16	27·26	436	
0·5	,,	9	16·58	149	
0·5	,,	13	38·36	499	
0·5	,,	12	12·35	148	
0·5	,,	12	18·22	219	
0·5	,,	9	22·74	205	
1·0	,,	30	36·99	1110	

Table III—*continued.*

Intervals of time during which respiration was counted, in minutes.	Anæsthetic.	Frequency of respiration.	Average depth of respiration.	Total ventilation, in c.c.	Remarks.
1·0	$CHCl_3$ 2 per cent.	37	26·03	863	
1·0	,,	43	26·44	1137	
1·0	,,	35	25·07	878	
1·0	,,	30	25·21	856	
1·0	,,	22	19·45	428	Held breath during half this minute.
1·0	,,	35	28·77	1007	Held breath for a short interval during this minute.
1·0	,,	38	21·65	843	
1·0	,,		not recorded		
1·0	,,	25	15·3	384	Irregular respiration.
1·0	,,	35	13·4	469	Very irregular respiration.
1·0	,,	36	9·18	691	
1·0	,,	37	14·5	537	
1·0	,,				Few irregular gasps.
1·0	,,				Died.

Experiment 4.—Showing the effect of 3 per cent. of chloroform following a deep and rapid respiration, but not so deep as in fig. 3. Cessation of respiration at the end of 1½ mins. from commencement of inhalation, and subsequent recovery (fig. 4):—

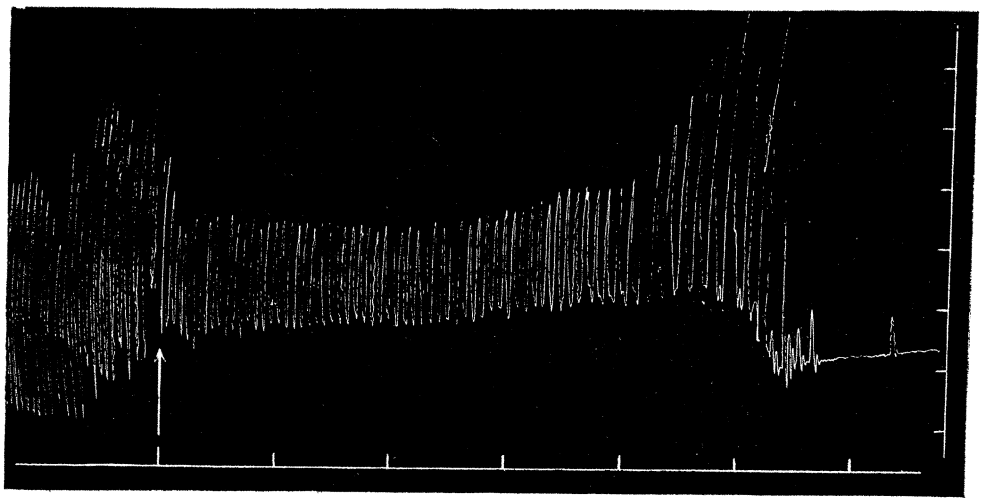


Fig. 4.

Depth of respiration, 1 division = 2·28 c.c.; time intervals, 15 secs. ↑, 3 per cent. chloroform on.

Table IV.—Measurements of Tracing in Fig. 4.

Intervals of time during which respiration was counted.	Anæsthetic.	Frequency.	Average depth of respiration.	Total ventilation, in c.c.	Remarks.
0·25 min. before	Recovery from $CHCl_3$	19	77·46	1472	
1st half-min.	N_2O 3 per cent. $CHCl_3$ on	32	37·24	1192	
2nd ,,	,,	25	36·6	915	
3rd ,,	,,	20	56·39	1128	Breathing ceased just before end of 3rd half-minute.
4th ,,	,,	2	18·08	36	$CHCl_3$ off after the 4th half-minute.

Experiment 5.—Effect of 3 per cent. chloroform with rapid but comparatively shallow respiration (fig. 5):—

