XXXVIII. THE HYDROGEN ION CONCENTRATION OF THE BLOOD IN CERTAIN PATHOLOGICAL CONDITIONS, AS DETERMINED BY THE HYDROGEN ELECTRODE AND THE INDIRECT METHODS OF BARCROFT AND HASSELBALCH.

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HASSELBALCH [1913] was the first to establish the conditions under which the hydrogen electrode can be used to measure accurately the reaction of the body fluids, and he constructed curves for the p_H of blood under varying CO_2 tensions.

More recently Peters [1914] has improved Hasselbalch's method by using completely reduced blood for the determinations, and Parsons [1917] has shown that by the C_H of blood is meant the C_H of the plasma it contains, *i.e.* the plasma obtained by centrifuging the blood without loss of CO_2 —which may be called the "true plasma" [Joffe and Poulton, 1920].

When once the hydrogen electrode apparatus has been set up the determinations do not occupy any great length of time; but as ordinarily arranged the apparatus itself tends to be somewhat complicated. A much simplified arrangement is, however, being designed by one of us (T. R. P.) especially for use with body fluids: it is soon to be placed on the market by the Cambridge and Paul Scientific Instrument Company. In this the manipulations are reduced to a minimum.

Barcroft's method [Barcroft and Peters, 1914] was introduced before the hydrogen electrode method had been finally perfected. It consists in determining at any required CO_2 pressure the percentage saturation with oxygen of the haemoglobin of the blood at a given oxygen pressure, and from this calculating the value of $\log K$ in Hill's equation. Barcroft and Peters [1914] showed for Barcroft's blood that $\log K$ was a linear function of p_H , and Hasselbalch [1916] found that in the case of six normal people the same relationship existed between the two values. Barcroft's method was used by Lewis, Ryffel, Wolf, Cotton and Barcroft [1913] in cases of cardio-renal disease, by Poulton and Ryffel [1913] in cases of uraemia, and by Poulton

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[1915] in cases of diabetic coma. Hasselbalch [1916, 1917] has pointed out that even if the relationship between p_H and $\log K$ holds for normal people, it does not necessarily hold for pathological cases; but unfortunately he did not test the method against the hydrogen electrode, but by calculations from the concentrations of free and combined CO_2 in the blood. In this method of calculating the p_H of blood there is a slight systematic error as pointed out by Parsons [1917].

1. METHODS.

Collection of blood, etc. The blood was obtained by venous puncture from patients in Guy's Hospital at about 11 a.m. It was immediately defibrinated, packed in ice inside a vacuum vessel, and sent by passenger train to Cambridge where it was received by T. R. P. at about 2 p.m. The determinations were carried out at once except in cases specially mentioned. The following investigations were made: (1) the p_H of this fully reduced blood at 37° at three or four CO_2 pressures by the method described by Parsons [1917]; (2) the CO_2 content of the same specimen of blood by means of Barcroft's differential apparatus; (3) the $\log K$ at the same temperature at varying CO_2 pressures, also with Barcroft's differential apparatus.

The alveolar CO_2 was obtained, by E. P. P. at the time that the blood was taken, by a modification of Hasselbalch and Lindhard's method which is described by Campbell, Hunt and Poulton [1923]. In this series of cases the patient, wearing Bohr's mask and valves, was told to expire deeply towards the end of his normal expiration. Inspiratory samples were not usually taken. In some of the earlier cases the ordinary Haldane-Priestley method was used.

In a few cases E. P. P. determined the CO_2 in the fully or partly oxygenated blood with Van Slyke's apparatus, the CO_2 pressure being measured as described in Joffe and Poulton's paper [1920]. A few determinations of $\log K$ were also made by him, according to Barcroft's original method [1914].

2. THE RELATION BETWEEN $\log K$ AND p_H IN PATHOLOGICAL BLOODS.

This relationship has been carefully tested with the normal blood of Barcroft [1914] and with Parsons' blood, with the addition of lactic acid [Donegan and Parsons, 1919] and by Barcroft and co-workers [1922]. In Fig. 1 the two lines indicate this relationship for the two bloods. The lines are parallel to one another; but they are obviously quite different. Thus at a p_H of 7.4 which is a normal p_H for reduced arterial blood, the $\log K$ for Barcroft's blood is 4.575, for Parsons' lactic acid blood it is 4.295. The few determinations carried out on Parsons' normal blood show that the $\log K$ - p_H relation is the same as for the lactic acid blood. The difference between these two lines is far outside the experimental error; it is to be partly accounted for by the fact that the p_H values obtained by Peters for Barcroft's blood are appreciably more acid than those obtained by Parsons working with his own blood. But Peters was more concerned with the differences in p_H produced

in blood under various physiological conditions than with the absolute value of the p_H at any time, and does not claim to have established this absolute value more than approximately in any given case. The average difference between Peters' result at any given pressure of CO_2 and that obtained by Parsons at the same carbon dioxide tension is about 0.1 in the value of the p_H , which is approximately half the difference between the p_H values corresponding to a given value of $\log K$ on the Peters-Barcroft curve and that found by Donegan and Parsons [1919]. It is to be noted, however, that Hasselbalch [1916] obtains values for normal blood which coincide with the original Peters-Barcroft curve, but he used p_H values calculated from the carbon dioxide content of the whole blood.

The $\log K$ - p_H relationship was tested on 16 cases (see Table I) and the results may be compared with Parsons' lactic acid blood curve in which the $\log K$ at $p_H = 7.4$ is 4.295 and with the P.-B. curve in which the $\log K$ at $p_H = 7.4$ is 4.575.

Fig. 1. $\log K$ - p_H curves for typical cases:

+	Case 4 (azotaemic nephritis).	◇	Case 11 (cardio-renal).
□	„ 6 (polycythaemia).	⊙	„ 12 (mitral stenosis).
x	„ 10 (diabetes).	—	P.B. line.
- - - - $\log K$ - p_H curve obtained with Parsons' blood to which 0.04 % of lactic acid had been added.			

Some typical examples of the relationship are shown in Fig. 1. In cases 4, 6 and 10 the lines joining the points are parallel with the curve for Parsons' blood and the P.-B. line, while in cases 11 and 12 there is no parallelism. Summarising our results, out of 21 examinations on 14 cases, there are six in which there is no parallelism, whereas in 18 the parallelism is fairly close.

Table I.

