THE CHANGE OF COMPOSITION OF ALVEOLAR AIR AFTER THE STOPPAGE OF NORMAL BREATHING.

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(With two Text-figs.)

Introduction.

The tension of carbon dioxide in the alveolar air of man is maintained, under conditions of rest and normal breathing, at a definite value in each individual, from which it deviates only slightly. The constant values for different individuals vary over a wider range. These facts were first established by Haldane and Priestly (1905), and by FitzGerald and Haldane (1905). Campbell, Douglas, and Hobson (1914) have recently shown that an increase of 2 mm.Hg in the alveolar tension of carbon dioxide is sufficient to double the amount of ventilation of the lungs. Under ordinary conditions of rest, then, the amount of air breathed in a given time is so adjusted as to keep the alveolar tension of carbon dioxide practically constant. Haldane and Priestly also showed that the alveolar tensions of oxygen may be varied widely by breathing atmospheres containing different percentages of oxygen, without sensibly affecting the amount of ventilation of the lungs. Within wide limits, therefore, the ventilation of the lungs is regulated solely by the alveolar tension of carbon dioxide, and is independent of the alveolar tension of oxygen.

When, however, the normal ventilation of the lungs is stopped by holding the breath, or by rebreathing the same air, the carbon dioxide given off by the blood will accumulate in the lungs, while the oxygen present will tend to disappear. The first investigation of the change of composition of the air in the lungs, when the breath is held, seems to be that of Becher (1855), who held the breath for various periods ranging up to 100 seconds, after taking a deep inspiration. He found that the percentage of carbon dioxide in the expired air rose at a continually decreasing rate, and, towards the end of the period of holding the breath, seemed almost to have reached a constant value.

By shutting off one lobe of the lung of an animal from the exchange of gases with the inspired air, and drawing off samples of the contents through a catheter, Wolffberg (1871) attempted to measure the final tension of carbon dioxide in this portion of the lung after a state of equilibrium with the venous blood had been reached.

Loewy and von Schrötter (1905) carried out similar experiments upon human beings. They found that the alveolar tensions of carbon dioxide and of oxygen eventually reached constant values, the former gas sooner than the latter. These values they regarded as the venous tensions of the gases.

Hill and Flack (1908) observed the length of time for which the breath could be held, under normal conditions, after breathing oxygen, and after muscular exercise. They measured the tensions of carbon dioxide and of oxygen in the alveolar air when the breaking-point was reached. They also measured the final alveolar percentages after breathing as long as possible from an anæsthetic bag, filled, in one case, with expired air, in another case, with oxygen. In each case, the time of holding the breath was longer, and the final tensions of carbon dioxide were higher than when similar gaseous mixtures were simply held in the lungs. The final tensions of carbon dioxide reached were also higher when oxygen was present in excess. These investigators made experiments to determine the alveolar percentages of carbon dioxide and of oxygen after holding the breath for various periods, and found that the percentage of oxygen fell more rapidly than that of carbon dioxide. They concluded that it was the alveolar percentage of oxygen, and not that of carbon dioxide, which determined the period for which the breath could be held. From their experiments on rebreathing the same air from a bag, they concluded that holding the breath obstructed the circulation and so hindered the exchange of gases between the alveolar air and the blood.

Leimdörfer (1909) determined the composition of alveolar air after inspirations of ordinary air, and of gaseous mixtures containing different percentages of carbon dioxide and oxygen, had been held in the lungs as long as possible. He, too, found that excess of oxygen raised the final percentage of carbon dioxide attained, and concluded that the time for which the breath could be held was determined by the percentage of oxygen in the alveolar air.

Du Bois-Reymond (1910) connected one lobe of the lung of an animal with a space filled with nitrogen, and observed the rate at which carbon dioxide was given off into this space. He found that the percentage of carbon dioxide rose at a logarithmically decreasing rate, and approached a certain final value.

Christiansen, Douglas, and Haldane (1914) carried out experiments to determine the composition of alveolar air after holding in the lungs mixtures of air containing various percentages of carbon dioxide. The lungs, in fact, were used as an aërotonometer. When the percentage of carbon dioxide in the inspired mixture was below a certain value, the percentage in the alveolar air was greater after holding the breath than that present in the original mixture. When, however, the percentage of carbon dioxide in the mixture was greater than this value, the alveolar percentage, after holding the breath, was less than that in the original mixture; that is, carbon dioxide had been absorbed by the blood. These investigators concluded that the percentage of carbon dioxide in the inspired air above which carbon dioxide was absorbed by the blood, and below which carbon dioxide was given off by the blood, was the percentage in the alveolar air with which the venous blood was in equilibrium in the lungs, and from which the venous tension of carbon dioxide in the lungs could be calculated. These workers also measured the percentages of carbon dioxide in the alveolar air after holding the breath for various periods. They found that the alveolar percentage of carbon dioxide continued to rise during the whole period for which the breath was held, and concluded that the venous tension of carbon dioxide could not be determined by observations of this kind.

Recently, Boothby and Sandiford (1916) have also used the above aërotonometric method for the determination of the venous tension of carbon dioxide, and have obtained results similar to those of Christiansen, Douglas, and Haldane (*loc. cit.*).

In the present investigation, the rate at which the composition of alveolar air changes, when the admission of fresh air to the lungs is discontinued, has been examined in greater detail. The rate of alteration of the composition of the alveolar air has been studied under two different sets of conditions. In the first series of experiments, the breath was simply held for measured periods after the completion of a normal inspiration, before taking a sample of alveolar air. In the second series of experiments, after the completion of a normal inspiration, breathing was continued into and out of an empty rubber bag, samples of alveolar air being collected from time to time. It was found that the rise in the alveolar tension of carbon dioxide and the fall in the tension of oxygen were considerably more rapid in the second series of experiments than the first.

Experiments have also been carried out to examine more closely the difference between the two sets of results. It was found that movement of the same air into and out of the lungs, alteration of pressure in the closed chest, or the maintenance of negative pressure in the chest, caused a marked increase in the rate of increase of the alveolar tension of carbon dioxide. The maintenance of positive pressure in the chest, however, slightly decreased the rate of change of composition of the alveolar air after the cessation of normal respiration.

Methods.

The experiments described in this paper were made upon one subject (H.S.H.W.). Before commencing to collect samples of alveolar air, the subject seated himself comfortably and rested for ten minutes in order to allow the respiration to become as steady as possible. The subject remained seated during the whole course of an experiment. The only work done by him was the opening of taps for the collection of samples of alveolar air, the starting and stopping of a kymograph, and the making of the deep expirations from which the samples were obtained. A complete rest of five minutes was taken after the collection of each sample. The experiments in each series in the Tables given below are recorded in the order in which they were made.

