THE ALVEOLAR CARBONIC ACID PRESSURE IN DISEASES OF THE BLOOD AND IN DISEASES OF THE RESPIRATORY AND CIRCULATORY SYSTEMS.¹

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It was shown by Haldane and Priestley (1905¹) that under normal conditions respiration is so regulated as to maintain in each individual a practically constant alveolar carbonic acid pressure. Later, Fitzgerald and Haldane (1905²), experimenting with a large number of normal individuals in a condition of rest, confirmed the individual constancy of the alveolar CO₂ tension, and determined the limits of normal variation in men and women and boys and girls respectively.

The investigations forming the substance of the present paper were made for the purpose of determining the alveolar CO₂ pressure, during rest, in conditions of disease. The experiments were carried out in the medical wards and in the out-patient department of the Radcliffe Infirmary, Oxford, and I take this opportunity of expressing my thanks to the physicians on both the senior and junior staffs for their courtesy in affording facilities for carrying out the research, and also to the sisters in charge as well as to the patients for their interested co-operation.

Over 400 experiments were made with patients suffering from diseases of the blood, respiratory, or circulatory systems. Many of the patients were under observation for several months.²

The method employed for determining the composition of the alveolar air was FitzGerald and Haldane's (1905²) modification of the Haldane and Priestley method, the small air analysis apparatus of Haldane being used for receiving the samples. This apparatus proved very adaptable to clinical use, and any difficulties arising either from weakness or other causes in conscious patients were readily overcome. The samples were generally taken both at the end of an inspiration and at the end of an expiration. In those cases in which difficulty was experienced in giving satisfactory "expiratory" samples only "inspiratory" samples were taken.

¹ Received September 30, 1909.

² The main results were communicated to a meeting of the Pathological Society of Great Britain and Ireland in January 1908; but, owing to the writer's absence abroad, the publication of the paper has been delayed.

As the CO_2 percentage found by analysis was very similar in both types of samples, only the mean result of the day's experiments with each individual is given in the tables. These results represent, and are recorded, as percentages of CO_2 in dry alveolar air. The actual partial pressure of CO_2 in the alveolar air saturated at 37°C . is expressed in millimetres of mercury, and is given in another column. This is calculated from the percentage of CO_2 in the dry alveolar air as found by analysis, and from the 8 a.m. reading of the barometric pressure recorded daily at the Radcliffe Observatory, adjacent to the Infirmary. In making the calculation the pressure of aqueous vapour in the saturated alveolar air was taken as 47 mm. of mercury. Determinations of the amount of hæmoglobin present and of the number of red blood corpuscles were made in as many cases as possible. For these estimations a Gowers-Haldane hæmoglobinometer and a Thoma-Zeiss hæmocytometer were used. For making the blood counts two pipettes of blood were generally taken (dilution, 1-100), duplicate counts made, and the mean result recorded. If the results obtained from the two pipettes differed by more than 10 per cent. the counts were discarded.

I. ALVEOLAR CARBONIC ACID PRESSURE IN DISEASES OF THE BLOOD.

Of diseases of the blood the alveolar CO_2 was examined in nineteen typical cases of chlorosis, in two cases of pernicious anæmia, one case of chronic polycythæmia with cyanosis and enlarged spleen (Vaquez and Osler's disease), and in two cases of secondary anæmia due to severe hæmorrhage. Over 200 experiments were performed.

Taking the average of the daily mean results (Tables II. and IV), the partial pressure of CO_2 in each of these conditions is seen to be within the normal limits of variation as previously determined (1905²), but the records also show that within these limits there is a general tendency in anæmic conditions towards a low pressure of CO_2 , since the average pressure is in each condition somewhat lower than the normal "mean" for men or women at ordinary atmospheric pressure.

Amongst the daily records, four examples occur which are below the minimum CO_2 pressure recorded as normal. These will be referred to again in dealing with the individual cases to which they belong.

A tendency to irregularity in the alveolar CO_2 pressure of the individual is also to be observed. In cases under observation for a long period a variation of from 1-3 mm. of mercury was frequently noted, and this occurred, generally speaking, either as an oscillation or as a rise.

In two cases of chlorosis—Table I. (2) A. R. and (7) A. S.—maximum variations of 6.8 (fall) and of 4 mm. of mercury (rise) were respectively recorded (Table I.).

No constant parallelism could be traced between the alveolar CO_2 pressure and either the percentage amount of hæmoglobin or the number of red-blood corpuscles present.

Owing to the similarity in the general results, brief mention only

is made of certain cases in each condition of disease investigated, together with a few general remarks.

(A) *Chlorosis.*

Taking the average of the mean results based on 152 experiments, the partial pressure of CO_2 found in chlorosis is slightly below the normal mean pressure for women (see Table II.); but *no record of tension as low as the normal minimum pressure occurs.*

The cases especially mentioned are selected from those who were under observation for several months, thus affording opportunity for the observation of any variation occurring during treatment and improvement in condition, and in relapse if such ensued.

