THE CARBON DIOXIDE COMBINING POWER OF THE BLOOD PLASMA, ITS DETERMINATION AND ITS SIGNIFICANCE IN CERTAIN PATHOLOGICAL CONDITIONS.

BY

JAMES LOCKHART COWAN,
MB.ChB.(Edin)., M.R.C.P.(Edin).

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PART I.

PHYSIOLOGY of ACID BASE EQUILIBRIUM of the BLOOD.

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INTRODUCTION

The determination of the CO_2 combining power of the blood plasma has been somewhat simplified of late by the many researches made by various workers, but in particular by Van Slyke. Its significance has been shown to be of estimable value in helping to assess, along with clinical findings and other blood findings, the presence or absence of acidosis or alkalosis in the blood.

Before discussing its importance it will be necessary to mention a few facts about the Blood Chemistry which will make matters much clearer. The "Alkali Reserve" of the blood serum, by means of which acids are neutralized, has been found to be made up of certain chemicals, the chief of which are small quantities of phosphates and the alkali protein compounds. If the acid base equilibrium is normal all these substances are present in constant quantities. So the reaction of the blood is maintained in a state of constant equilibrium. I will go more fully into this point in my second section where the Physiology of the combining power of the blood will be dealt with. Also in the third section I will deal with the method I have used, and other methods used, in determining the degree of acidosis or alkalosis present.

Carbon dioxide is the acid product which is normally present, and this is taken up by the serum partly in solution and partly combined with carbonates. When the carbon dioxide is increased in amount then follows over-stimulation and over-excitability of the respiratory centre. This allows of an increased loss of carbon dioxide, so that the reaction of the blood is kept within normal limits. This process may go on for some time without any necessity of drawing on the "Alkali Reserve." However, as the amounts of acid are increased so non-volatile acids combine with the carbonates. The production of this overflow of acids cannot be compensated for by an increased pulmonary excitability and so they combine with the carbonates. This has been called by Henderson "the first line of defence" so encroaching upon the "Alkali Reserve." This produces a condition of acidosis or acidaemia and even the normal amount of carbon dioxide lowers the already depleted "Alkali Reserve."

As a result of this the respiratory centre is overstimulated and hyperpnoea occurs. The carbon-dioxide tension of the alveolar air becomes greatly reduced.

Urinary excretion may for some time compensate for the above since the kidneys have the power of excreting an acid urine from a neutral blood. In certain forms of nephritis this mechanism fails. More of this anon.

It is my intention to show how the carbon-dioxide combining power of the blood varies in several forms of nephritis, and how some therapeutic as well as diagnostic value can be obtained from its estimation.

The assessment of the carbon-dioxide combining power of the blood is of definite value in numerous pathological conditions. My endeavour is to show its value in certain forms of nephritis. It can be of diagnostic value in a good number of cases and also gives one an insight into the ultimate prognosis.

My intention is not to show that it is of value alone, but its value taken in conjunction with other findings, both clinical and biochemical, is of great significance.

The bicarbonate of the body fluids are the most important "Alkali Reserve" of the tissues. If this first line of defence is affected then its estimation will undoubtedly show deviations from normal in acidotic or acidaemia conditions. The bicarbonate of the blood is depleted in acidotic conditions caused by fixed acids. An example of this is the production of B oxybutyric acid and aceto-acetic acid in diabetes. In nephritis the bicarbonate is also depleted, due in this case to improper elimination of acids produced in normal metabolism. In the first case the trouble is due to faulty metabolism, in the second due to faulty excretion, metabolism being normal. In other cases where there is an accumulation of CO_2 in the blood, the bicarbonate of the blood is elevated above the normal. The following is a list of the various conditions in which the carbon dioxide combining power of the blood has been found by previous workers to be increased or decreased. It is interesting to place this in the introduction to show the far-reaching effects on the various systems of the body.

CO_2 COMBINING POWER OF THE BLOOD PLASMA IN VARIOUS CONDITIONS /

CO_2 COMBINING POWER OF THE BLOOD PLASMA IN VARIOUS CONDITIONS.

TYPE OF DISTURBANCE.	TOTAL CO_2 CONTENT.	OCCURS IN
ACIDOSIS $^{(1)}$ (1) Due to Bicarbonate Deficiency. (Non Gaseous) (a) Compensated. $BHCO_3$ is diminished H_2CO_3 is diminished to same extent. pH is normal. (b) Uncompensated. $BHCO_3$ is diminished H_2CO_3 is diminished to less extent. pH is diminished.	DECREASED	Diabetic Coma. Cyclical Vomiting Gastro-enteritis in infants. Dysentery in older children. Uraemia Salicylate Poisoning.
ACIDOSIS $^{(2)}$ (2) Due to Carbon Dioxide Excess. (Gaseous) (a) Compensated. $BHCO_3$ is increased H_2CO_3 is increased pH is normal. (b) Uncompensated. H_2CO_3 is increased $BHCO_3$ is increased to less extent. pH is diminished	INCREASED	Morphine Poisoning. Emphysema

ALKALOSIS /

CO_2 COMBINING POWER OF THE BLOOD PLASMA IN VARIOUS CONDITIONS (CONTD.)

TYPE OF DISTURBANCE.	TOTAL CO_2 CONTENT.	OCCURS IN
ALKALOSIS (1) (1) Due to Bicarbonate Excess. (Non Gaseous) (a) Compensated. $BHCO_3$ is increased. H_2CO_3 is increased. pH is normal. (b) Uncompensated. $BHCO_3$ is increased. H_2CO_3 is increased to less extent. pH is increased.	INCREASED	Administration of Sodium Bicarb. High Intestinal Obstruction. Pyloric Stenosis. Prolonged Vomiting.
ALKALOSIS. (2) (2) Due to Carbon Dioxide Deficit. (Gaseous) (a) Compensated $BHCO_3$ is diminished. H_2CO_3 is diminished to same extent. pH is normal. (b) Uncompensated. H_2CO_3 is decreased. $BHCO_3$ is decreased to less extent. pH is increased.	DECREASED	Anoxaemic Conditions. High Altitudes. Hyperpnoea.

We can see from this diagram that estimation of CO_2 content can be of far-reaching value.

I have been fortunate in being allowed material from patients in one of the Wards of the Royal Infirmary, Edinburgh, and also the use of the ingenious Van Slyke apparatus for the estimation of the carbon dioxide combining power. *

In later sections there will be dealt with fully the Physiology of Acid base equilibrium of the blood, the production of acidosis and alkalosis under experimental conditions, and their laboratory determination by means of the Van Slyke apparatus.

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* I have to acknowledge my indebtedness to Professor Ritchie for the use of the clinical material in his Wards and also for the use of the Van Slyke apparatus in his department.

PART I.

PHYSIOLOGY OF ACID BASE EQUILIBRIUM OF THE BLOOD.

It has been shown that the reaction of the blood and tissues of the body are preserved at a fairly constant level by a series of delicate mechanisms. I intend to make a survey of three mechanisms in this section.

The chief mechanisms available in the body for the maintenance of these reactions are:-

1. Physico-chemical processes which occur in the blood itself.
2. The vital reactions of the Respiratory Centre.
3. The excretory powers of the Kidney tissues.

It is necessary to deal with the first mechanism to some extent as it is all important. The other two will be dealt with later. Firstly we have to consider the H ion concentration of the blood and define this term.

(a) H ion Concentration of the Blood.

The Electrolyte dissociation theory tells us that pure water is almost entirely made up of molecules of H_2O. The H_2O can be dissociated into the two equally and oppositely charged ions. The two ions are the Hydrogen ions and the Hydroxyl ions, i.e. H' and OH'.

This works according to the equation:-

$$H_2O \rightleftharpoons H' + OH'$$

An ion is an electrically charged particle, the Hydrogen ions being charged with positive electricity and the Hydroxyl ions with negative electricity. The reaction of any fluid is thus dependent on the relative number of H' and OH' ions. Pure water, as an example, is a neutral substance, and the H' ions and OH' ions are therefore equal in number. By experimental work it has been possible to actually estimate the number of ions in pure water. The concentration of Hydrogen ions is often expressed as C H. This concentration is expressed in terms of gramme equivalents per litre of the solution. In pure water the concentration of Hydrogen ions set free is 10^{-7} gramme equivalents at 22° C. temperature. H and O H mean that the concentration of H and O H ions are being expressed in terms of gramme equivalents on the ion per litre of the solution.

10^{-7} means that in 10,000,000 litres of water there is 1 gramme of Hydrogen in the ionic state. As number of O H ions is similar to that of H ions $(\bar{O}H)$ is also 10^{-7} or 1 gramme equivalent of OH in the ionic form is present in 10 million litres of water.

The equivalent weight of O H (O = 16 and H = 1) is 17. The actual weight of ionic OH is 17 grammes in 10,000,000 litres of water.

In pure water the number of OH ions is the same as that of H ions, as already stated. Now the law of mass action shows that in such an equilibrium as the above, the product of the concentration of two ions is a constant; i.e. if $(\overset{+}{H})$ is multiplied by $(\overset{-}{OH})$ the product is constant for all solutions whatever their reaction may be.

The equation in case of pure water can now be worked out:-

$$(\overset{+}{H}) \times (\overset{-}{OH}) = 10^{-7} \times 10^{-7} = 10^{-14}$$

$$= \frac{1}{10 \text{ million}} \; \frac{1}{10 \text{ million}} = \frac{1}{100 \text{ million million.}}$$

It follows from this that if we know the $(\overset{+}{H})$ of any solution we can deduce the $(\overset{-}{OH})$ as the product must be 10^{-14}.

By comparison of the H ion concentration and the OH ion concentration to see which is greater, we can determine the reaction of the fluid in question.

In other words, we can determine the degree of acidity of an actual fluid acid or alkaline in terms of normality in Hydrogen ions.

That is as the following equations will now show:-

$(\overset{+}{H}) = 10^{-7} (\overset{-}{OH}) = 10^{-7}$ neutral solution.

$(\overset{+}{H}) = 10^{-6} (\overset{-}{OH}) = 10^{-6}$ acid solution.

$(\overset{+}{H}) = 10^{-8} (\overset{-}{OH}) = 10^{-8}$ alkaline solution.

Acids dissociate in water such as Hcl yielding two ions.

$$Hcl \rightleftharpoons H + Cl'$$

Alkalis also dissociate and yield two ions.

$$NaOH \rightleftharpoons Na + OH'$$

A normal solution of an acid or base is one which contains the equivalent weight of an acid or base expressed in grammes in one litre of the solution.

The products of the concentrates of the two ions of water are unaltered when acid or base are added. In the former case, e.g. acid, the Hydrogen ion, and in the latter case e.g. base, the Hydroxl ion, concentration is increased.

The other ion is proportionately reduced by a depression of the ionization reaction of the water.

Furthermore, if, say

in 1/10,000 normal solution of strong acids the concentration of H' ions is approximately 10^{-4}N.

Evidently in

1/100,000 N Solution of strong acid

$H^{\cdot} = 10^{-5}$; $OH' = 10^{-9}$; $(H) + (OH) = 10^{-14}$

1/1000 N Solution of strong acid.

$H^{\cdot} = 10^{-3}$; $OH' = 10^{-11}$; $(H) + (OH) = 10^{-14}$

Also we find the same procedure in base.

1/100,000 N Solution of strong base

$H^{\cdot} = 10^{-9}$; $OH' = 10^{-5}$; $(H) + (OH) = 10^{-14}$

And so on.

The effect of addition of strong ionized acid to water is to depress the ionization of water itself. This is so until a fresh equilibrium is reached.

The produce of the two ions is still 10^{-14} as shown above. The negative power of 10 is a convenience in writing.

Sorensen introduced a new momenclature, that of pH.

p. is an arbitrarily chosen letter to notify that the negative exponent to the base 10 is employed.

To explain further:- if

$CH = 10^{-7}$ = neutral solution, this would be expressed as a pH of 7, and if $CH = 10^{-5}$ acid solution it would be expressed as a pH of 5; and lastly, if $CH = 10^{-8}$ = alkaline solution it would be expressed as a pH of 8.

If pH is above 7 the solution is alkaline, and if it is less than 7 then solution is acid.

The reaction of water is a pH = 7 at 22°C. temperature.

Again in other words, as the H ion concentration rises the pH becomes smaller, and if H ion concentration falls, as in alkaline solutions, the pH will be proportionally increased.

We will now see how this H ion concentration of fluids affects the reaction of the blood and the carbon dioxide combining power of the plasma.

The determination of the H ion concentration of the blood is not a method of great clinical value. There are great difficulties to be encountered in colorometric determination. It has also been shown by various workers that often no decided change in the H ion concentration occurs even in advanced pathological conditions.

It has, however, been necessary to explain the terms used and their significance.

I will now go on to show, by means of various phenomena, the blood remains at a constant pH, and also explain how the carriage of carbon dioxide takes place in the blood.

If any non-volatile acid, such as lactic acid, phosphoric acid or sulphuric acid, gets into the blood stream it acts with the bicarbonate present in the plasma.

The following equation shows exactly how lactic acid behaves.

$$\text{(i)}\quad \underset{\text{Lactic acid}}{Hl} + Na\,HCO_3 \rightleftharpoons \underset{\text{Sodium lactate.}}{Na\,L} + H_2CO_3$$

We find from this equation that the products are sodium lactate and carbonic acid. Lactic acid being a strong non-volatile acid this means that it dissociates freely, giving rise to many H ions. This also means that it does two things:-

(a) makes any solution in which it is in contact with very acid.

(b) It is excreted slowly in the urine.

H_2CO_3 is a much weaker acid, giving rise to fewer H ions; also it is a volatile acid which is readily eliminated in the lungs.

The sodium bicarbonate has in this case acted as a Buffer substance.

It has caused H ions to be used up so that there are fewer left in the blood. By so doing the reaction of the blood has remained unaltered.

This buffering is one of the great means by which the reaction of the blood is kept at a constant level.

It is convenient at this stage to discuss further the buffering action of the blood.

BUFFERING.

It follows from what has been previously stated, that as long as $NaHCO_3$ is present in the plasma no acid stronger than CO_2 can exist in the blood as such. The acid formed in the body to the greatest extent is H_2CO_3. This cannot all be dealt with by $NaHCO_3$. The H_2CO_3 is dealt with as shown by the following equations.

$$(i)\ H_2CO_3 + NaCl \rightleftharpoons NaHCO_3 + Hcl$$

$$(ii)\ Hcl + \underset{\underline{\text{Potassium Salt of reduced Haemoglobin}}}{\underset{\downarrow}{Khb}} \rightleftharpoons Kcl + H\,HC$$

The H_2CO_3 interacts with sodium chloride of the plasma to form sodium bicarbonate and Hcl. Instead of the weak acid we have now formed a strong acid, namely Hydrochloric acid. This would seem to indicate that the H ion concentration of the blood should rise higher instead of falling. Also a weak acid such as H_2CO_3 cannot displace Chloride from its union with Na in NaCl. However we find that an equation such as (i) can act in either direction if the product of the reaction that would tend to drive the process the opposite way is at once removed.

That is to say, the equation will go from left to right if the Hydrochloric acid so formed is removed from the plasma. This is what actually happens.

If blood is exposed to increased tensions of CO_2 the amount of $NaHCO_3$ in the plasma increases and the Chloride diminishes in the plasma but increases in the interior of the red blood corpuscles.

The Hcl, as in equation (i), as it is formed migrates quickly through the corpuscular wall to be dealt with suitably in the red cells.

This has been called the Hamburger phenomenon or Chloride shift.

There are various buffer substances in the blood. These are the phosphates, both monobasic and dibasic, bicarbonates, alkali salts of Haemoglobin and other proteins in a smaller degree. They are all salts of weak acids and they can yield alkali to a stronger acid which comes into competition with them. This is best explained by illustrating a chemical reaction.

If a solution of Hcl is neutralized slowly with caustic soda and resulting H ion concentration, change is plotted on a graph. The H ion concentration changes at first in proportion to the amount of base added. This takes place until near neutral point. There is an abrupt fall of CA or rise of pH, and Solution becomes alkaline.

If 10 cc. of N/10 Hcl and 9 cc. of N/10 NaOH are used the pH will be 3. The addition of 2 cc. more of alkali will make pH top 11; i.e. the cH is reduced to 1/100,000,000th of its former value.

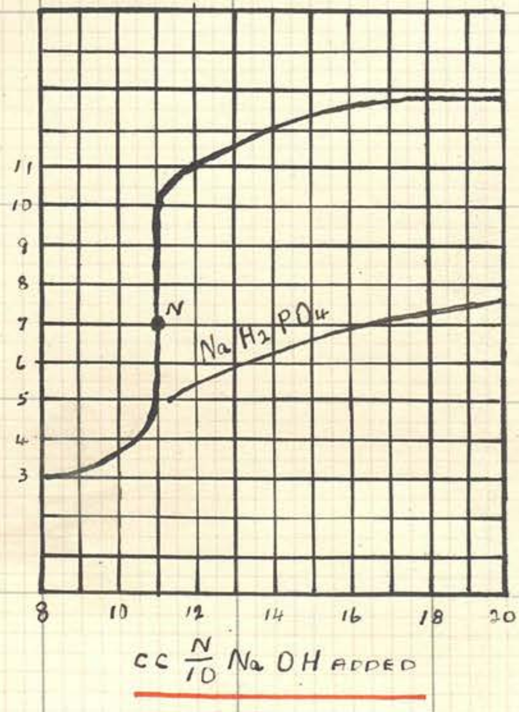
We will now consider the effect of addition of alkali to a solution of NaH_2CO_4. Here even in the neighbourhood of neutral point the addition of 2 cc. of N/10 alkali causes a relatively small change in H ion concentration.

Solutions such as NaH_2PO_4 are able to support the addition of considerable quantities of acids or alkalis without there being a rapid change in H ion concentration of the solution.

If water, or a solution such as NaCl, were taken, addition of strong alkali to it would give a curve like the one proceeding upwards from point marked N, while addition of strong acid would give a curve like the one proceeding downwards from N. A solution of acid sodium phosphate would thus behave very differently from one of an ordinary neutral salt and would tend to stabilize or buffer the solution towards alkalis or acids.

FIG. 1.

CURVES OF NEUTRALIZATION OF HCl AND NaH_2PO_4 IN EACH CASE 10 cc OF THE N/10 SOLUTION ARE TREATED WITH THE AMOUNTS OF N/10 ALKALI SHOWN IN THE ABSCISSAE AND THE MIXTURE MADE UP TO 100 cc ORDINATES = pH ; N = NEUTRAL POINT



I will now discuss the Theory of Buffer Action.

It has been shown on physico-chemical grounds that the H ion concentration of such a buffered solution depends on the ratio HA/BA when HA = the free acid and BA = a salt of the acid with a strong base such as sodium. Thus a sodium bicarbonate solution in equilibrium with CO_2 has an H ion concentration which is determined by the ratio $\frac{H_2CO_3}{NaHCO_3}$

Since it is the ratio between free acid and its sodium salt which determines the H ion concentration, an important factor in connection with a buffered solution is, that when H ion concentration is unchanged by moderate dilution with water because the ratio is unaltered - in this respect they differ fundamentally from unbuffered solutions having a definitely acid or alkaline reaction and which on dilution show respectively a fall or a rise of H ion concentration. The proof that the H ion concentration is dependent upon this ratio belongs to the province of physical chemistry.