Case no.	Age	Disease	Date	Alv. CO ₂ mm.	p _H at alv. CO ₂ reduced (blood)	Fixed CO ₂ p _H at 40 mm. (reduced blood)	Buffer value		O ₂ capacity	Average difference		log K at p _H = 7.4	
							red blood	oxyg. blood		p _H (calc. from blood-true curve) - p _H observed	p _H (calc. from Warburg) - p _H observed		
5	36	Normal	June 5, '18	(39.4 May 26)	7.34	7.34	43.8	—	4.0 (3)	17.8	-0.033	-0.045	4.28
15	37	" (after oxygen chamber)	" 10, '18	(34.9 June 11)	7.34	7.29	43.8	3.3 (4)	4.4 (4)	17.6	+0.039	+0.029	4.295
1	61	Tubae with myatrophly	Sept. 24, '19 ¹	39.4	7.375	7.37	40.0	11.2 (2)	—	—	-0.088	-0.103	4.35 ²
		Uraemic coma	Feb. 4, '18	9.6	—	6.72	—	—	1.1 (2)	10.2	—	—	4.23 (extrap.)
4	32	Azotaemic nephritis	Mar. 13, '18	34	7.39	7.34	40.3	5.3 (2)	7.2 (2)	22.0	-0.053	-0.048	4.44
		"	"	"	—	—	40.5	—	—	—	+0.01	+0.003	—
		"	June 24, '18	(36 June 11)	7.26	7.23	39.8	3.95 (4)	3.8 (3)	15.9	+0.057	+0.037	4.35
		"	" 29, '18	(32.7 July 1)	7.31	7.22	42.3	7.3 (4)	2.5 (3)	16.5	+0.08	+0.068	4.35
8	19	(after O ₂ chamber)	Dec. 18, '18	34.9	7.33	7.29	42.3	—	—	17.8	-0.01	-0.005	4.33 ²
		Tubal nephritis, lipaemia	"	"	—	—	(extrap.)	—	—	—	—	—	—
		"	Jan. 28, '19	34.2	7.34	7.295	43.8	—	8.4 (2)	17.4	+0.03	+0.02	4.42
2	56	Cardio-renal	Feb. 12, '18	32.0	—	—	40.5	—	—	—	-0.025	-0.053	—
16	55	"	Nov. 4, '19	29.8	—	7.335	45.3	6.1 (3)	—	15.2	0.0	-0.015	4.29
11	65	"	Feb. 7, '19	23.5	—	7.36	41.6	5.9 (2)	—	24.5	-0.065	-0.05	4.34
17	56	Myocardial, emphysema	" 25, '20	31.2	—	7.35	44.3	7.5 (2)	—	16.5	-0.008	-0.023	4.10 ²
12	21	Mitral disease	" 14, '19	32.3	—	7.36	—	—	—	—	—	—	—
14	14	"	July 14, '19	35.1	7.42	7.37	50.0	9.9 (3)	—	12.6	+0.025	+0.002	4.295 ²
7	27	" pregnancy	Dec. 11, '18	28.1	7.50	7.46	—	—	—	22.2	—	—	4.19 ²
		"	"	"	7.35	7.26	39.3	3.3 (2)	—	16.7	+0.025	+0.008	4.15 (extrap.)
6	46	Erythraemia	Aug. 3, '18	(37.5 July 27)	7.27	7.25	33.6	—	7.3 (3)	30.5	+0.005	+0.013	4.27
		" (after O ₂ chamber)	8, '18	—	7.37	7.35	39.3	—	8.8 (3)	30.2	-0.031	+0.005	4.27
3	42	Diabetes	Feb. 27, '18 ¹	36.9	—	7.25	34.3	3.6 (2)	7.9 (2)	18.5	-0.048	-0.06	4.29 ²
10	20	" Ketosis	Mar. 4, '18	43.2	7.38	7.39	43.3	—	—	—	-0.08	-0.08	—
		"	Jan. 21, '19	35.3	7.32	7.295	36.8	5.1 (2)	8.2 (2)	19.6	-0.025	-0.038	4.45
9	18	"	Jan. 14, '19	23.2	7.27	7.14	28.8	—	—	—	-0.038	-0.068	—
		"	"	"	—	—	—	3.8 (3)	—	17.0	+0.04	+0.004	4.32
		"	Feb. 4, '19 ¹	16.3	7.23	7.04	—	—	—	—	+0.055	+0.01	4.85 ²
		"	"	"	—	—	—	—	—	18.0	+0.113	+0.04	(extrap.)
		"	"	"	—	—	—	—	—	—	—	—	(extrap.)
13	42	"	" 11, '19	19.6	7.32	7.15	29.8	4.7 (3)	—	18.1	+0.073	+0.042	4.27 ²
		"	June 2, '19	24.5	7.56	7.39	—	—	—	—	—	—	4.64
		"	Oct. 21, '19	21.8	7.435	7.265	—	—	—	—	—	—	4.295
		Parson's lactic acid blood	—	—	—	—	—	—	—	—	—	—	4.575
		P.-B. curve	—	—	—	—	—	—	—	—	—	—	—

¹ Blood kept in ice overnight.² Only one point available for log K-p_H relation.³ In this case the log K-p_H relation is not parallel to that of Parsons' blood.

There was no parallelism in a case of tabes (15) where the blood had been kept overnight, but had not apparently developed much acid; in a cardio-renal case (11); in tubal nephritis (8) on one occasion, but not on another; in mitral stenosis (12); in diabetic ketosis (9) on two occasions out of three, on one of which the blood had been kept, and on these two occasions the lines were not parallel to each other. It may be said that there is usually parallelism, but we cannot find any reasons for the exceptions.

In Table I (last column) we have defined the relationship by the value of $\log K$ at p_H 7.4. Analysing these 23 results (two of which are rather doubtful, as only single $\log K$ determinations were made) we find that they group themselves roughly about the curve for Parsons' blood. Thus eight results are greater than $\bar{4}\cdot34$ and eight are less than $\bar{4}\cdot28$, while seven are intermediate and the mean of these seven is $\bar{4}\cdot30$, which is practically the same as for Parsons' blood ($\bar{4}\cdot295$).

In cardio-renal disease and mitral disease with heart failure the $\log K$ at p_H 7.4 tends to be low, the mean value for cases 2, 16, 11, 12, 14 and 7 being $\bar{4}\cdot23$. This may have some bearing on Lewis, Ryffel, Wolf, Cotton and Barcroft's [1913] determinations of $\log K$ in cases of breathlessness. These authors found that the $\log K$ was low and considered that this was due to the presence of fixed acid in the blood in abnormal amounts, which produced an acidæmia. In Campbell, Hunt and Poulton's [1923] paper it has been pointed out that the fixed CO_2 of the blood is hardly diminished at all in these cases. Our present results suggest that there is a distinct tendency in cardiac cases for the $\log K$ to be low when compared with the p_H . This might possibly explain Lewis and Barcroft's findings; for, out of 13 determinations on the special cases showing meionexy in their paper there are only five in which the p_H at 40 mm. would be more acid than 7.40, supposing that $\log K$ was $\bar{4}\cdot10$ at p_H 7.40, as in our case of myocardial degeneration (case 11). In making this estimate we have calculated $\log K$ at 40 mm. CO_2 assuming that alteration of $\log K$ with CO_2 pressure was the same as in Parsons' lactic blood.

