THE INDIRECT DETERMINATION OF THE pH OF THE BLOOD IN CHILDREN.

BY

STANLEY GRAHAM, M.B., and NOAH MORRIS, M.D.

(From the Medical Department, Royal Hospital for Sick Children, Glasgow.)

In any indirect method of determining the pH of the blood a knowledge of the ratio $H_2CO_3 : BHCO_3$ becomes essential. The sum of these two factors, or the total CO_2 , can readily be estimated by an analysis of a sample of blood in the Haldane or the Van Slyke blood-gas apparatus, but the proportion of free CO_2 (H_2CO_3) to the combined CO_2 ($BHCO_3$) is much more difficult to determine.

It has long been known that the tension of CO_2 in arterial blood is approximately the same as that of the alveolar air. Thus, by obtaining samples of alveolar air, one can readily calculate the CO_2 tension in the blood and, by using Bohr's coefficient, arrive at the figure for the free CO_2 content (H_2CO_3). The total CO_2 content less this figure will then represent the combined CO_2 ($BHCO_3$) of the blood.

In infants and children, we have tried various ways of obtaining alveolar air, including the original Haldane-Priestley method as well as that recently used by Henderson⁽¹⁾ in his method of estimating the blood-flow. The results of the CO_2 analysis, however, always confirmed our doubts as to the genuineness of the samples obtained. Consequently, it became necessary to devise some other method for the determination of the CO_2 tension of the blood.

It has been stated that air injected into any body cavity assumes the same partial pressure or tension of oxygen and carbon dioxide as exists in the arterial blood. Argyll-Campbell⁽²⁾ has injected air subcutaneously as well as intra-peritoneally in rabbits and has demonstrated that the CO_2 content of the air so injected in about one hour becomes the same as that in the alveolar air obtained by the usual Haldane-Priestley method. Haggard and Henderson⁽³⁾ in a study of the effect of ether anæsthesia on the CO_2 content of air injected intra-peritoneally in dogs have concluded that the tension of the CO_2 in the injected air becomes after a period of time identical with that of the arterial blood. Henderson⁽¹⁾ has also suggested that the same equilibration of gases takes place if air be held in the mouth with the lips closed and the cheeks distended. In this way he obtains samples, the CO_2 content of which is the same as that of alveolar air. We, however, have repeatedly tried this method

of holding air in the mouth but, whether from inexperience or not, we were unable to obtain in ourselves concentrations of CO_2 which fell within the usual limits of normal.

During a conversation with Henderson on this question the possibility was suggested that a figure approximating the CO_2 content of alveolar air might be obtained by injecting air into the rectum and, after allowing time for the diffusion of gases, removing samples for analysis. It is this method and the results obtained by it which form the basis of this paper.

METHOD :—The technique adopted was as follows :—After a simple enema, a rectal wash-out with an 0.5% NaHCO_3 solution was given until the return was clear. Then, by means of a catheter and a large (100 cc.) syringe, 100 to 200 cc. of air were slowly injected into the rectum. The catheter was left *in situ*, the free end being clamped. At the end of half an hour a sample was removed in the syringe by means of a three-way stop-cock, care being taken always to discard the air which had been in the catheter and consequently not exposed to the bowel wall. This sample was transferred directly to a Haldane air-gas analysis apparatus and its CO_2 content determined. Subsequent samples were taken every ten minutes for analysis. In later experiments, we found it of value to mix the air at the end of 15 minutes by withdrawing it into the syringe and re-injecting it. The whole procedure can be accelerated by injecting air containing approximately 4% CO_2 . Ordinary expired air serves this purpose quite well.