Two preliminary series of experiments, in which about two hundred analyses were performed, were carried out on two different subjects. In these experiments, attention was not paid to the necessity of allowing the subject to rest completely before taking a sample of alveolar air. The variations among individual experiments were, consequently, too great to allow precise conclusions to be drawn. The average results of each series, however, showed the same features as the experiments recorded here.

The samples of alveolar air were collected over mercury in exhausted gas-burettes. The deep expirations from the last portions of which the samples were obtained (Haldane and Priestly, *loc. cit.*) were made through a brass mouth-piece, 20 cm. long, into a rubber-lined anæsthetic-bag. The mouth-piece was provided with ten side-tubes of capillary bore; to these tubes, burettes were attached. In this way, a number of samples of alveolar air could be collected without other manipulation than the opening of spring-clips.

The instant at which an expiration was made was recorded on the drum of a kymograph by means of a manometer connected with one of the side-tubes of the mouth-piece. The instant at which respiration was stopped and the holding of the breath commenced, was recorded on the kymograph by pinching the tube leading to the manometer. A Jaquet clock was arranged to make a time-tracing, showing seconds, immediately below the tracing of the manometer. The periods elapsing between the commencement of holding the breath and the making of the expiration from which the sample of alveolar air was obtained, were determined by measurement of the graphic records. In the cases in which the subject breathed into and out of a closed bag, the intervals of time between the successive expirations were measured in the same way. Time could be measured on the tracings with an error of about 0·5 second.

Periods of holding the breath, or, between expirations into a bag, are given in the Tables to the nearest second.

The analyses of the samples of alveolar air were carried out in a small Haldane-apparatus. About 20 cc. of alveolar air were collected for each sample, about 9 cc. being used for an analysis. Duplicate analyses were performed only in those cases in which there was doubt as to the reliability of a result. The results of duplicate analyses showed divergences ranging up to 2%. The deviation from the mean is only half this figure. The results given in the Tables, therefore, have an error of less than 2%; that is to say, the percentages of carbon dioxide and of oxygen are correct to less than one-tenth of one per cent. The amounts of carbon dioxide and of oxygen in the alveolar air are expressed as percentages by volume of the dry gas. The partial tensions of carbon dioxide and of oxygen, in millimetres of mercury, are also given. The tensions were calculated from the percentage composition of the dry gas, the barometric pressure at the time of the experiment, and the tension of aqueous vapour in the lungs [43 mm.Hg, Loewy and Gerhartz (1913), Osborne (1913)]. The tensions have an error of less than 1 mm.Hg.

Effect of holding the Breath.

In the following Table are shown the percentages and tensions of carbon dioxide and of oxygen in alveolar air after holding the breath for various periods. In the last portion of the Table, the averages of the values obtained in the individual experiments are given.

Table i.

Composition of alveolar air after holding breath for various periods.

Number.	Time.	Carbon dioxide.		Oxygen.	
		Per cent.	Mm.Hg.	Per cent.	Mm.Hg.
1	0	5·26	38·4		
2	5	5·75	42·0		
3	10	5·97	43·6		
4	16	6·19	45·1		
5	20	6·25	45·6		
6	27	6·56	47·8		
7	31	6·50	47·5		

TABLE i.—*continued.*

Number.	Time.	Carbon dioxide. Per cent.	Carbon dioxide. Mm.Hg.	Oxygen. Per cent.	Oxygen. Mm.Hg.
8	0	5·53	40·4		
9	5	5·90	43·0		
10	11	6·01	43·9		
11	16	6·42	46·9		
12	20	6·58	48·0		
13	27	6·57	48·0		
14	30	6·67	48·7		
15	37	6·91	50·5		
16	0	5·20	37·6	16·00	115·8
17	6	5·79	41·9	14·75	106·8
18	12	6·21	45·0	13·68	99·0
19	16	6·18	44·8	13·81	100·0
20	21	6·49	47·0	12·76	92·3
21	26	6·33	45·8	12·74	92·2
22	31	6·55	47·4	11·93	86·4
23	36	6·75	48·8	11·20	81·1
24	0	5·11	36·9	16·48	118·8
25	7	5·87	42·4	14·98	108·1
26	11	6·06	43·8	14·43	104·2
27	16	6·37	46·0	13·65	98·5
28	20	6·51	47·0	12·95	93·5
29	26	6·57	47·4	12·39	89·4
30	30	6·70	48·3	11·89	85·8
31	35	6·65	48·0	12·10	87·4
32	0	5·10	36·8	16·21	117·0
33	6	5·89	42·5	14·83	107·0
34	10	6·28	45·3	14·04	101·4
35	16	6·29	45·4	13·70	98·9
36	21	6·49	46·8	12·85	92·8
37	25	6·52	47·1	12·46	89·9
38	30	6·78	49·0	11·64	84·1
39	35	6·77	48·9	11·13	80·4
40	0	5·34	37·9	16·40	116·5
41	5	5·89	41·8	14·21	101·0
42	11	5·99	42·5	14·04	99·9
43	17	6·43	45·1	12·69	90·1
44	21	6·57	46·7	12·13	86·2
45	26	6·77	48·1	11·83	84·1
46	31	6·78	48·1	11·31	80·5
47	36	6·98	49·6	10·42	71·1