In three cases of diabetes with much ketosis $\log K$ at p_H 7.4 tended to be greater than in Parsons' blood, sometimes reaching the P.-B. curve, as follows: case 9 (lipaemia) $\bar{4}\cdot32$ on the first occasion; $\bar{4}\cdot85$, *i.e.* beyond the P.-B. curve on the second occasion when the blood was kept overnight; $\bar{4}\cdot27$ on the third occasion; case 10, $\bar{4}\cdot45$; case 13, $\bar{4}\cdot64$. In order to draw conclusions as to the p_H of blood from determinations of K in six cases of diabetes verging on coma or actually comatose, Poulton [1915] used the P.-B. curve for his calculations of p_H from $\log K$. Our present results indicate that this possibly gave correct results at any rate in some of the cases.

In five cases we have determined the $\log K$ - p_H relation on more than one occasion. In cases 4 and 6 (azotaemic nephritis, and erythraemia) there was no alteration before and after treatment in the oxygen chamber; but in case 4 $\log K$ at p_H 7.4 changed from $\bar{4}\cdot44$ to $\bar{4}\cdot35$ in three months, while the fixed acid in the blood increased considerably. On the other hand in case 5 (normal)

the fixed acid apparently increased during oxygen treatment but there was no alteration in $\log K$. There was some slight alteration in the slope of the $\log K-p_H$ curve and of the $\log K$ value at p_H 7.4 in case 8 (tubal nephritis, lipaemia) after six weeks. Case 9 (diabetes with a marked ketosis) showed great changes in the relation within the space of a month.

It is of course unsafe to generalise on a few cases; but our results would appear to suggest that in diabetes with severe ketosis $\log K$ tends to be rather high for a given value of p_H . On the other hand in cardiac disease with circulatory failure, including valvular disease and myocardial degeneration, $\log K$ tends to be rather low.

3. THE COMPARISON OF THE p_H OF BLOOD CALCULATED FROM THE CO_2 OF THE BLOOD WITH THE p_H DETERMINED BY THE HYDROGEN ELECTRODE.

It has been pointed out by Parsons [1917] that the p_H of blood means the p_H of the "true plasma." Consequently the most direct way of comparing Hasselbalch's CO_2 method with the hydrogen electrode would be to determine at a given CO_2 pressure the CO_2 content of the true plasma and from this to calculate the p_H by means of the formula [see Joffe and Poulton, 1920], and also to measure the p_H of the same specimen directly by the hydrogen electrode. In the case of reduced blood it is unnecessary to use the "true plasma" for the electrode measurement, as the same results are obtained with whole blood.

We have made determinations of this kind in two cases of myocardial degeneration (Figs. 2 and 3). In case 16 the p_H (observed) of the oxygenated plasma was less than that of the reduced blood as would be expected from Parsons' work [1917]. The calculated values from the CO_2 of the plasma agree fairly well with these results, as shown in Fig. 2. [For some unexplained reason the values calculated from the CO_2 of the blood are much too low in this case.] In case 17 (Fig. 3) we have five calculations from the CO_2 of the plasma, and two calculations from the CO_2 of the blood, but, unfortunately, only two values for the observed p_H . The correspondence between them is fair. Further observations of a similar nature would be desirable before it would be possible to say that the truth of this proposition had been conclusively demonstrated.

In case 13 (diabetes with ketosis) we have determinations of p_H both for the reduced blood and oxygenated true plasma. Parsons found that the average difference between the p_H of his oxygenated and reduced blood was 0.038. The differences in the case of the patient's blood were 0.03 and 0.035, agreeing fairly well with Parsons' figures. This difference of course depends primarily on the fact that oxyhaemoglobin is a stronger acid than reduced haemoglobin; and it is satisfactory to be able to conclude that in a pathological state such as diabetes the same theory also holds good.

In all our calculations we have used the Hasselbalch formula [1916] with a constant value of 6.096 for p_{K_1} , according to Warburg's recommendation

[1922, p. 207]. In calculating the free CO_2 we have used Bohr's solubility coefficient for CO_2 in serum, viz. 0.541 [Hasselbalch, 1916].

The true significance of the CO_2 content of true plasma had not been realised during the earlier part of the work, and although we made many determinations of the CO_2 content of whole blood the CO_2 of the "true plasma" was not determined. However, Campbell, Hunt and Poulton [1923] have

Fig. 2. The dotted line represents the normal relation between p_{H} and CO_2 tension in the reduced blood of T. R. P.

The points indicate values of this relationship in the blood of case 16, obtained as follows:

- By direct electrometric measurements on the completely reduced blood (T. R. P.).
- × By calculation from the CO_2 content of the completely reduced blood (T. R. P.) using the blood-true plasma CO_2 curve.
- + By calculation from the CO_2 content of the completely reduced blood, using Warburg's method.
- By calculation from the CO_2 content of the true plasma of the partly oxygenated blood (E. P. P.).
- By electrometric measurement on the true plasma of the fully oxygenated blood (T. R. P.).
- ⊕ By calculation from the CO_2 content of the true plasma of the fully oxygenated blood (E. P. P.).

determined the CO_2 both in whole blood and in the corresponding true plasma in quite a number of pathological conditions. In Fig. 1 of their paper, where these two values are plotted at right angles to one another, the results fall on a straight line, provided the haemoglobin content of the blood is about normal. Using their diagram we have calculated the CO_2 of the true plasma corresponding to our determinations in whole blood, and these plasma results have then been used for calculating the p_{H} by Hasselbalch's formula. This has been carried out for all our determinations of CO_2 in blood. It has been thought advisable to make one small correction. Campbell, Hunt and Poulton's curve

applies only to oxygenated blood, while we are dealing here almost entirely with reduced blood. Now Joffe and Poulton found that the difference between the CO_2 content of blood and that of its true plasma was slightly less, if the blood was reduced, than if it was oxygenated. This difference was about 1.7 cc. % and this has been subtracted from the plasma figures obtained from Campbell and Poulton's curve.

Fig. 3. The dotted line represents the normal relation between p_{H} and CO_2 tension in the reduced blood of T. R. P.