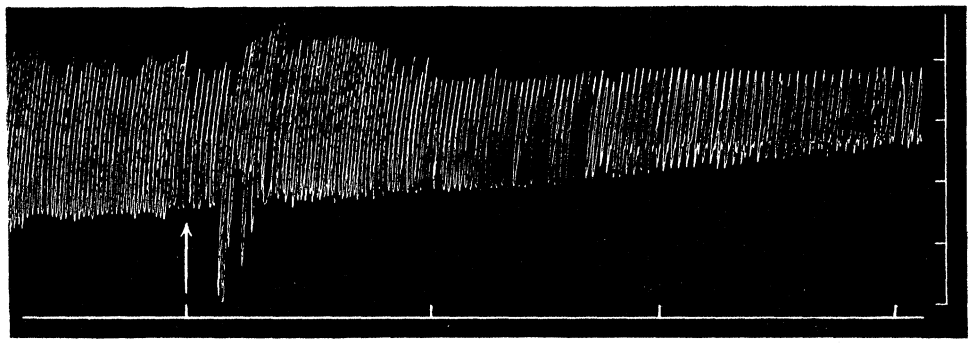


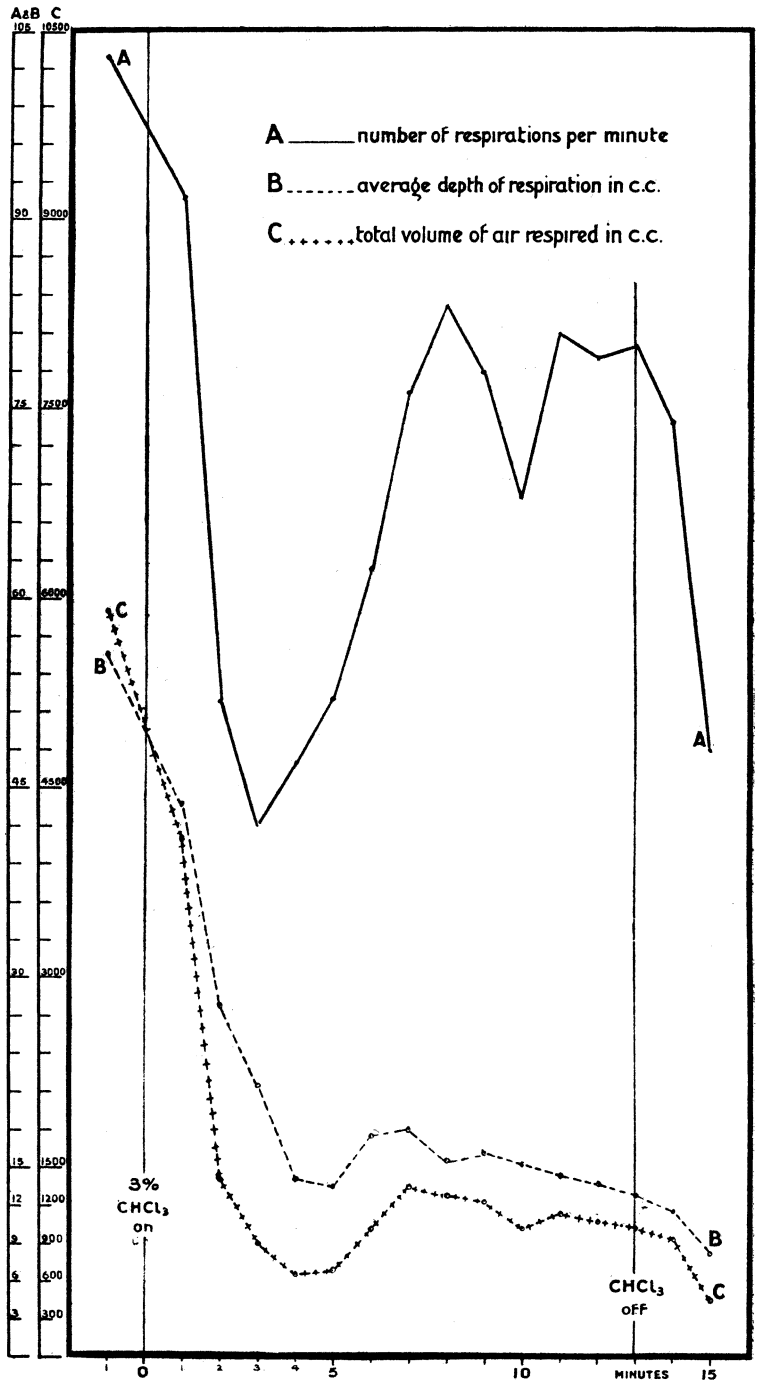
Fig. 5.

Depth of respiration, 1 division = 21·28 c.c. ; time intervals, 30 secs. ; ↑, 3 per cent. chloroform on.

Table V.—Measurements of Tracing in Fig. 5.

Intervals of time. in minutes.	Anæsthetic.	No. of respirations per minute.	Average depth of respiration.	Lung ventilation, in c.c.	
1	0	106	55·38	5870	
0·5	3 per cent. $CHCl_3$	56	51·91	2907	4101
0·5	,,	36	35·96	1294	
0·5	,,	30	31·06	932	1470
0·5	—	—	—	538	

The whole data of this experiment are given in Curve II.


A & B
C
A ——— number of respirations per minute
B ------- average depth of respiration in c.c.
C ..... total volume of air respired in c.c.
A
B
C
3% CHCl3 on
CHCl3 off
MINUTES
0
1
2
3
4
5
10
15

Curve II.

Experiment 6.—Example in which the respiration is comparatively slow (40 in 30 secs.) and also shallow; average depth, 47·88 c.c., and a low total ventilation of 1915 c.c. per 30 secs. There is no trace of an initial danger-point (fig. 6):—

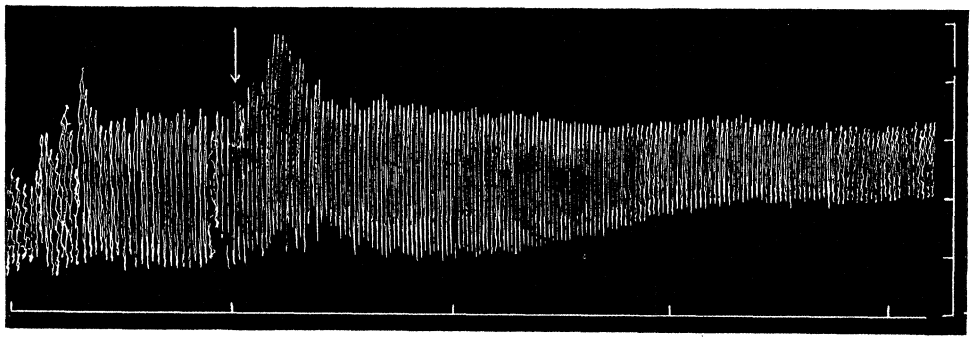


FIG. 6.

Depth of respiration, 1 division = 21·28 c.c.; time intervals, 30 secs.; ⅄, chloroform on.

Table VI.—Measurements of Tracing in Fig. 6.

Intervals of time, in minutes.	Anæsthetic.	No. of respirations per minute.	Amplitude of respiration.	Lung ventilation, in c.c.
0·5	—	51	54·39	2772
0·5	—	52	48·82	2272
0·5	—	48	28·41	1364

The cat continued to breathe for several minutes without any marked alteration in the type of respiration, and the experiment was then stopped.

It is clear, from the typical experiments quoted, that the initial effect of chloroform is to produce a marked diminution in the average depth of respiration. This occurs during the first few minutes of anæsthesia, but subsequently the depth of respiration becomes constant at a lower level. The rate is not affected to anything like the same extent. In the initial stage a slight increase in the frequency, followed by a decrease, generally occurs, but sometimes a slight decrease takes place at once. The cessation of respiration, which is an initial danger-point in chloroform anæsthesia and may result in death, is the direct effect of deep and rapid respiration prior to the administration of the drug, and the higher the percentage of the drug administered the more likely it is to occur. This can be rendered negligible by a low percentage of chloroform. An examination of many

curves has convinced us that some trace of an initial danger-point is rarely absent.