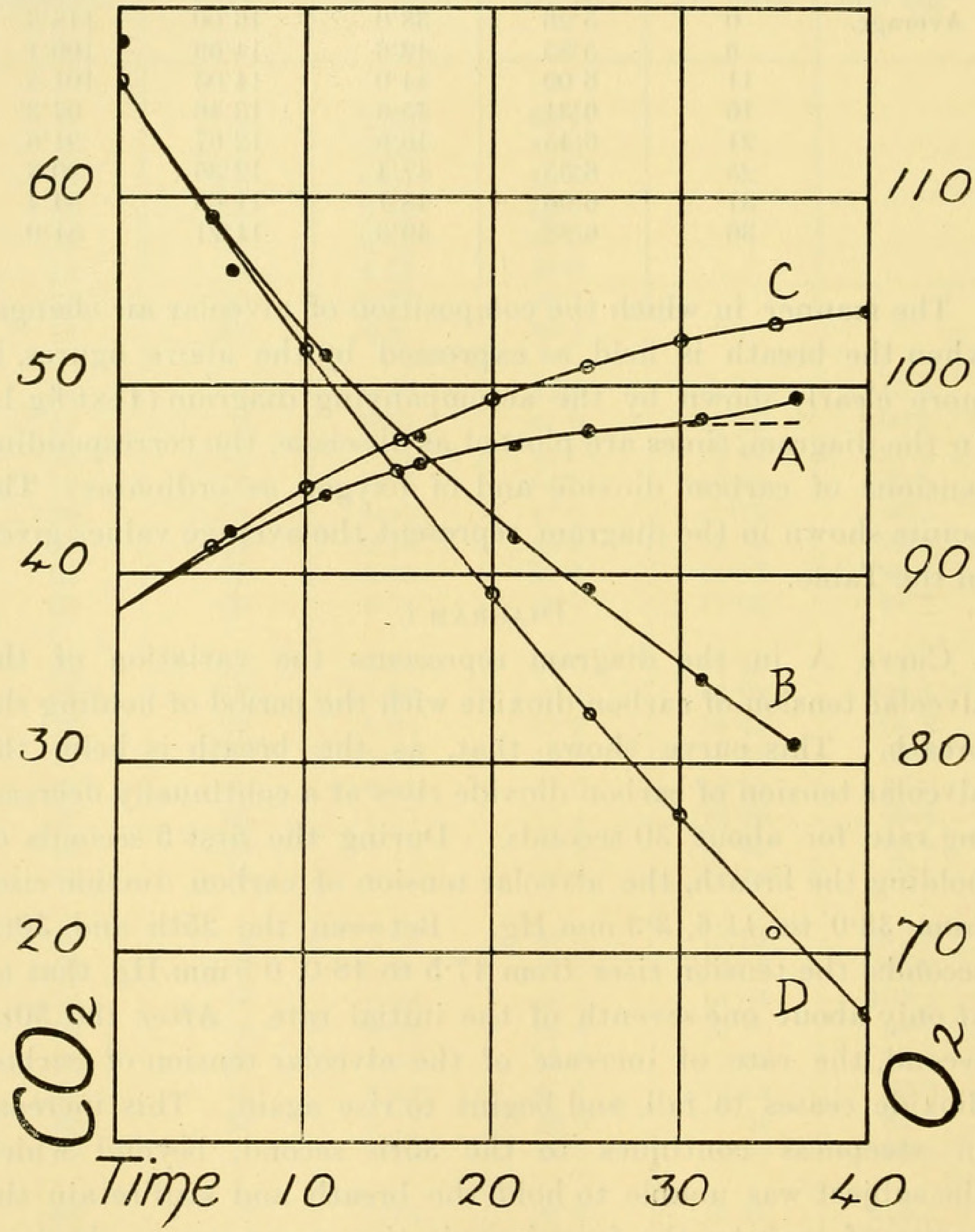
TABLE i.—*continued.*

Number.	Time.	Carbon dioxide.		Oxygen.	
		Per cent.	Mm. Hg.	Per cent.	Mm. Hg.
Average.	0	5·26	38·0	16·00	118·3
	6	5·85	42·6	14·69	106·1
	11	6·09	44·0	14·05	101·5
	16	6·31	45·6	13·46	97·3
	21	6·45	46·6	12·67	91·6
	25	6·55	47·4	12·36	89·3
	31	6·66	48·1	11·69	84·4
	36	6·82	49·3	11·21	81·0

The manner in which the composition of alveolar air changes when the breath is held, as expressed by the above figures, is more clearly shown by the accompanying diagram (Text-fig.1). In the diagram, times are plotted as abscissæ, the corresponding tensions of carbon dioxide and of oxygen as ordinates. The points shown in the diagram represent the average values given in the Table.

DIAGRAM i.

Curve A in the diagram represents the variation of the alveolar tension of carbon dioxide with the period of holding the breath. This curve shows that, as the breath is held, the alveolar tension of carbon dioxide rises at a continually decreasing rate for about 30 seconds. During the first 5 seconds of holding the breath, the alveolar tension of carbon dioxide rises from 38·0 to 41·6, 3·3 mm.Hg. Between the 25th and 30th seconds, the tension rises from 47·5 to 48·0, 0·5 mm.Hg, that is, at only about one-seventh of the initial rate. After the 30th second, the rate of increase of the alveolar tension of carbon dioxide ceases to fall, and begins to rise again. This increase in steepness continues to the 35th second, beyond which the subject was unable to hold the breath and still retain the power of making the forced expiration necessary to obtain a sample of alveolar air. The increase in the rate at which the alveolar tension of carbon dioxide rises, after holding the breath for about 30 seconds, is due to the fact that the subject then begins to make involuntary movements of the diaphragm and of the muscles of the chest, which grow in intensity as the holding of the breath is continued. These movements, as will be shown later, markedly hasten the passage of carbon dioxide into the alveolar air. The total rise of the tension of carbon dioxide, on holding the breath for 35 seconds, is 11·5 mm.Hg.



Text-fig. 1.—Variation of alveolar tensions of carbon dioxide and of oxygen with period of holding the breath (A, B), and with period of re-breathing expired air (C, D). Times (abscissæ) in seconds, tensions (ordinates) in mm.Hg.

Curve B, in the above diagram, shows how the alveolar tension of oxygen changes as the breath is held. It will be seen that the rate, at which the tension of oxygen falls, is very much greater than the rate at which the tension of carbon dioxide rises. In 35 seconds, the tension of oxygen falls from 116·5 to 81·0, 35·5 mm.Hg, or more than three times as much as the tension of carbon dioxide rises. It will be noticed also that, although the rate of change of the alveolar tension of oxygen slows down with time, this slowing down is much less marked than in the case of the tension of carbon dioxide. During the first 5 seconds of the experiment, the tension falls 7·5 mm Hg; during the last 5 seconds, 3·5 mm.Hg or at about one-half the initial rate. The tremors of the respiratory muscles, which make their appearance towards the end of the experiment, apparently do not become of sufficient intensity to affect noticeably the rate of absorption of oxygen in the lungs.

When the breath is held for a long enough period, therefore, the tension of carbon dioxide gives indications of attaining a certain fixed value. The alveolar tension of oxygen, on the other hand, falls rapidly during the whole period for which the breath can be held.

Effect of rebreathing the same Air.

In the following Table are given the alveolar tensions and percentages of carbon dioxide and of oxygen after the air in the lungs at the end of a normal inspiration, instead of being held there for a certain period, is breathed into and out of a closed, empty bag. Under these circumstances, the air of the lungs does not remain stagnant, but is mixed together by the movements of breathing. The contents of the lungs are also mixed with the air in the mouth-piece, and in the bag, which cannot be emptied completely. The volume of this air is not more than 100 cc. The average volume of the deepest expiration which the present subject can make, after taking a normal inspiration, is 2200 cc. As the volume of the residual air may be taken as 800-1000 cc., the total volume of the air in the lungs, at the end of a normal inspiration, amounts to approximately 3000 cc. The contents of the lungs are mixed, therefore, with about 3% of their volume of air by breathing into and out of the bag. If the rate at which the alveolar tension of carbon dioxide rises, and that at which the alveolar tension of oxygen falls, be the same, when the contents of the lungs are breathed in this way as when the breath is held, the changes in the tensions of the gases will be about 3% less in the former case than in the latter. The figures given in the following Table, however, show that, on the contrary, the changes in the tensions of the gases are considerably greater in the former case.