The points indicate values of this relationship in the blood of case 17, obtained as follows:

● By direct electrometric measurement on the completely reduced blood, and subtraction of 0.038 from each observed value of p_{H} , in order to bring the readings into comparison with the calculations made on the oxygenated blood.

○ By calculation from the CO_2 content of the true plasma of oxygenated oxalated blood (E. P. P.).

⊕ By calculation from the CO_2 content of the true plasma of oxygenated defibrinated blood (E. P. P.).

× By calculation from the CO_2 content of the whole oxygenated blood (E. P. P.), examined a week later.

In addition to CO_2 determinations on fully reduced blood by T. R. P. with the differential apparatus, in some cases the CO_2 was determined by E. P. P. with Van Slyke's apparatus using the technique described [Joffe and Poulton, 1920]. Sometimes fully oxygenated blood was used and sometimes partly oxygenated

blood. We have calculated the p_H for these results also, but where we are dealing with fully oxygenated blood we have added 0.038 to the result, which is the difference in p_H found by Parsons [1917] between oxygenated and reduced blood, in order to make the results comparable with the p_H measurements on reduced blood. When the blood was partly oxygenated a correspondingly smaller figure was added. These results of E. P. P.'s form a useful check on T. R. P.'s results especially as the methods used are quite different. On the whole the agreement is good.

We have used the same blood-true plasma CO_2 relation in calculating the p_H in our case of polycythaemia, because there is evidence that this relation is unchanged in polycythaemia, where the fixed acid of the blood is increased.

There is one other point. Campbell, Hunt and Poulton constructed their blood-plasma CO_2 relation for oxalated blood, while we are dealing here almost exclusively with defibrinated blood. Thus we have neglected any slight alteration there may be in the distribution of CO_2 between corpuscles and plasma, as the result of adding 0.5 % potassium oxalate.

The p_H values obtained by calculation and by actual experiment are given in detail in Table IV.

In Table II the differences between the values have been collected and it will be seen that out of the 57 calculations 71.9 % are not further from the observed values than 0.05. In Table I the average differences of the several determinations in each case are stated. When the fixed acid of the blood is increased, as indicated by the low value of p_H at 40 mm., there is a decided tendency for the p_H calculated from the blood-true plasma CO_2 curve to be higher than the observed value. This is shown in the last two experiments in case 4, in case 7 and in case 9. In the last case when the fixed acid in the blood due to keeping had increased greatly, the difference was 0.113, which is much the largest we found.

Table II.

Total No. of observations Percentage	No. of observations showing a difference between p_H (calculated) and p_H (observed) not greater than				Greater than 0.1
	0.01	0.03	0.05	0.1	
<i>Blood-true plasma CO₂ curve used:</i>					
57	14	26	41	53	4
%	24.6	45.6	71.9	93	
39*	13	23	31	38	1
%	33.3	59	79.5	97.4	
<i>Warburg's method used:</i>					
57	15	31	45	55	2
%	26.3	54.4	79	96.5	
39*	10	22	32	38	1
%	25.6	56.4	82.1	97.4	

* After deducting the cases in which there was a considerable increase of fixed acid, but not case 6.

On the other hand in case 3, where acid had accumulated owing to keeping, the difference was -0.048 ; but the difference was -0.06 for the same case when there was no acid, *i.e.* the alteration due to acid was in the same direction as in the other cases.

We think it possible that the relationship between the CO_2 in the corpuscles and plasma is altered by the addition of acid, so that the plasma, owing to the greater neutralisation of sodium bicarbonate contains relatively less CO_2 than the corpuscles [see Campbell, Hunt and Poulton, 1923, Section 3]. This would account for the difference. It is clear that these cases with increased fixed acid should be omitted from our test of the accuracy of the Hasselbalch formula applied to the plasma. This leaves 39 determinations and Table II shows a considerable improvement in the agreement, 79.5 % of the calculated p_{H} values not being further from the observed p_{H} than 0.05. Seven of the calculated p_{H} values coincide with the observed p_{H} , 20 are too small and 12 are too large.

Warburg¹ has recently described a modification of the Hasselbalch formula by means of which it is possible to calculate the p_{H} of blood (*i.e.* of the true plasma) from the CO_2 content of the blood and the CO_2 pressure, provided the oxygen capacity of the blood is known.

The oxygen capacities were obtained by Parsons during his log K determinations. They were carried out with various Barcroft differential apparatus in which (except for case 15) the oxygen capacity of Parsons' own blood had also been obtained. In making the calculations the value for Parsons' blood was taken at 18.5 vols. %; but it had not been determined. The haemoglobinometer value was 98 % (Price Jones).

As some of the examples in Warburg's paper are not quite accurately calculated and as the method is a valuable one, we think it best to give a fresh example of the calculation and Dr Warburg has kindly agreed to this.

Example. Case 8, on Jan. 28, 1919.

Partly oxygenated blood (% saturation = 60.3) contained 41.2 cc. CO_2 % at 41.7 mm. CO_2 pressure. It is required to find the p_{H} of this blood. The oxygen capacity (*i.e.* combined oxygen) of the blood was 17.4 vols. %.

In order to calculate the volume of free CO_2 , Warburg calculates the absorption coefficient Ψ by equation 128 and multiplies the pressure of CO_2 by the factor $\frac{0.5554}{7.6} \times \Psi$. We have shortened the process considerably by calculating a graph of the blood, which relates the oxygen capacity of the blood as abscissa with the above factor as ordinate directly. The graph is a straight line, drawn through two points such that an oxygen capacity of 1.5 vols. % corresponds to the factor 0.0709 and an oxygen capacity of 37.5 vols. % corresponds to the factor 0.0620 (see Fig. 4). In the present example the factor corresponding to 17.4 vols. % oxygen is 0.0670.

¹ Dr Warburg has pointed out a mis-print to us in equation 206 [1922, p. 327] which should read $x_1 = 100 - \text{the fraction}$.

The free CO_2 is $41.7 \times 0.067 = 2.794$.

$$\begin{aligned} \text{Now } p_{\text{H}}(\text{uncorrected}) &= 6.155 + \frac{\log \text{combined } \text{CO}_2}{\log \text{free } \text{CO}_2} [\text{see Warburg, 1922, p. 202}] \\ &= 6.155 + \frac{\log (41.2 - 2.794)}{\log 2.794} \\ &= 7.293. \end{aligned}$$

Fig. 4. Calculation of p_{H} (Warburg). Ordinate, values of F in equation—Free CO_2 (cc. per 100 cc. blood) $= F \times \text{CO}_2$ partial pressure (mm. Hg.). Abscissa, oxygen capacity of blood (cc. per 100 cc.).

