A C I D O S I S

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Acidosis is a subject as yet imperfectly understood. Recently the literature on the subject has been greatly added to, but there is much ground to cover before the disease is made one that the General Practitioner can readily diagnose. An attempt is made in this paper to bring together much that has been written on the subject, and to contrast some of the diagnostic methods in use at present.

It is seventy years since the subject was first investigated. Bousingault was the first to turn his attention to the subject of Acidosis. In 1850 he discovered that large amounts of ammonia was found in diabetic urine. His methods and results were not accepted by contemporary investigators.

Miquel administered sulphuric acid by the mouth to dogs, and Salkowski used taurin, which yields sulphuric acid in the body, to poison rabbits; he demonstrated excessive loss of alkalies in the urine.

Walter was the investigator who placed beyond doubt the pathological significance of the withdrawal of alkalies by the administration of mineral acids. He showed that 0.9 grammes of Hydrochloric acid by the mouth per diem was constantly fatal for rabbits, and/

and that the carbon dioxide content of the still faintly alkaline blood of such animals was greatly reduced. The study of the effect of administration of acids in animals has been pursued for the past thirty years, with the result of greatly extending, and in the main confirming, the conclusions of Walter.

In 1857 Petter showed that the penetrating odour of the breath of diabetics is caused by acetone, and he first referred the coma of diabetics to acetone poisoning. Later Kaulich described a group of nervous symptoms as a characteristic clinical picture of acetonemia.

The first demonstration of acid substances in the acetone series was accomplished by von Jaksch, who in 1883 showed that the ferric chloride reaction in diabetic urine was due to the presence of diacetic acid.

Stadelmann proved that diabetic urine contains a great excess of bases over that required to neutralize the inorganic acids, and hence that some unknown organic acid must exist in the highly acid urine.

Kulz and Minkowski demonstrated beta-oxybutyric acid as the questionable acid in diabetic urine.

The term Acidosis has called forth a great variety of definitions.

Naunyn/

Naunyn describes the term as "the appearance of large quantities of non-combustible acids in the metabolism." This is what is recognised as "true" or "absolute acidosis."

Steinitz introduces a "relative acidosis", which has in common with the true acidosis of Naunyn an increase of ammonia in the urine. It is not an absolute increase of acids, but a relative predomination of them, which is a normal occurrence in consequence of the deprivation of carbohydrates. Relative acidosis is really a deficiency in the alkalies.

Cantley defines acidosis as an abnormal metabolism of carbon, leading to the appearance of organic acids in the blood and urine, and the formation of ammonia to neutralize these acids.

Metcalf believes that acid auto-intoxication, recurrent vomiting, and cyclic vomiting are merely degrees of acidosis.

Beddard says that if we take a normal man on an ordinary diet as our standard, we say that whenever there is evidence that the body is using these neutralizing bases to an excessive degree an acidosis is present.

The/

The cause of acidosis.

Life is incompatible with acidity, for not only animal but plant life as well demands for its continuence an alkaline or at least a neutral medium. The tissue fluids and blood with which the living cells of the body are bathed, have a reaction, which may be roughly described as being just on the alkaline side of neutral. Acidosis existed whenever the acidity of the urine was higher than normal.

Man depended upon the removal of acid by the liver and the kidneys. When this was not readily performed, or when the acid content of the blood appeared greater than neutral, death ensued automatically.

Beddard says there are three groups of acids which produce acidosis.- (a) acids introduced into the body from the outside as hydrochloric acid, (b) inorganic acids formed in the body, as sulphur and phosphoric acids, these are formed from proteids; (c) organic acids, also formed in the body, they include lactic acid and acetone bodies.

When acids are either absorbed from the intestine or formed out of intermediary products there is absolute acidosis, but if acids while still in the intestine/

intestine are neutralized by alkalies taken in food or obtained from the tissues, or if fixed alkalies are withdrawn from the body in some other way (as Diarrhoea), a relative acidosis results.

The most dangerous result of the formation of acetone and its allies is the flooding of the circulation and tissues with acids.