CASE 13, A. W.—This patient had been under treatment, on and off, for four years, but had never entirely regained her health. When she was first seen the hæmoglobin was reduced to 29 per cent. and the red blood corpuscles to 80 per cent. of the normal. Breathlessness was very great on any exertion.

The partial pressure of CO_2 was then 35.9 mm. of mercury, or just below the normal mean for women.

Under treatment and on cessation of work improvement took place, the hæmoglobin rising to 73 per cent. The CO_2 tension increased during this time to 38.4 mm. Hg, a value just above the normal mean.

After her return to work (domestic service) the hæmoglobin again began to fall, and breathlessness returned on exertion, but the alveolar CO_2 pressure was maintained at 38.4 mm. of mercury.

CASE 15, E. W. (Tables I. and II.).—This patient was under observation for six months. On presenting herself for treatment she complained of feeling ill for five months prior to this, and was ultimately forced to abandon work. Breathlessness was very great. The CO_2 pressure was found to be 32 mm. of mercury, a value that is above the normal minimum pressure for women. The hæmoglobin at this time was reduced to 31 per cent. The CO_2 pressure varied very little during the improvement in her condition.

In a relapse that followed three months later the hæmoglobin was reduced to 28 per cent., and the CO_2 tension, whilst decreasing slightly, was still within normal limits. During the six months of observation the alveolar CO_2 pressure showed a maximum variation of 2.4 mm. of mercury.

CASE 5, F. M. (Tables I. and II.).—This was another severe case. The CO_2 pressure, although very low (31.6 mm. Hg), was nevertheless maintained within normal limits, while the hæmoglobin was reduced to 27 per cent.

In CASE 9, E. H. (Tables I. and II.), the records show the same tension of CO_2 in the alveolar air (34 mm. Hg) with 25 per cent. of hæmoglobin as with 78 per cent.

Similar results were obtained in Case 1, E. T. (Tables I. and II.), whose alveolar CO_2 pressure oscillated between 31.7 and 33.9 mm. of mercury; the pressure being almost the same with 36 per cent. as with 74 per cent. of hæmoglobin.

CASE 14, A. C. (Tables I. and II.), was an instance of the maintenance of the CO_2 pressure nearer the higher limit for normal (average 39.6 mm. Hg), and on one occasion the records show a tension higher than normal maximum pressure for women.

TABLE I.—*Diseases of the Blood.*

CHLOROSIS.

No.	Initials and Age.	Date.	Percentage of Red Corpuscles per c.mm.	Hæmoglobin Percentage by Scale (Haldane's Hæmoglobinometer).	CO ₂ Percentage in Dry Alveolar Air (mean).	Pressure of CO ₂ in Alveolar Air (mm. Hg).	Number of Determinations.	Remarks.
			(4,500,000 = 100)					
1	E. T., 17	Jan. 10, 1906	86	36	4.53	31.7	3	Very breathless ; unable to work.
		„ 25, „	119	63	4.71	33.2	4	After fourteen days in bed.
		Feb. 6, „	114	74	4.36	31.3	2	...
		„ 23, „	105	66	4.85	33.9	5	...
2	A. R.	Dec. 20, 1905	90	45	5.66	40.5	2	In bed.
		Jan. 4, 1906	94	68	4.85	33.7	3	...
		Dec. 22, 1905	76	33	5.06	36.5	2	In bed.
3	E. B.	„ 28, „	...	...	5.58	38.9	4	Up.
		„ 29, „	91	47	5.35	37.0	3	Up; respirations, 28; pulse, 94.
4	D. D., 17	Aug. 3, „	...	...	5.27	36.9	3	...
		„ 31, „	...	...	5.27	37.8	5	...
5	F. M., 18	Nov. 8, „	61	28	4.39	31.1	2	Very breathless ; at work as housemaid.
		Dec. 7, „	50	27	4.53	31.9	4	...
6	B. P., 17	Nov. 11, „	100	49	4.42	31.3	3	...
		„ 23, „	75	39	4.73	33.2	3	...
7	A. S., 28	Aug. 23, „	...	...	4.40	31.4	3	Very breathless.
		Sep. 30, „	...	...	4.98	35.4	4	...
8	E. S., 14	Aug. 23, „	...	...	4.80	33.8	4	Breathless ; still able to work.
		Sep. 30, „	...	...	5.16	36.7	4	Very breathless ; forced to abandon work ; ill for past two years ; without treatment until now.
		Oct. 7, „	65	25	4.73	34.0	4	...
		„ 28, „	95	60	4.54	32.6	4	...
9	E. H., 17	Nov. 25, „	85	78	4.82	34.0	3	...
10	R. B., 20	Feb. 10, 1906	103	59	4.66	32.0	2	...
11	L. M., 15	Aug. 24, 1905	...	...	5.33	37.8	5	...
12	G. L., 17	Sep. 2, „	...	...	4.66	33.0	4	...
		Oct. 7, „	80	29	5.00	35.9	5	Breathless, but at work ; under treatment, on and off, for four years, but never got quite well.
13	A. W., 20	Oct. 21, „	77	48	5.15	36.7	4	Stopped work, and resting.
		Nov. 4, „	78	53	5.24	36.9	4	Returned to work as a general servant ; stairs trying.
		„ 18, „	77	73	5.36	38.4	4	...
		Dec. 2, „	72	62	5.34	38.4	3	...
14	A. C., 20	Aug. 23, „	...	...	4.96	35.0	3	Breathlessness for twelve months ; very pale.
		Sep. 2, „	...	...	5.75	40.0	4	...
		„ 30, „	...	...	5.76	41.0	3	...
		Oct. 14, „	...	...	5.92	42.3	4	...