The correction is obtained as follows: a value of p_{H} depending on the percentage saturation of the blood (60.3) is first calculated, viz.

$$\begin{aligned} 7.293 - \frac{100 - 60.3}{100} \times 0.40 \\ = 7.13. \end{aligned}$$

The correction corresponding to this (7.13) is obtained from Fig. 10 of Warburg's paper corresponding to 17.4 % oxygen. This is + 0.005. This is added to the original figure 7.293, so that the p_{H} is 7.298. Warburg has expressed his values

of p_H on Bjerrum's scale [see p. 167 of his paper]. Hence 0.048 must be deducted, so that the finally corrected p_H of the blood is 7.25 on the Sørensen scale. We have made an addition of 0.025 to this figure in this particular case, so as to make the result comparable with the observed p_H which was carried out on reduced blood.

We have calculated all our available results by Warburg's method and their accuracy can be compared with those calculated from the blood-true plasma CO_2 curve. A summary of the 57 results in Table II shows that the accuracy of Warburg's method is rather greater. This is because in cases 4, 7 and 9, in which the fixed acid of the blood was increased, the error is not so great by this method of calculation, as can be seen in Table I. After deducting these cases the accuracy of the two methods in the 39 remaining determinations is very much the same (see Table II). Of the 39 values calculated by Warburg's method 26 were less and 11 were greater than the observed p_H .

In this connection case 6 (erythraemia) is of special interest (Table I). On Aug. 8th after oxygen treatment the fixed acid in the blood was about normal. Under these circumstances Warburg's method of calculation would be expected to give a more accurate result, while the result calculated from the blood-true plasma CO_2 curve would be too low because with increase of blood cells there would be relatively more CO_2 in the plasma compared with the blood [see Campbell, Hunt and Poulton, 1923, Section 9]. The Warburg figure is 0.005 too large and the figure from the curve is 0.031 too small. Before treatment with oxygen the blood contained excess of fixed acid. This causes a relative diminution in the CO_2 of the plasma which neutralises the previous error in the calculation from the blood-true plasma CO_2 curve. On the other hand this makes the Warburg calculation too large. In accordance with this we find that on Aug. 3rd the former value was the more accurate, being only 0.005 too large, while the Warburg calculation was 0.013 too large.

In case 12 the oxygen capacity was rather low, without increase of fixed acid. This would make no difference to the Warburg figure but would make the figure calculated from the curve too high. In accordance with this we find that the former was only 0.002 too high, while the latter was 0.025 too high.

The conclusion we would draw is that when the haemoglobin content is about normal both methods of calculation from the CO_2 content of the blood are available; where the haemoglobin is distinctly too high or too low and there is no increase of fixed acid or base, Warburg's method is the better; where there is increase or diminution in fixed acid, it is necessary to determine the CO_2 in the true plasma and make the calculation from this by Hasselbalch's formula using a constant value of 6.096 for p_{K_1} .

4. THE p_H OF REDUCED BLOOD AT 40 MM. CO_2 PRESSURE.

The method which has been widely adopted for obtaining a measure of the fixed acid in the blood was described by Van Slyke and Cullen [1917],

viz. determining the alkali reserve of separated plasma (the CO_2 combined at 40 mm.). A better plan is to determine the CO_2 combined at 40 mm. in whole blood [Joffe and Poulton, 1920]. It is permissible in most cases to draw conclusions as to the fixed acidity of the blood from these measurements, providing that the blood has about a normal haemoglobin content. It is still better to determine the CO_2 combined in the true plasma, as this gives a measure of the amount of fixed acid present, irrespective of the haemoglobin content of the blood. Undoubtedly the best method of measuring variations in fixed acidity is to determine the reaction of the blood by some direct method at a known pressure of CO_2 such as 40 mm. For this purpose we have used the hydrogen electrode, and figures have been obtained for 17 cases, some of them being examined on several occasions.

The normal limits for the p_{H} of reduced blood at 40 mm. CO_2 pressure have been determined by Barcroft and his co-workers [1922] by observations on nine different subjects. The values ranged from 7.38 to 7.47. Parsons' blood at one time gave a value of 7.36 [Donegan and Parsons, 1919], so that we may regard 7.36–7.47 as the normal limits.

In our series of 17 cases results between normal limits were obtained in seven and six of them lay between 7.36 and 7.39, so that they were on the acid side of Barcroft and his co-workers' mean value. The seven cases comprised two each of diabetes, mitral disease, and myocardial disease, and one normal (15) in which the blood had been kept overnight. In the other normal case (5) the value was 7.34, which is slightly acid; but for some unexplained reason the fixed acidity was still further increased after treatment in an oxygen chamber.

Cases with evidence of heart failure also gave mostly normal results. These included two cases of mitral stenosis—case 12, $p_{\text{H}} = 7.37$, and case 14, $p_{\text{H}} = 7.46$, and four cases of myocardial degeneration which were clinically similar to the cases described by Lewis and his colleagues [1913]. They were: case 2, 7.335; case 11, 7.35; case 16, 7.36; and case 17, 7.36. These results agree with those of Campbell, Hunt and Poulton [1923] and indicate that there is no large amount of fixed acid present in the blood, as has been suggested.

In one case of diabetes with very little ketosis (case 3) the p_{H} was normal, 7.39. In case 13 where the ketosis was not marked on one occasion, due to treatment, the p_{H} was 7.39, though on a second occasion when ketosis had increased the value of 7.265 was obtained showing considerable increase in the fixed acid of the blood. Case 4, azotaemic nephritis, gave a value of 7.34 on one occasion, but on a second occasion three months later the value was 7.23 before and 7.22 after oxygen, showing a considerable increase in the fixed acid of the blood.

Six of our cases showed a marked increase in the fixed acidity. One of these (case 1) was a case of uraemia following septic pyelonephritis. The p_{H} of the blood while the patient was unconscious shortly before death was 6.72, the blood being actually acid, but it had been kept 16 hours longer than usual

although in ice all the time. The other was a case of parenchymatous nephritis with oedema, 7.29 and 7.295 on two occasions.

Two cases of diabetes with ketosis showed increase in the fixed acidity. In case 10 this was slight, the p_H being 7.295. In case 9 values of 7.14, 7.04 and 7.15 were obtained. The middle one of these determinations—7.04—was done when the patient was approaching coma, but the blood had been kept in ice overnight.

In one case of mitral stenosis (case 7) with pregnancy the p_H was 7.26, the acid value being probably accounted for by the pregnancy (see Hasselbalch and Gammeltoft, 1915].