It is a fact that the H ion concentration depends on the ratio of free acid to that of its salt.

Hasselbatch's Formula has been used for calculation of H ion concentration of the Blood.

It is determined by ratio of free carbonic acid to bicarbonate (i.e. fixed carbonic acid). The equation is -

$$(H) = K_1 \frac{(H_2CO_3)}{(BHCO_3)}$$

We must go further than this. Haemoglobin exists in the body in an oxidized and a reduced form. Oxyhaemoglobin is a much stronger acid than reduced haemoglobin. It is in fact 70 times as strong. As it is much easier to take base from the salt of a weak acid CO_2 is formed in the tissues. Therefore when CO_2 is diffusing into the blood to form H_2CO_3 the reduced Hb is chiefly present which gives up base readily. In this way equation previously described comes about.

H_2CO_3 also contains base from the protein of the plasma $NaHCO_3$ being formed.

Thus - $H_2CO_3 + \underset{\substack{\downarrow \\ \text{Sodium} \\ \text{Proteinate}}}{NaPr} \rightleftharpoons NaHCO_3 + NP_2$

The Proteic Acid NP_2 is a very weak acid and dissociates very feebly, so again there is a removal of H ions. H_2CO_3 diffuses into interior of red cell and obtains base directly from Hb.

i.e. $H_2CO_3 + KHb = KHCO_3 + H\,Hb.$

Van Slyke has estimated that 84% to 90% of the base which is required to deal with H_2CO_3 is supplied directly or indirectly by the Haemoglobin.

The serum proteins only constitute 8% of the plasma compared with 30% of Hb in the corpuscles and their buffering action is relatively unimportant.

Whole blood is therefore much more effectively buffered than plasma alone. If the corpuscles are diminished in number, as in anaemia, the H ion concentration tends to rise excessively when CO_2 enters the blood.

It will be noted that such an equation

$$H_2CO_3 + KHb \rightleftharpoons Kl + CO_3 + H\ Hb, H_2CO_3$$

disappears and is replaced by bicarbonate which is actually an alkaline substance giving rise to an excess of OH ions. The Haemoglobin formed, like all proteins, is a weak acid which dissociates very feebly. The buffering reaction is therefore very effective.

As has already been pointed out H_2CO_3 is dealt with first by Haemoglobin, then by the plasma proteins; only in the last resort and to an unimportant extent is it buffered by the phosphates which are only present in sufficiently high concentration in the corpuscles.

$$H_2CO_3 + Na_2HPO_4 \rightleftharpoons NaHCO_3 + NaH_2PO_4$$

The alkaline sodium phosphate Na_2HPO_4 gives up some of its base to H_2CO_3 to form bicarbonate and is itself converted into NaH_2PO_4 which is very feebly acid.

The equations given represent what occurs when H_2CO_3 is accumulating in the blood, and show how the expected acidaemia is minimized. When CO_2 is given off in the lungs the processes will take place in the reverse direction, preventing excessive alkalaemia.

I shall now gather the equations together and consider them again. The Hb is now in the more acid oxidised form and will be written as HbO_2 and $KHbO_2$ to indicate this.

$$\left\{\begin{array}{lcll} \mathrm{Hcl} + \mathrm{Na\,HCO_3} & \rightleftharpoons & \mathrm{NaCl} + \mathrm{H_2CO_3} & \text{(plasma)} \\ \mathrm{H\,HbO_2} + \mathrm{Kcl} & \rightleftharpoons & \mathrm{KHbO_2} + \mathrm{Hcl} & \text{(corpuscle)} \\ \mathrm{NaHCO_3} + \mathrm{H\,Pr} & \rightleftharpoons & \mathrm{NaPr} + \mathrm{H_2CO_3} & \text{(plasma)} \\ \mathrm{KHCO_3} + \mathrm{H\,HCO_2} & \rightleftharpoons & \mathrm{KHbO_2} + \mathrm{H_2CO_3} & \text{(corpuscle)} \\ \mathrm{NaH_2PO_4} + \mathrm{NaHCO_3} & \rightleftharpoons & \mathrm{Na_2HPO_4} + \mathrm{H_2CO_3} & \text{(corpuscle)} \end{array}\right.$$

Not only do these equations represent buffering actions tending to maintain normal blood reaction but they also explain how CO_2 is carried in the blood.

The problem of CO_2 carriage is, - how base is obtained to form bicarbonate in the tissues and how that bicarbonate is decomposed and CO_2 liberated in the lungs.

To sum up:- The simplest explanation that one gets is that the CO_2 in the blood is held in combination with bases such as sodium in the form of bicarbonates. Researches during the last ten years have shown that the CO_2 is carried in the blood by the interesting chemical mechanisms described.

The most valuable information has been obtained by the study of the CO_2 dissociation curves of the blood. The most accurate dissociation curves were obtained by Christiansen, Douglas and Haldane.

I will now mention a few facts about the carbon dioxide dissociation curve.

If we compare the dissociation curve of CO_2 for blood with that of a solution of sodium bicarbonate containing the same amount of available base as is shown in Figure 5, it is evident that there is a great difference between them. All the CO_2 is removed from the blood when the pressure of CO_2 is reduced to zero (i.e. in a vacuum). It is not possible to remove from the bicarbonate solution more CO_2 than corresponds to its conversion to carbonate according to the equation -

$$2\ NaHCO_3 = Na_2CO_3 + CO_2 + H_2O$$

i.e. from an aqueous bicarbonate solution only half as much CO_2 can be expelled by a vacuum as by addition of a strong acid.

$$2\ Na\ HCO_3 + 2\ Hcl = 2\ NaCl + 2\ CO_2 + 2H_2O$$

If it is believed that CO_2 is fixed in the form of bicarbonates in the blood then it must also be believed that we have in the blood some substance.

This substance while not interfering with the building up of CO_2 by the base when the blood is exposed to increasing pressures of CO_2 will yet act as an acid does in allowing withdrawal of CO_2 ultimately to completion as the partial pressure of CO_2 falls.

It is convenient here to give the following data of average findings in man.

Tensions of CO_2.

i. In alveolar air 40 mm. Hg.

ii. In arterial blood 40 mm. Hg.

iii. In venous blood 46 mm. Hg.
at rest and higher during exertion (up to 60 mm. Hg.)

Volumes of CO_2.

i. Arterial blood - 52 ccm.
Average of normal is from 45 to 65 ccm. per 100 ccm. of blood.

ii. Venous blood at rest - 55 ccm.

iii. Venous blood during exercise up to 65 ccm. or even more.

We will now examine the dissociation curves of blood plasma to see if it behaves as blood does.

First of all, the Technique of construction of CO_2 dissociation curve.

The sample of blood is withdrawn from a vein and by addition of Potassium oxalate (about 0.2%) coagulation is prevented. There is also added to this about 0.05% sodium fluoride. Sodium fluoride is added to prevent conversion of blood glucose into lactic acid. The lactic acid by combining with base would lower the carbon dioxide combining power of the blood if kept for long at body temperature. About 3 to 5 cc. of blood is placed in a saturating chamber. That of Barcroft is the one in general use.

This is a glass cylinder about 300 cc. capacity with a neck at one end while at the other end the cylinder is drawn out to a narrow portion of a few cubic cc. capacity bearing a three-way tap. After blood is introduced the neck of the funnel is closed with a rubber stopper which may conveniently also carry a three-way stopper.

Suppose now we want to plot a point on the curve corresponding to a CO_2 pressure of, say, 5% of an atmosphere. This would mean that it would be necessary to add to the 300 cc. of air about 15 cc. of CO_2. The saturator is connected to a filter pump and partially evacuated. The use of a mercury barometer is convenient as a guide to the degree of exhaustion reached; for the example under consideration about 70 atmosphere of vacuum would suffice. The tap is now closed and the saturator connected with a measuring burette containing CO_2 over mercury. The required amount of the gas is allowed to enter the partially exhausted cylinder and then the gas burette is disconnected. There should still be a partial vacuum in the Saturator, and this is now filled by momentarily turning the tap to the atmosphere so that air enters and equalizes the pressure.

The Saturator is now immersed in a water bath at the required temperature, 38°, and is rotated in a horizontal position so that the blood spreads in a thin film over the inside of the cylinder. After about 5 minutes of this spinning the Saturator is tilted so that the blood runs to the narrow end and the tap at the other end just emerges from the surface of the water in the bath. This tap is now momentarily turned, and thus the pressure in the Saturator, which has risen owing to expansion from rise of temperature, is equalized by escape of gas. The tap is now closed, the Tinometer restored to its horizontal position beneath the water, and the rotation continued for a further 15 to 20 minutes. After this time the Saturator is held vertically in the bath so that the blood runs down to the narrow end while the top tap just emerges from the water. The tap is now connected to a small pattern of Haldane's gas analysis Apparatus and a sample of the gas in the Saturator is withdrawn, with proper precaution, for analysis.

The analysis gives the exact CO_2 content of the gas mixture in the Saturator.

Immediately after the withdrawal of the gas sample, the Saturator is opened by removal of the stopper, a pipette is passed down and a sample of 1 to 2 cc. of the blood taken. In this blood the total CO_2 is determined by any suitable method, e.g. by means of the small blood gas analysis apparatus of Barcroft or that of Haldane or Van Slyke.

When the CO_2 pressure required is small, the CO_2 content of the blood is first removed nearly completely by warming in vacuo. Another method of reaching small CO_2 tension is to place the blood in air equilibrate with it in the Saturator (when CO_2 will be given off in the air) and then make an analysis of the gas contained in the Saturator. If this is not low enough in CO_2 the gas is blown out with a hand pump and a new equilibration carried out. When a pressure of about 40 mm. is required the Saturator is filled with alveolar air by blowing into it.

In this way we get as many points on the curve as we choose to make. At each point we have the CO_2 pressure of the gas mixture with which the blood is in equilibrium, and also the amount of CO_2 which the blood holds at that pressure. The results are then plotted in the form of a curve.

The method just described gives the CO_2 dissociation curve of oxygenated blood. If we require that for reduced blood the procedure is the same except that we start by reducing the blood and then filling the saturator with Hydrogen or Nitrogen instead of with air.

In the calculation of gas present we must remember to deduct the tension of aqueous vapour at the equilibration temperature. At 38° C. this is 49 mm.Hg. Suppose that at 38° the gas contained 42% CO_2 and that the barometric pressure at the time was 758 mm. Then the effective gas pressure in the saturator would be 758-49 = 709 mm., and the partial pressure of CO_2 $\frac{4.2 \times 709}{100}$ mm. = 29.7 mm.Hg.

Separated plasma behaves less like blood than like an aqueous bicarbonate solution. This is confirmed by the well known fact that although all the CO_2 can be removed from blood by a vacuum this cannot be done with blood plasma. After plasma has been thoroughly pumped in vacuo, addition of acid can still set free CO_2 from it. It is evident that the carrying power of blood for CO_2 is largely dependent on some substance contained in the corpuscles.

It is the corpuscles which in vacuo act like the acid expelling CO_2. This can be proved by the simple experiment of rinsing thoroughly well evacuated plasma with corpuscles when CO_2 is at once evolved in evacuation.

I will illustrate the above by a drawing of three carbon dioxide dissociation curves - namely, comparison between CO_2 dissociation curves of blood and of sodium bicarbonate solution, Figure 2. - Comparison between CO_2 dissociation curves of blood and of separated plasma, and of true plasma from same blood: Figure 3; and lastly the carbon dioxide dissociation curve of foetal blood in comparison with that of a normal pregnant woman and that of a non-pregnant adult, Figure 4.

Considering the CO_2 dissociation curves of foetal blood the following conclusions have been arrived at.

1. At gas tensions between 25 and 60 mm. of Hg. foetal blood absorbs oxygen more effectively than the blood of the mother.

2. At all gas tensions foetal blood releases CO_2 more readily than the blood of the mother.

3. The two adjustments facilitate the placental interchange of the gases but result in a low oxygen tension in foetal tissues and a high partial pressure of carbon dioxide.

4. At the moment respiration begins at birth the CO_2 tension of umbilical vein blood varies within normal limits. This is a circumstance which suggests that some factor other than

FIG. 2

Comparison between the CO_2 dissociation curves of blood and of sodium bicarbonate solution of a concentration of 0.0484N. The amounts of CO_2 held in physical solution in water are also shown (lowest line). (Redrawn from data by Parsons Journal of Physiology 1919. 53 page 57.)

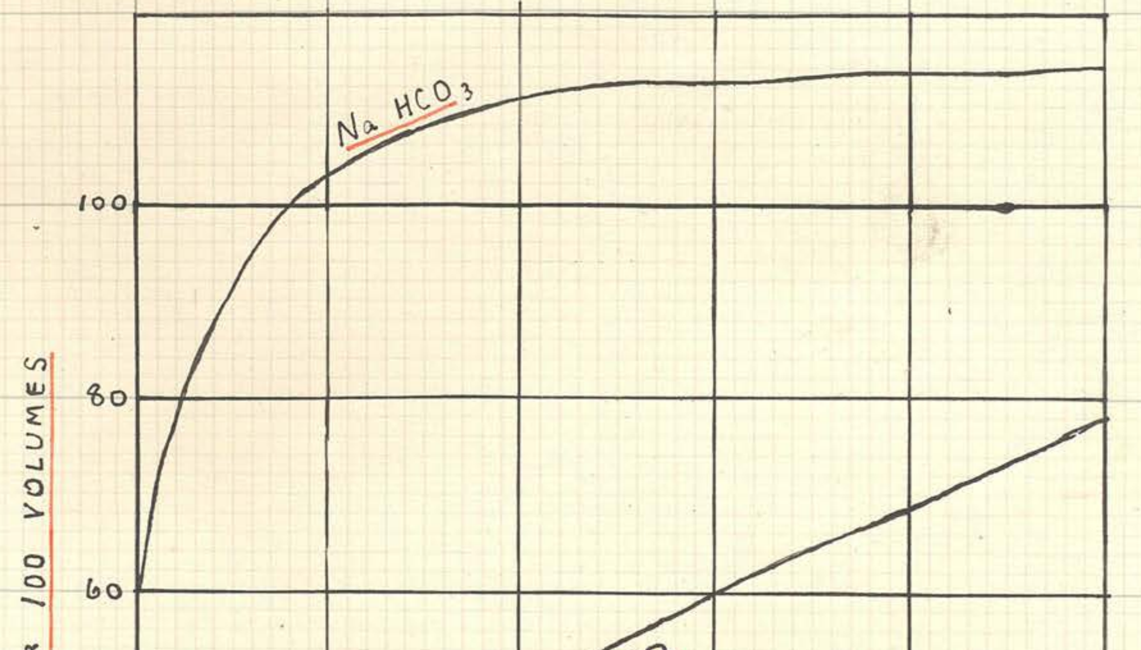


FIG. 3

COMPARISON BETWEEN THE CO_2 DISSOCIATION CURVES OF BLOOD AND OF SEPARATED PLASMA AND TRUE PLASMA FROM SAME BLOOD.
(REDRAWN FROM DATA BY JOFFE AND POULTON, JOURNAL OF PHYSIOLOGY 1920 54 p. 129.