TABLE I.—*Diseases of the Blood* (continued).

No.	Initials and Age.	Date.	Percentage of Red Corpuscles per c.mm.	Hæmoglobin Percentage by Scale (Haldane's Hæmoglobinometer).	CO ₂ Percentage in Dry Alveolar Air (Mean).	Pressure of CO ₂ in Alveolar Air (mm. H g.	Number of Determinations.	Remarks.
			(4,500,000 = 100)					
15	E. W., 18	Oct. 26, 1905	71	31	4.45	32.0	4	Anæmic for past five months; obliged to abandon work as domestic servant.
		Nov. 11, "	88	59	4.61	32.0	4	
		" 25, "	108	63	...	...	...	
		Dec. 9, "	84	53	4.62	33.1	5	
		Mar. 3, 1906	60	28	4.38	31.6	4	
		" 17, "	...	...	4.34	30.9	3	Relapse after return to work. Breathlessness extreme, and faintness.
16	E. N. .	Aug. 2, 1905	...	...	4.55	32.3	2	...
17	R. G., 14	Sep. 9, "	...	...	5.12	36.2	2	...
18	M. K., 21	" 20, "	...	...	4.53	32.3	3	...
19	W. N., 14	" 30, "	...	...	5.01	35.6	3	...
		" 20, "	...	...	5.10	36.6	3	...

TABLE II.—*Diseases of the Blood.*

CHLOROSIS.

Number in Table I.	Mean CO ₂ Pressure in Alveolar Air (mm. of Hg).	Number of Determinations.
14	39.6	14
11	37.8	11
3	37.5	9
4	37.4	8
13	37.3	5
2	37.1	20
19	36.6	3
17	36.2	2
8	35.3	8
18	33.9	6
9	33.6	11
7	33.4	7
12	33.0	4
1	32.5	14
6	32.3	2
10	32.2	6
16	32.3	2
15	31.9	23
5	31.6	6
	Mean 34.9	Total 152
Normal Women { Mean . . . 36.3		
{ Maximum . . . 41.0		
{ Minimum . . . 30.4		

(B) *Pernicious Anæmia.*

CASE 20, F. S., male (Tables III. and IV.).—This was a very marked case of pernicious anæmia, and was under observation for two and a half months. This period embraced part of his second attack, and a brief spell of improvement prior to the onset of the third and fatal attack.

The partial pressure of CO₂ oscillated between 31·3 and 33·9 mm. of mercury, giving a mean of 32·6, a value corresponding to the minimum CO₂ pressure recorded for normal men at ordinary atmospheric pressure.

TABLE III.—*Diseases of the Blood.*

PERNICIOUS ANÆMIA

(MEN).

No.	Initials and Age.	Date.	Percentage of Red Corpuscles per c.mm. (5,000,000 = 100)	Hæmoglobin Percentage by Scale (Haldane Hæmoglobinometer).	CO ₂ Percentage in Dry Alveolar Air (Mean).	Mean Pressure of CO ₂ in Alveolar Air (mm. Hg).	Number of Determinations.	Remarks.
20	F. S., 45	Aug. 2, 1905	...	...	4·61	32·7	2	Very weak; brought down in chair. Up; able to walk about garden and to go upstairs without discomfort. Walking about. Died a few weeks later.
		" 10, "	...	...	4·50	31·9	3	
		" 24, "	34	42	4·60	32·7	4	
		Sept. 2, "	43	46	4·78	33·9	4	
		" 22, "	29	45	4·70	33·6	5	
		Oct. 7, "	31	42	4·36	31·3	4	

PERNICIOUS ANÆMIA

(WOMEN).

No.	Initials and Age.	Date.	Percentage of Red Corpuscles per c.mm. (4,500,000 = 100)	Hæmoglobin Percentage by Scale (Haldane Hæmoglobinometer).	CO ₂ Percentage in Dry Alveolar Air (Mean).	Mean Pressure of CO ₂ in Alveolar Air (mm. Hg).	Number of Determinations.	Remarks.
21	F. M., 44	Aug. 8, 1905	...	...	5·06	36·0	2	Has been very short of breath; patient in bed. Up; able to walk about garden and to go upstairs. At work. Died a few weeks later.
		" 14, "	66	50	4·61	33·1	3	
		" 23, "	65	70	...	...	...	
		Sept. 9, "	52	75	4·81	34·0	3	
		" 22, "	...	...	4·60	33·0	4	
		Oct. 14, "	58	...	4·99	35·7	3	
		Nov. 11, "	69	82	4·99	34·0	4	
		Dec. 9, "	70	83	4·70	33·7	5	

TABLE III.—*Diseases of the Blood* (continued).