TABLE ii.—*Composition of alveolar air after breathing into and out of closed bag for various periods.*

Number.	Time.	Carbon dioxide.		Oxygen.	
		Per cent.	Mm. Hg.	Per cent.	Mm. Hg.
48	0	5·07	36·5	15·70	112·8
49	7	5·91	42·5	14·13	101·5
50	15	6·52	46·9	12·44	89·5
51	22	6·73	48·9	11·22	80·7
52	29	7·07	50·8	10·03	72·2
53	34	7·03	50·5	9·35	67·2
54	41	7·29	52·4	8·74	62·8
55	46	7·30	52·5	8·23	59·1
56	0	5·03	35·7	15·92	113·2
57	7	5·77	41·0	14·93	106·1
58	16	6·33	45·0	13·53	96·2
59	23	6·74	47·9	12·13	86·2
60	31	6·96	49·5	11·32	80·5
61	38	7·20	51·2	10·14	72·1
62	44	7·34	52·1	9·35	66·5
63	51	7·37	52·4	8·65	61·5
64	0	5·35	38·4	15·84	113·8
65	8	6·09	43·3	14·51	104·2
66	14	6·60	47·4	13·36	95·9
67	20	6·94	49·8	11·95	85·8
68	27	7·24	49·8	10·87	78·0
69	33	7·47	53·6	9·91	71·2
70	38	7·59	54·5	8·70	62·4
71	44	7·77	55·7	7·97	57·2
72	0	5·30	38·6	16·20	118·0
73	7	5·99	43·6	15·25	110·3
74	13	6·63	47·8	13·88	100·3
75	19	7·09	51·2	12·88	93·1
76	25	7·25	52·4	11·80	85·4
77	31	7·45	53·8	11·00	79·6
78	36	7·61	55·0	9·94	71·8
79	42	7·78	56·2	9·08	65·6

TABLE ii.—*continued.*

Number.	Time.	Carbon dioxide.		Oxygen.	
		Per cent.	Mm.Hg.	Per cent.	Mm.Hg.
Average	0	5·25	38·0	16·1	116·4
	5	5·70	41·0	15·1	109·1
	10	6·15	44·5	14·1	101·9
	15	6·5	47·0	13·2	95·5
	20	6·8	49·2	12·3	89·0
	25	7·05	51·0	11·4	82·5
	30	7·25	52·4	10·7	77·2
	35	7·35	53·1	9·8	70·9
	40	7·45	53·9	9·2	66·5

The intervals of time between the taking of each sample of alveolar air and that of the next in the above series of experiments, are not considered to be uniform enough to allow average values to be calculated from them arithmetically. The average figures given in the last portion of the Table, therefore, have been determined graphically by plotting the individual experiments on squared paper, drawing a curve through the points representing each series of results, and, from the curves, determining the tensions of carbon dioxide and of oxygen for corresponding times. From the figures got thus, the average values have been calculated in the ordinary way. These values are represented in the diagram by the points on the curves C and D.

The curve C represents the manner in which the alveolar tension of carbon dioxide rises when the contents of the lungs are breathed into and out of a closed, empty bag. It will be seen that the alveolar tension of carbon dioxide rises at a continually decreasing rate. During the first 5 seconds of the experiment, the tension of carbon dioxide rises 3·5 mm.Hg, or by practically the same amount as when the breath is held in the lungs. Between the 25th and 30th seconds, however, the rise is 1·4 mm. Hg, or about thrice as great as when the breath is held. The total rise in the alveolar tension of carbon dioxide in 35 seconds is from 38·0 to 53·0, 15·0 mm.Hg, or nearly 40% greater than the rise occurring in the same period when the breath is simply held.

Curve D shows the rate at which the alveolar tension of oxygen falls when the contents of the lungs are breathed into and out of a closed bag. This rate decreases very slowly with time. The fall in the alveolar tension of oxygen during the first 5 seconds of the experiment is 7·5 mm.Hg, the same as when the breath is held. Between the 25th and 30th seconds, the fall is 6 mm.Hg, or nearly twice as great as when the breath is held. The total fall in the alveolar tension of oxygen, after breathing into and out of the bag for 35 seconds, is from 116·4 to 70·9, 45·5 mm.Hg, or nearly 30% greater than when the breath is simply held. Thus, when the same air is rebreathed, not only is there an increase of the rate at which the composition of the alveolar air changes, but the amount of the change itself is also greater than when an equal quantity of air is held in the lungs for an equal period. Although the increase in the alveolar tension of carbon dioxide and the decrease in the alveolar tension of oxygen are so much greater, when the air in the lungs is breathed to and from a bag for a given time, than when the breath is held for the same length of time, the period which elapses before the subject begins to feel acutely the need of fresh air is considerably extended in the former case. In the present subject, the feeling of distress is as pronounced after holding the breath for 35 seconds as it is after breathing to and from the bag for about 50 seconds.

Discussion of Results.

The curves in the above diagram show the rates of change of the alveolar tensions of carbon dioxide and oxygen at different times after the stoppage of normal respiration. They depict the rates of movement of these gases to and from the alveolar air. Carbon dioxide and oxygen can move only to and from the alveolar out of or into the pulmonary tissues and the blood, on the one hand, and the air of the dead space. on the other hand. At the end of a normal inspiration, the dead space amounts to about 5% of the total volume of the lungs. Even when the dead space is increased by the addition of the mouthpiece and bag, the alveolar air of the lungs still accounts for more than 90% of the air with which the blood can exchange gases. Exchanges of gases between the alveoli and the dead space, therefore, will affect but slightly the alveolar tensions, and the above curves may be taken as exhibiting the exchange of carbon dioxide and of oxygen between the blood and pulmonary tissues, and the alveolar air under the conditions of the experiments.

If diffusion play a part in this exchange of gases between the alveolar air and the blood, the variations in the rates of exchange are likely to be expressed by an equation of the form

$$d(P-p)/dt = -n(P-p) \qquad (1)$$

where P is the effective, not necessarily the actual, tension of the gas in the venous blood *entering* the lungs, p the tension in the alveolar air at the moment, and n a constant. The work of Mosso (1904), of Haldane and his collaborators (*loc. cit.*, and Christiansen and Haldane, 1914), of Krogh and Krogh (1910), and of others, has shown that the tensions of the carbon dioxide in the arterial blood *leaving* the lungs must be very close to the alveolar tension.