The pollution of the air in the rectum with fæcal gas from the bowel above is, of course, a probable source of serious error. Such fæcal gas, however, would only influence the analysis if it were acid in reaction. If neutral, the gas would simply dilute the percentage in the equilibrating air and so delay the equilibration, but the tension of CO_2 in the rectum would gradually return to that of the blood, provided the air were left sufficiently long in the rectum. Should the polluting gas be acid in character, it would undoubtedly raise the percentage of CO_2 obtained on analysis and it was to obviate this possibility that a preliminary wash-out of NaHCO_3 was given. The small amount of NaHCO_3 left in the rectum we believe is sufficient to neutralise any polluting acid gas. The presence of any polluting acid gas would cause an evolution of CO_2 , but this, of course, would gradually be equilibrated. In our investigations, the interval between the taking of successive samples was never less than ten minutes and any results differing by more than 0.3 from the mean of three successive readings should be accepted with caution. Unfortunately, in infants and in children under two years of age we have found it impossible to prevent the air being expelled around the catheter, even when very small amounts were injected. In children over two years however, no such difficulty was experienced and the procedure did not disturb them in the least. On many occasions, as much as 300 cc. of air was injected without causing the slightest inconvenience.

TABLE I.

Observation No.	Age in Years.	Sex.	Time in Mins. after Injection at which sample was taken.								Average CO ₂ Content. Rectal Air.
			30	40	50	60	70	80	90	100	
1	7	F	—	6.0	6.5	6.2	6.4	6.4	6.6	6.4	6.4
2	7	F	5.9	5.6	5.5	5.5	—	—	—	—	5.5
3		M	4.9	6.0	6.0	5.9	6.0	—	—	—	6.0
4	12	M	4.4	5.1	5.9	5.7	6.2	6.6	6.2	6.3	6.3
5	2	M	—	3.7	5.0	5.0	5.0	—	—	—	5.0
6	7	M	5.0	5.0	5.2	6.0	4.5	5.0	4.9	—	5.0
7	10	F	4.8	5.0	5.4	5.0	5.0	—	—	—	5.0
8	9	M	—	—	5.8	6.7	6.6	7.0	6.9	6.9	6.8
9	10	F	4.4	4.3	4.3	—	—	—	—	—	4.4
10	7	F	4.4	5.3	5.4	5.7	5.4	—	—	—	5.5
11	2	M	—	4.8	5.0	4.9	—	—	—	—	4.9
12	4	M	—	5.9	5.7	6.0	5.7	—	—	—	5.8
13	4	M	—	5.3	5.7	5.7	—	5.5	—	—	5.5
14	8	M	4.5	5.0	5.0	5.0	—	—	—	—	5.0
15	8	M	—	—	4.9	5.0	4.8	5.3	5.5	5.3	5.4
16	11	M	5.2	5.5	5.7	—	—	—	—	—	5.5
17	4	M	—	5.8	6.8	6.8	—	—	—	—	6.8
18	4	M	5.3	5.4	5.8	4.6	5.3	—	—	—	5.3
19	6	M	—	6.0	6.6	7.2	7.1	7.3	6.7	—	7.0
20	9	M	—	6.0	6.6	6.6	—	—	—	—	6.6
21	6	M	—	4.2	4.2	4.2	—	—	—	—	4.2
22	7	F	—	5.2	5.0	6.4	5.6	6.0	6.5	—	6.1
23	7	F	—	5.3	5.3	6.8	6.3	5.8	5.7	—	5.9

The above table (Table I) gives a few of the results obtained and it is seen that on the whole, the successive readings at ten minute intervals agree fairly well, once the tension has become established. Occasionally for some reason, perhaps an unusual degree of pollution by faecal gas from above, a high figure is obtained. For example, the 60 minute sample in Case 6 is obviously wrong, but the 70 minute reading shows that equilibration had again taken place. With 100 cc. of air it is usual to get only three samples of 15 to 20 cc. each or,

at the most four, but if the first sample is taken at the 40 minute period a good result can be obtained in almost every case.