SECONDARY ANÆMIA

(WOMEN).

No.	Initials and Age.	Date.	Percentage of Red Corpuscles per c.mm. (4,500,000 = 100)	Hæmoglobin Percentage by Scale (Haldane's Hæmoglobinometer).	CO ₂ Percentage in Dry Alveolar Air (Mean).	Mean Pressure of CO ₂ in Alveolar Air (mm. Hg).	Number of Determinations.	Remarks.
22	M. S., 34	Aug. 24, 1905	45	23	4.19	29.8	2	Placenta prævia; severe hæmorrhage; very weak; in bed. Able to get up. ... (Deaf and Dumb) Hæmatemesis (gastric ulcer). Very pale; lips quite white; unable to sit up in bed.
		" 30, "	...	...	4.69	33.0	1	
		" 31, "	...	...	4.56	32.7	3	
		Sept. 5, "	83	52	...	...	...	
		" 1, "	...	...	5.03	36.1	2	
23	K. T., 33	" 4, "	...	...	5.33	38.1	1	
SPLENOMEGALY WITH CHRONIC POLYCYTHEMIA AND CYANOSIS (WOMEN).								
24	E. H., 45	Dec. 4, 1907	175	148	4.13	28.7	3	In bed.
		" 11, "	145	161	4.61	32.1	4	"

TABLE IV.—*Diseases of the Blood* (continued).

	Number in Table III.	Mean Pressure of CO ₂ in Alveolar Air (mm. of Hg).	Number of Determinations.
Pernicious anæmia (man) . .	20	32.6	22
" " (woman) . .	21	34.2	24
Secondary anæmia (") . .	23	37.1	3
" " (") . .	22	31.8	6
Polycythemia with cyanosis and enlarged spleen . .	24	30.4	7
Normal men . .			
{ Maximum . .	...	44.5	...
{ Minimum . .	...	32.6	...
{ Mean . .	...	39.2	...
Normal women . .	...	41.0	...
{ Maximum . .	...	30.4	...
{ Minimum . .	...	36.3	...

On two occasions the CO_2 pressure was below the minimum normal for men, and equivalent to 31.3 and 31.9 mm. of mercury respectively.

When the first samples of alveolar air were taken, the patient was very weak,—barely able to sit up, and complained much of shortness of breath. At this time the CO_2 partial pressure was 32.6 mm. of mercury, the normal minimum pressure. The same tension was recorded three weeks later, when the patient was able to walk about the hospital grounds and upstairs without discomfort or shortness of breath.

The hæmoglobin was reduced to less than half the normal amount, and the red blood corpuscles to less than one-third normal; the hæmoglobin varying between 42 and 46 per cent., and the red corpuscles between 29 and 43 per cent. of the normal.

The higher pressures of CO_2 recorded (33.6 and 33.9 mm. Hg) were in this case associated with the higher percentage values of hæmoglobin.

CASE 21, F. M., female (Tables III. and IV.).—During the five months this patient was under observation, both as an in-patient in a serious condition and as an out-patient able to work, the alveolar CO_2 pressure varied between the normal minimum and the normal mean pressure for women (mean 34.2 mm. Hg). Shortness of breath was a marked feature at different times.

(C) *Chronic Polycythæmia and Cyanosis with Enlarged Spleen.*

CASE 24, E. H., female (Tables III. and IV.).—In this very interesting case of Vaquez and Osler's disease the average alveolar CO_2 pressure was found to be the same as the minimum normal pressure for women.

One record, however, shows a tension still lower (28.7 mm. Hg). Breathlessness had not been a marked symptom.

It must also be observed that very high percentages of hæmoglobin, and red corpuscles numbering between 6 and 7 millions to the cubic millimetre, are here associated with an alveolar CO_2 tension corresponding to the minimum normal.

(D) *Secondary Anæmia.*

At the time of obtaining the earlier samples of alveolar air, extreme weakness and pallor marked the condition of both patients suffering from secondary anæmia, ascribable in the one case (22), M. S., to severe post-partum hæmorrhage and in the other (23), K. T., to hæmorrhage from a gastric ulcer.

With K. T., 23 (gastric ulcer) (Tables III. and IV.), the CO_2 pressure was the same as the normal mean for women, and later increased 2 mm. of mercury.

In the case of M. S., 22, placenta prævia (Tables III. and IV.), the CO_2 pressure kept very near the normal minimum pressure of 30.6 mm. of mercury, the first samples recording a tension 0.6 mm. below this.

The hæmoglobin at the same time was reduced to less than one-fourth of the normal and the red corpuscles to less than one-half of the normal.