In case 6 (erythraemia with splenomegaly) the p_H was 7.25, showing increase in fixed acidity. The interesting point was that after treatment with oxygen the p_H rose to 7.35 a normal figure, so that the acid, whatever it was, was abolished by oxygen. Dr Price Jones found that the condition of the blood remained unaltered (Table III). This suggests that the polycythaemia was not secondary to want of oxygen [see Weber, 1921].

In Table I the fixed CO_2 blood at 40 mm. is also given. On the whole the values diminish with the p_H , as would be expected; but there are surprising exceptions, *e.g.* case 4, where the CO_2 remained much the same, while the fixed acid, as indicated by the p_H , had increased considerably.

Table III.

Case	Date	Red cells $\times 10^6$ white cells per cu. mm.	Hb. per cent. colour index	Mean diameter of red cells	Differential Count, per cu. mm.				
					Poly- morphs	Lympho- cytes	Hyalines	Eosino- phils	Mast cells
4	24. vi. 18	5.41	86	7.44	6922	6306	1050	293	117
		14,666	0.79	—	—	—	—	—	—
	29. vi. 18 (after O_2 chamber)	4.136 8,700	88 1.07	7.55	3793	3863	835	157	52
5	5. vi. 18	4.856	94	7.56	7330	2415	588	147	21
		10,500	0.96	—	—	—	—	—	—
	10. vi. 18 (after O_2 chamber)	4.86 11,700	98 1.01	7.34	6271	4680	468	281	0
6	3. viii. 18	8.346	158	6.87	4350	390	150	100	10
		5,000	0.95	—	(10 normoblasts, 10 myeloblasts)				
	9. viii. 18 (after O_2 chamber)	8.646 6,600	164 0.95	6.91	5504	647	251	145	53
					(40 normoblasts)				

5. p_H OF REDUCED BLOOD AT ALVEOLAR CO_2 PRESSURE.

This calculation has often been made in order to express the p_H of the arterial blood on the assumption that the alveolar and arterial CO_2 pressures are identical. In the paper by Campbell, Hunt and Poulton [1923] it is shown that this approximately holds in people who are not breathless, and in anaemia and erythraemia, while in cases of mitral stenosis there is sometimes fairly good correspondence and sometimes not. However in breathless cases where there was evidence of pulmonary disease the alveolar samples gave results very much below the arterial CO_2 pressure. Many of these cases might be classified as cardio-renal, although there was evidence that the lungs were

also affected. On this account we have not calculated the p_{H} at alveolar CO_2 pressure for cases 2, 16, 11 and 17, as we think the results would be misleading.

The figures in column 5 (Table I) are for fully reduced blood and it is necessary to deduct about 0.04 to make these strictly comparable to the figures for arterial blood. The results, as is the case with all figures hitherto published, may err somewhat on the acid side, as the observations were made before Lovatt Evans' work on glycolysis was published. This subject is dealt with fully elsewhere [Campbell, Hunt and Poulton, 1923].

Approximately normal results were obtained in cases 5, 15 (normals) and in case 4 on March 4th while the p_{H} fell somewhat as the fixed acid in the blood was increased later and in case 8 (tubal nephritis). In case 6 (erythraemia) the p_{H} was 7.27 which is low and this was fairly close to the arterial value for case 13 of the next paper. In case 12 (mitral stenosis) the value 7.42 was quite close to the arterial value 7.395 of the same patient in Campbell, Hunt and Poulton's paper (case 9). In case 27 the value was normal showing that the increase of fixed acid due to pregnancy had been approximately compensated. In case 1 (uraemia) there was great acidemia, but the blood had been kept longer than normal. Still, taken in conjunction with case 33 of Campbell, Hunt and Poulton's paper there can be little doubt that acidemia is present in uraemic coma, but evidence that the coma is not itself due to the acidemia is given in their paper.

In the ketosis of severe diabetes there are reasons [Campbell, Hunt and Poulton, 1923] for believing that the alveolar samples may give too low values for the arterial CO_2 . If this is the case, the arterial p_{H} would probably lie somewhere between the value at alveolar CO_2 pressure and the value at 40 mm. This would suggest that there was a measurable amount of acidemia in case 9 who was verging on a state of coma when the examinations were made. Sonne and Jarlöv [1918] found the same thing by determinations of the CO_2 of blood at 40 mm. Poulton [1918] also came to this conclusion from log K determinations. However it does not follow that this acidemia is itself the cause of diabetic coma. Cases of emphysema with myocardial changes are described by Campbell, Hunt and Poulton, and in these cases there was for months some degree of acidemia due to CO_2 without any symptoms of drowsiness. However it must be admitted that in the case of diabetes further observations with analysis of the arterial blood are necessary before conclusions can be drawn as to whether acidemia plays any part in the symptomatology of coma. On other grounds this is unlikely [Poulton, 1918].

6. THE BUFFER VALUE OF BLOOD.

Following Barcroft, Bock, Hill, Parsons, Parsons and Shoji [1922] we have considered that buffer value should be expressed as a change in c_{H} and we define it as the percentage volume of CO_2 it is necessary to add to blood within the physiological range, to increase the c_{H} by 1×10^{-8} .

The buffer value of blood is difficult to estimate because if only a few p_{H}

and CO_2 points are determined, a slight error in the determination will make a considerable change in the values obtained. In many of our cases we have not only the CO_2 volumes determined on the same samples of reduced blood which were used for the p_{H} measurements, but we have also CO_2 measurements on the partly oxygenated blood used for the $\log K$ determinations. These latter CO_2 determinations have not so far been employed, and are not given in the protocols, because the constant of the differential apparatus used was not known with the same degree of accuracy as that of the apparatus used for the reduced blood. However the results are comparable among themselves, so that they can be used for obtaining the buffer value. In Table I calculations from the CO_2 of both reduced and partly reduced oxygenated blood are given and the number of points available for the calculation are put in brackets after the value.

The most striking fact arising out of these results is the effect that increasing the fixed acid of the blood has in diminishing the buffer value. Taking cases 3, 4, 7 and 9, when the p_{H} at 40 mm. was not above 7.26 the average buffer value was 4.54, while taking the cases where the p_{H} at 40 mm. was above 7.33, the average buffer value was 7.0.

Anaemia also diminishes buffer value; but this can hardly be of much importance in these cases because the average oxygen capacity was not very different in the two groups, being 17.1 in the first and 19.1 in the second.

The remarkably low value of 1.1 was obtained in case 1 (uraemia), where the fixed acid was very greatly increased, and there was also considerable anaemia.