With regard to the tension of oxygen in the arterial blood, opinion is not so unanimous. Barcroft and Cooke (1913) found arterial blood (human) to be 94% saturated with oxygen. Twort and Hill (1915) showed, however, that, during rest and shallow respiration, the degree of saturation may be considerably lower.

According to the above equation, if the tensions of the gases in the venous blood entering the lungs, after the stoppage of the exchange with the air occurring in normal respiration, remain constant for a period long enough, the alveolar tensions will approach very closely to the venous, and the blood will pass through the lungs practically unchanged.

Equation (1) is converted by integration into the form

$$\log (P-p) = \log a - nt \qquad (2)$$

where a is another constant

If the figures for p given in the above tables vary with the times of stoppage of normal respiration in the manner described by this equation, then, if instead of plotting the tensions against times, the logarithms of the differences of these tensions from certain constant tensions, P, be plotted, the curves obtained will be straight lines. The values of the constant tensions, P, towards which the tensions, p, approach, may be calculated by converting equation (2) into the form

$$P - p = a/10^{nt} \qquad (3)$$

by eliminating the logarithms. If the values of p and t be inserted into the equation for pairs of equidistant values of t, equations containing only P and p may be obtained, and, from these, the values of P may be determined. In this way, it may be calculated that, when the breath is held, the alveolar tension of carbon dioxide (curve A) rises from the initial value of 38·0 mm.Hg towards a final value of 50·0 mm.Hg. When the air in the lungs is breathed into and out of a closed bag, the alveolar tension of carbon dioxide (curve C) rises from the same initial value towards the value of 59·0 mm.Hg. The value towards which the alveolar tension of oxygen sinks when the breath is held (curve B) is found by a similar calculation to be 55 mm.Hg, the initial value being 116·4 mm.Hg. The curvature of curve B is much less than that of the two preceding curves, and the accuracy with which the value of P can be calculated is correspondingly less. In the case of curve D, representing the variation of the alveolar tension of oxygen when the air of the lungs is breathed into and out of a bag, the curvature is so small, that the value of the tension which would be reached eventually, if the tension continued to fall in the same manner, cannot be determined with any precision by the above calculation. This is due to the fact that, in the calculation, the differences of observed values appear. These differences become smaller as the curvature decreases, and as the whole experimental error falls on the differences, the uncertainty of their values soon becomes so great as to render them useless for calculation. The value given for P for each of the curves A, B, and C, is the mean of six values calculated from six different sets of points on the curve.

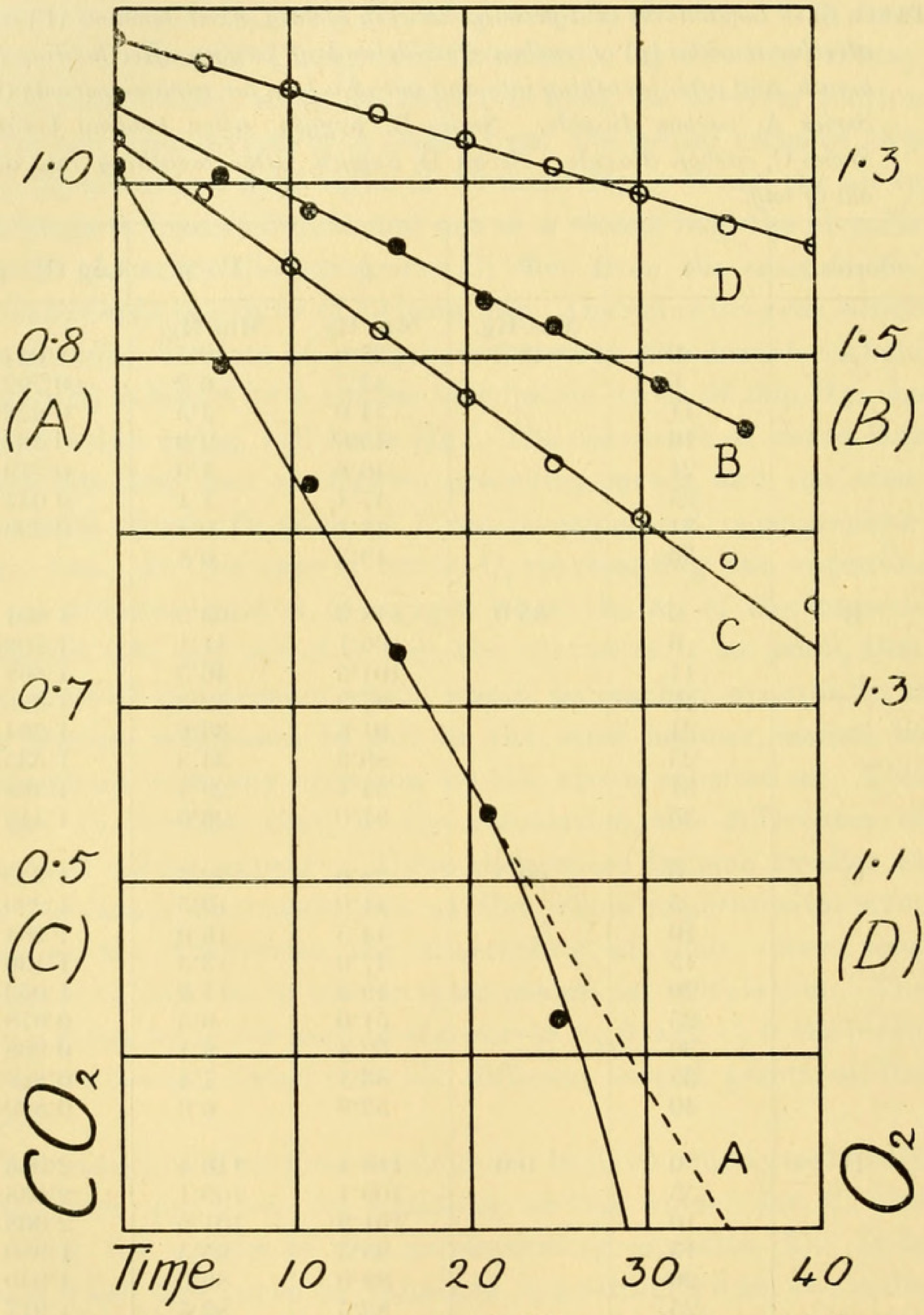
The values of these final tensions can be determined graphically with more precision by assuming certain values for P, and plotting the graphs of the corresponding equation (2). It is found that the curve so obtained is a straight line, *i.e.*, is described by equation (2), only when the value chosen for P lies between certain limits.