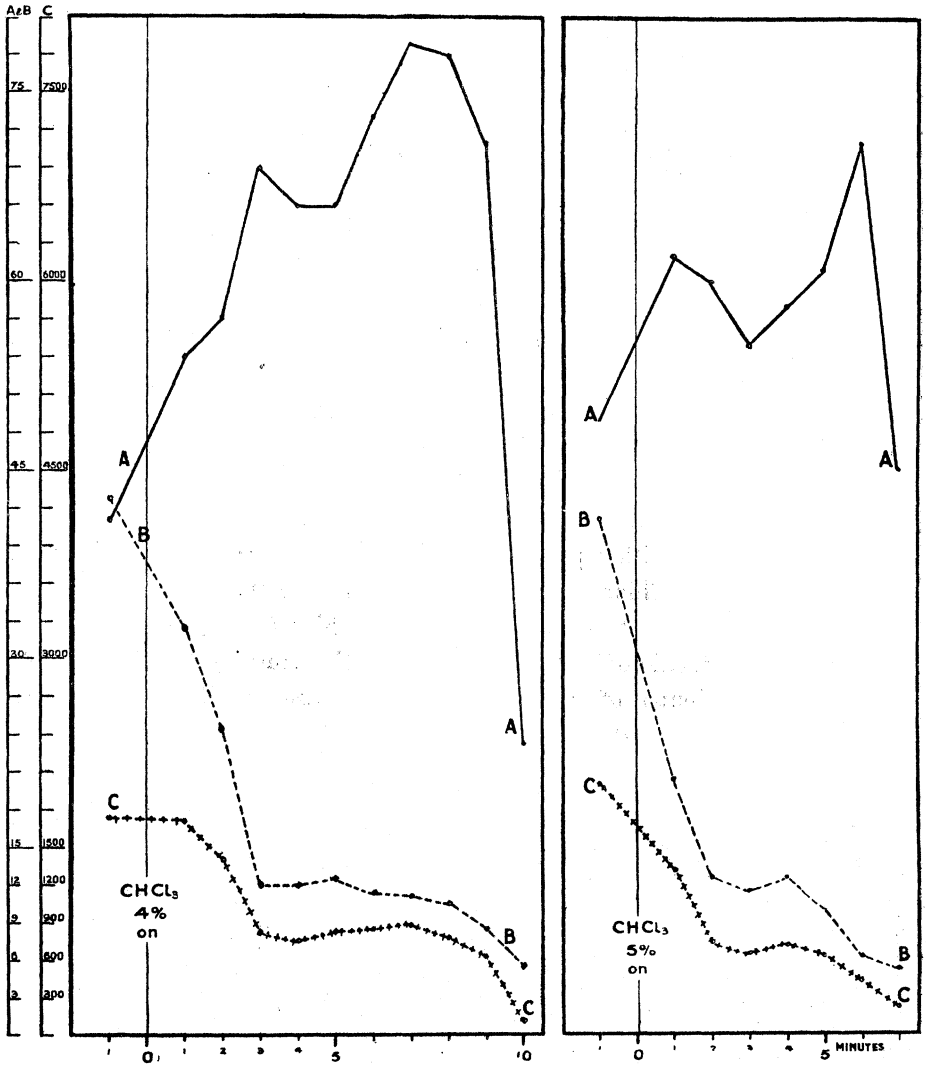
Effect on the Lung-ventilation of Re-anæsthetisation of Animals by Chloroform after Recovery from a Previous Anæsthetisation by this Drug when the Reflexes are well marked and Voluntary Movements begin.

In former papers we have shown that the chloroform content of the blood rises in the initial stage of anæsthesia with great rapidity to a value which approaches a maximum. During this period the amount of chloroform in the blood appears to affect chiefly the respiratory centres, so that the breathing becomes slower, and sometimes ceases altogether, and this is illustrated in the experiments already described. If the animal passes this stage naturally, or recovers on cessation of the anæsthetic, or is revived by means of artificial respiration, then, on continuing the anæsthetic, the amount of chloroform in the blood again rises quickly towards a maximum value, and an equilibrium between the factors which determine the amount of chloroform in the blood is established, the processes of intake and elimination at the pulmonary surface going on side by side.* After the animal passes this first stage of anæsthesia, or if an animal is re-chloroformed after it has so far recovered from a previous anæsthetic that the reflexes have become well marked, it appears to acquire a certain degree of apparent tolerance to the drug, with the result that the drug has a much less effect than would be the case, had not the animal been previously chloroformed. After recovery from chloroform to the point mentioned, the ventilation of the lung takes place at a lower level, both as regards frequency and depth of respiration. If the respiration happens to be deep, the frequency is generally correspondingly diminished. At this lowered level of respiration, the initial effects, when chloroform is again administered, are much less marked, even with very high percentages of chloroform. These points are well illustrated in the following examples :—

Example I.—The cat, from which the data of fig. 5 and Curve II were constructed, one minute after cessation of respiration, exhibited asphyxial convulsions, from which it recovered naturally, and, four minutes later, was respiring normally and regularly. Eighteen minutes after cessation of respiration, the animal had so far recovered as to make voluntary movements. It was then re-chloroformed with 4–5 per cent. chloroform. The frequency, amplitude, and total lung ventilation are given in Curve III.

After 10 minutes the animal ceased to breathe for one minute, and the chloroform was taken off, then a series of asphyxial gasps set in for five

* 'Roy. Soc. Proc.,' 1907, B, vol. 79, pp. 255 and 580.



CURVE III. CURVE IV.

A, B, C as in Curve II.

or six minutes, which passed into normal respiration nine minutes after cessation of respiration.

The respiration data during recovery are given in Table VII.

The animal was then again chloroformed with 5 per cent. chloroform, and the results are given in Curve IV. The animal died in seven minutes.

Table VII.

	Frequency.	Average depth.	
9th min.	20	27·66	553
The respiration lessened steadily after—			
14th min.	33	40·4	1333
17th ,,	38	42·5	1615
18th ,,	37	42·5	1572
20th ,,	Reflexes observed and voluntary movements.		

Example II.—The animal from which the tracing of fig. 4 was obtained ceased to breathe during the first minute of anæsthesia, and the chloroform was stopped. Asphyxial gasps then set in, which gradually passed into normal respiration. During the 10th minute the respiration was deep, slow, and regular, and at the end of the 12th minute the reflexes re-appeared, and also voluntary movements. The animal was now chloroformed a second time for 8 minutes with 3 per cent. chloroform. There was no evidence of any danger-point. Chloroform was stopped, and the animal allowed to again recover to the same state as above. It was re-chloroformed for a third time with 3·2 per cent. chloroform, and the effect of the drug was still less marked. The first few minutes of the tracings in each case are given below (figs. 7 and 8) and the comparative figures of all three chloroformings in Table VIII.