In conclusion, we should like to thank Dr Price Jones for allowing us to quote some of his blood findings, and Dr W. N. Hurtley for kindly analysing the urine in case 13.

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7. CONCLUSIONS.

(1) The $\log K$ - p_{H} relationship was a straight line, in most cases parallel to the P.-B. line and to the line for Parsons' blood, but it was usually closer to the latter. In cardio-renal disease and mitral disease with heart failure the $\log K$ at p_{H} 7.4 tended to be rather low. It was rather higher in a few cases of diabetes with ketosis.

(2) The p_{H} can be calculated from the CO_2 content of blood and the CO_2 partial pressure, (a) by calculating the "true" plasma CO_2 from the blood—true plasma CO_2 curve given by Campbell, Hunt and Poulton [1923], (b) by Warburg's method. The latter method must be used where there is any great increase or diminution in the oxygen capacity of the blood. If there is increase or diminution of CO_2 fixing power, it is essential to determine the CO_2 content of the true plasma and use this for the calculation. In suitable cases 80 % of values were found not to be further away from the observed p_{H} than 0.05.

(3) A graph has been constructed which should be useful in calculating p_H values by Warburg's method.

(4) A case of erythraemia with splenomegaly, treated for five days in an oxygen chamber, at Cambridge, showed no alteration in the blood picture. There was a marked diminution in the fixed acid of the blood, which was previously abnormally high.

(5) In cases of diabetes with ketosis, in mitral disease with pregnancy, in uraemia and renal disease and erythraemia, the p_H observed at 40 mm. was abnormally low. In other cases normal values were usually obtained.

(6) The buffer value of blood is diminished, as the fixed acid in blood is increased.

8. CLINICAL NOTES ON CASES AND PROTOCOLS.

Case 1. *Male*. Enlarged prostate. Suppurative pyelo-nephritis. Uraemia. Blood urea 0.4 %.

Case 2. *Male*. Myocardial degeneration, nephritis and bronchitis, anasarca, blood urea 0.046 %.

Case 3. *Female*. Diabetes mellitus. Faint Rothera reaction.

Case 4. *Male*. Azotaemic nephritis following streptococcal pneumonia. Blood urea on Oct. 26, Nov. 10, 1917, Feb. 7, March 15, June 12, 1918, respectively 0.2, 0.09, 0.08, 0.05, 0.07 %. B.P. (Mar. 19) 183/110. Uraemia and death in March 1921. Blood urea 0.44 %.

Case 5. *Healthy Male*. Recovery after having suffered in Jan. 1918 from acute nephritis and uraemia with hemiplegia. Blood urea on Jan. 29, Feb. 12, April 10, 25, May 7, respectively 0.23, 0.03, 0.03, 0.03, 0.02 %.

Case 6. *Male*. Erythraemia with enlarged spleen. B.P. 160.

Case 7. *Female*. Mitral stenosis, 4-5 months pregnancy. Some bronchitis.

Case 8. *Male*. Chronic tubal nephritis, lipaemia, oedema. Blood urea 0.02 %.

Case 9. *Male*. Diabetes, ketosis, lipaemia, sepsis. Ammonia index 23.3 %. Coma threatening on Feb. 3 with subsequent recovery. Died a few weeks later.

Case 10. *Male*. Diabetes, ketosis, septic glands.

Case 11. *Male*. Myocardial degeneration; emphysema, pulsus alternans, anasarca, oedema of lungs, albuminuria. Blood urea 0.04 %. Cheyne-Stokes respiration. No cyanosis. Large tender liver.

Case 12. *Female*. Mitral stenosis and regurgitation. Bronchitis. Oedema. Large liver. No cyanosis. (The same as case 9 of Campbell, Hunt and Poulton's paper.)

Case 13. *Female*. Diabetes, ketosis. Given 3 drachms sod. bicarb. daily. June 2, Urine sugar 3.6 %; Ammonia index 8 %; Aceto-acetic acid slight. Oct. 21, ketosis had much increased. Dr W. N. Hurtley of St Bartholomew's Hospital very kindly analysed the urine (184 cc.) collected during the 12 hours, 8 p.m. to 8 a.m., before the blood sample was taken. Aceto-acetic acid was

0.19 %; total 3.51 gm. The β -hydroxybutyric acid was 0.63 %; total 11.6 gm. as determined by rotation and 0.94 %; total 17.3 gm. as determined by titration. The ratio $\frac{\beta\text{-hydroxybutyric acid}}{\text{total acetone bodies}}$, was 82.6 % agreeing with Neubauer's and Kennaway's findings [1914] in severe diabetes.

Case 14. *Female*. Mitral stenosis and regurgitation, large pulsating liver, ascites, right sided dilatation of heart, lips slightly cyanosed, orthopnoea.

Case 15. *Male*. Tabes with myatrophie, taken as a normal control.

Case 16. *Male*. Fibroid heart (650 g.), Atheroma of coronary arteries, Infarcts of spleen and kidneys. Auricular fibrillation. Oedema, periodic breathing and orthopnoea. Distinct cyanosis of face and hands. Blood urea 0.04 %. Slight albuminuria.

Case 17. The same as case 26 [Campbell, Hunt and Poulton, 1923].

Table IV.