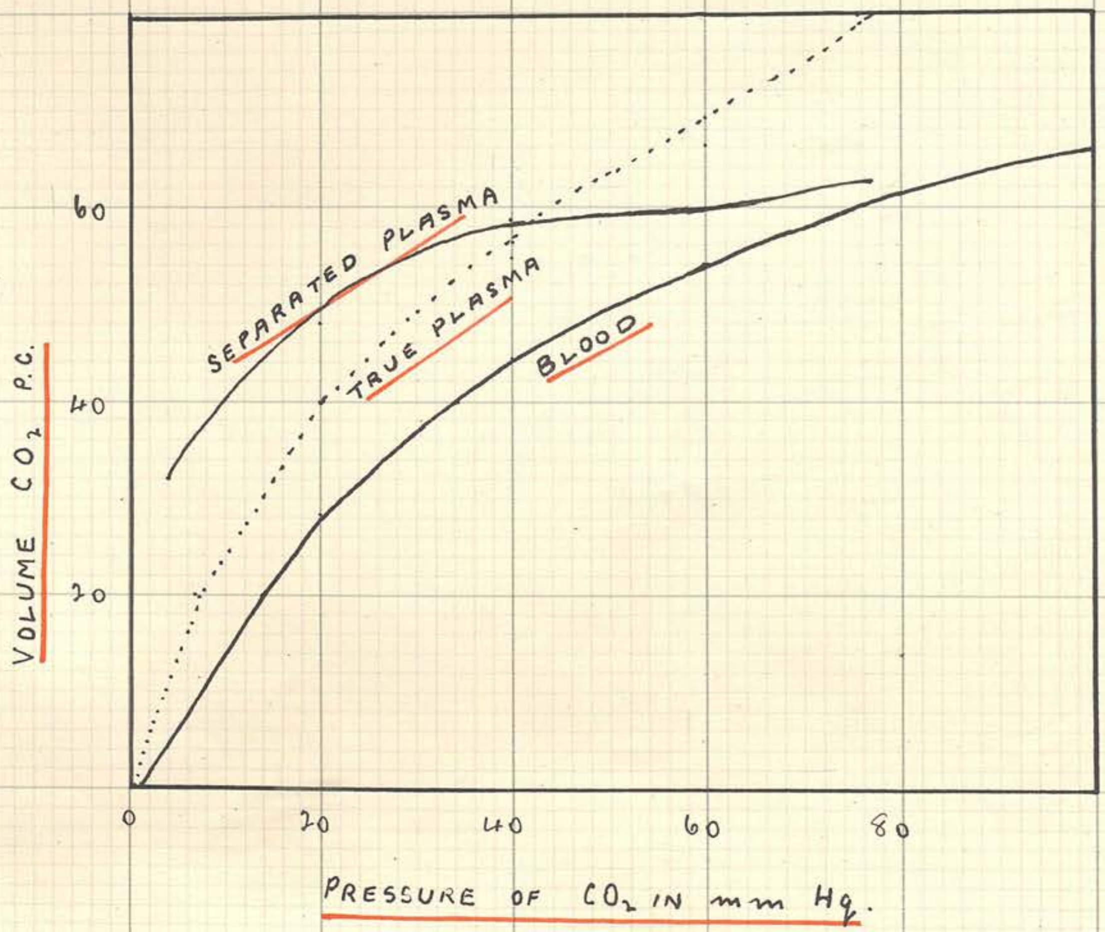
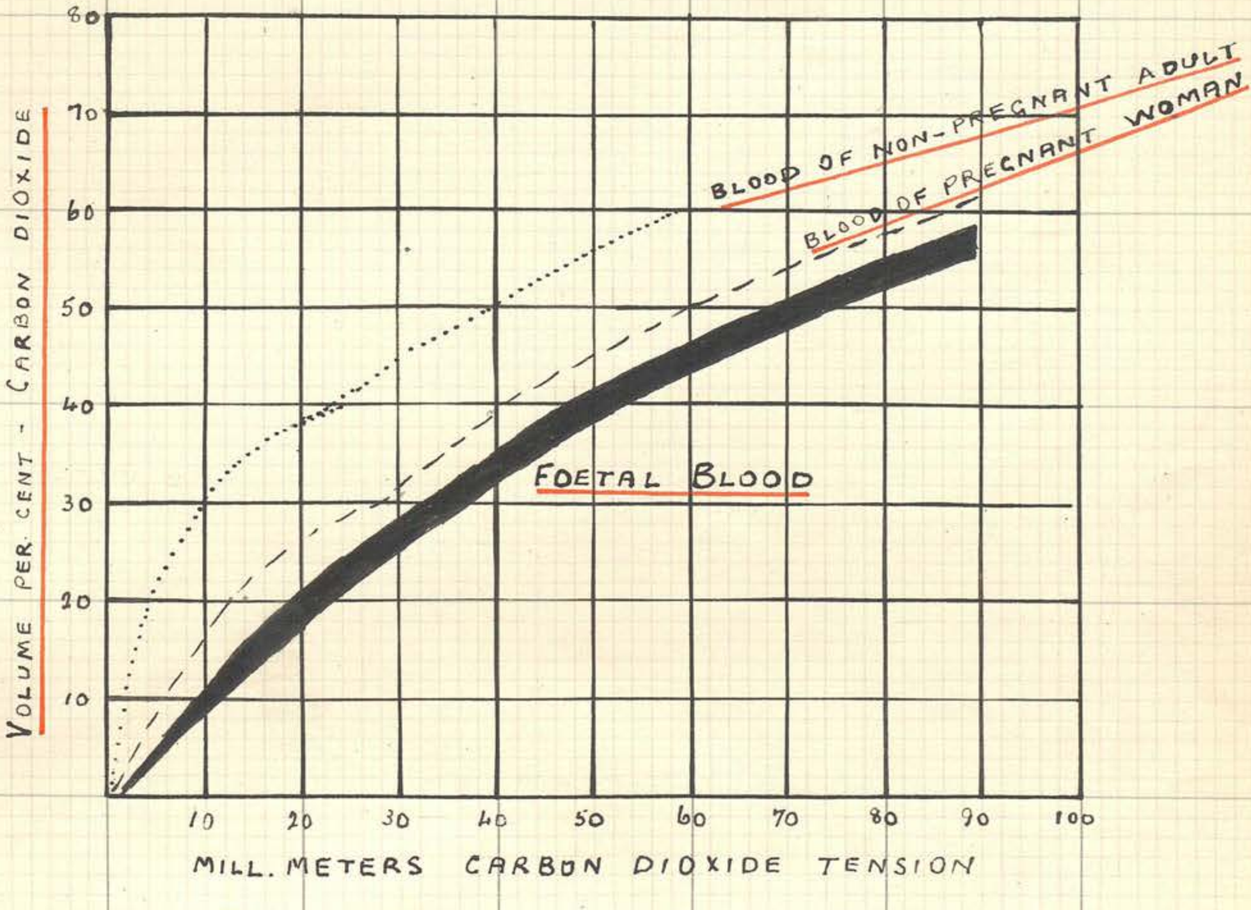
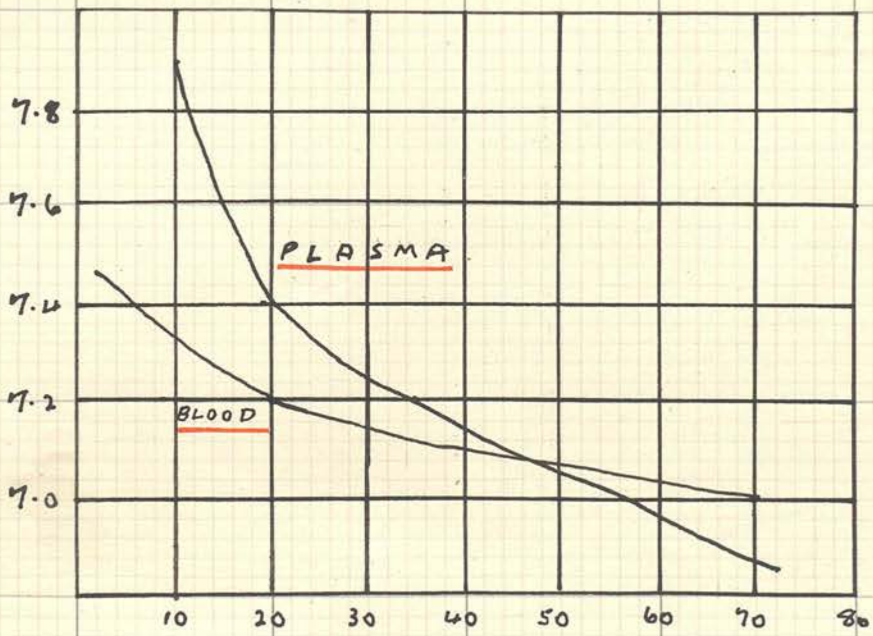


FIG. 4



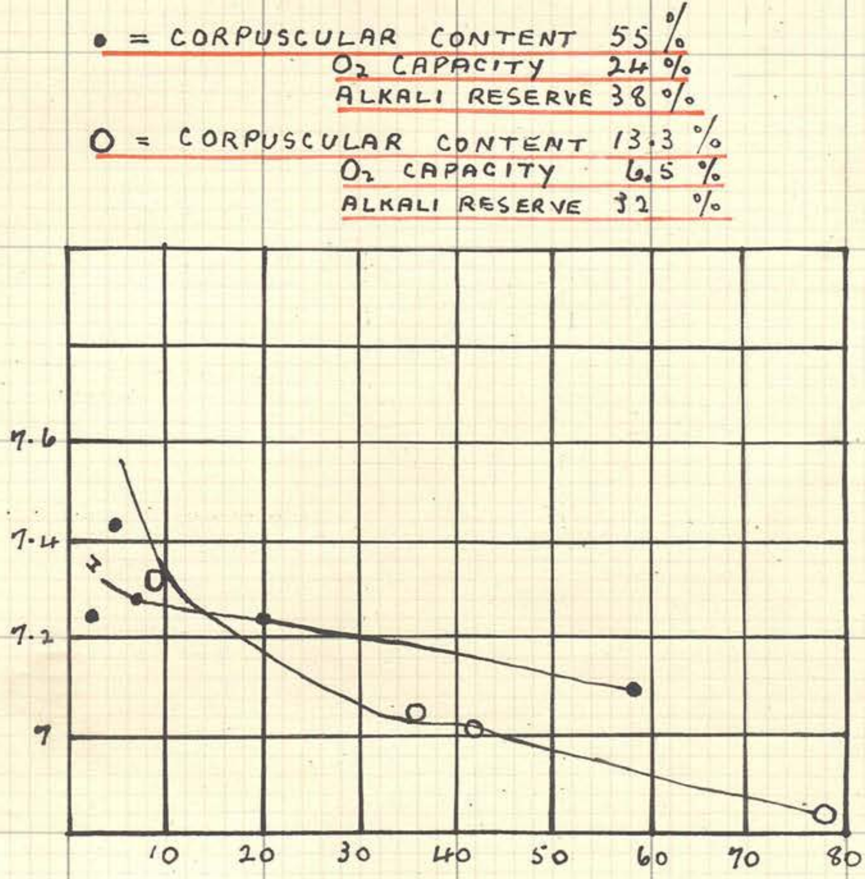
Showing the carbon dioxide dissociation curve of foetal blood in comparison with that of a normal pregnant woman and with that of a normal non-pregnant adult.

FIG. 5



CO_2 REACTION CURVES OF BLOOD AND OF PLASMA SEPARATED FROM IT.

Fig. 6.



EFFECT OF CORPUSCULAR CONTENT ON THE BUFFERING OF THE BLOOD

(FROM JOURNAL OF PHYSIOLOGY 1921. 55)

CO_2 tension of the foetal blood is the dominant one in initiating this phenomenon.

It seems probable that the depressed level of the CO_2 dissociation curve of foetal blood in comparison with that of normal adult blood is largely the result of two factors. In the first place the total serum base of foetal blood, like that of the pregnant woman, is low. Whereas the serum base of normal adult blood is usually about 154 mm., that of foetal blood averages 148 mm. At a blood pH of 7.35 this difference of 6 mm. would decrease the CO_2 capacity of the serum by approximately 14 volumes percent. Secondly, the large amount of Haemoglobin in foetal blood would produce an effect in the same direction since the total CO_2 content tends to vary inversely to the haemoglobin concentration.

The CO_2 reaction curve of blood and of separated plasma tells us at once that blood is much more perfectly buffered than is separated plasma. By the reaction of the blood as ordinarily expressed we mean the reaction of the true plasma of the blood.

There is a great difference between the buffering power of separated plasma which relies on its own buffers and that of true plasma, which has the resources of the red blood corpuscles as well.

If, as we have said, the secondary and principal buffering of the blood is due to the presence of its corpuscles which act in the manner described, it would be expected that the perfection of buffering of the blood would largely depend on its corpuscular or haemoglobin content. That this is so may be seen from the next diagram, Figure 6, in which the CO_2 reaction curves of two bloods of different corpuscular content are compared. Both were made from the same blood by separating off plasma from one portion of the blood and adding it to the remaining portion, thus effecting a concentration of corpuscles in the first and a dilution in the second. It is obvious that the one with the higher corpuscle content has much the better buffering.

As regards the primary buffering of the plasma, this is almost entirely due to the bicarbonate which it contains. As the primary buffering of the plasma is increased, as it can be by addition of sodium bicarbonate, the only effect is to raise the curve to a higher level which means that its relative, but not its absolute, buffering power is increased, all the curves being approximately parallel.

The facts mentioned confirm and extend what we have learned from the study of the CO_2 carriage of the blood, and we see, by reason of the ionic interchange (secondary buffering) and by reason of the plasma bicarbonate, additions of CO_2 to blood produce but little change in the H ion concentration.

From this study we go on to discuss the reaction of the corpuscles. This entails a description of the Donnan membrane equilibrium.

The Reaction of the Corpuscles.

The general principles governing the reaction of the corpuscles are the same as those which operate in the plasma or elsewhere, that is to say, we have inside the corpuscles an equilibrium between certain weak acids - (Hb, HbO_2, KH_2PO_4, H_2CO_3) and their salts. There must also be a state of equilibrium between the contents of the corpuscles and the substances in the plasma. Owing to the fact that the envelope of the red cell is only partially permeable to the constituents of the cell on the one hand, and those of the plasma on the other, this equilibrium between corpuscular contents and plasma is not so simple as would at first sight appear. In addition to the possibilities of the existence of an equilibrium on the basis of the law of mass action, we have to take into account what is known as the Donnan membrane equilibrium. This is due to the fact that there are inside the corpuscle large ions, e.g. that of Haemoglobin to which the envelope of the corpuscle is not permeable. Suppose that the potassium salt of Haemoglobin ionises in solution to give K ions and HO' ions. When carbon dioxide is added to the blood the Hcl produced passes through the corpuscular membrane and reacts with haemoglobin to form the acid H Hb and Kcl. Carbon dioxide entering the cell will similarly form H Hb and $KHCO_3$. The free acid of Haemoglobin (H Hb) will be dissociated into its ions H and Hb' but since the Hb ion is unable to diffuse out it restrains the H ions by electrostatic attraction from wandering through the membrane. Hence the Hydrogen ion inside the corpuscle keeps at a higher level than that in the plasma. The Hamburger ionic interchange is due to the peculiar partial permeability of the envelope of the red cell.

By direct experiment it has been shown (see M.R.C. report) that haemolyted corpuscles have, at the same CO_2 pressure, a higher H ion concentration than plasma.

Further the value of K, the dissociation constant for oxyhaemoglobin, varies in blood inversely as the cH of the plasma, and this has been interpreted by A.V.Hill as indicating that the dissociation of oxyhaemoglobin depends on the reaction inside the corpuscles. When CO_2 is added to blood the greater ease with which the O_2 can be dissociated from it can only be due to alteration of the reaction inside the corpuscles.

By determining the value of K we have therefore a valuable means of determining indirectly the reaction of the interior of the corpuscles, which is thus known to vary in the same direction as that of the plasma.

A word or two about the Monogram described by L. J. Henderson.

It is known from the researches of Barcroft and other workers that the saturation of the blood with O_2 is a function of the O_2 pressure which may be expressed by the O_2 dissociation curve. Further, from the investigations of Christiansen, Douglas and Haldane and subsequent work in the same field, we have also learned that the amount of CO_2 held in the blood varies with the CO_2 pressure as shown by the CO_2 dissociation curve.

It has also been learned that there is a relation between the two curves, for addition of CO_2 affects the oxygen dissociation curve in a definite manner and conversely the addition of oxygen has a definite effect on the CO_2 dissociation curve. We also know that the alteration of the CO_2 pressure alters the H. ion concentration and also the chloride content of the plasma.

Finally it has been demonstrated that alteration of H ion concentration affects the O_2 dissociation.

All these properties of the blood are related to each other.

L.J.Henderson has shown that in fact blood can be regarded as a complex physico-chemical system in which at least six important varieties are concerned. These varieties he states are:-

(1) The free oxygen (expressed by O_2 partial pressure).

(2) The combined oxygen (oxygen saturation of Haemoglobin).

(3) The free CO_2 (CO_2 partial pressure).

(4) The combined CO_2 (fixed CO_2).

(5) The H ion concentration of the plasma.

(6) The Chloride concentration of the plasma.

Now, the relation of these six varieties is such that if any two of them are arbitrarily fixed at definite values the remaining four will thereby be fixed according to definite laws of chemical equilibrium. For example, we know that, if the partial pressures of oxygen and of CO_2 are given particular values, the H ion concentration, the O_2 saturation, CO_2 content and chloride content will acquire certain fixed values.

The formulation of this principle as stated by L.J.Henderson leads us to believe that whichever two varieties are fixed, the value of the remainder is thereby pre-determined. Conversely, if we take blood in a state of equilibrium all six varieties will have a certain value. If we alter any one of the six there will result compensatory changes in the other five, - a new state of equilibrium being obtained.

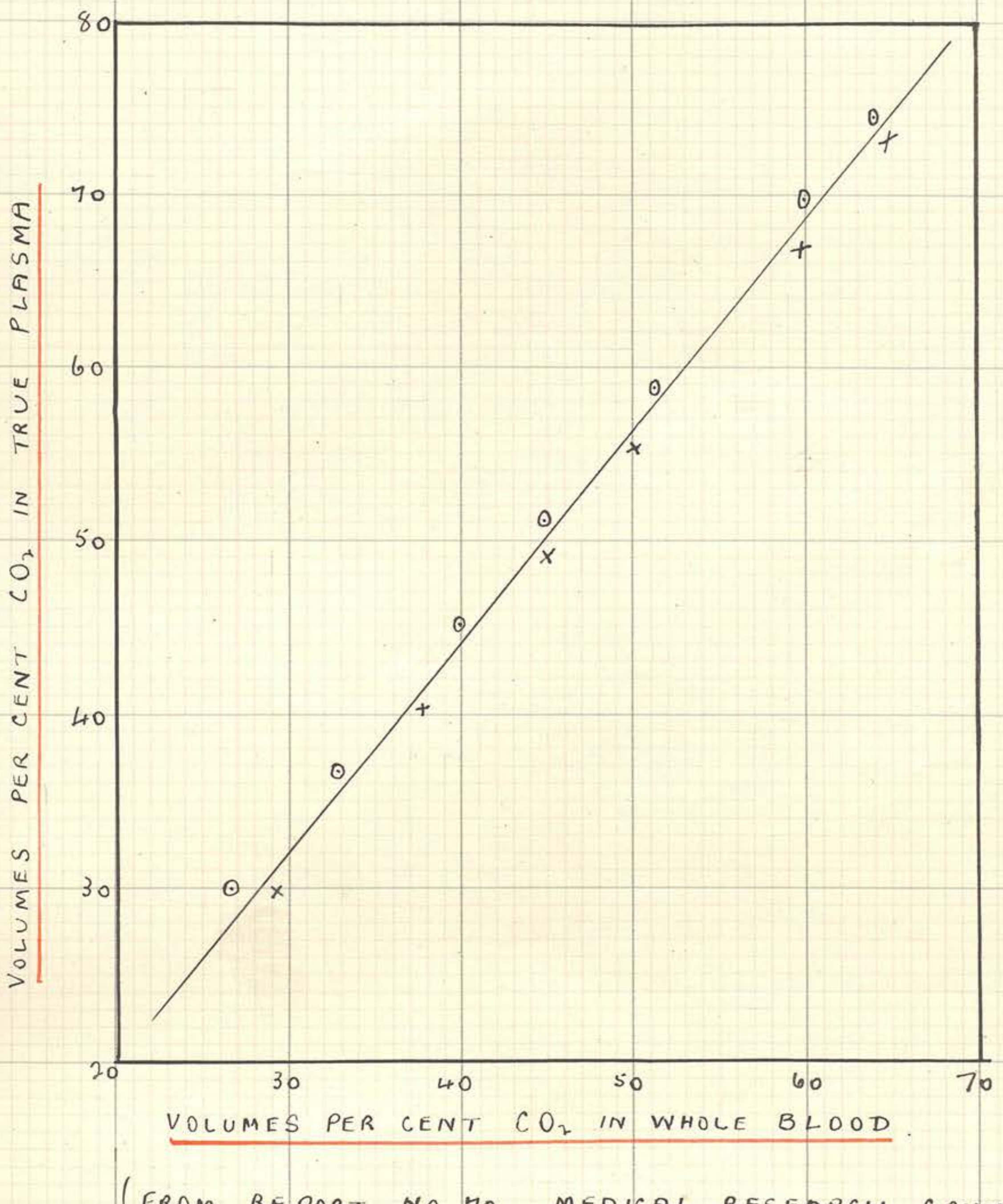
L.J.Henderson has shown that the natural relationships of these six varieties can be expressed in a chart called a Monogram. This chart contains six different isopleths corresponding to the six varieties, and it will be possible when the necessary data have been fully worked out to predict all the changes that will occur in these varieties when one of them is altered to a given extent.

A short Note on the Relation of CO_2 content of whole Blood to that of true Plasma.

It is often desirable to know the CO_2 content of the true plasma, but it is not always convenient to prepare the plasma for this determination. The amount of CO_2 in the true plasma has been found by Campbell and Poulton to be greater than that in whole blood but they found that for ordinary ranges of CO_2 pressure there is a linear relationship between the two. Hence if the CO_2 content of whole blood is known, that of the true plasma can be determined by reference to a graph showing the relationship between the two quantities. Such a graph is shown in Figure 7.

It has been shown by Christiansen, Douglas and Haldane in their classical paper on the Carbon Dioxide of the Blood that, at equal partial pressures of CO_2, a greater amount of it is fixed by reduced than by oxygenated blood.

FIG. 7.



(FROM REPORT NO 72 . MEDICAL RESEARCH COUNCIL)

In other words O_2 tends to displace CO_2 from the blood just as CO_2 is known to displace O_2.

They explained this phenomenon on the hypothesis that oxyhaemoglobin is a stronger acid than reduced haemoglobin, and all subsequent work has confirmed this belief. Figure 8, reproduced from the paper of Christiansen Douglas and Haldane, gives the curves for oxygenated and reduced blood, and shows that at pressures of CO_2 which fall within physiological limits, from 5 to 6 volumes per cent more of CO_2 is taken up by reduced than by oxygenated blood.

The importance of this observation lies in the fact that during its passage along the systemic capillaries not only is CO_2 added to the blood but also CO_2 is withdrawn from it and _vice versa_ in passing the lungs.

When two acids compete for possession of a base which is present in amount insufficient to satisfy both, the base will be distributed between the acids according to their strengths. The stronger acid will seize the greater part of the base. Now, if oxyhaemoglobin is a stronger acid than reduced haemoglobin, we may consider the following changes to occur when, at the same time, CO_2 is added to the blood and O_2 withdrawn from it.