Since the alveolar CO_2 is maintained at nearly normal pressure in chlorosis and in other anæmic conditions, and since even a slight deficiency in the oxygen supply to the tissues would lower the alveolar CO_2 ,¹ it appears evident that a compensatory process, almost com-

¹ See the papers of Boycott and Haldane, of Ward, and of Haldane and Poulton, *Journ. Physiol.*, 1908, Cambridge and London, vol. xxxviii. pp. 355, 378, and 390; also Haldane, *Brit. Med. Journ.*, 1908, vol. ii. p. 578.

pletely effective during rest, is brought into play; and this can only be an increased rate of blood flow. With the oxygen-carrying power of the blood reduced to one-third or less of the normal, as has been frequently observed in the cases above mentioned,¹ marked symptoms of want of oxygen would appear (as is actually the case in CO-poisoning, as shown by Haldane) even in rest, unless the circulation was increased. The fact that compensation occurs in this way, the heart being unable at times (as during muscular exertions) to respond fully, will therefore account for many of the circulatory and respiratory symptoms met with in anæmia.

II. ALVEOLAR CARBONIC ACID, PRESSURE IN DISEASE OF THE RESPIRATORY SYSTEM.

Fourteen patients were examined suffering from diseases of the respiratory system, which included pneumonia, early and advanced phthisis, tuberculous pleurisy and empyema, asthma, emphysema, and one case of hysterical dyspnoea.

Ninety-one experiments were performed.

With but three exceptions in the mean records, to be referred to later, the partial pressure of CO₂ in the alveolar air was maintained within the normal limits. Generally speaking, the tension was found to vary between the normal minimum and the normal mean pressure for men, women, boys, or girls respectively.

Low tensions, *i.e.* near the normal minimum, were found in advanced cases of phthisis; tensions near the normal mean in early cases of the same disease, and in tuberculous pleurisy and empyema.

To take a special case, R. G. (31, Tables V. and VI.) was suffering from an empyema that had persisted for some time. The left lung was in a condition of partial collapse and very little air was entering on this side; the chest wall was markedly deformed. The CO₂ tension was, however, maintained at the normal mean for boys (37.2 mm.).

A partial pressure of CO₂ lower than the minimum normal for men was found with D. K. (26, Tables V. and VI.), the severest of the four cases of pneumonia investigated. The first samples were taken six days after the crisis, but at a time when the patient was still very ill and weak. The tension of CO₂ was then only 26.3 mm. of mercury, the temperature of the body 97, and respiration 25. As improvement took place the CO₂ pressure rose, at first to the minimum pressure for men, and fifteen days later to just below the normal mean for men. The increase in tension recorded was 8 mm. of mercury.

Another instance of the CO₂ pressure being on two occasions outside the normal limits is found in the case of A. C. (35, Tables V. and VI.), a nervous woman suffering from bronchitis and asthma.

¹ That the oxygen carrying power of the hæmoglobin in anæmia and other pathological conditions is accurately indicated by the Gowers-Haldane hæmoglobinometer, has recently been experimentally proved by Morawitz and Röhmer, *Arch. f. klin. Med.*, 1908, Bd. xciv. S. 540.

A mean CO_2 pressure of 25 mm. of mercury was recorded at a time when the breathing was very distressed. The pulse was 116 (usually 96), and respirations 24.

With this subject the alveolar CO_2 tension was very variable, the samples on each day were consistent, but from the records it will be seen that there is a maximum difference of over 8 mm. The total mean of 29.6 mm. of mercury is just below the value for the minimum pressure in women.

The fact that in most of the cases investigated the alveolar CO_2 pressure was about normal indicates that almost all the blood passing through the lungs was normally arterialised. Had any considerable

TABLE V.—*Diseases of the Respiratory System.*

MEN.

No.	Initials and Age.	Disease.	Date.	Percentage of Red Corpuscles per c.mm. (5,000,000,000 = 100)	Hæmoglobin Percentage by Scale (Haldane's Hæmoglobinometer).	CO_2 Percentage in Dry Alveolar Air (Mean).	Pressure of CO_2 in Alveolar Air in mm. Hg.	Number of Determinations.	Remarks.
25	B. . .	Pneumonia (left side)	Jan. 10, 1906	..	70	5.37	37.5	3	In bed; crisis, Jan. 7; temperature normal.
			" 17, "	..	..	5.50	38.9	4	Up.
			" 15, "	69	87	3.72	26.3	4	Crisis, Jan. 9; very weak and ill; temperature, 96.8; respirations, 23.
26	D. K. .	Pneumonia (right side)	" 17, "	..	..	4.11	29.1	4	Temperature, 97.8
			" 27, "	..	..	4.27	30.5	2	..
			" 30, "	..	..	4.78	34.4	4	..
27	W. H., 16	Pneumonia (both lungs)	" 10, "	81	98	6.01	41.9	5	Lungs now clear.
28	E. J. W., 27	Advanced phthisis, Dyspnoea (hysterical)	Sept. 16, 1905	93	64	..	..	..	Temperature, normal.
			" 30, "	..	..	4.60	32.7	2	..
29	R. S., 29		Nov. 17, "	..	105	4.68	33.3	6	..
30	C. B., 66	Empyema	Oct. 13, 1906	..	..	5.52	39.2	3	Mitral regurgitation.
Boys.									
31	R. G., 12	Empyema (left side).	Jan. 9, 1906	..	..	5.34	37.2	3	Large empyema on left side.
			" 10, "	..	..	5.34	37.3	3	..
			" 11, "	84	85	..	..	..	..
			" 15, "	..	89	5.26	37.2	2	Very little air entering left side; great fluttering over left side.
			Aug. 28, "	..	..	5.19	36.1	2	In bed; deficient aeration of lower lobe of right lung, possibly also of left, and falling in of chest wall; temperature normal.
			" 29, "	..	..	5.21	36.2	4	..
32	A. P., 13	Tubercular pleurisy (right side)							

TABLE V.—*Diseases of the Respiratory System* (continued).