In adults, the average normal CO₂ content of alveolar air is approximately 5.5% but owing to the technical difficulty in obtaining good samples, wide variations occur and figures well above or below 5% to 6% are required before much significance can be attached to them. Our results obtained by analysis of rectal air showed a variation of from 4.2 to 7%. Although this variation appears wide, we believe that such does occur in young children. We know that the younger the child the more often and the more readily does the acid-base balance shift and in the routine estimation of the alkaline reserve of the blood one is struck with the wide variations which occur in children who are to all intents and purposes normal so far as their acid-base balance is concerned. If this total CO₂ combining power is so frequently altered, it seems only natural that the free CO₂ content would also be subject to fluctuation. Indeed, it is now known that this content of CO₂ in the alveolar air which changes, of course, with the free CO₂ content of the blood, is not as constant as it was formerly thought to be. Dodds⁽⁴⁾ has recently demonstrated that following the intake of food there is at first a rise in the CO₂ tension of the alveolar air of 2–6 mm. followed later by a fall of a similar magnitude below the original level. Our determinations were done usually in the afternoon but irrespective of meals.

We have made use of the figure for the CO₂ content of air after equilibration in the rectum. The free CO₂ content of the blood was calculated from the figure as follows:—

The partial pressure or tension of CO₂ in the rectal air can be determined from the equation

$$\text{Tension} = \frac{\text{Percentage of CO}_2 \times (\text{Bar. press.} - \text{water vapour pressure})}{100}$$

If the barometric pressure be taken as 760 mm. Hg. and the water-vapour as 47 mm. Hg., the equation reads

$$\text{Tension} = \frac{\text{Percentage of CO}_2 \times 713}{100}$$

In order to determine the amount of CO₂ in the blood at this tension, use has been made of the coefficient of solubility of CO₂ in blood plasma which has been worked out by Bohr to be 0.54. This means that 1 c.c. of blood exposed to a pressure of 760 mm. Hg. of CO₂ will hold 0.54 c.c. of CO₂ at N.T.P. Accordingly it becomes easy to calculate the free CO₂ content of the blood from the following formula

$$\text{Free CO}_2 = 0.54 \times \frac{\text{Tension of CO}_2 \text{ in Rectal Air} \times 100}{760}$$

The total CO₂-combining power of the blood-plasma was determined by the method of Van Slyke. As we questioned the accuracy of the samples of true plasma, the plasma was in each case saturated with CO₂ at a tension of approximately 40 mm. Hg (the worker's own alveolar air). The difference

between the total CO₂ combining power and the free CO₂ we have taken to represent the combined CO₂.

It was thus possible to ascertain the pH of the blood by making use of the Hasselbalch formula, $pH = pK_1 + \log \frac{BHCO_3}{H_2CO_3}$ in which the Sorensen nomenclature is employed as shown in the following example. pK_1 is a constant and was taken as 6.1.

EXAMPLE :—

Percentage of CO₂ in rectal air

Tension of CO₂ in rectal air 5.5 × 713

— 5.5%

— 39.2 mm.

100

0.54 × 39.2 × 100

Percentage of CO₂ in arterial blood

760

— 2.79%

— 62.7%

— 59.91%

CO₂ combining power

Combined CO₂ (62.7 — 2.79)

$pH = pK_1 + \log \frac{BHCO_3}{H_2CO_3}$

$= 6.1 + \log \frac{59.91}{2.79}$

$= 7.43$

TABLE II.