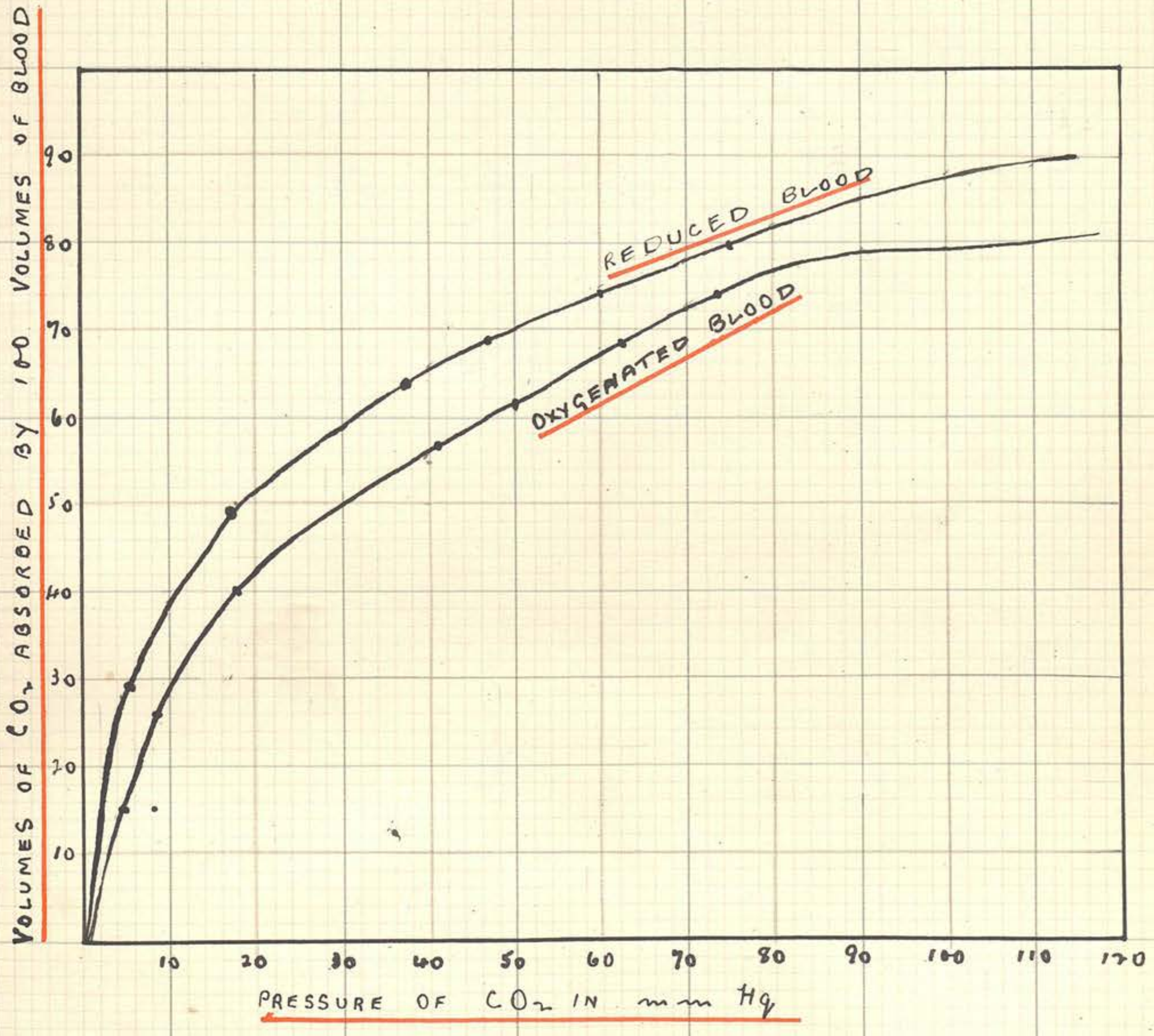
First we have the oxyhaemoglobin present chiefly as a potassium salt. O_2 leaves the corpuscles let us suppose, completely, and this weakens the acidic properties of the haemoglobin so that it holds

FIG. 8.

CARBON DIOXIDE DISSOCIATION CURVES FOR OXYGENATED AND REDUCED BLOOD.

NOTE EXTRA CO_2 TAKEN UP BY THE REDUCED BLOOD AT ALL TENSIONS OF THE GAS.

(FROM CHRISTIANSEN DOUGLAS AND HALDANE.



the combined base less firmly. At the same time Hcl and CO_2 enter the corpuscle from the plasma, as we have previously explained, and against it here the feebly-acting acidic haemoglobin can compete very little. It therefore gives up its base more readily than it would if it were oxygenated. Hence the reactions

$$\text{(i) } KHb + Hcl = Kcl + H\,Hb.$$

$$\text{(ii) } KHb + H_2CO_3 = H.Hb + KHCO_3$$

In consequence of reaction (i) the ionic interchange with the plasma is more extensive and more $NaHCO_3$ is found in it, while in consequence of reaction (ii) the amount of bicarbonate stored in the corpuscles is also greater than it would be if oxygen had not left the corpuscle.

Exactly the reverse changes take place in the conversion of venous into arterial blood.

Again summing up:

We can say that when CO_2 is added to the blood it mostly combines directly or indirectly with base which is set free from combination with haemoglobin.

According to calculations by Van Slyke from various available data, about 80 to 85% of the base set free is liberated by the change of oxyhaemoglobin to reduced haemoglobin.

The direct "buffer" action of oxyhaemoglobin without simultaneous reduction, as in the simple

Hamburger ionic interchange, probably accounts for about 10% of the change. Haemoglobin is therefore the chief carbon dioxide "carrier" of the blood, though under normal conditions it does not appear to combine with it directly.

PART II.

ACIDOSIS AND ALKALOSIS AND THEIR LABORATORY DETERMINATION.

PART II.

ACIDOSIS AND ALKALOSIS AND THEIR LABORATORY DETERMINATION.

(a) Pathological conditions under experimental conditions.

We will now go on to discuss the production of acidaemia and alkalosis in various conditions and how their variation in the reaction of the blood is brought about.

First of all -

Acidaemia or acidosis.

This may be present by addition of acid substances to the blood, or by removal of alkaline substances from the blood. In other words, owing to an increase in H_2CO_3 or a diminution of bicarbonate content of the blood. There is a tendency towards an actual reduction of $\frac{H_2CO_3}{B\ H\ CO}$ ratio.

1. To begin with conditions in which bicarbonate content of blood is lowered. The bicarbonate has been used in most cases to buffer the acid which has accumulated in the body.

In this condition we have a lowered alveolar CO_2 tension, an increased pulmonary ventilation, acid urine and an increased ammonium content. To begin with the "alkali deficit" is compensated.

(a) Ingestion of wood spirit, i.e. methyl alcohol, gives rise to formic acid in the body.

(b) Ammonium Chloride after absorption is deaminized in the body: NH_3 is split off and Hcl is left which enters the blood.

(c) In starvation and diabetes - fat metabolism stops short at the stage of B.oxybutyric and aceto-acetic acid.

(d) In nephritis there is retention of a non-volatile acid. This may be due to defective elimination of phosphate by diseased Kidney.

(I will discuss this fact more fully later)

(e) In many cases of infantile diarrhoea and vomiting, acidaemia is present owing to lowering of plasma bicarbonate.

In the case of infantile diarrhoea many factors are involved. There is a decreased water content of the blood, therefore the circulation through the Kidneys is closed down, the renal excretion becomes imperfect, and phosphate retention occurs as in nephritis.

Because of tissue anoxaemia, lactic acid or other organic acids derived from incomplete acidulation may pass into the blood. Also a certain amount of Ketosis may be present - as well as an excess of base compared with acid which may be lost in the stools.

2. Acidaemia may be caused by excess of CO_2 in the blood.

This occurs in:

(a) Experimental breathing of air containing increased percentages of CO_2

(b) Morphine poisoning owing to depression of respiratory centre.

In this case pulmonary ventilation becomes inadequate and so CO_2 is not eliminated in sufficient amounts. During sleep the alveolar CO_2 rises because of inadequate pulmonary ventilation.

(c) Very often in cardiac failure, when the pulmonary epithelium is so damaged that CO_2 cannot diffuse out readily.

(d) In Emphysema where CO_2 tension in alveolar air is raised.

Another classification of Acidaemia.

(1) Non-gaseous.

where the pathological factor affects the denominator primarily.

(a) Reduction of $BHCO_3$ due to neutralization of acids due to:-

- (i) increased formation of acid, e.g. Ketone bodies in diabetes, acidosis or lactic acid in muscular exercise.
- (ii) administration of acid-producing substances, e.g. Hcl NH_4Cl, $CaCb_2$. High fat diet, e.g. Ketogenic diet leading to production of Ketone bodies.
- (iii) impaired urinary excretion of acids: e.g. phosphates as in interstitial nephritis.

(b) Ions of fixed base - excessive excretion as in

- (i) Diarrhoea - intestinal tract.
- (ii) Urine - when ammonia formation is impaired by Kidney.

(2) Gaseous

where pathological factor affects the numerator (H_2CO_3) primarily.

(a) Increase of H_2CO_3 as in:-

(i) Depression of respiratory centre

(ii) Impairment of circulation

(iii) Pulmonary impairment.

We will now discuss the production of alkalosis or alkalaemia.

In this condition there is a tendency toward, or actual rise of $\frac{H_2CO_3}{BHCO_3}$ ratio.

There is depression of the respiratory centre. The pulmonary ventilation is diminished and the alveolar CO_2 rises. There is less acid urine and less NH_4 in urine.

These conditions may be caused by:-

1. Excessive breathing at rest which washes out an excessive amount of CO_2 from the alveolar air and lowers CO_2 tension in the arterial veins.

This may be due to:-

(a) Voluntary hyperpnoea.

(b) Exposure to high external temperature, especially when air is moist.

The respiratory centre is stimulated by raised temperature of the blood.

(c) Anoxaemia stimulating the respiratory centre as in high altitudes and in cardiac failure.

The lowered alveolar CO_2 tension gives alkalaemia of the arterial blood consequent upon stimulation of respiratory centre by O_2 want.

In some cases, however, of cardiac failure the CO_2 cannot be properly eliminated from the lungs because of the altered condition of the pulmonary epithelium. The CO_2 content of the blood is therefore raised and consequent tendency to acidaemia is a contributing factor in stimulating the respiratory centre.

2. Increase in the bicarbonate content of the Body.

This may be due to:-

a. Ingestion of overdoses of bicarbonate.

b. Pyloric obstruction.

c. High intestinal obstruction.

d. Infantile diarrhoea and vomiting.

The explanation of alkalaemia in b. c. d. is as follows. When vomiting takes place chloride is lost from the body. If diarrhoea is present there is further loss of chloride in the faeces. As a result the chloride content of the plasma is lowered and the osmotic pressure falls.

In cases of pyloric obstruction the alkalaemia is sometimes due to the loss of Hcl. from the body in the vomit, leaving an excess of base in the blood which unites with CO_2 to form bicarbonate. But alkalaemia may also develop if condition is due to carcinoma as in that case achlorydria is usually present.

Another classification of Alkalosis or Alkalaemia is :-

(1) Non-gaseous,

where pathological factors affect the denominator primarily.

- (a) Increase of bicarbonate.
  - (i) Administration of alkali;
  - (ii) Deficit of acid and its replacement by H_2CO_3 as in:-
    - (a) Loss of chloride by vomiting.
    - (b) Oxidation of Ketone acids after insulin in diabetes.

(2) Gaseous.

where pathological factors affect the nominator (H_2CO_3) primarily.

- (a) Decrease in H_2CO_3 as in
  - (i) Higher ventilation.

In a	(non-gaseous acidosis and (gaseous alkalosis	we have	a low total CO_2 content and a low alkali receive.
In a	(gaseous acidosis (and (non-gaseous (alkalosis	we have	a high total CO_2 content and a high alkali receive.

The tendencies to acidaemia or alkalaemia we have shown are dealt with by the various physiological mechanisms described.

Before discussing fully the disordered equilibrium and method of production in nephritis, I will mention a few of the more evident clinical manifestations of acidosis and alkalosis, especially form of breathing.

Of course the clinical signs and symptoms depend on the cause of the acidosis or alkalosis. In the gaseous type of acidosis, which is rare, the breathing is slow. This is due to the respiratory centre being depressed, and therefore requires more CO_2.to stimulate it. The patient is generally comatose or very drowsy. In the non-gaseous acidosis, which is much commoner, the symptoms are well known. They are those of Diabetic acidaemia. Air hunger described by Kussmaul is marked. The breathing is pauseless and noisy; the increase in rate is not so marked as increase in depth. It is important to recognize this type of breathing as it may cause some difficulty, especially as it may be mistaken for the breathing in pneumonia. In pneumonia there is usually marked frequency and less depth than in acidosis. You do not get the cyanosis that is present with pneumonic conditions.

In non-gaseous alkalosis the breathing is depressed in order to control CO_2. In pyloric stenosis in infancy the respiratory rate has been known to fall to 6 per minute. There are long periods of apnoea, and respirations are very shallow. These infants have often the appearance of being drugged.

Gaseous alkalosis is produced by rapid breathing which washes out CO_2. This is seen experimentally in forced respirations and clinically in mountain sickness and as a sequel of encephalitis lethargica.

I will now go on to discuss the type of disordered equilibrium found in nephritis and its method of production.

The chief functions of the Kidney in helping to keep a normal acid base equilibrium, are:-

1. Excretion of Water.

Tissue water must be maintained at a constant level, otherwise if dehydration occurs, there is breakdown of tissue and excessive acid metabolites are formed with the production of acidaemia.

2. Excretion of Excess Salts, both acid and Alkaline.

This must be carried out to maintain the ionic concentration of the plasma and tissues at the normal level.

3. Production of Ammonia as a sparer of fixed base.

4. Excretion of bicarbonate as an acid sparer.

If there is a deficiency of non-volatile acid, either relative or absolute, for neutralization of base, the carbonic acid is held back in the tissue fluids and blood, in order to unite with the base, and in consequence is excreted in the urine as bicarbonate. If, on the other hand, there is sufficiency of non-volatile acid present in the body, bicarbonate does not appear in the urine. The carbonic acid is readily expelled by the lungs.

It has been shown, in relation to carriage of CO_2, that the alkali available for the transport of this and other acids is known as the alkali reserve. But in addition the body makes use of ammonia which is produced as a product of protein metabolism. This function is carried out by the Kidney, as previously stated, and is due to the fact that the Kidney has the power of breaking down urea and of utilizing the ammonia found to neutralize acid.

The evidence that the Kidney does this is that the renal vein may contain more ammonia than the artery, and in renal disease, although an acidaemia may be present, the ammonia -urea ratio is unaltered (McLean).

To further expand the above:- the Kidney has the power of modifying the reaction of the urine. It varies proportions of the acid phosphate NaH_2PO_4 and the alkaline phosphate Na_2HPO_4. If there is a tendency to acidaemia the acid phosphate is excreted, the blood thereby being made more alkaline, - the reverse occurs if there is a tendency to alkalaemia.

The Kidney is, however, less sensitive than the respiratory centre in its recognition of alterations in blood reaction and it may take some time before it really comes into action.

Nash and Benedict have shown that the epithelium of the renal tissues manufactures NH_3 and passes it into the blood stream. As stated above the renal vein contains more NH_3 than the renal artery. In conditions of acidaemia the Kidney makes more NH_3 to deal with excess of acid radicles present. The NH_3 forms ammonia salts in the blood which are subsequently eliminated by filtration in the glomerular and passed out in the urine.

The urinary ammonia is increased in acidaemia and decreased in alkalaemia.

It is doubtful whether other organs make NH_3 which can be used in this manner.

Under normal conditions the Kidney may excrete the equivalent of 60 or 70 cc.cm. of normal solution of acid per day. The glomeruli of the Kidney filter a mixture of acid and basic phosphate which is slightly alkaline. The proportion of NaH,PO_4 to Na_2HPO_4 in plasma is 1 : 4. The Kidney normally eliminates the acid while retaining the base as far as is possible. It excretes NaH_2O_4 and Na_2HPO_4 in the ratio of 9 : 1. The basic phosphate is changed into the acid form and one molecule of five is retained in the body.

$Na_2 HPO_4 + H_2O = Na + OH + NaH_2PO_4$

excreted.

The base may be absorbed as bicarbonate. When there is a tendency to alkalaemia the base phosphate is eliminated and bicarbonate as well. At times the Kidney sacrifices H ion concentration in order to preserve the salt concentration of the blood.

It must be mentioned that the ammonia excretion takes some days to reach its maximum, so that some other arrangement is necessary to tide over the delay. This is produced by a supply of extra base directly from the bones as calcium, and from the soft tissues as sodium and potassium. In contrast to the ammonia output the excretion of this fixed base takes place immediately.

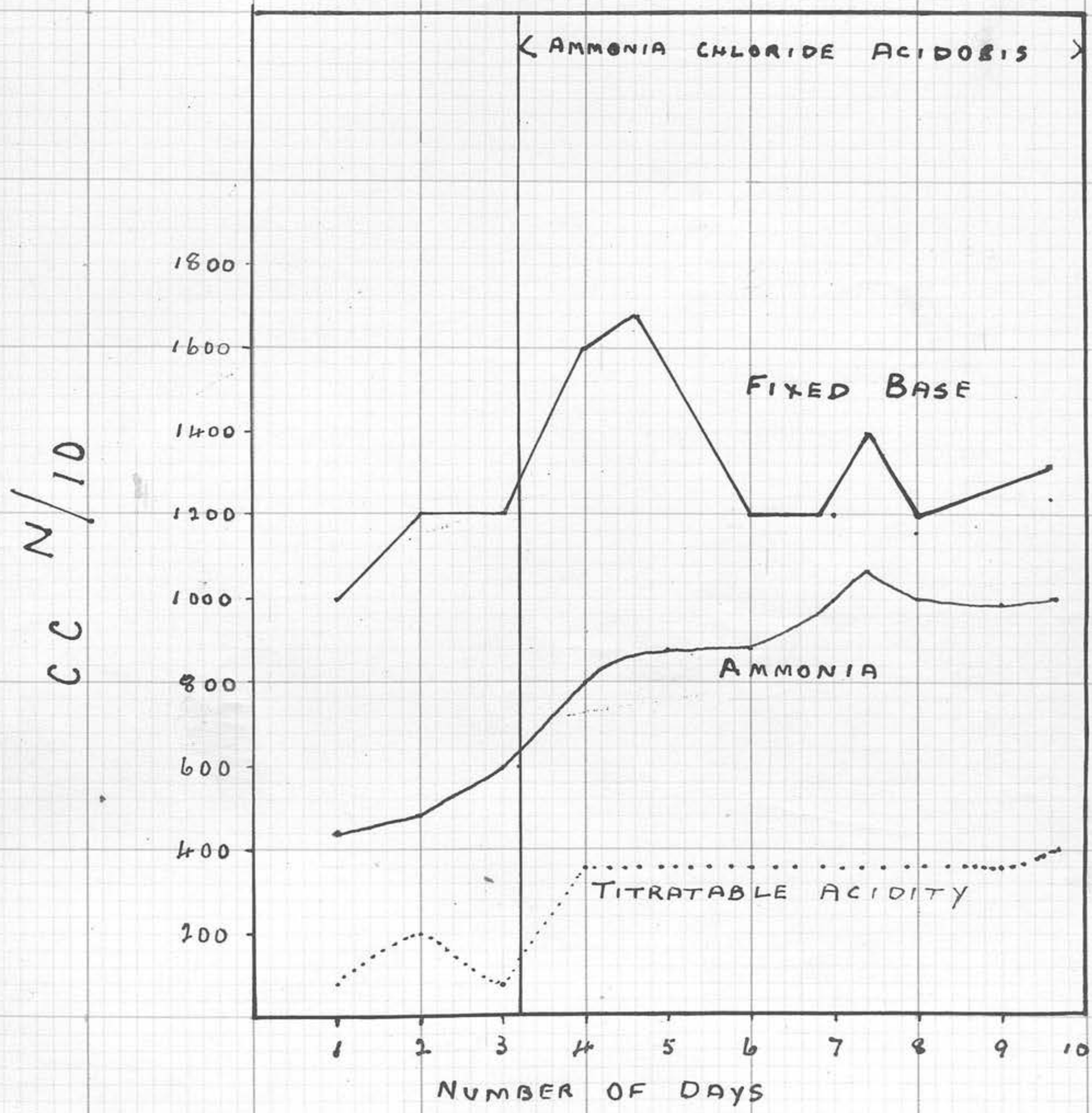
The next illustration shows the daily output of ammonia, fixed base and titratable acid before and during acidosis produced by ammonium chloride.