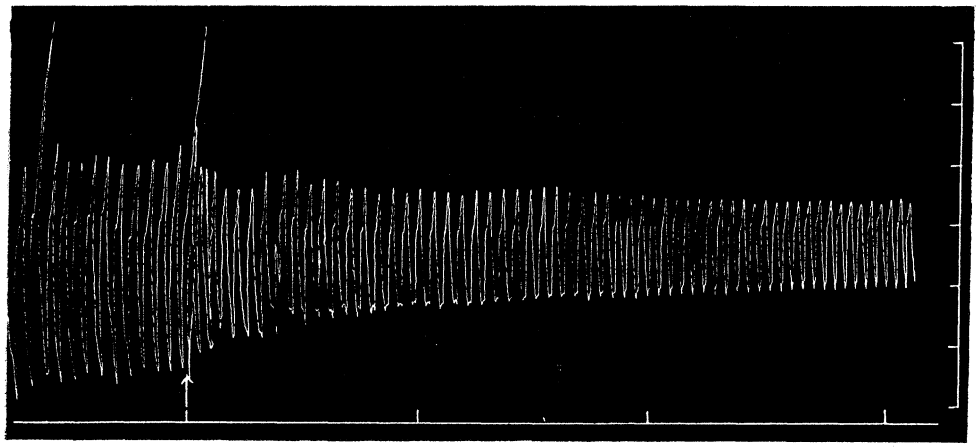


Fig. 7.

Depth of respiration, 1 division = 21·28 c.c.; time intervals, 30 secs.; ↑, 3 per cent. chloroform on.

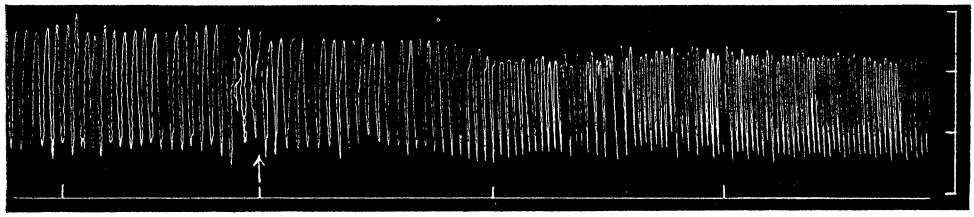


Fig. 8.

Depth of respiration, 1 division = 21·28 c.c.; time intervals, 30 secs.; ↑, 3·2 per cent. chloroform on.

Table VIII.

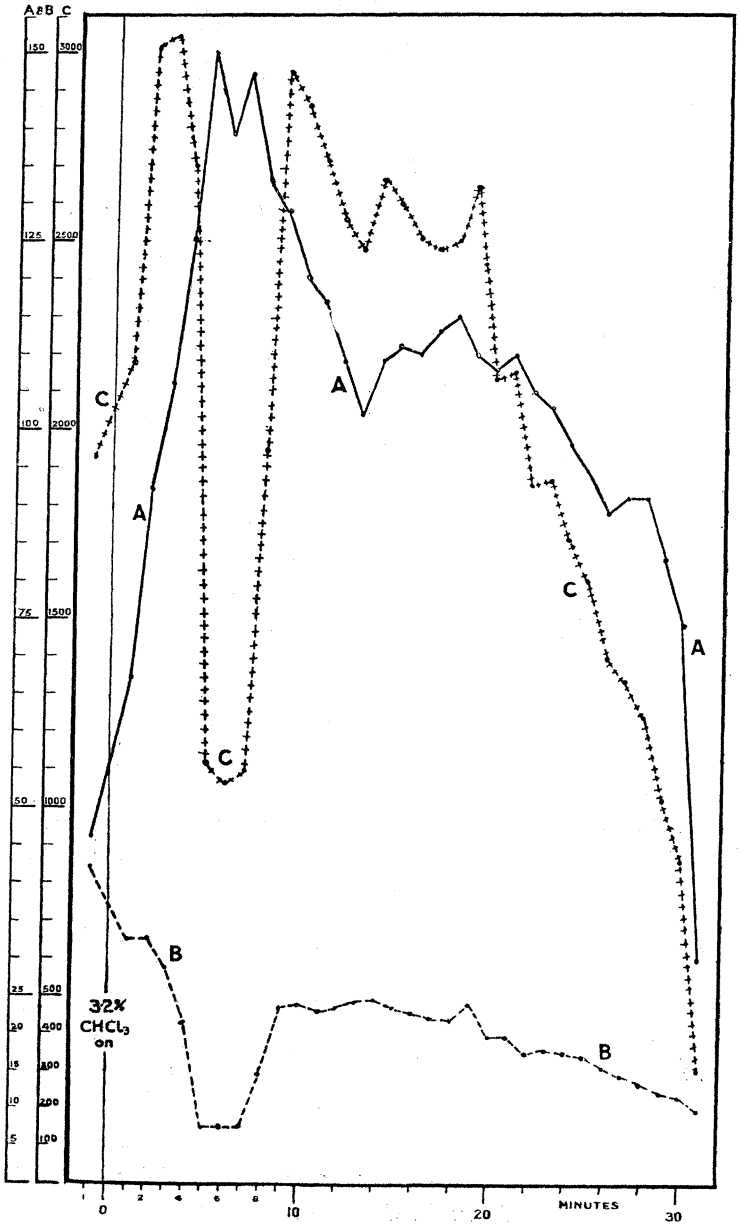
Intervals of time.	Anæsthetic.	1st chloroforming.			2nd chloroforming.		
		Frequency.	Amplitude.	Ventilation.	Frequency.	Amplitude.	Ventilation.
1 min. before $CHCl_3$	None	76	77·46	5887	32	83·63	2676
0·5 min.	$CHCl_3$ on 3 per cent.	32	37·24	1102 } 2017	17	49·37	839 } 1523
0·5 „	„	25	36·6	915 }	18	38·30	684 }
0·5 „	„	20	56·39	1128 } 1164	22	32·56	716 } 1445
0·5 „	„	2	18·08	36 }	25	29·15	729 }
3rd „	$CHCl_3$ off. A few gasps asphyxial.				65	24·54	1660
4th „	„	„	„		81	23·4	1895
5th „	„	„	„		89	21·28	1894
6th „	„	„	„		89	20·64	1837
7th „	„				$CHCl_3$ off.		