Case	Date	Fully reduced blood					Partly oxygenated blood	
		CO ₂ mm.	p_{H} (calculated)			CO ₂ cc. %	CO ₂ mm.	log K
			p_{H} (observed)	Bl. t. pl. curve	Warburg			
1.		9.9	6.92	—	—	—	10.5 ¹	5.74
		26.0	6.81	—	—	—	23.7 ¹	5.66
		40.2	6.72	—	—	—	—	—
2.		23.1	7.51	7.51	7.49	39.4	20.1	4.43
		33.1	7.39	7.39	7.38	44.2	29.0	4.33
		41.7	7.33	7.33	7.315	49.0	41.4	4.25
3. Feb. 27		27.1	7.40	7.34	7.33	31.8	25.3	4.32
		35.4	7.30	7.265	7.25	35.5	—	—
		44.3	7.37	7.29	7.29	48.1	—	—
4. Mar. 13		27.3	7.465	7.39	7.40	36.7	30.4	4.44
		48.9	7.27	7.24	7.24	47.0	56.4	4.29
		June 24	2.5	7.84	—	8.2	11.6	4.19
		25.0	7.34	7.435	7.42	36.2	35.7	4.05
		40.8	7.23	7.265	7.24	40.6	49.2	4.52
		61.6	7.11	7.15	7.13	48.8	63.3	5.96
	June 29	2.3	7.96	—	—	5.0	0.5	3.13
		23.5	7.37	7.42	7.405	33.0	18.6	4.56
		42.7	7.20	7.31	7.30	47.9	32.9	4.22
	June 5	64.9	7.07	—	—	—	64.5	5.95
		1.7	8.17	—	—	11.8	11.8	4.72
		16.8	7.61	7.555	7.54	30.9	26.9	4.31
	June 10	45.6	7.32	7.29	7.285	49.4	38.8	4.21
		33.2	7.39	7.375	7.37	42.7	52.4	4.10
		1.9	8.18	—	—	5.6	10.2	4.67
		17.9	7.56	7.60	7.605	38.0	20.8	4.41
		31.0	7.37	7.41	7.395	42.4	41.1	4.15
		45.3	7.24	7.285	7.28	48.4	57.1	4.10
	Aug. 3	58.9	7.17	7.20	7.175	50.7	55.7	4.06
		22.2	7.36	—	—	—	—	—
		40.6	7.24	—	—	—	—	—
	Aug. 8	60.4	7.13	—	—	—	—	—
		12.5	7.63	—	—	—	—	—
		38.8	7.36	—	—	—	—	—
	7.	60.7	7.23	—	—	—	—	—
		35.0	7.29	7.335	7.315	40.8	31.6	4.08
		49.8	7.20	7.205	7.19	44.7	45.8	4.01
8. Dec. 18		30.0	7.38	7.37	7.375	39.3	24.0	4.43
		39.6	7.30	—	—	—	38.8	5.16
		—	—	—	—	—	50.3	4.93
Jan. 28		37.5	7.32	7.35	7.34	45.4	16.7	4.595
		—	—	—	—	—	30.3	4.44
		—	—	—	—	—	40.0	4.26

Table IV *continued*.

		Fully reduced blood				Partly oxygenated blood		
		p_H (calculated)						
Case	Date	CO ₂ mm.	p_H (observed)	Bl. t. pl. curve	Warburg	CO ₂ cc. %	CO ₂ cm.	log K
9.	Jan. 14	16.0	7.33	7.405	7.36	20.3	16.1	4.26
		29.3	7.22	7.24	7.205	27.0	31.4	4.13
		49.1	7.08	7.105	7.07	34.5	—	—
Feb. 4	15.1	7.245 ²	7.425	7.355	18.8	14.0	4.496	
	14.6	7.25	—	—	—	29.4	4.14	
	29.2	7.105	7.15	7.065	20.1	—	—	
Feb. 11	9.4	7.44	7.555	7.525	16.8	11.2	4.27	
	26.8	7.22	7.26	7.225	25.5	39.2	4.20	
	36.3	7.17	7.235	7.205	33.6	—	—	
10.	20.3	7.465	7.465	7.455	31.0	22.1	4.47	
	42.9	7.28	7.23	7.215	40.3	35.4	4.40	
	—	—	—	—	—	43.4	4.29	
11.	16.3	7.59	7.59	7.58	32.8	16.2	4.16	
	41.2	7.345	7.33	7.31	47.5	37.2	4.09	
12.	19.8	7.545	7.59	7.565	39.8	19.5	4.58	
	28.3	7.45	7.48	7.45	44.4	29.5	4.02	
	41.7	7.37	7.37	7.355	53.8	46.7	4.17	
13. June 2	20.5	7.62	—	—	—	—	—	
	28.9	7.52	—	—	—	—	—	
	44.3	7.34	—	—	(Oct. 21)	11.7	4.80	
Oct. 21	20.9	7.45	—	—	—	26.0	4.64	
	39.6	7.27	—	—	—	35.5	4.57	
	27.8	7.575	—	—	—	29.9	4.41	
14.	40.4	7.46	—	—	—	—	—	
	29.3	7.46	7.325	7.30 ³	32.8	28.2	4.37	
15.	49.8	7.30	7.26	7.255 ³	50.1	47.7	4.29	
	20.7	7.565	7.495	7.515	34.4	21.7	4.49	
16.	41.7	7.35	7.29	7.30	44.8	41.0	4.30	
	21.5	7.56	—	—	—	—	—	
	41.5	7.35	—	—	—	—	—	
Experiments on fully oxygenated blood								
4. Mar. 13	29.8	7.43 ⁴	7.415	7.42	36.5	—	—	
	38.4	7.35 ⁴	7.385	7.365	42.3	—	—	
13. Oct. 21	21.0	7.415 ⁵	—	—	—	—	—	
	39.3	7.24 ⁵	—	—	—	—	—	
16. Mar. 13	20.7	7.51 ⁵	—	—	—	—	—	
Experiments on partly oxygenated blood (Hb. circ. 50 % saturation)								
6. Aug. 3	16.0	7.41 ⁶	7.41 ⁷	7.405 ⁷	19.1	—	4.39	
	37.2	7.26 ⁶	7.265 ⁷	7.28 ⁷	34.5	—	4.12	
	53.3	7.17 ⁶	7.18 ⁷	7.195 ⁷	42.7	—	5.98	
Aug. 8	9.9	7.66 ⁶	7.665 ⁷	7.705 ⁷	21.4	—	4.50	
	27.9	7.455 ⁶	7.385 ⁷	7.415 ⁷	33.8	—	4.36	
	43.1	7.335 ⁶	7.305 ⁷	7.34 ⁷	45.0	—	4.17	
8. Jan. 28, '19	58.4	7.24 ⁶	7.21 ⁷	7.24 ⁷	50.0	—	4.09	
	15.4	7.53 ⁶	7.475 ⁷	7.435 ⁷	21.9	—	—	
	41.7	7.285 ⁶	7.29 ⁷	7.275 ⁷	41.2	—	—	
9. Jan. 14, '19	32.6	7.19 ⁶	7.245 ⁷	7.20 ⁷	28.6	—	—	
	14.8	7.53 ⁶	7.48 ⁷	7.435 ⁷	20.6	—	4.66	
10.	35.7	7.32 ⁶	7.295 ⁷	7.28 ⁷	35.9	—	4.327	

¹ Corresponding values for CO₂ content were 5.9 and 8.6 cc. %.² By extrapolation.³ Assuming haemoglobin content of blood was normal.⁴ Values obtained by interpolation from reduced blood, with 0.038 added, so that they represent p_H of fully oxygenated blood [see Parsons, 1917].⁵ Oxygenated true plasma was used for these determinations.⁶ These values are for reduced blood, obtained by interpolation from the values given earlier in the table.⁷ CO₂ in partly oxygenated blood was used in these calculations, which were subsequently corrected so that they represent values of p_H for reduced blood.

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