The Illustration is from Morris and McRae, Archives, Diseases of Children 1930, V. 218.

FROM MORRIS & MCRAE

ARCHIVES DISEASES CHILDREN

1930 V. 218



ACID BASE VALUE of CERTAIN FOODS.

FOOD.	Keto: genic Value gms.p. 100 gm	AntiKeto: genic Value gms. p.100 gms.	Calories per 100 gms.	Alkali cc.N/1 per 100 gms.	Acid cc.N/1 per 100 gms.	ACIDITY / ALKALINITY (cc.N/1 p. 100 gms.)
APPLES	0	11	63	4.8	1.3	3.5
BACON	62	12	625	7.5	15.9	8.4
BANANAS	1	15	99	14.5	6.2	8.3
BEANS	12	71	345	65.0	46.0	19.0
BEEF	19	13	200	17.2	30.4	13.2
BREAD (White)	5	58	263	22.8	29.7	6.9
BRUSSELS SPROUTS	1.7	7.8	40	14.4	21.0	6.6
BUTTER	77	9	770	35.5	35.7	.2
CABBAGE	1	6	32	11.0	6.7	4.3
CARROTS	1	8	45	11.9	5.4	6.5
CAULIFLOWER	1	6	30	16.0	10.7	5.3
CELERY	1	3	18	17.2	8.2	9.0
CHEESE	47	22	454	78.3	85.3	7.0
CHOCOLATE	50	42	625	43.9	36.1	7.8
COCOA	37	51	500	66.2	57.9	6.3
CREAM	19	8	224	9.8	8.4	1.4
EGGS	16	8	147	8.0	26.8	18.8
FISH	9	9	71	13.3	28.0	15.3
FLOUR	6	81	357	8.1	19.0	10.9
LEMON JUICE	0	10	40	5.4	1.6	4.3
LETTUCE	1	4	19	13.0	5.6	7.4
LIVER	14	12	128	-	-	-
MILK	2	6	36	13.3	10.7	2.6
MILK (Skim)	2	7	30	12.0	11.2	.8
MILK (Whole)	5	7	60	12.9	11.0	1.9
OATMEAL	15	76	400	24.2	27.2	3.0
ONIONS	1	11	49	8.0	7.6	.4
ORANGES	1	12	51	8.0	2.2	5.8
PEAS	13	74	357	33.0	40.4	7.4
PORK	55	10	500	7.5	15.1	7.6
POTATOES	1	20	83	14.9	6.7	8.2
PRUNES	1	74	303	35.3	9.7	25.6
RHUBARB	1	4	23	12.9	3.8	9.1
RICE	4	83	395	6.0	15.0	9.0
TOMATOES	1	4	23	8.8	3.4	5.4
TURNIPS	1	9	39	15.7	8.2	7.5

For purpose of discussion of disturbance of acid base balance we will consider three main types of nephritis.

1. Acute nephritis (commonly seen in children).
2. Chronic interstitial nephritis.
3. Chronic parenchymatous nephritis.

In 1. Acute nephritis

the whole kidney is temporarily thrown out of action; water, salts, nitrogenous bodies and acids are all retained in the blood. The volume of urine is reduced to a few ounces daily and it contains protein blood and casts.

The CO_2 combining power of the blood varies within normal limits but tends to be low. Even when well marked oedema is present the acid base balance is little, if at all, disturbed. Some workers state that the CO_2 combining power is definitely lowered and this forms the basis of the intensive alkaline treatment recommended. It is used also as a means of prophylaxis in Scarlet Fever in which nephritis is feared. The convulsions seen frequently in acute nephritis are not due to uraemia but to cerebral oedema and high blood pressure. The treatment is therefore an intravenous administration of alkalies, by venesection, and lumbar puncture. These so-called "uraemic" convulsions can often be differentiated from true uraemia by a knowledge of the CO_2 combining power of the blood. Acute nephritis without uraemia rarely shows a CO_2

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combining power of below 40 vols.%, but uraemia with convulsions rarely shows one above this figure (Dunlop and Stewart). Moreover the N.P.N. in acute nephritis without uraemia is usually at a normal figure.

In 2. Chronic Interstitial Nephritis

restriction of the CO_2 combining power of the blood is usually a fairly reliable guide to the extent of acidosis prevailing in interstitial nephritis. Dunlop and Stewart state, however, that as a general rule cases of chronic interstitial nephritis show a CO_2 combining power rather above the normal range, and it is only in the terminal stages of the disease with commencing uraemic manifestations that it is lowered below 53 vols. %. They also state that the onset of chronic uraemia is frequently accompanied by symptoms which are so varied and which so often simulate those of many other possible conditions that it may be difficult to decide whether they are due to underlying renal disease or to other possible causes. In these circumstances the discovery of a lowered carbon dioxide combining power may be of some significance. When uraemic coma supervenes the CO_2 combining power of the blood is always markedly lowered though possibly less so than in diabetic coma. This may become a valuable diagnostic sign, for even with coma present the diagnosis of uraemia may not be perfectly obvious.

Some cases of cerebral haemorrhage with albuminuria may present many features in common with uraemic coma but show no lowering of the CO_2 combining power.

Also from a point of view of treatment a knowledge of the alkali reserve may be useful for the distressing breathlessness which is one of the characteristic features of one type of uraemia. In some cases life may even be prolonged by the therapeutic use of alkalies.

The fall of CO_2 may be associated with one or more of the following:-

1. Low plasma base.
2. High inorganic phosphate.
3. High organic content of the blood.

Total acid only exceeds the normal limits when the organic acid is greatly increased. This latter occurrence takes place with excessive vomiting, carbohydrate starvation or dehydration.

When the supply of carbohydrate is deficient the excess organic acid is mainly Ketone, but in the other conditions the organic acid falls into the group of undetermined acid.

Excess of phosphate sulphate and other acid radicles may explain the slight degree of acidaemia associated with a blood carbon dioxide bordering on the lower limits of normal.

It is, however, to the kidneys tissues fault to regulate water, and salt loss, that must be attributed the dehydration which, with the inability to form ammonia, is the potent cause of the acidaemia found with chronic interstitial nephritis.

The more severe the nephritis the more delicate must be the adjustment between the water and salt intake. Too much water will deplete water of its salt content, as an increased urinary output will carry an increased amount of salt with it. On the other hand, if salt be given in excess the tissue fluid will be diminished, since the water is required to excrete the salt.

A word here about the effect of acid and alkali administration. The kidneys do not react well to injection of acid substances. The administration of alkali relieves the situation to some extent, but alkali may lead to an excessive amount of CO_2 in the blood although urine remains acid. This suggests defective bicarbonate excretion by the kidney, and it is possible in such cases that the kidney is only able to secrete a urine the pH of which varies within comparatively narrow limits. Peters and Van Slyke attribute this state of affairs to deficiency of the fixed base of the plasma, any base absorbed being retained as bicarbonate.

Lyon, Dunlop and Stewart point out the advantages of giving a diet containing a more adequate supply of protein than is usually advised in chronic nephritis, and recommend diet with ample protein in addition to administration of alkali. I have included a diet sheet from Steiman's tables 'Chemistry of Food,' showing acid base value of various common food stuffs.

By above means CO_2 content of the blood is kept up and N.P.N. falls to a lower level. The excretion of urea also seems to be favourably influenced, although the administration of other substances, such as Creatine, is not altered. The advantage of an adequate protein intake is to spare the tissue protoplasm and thus prevent its excessive catabolism. The beneficial effect produced on the acid base equilibration is entirely due, however, to the alkali nature of the diet.

The next two tables show observations made by various workers on the CO_2 combining power and N.P.N. in various cases of nephritis.

TABLE 1. /

TABLE 1.

By Lyon, Dunlop and Stewart.

Showing incidence of acidosis in a series of 135 observations on advanced nephritis.

Two observations made, namely -

1. Blood. Non protein nitrogen.
2. Carbon dioxide combining power of blood plasma

BLOOD N.P.N. per 100 ccm.	Blood CO_2 combining power in volumes per cent.				
	over 70	60.70	53.60	45.53	under 45
under 40	26	17	2	-	-
40-75	3	39	15	5	-
75-100	-	2	3	7	1
over 100	-	-	2	3	10

TABLE 2.

Showing changes in certain blood constituents in various forms of nephritis.

TYPE.	CO_2 combin: ing power.	N.P.N. mgm.%	Phosphorus mgm.%
Average normal	50	25	4
Acute nephritis non complicated	45.5	56	4
Acute nephritis with oedema	49.7	48	6
Acute nephritis with uraemia	38.9	67	3.6
Chronic intersti: tial nephritis	45.9	174	12.1
Uraemia	20.6	343	16.0
Chronic parenchy-matous nephritis	48.4	29	5.5

3. In Chronic parenchymatous Nephritis.

The CO_2 combining power of the blood plasma is usually unchanged but this is dependent upon changes in chronic fixed base and protein. In this condition there is marked oedema present. Protein +++ in urine and the urea concentration is normal. There is no chloride retention in the blood but the blood cholesterol is increased. There is no tendency to uraemia and no marked cardio vascular changes are noted.

The diet in this case should contain

1. Diet rich in protein,
2. Diet poor in ash,
3. Administration of an acid producing substance.

A diet of this nature is acid-producing, and fortified by an acid-producing salt will tend to induce a flow of fluid from the tissue spaces to the plasma and thence to the kidney for excretion. A low ash diet is clearly indicated because of the inability to excrete minerals which are retained in solution and lead to an increase of the tissue fluids with consequent increase in oedema.

It is my intention now to describe the Van Slyke method for estimating the CO_2 combining power of the blood, as this is the method I have employed.

In order to estimate the alkali reserve of the blood, Haldane introduced a method by means of which, by determining the percentage of CO_2 in the alveolar air, this can be done. This depends on the principle that in acidaemia the power of the blood to carry carbon dioxide is reduced, with a proportional reduction in the CO_2 content of the alveolar air. Van Slyke's method has, however, superseded this. His method is based on the principle that blood, if exposed to an absorption containing a definite amount of CO_2, absorbs that gas in proportion to its supply of available base.

Thus the method of Van Slyke measures the CO_2 combining power of the blood and not directly its alkali reserve. With certain reservations the terms are interchangeable.

The technique of the Van Slyke method is now described.

The Estimation of the CO_2 Combining Power of the blood by the method used by Van Slyke and employing his apparatus.

If a patient is suspected to be suffering from acidosis then two tests of value can be performed. They are:-

1. Estimation of the alkali reserve by Van Slyke's method.
2. Determination of the alveolar Carbon Dioxide tension.

Method One is the method of choice, and is the method I have used.

1. Van Slyke's Method for estimation of the CO_2 Combining Power of the Blood Plasma.

By this method the alkali reserve is estimated in the form of sodium bicarbonate. It really consists in the addition of acid to a measured quantity of blood plasma and extracting the CO_2 produced by reducing the pressure. The fluid is trapped by a very ingenious device and the CO_2 is measured. The alkali reserve can be calculated from this volume by reference to a table. These tables I will reproduce later.

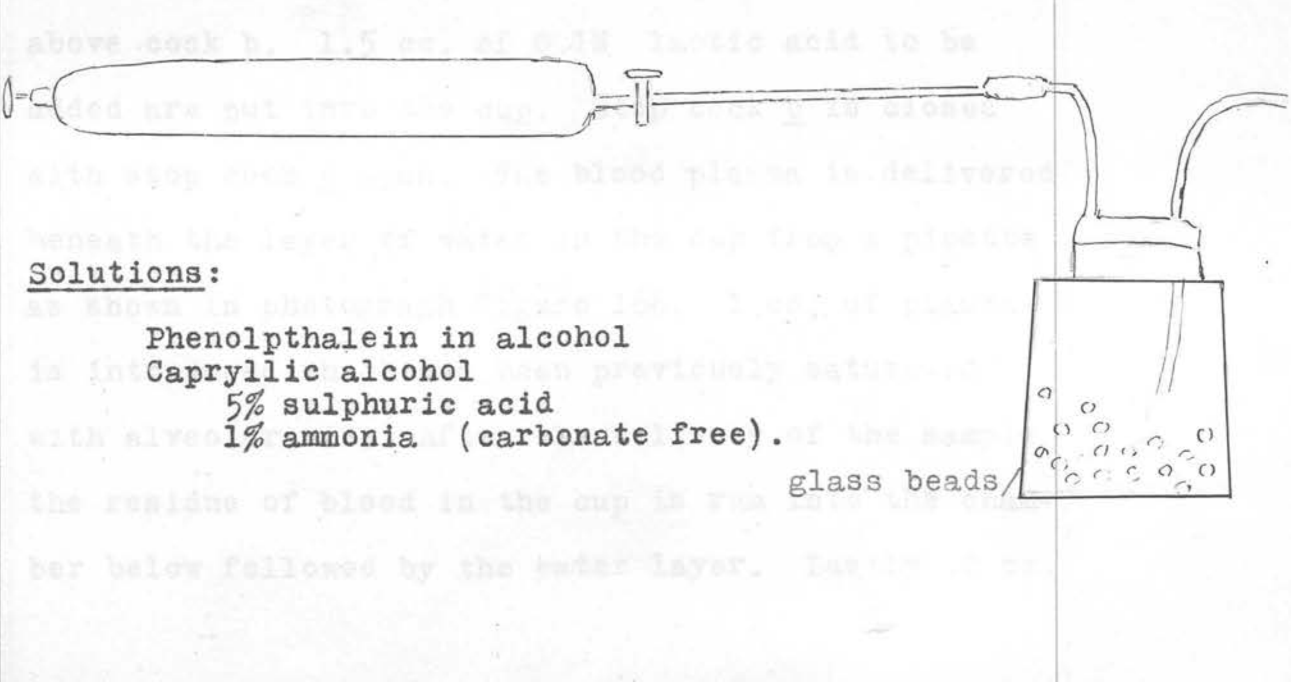
The actual CO_2 content of the blood plasma, or else its CO_2 combining power, can be determined.

Blood is drawn off from the patient in the usual way. About 5 or 6 cc. of venous blood drawn from the median basilic vein is quite sufficient. This blood is run into a glass tube from the syringe. In the glass test tube are a few crystals of Potassium oxalate. The blood is then shaken up with the crystals. The experiment of investigating the CO_2 combining power must be carried out within the space of 6 hours at the most. About 3 or 4 cc. of the oxalated blood is run into a glass tinometer. This blood has now to be saturated with CO_2 at about atmospheric pressure.

If no cylinder of CO_2 is available the plasma can be saturated with operator's own alveolar air. It is advisable to pass breath through some form of condensation bottle first, as shown in Figure 1. The funnel or tinometer containing the plasma is then rotated around its long axis in such a way that the plasma is spread over the sides in the form of a thin layer. If too much blood is used for the estimation then the layer will be too thick, and if too little then there will not be enough plasma left for the estimation. About 4 cc. is a fairly useful amount to use. Two minutes of this rotation is sufficient to saturate the plasma with CO_2.

Figure 1. Apparatus for saturating plasma with CO_2. The bottle contains glass beads.

This is a condensation bottle used when utilizing own alveolar air.



Solutions:

- Phenolpthalein in alcohol
- Caprylic alcohol
  - 5% sulphuric acid
  - 1% ammonia (carbonate free).

If a cylinder of CO_2 is available then the blood plasma is saturated with a known quantity of carbon dioxide. In the method used the tinometer was graded 15 cc. 15 cc. of CO_2 were run into tinometer and saturation was allowed to go on for two to four minutes.

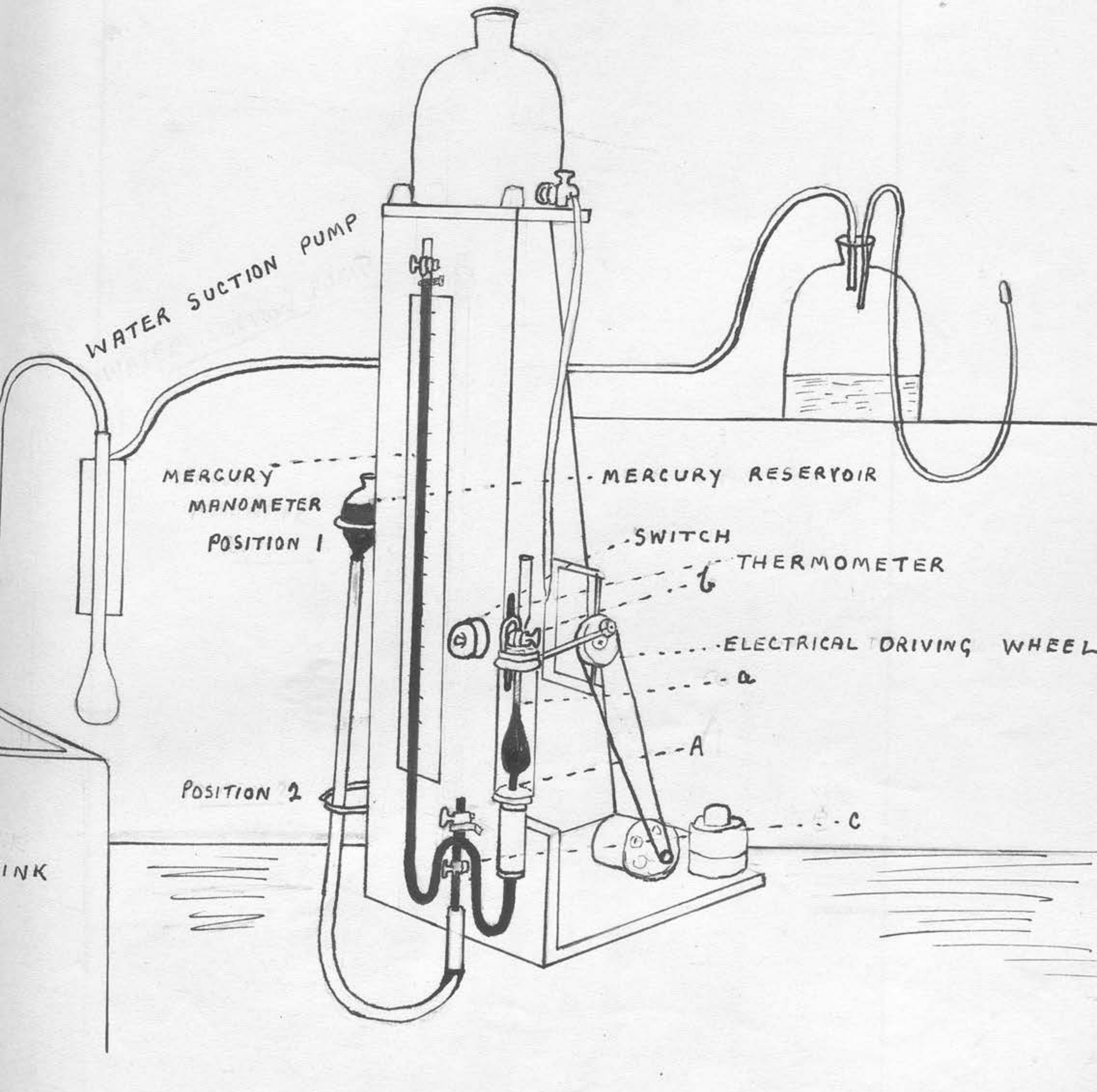
I have included here rough diagrams of:-

1. Van Slyke apparatus.
2. Water Suction Pump.
3. Gas free lactic acid apparatus.
4. CO_2 Saturation apparatus.

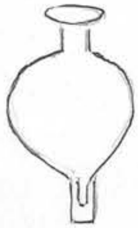
Also are included two photographs which I had taken of the Extraction chamber in full detail, and also a photograph of operation of delivery pipette. The other photograph shows roughly the appearance of the Van Slyke apparatus.