Intervals of time.	Anæsthetic.	3rd chloroforming.		
		Frequency.	Amplitude.	Ventilation.
1 min. before $CHCl_3$	None	46	41·92	1928
0·5 min.	$CHCl_3$ on 3·2 per cent.	25	38·3	958 } 2182
0·5 „	„	42	29·15	1224 }
0·5 „	„	92	32·77	3015
0·5 „				
3rd „	„	106	28·73	3045
4th „	„	125	21·57	2699
5th „	„	150	7·45	1117
6th „	„	139	7·66	1065

The complete course of the third chloroforming, which was continued until death in 31 minutes, is shown in Curve V.

No doubt the early cessation of respiration in the first chloroforming was largely due, as we have pointed out, to the excessive lung ventilation prior to the anæsthetic, combined with the high percentage of chloroform;

in subsequent chloroformings the respiratory centres are depressed to such an extent that the respiration is at a lower level, and consequently



CURVE V.—A, B, C as in Curve II.

identical or even higher percentages of chloroform have a less effect on the ventilation, and no sign of any initial danger-point is present.

Example III.—In the following experiment the animal was anæsthetised under a bell-jar with chloroform, the necessary operative procedures carried out, and then placed in the plethysmograph and allowed to recover until all the reflexes were well marked and voluntary movements returned. When the respiration was steady and equable, 2·5 per cent. of chloroform was given, and, as the tracing (fig. 9) shows, there is no very marked effect on the respiration leading to a danger-point. After the third minute

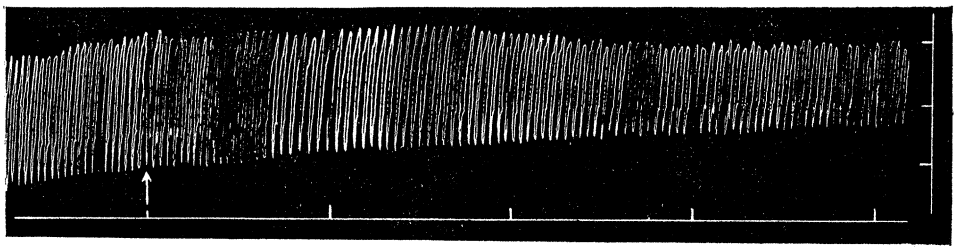


Fig. 9.

Depth of respiration, 1 division = 22·22 c.c.; time intervals, 30 secs.; ↑, 2·5 per cent. of chloroform.

the percentage of chloroform was gradually reduced to 1 per cent., and the lung ventilation remained practically the same. After the 10th minute the chloroform was stopped, the animal allowed to recover until the reflexes returned seven minutes later. A high percentage of chloroform (5 per cent.) was now given, and the animal died in nine minutes. A slowing of the respiration occurred at first, but no cessation. Such a percentage administered to an animal not previously anæsthetised with chloroform would almost

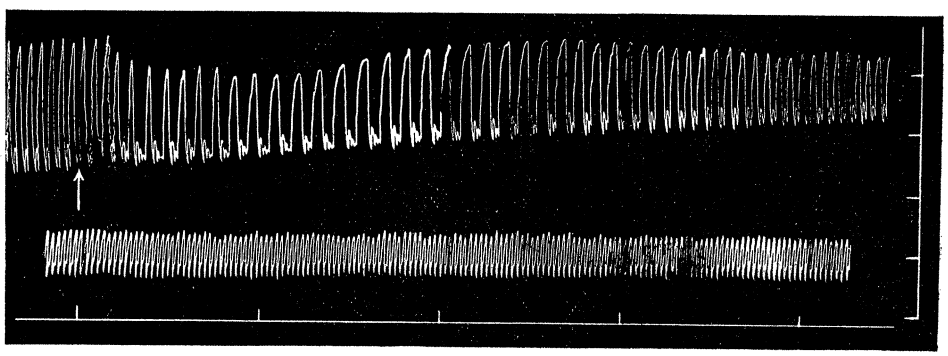


Fig. 10.

Depth of respiration, 1 division = 22·22 c.c.; time intervals, 30 secs. Upper tracing represents the first 2 mins. of 5 per cent. chloroform, the lower the 4th to 6th mins.

certainly have produced death within the first few minutes. This initial slowing was followed by increase in rate and decrease in depth. This is a typical result and well illustrated in the tracing, fig. 10.

The data of this experiment are given in Table IX.

Table IX.

Intervals of time.	Anæsthetic.	Frequency.	Amplitude, in c.c.	Ventilation.	
1 min. before $CHCl_3$		53	48·73	2705	
0·5 min.	$CHCl_3$ 2·5 per cent. on	24	27·11	1131	2131
0·5 ,,	,,	22	45·33	1000	
0·5 ,,	,,	24	34·89	837	1637
0·5 ,,	,,	25	32·00	800	
3rd ,,	,,	55	29·34	1614	
4th ,,	,,	60	27·11	1628	
5th ,,	Reduced percentage of $CHCl_3$	64	24	1536	
6th ,,	1·3 $CHCl_3$	62	23·11	1433	
7th ,,	1·0 ,,	54	24·39	1344	
8th ,,	1·0 ,,	52	29·11	1514	
9th ,,	1·0 ,,	50	33·34	1666	
10th ,,	1·0 ,,	49	39	1905	
	$CHCl_3$ off for 8 mins. Reflexes and voluntary movements.				
1 ,,	No $CHCl_3$	35	46·89	1642	
0·5 ,,	5 per cent. $CHCl_3$	11	36·98	407	705
0·5 ,,	,,	9	33·11	298	
0·5 ,,	,,	10	34·89	349	744
0·5 ,,	,,	14	28·22	395	
0·5 ,,	,,	18	22·67	408	891
0·5 ,,	,,	25	19·33	483	
1 ,,	,,	61	18·23	1111	
1 ,,	,,	71	16·00	1137	
1 ,,	,,	70	15·71	1100	
1 ,,	,,	70	15·55	1089	
1 ,,	,,	64	14·78	946	
1 ,,	,,	55	13·87	749	
1 ,,	,,	Ceased to breathe			
1 ,, (11th)	,,	Asphyxial convulsions			

Example IV.—In this experiment the animal was anæsthetised with nitrous oxide; the breathing after recovery was regular.