The acetone bodies found in urine in the condition known as acidosis, are Acetone $CH_3 CO. CH_3$, Aceto-acetic acid $CH_3 CO.CH_2 COOH$, B Oxybutyric acid $CH_3 CH(OH)CH_2 COOH$. B Oxybutyric acid is readily oxidised to aceto-acetic acid, and this is converted into acetone by the loss of CO_2. The two acids are never found in urine unaccompanied by acetone, but acetone may be present without the acids. The excretion of the acetone bodies depends on the inability of the tissues to oxidise completely the fatty acids generally derived from the fats, but sometimes from certain of the amino-acids formed in the metabolism of proteins. The condition that usually gives rise to acetonuria or acidosis is the inability of the tissues to obtain or to utilise an adequate amount of glucose. Thus these acetone bodies are excreted in starvation, on a diet of fats with a limited amount of protein, in certain fevers, severe anaemias, and after phosphorus poisoning, and finally in diabetes mellitus,/

mellitus, in which condition the tissues are unable to utilise the glucose provided.

The three closely related substances, B-Hydroxybutyric acid, Aceto-acetic acid, and acetone, are generally referred to in medical literature as the acetone bodies. There is no basis for the older statement that mild cases of diabetes excrete only acetone, that severer cases excrete acetone and aceto-acetic acid, and that still severer cases excrete B-Hydroxybutyric acid in addition. It seems to have been due to the misinterpretion of the tests, and to the inadequacy of our methods of estimating these substances.

The occurrence of acetone in the breath can be accounted for by the difference in the blood circulation. This is slow through the systemic systems and lung capillaries, through which the blood passes before it goes to the kidney. Venous blood is more acid than arterial blood, so that the conditions for the decomposition of aceto-acetic acid are most favourable. Acetone is very volatile, and if decomposition occurs during the passage of the blood through the lungs, it would pass into the expired air.

The origin of the aceto-acetic acid in the urine appears to be partly from the proteins of the food, but mainly from the fat. The work of Knopp and of Dakin has shown that the oxidation of the fatty acids takes/

takes place at the B-carbon atom; the long chains are broken down with the loss of two carbon atoms at a time. This accounts in part for the occurrence of those fatty acids in nature containing an even number of carbon atoms. Butyric acid if present as such, or formed by the oxidation of higher fatty acids by B-oxidation, is oxidised and converted into aceto-acetic acid or B-hydroxybutyric acid.

In "Metabolism and Practical Medicine" Oxybutyric acid is said to be par excellence the cause of acidosis, though acetic acid and perhaps a few other volatile organic acids may assist. The figures on this point are quite clear, considerable quantities of the acid have been found in the body. Hugounenq recovered 4.27 grammes from the blood of a diabetic patient.

Oxybutyric acid is formed in the body chiefly from fats, possibly from proteids and carbohydrates as well; it is completely destroyed in the normal body probably in the liver, and is therefore not found in the healthy urine. Whenever in disease any beta-oxybutyric acid escapes destruction some of it is converted into diacetic acid and is found as such in the urine. Diacetic acid is readily converted into a nonacid substance, acetone, which being volatile is excreted in the breath as well as in the urine. While the daily excretion of acetone exceeds half a gramme/

gramme, diacetic acid is present, and when the acetone is more than one gramme beta-oxybutyric acid is there as well, and forms the main portion of the acetone bodies present. Whenever diacetic acid alone or with beta-oxybutyric is found in the urine, acidosis must exist, but when acetone alone is excreted there is no acidosis due to the acetone bodies.

W. S. Gordon concludes that the processes concerned in producing acidosis are not thoroughly understood, and that they revolt from a disturbed metabolism due to various pathological conditions. While acetonemia may appear with carbohydrate starvation, and disappear with a corresponding regulation of diet, it does occur on a full carbohydrate diet. The gravity of the condition may be out of proportion to the amount of acetone in the urine, and while a large number of cases of acetonemia are relieved even when unrecognized and untreated the toxaemia is frequently of serious import. Its occurrence with alkaline and phosphatic urine should not be overlooked.

Frierichs is of opinion that none of these three substances, acetone, aceto-acetic acid, and hydroxybutyric acid exerts a specific toxic action, the last in particular cannot be very toxic for it has been shown to be present in the urine of patients in/

in large amounts and by the year together, without the appearance of any typical functional derangement.

For the purpose of neutralizing these acids the body uses bases of two kinds, (a) ammonia, which would otherwise be converted into urea; and (b) mineral bases, the sodium of the blood and other juices, the potassium of cells and calcium of bones.

If by any means a portion of the alkalies which neutralizes the mineral acids in the urine be withdrawn, then a percentage increase in the ammonia in the urine may occur. In the great majority of slight diabetic cases one finds between one and one-and-a-half grammes in the twenty-four hours urine, and the relation between the total nitrogen and the ammonia nitrogen is about eleven to one. On the other hand in severe cases it is not unusual to find four to six grammes in the urine per diem, continuing for weeks and months. Larger amounts still, such as ten grammes or more, are only found when coma is imminent.