The apparatus is thoroughly cleaned by means of rinsing out chamber with N/10 lactic acid. A drop of capryllic alcohol is then drawn into the capillary above cock b. 1.5 cc. of 0.1N lactic acid to be added are put into the cup. Stop cock b is closed with stop cock c open. The blood plasma is delivered beneath the layer of water in the cup from a pipette as shown in photograph Figure 166. 1 cc. of plasma is introduced which has been previously saturated with alveolar air. After the delivery of the sample the residue of blood in the cup is run into the chamber below followed by the water layer. Lastly .2 cc.

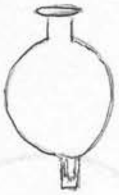
VAN SLYKE APPARATUS


WATER SUCTION PUMP
MERCURY MANOMETER
POSITION 1
MERCURY RESERVOIR
SWITCH
THERMOMETER
b
ELECTRICAL DRIVING WHEEL
a
A
POSITION 2
C
INK

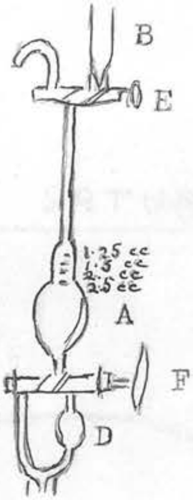
ANALYSIS APPARATUS.



Position 1.



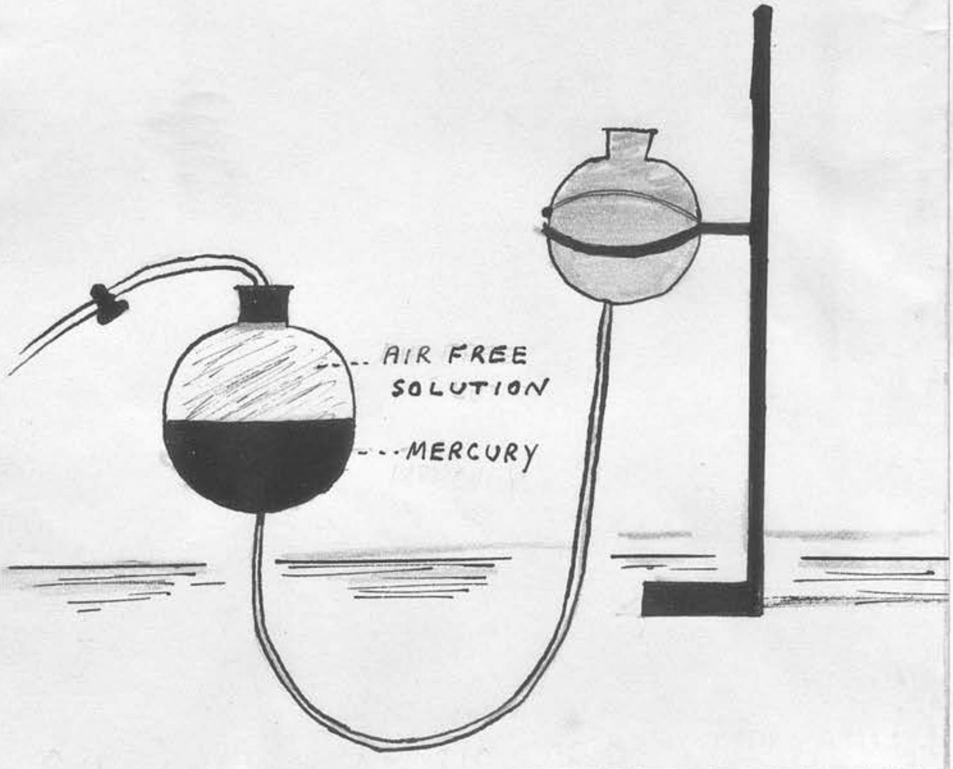
Position 2.


B
E
1·25 cc
1·5 cc
2· cc
2·5 cc
A
F
C
D

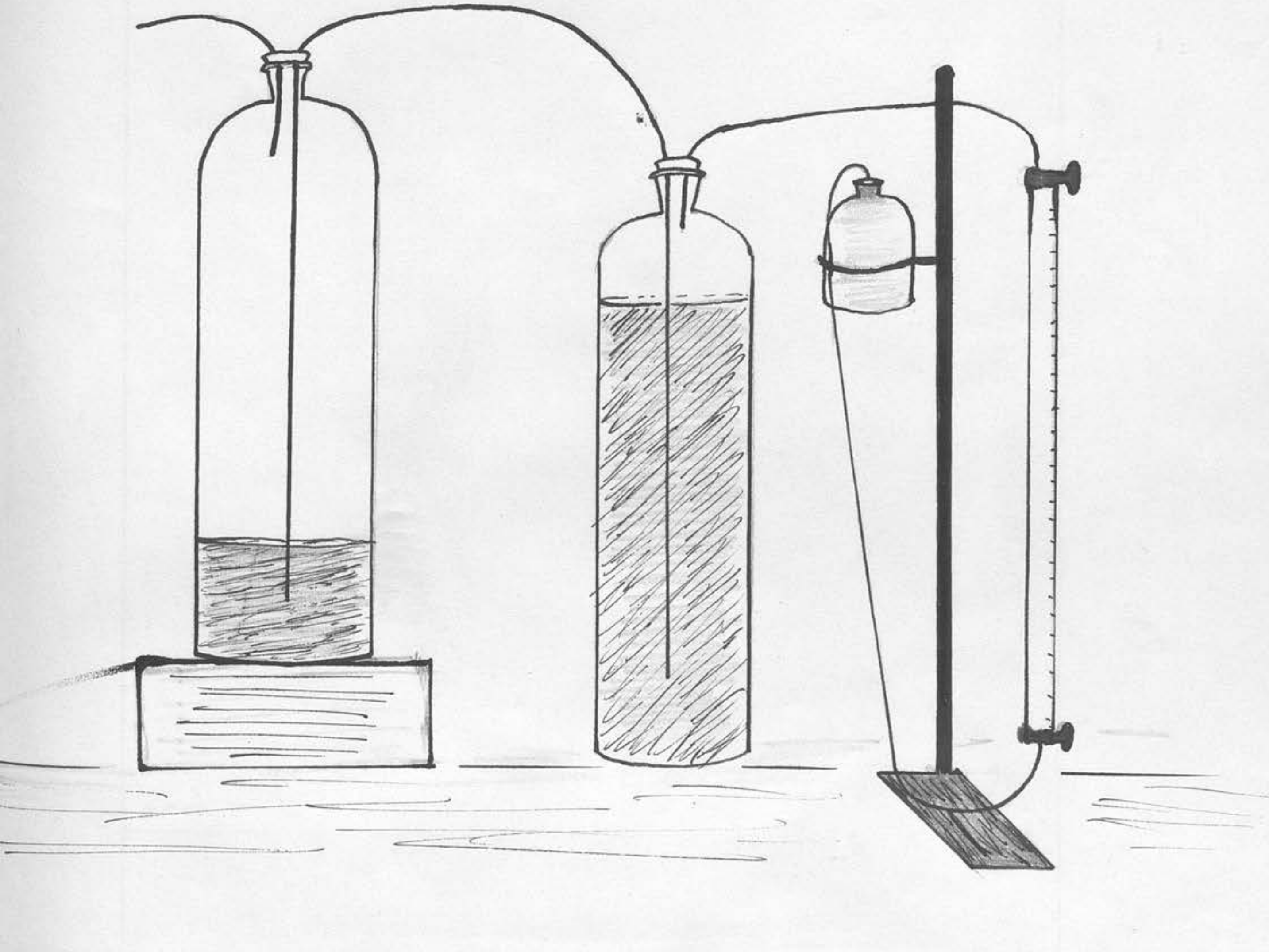
Van Slyke's apparatus for estimation of alkali reserve.

The reservoir is connected to the main apparatus by means of a rubber tube the ends of which are shown cut across.

GAS FREE LACTIC ACID APPARATUS.


AIR FREE SOLUTION
MERCURY

CO_2 SATURATION APPARATUS



EXTRACTION CHAMBER.

Operation of DELIVERY PIPETTE

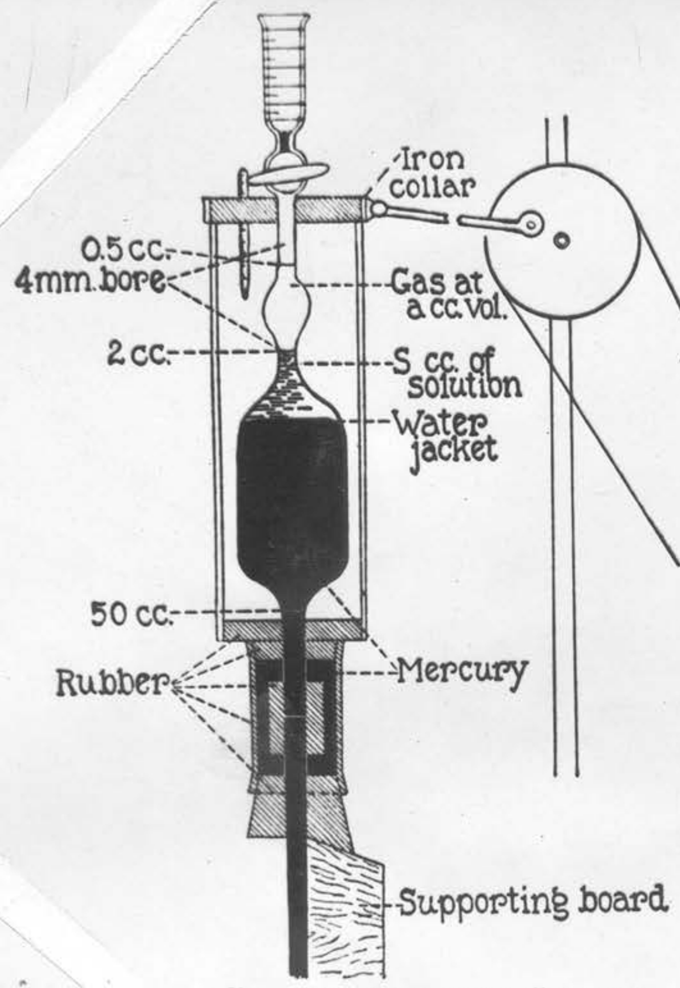

Iron collar
0.5 cc.
4mm. bore
Gas at a cc. vol.
2 cc.
S cc. of solution
Water jacket
50 cc.
Rubber
Mercury
Supporting board

Fig. 165.—Extraction Chamber.

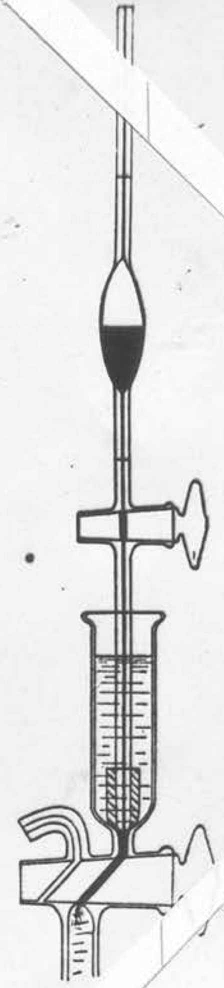
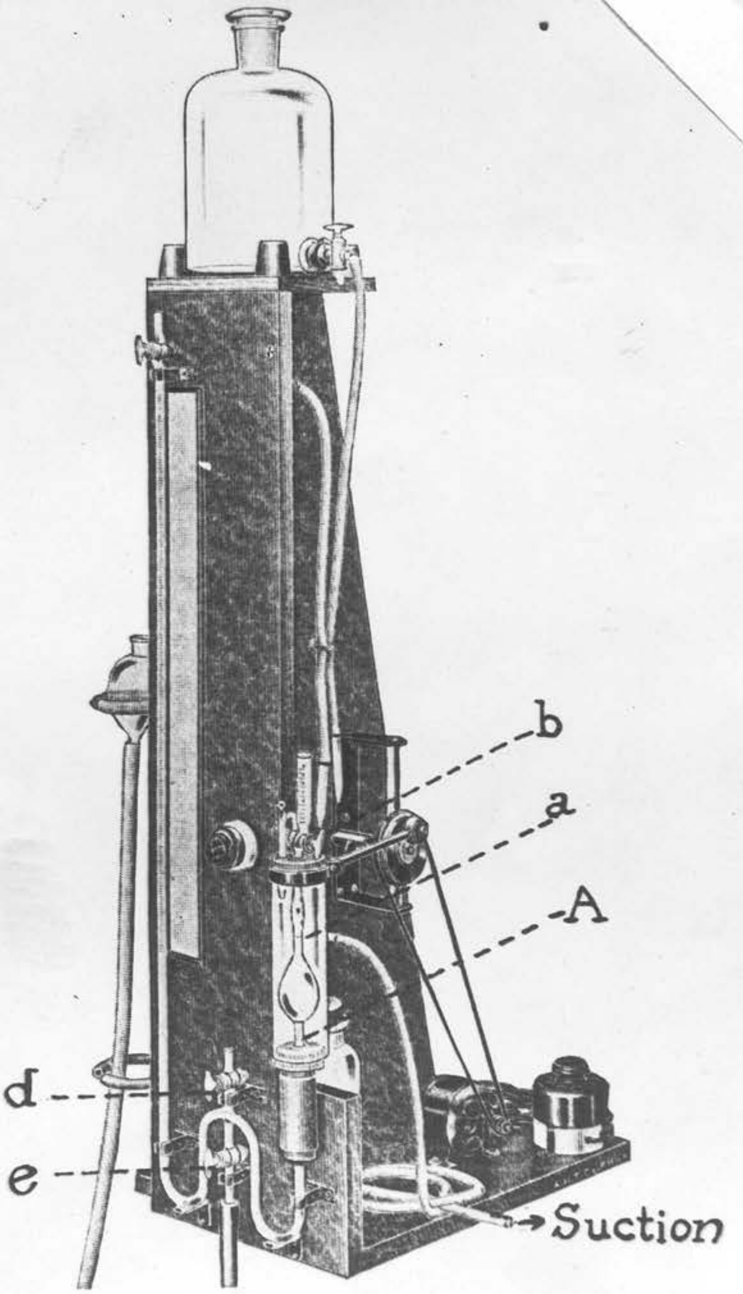


Fig. —Opera-
tion Delivery
Pi te.

Appearance of VAN SLYKE APPARATUS.


b
a
A
d
e
Suction

CO_2 free .1N lactic acid per cc. of plasma is added. Gas-free lactic acid diagram roughly shown. Stop cock b is then sealed with a drop of mercury. The CO_2 is then liberated by lowering the levelling bulb until the surface of the mercury has fallen to the mark A, closing cock e and shaking mixture for three minutes. This is done by an electrical wheel and rod; the speed of the movement can be gauged by a sliding rule. The extracted gas is reduced to 2 cc.(a), the admission of mercury being regulated by stop cock e and the levelling bulb. If the fluid meniscus should pass this point readjustment must be made by first bringing the mercury meniscus to the A mark and equilibrating for one minute. If you do not do this more re-absorption of CO_2 will take place than is provided for in the calculation. The adjustment having been done, the manometer is tapped with the finger and the height of the mixing column read off. We will call this reading $p_1$mm.

The variable amounts of CO_2 extracted from whole blood make it necessary to determine CO_2 by absorption. After measuring p_1 the pressure is diminished so that a space of several cc. is left between the water meniscus and the lower A mark. 2 cc. gas-free alkali are measured into the cup from the reservoir, avoiding re-absorption of air. 1 cc. of alkali is admitted into the chamber. Absorption is complete in 30 seconds.

After absorption of CO_2 cock b is sealed with mercury and the meniscus of the solution in the cylinder is lowered a little below the a mark. Mercury is re-admitted from cock e until the solution meniscus is again on the a mark. Cock e is left open and the reading on the manometer is taken. This is $p_2$mm.

The CO_2 pressure $P CO_2 = p: - p_2 - C$

when e is corrective.

The temperature is also read.

The CO_2 capacity - obtained from this pressure by the use of the Monogram, a copy of which I have enclosed.

The efficiency of the taps is tested by turning them off and lowering the mercury reservoir until a Torricellian vacuum is produced. It is essential that the taps are in good working order, otherwise the finer touches are lost. If the taps are efficient a sharp click will be heard on raising the reservoir.

The taps a and b are set so that the reservoir communicates with the main chamber. The mercury reservoir is raised to position 1, when the mercury will just fill the capillary stem. The cup is washed out with N/10 lactic acid. The residue is removed by means of a water suction pump. One cc. of the plasma is measured into a 1 cc. pipette (Ostwald) and is then run into cup. Before this procedure the stem is filled with about 3 or 4 cc. of N/10 gas-free lactic acid. On the end of the Ostwald pipette is a rubber stem which fits exactly the capillary stem B. As this is inserted the lactic acid runs up above the glass nozzle. The tap is closed and mercury reservoir is lowered to position 2. The tap is then cautiously opened and the liquid contained in the cup is run into the main cylinder until the upper surface of the liquid reaches the top of the capillary stem when the tap is shut. A small drop of caprыllic alcohol has been formerly sucked into chamber to prevent frothing of the mercury. 1.5 cc. of N/10 lactic acid is now sucked into chamber and mercury seal applied. The tap b is then closed. Great care has to be taken to avoid introduction of air into apparatus as whole experiment will be spoiled, and after, through waiting and getting rid of air, experiment has to be commenced again with fresh plasma.

The reservoir is now lowered still further, producing a Torricellian vacuum in the apparatus and causing CO_2 to be liberated.