It was then anæsthetised with 2 per cent. of chloroform for three minutes, with slight evidence of a danger-point during the first minute, but the effect was not very marked. The measurements are given in Table X.

Table X.

Intervals of time.	Frequency.	Amplitude.	Ventilation.	
1 min. before $CHCl_3$	55	48·28	2656	
0·5 min., 2 per cent. $CHCl_3$ on	24	26·86	645	1161
0·5 ,,	19	29·14	516	
0·5 ,,	26	30·71	798	1755
0·5 ,,	33	29·00	957	
1 ,,	64	26·14	1699	

The animal was allowed to recover for six minutes; when the reflexes had reappeared, 1·5 per cent. chloroform was given for 10 minutes, after which it was increased to 2·5, and finally to 3 per cent. The increasing percentage of chloroform produced an increase in rate and considerable decrease in the average depth, but had a comparatively slight effect on the total ventilation of the lung, as may be seen from the data given in Table XI.

Table XI.

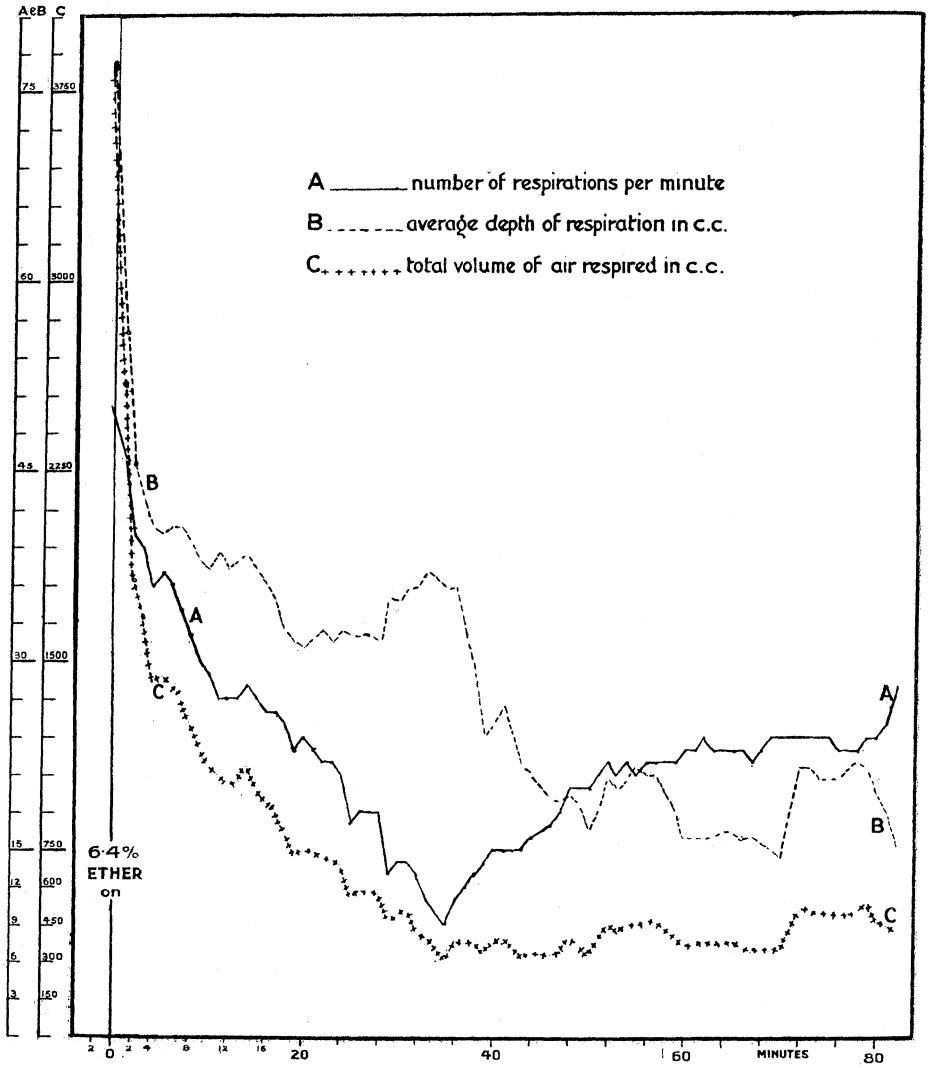
Intervals of time.	Anæsthetic.	Frequency.	Amplitude.	Ventilation.	
0·5 min. before $CHCl_3$		30	34·29	1028	
0·5 ,,	1·5 per cent. $CHCl_3$ on	27	25·71	694	1225
0·5 ,,	,,	24	22·14	531	
1 ,,	,,	49	21·44	1050	
1 ,,	,,	57	22·14	1129	
4 ,,	,,				
5 ,, Not counted	,,				
6 ,,	,,	65	27·71	1194	
7 ,,	,,				
8 ,, Not counted	,,				
9 ,,	,,				
10th ,,	,,	56	18·43	1032	
11th ,,	2·5 per cent. $CHCl_3$ on	59	16·66	983	
12th ,, Not counted	,,				
13th ,,	,,	56	12·57	830	
14th ,,	3 per cent. $CHCl_3$ on	66	11·57	764	
15th ,,	,,	60	11·19	738	
16th ,,	,,	64	10·14	648	
0·5 ,,	,,	30	6·97	209	
0·5 ,,	,,	Ceased to breathe			

Ventilation of the Lung during Narcosis with Ether.

Adopting the same methods of experiment as with chloroform, a number of plethysmographic records were taken of cats anæsthetised with ether, the percentage of which varied between 6·4 and 14 per cent. These values were controlled by Waller's balance. It was found, on comparing the various tracings, that, as in the case of chloroform, the effect of the drug on the

ventilation of the lung depended on the rate and depth of the respiration before the administration of the anæsthetic. The general effect of ether is to reduce the respiration to a lower level. This reduction is at first rapid, and then, after the first few minutes, proceeds slowly. This is illustrated by the two following examples :—

Example V.—The cat, weight 3·2 kgrm., was anæsthetised with nitrous oxide, the necessary operations performed, placed in the plethysmograph, and allowed to recover. Ether 6·4 per cent. was administered. The data of the first 10 minutes of this experiment are given in Table XII.