WOMEN.

No.	Initials and Age.	Disease.	Date.	Percentage of Red Corpuscles per c.mm.	Hamoglobin Percentage by Scale (Haldane's Hamoglobinometer)	CO ₂ Percentage in Dry Alveolar Air (Mean).	Pressure of CO ₂ in Alveolar Air in mm. Hg.	Number of Determinations.	Remarks.
				(4,500,000 = 100)					
33	M. B., 23 .	Pneumonia Bronchial asthma	Jan. 13, 1906	93	101	5·60	39·6	4	..
34	M. H. . {		April 7, "	..	..	4·69	33·9	3	..
			Jan. 1, "	98	92	4·33	30·1	2	In bed; respira- tions, 22; pulse, 80.
35	A. C., 22 {	Bronchial asthma	" 6, "	..	..	4·13	28·5	4	In bed.
			" 11, "	..	..	4·77	34·1	4	..
			" 15, "	..	..	3·61	25·6	3	Up; breathing very difficult; respirations, 24; pulse, 116.
36	E. B., 22 {	Phthisis (early)	Sept. 7, 1905	..	..	5·39	37·7	4	..
			" 21, "	..	..	5·73	41·1	4	..
37	E. T. . {	Phthisis (advanced)}	Aug. 8, "	..	..	4·53	32·2	2	Unable to walk for last 2 months; very breathless.
GIRLS.									
38	E. W., 15 .	Empyema {	Jan. 6, 1906	..	..	5·00	34·5	4	..
			" 11, "	..	..	5·21	37·2	4	..
			" 13, "	100	95	..	..	..	..
			" 15, "	..	..	5·03	35·6	3	..
							Total	91	

TABLE VI.—*Diseases of the Respiratory System.*

MEN.

	Number as in Table V.	Mean CO ₂ Pressure in Alveolar Air.	Total Number of Determinations.
Normal men (Alveolar CO ₂ pressure)	27	41·9	5
	30	39·2	3
	25	38·2	7
	29	33·3	6
	28	32·7	2
	26	29·8	15
		Mean 35·8	Total 38

TABLE VI.—*Diseases of the Respiratory System (continued).*

BOYS.

	Number as in Table V.	Mean CO ₂ Pressure in Alveolar Air.	Total Number of Determinations.
Normal boys { Maximum 42·1 Minimum 30·6 Mean . . 37·2 }	31 72	37·2 36·2	8 6
		Mean 36·7	Total 16
WOMEN.			
Normal women { Maximum 41·0 Minimum 30·4 Mean . . 36·3 }	33 36 34 37 35	39·6 39·4 33·9 32·2 29·6	4 8 3 2 11
		Mean 34·9	Total 28
GIRLS.			
Normal girls { Maximum 40·1 Minimum 31·2 Mean . . 35·2 }	38	35·8	11

amount of blood passed through the blocked portions of lung, and thus escaped arterialisatation, the breathing would certainly have been increased, with consequent fall in the alveolar CO₂ pressure. The circulation is thus concentrated in the sound portions of the lung, and must be normal in amount.

III. ALVEOLAR CARBONIC ACID PRESSURE IN DISEASES OF THE CIRCULATORY SYSTEM.

In general, the alveolar CO₂ pressure in men, women, or children suffering from diseases of the circulatory system is maintained within normal limits. The average tension is somewhat low, the total mean for each class as seen in Table VIII. being below the normal mean pressure in the same. One hundred and forty-one experiments were performed. A greater variation in the alveolar CO₂ pressure pertaining to each individual was met with in this class of patients than in those previously mentioned, with a maximum variation of 8 mm. of mercury. A fall in pressure of 7 mm. of mercury occurred in two

cases of mitral incompetency (V.S., 39, and F.L., 40) as the condition improved. In the latter case the CO_2 tension decreased as the hæmoglobin and red corpuscles increased.

On the other hand, with J. E. (No. 42), an old man, the tension increased 6 mm. of mercury. Oscillations in tension were observed in other cases.

Departure from the normal was observed in one case of mitral stenosis, one case of mitral incompetency, and to a *very marked degree in congenital heart disease* (pulmonary stenosis). Taking these in order:—

1. *Mitral Stenosis* (E. B., 47, Tables VII. and VIII.). The partial pressure of CO_2 in this case, a young woman, was invariably below the minimum pressure for normal women, and varied from 27 to 29 mm. of mercury. When first seen she was unable to work. Cyanosis and breathlessness were marked features.