The mercury level inside the apparatus will now have fallen to the 50 cc. mark and the tap e is closed.

The bulb is now shaken by means of an electrically driven machine which causes apparatus to move backwards and forwards. The speed of this movement can be controlled by a slide. This shaking should go on for 2 to 4 minutes. The tap e is now opened and solution is allowed to run into trap. When the upper surface of the liquid reaches the top of the capillary in the tap it is rapidly reversed and the mercury reservoir raised. The mercury will then run into the main chamber. The height of the reservoir is so arranged that the levels inside and outside the apparatus are the same when the volume of gas is read off.

Despite the ingenious method of trapping, a minute quantity of water will collect above the mercury, but if the reading be made at once no correction need be applied for the amount of CO_2 absorbed by this minute volume.

The volume of gas is then reduced to standard pressure by multiplying by the factor obtained from Table I, balancing the figure corresponding to the barometer reading for the day.

By means of Table II. the temperature factor is allowed for, and by means of the right hand columns the bicarbonate equivalent can be determined.

Monogram for calculation is attached. Devised by Van Slyke and J. M. Neill.

It is convenient here to give the percentage of CO_2 combining power as estimated by Van Slyke in various conditions.

PERCENTAGES found by VAN SLYKE.

	CO_2 capacity cc. per 100 cc.
30 normal students	52 to 79
acidosis (mild)	44
acidosis (severe in terminal stages of chronic interstitial nephritis)	34
acidosis severe after anaesthesia	32
Fatal diabetic coma	21
Diabetes without coma	34

Van Slyke suggests that if a number of determinations have to be made each day it is advisable to instate special apparatus.

The saturation of plasma with CO_2 is effected by passing a mixture of 5.5 % CO_2 in air from a cylinder (supplied by the British Oxygen Company), through the plasma for five minutes after the addition of capryllic alcohol. If a long glass tube with a number of side tubes at right angles be employed, a number of sera can be saturated at once. This method standardizes the saturation and eliminates the individual factor of alveolar air. This method is now used universally and the old method of using your own alveolar air is discarded as each alveolar air varies and also causes operator much respiratory embarrassment.

The apparatus nowadays is incorporated in a vertical board hinged to the base board of the apparatus. This is connected to a wheel by an eccentrically placed connecting rod, so that on rotation of the wheel by a motor, mechanical shaking of the apparatus occurs. This is done for two minutes as already described. By this means every part of the estimation is standardized and consistent results are obtained. The normal limits of CO_2 capacity were found by Van Slyke to be from 53 to 77 cc. per 100 cc. of plasma.

TABLE I.

BAROMETER	BAROMETER / 760	BAROMETER	BAROMETER / 760
732	0.961	756	0.995
734	0.966	758	0.997
736	0.968	760	1.000
738	0.971	762	1.003
740	0.974	766	1.008
742	0.976	768	1.011
744	0.979	770	1.013
746	0.981	772	1.016
748	0.984	774	1.018
750	0.987	776	1.021
752	0.989	778	1.024
754	0.992		

Van Slyke.

TABLE II.

TABLE FOR CALCULATION OF CO_2 COMBINING POWER OF PLASMA.

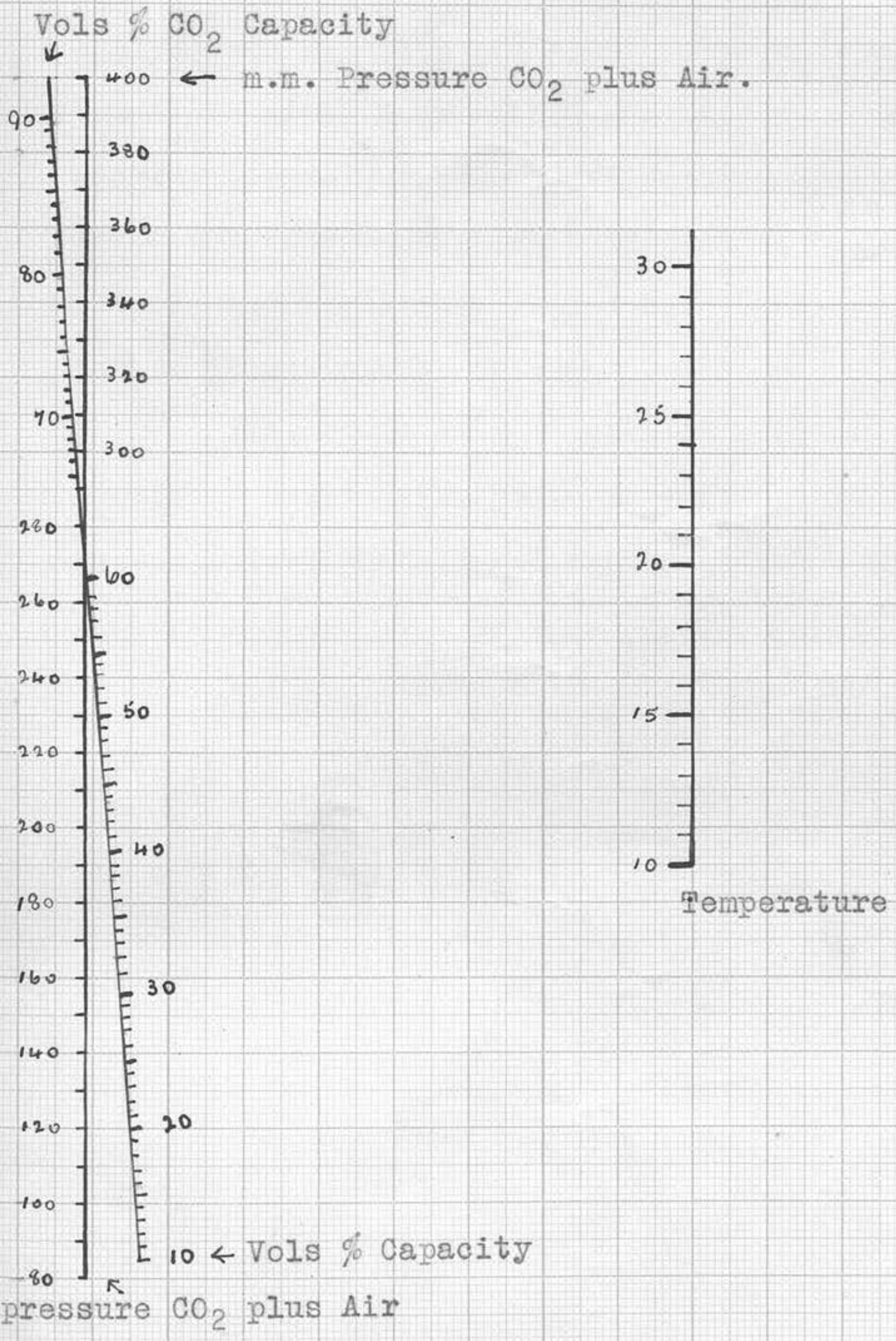
Observed Vol.Gas x $\frac{B}{760}$	Cc. of CO_2 reduced to 0°760 mm. bound as bicarbonate by 100 cc. of Plasma.				Observed Vol.Gas x $\frac{B}{760}$	Cc. of CO_2 reduced to 0° 760 mm. bound as bicarbonate by 100 cc. of Plasma.			
	15	20	25	30		15	20	25	30
0.20	9.1	9.9	10.7	11.8	0.60	47.7	48.1	48.5	48.6
1	10.1	10.9	11.7	12.6	1	48.7	49.0	49.4	49.5
2	11.0	11.8	12.6	13.5	2	49.7	50.0	50.4	50.4
3	12.0	12.8	13.6	14.3	3	50.7	51.0	51.3	51.4
4	13.0	13.7	14.5	15.2	4	51.6	51.9	52.2	52.3
5	13.9	14.7	15.5	16.1	5	52.6	52.8	53.2	53.2
6	14.9	15.7	16.4	17.0	6	53.6	53.8	54.1	54.1
7	15.9	16.6	17.4	18.0	7	54.5	54.8	55.1	55.1
8	16.8	17.6	18.3	18.9	8	55.5	55.7	56.0	56.0
9	17.8	18.5	19.2	19.8	9	56.5	56.7	57.0	56.9
0.30	18.8	19.5	20.2	20.8	0.70	57.4	57.6	57.9	57.9
1	19.7	20.4	21.1	21.7	1	58.4	58.6	58.9	58.8
2	20.7	21.4	22.1	22.6	2	59.4	59.5	59.8	59.7
3	21.7	22.3	23.0	23.5	3	60.3	60.5	60.7	60.6
4	22.6	23.3	24.0	24.5	4	61.3	61.4	61.7	61.6
5	23.6	24.2	24.9	25.4	5	62.3	62.4	62.6	62.5
6	24.6	25.2	25.8	26.3	6	63.2	63.3	63.6	63.4
7	25.5	26.2	26.8	27.3	7	64.2	64.3	64.5	64.3
8	26.5	27.1	27.7	28.2	8	65.2	65.3	65.5	65.3
9	27.5	28.1	28.7	29.1	9	66.1	66.2	66.4	66.2
0.40	28.4	29.0	29.6	30.0	0.80	67.1	67.2	67.3	67.1
1	29.4	30.0	30.5	31.0	1	68.1	68.1	68.3	68.0
2	30.3	30.9	31.5	31.9	2	69.0	69.1	69.2	69.0
3	31.3	31.9	32.4	32.8	3	70.0	70.0	70.2	69.9
4	32.3	32.8	33.4	33.8	4	71.0	71.0	71.1	70.8
5	33.2	33.8	34.3	34.7	5	71.9	72.0	72.1	71.8
6	34.2	34.7	35.3	35.6	6	72.9	72.9	73.0	72.7
7	35.2	35.7	36.2	36.5	7	73.9	73.9	74.0	73.6
8	36.1	36.6	37.2	37.4	8	74.8	74.8	74.9	74.5
9	37.1	37.6	38.1	38.4	9	75.8	75.8	75.8	75.4
0.50	38.1	38.5	39.0	39.3	0.90	76.8	76.7	76.8	76.4
1	39.1	39.5	40.0	40.3	1	77.8	77.7	77.7	77.3
2	40.0	40.4	40.9	41.2	2	78.7	78.6	78.7	78.2
3	41.0	41.4	41.9	42.1	3	79.7	79.6	79.6	79.2
4	42.0	42.4	42.8	43.0	4	80.7	80.5	80.6	80.1
5	42.9	43.3	43.8	43.9	5	81.6	81.5	81.5	81.0
6	43.9	44.3	44.7	44.9	6	82.6	82.5	82.4	82.0
7	44.9	45.3	45.7	45.8	7	83.6	83.4	83.4	82.9
8	45.8	46.2	46.6	46.7	8	84.5	84.4	84.3	83.8
9	46.8	47.1	47.5	47.6	9	85.5	85.3	85.2	84.8
0.60	47.7	48.1	48.5	48.6	1.00	86.5	86.2	86.2	85.7

Van Slyke.

MONOGRAM FOR CALCULATION OF PLASMA CO_2 CAPACITY

A straight line connecting the observed points on the pressure and temperature scale cuts the CO_2 capacity scale at the point indicating the capacity.

D.D. Van Slyke and J.M. Neill.


Vols % CO2 Capacity
m.m. Pressure CO2 plus Air.
400
380
360
340
320
300
280
260
240
220
200
180
160
140
120
100
80
90
80
70
60
50
40
30
20
10 ← Vols % Capacity
30
25
20
15
10
Temperature
m.m. pressure CO2 plus Air

MONOGRAM FOR CALCULATION OF PLASMA CO_2 CAPACITY.

A straight line connecting the observed points on the pressure and temperature scale cuts the CO_2 capacity scale at the point indicating the capacity.

Stewart and Dunlop state that the CO_2 combining power of the blood of normal healthy individuals actually varies within wide limits. They have obtained values as low as 53 vols.%, and as high as 79% in individuals who were apparently perfectly normal. Van Slyke gives values from 52% to 79%, as already stated. These variations are not due to experimental error but represent actual differences between individuals and variations in the same individual purely due to physiological causes.

They state that an acidaemia exists when CO_2 combining power falls below 53 vols.%, and an alkalaemia exists when it has risen above 80 vols.%.

PART III.

CASES.

I will describe a number of cases which I have examined and in which a fairly full blood chemistry examination has been made. These cases are of various pathological conditions, and all have some significance in their evidence of the state of the acid base equilibrium.

First of all I will tabulate the number of cases under the headings of the various diseases. Nextly will be tabulated the CO_2 combining power result measured in each case, and give the average CO_2 combining power for the given condition as found.

Following on this I will give a brief clinical history of each case, noting any special investigation made and also the other Blood Chemistry findings.

CASES.

1. Chronic Interstitial Nephritis....	11	Cases
2. Myocarditis with no primary renal lesion	3	"
3. Acute Nephritis	1	"
4. Epilepsy	2	"
5. Toxic Goitre	1	"
6. Alcoholic Neuritis	1	"
7. Tb. Meningitis & ? Cerebral Tumour	2	"
8. Abdominal Colic with Abdominal obstruction	1	Case

PART III.

CASES.

The next table will show the estimation of the CO_2 combining power made in each of these Cases, and also the age of the patient. The pathological condition in each case will also be included.

1. CHRONIC INTERSTITIAL NEPHRITIS.

	Patient.	Diagnosis.	CO_2 Combining Power vols.%
1.	S.F.	Uraemia + oedema + Cardiac failure.	58 vols.%
2.	W.T.	No uraemia-cardial feature.	64 vols.%
3.	S.R.	No uraemia.	69 vols.%
4.	S.R.	Uraemia. Secondary anaemia, Cardiac failure.	49 vols.% 49 vols.%
5.	W.C.	Uraemia with progressive Cardiac failure.	47.5 vols.% 40.5 vols.% 53 vols.% 50 vols.%
6.	H.M.	Uraemia	43.5 vols.%
7.	M.F.	No uraemia - no dropsy Albumenine retention.	70 vols. %
8.	W.A.	No uraemia; marked hyperpieris .	65 vols. %
9.	R.D.	Uraemic seizures. Albumen retention	65 vols. %
10.	D.McL.	Uraemia - cardio-renal syndrome. Albumine retention.	40 vols. %
11.	J.McN.	No uraemia - hyperpieris	69 vols. %

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2. MYOCARDITIS with no Primary Renal Lesion.

1. J.W. Oedema 56 vols.%

Patient.	Diagnosis	CO_2 combining Power vols.%
2. A.C.	Oedema, marked.	later 59 vols.% 68 vols.%
3. J.E.	Marked oedema.	58 vols.%

3. ACUTE NEPHRITIS.

1. J.B.	64.5 vols.% 69 vols.% 69 vols. % 65 vols. %

4. EPILEPSY.

1. H.S.	60 vols.%
2. J.B.	67 vols.%

5. TOXIC GOITRE.

1. H.McE.	63.5 vols.%

6. ALCOHOLIC NEURITIS.

1. S.K.	56 vols. %

7. Tb. MENINGITIS & ? CEREBRAL TUMOUR.

1. H.B.	65 vols. %
2. E.G.	68 vols. %

8. ABDOMINAL COLIC.

1. J.B.	63.5 vols. %

From perusal of the following figures we can work out the average. CO_2 combining power reading for each condition investigated. The average age of the patient under survey will also now be tabulated. The patients were all in-patients in one of the Wards of the Royal Infirmary and the investigations were carried out while they were as such.

1. CHRONIC INTERSTITIAL NEPHRITIS.

(a) Uraemias.

Average age = 61-32-53-60-43 = 49.8 years.

Average CO_2 combining power reading. = 58-49-47.5-43.5-40 = 47.6 vols.% CO_2 combining power

(b) Non-uraemias.

Average age: 54-55-53-53-41-47 = 50.5 years.

Average CO_2 combining power reading: 64-69-70-65-63-69 = 66.6 vols.% CO_2 combining power

2. MYOCARDITIS with no Primary Renal Lesion.

Average age: 40 - 56 - 57 = 51 years.

Average CO_2 combining power reading: 56-59-58 = 57.8 vols.% CO_2 combining power.

3. ACUTE NEPHRITIS with no Uraemic Symptoms.

Age: 32 years.

Average CO_2 combining power reading: 64.5-69-69 = 67.5 vols.% CO_2 combining power.

4. EPILEPSY.

Average age : 35 - 45 = 40 years.

Average CO_2 combining power reading: 60 - 67 = 63.5 vols.% CO_2 combining power.

5. TOXIC GOITRE.

Age = 35 years.

CO_2 Combining power reading = 63.5 vols.% CO_2 Combining power.

6. ALCOHOLIC NEURITIS.

Age = 45 years.

CO_2 Combining power reading = 56 vols.% CO_2 combining power.

7. TB. MENINGITIS & ? CEREBRAL TUMOUR.

Average age = 63 - 20 = 41.5 years.

Average CO_2 combining power reading: 65 - 68 = 66.6 vols.% CO_2 combining power.

8. ABDOMINAL COLIC.

Age = 43 years.

CO_2 combining power reading = 63.5 vols.% CO_2 combining power.

Now, taking each case separately, I will describe where possible a short clinical history with salient features regarding the Blood Chemistry findings.

To begin with:-

Cases 1 - 11. All are cases with chronic interstitial nephritis, with or without uraemic symptoms, as already stated.

Case 1. S.F. Aged 61 years.

He was admitted to the Royal Infirmary with a history of breathlessness on even slight exertion for one week. He stated he had been previously quite healthy until January 1933, when he had an attack of influenza. This, he states, left him with a chronic cough and some breathlessness on exertion.

On examination it was found that he had some incompetency of the aortic valve and concomitant chronic interstitial myocarditis. He had renal changes suggestive of chronic interstitial nephritis.

His Wasserman reaction was negative.

On admission oedema was present but not markedly so; later it increased in spite of diuretics.

His blood pressure was on the high side but not markedly so for a man of his age.

His oedema increased and he gradually grew worse. He had what was diagnosed as a slight cerebral haemorrhage and he died a short time after this, in a semi-comatose state until near the end.

Unfortunately no blood chemistry findings were able to be carried out later.

After he had been in hospital one week his Blood Chemistry was:-

CO_2 combining power	58 vols.%
Albumen	3.85 grams %
Globulin	2.10 " %

CASE 2. W.T. Aged 54 years.

He was found to be suffering from chronic interstitial nephritis. His blood pressure was 180 systolic, 120 diastolic.

His blood chemistry figures were:-

CO_2 combining power 64 vols.%

N.P.N...... 34 mgs.%

Creatine .. 1.4 mgs.%

Urea concentration test - normal.

Urine contained blood - albumen - urates and casts.

CASE 3. S.R. Aged 54 years.

He was found to be suffering from chronic interstitial nephritis with cardiac failure.

His blood chemistry findings were:-

CO_2 combining power 69 vols.%

Albumen .. 2.94 grams %.

Globulin . 1.94 grams %

CASE 4. S.R. Aged 32 years.

She was diagnosed as chronic interstitial nephritis with uraemia and marked secondary anaemia.

Blood Chemistry findings:-

On admission: N.P.N. 211 mgs.%
Creatine 5 mgs.%

1 week after admission: N.P.N. 212 mgs.%
Creatine 5 mgs.%

3 weeks after admission: CO_2 combining power: = 49 vols.%

CO_2 combining power on day of death was 49 vols.%

She had continuous haemorrhages from the bowel which were found at autopsy to be due to uraemic ulceration.