We are therefore compelled to regard increased ammonia excretion by the kidneys as the expression of an acidosis, and to take the ammonia as the index of the acidity. The amount of ammonia excretion which is the index of acidosis depends on the alkalinity of the tissues as a whole.

When an alkali is given the ammonia excretion may/

may drop tremendously. In ten cases when the ammonia excreted was four to six grammes, the taking of 30 grammes soda bicarb. per diem was followed by a reduction of 10 to 22 per cent.

Another evidence of the toxic effect of the withdrawal of alkalies from the blood and tissues is suggested by the diminished alkalescence of the blood and its lowered content in carbon dioxide. In fatal acid intoxications the blood may contain only two or three volumes per cent, as compared with the normal twenty-eight to thirty per cent.

Any chronic condition may promote acute attacks of the acidosis, such as due to adenoids, to chronically inflamed tonsils, to chronic appendicitis, to maldigestion of fats, to long privation from carbohydrates, or to an insufficient amount of carbohydrate food, to profuse continuous vomiting, to imperfect liver function, to chronic pain, and to severe headaches.

The acidosis of surgical shock and Graves' disease is the result of the kinetic driving of the entire system, to such an extent that an undue strain is put upon all the organs of elimination. This is also the explanation of the acidosis which results from overwork or from excessive exertion. For the same reason also great emotion may produce an acute/

acute acidosis.

Another interesting and significant fact proved by experiments is that nitrous oxide, ether and chloroform during their administration all produce increased acidity of the blood and urine.

Acidosis in children is induced by an excess of fat in the diet.

In infants suffering from gastro-intestinal affections who received a large quantity of fat in their food, it was found that considerably more alkaline earths and alkalies in the fatty stools than usual, and as regards potassium often even more than the food had contained. As however the body endeavoured so far as possible to maintain its relative alkalinity, the alkalies in the urine were markedly diminished, and ammonia appeared in increased quantity to take their place. It is not however by any means decided whether in such cases a genuine acidosis is not present at the same time, in addition to the relative acidosis. It is indeed quite possible that under these circumstances organic acids are compelled to form a union with ammonia and participate in the increase.

Magnus Levy says the diabetic dies not from the acid excreted in the neutralized state in the urine, but from that left in the body, which he has not the power wholly to neutralize.

The symptoms or phenomena accompanying acidosis.

Whenever there is increased acidity in the blood there is thirst, when one exercises he is thirsty, as he is also if he has a fever, or is in emotional distress; Anaesthesia is followed by thirst.

Acidosis is accompanied by sweating, which is nature's attempt to aid the kidneys and the lungs in their efforts to eliminate acids.

An increase of pulse rate is another phenomena of acidosis, also increased respiration - (air hunger), and cerebral symptoms.

The urine gives the reaction of acetone and diacetic acid.

Kraus and Honigmann made a careful comparison of the symptoms of acid poisoning and diabetic coma. The similarities are, - the peculiar dyspnoea, the accelerated pulse, the fall of temperature, the cessation of the respiratory before the cardiac activity. They say that these points of contact place the acid intoxication theory of diabetic coma far ahead of all other theories.

The symptoms of acidosis may be erroneously attributed to other morbid states, especially in pregnancy should we be on the watch for a toxaemia due/

due directly to acetone, and not accounted for by kidney involvement, or the retention of urea.

Beddard in arguing the point as to whether acidosis per se can produce symptoms, says that the answer to the question can be readily given by considering the condition of a healthy man who voluntarily fasts or of a case of haematemesis from gastric ulcer, who receives nothing but salines per rectum. In both of these instances an acidosis in every way identical in magnitude with those of a really severe case of diabetes may be produced, and may be allowed to go on for a fortnight or more, without the patient showing any signs of functional upset or illness. It is manifest therefore, he says, that an acidosis associated with the excretion of large quantities of beta-oxybutyric acid, together with diacetic acid and acetone - both in the breath and urine - even when it lasts for several days, does not of itself produce any symptoms, and yet there are many clinical conditions associated with much less severe acidosis, in which the acidosis has been held responsible for producing grave illness, serious vomiting, cerebral symptoms, and even death.

Gordon says that the nausea, vomiting and consequent abstinence from food, which are often supposed to cause acidosis, may frequently be results instead of causes/

causes, and that so far as symptoms and treatment are concerned, the toxaemia should in such cases be regarded as a primary and not a secondary or incidental disorder.