2. *Mitral incompetency*. CO_2 tensions above the normal maximum record for any class of subjects were found in the case of E. C. (44, Tables VII. and VIII.), an elderly woman suffering from mitral obstruction and incompetency with failing compensation, together with asthma. Cyanosis of the cheeks and lips was very marked and dyspnoea present. Possibly her respiratory centre was failing. From the analyses of the alveolar air obtained soon after her entry to the hospital, the CO_2 tension was found to be 49 mm. of mercury. At that time she was in bed, and the respiration was very distressed. Twelve days later, when up, much relieved and cyanosis less evident, the partial pressure of CO_2 had fallen to 45·7 mm. of mercury.

Taking even the mean of these values, 47·4 mm., the tension is considerably higher than the maximum recorded for normal men or women at ordinary atmospheric pressure.

3. *Congenital heart disease*.—A very interesting departure from the normal was observed in the case of L. M. (50, Tables VII. and VIII.). This case was one of a girl of 16 afflicted with pulmonary stenosis. Cyanosis was very marked and dyspnoea often great. During the six months that she was under observation, samples of the alveolar air were obtained under varied conditions, such as when keeping her bed, when up but barely able to walk about, and also at times when walking upstairs slowly could be accomplished without shortness of breath.

The partial pressure of CO_2 varied from 21 to 25·3 mm. of mercury, the percentage of CO_2 from 2·98 to 3·59, the maximum pressure and percentage being recorded at a time when breathlessness was again becoming more manifest.

When she was feeling at her best the CO_2 pressure was 22·5 mm. of mercury, the percentage of CO_2 3·18. The tensions here recorded are markedly lower than any observed under normal conditions. The hæmoglobin varied in amount from 157 to 165 per cent., and the red corpuscles from 158 to 184 per cent. of the normal.

In this case, and in No. 1, it would seem that the circulatory defect was not compensated even during rest, and that as a consequence the respiratory centre was abnormally active. In the other cases the circulatory compensation was apparently almost complete

TABLE VII.—*Diseases of Circulatory System.*

MEN.

N	Initials and Age.	Disease.	Date.	Percentage of Red Corpuscles per c.mm. (500,000,000 = 100)	Percentage of Hemoglobin by Scale (Haldane's Hemoglobinometer.	CO ₂ Percentage in Dry Alveolar Air (Mean).	Pressure of CO ₂ in Alveolar Air in mm. Hg.	Number of Determinations.	Remarks.
39	J. O. S., 20	Mitral regurgitation	Aug. 28, 1905	..	..	6.00	41.8	3	Two attacks of rheumatic fever; walking about in hospital.
			" 29, "	..	..	5.55	38.6	5	Respirations, 24.
			Oct. 7, "	..	..	4.78	34.3	5	At work on farm; breathless on exertion.
40	J. L., 17	"	Aug. 25, "	75	40	5.53	39.0	3	In bed; rheumatic fever; hæmaturia.
			Sept. 1, "	68	63	5.20	37.3	4	
			" 8, "	..	..	4.91	34.7	5	Walking about hospital.
41	C. C., 64	Mitral stenosis and regurgitation.	Nov. 25, "	..	83	4.67	33.0	3	At work as page.
			" 3, "	89	96	5.14	35.9	3	Shortness of breath for last two months; in bed.
			" 7, "	..	..	5.14	36.1	4	
42	J. E., 73	Mitral incompetency	" 3, "	..	..	5.06	34.4	2	Cyanosis; very short of breath; in bed.
			" 7, "	..	..	5.42	38.0	2	
			" 15, "	123	114	..	..	..	
			" 20, "	..	..	5.74	40.1	4	

BOYS.

43	W. B., 12	Mitral incompetency.	Jan. 17, 1906	..	..	4.37	30.1	3	In bed.
			" 20, "	..	..	5.28	38.3	2	..
			" 25, "	..	..	4.60	32.4	3	..
			" 29, "	..	97	4.99	35.6	4	..

WOMEN.

44	E. C., 64	Mitral regurgitation, failing compensation, asthma	Sept. 9, 1905	..	..	6.94	49.1	2	Cyanosis, marked; respirations, 28; just able to sit up in bed.
			" 20, "	..	..	6.39	45.7	3	Before leaving hospital, walking about.
			Aug. 19, "	..	..	4.65	33.0	3	Cyanosis; very breathless, but able to work; rheumatic fever twice.
			Sept. 2, "	..	..	4.60	32.6	3	
			" 16, "	..	..	4.50	32.3	3	
			" 30, "	..	..	4.54	32.3	4	
			Oct. 27, "	..	..	4.12	29.6	4	
			Nov. 11, "	..	..	4.38	30.4	4	
45	S. B., 39	Mitral obstruction and regurgitation, tricuspid incompetency	" 30, "	..	..	4.28	30.4	3	Patient in bed; œdema of legs and ascites; breathlessness had been very marked.
			Dec. 1, "	87	86	..	..	..	
			" 19, "	..	..	5.16	36.6	3	In bed; less breathless.
			Jan. 19, 1906	..	..	5.12	36.5	4	
			Feb. 2, "	87	94	4.31	30.7	5	
46	A. W., 32	Mitral incompetency	Oct. 9, "	..	..	4.22	30.4	2	Cyanosis, slight.
			Aug. 19, 1905	..	..	4.15	29.4	3	Breathlessness; marked cyanosis; unable to work.
47	E. B., 15	Mitral stenosis	Sept. 16, "	..	..	4.04	29.0	3	Less blue.
			" 30, "	..	..	3.81	27.1	5	
			Oct. 14, "	..	..	4.03	28.8	5	Able to start work.