In the following Table are given the values of log (P – p) when the values assumed for the final tension, P, are 48·5 mm.Hg for curve A, 60·5 mm Hg for curve C, 55·0 mm.Hg for curve B, and 0·0 mm.Hg for curve D.

TABLE iii.—*Logarithms of differences between certain fixed tensions* (P) *and alveolar tensions* (p) *of carbon dioxide and of oxygen after holding the breath, and after breathing into and out of a bag for various periods* (t). *Series* A, *carbon dioxide. Series* B, *oxygen, after holding breath. Series* C, *carbon dioxide. Series* D, *oxygen, after breathing into and out of bag.*

Series.	t	P	p	P – p.	Log (P – p).
		Mm.Hg.	Mm.Hg.	Mm.Hg.	
A	0	48·5	38·0	10·5	1·021
	6		42·3	6·2	0·792
	11		44·0	4·5	0·653
	16		45·6	2·9	0·462
	21		46·6	1·9	0·279
	25		47·4	1·1	0·041
	31		48·1	0·4	– 0·398
	36		49·3	– 0·8	
B	0	55·0	118·3	63·3	1·801
	6		106·1	51·1	1·708
	11		101·5	46·5	1·668
	16		97·3	42·3	1·626
	21		91·6	36·6	1·564
	25		89·3	34·3	1·535
	31		84·4	29·4	1·468
	36		81·0	26·0	1·415
C	0	60·5	38·0	22·5	1·352
	5		41·0	19·5	1·290
	10		44·5	16·0	1·204
	15		47·0	13·5	1·130
	20		49·2	11·3	1·053
	25		51·0	9·5	0·978
	30		52·4	8·1	0·908
	35		53·1	7·4	0·869
	40		53·9	6·6	0·820
D	0	0·0	116·4	116·4	2·066
	5		109·1	109·1	2·038
	10		101·9	101·9	2·008
	15		95·5	95·5	1·980
	20		89·0	89·0	1·949
	25		82·5	82·5	1·917
	30		77·2	77·2	1·888
	35		70·9	70·9	1·851
	40		66·5	66·5	1·823

In the following diagram (Text-fig.2). the values of log (P – p) are shown plotted as ordinates against periods of holding the breath or of breathing into and out of a bag as abscissæ.



Text-fig. 2.—Variation of logarithms of differences between existing and final alveolar tensions of carbon dioxide and of oxygen (ordinates), with period of holding the breath (A, B), and with period of re-breathing expired air (C, D). Times (abscissæ) in seconds. In each curve, the logarithms are plotted to the same scale, but the zero ordinates are adjusted to bring the curves together.

This diagram shows that, when the above values are assumed for the final tensions, P, the points obtained for the value of log (P − p) fall upon straight lines. The curves through these depart visibly from straight lines when the values chosen for P lie outside of the following limits: 48·5±1·0 mm.Hg for curve A; 60·5±2 mm.Hg for curve C; 55·0±5 mm.Hg for curve B; 0±10 mm.Hg for curve D.

The figures for the variations of the alveolar tensions of carbon dioxide and of oxygen after the stoppage of normal breathing, according to the above relations between them, may have the following interpretation.

When the breath is held, the alveolar tension of carbon dioxide rises, during the first 25 seconds, from its initial value of 38·0 mm.Hg at such a logarithmically decreasing rate that, if the rise were to continue in the same manner, a final tension of 48·5 mm.Hg would be approached closely. This final tension is actually passed during the period of the experiment. The effective difference of tension driving carbon dioxide from the blood into the alveolar air, when the holding of the breath begins, is thus 10·5 mm.Hg in the present subject. This final tension of carbon dioxide lies within the range of values found by Christiansen, Douglas, and Haldane (*loc. cit.*) for the tension of carbon dioxide in venous blood by their aërotonometric method. It is also within 2 mm.Hg of the value calculated by Boothby (1915) from the consumption of oxygen, the flow of blood through the lungs, and the respiratory quotient.

With regard to the variation of the alveolar tension of oxygen when the breath is held, the results of the present investigation show that the tension falls at a logarithmically decreasing rate such that, starting from the initial value of 116·4 mm.Hg, a final value of 55 mm.Hg would be approximated to if the fall continued in the same way. The difference of tension driving oxygen from the alveolar air into the blood is thus about 61 mm.Hg, when the holding of the breath begins. At the end of the experiment, the alveolar tension of oxygen is still 26 mm.Hg above this final value.

When the air in the lungs is breathed into and out of an empty bag, instead of being held in the closed chest, the alveolar tension of carbon dioxide rises from its initial value of 38·0 mm. Hg at a logarithmically decreasing rate such that, if the rise continued in the same way, a final tension of 60·5 mm Hg would be approached closely. During the period of the experiment, the alveolar tension of carbon dioxide rises to within 6·5 mm.Hg of this final value. The initial difference of tension driving carbon dioxide from the blood into the alveolar air is, in this case, 22·5 mm.Hg, or about double that acting when the breath is held.

The alveolar tension of oxygen, when the air in the lungs is rebreathed, falls from its initial value of 116·4 mm.Hg at a logarithmically decreasing rate such that the final tension of oxygen would approach zero, if the fall continued in the same way. The initial difference of tension driving oxygen from the alveolar air into the blood is, in this case, 116·4 mm.Hg, again practically double the effective difference existing when the breath is held. During the period of the experiment, the alveolar tension of oxygen falls to a value which is still about 66 mm. Hg above this final value.

These experiments show that the rate and extent of the exchange of gases between the blood and the alveolar air are very much increased by the movements of breathing.

In the experiments of Hill and Flack (*loc. cit.*), a similar effect of respiration on the gaseous exchange in the lungs is to be observed. The experiments of these authors on the effect of breathing from a bag are not strictly comparable with those of the present work. Hill and Flack's subjects breathed from an anæsthetic bag "filled" with expired air. The volume of air with which the blood could exchange gases was very much greater, therefore, than that present in the lungs alone, and the period for which the experiments could be continued was correspondingly extended to about two minutes, or three times as long as when the breath was held. In the present experiments, the bag was empty, and the volume of air in the lungs was hardly added to. The period for which the experiment could be continued was not greatly extended beyond that for which the breath could be held in the ordinary way.

Effect of Respiratory Movements.

Hill and Flack considered, as was mentioned earlier, that the smaller respiratory exchange during the holding of the breath was due to hindrance of the circulation. They supposed that the normal respiratory movements hastened the flow of blood. Dogiel and Kowalewsky (1870) showed, however, that stoppage of artificial respiration in curarised dogs for periods of less than 10 seconds exerted no hindering effect on the circulation. More recently, Ebert (1914) has shown that the state of distension of the lungs has, of itself, no influence on the circulation through them, and that the actual movements of inspiration and of expiration respectively hasten and hinder the circulation to corresponding extents.