Case No.	Name.	Age in years.	Mean CO ₂ content of rectal air.	Tension of CO ₂ in arterial blood.	Free CO ₂ content of arterial blood.	Total CO ₂ combining power.	Combined CO ₂ content of blood plasma.	pH of the Blood.
1	W.F.	11	5.5	39.2	2.79	62.7	59.91	7.43
2	A.McL.	12	6.3	44.9	3.19	67.1	63.91	7.40
3	W.McC.	7	5.0	35.7	2.53	62.3	59.77	7.47
4	C.F.	10	5.0 4.4	35.7 31.4	2.53 2.23	61.3 58.4	58.77 56.17	7.47 7.50
5	J.T.	6	7.0	49.9	3.55	71.9	68.35	7.38
6	W.McM.	4	5.3 5.5 6.8 5.8	37.8 39.2 48.5 41.4	2.69 2.79 3.45 2.94	52.6 58.4 64.0 61.3	49.91 55.61 60.55 58.36	7.37 7.40 7.34 7.40
7	W.C.	9	6.8 6.6	48.5 47.1	3.45 3.34	61.0 65.2	57.55 61.86	7.32 7.37
8	W.C.	6	4.2	30.0	2.13	49.7	47.57	7.45
9	S.K.	7	6.1 5.9	43.5 42.1	3.09 2.99	55.0 57.4	51.91 54.41	7.33 7.36
10	V.McK.	7	6.4 5.5	45.6 39.2	3.24 2.79	63.2 59.4	59.96 56.61	7.37 7.40

In Table II are shown the *pH* values worked out on cases taken indiscriminately in the wards. In no instance was the subject suffering from fever or any obvious disturbance of the acid-base balance. It will be seen that in this series of "normals" the variation in the *pH* values lies between 7.32 and 7.50. This agrees quite well with the findings of other investigators who have arrived at the *pH* by using Hasselbalch's formula. Peters, Barr and Rule⁽⁵⁾ in normal controls (adults) found variations from 7.23 to 7.45 and Straub and Meier⁽⁶⁾ from 7.30 to 7.42.

Several points of interest emerge from a consideration of the findings in our cases. In case 5 the tension of CO₂ in the rectal air was practically 50 mm. Hg. which in comparison with the usual normal alveolar air tension of 40 mm. Hg. seems much too high, but on estimating the CO₂-combining power, it was also found to be correspondingly high and the result was a normal *pH* value of 7.38. It is also noteworthy that in the second observation in Case 4 and in Case 8, where the tensions are both approximately 30 mm. Hg, the *pH* values as determined by this method are tending to alkalinity, namely 7.50 and 7.45. In addition the table serves to exemplify the extraordinary variations which occur in the CO₂ combining power (alkaline reserve) in cases which are presumably normal so far as their acid-base balance is concerned.

TABLE III.

No.	Name	Age Yrs.	Date.	Remarks.	Mean CO ₂ Content of rectal air.	Tension Free of CO ₂ CO ₂ in art.-arterial blood.		Total CO ₂ combining power.	Combined CO ₂ content.	<i>pH</i> of the Blood.
1	W.C.	6	12/2/26	Ketogenic diet begun 13/2/26, discontinued on 18/2/26.	5.6	39.9	2.84	57.4	54.56	7.38
			17/2/26		4.4	31.4	2.23	37.1	34.87	7.29
			18/2/26		4.3	30.7	2.18	42.9	40.72	7.37
			22/2/26		6.2	44.2	3.14	62.3	59.16	7.38
2	A.M.	9	27/2/26	Ketogenic diet begun 28/2/26, discontinued on 5/3/26.	5.5	39.2	2.79	56.5	53.71	7.38
			5/3/26		5.5	39.2	2.79	49.7	46.91	7.33
			7/3/26		6.9	49.2	3.49	72.0	68.51	7.39
3	J.R.	2	10/1/26	CaCl ₂ gr. XXX 6x begun on 11/1/26 and continued till 17/1/26	3.9	27.8	1.97	50.7	48.73	7.49
			14/1/26		4.9	34.9	2.48	50.7	48.22	7.39
			17/1/26		5.0	35.7	2.53	47.7	45.17	7.35
4	T.R.	8	4/1/26	Mild clinical acidosis.	5.0	35.7	2.53	38.1	35.57	7.25
			5/1/26		5.4	38.5	2.73	38.1	35.37	7.22
			6/1/26		6.0	42.8	3.04	62.3	59.26	7.39
			8/1/26		4.4	31.4	2.23	52.6	50.37	7.45
5	A.L.	12	19/2/26	Diabetes.	5.5	39.2	2.79	46.8	44.01	7.30
			25/2/26		6.4	45.6	3.24	62.3	59.06	7.36
			4/3/26		6.6	47.1	3.34	61.3	57.96	7.34