CURVE VI.

Table XII.

Intervals of time, in minutes.	Anæsthetic.	Frequency of respirations.	Amplitude of respiration, in c.c.	Lung ventilation, in c.c.
0·5	0	25	77·14	1929
0·5	6·4 per cent. ether	25	59·77	1494 } 2584
0·5	,,	21	51·92	1090 }
1·0	,,	40	45·47	1820
1·0	,,	39	42·86	1672
1·0	,,	36	40·59	1461
1·0	,,	37	39·93	1478
1·0	,,	36	40·48	1457
1·0	,,	34	40·48	1358
1·0	,,	32	39·29	1057
1·0	,,	30	38·10	1043
1·0	,,	29	37·27	1081

The whole experiment lasted 82 minutes, and, during the last four minutes, a very high percentage of ether was given in order to kill the animal. The whole data of this experiment are given in Curve VI.

Example VI.—The procedure was the same as in the last experiment, except that the percentage of ether administered was 13–14 per cent. The measurements are given in Table XIII.

Table XIII.

Intervals of time, in minutes.	Anæsthetic.	Frequency of respirations.	Amplitude of respiration, in c.c.	Lung ventilation, in c.c.
1·0	0	75	59·96	4498
1·0	13—14 per cent. ether	57	30·47	1737
1·0	,,	63	26·69	1644
1·0	,,	68	25·37	1726
1·0	,,	Not counted: even and regular.		
1·0	,,	,, ,,		
1·0	,,	,, ,,		
1·0	,,	,, ,,		
1·0	,,	46	25·05	1153
1·0	,,	Not counted: even and regular.		
1·0	,,	37	26·15	967
1·0	,,	Not counted: even and regular.		
1·0	,,	29	23·92	693
1·0	,,	Not counted: even and regular.		
1·0	,,	,, ,,		
1·0	,,	33	21·8	719
1·0	,,	31	21·59	669

During the 16th minute the respiration was shallow, and irregular until the 18th minute, when the ether was discontinued.

In no case, with the percentage of ether used, up to 15 per cent., did we

notice any cessation of respiration constituting a danger-point, such as is generally found constituting an initial danger-point in chloroform narcosis.

In experiments with re-etherisation after recovery from ether, the effects of the drug on the lung ventilation are less marked, a state of things already referred to in connection with chloroform.

General Discussion of Results.

With unimpeded respiration under anæsthesia by chloroform, given at a slight positive pressure, the ventilation of the lung takes place at a lowered level. Whatever may be the condition of the gas exchange between the alveolar air and the blood, the total exchange of gases between the animal and the atmosphere is diminished in amount, and this continues throughout the whole period of anæsthesia. From our data it will be seen that during chloroform narcosis (in which breathing does not stop) the lung ventilation is diminished in the first three minutes by from 30 to 80 per cent., or on an average about 60 per cent. of its original value, and by a similar amount after prolonged anæsthesia.

It is during this early period that the initial danger-point occurs, and an entire cessation of the respiration may take place, which may result in death.

A simple explanation of this cessation of breathing on administration of chloroform after deep and rapid respiration may, we think, be found in the carbon dioxide content of the blood. The hyperpnœa, prior to the administration of the anæsthetic, probably reduces the carbon dioxide content below normal, so that, as Mosso, Miescher, Haldane and Priestley, and Yandell Henderson* have pointed out, the chemical stimulus necessary to keep the respiratory centre in activity is reduced. The effect of the anæsthetic would be to reduce the excitability of the centre to the effect of the carbon dioxide, so that the quantity of this gas, even after a minute or two of reduced respiration consequent on the administration of the drug, would not be sufficient to maintain respiration, which accordingly would cease. If this is the case, the stoppage of respiration after administration of the drug would obviously depend on two factors, viz., the alveolar ventilation prior to anæsthesia and the strength of the anæsthetic. If the ventilation were sufficient to reduce the carbon dioxide much below normal, and the anæsthetic were strong enough, cessation of breathing would occur; if either of these factors were reduced in a less degree, the effects would vary from slowing of respiration or temporary stopping to a scarcely appreciable change. In all

* 'Amer. Journ. Physiol.,' 1908, vol. 21, p. 126; 1909, vol. 23, p. 345; 1909, vol. 24, p. 66; 1910, vol. 25, pp. 310 and 385; 1910, vol. 26, p. 260.

the cases of death at this stage which we have investigated, the heart continued to beat for some little time after respiration ceased.

In order to throw light on this question, we made analyses of the blood gases of cats under urethane, in which, as the plethysmograph showed, the respiration was extremely regular and constant and the lung ventilation medium in amount. The results are given in Table XIV, and compared with the average of four analyses of the blood of unanæsthetised cats which exhibited marked hyperpnœa, taken from our former paper.*

Table XIV.

	Composition of the blood gases of cats under urethane in c.c. per 100 c.c. of blood.				Remarks.	Alveolar air. Composition of lung gases.		
	Total gas.	CO_2.	O.	N.		CO_2.	O.	N.
1	60·70	49·48	10·01	1·21	10 c.c. of blood			
2	53·54	42·03	12·56	0·95	Same cat as 1, 1 hour later			
3	51·17	38·68	17·43	1·07	Shallow panting respiration	5·74	9·66	84·59
4	60·70	49·48	10·01	1·21				
5	55·54	42·03	12·56	0·95	Same cat as 4, 1 hour later			
6	50·01	31·77	16·68	1·55				
7	64·71	47·84	15·66	1·22	Respiration slow and shallow	6·24	9·15	84·69
8	51·57	35·76	14·89	0·91		4·93	—	—
9	51·17	38·03	12·03	1·07		6·25	9·74	84·02
	Average of four analyses of the blood of unanæsthetised* cats in which the respiration was rapid and deep and the lung-ventilation abnormally great.							
	35·03	20·56	13·49	0·96				

* 'Journ. Physiol.,' October 11, 1910, vol. 41, p. 62.