It is evident also in the present experiments, that the slower respiratory exchange during the holding of the breath is not due to a slowing of the circulation brought about by the absence of the movements of breathing. When the breath is held for 30 seconds, the four or five respirations, which would normally be made in that time, do not occur to exert their effect on the circulation. If circulatory disturbances due to the absence of respiratory movements be the cause of the slower gaseous exchange when the breath is held, then, as each succeeding respiration is missed, the exchange will be retarded more and more. When one respiratory movement is made during a period of 20 seconds, instead of the normal four, then the respiratory exchange will be increased, above that occurring when the breath is held, by about one-fourth of the amount of increased respiratory exchange occurring during normal respiration. The rate of the pulse of this subject is the same, after holding the breath for 30 seconds, as immediately before.

The accompanying figures give the results of experiments in which the effect of one respiratory movement in 20 seconds, and of three respiratory movements, are compared with the effect on the gaseous exchange of holding the breath for the same period. The figures in column "a" represent the alveolar percentages of carbon dioxide after holding the breath for 20 seconds. The figures in columns "b" and "c" are the corresponding alveolar percentages when one and three respirations, respectively, are made in this period.

TABLE IV.

Effect of frequency of respiratory movements on gaseous exchange,

Expt.	a	b	Expt.	a	c
1	6·00	6·40	5	6·09	6·49
2	5·96	6·42	6	6·29	6·57
3	5·99	6·51	7		6·65
4	6·13	6·47	8	6·00	6·51
Mean	6·01	6·45	Mean	6·13	6·56
	Increase	0·44		Increase	0·43

The above experimental results show that the alveolar tension of carbon dioxide is not raised any higher, above that found after holding the breath for 20 seconds, by making three respirations than by making one respiration in the same period. Increasing the rate of the respiratory movements three times, therefore, causes no parallel increase in the alveolar percentage (and tension) of carbon dioxide, within these limits.

The following experiments show that not only is the increase in the respiratory exchange in a given time independent, within the limits of the work, of the number of respiratory movements in a given time, but also of the extent of these movements. In these experiments, the alveolar tensions of carbon dioxide, after holding the breath quietly for 20 seconds, are compared with those reached when the four respiratory efforts are made in the same time with the pharynx closed, "d".

TABLE V.

Effect of respiratory efforts with closed chest on gaseous exchange.

Expt.	a	d
9	6·36	6·76
10	6·26	6·71
Mean	6·31	6·74
	Increase	... 0·43

The increase in the respiratory exchange in this case is as great as in experiments "b" and "c", although the movements of the chest were very much smaller than in those experiments. It is evident, then, that neither the extent, nor the frequency of the respiratory movements in a given time, has any effect on the respiratory exchange under the conditions of these experiments, in which the renewal of the air in the lungs was prevented. There still remain to be considered, however, the variations of pressure of the air in the lungs, which accompany the respiratory movements.

Effect of Variations of Pressure.

To enable the pressure in the lungs to be measured, the mouthpiece, through which the expirations were made, was provided with a small, lateral opening near its end. This opening lies inside the mouth of the subject when the mouthpiece is in position. Another small hole was drilled through the wall of the mouthpiece at a position lying outside of the mouth of the subject. These two small holes were connected together by a very narrow brass tube lying inside the bore of the mouthpiece, and soldered in place. The end of the narrow tube, which is to lie inside of the mouth of the subject, terminates flush with the wall of the mouthpiece. The end of the tube lying outside of the mouth of the subject projects through the wall of the mouthpiece and is connected with a mercury-manometer. When in position during an experiment, the mouthpiece is held firmly between the lips, the end being tightly closed by the tongue. The nose of the subject is held at the same time. Pressures existing in the mouth are then registered by the manometer. When the pharynx is kept open, the pressure in the mouth will be practically equal to that in the lungs, if no sudden variations of pressure occur. The maximal differences of pressure between the air in the lungs and the atmosphere, which the present subject is able to maintain for about 20 seconds, are approximately plus and minus 30 mm.Hg. When these differences are greater than about 10 mm.Hg, it is found impossible to keep them absolutely steady. These variations, which cannot be avoided, lie within a range of about 2 mm.Hg from the average pressure.

Positive pressures.—In the following Table are given the percentages of carbon dioxide found in the alveolar air after holding the breath under various pressures in excess of that of the atmosphere. The corresponding percentages of carbon dioxide reached, when the breath is held under normal pressure, are given for comparison.

When the breath is held under pressures differing from that of the atmosphere, it is found to be rather difficult to note the time to within a second. The subject is obliged to watch the manometer as well as to observe the time. The figures in the accompanying Tables show that variations of several seconds occur in the periods of holding the breath, as determined from the graphic records. The percentages of alveolar carbon dioxide found, therefore, cannot be compared directly with one another, and it has been necessary to reduce the results to a common period. In the last column of the Tables, the alveolar percentages of carbon dioxide are given, reduced to a period of holding the breath of 20 seconds. In the case of Table vi., this reduction has been made from the data given in the average figures in Table i. From these figures it will be seen that, between the 21st and 26th seconds of holding the breath, the alveolar carbon dioxide rises at the rate of 0·025% per second. During a period of this length, the rise is very nearly uniform, as is shown by curve A (Text-fig. 1). For each second for which the breath was held longer than 20 seconds, 0·025 has been subtracted, therefore, from the percentage of carbon dioxide found.

TABLE vi.

Effect of increased pressure on alveolar percentage of carbon dioxide after holding the breath for 20 seconds.

Expt.	Pressure.	Period.	CO_2 found.	CO_2 at 20 sec.
11	0 mm. Hg	20 sec.	6·24%	6·24%
	10	23	6·09	6·01
	20	25	6·29	6·16
	30	26	6·34	6·19
12	0	20	6·18	6·18
	10	22	5·98	5·93
	20	21	6·06	6·03
	30	23	5·94	5·86
Mean	0	20		6·21
	Positive	20		6·03
			Increase	... -0·18

These figures show, that holding the breath under increased pressure certainly does not increase the gaseous exchange in the lungs. Indeed, the average alveolar percentage of carbon dioxide reached in 20 seconds, when the pressure in the lungs is greater than atmospheric pressure, is lower than that reached when the breath is held under normal conditions.

The average deviation of the above results from the mean, calculated as described by Krogh (1916), is $\pm 0{\cdot}13$. This number is not much smaller than the amount by which the alveolar percentage of carbon dioxide, after holding the breath under normal pressure, exceeds that found after holding the breath for the same period under positive pressure. The results, therefore, only show definitely that holding the breath under increased pressure does not accelerate the gaseous exchange. The differences observed are too small to allow any more precise conclusions to be drawn from them.