We have also investigated the change in the *pH* of the blood in children in whom a mild acidosis has been produced either by a ketogenic diet or by the administration of calcium chloride. Case 1 and 2 (Table III) show the influence

of a ketogenic diet. In Case I, the pH had already swung back before the diet was discontinued. This we believe to be correct as it is recognised by those who have carried out investigations with subjects on this diet that the acidosis tends to disappear very often as the subject becomes accustomed to the diet⁽⁷⁾. Case 3 appeared to be an ideal case in which to administer the acid therapy, because although the alkaline reserve was normal or even on the low side, the CO_2 tension of the rectal air was very low and the pH was therefore tending to the alkalotic side. On administration of calcium chloride 30 grains four-hourly, the pH fell from 7.49 to 7.39 and later to 7.35. The readings were obtained in Case 4 during the recovery from a mild clinical acidosis. In this case the pH value was 7.45 four days after admission, although on this occasion the lowest CO_2 tension in the rectal air was recorded. Case 5 is that of a diabetic admitted with a mild acidosis (acetone++) and in which two subsequent determinations were made when the acetone had disappeared from the urine.

It is of course a debatable point whether the air injected into the rectum equilibrates with arterial, capillary or venous blood, or with the tissue juices. The figures for the CO_2 tension are very similar to those found by Argyll-Campbell⁽²⁾ in his experiments on rabbits with air injected subcutaneously or intra-peritoneally. He states that the tension of CO_2 in air injected under the skin or into the peritoneal cavity is the same as that in the alveolar air, which is usually believed to be in equilibration with the arterial blood.

It may be asserted that a direct determination of the pH by the hydrogen electrode or by a colorimetric method is more accurate. Such a method, however, only gives an indication of the reaction of the blood without throwing any light on the processes which the body brings into play to produce this reaction. Haldane⁽⁸⁾ has stated that the animal organism tends to regulate the reaction of the blood in a much more delicate way than can be determined by even the finest chemical means. Hence, whether the figure obtained by this method represents arterial CO_2 tension or not, at any rate, when correlated with the total CO_2 combining power as shown above, the information obtained is of significance in two definite directions. First, it gives an indication of the state of the acid-base balance, whether tending to an acidosis or an alkalosis, and secondly, it throws some light on the mode of operation in the production of such a change, as well as showing compensated changes not recorded by a pH determination.

CONCLUSIONS.

1. An indirect method of determining the CO_2 tension of arterial blood in children by means of air injected into the rectum is described. The method unfortunately is inapplicable in children under two years of age.
2. A method of determination of the pH of the blood by means of Hasselbalch's formula is outlined and some results reported.
3. The pH of the blood calculated by this method varies in normal children over two years from 7.32 to 7.50.

We desire to express our gratitude to the Medical Research Council, by whom the expenses of this research were defrayed.

REFERENCES.

1. Henderson, Y., *Amer. J. of Phys.*, Baltimore, 1925, LXXIII, 193.
2. Campbell, A., *J. of Phys.*, London, 1924, LIX, 1.
3. Haggard, H. and Henderson, Y., *J. Biol. Chem.*, N.Y., 1919, XXXVIII, 71.
4. Dodds, E., *J. of Phys.*, London, 1920—21, LIV, 342.
5. Peters, F., Barr and Rule, *J. Biol. Chem.*, N.Y., 1921, XLV, 489.
6. Straub, J., and Meier, D., *Deut. Arch. f. Klin. Med.*, Leipzig, 1918, CXXV, 477 : 1922, CXXXVIII, 208. (Quoted from M.R.C. Special Report Series, London 1923, No. 72, 47.)
7. Brown, G., and Graham, M., *Arch. of Dis. in Childhood*, London, 1926, I., 302.
8. Haldane, J. S., *Respiration*, Yale Univ. Press, New Haven 1922, 185.