TABLE VII.—*Diseases of Circulatory System* (continued).
WOMEN (continued)

No.	Initials and Age.	Disease.	Date.	Percentage of Red Corpuscles per c.mm.	Percentage of Hemoglobin by Scale (Haldane's Hemoglobinometer).	CO ₂ Percentage in Dry Alveolar Air (Mean).	Pressure of CO ₂ in Alveolar Air in mm. Hg.	Number of Determinations.	Remarks.
48	E. H., 36	Mitral stenosis	Nov. 8, 1905	111	89	4.58	32.6	2	In bed; has been very breathless; cyanosis, marked.
			" 14, "	..	..	5.04	35.1	4	In bed.
			" 21, "	..	..	4.90	34.9	4	Cyanosis, less marked; in bed.
49	M. I., 17	Mitral incompetency systolic murmur	Aug. 3, "	..	..	4.30	30.1	2	..
			" 4, "	158	..	..	..	..	In bed; cyanosis very marked; very short of breath.
			" 6, "	..	..	2.98	21.1	2	
			" 8, "	..	..	3.38	24.0	3	
			" 22, "	..	..	3.18	22.5	4	Able to walk upstairs without getting breathless; less cyanosed.
			" 23, "	184	157	..	..	..	
50	L. M., 16	Congenital pulmonary stenosis	Nov. 11, "	..	165	3.59	25.3	4	Increased breathlessness.
			Dec. 13, "	..	..	3.27	23.8	2	
			" 22, "	..	..	3.29	23.7	4	Unable to walk length of ward without breathlessness.
			Jan. 1, 1906	..	..	3.23	23.4	5	
Total number of experiments, 141									

TABLE VIII.—*Diseases of the Circulatory System.*
MEN.

	Number as in Table VII.	Mean CO ₂ Pressure in Alveolar Air. In mm. Hg.	Total Number of Determinations.
Normal men { Maximum 44.5 (Alveolar CO ₂ pressure) Minimum 32.6 Mean . . 39.2	{ 39 42 41 40	38.2 37.5 36.0 36.0	13 9 7 15
		Mean 36.9	Total 44
Boys.			
Normal boys { Maximum 42.1 Minimum 30.6 Mean . . 37.2	43	33.6	12
WOMEN.			
Normal women { Maximum 41.0 Minimum 30.4 Mean . . 36.3	44	47.4	5
	48	35.5	10
	45	32.4	36
	46	30.4	2
	49	30.1	2
	47	28.5	16
	50	23.4	24
		Mean 32.5	Total 95
Total number of determinations, 141.			

during rest. The alveolar air in several further cases of congenital heart disease with cyanosis has quite recently been observed by French, Pembrey, and Ryffel.¹ In every case the alveolar CO₂ pressure was very low. A preliminary account by Beddard and Pembrey of the alveolar air in several other very interesting cases appeared recently.²

CONCLUSIONS.

1. During rest and at ordinary atmospheric pressure a normal or nearly normal alveolar CO₂ pressure may be said to be maintained in the following diseases of the blood: Chlorosis, pernicious anæmia, chronic polycythæmia with cyanosis and enlarged spleen, and secondary anæmia due to severe hæmorrhage.

2. Except in the condition of congenital heart disease a normal or nearly normal alveolar CO₂ pressure was found as a rule to be maintained during rest in all the diseases of the circulatory and respiratory systems investigated. This fact points to complete circulatory compensation during rest.

3. In a case of congenital heart disease the alveolar CO₂ was maintained at a tension considerably lower than normal.

4. No constant parallelism could be traced between the partial pressure of CO₂ in the alveolar air and either the amount of hæmoglobin present or the number of red blood corpuscles.

5. From the maintenance of the alveolar CO₂ at a normal pressure in chlorosis and in other anæmic conditions, it must be inferred that a circulatory adaptation of increase in rate of blood flow gradually occurs, so that no want of oxygen results during rest. With a normal rate of circulation, and the oxygen-carrying power of the blood reduced to one-third of the normal or less, there would be symptoms of oxygen asphyxia.

At high altitudes, where the alveolar CO₂ pressure is diminished, such an adaptation does not succeed, owing to the incomplete saturation of the arterial blood with oxygen, while in CO poisoning there is insufficient time for the adaptation to take place.

In conclusion, I desire to express my sincere thanks to Dr. J. S. Haldane for his valuable suggestions and for the loan of apparatus.

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2. FITZGERALD AND HALDANE *Ibid.*, 1905, vol. xxxii. p. 486.

¹ *Journ. of Physiol.*, Cambridge and London, "Proc. Physiol. Soc.," 1909, vol. xxxix. p. ix.

² *Brit. Med. Journ.*, London, 1908, vol. ii. p. 580.