Negative pressures.—In Table vii., are given the alveolar percentages of carbon dioxide found after holding the breath for definite periods, under pressures lower than that of the atmosphere. The control-determinations for normal pressure are given also. In the last column of the Table, the figures are reduced to a common period of holding the breath of 20 seconds, in the manner explained above.

TABLE vii.

Effect of decreased pressure on alveolar percentages of carbon dioxide after holding the breath for 20 seconds.

Expt.	Pressure.	Period.	CO_2 found.	CO_2 at 20 sec.
13	0 mm.Hg	20 secs.	6·34%	6·34%
	-2	22	6·41	6·31
	-6	22	6·63	6·53
	-10	23	6·95	6·80
	-14	23	7·22	7·07
	-18	23	7·08	6·93
	-22	25	7·19	6·94
	-26	24	7·28	7·08
14	0	20	6·47	6·47
	-2	21	6·58	6·53
	-6	23	6·72	6·57
	-10	25	6·80	6·55
	-14	27	7·22	6·87
	-18	23	6·94	6·79
	-22	26	7·11	6·81
	-26	25	7·21	6·96
15	0	21	6·35	6·30
	-2	22	6·40	6·30
	-6	24	6·83	6·63
	-10	27	7·23	6·88
	-14	25	7·05	6·80
	-18	26	7·19	6·89
	-22	27	7·29	6·94
	-26	25	7·29	7·04
Mean	0	20		6·37
	-2-6	20		6·48
	-10-30	20		6·88
			Increase ...	... 0·51

These figures show at once that holding the breath under pressures less than that of the atmosphere increases the gaseous exchange in the lungs. As the percentage of carbon dioxide is rising, in this case at a rate about equal to that at which it rises when the contents of the lungs are breathed to and from a bag, the data given in Table ii. have been used for the calculation of the percentages of carbon dioxide after holding the breath for 20 seconds. The figures in Table ii. show that, between the 20th and 25th seconds of breathing into the bag, the alveolar carbon dioxide is rising at the rate of 0·05% per second. Curve C, in Fig. 1, shows that, during this period, the rise is practically uniform. From the percentages of carbon dioxide found, therefore, 0·05 has been subtracted for each second for which the breath was held longer than 20 seconds.

The above results may be divided into two groups, (1) those obtained when the breath is held under pressures numerically less than − 10 mm.Hg, (2) those obtained under pressures numerically greater than − 10 mm.Hg. The alveolar percentages of carbon dioxide shown in the first group of results vary with the pressure under which the breath is held. The lower the negative pressure is, the higher the percentage of carbon dioxide is. In the second group of results, however, the percentages of carbon dioxide found are, with one exception, practically constant and independent of variations of the pressure under which the breath is held. The mean alveolar percentage of carbon dioxide reached, when the breath is held for 20 seconds under negative pressures numerically greater than − 10 mm.Hg, is 0·51 higher than that reached in an equal period under normal pressure. The average deviation of these results from the mean is ±0·12. Practically the same increase of the rate of gaseous exchange is produced, therefore, by holding the breath under pressures more than 10 mm.Hg below that of the atmosphere, as by performing the movements of breathing into a closed bag. This fact is additional evidence that the increased respiratory exchange, caused by the movements of breathing, is not brought about by a quickening of the circulation. The respiratory exchange is increased during breathing owing to the existence of negative pressure in the chest during the act of inspiration. The figures indicate that the pressure in the lungs, during inspiration, must fall at least as low as − 10 mm.Hg.

In these experiments, the alveolar percentages of oxygen have not been estimated, as a knowledge of the variations in the percentages of carbon dioxide alone is sufficient to lead to the recognition of differences in the rates of gaseous exchange. The accompanying figures, however, give the results of experiments in which the alveolar percentages of oxygen, as well as of carbon dioxide, were determined after holding the breath for about 20 seconds under various pressures below that of the atmosphere.

TABLE viii.

Effect of negative pressure on respiratory exchange in lungs.

Expt.	Pressure.	CO_2	O_2
16	0 mm.Hg	6·32%	13·60%
	-10	7·01	11·48
	-20	7·09	11·90
	-30	7·06	11·62
17	0	6·58	12·70
	-5	6·87	11·60
	-10	6·83	11·62
	-15	6·81	11·62

These figures show that higher percentages of carbon dioxide are accompanied by lower percentages of oxygen in the same way, when the breath is held under negative pressures, as when the air of the lungs is rebreathed from a bag.

The results of these experiments indicate that the movements of breathing, or the negative variations of the intrapulmonary pressure which accompany them, accelerate, under certain conditions, the respiratory exchange of gases in the lungs. This acceleration is brought about not only by increase of the rates at which the alveolar tensions of carbon dioxide and of oxygen tend toward certain final (venous) tensions, but by a seeming alteration of these final tensions themselves. Negative intrapulmonary pressures increase the effective gradient of tension between the gases of the alveolar air and those of the venous blood entering the lungs. It is unlikely that the movements of breathing, or negative pressures in the chest, have any actual effect on the tensions of the gases of the venous blood. These factors also can have only a very slight effect on the partial tensions of the gases of the alveolar air. It seems, therefore, that, in the lungs, some mechanism must exist by which the effective difference of tension between the gases of the alveolar air and the gases of the venous blood may be altered.

Summary.

1. When the normal ventilation of the lungs is discontinued by holding the breath, the alveolar tensions of carbon dioxide and oxygen may be expressed as exponential functions of the period for which the breath is held.

2. When the normal ventilation of the lungs is discontinued by breathing into and out of an empty bag, the alveolar tensions of carbon dioxide and oxygen may be expressed as exponential functions of the period for which the contents of the lungs are rebreathed.

3. The rate of the gaseous exchange in the alveolar air is about twice as great when the movements of breathing are performed, as when the breath is held under normal pressure.

4. The rate of gaseous exchange in the lungs is also increased to the same extent when the breath is held under pressures less than that of the atmosphere by a certain amount.

5. Holding the breath under pressures greater than that of the atmosphere slightly decreases the rate of respiratory exchange.

6. The rate of the gaseous exchange, when the renewal of the air in the lungs is prevented, is not affected by the depth or frequency of the respiratory movements during the period of these experiments.

In conclusion, I wish to express my thanks to Professor Sir Thomas Anderson Stuart, in whose laboratory this work was done, to Dr. H. G. Chapman, whose advice and criticism were of the greatest value, and to Miss E. C. Pinkerton, B.Sc., who assisted in the preliminary experiments.

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