CASE 5. W.C. Aged 53 years.

This was a case of chronic interstitial nephritis. His previous history was not of any note excepting history of Scarlet Fever at the age of 10. Blood pressure on admission was systolic 230, diastolic 110.

Patient had a relative mitral incompetence and a dilated heart. He was very breathless and oedematous. All the clinical signs of cardiac insufficiency were very marked.

For a time in hospital he improved, his blood pressure came down although the diastolic pressure always remained about 120 to 130 mm. Hg.

The urinary output was fairly satisfactory. Patient was given ammonium chloride + neptal with fairly satisfactory results.

Later, however, every diuretic tried was of no avail - patient becoming very oedematous and very drowsy. Diastolic blood pressure fell from 130 to 120, 110, 100 and 60 mm. Hg. The systolic blood pressure more or less remained high throughout this fall of diastolic pressure.

Patient towards the end was semi-conscious and showed marked twitching movements of the limbs.

Blood Chemistry findings were:-

On admission.	10 days later.	16 days later	32 days. later.
CO_2 combining power ....47.5 vols.%	40.5 vols.%	53 vols. %	50 vols.%
N.P.N. ... 75 mgs.%	70 mgs. %	-	7 mgs. %
Creatine .. 3 mgs.%	2.4 mgs.%	-	2.9 mgs.%
Albumen ... 3.53 gr.%	-	4.53 grams %	3.13 grams %
Globulin .. 1.82 gr.%	-	1.88 grams %	2.75 grams %

CASE 6. H.M. Aged 60 years.

Diagnosed as chronic interstitial nephritis with uraemia. She was comatose on admission and for subsequent 3 days before death. Suppression of urine necessitated passing of catheters. Venesection and lumbar puncture with high colon lavage and massive doses of purgatives was the line of treatment.

Her blood pressure was - systolic 166, diastolic 110. There was no marked oedema.

Findings.

CO_2 combining power	43.5 vols. %
N.P.N.	40 mgs. %
Creatine	2.3 mgs.%

C.S.F. - Wasserman neg.
Blood - Wasserman neg.
Colloidal Gold Reaction C.S.F = 0 00,000 00

CASE 7. M.F. Aged 53 years.

She was suffering from chronic interstitial nephritis. There was no oedema. Urine contained blood albumen and casts. There was very marked albuminuric retinitis. Centrifuged urine showed granular and hyaline casts.

Blood Chemistry Findings:-

	3 weeks later.
CO_2 combining power..... 70 vols.%	CO_2 combining power ... 72 vols.%
N.P.N. ... 74 mgs. %	N.P.N. .. 70 mgs.%
Creatine..3.6 grams %	albumen. 3.4 grams %
Cholesterol 143 mgs.%	globulin 2.16 " %

CASE 8. W.A. Aged 42 years.

Case of chronic interstitial nephritis and hyperpiesis. Blood pressure was systolic 250, diastolic 154. There was no oedema.

His Blood Chemistry readings were as follows:

CO_2 combining power ... 65 vols.%
N.P.N. .... 90 mgs.%
Creatine ...... 3 mgs.%
Cholesterol ....320 mgs.%
Phosphorus .... 7.7 mgs.%
Chlorides ..... 350 mgs.%
Calcium .... 7.9 mgs.%

3 weeks later:-

N.P.N. .... 100 mgs.%
albumen ...... 4.0 mgs.%
globulin ...... 198 mgs.%

CASE 9. R.D. Aged 41 years.

He had clear evidence of chronic interstitial nephritis as shown by state of urine and of fundus oculi. On admission patient was lethargic. Ten days after admission he commenced to have seizures. These occurred frequently for one day and for the subsequent two days. Later he developed a noisy delirium for which he was given morphia and hyoscine. He has slowly but gradually improved. His present diet includes fish and chicken. Regarding present state of urine there is some little albumen but no blood. Systolic blood pressure is 200 and diastolic 130. Progress is, however, far from favourable - liability to cerebral haemorrhage or uraemia.

Blood Chemistry Findings:

On admission:

N.P.N. 33 mgs.%
Creatine 2 mgs.%

1½ weeks later:

N.P.N. 48 mgs.%
Creatine 3.1 mgs.%
CO_2 combining power 63 vols.%

1 month later:

N.P.N. 29 mgs.%
Creatine 3 mgs.%

Patient had marked albuminuric retinitis.

CASE 10. D.McL. Aged 43 years.

He was suffering from chronic interstitial nephritis with cardio-renal syndrome. On admission he had chronic congestive heart failure with pronounced dyspnoea and considerable dropsy. His blood pressure was very high and average findings were systolic 240, diastolic 130. His progress was consistently unsatisfactory. In spite of various diuretics the dropsy increased. Patient became very restless and required Sedormid, Chloral amide and latterly morphia. End came gradually with marked super-added renal failure leading up to the fatal issue.

Patient had always suffered from sore throats. There was a history of Scarlet Fever in childhood, - family history of arterio sclerosis, renal trouble and shock.

Blood Chemistry Findings:

On admission:

N.P.N. 43 mgs.%
Creatine 2.2 mgs.%

1 week later:

CO_2 combining power 40 vols.%
N.P.N. 106 mgs. %

Wasserman Reaction negative.

Urine contained - trace of albumen, one or two granular casts.

Urea Conc.Test.

Specimen 1. - 1.8 gr.%
Specimen 2. - 2.5 gr.%

CASE 11. J.McN. Aged 47 years.

He was suffering from chronic interstitial nephritis with a persistently high blood pressure, and made a fairly satisfactory recovery. There is impairment of renal function but no nitrogen retention according to blood chemical findings. The prognosis is, however, grave. He had also, on admission, acute nephritis which soon responded to dietetic treatment and rest. He also, six months previously, had a painless profuse haematuria.

Patient also had chronic interstitial nephritis as evidenced by impaired excretion of urea concentration test. His blood pressure was previously very high, necessitating on two occasions venesection.

Blood Pressure - Systolic 190 mm.Hg.
Diastolic 130 mm.Hg.

He had marked albuminuric retinitis - woolly patches and one or two flame-shaped haemorrhages.

Urine: Albumen +

micros numerous granular and a few hyaline casts and R.B.C.

Treatment given was light diet - low protein
Pot.iod. gr.X t.i.d.
later Trinitrin gr.$\frac{1}{100}$ t.i.d.

Blood Chemistry Findings:

After 2 weeks:

CO_2 combining power	69 vols.%
N.P.N.	28 mgs. %
Creatine	2.0 mgs.%

11 days later.

Albumen	4.5 grams %
Globulin	2.87 " %
N.P.N.	30 mgs.%
Creatine	2.2 mgs.%
Calcium	12.1 mgs.%

Urea concentration.

No specimen before urea.

2nd specimen	.8 grams %
3rd specimen	1.0 grams %

CASES 12 to 14 are cases of myocarditis with no primary renal lesion.

CASE 12.

J.W. Aged 40 years.

He was suffering from chronic interstitial myocarditis with no primary renal lesion. There was some initial stenosis present. He had one year's history of breathlessness on exertion. At present breathlessness even when lying in bed. He has marked oedema.

Blood Chemistry Findings.

CO_2 combining power .. 56 vols.%
Albumen ...... 3.6 grams %
Globulin ...... 2.33 " %

Wasserman Reaction negative.

CASE 13. A.C. Aged 56 years.

His complaint was breathlessness on exertion for six weeks. He was suffering from chronic myocarditis.

His Wasserman reaction was negative and he was markedly oedematous.

On admission.

CO_2 combining power was 68 vols.%
Albumen ... 3.8 grams %
Globulin .. 2.52 " %
Icteric index .. 5

3 weeks later.

CO_2 combining power was 59 vols.%
Albumen ..... 3.7 grams %
Globulin .... 2.19 " %
Icteric index .. 5.

CASE 14.

J.E. Aged 57 years.

Was only six days in hospital. She had marked myocardial failure. She was very oedematous on admission and never made much progress in spite of diuretics, digitalis, and finally Southey's tubes.

She was a case of marked cardiac failure with no previous rheumatic history. There was a considerable pulse deficit.

Treatment included:-

Tinc. Digitalis mxx t.i.d.
Theocin Sod. acet. gr.iii t.i.d.

later Nativelle's Digitalein gr. $\frac{1}{240}$ tds.
Diuretin gr.XV tds.

Urine contained - Pus cells + B.Coli, Squamous epithelium and granular debris and casts.

Blood Chemistry Findings:

CO_2 combining power .. 58 vols.%
Albumen ..... 4.06 grams %
Globulin .... 1.13 grams %

Wasserman reaction - negative.

CASE 15.

J.B. Aged 32 years.

He was suffering from acute nephritis. On admission he was dropsical and urine contained blood albumen and tube casts. His progress was satisfactory though slow. It was interrupted by a slight recrudescence of haematuria. His urine still contains a trace of albumen. His blood pressure is within normal limits.

Treatment prescribed was:- Light diet with restriction of proteins of animal origin, - jalap and hot-air baths. Fruit juice daily with glucose 20 grams. Later he got cornflour and banana, then bread and butter, and later still potato and vegetable.

Microscopic examination of urine showed -

Numerous R.B.C.
few W.B.C.
Hyaline and cellular casts and
granular débris.

Blood Chemistry Findings.

On admission.	1 month later.	2 months later.
CO_2 combining power .....64.5 vols.%	69 vols.%	65 vols.%
Albumen .. 4.63 grams.%	3.15 grams %	3.94 grams %
Globulin . 2.13 " %	2.8 " %	2.75 " %

His blood pressure on discharge was -

systolic ... 110
diastolic .. 75.

CASES 16 and 17 were both suffering from Epilepsy.

CASE 16. H.S. Aged 35 years.

He was suffering from recurring fits which were diagnosed as being epileptic in nature.

Blood Chemistry Findings.

CO_2 combining power .. 60 vols.%
N.P.N. ..... 30 mgs. %
Sugar ..... 94 mgs. %

CASE 17. J.B. Aged 45 years.

He was suffering from recurring fits which were diagnosed as being of an epileptic form.

Blood Chemistry Findings.

CO_2 combining power .. 67 vols.%
N.P.N. ...... 34 mgs. %
Sugar ...... 80 mgs. %

CASE 18.

H.McE. Aged 35 years.

He was suffering from toxic goitre.

Blood Chemistry Findings.

CO_2 combining power ... 63.5 vols.%
Sugar .... 95 mgs. %

B.M.R. on two occasions was +70%
later +47%.

CASE 19.

G.R. Aged 45 years.

She had a large mass on the right side which was considered to be renal in origin. It was found on urological examination that there was present two renal pelvi on the right side. There was no evidence of nitrogenous products on blood examination.

Blood Chemistry Findings.

CO_2 combining power ... 56 vols.%
N.P.N. ..... 26 mgs. %
Creatine .... 1.8 mgs.%

She was also suffering from neuritis of the lower limbs, which was found to be caused by over-indulgence in alcohol.

CASE 20.

H.B. Aged 63 years.

This patient was admitted in a semi-comatose condition. Her condition was considered to be one of uraemic coma. Her urine had albumen and casts but no sugar. On autopsy, however, her condition was found to be one of tuberculous meningitis.

Blood Chemistry Findings.

CO_2 combining power .... 65 vols.%
N.P.N. .... 40 mgs. %
Creatine .... 2.1 mgs.%

CASE 21.

E.G. Aged 20.

She was admitted in a semi-conscious state and last time seen was very lethargic, suffering from very severe headache and showing marked eye symptoms.

Her condition has been diagnosed as one of cerebral tumour or cerebral abscess.

She is running a slight temperature and has a leucocytosis of 12,000. Her previous history included a discharging ear two years ago.

Blood Chemistry Findings.

CO_2 combining power .... 68 vols.%
N.P.N. .... 30 mgs. %
Chlorides ....560 mgs. %

No lumbar puncture has as yet been done.

CASE 22.

J.B. Aged 43 years.

He was admitted suffering from severe abdominal colic and obstruction. He had no vomiting.

Blood Chemistry Findings.

CO_2 combining power ....63.5 vols.%
Albumen .... 3.78 grams %
Globulin .... 2.14 grams %
N.P.N. .... 29 mgs. %

It would be convenient here to summarize all chemical findings in the form of a Chart. In this way they can all be compared one with another.

To begin with, summarizing the CO_2 combining power findings in the cases of chronic interstitial nephritis, we find:-

A. URAEMIAS.		B. NON-URAEMIAS.	
1. S.F.	58 vols.%	1. W.T.	64 vols.%
2. S.R.	49 vols.%	2. S.R.	69 vols.%
3. W.C.	47.5 vols.%	3. M.F.	70 vols.%
4. H.M.	43.5 vols.%	4. W.A.	65 vols.%
5. D.McL.	40 vols.%	5. R.D.	63 vols.%
		6. J.McN.	69 vols.%

The average as already stated for

A is 47.6 vols.% CO_2 combining power.

B is 66.6 vols.% CO_2 combining power.

COMPARISONS of OTHER CHEMICAL FINDINGS and THE CO_2 COMBINING POWER.

Case	Name.	Vols. CO_2 combin- -ing Power.	Albumen Globulin	N.P.N.	Creatine.	Choles- -trol.	Chlorides.	Phosphorus.	Cal- cium.
1.	S.F.	58	3.85 mgs.% 2.10 mgs.%	-	-	-	-	-	-
2.	W.T.	64	-	34 mgs.%	1.4 mgs.%	-	-	-	-
3.	S.R.	69	2.94 gms.% 1.94 " %	-	-	-	-	-	-
4.	S.R.	(a) 49 (b) 49	-	(a) 211 mgs.% (b) 212 " %	(a) 5 mgs.% (b) 5 " %	-	-	-	-
5.	W.C.	(a) 47.5 (b) 40.5 (c) 53 (d) 50	(a) 3.53 gms.% 1.82 " % (c) 4.53 " % 1.88 " % (d) 3.13 " % 2.75 " %	(a) 75 mgs.% (b) 70 " % (d) 71 " %	(a) 3 mgs.% (b) 2.4 " % (d) 2.9 " %	-	-	-	-
6.	H.M.	43.5	-	40 mgs.%	2.3 mgs.%	-	-	-	-
7.	M.F.	(a) 70 (b) 72	(b) 3.40 gms.% 2.6 " %	(a) 74 mgs.% (b) 70 " %	(a) 3.6 mgs.% (b) 3.6 " %	(a) 143 mgs.%	-	-	-
8.	W.A.	(a) 65	(b) 4.00 gms.% 1.98 " %	(a) 90 mgs.% (a) 100 " %	(a) 3 mgs.%	(a) 320 mgs.%	(a) 350 mgs.%	(a) 7.7 mgs.%	(a) 7.9 mgs %
9.	R.D.	(b) 63	-	(a) 33 mgs.% (b) 48 " % (c) 29 " %	(a) 2 mgs.% (b) 3.1 " % (c) 3 " %	-	-	-	-
10.	D.McL.	(a) 40	-	(a) 166 mgs.% (b) 43 " %	(b) 2.2 mgs.%	-	-	-	-
11.	J.McN.	68.5	-	40 mgs.%	-	-	-	-	-
12.	J.W.	56	3.6 gms.% 2.33 " %	-	-	-	-	-	-

COMPARISONS of OTHER CHEMICAL FINDINGS and the CO_2 COMBINING POWER (Contd.)

Case.	Name.	Vols.CO2 Combining Power	Albumen Globulin	N.P.N.	Creatine.	Chole: strol	Chlorides	Phos: phorus	Cal- cium.	Sugar.
13.	H.C.	(a) 68 (b) 59	(c) 3.8 gms.% 2.52 " % (b) 3.7 " % 2.19 " %	-	-	-	-	-	-	-
14.	J.E.	58	4.06 gms.% 1.13 " %	-	-	-	-	-	=	-
15.	J.B.	(a) 64.5 (b) 69 (c) 65	(a) 4.63 gms.% 2.13 " % (b) 3.15 " % 2.8 " % (c) 3.94 " % 2.75 " %	-	-	-	-	-	-	-
16.	H.S.	60	-	30 mgs.%	-	-	-	-	-	94 mgs. %
17.	J.B.	67	-	34 mgs.%	-	-	-	-	-	80 mgs. %
18.	H.McE.	63.5	-	-	-	-	-	-	-	95 mgs. %
19.	S.R.	56	-	26 mgs. %	1.8 mgs.%	-	-	-	-	-
20.	H.B.	65	-	40 mgs. %	2.1 mgs.%	-	-	-	-	-
21.	E.G.	68	-	30 mgs. %	-	-	56 mgs.%	-	-	-
22.	J.B.	63.5	3.98 gms.% 2.14 " %	29 mgs. %	-	-	-	-	-	-

PART IV.

SUMMARY.

PART IV.

SUMMARY.

It will be seen from this investigation that the Physiology of Acid Base Equilibrium is a complicated one. Recently, however, by the numerous excellent observations made it has been shown in a clearer light. One can see that it is essential that the excretory powers of the Kidney must be in first class order or, as has been shown, the acid base equilibrium is in time thrown out of gear. There are various compensating mechanisms, but as the damage to the excretory cells of the Kidney increase, then, even allowing for balance of compensation, the normal reaction of the blood changes, and we get an excess acid state which gives one all the noted clinical features of uraemia.

It is noted that the Kidney is less sensitive than the respiratory centre in its recognition of alterations in blood reaction, and, as is often the case, it takes some time before it really comes into action.

The Van Slyke apparatus is an excellent means by which this state of acid or alkaline toxaemia can be examined. The investigation of the CO_2 combining power of the blood plasma is fairly simply carried out and it should be one of the essential investigations in any case where the acid base equilibrium is suspected to be altered.

At this stage it is convenient to give a list of the conclusions which I have arrived at in this investigation. I mention them in half sentences and not in any order of importance.

CONCLUSIONS.

1. There is a marked fall in the CO_2 combining power of the blood plasma in states of uraemia as estimated by the Van Slyke apparatus.

2. Relative normal in Chronic Interstitial Nephritis where there is no clinical evidence of uraemia.

3. If the CO_2 combining power reading of the blood plasma remains high then less likelihood of uraemia supervening.

4. Suggested early treatment of uraemia before definite clinical signs of this condition appear if one finds the reading of the CO_2 combining power commencing to fall.

5. Patient is more likely to die suddenly of cerebral haemorrhage than go into uraemic coma if the CO_2 combining power reading remains high. (It

is in cases of high blood pressures:- all the cases I have mentioned had relatively high blood pressures.)

6. CO_2 combining power reading of the blood plasma is of useful diagnostic value in comatose or semi-comatose patients. If the CO_2 combining power reading is high then less likelihood of patient being in uraemic coma.

7. If CO_2 combining power reading is low in an unconscious patient and after examination of urine no sugar is found, the patient is likely to be in uraemic coma.

8. Findings are not so low in this short series of cases as others have found (i.e. the CO_2 combining power readings of the blood plasma).

9. There is no particular correlation between the CO_2 combining power findings and the blood chemistry findings.

10. CO_2 combining power readings useful in diagnosis of epileptic seizures from uraemic convulsions, if any dubiety should arise in the diagnosis.

11. Relative lowness of supposed normal figures found as compared to those found by Van Slyke, Dunlop Stewart and others. (as in cases 16, 17, 18, 20, 21 & 22)

12. Findings certainly suggest that if CO_2 combining power of the blood plasma readings are below 50 patient in serious danger of going into uraemic coma if not already so.

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