The comparison of these analyses clearly shows that with a deep and rapid respiration the carbon dioxide content of the blood is much less than when the lung-ventilation is normal in character.

Since the dead-space in respiration is constant, it is evident that, with reduced ventilation, a proportionately less amount of inspired air is introduced for diffusion with alveolar air, and consequently the carbon dioxide and nitrogen should accumulate in the alveolar air, and the oxygen content should diminish. These variations, however, could not be very great; at any rate

* 'Journ. Physiol.,' Oct. 11, 1910, vol. 41, Nos. 1 and 2, p. 62, Expts. I, II, III, and IV.

would not vary directly as the change in ventilation. From these considerations we might expect the oxygen content of arterial blood to fall a little below the normal and the carbon dioxide to augment, and to a slight extent also the nitrogen, at about the point of the vanishing of the reflexes in the initial stages of anæsthesia, and in the second stage of anæsthesia. On the other hand, when the animal is recovering from the anæsthetic and the lung ventilation is improving, we might expect the gas-content of the blood at the reappearance of the reflexes to again approach the normal, or even be normal. In Table XV we give analyses, taken from our paper on "The Composition of the Blood Gases in Chloroform Narcosis,"* and the blood gases at the various stages referred to.

Table XV.—Gas Content of the Arterial Blood of Cats at 0° and 760 in c.c. per 100 c.c. of Blood.

		CO_2.	O.	N.
1	Normal (average of six observations)	25·07	13·60	1·0
2	Disappearance of reflexes (in 3—5 mins.)	27·76 26·45 34·51	9·52 6·11 7·71	3·05* 2·03* 1·38
3	Re-appearance of reflexes after cessation of $CHCl_3$ for 25—35 mins.	26·62 26·31 32·83	15·41 12·14 12·58	1·18 1·19 1·28
4	Second stage of anæsthesia (average of eight experiments)	36·00	8·14	1·49
	Variations	16·98—48·38	3·51—11·63	1·16—2·53

* Uncorrected for the nitrogen contained in the oxygen used for combustion of the chloroform.

In normal cats the amount of hæmoglobin, as given by the Gowers-Haldane hæmoglobinometer, lies between 70 and 80, which, in terms of the percentage of oxygen content, would give a value a little above 13·6, the average volume of oxygen found by gas analysis. The fall in oxygen content during the second stage of anæsthesia is about 40 per cent., and in the initial stages often even more than this. The hæmoglobin is then only partially saturated with oxygen during narcosis—indeed not more than 60 per cent. The blood of the normal cat, on the assumption that the alveolar air contains 14 per cent. of oxygen, must, when allowance is made for tension of aqueous vapour at 38° (49·3 mm.) and with 40 mm. carbon dioxide tension in blood,

* 'Journ. Physiol.,' Nov. 9, 1910, vol. 41, p. 255.

be saturated to the extent of 19 c.c. per 100 c.c. of blood, 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. The diminution of oxygen in the blood during chloroform narcosis seems too great to be accounted for by the lowered level of respiration, particularly in the initial stages, judging by the figures obtained by Loewy and Zuntz and others.*

The diminution of oxygen might, however, be to some extent accounted for by a piling up of carbon dioxide in the blood during narcosis, a condition which, as is well known, favours the dissociation of oxyhæmoglobin.

In order to test whether a lowered level of respiration, such as one finds in chloroform narcosis, does result in a marked diminution of oxygen due to the diminished respiration alone, we made the following experiment with a low percentage air-ether mixture, ether being selected as it has a less marked poisonous effect than chloroform:—

A cat was anæsthetised with ether, the necessary operations performed, and placed in the plethysmograph. It was then allowed to recover, and was anæsthetised with 6 per cent. ether-air. Samples of the blood were taken at two stages at which the number of respirations per minute was the same, but the average depth of respiration much less in one than the other.

The following was the breathing during the three minutes before Sample I was taken:—

	No. of respirations.	Average depth, in c.c.	Total ventilation, in c.c.
1st min.	27	39·45	1065
2nd „	27	38·00	1026
3rd „	29	37·28	1084

and before Sample II—

1st min.	27	25·22	681
2nd „	26	25·38	657
3rd „	28	25·20	706
4th „	22	26·60	585

The following results were obtained:—

Sample I.—Volume of blood = 10·3 c.c.

Pressure of gas at 13·8° C. and constant volume (48·65 c.c.) = 8·2 cm.; after addition

* 'Archiv f. Anat. u. Physiol.,' 1904, p. 166.

of oxygen, 23·6 at 13·8° ; after explosion, 23·08 at 13·9° ; after absorption by KOH, 16·14 at 13·9° ; after absorption by "pyro," 0·40 at 13·9° and constant volume (12·60).

Sample II.—Volume of blood = 10·3 c.c.

Pressure of gas at 14·2° and constant volume (48·65 c.c.) = 8·98 cm. ; after addition of oxygen, 25·81 at 14·2° ; after combustion, 24·75 at 14·2° ; after treatment with KOH, 16·65 at 14·2° ; and after "pyro," 1·48 at 14·5° and constant volume (12·60 c.c.). The oxygen used for combustion contained 1·3 per cent. of nitrogen.

Composition of Gas in c.c. per 100 c.c. of Blood.

	Gas.	Ether.	CO_2.	O.	N.
1	48·51	1·04	36·87	9·63	0·96
2	53·05	2·09	39·50	10·48	0·98

Hæmoglobin by hæmoglobinometer: first sample, 70 per cent. ; second sample, 68 per cent. This is equivalent to about 12·6 of oxygen.

It is clear from this that a change of total respiration from an average of 1058 to 657 had no effect on the oxygen-content of the blood. It may thus be fairly concluded that the diminution of oxygen-content of blood in chloroform narcosis is not mainly due to diminished respiration, but to the action of the drug on the red corpuscles ; since, in agreement with the observations of Pohl and Nicloux, we found that as much as 97 per cent. of the chloroform in blood may be actually associated with the red corpuscles.* The views of B. Moore and Roaf and Gangitano may also be regarded as supporting the idea that there is some direct combination between chloroform and the protein of the corpuscles.

We take this opportunity of thanking the Government Grant Committee of the Royal Society for help in carrying out this work.

* 'Roy. Soc. Proc.,' 1906, B, vol. 78, p. 450.