Diseases in which acidosis is seen.

Diabetes is the best and most important example of acidosis, every case of the severe type shows it. The diabetic coma is an almost pure example of the acid intoxication by the acetone bodies. The clinical status of the whole subject appears to depend on its position in this disease, and it is in connection with this affection that the clinical developments of the theory has occurred.

Acidosis is also met with in uraemia and eclampsia.

In the cycles of exophthalmic goitre there are periods of vomiting, of acid breath, of restlessness, of rapid heart action, and of rapid respiration, - all characteristic phenomena of acidosis.

In acute yellow atrophy of the liver and phosphorus poisoning, a severe acidosis is certainly present, which may aid the fatal result by passing into an acid intoxication.

In/

In delayed chloroform poisoning we are dealing with a condition in many respects similar to the severe stages of poisoning by phosphorus.

Coombs describes two cases of chronic myocardial disease, in which the terminal phase was marked by clinical evidence of acid intoxication (acetone smell in the breath, air hunger, dyspnoea, thirst, and cerebral symptoms). This acidosis was apparently not of the type associated with diabetes, as that the beta-oxybutyric acid was not present in excess in the urine, and that neither alkalies nor oxygen inhalation had any effect on the course of the intoxication.

Acidosis in children. Howard concludes that acidosis in children is of frequent occurrence. Recurrent or cyclic vomiting, as distinguished by the absence of predisposing factors is extremely rare. The common clinical type of acidosis is what might be termed a complicatory acidosis with predisposing factors.

Metcalf reports an epidemic of acidosis, which occurred in Concord, N.H., in 1913-14. There were two hundred cases, with nine deaths. The epidemic was one of first attacks, eighty-four patients were ill of acidosis for the first time. So great was the loss of fat in fatal cases that children in a relatively few hours shrivelled from plumpness to emaciation./

emaciation. In forty-five cases the test for diacetic acid was made, only fifteen gave a positive reaction with ferric chloride. Of the fatal cases three were positive while two were negative. Oxybutyric Acid was found but once. Recovery was rapid in sixty cases. This seems to me not to have been a case of acidosis at all.

In many of these diseases we have to recognise the fact that an acidosis often seriously aggravates, if it does not entirely overshadow the original malady. If not, the recovery will be unduly delayed, or the life of the patient seriously endangered.

Methods used for ascertaining the degree of acidosis present.

It is very important to the ordinary clinician that he should have some method or methods that will enable him to confirm his diagnosis at once. Many methods have been brought forward, but none have proved their adaptability sufficiently to be universally accepted.

The following are some of the methods used.-

Beddard suggests three simple methods, (a) Colour tests for acetone and diacetic acid. The sodium nitro-prusside test for acetone and the reaction of diacetic/

diacetic acid with a solution of ferric chloride are the tests in question. The depth of the colour, he says, of the reaction may be taken as roughly corresponding to variations in the percentage of these two substances in the urine. It is necessary to remember that these colour tests do not enable us to distinguish a severe acidosis, which can produce no symptoms, from an acid intoxication which will. (b) Estimation of the ammonia in the urine. For ordinary clinical purposes it is sufficiently accurate to estimate the ammonia by the formalin method and the total nitrogen by a reliable hypobromite method. An acidosis is present only when the ammonia figures are raised absolutely and relatively to the total nitrogen above the normal. (c) Giving alkalies by the mouth or rectum. He goes on increasing the dose of the alkalies until the urine becomes either neutral or alkaline, and in this way obtains a rough measure of the quantity of acid which the body is producing, and therefore of the degree of acidosis. Any patient that requires more than about one ounce of sodium bicarbonate to make his urine alkaline is certainly suffering from an acidosis of very considerable severity.

There are various other methods commonly employed for measuring acidosis in diabetes, such as estimating the amount of ammonia or total acetone in the day's urine./

urine. The disadvantages of these methods are the labour involved in the determination, and the fact that it is necessary to get the patient to collect his urine for a period of twenty-four hours. However the greatest disadvantage of all is that it is impossible to obtain the result at once. A device for overcoming this difficulty is to determine the ratio of the ammonia nitrogen to the total nitrogen in a specimen of urine. This ratio, the so called ammonia index, is usually about three or four per cent in health. In severe acidosis values of about twelve to thirty per cent are obtained. These analyses take some time to perform, and they are essentially methods for the laboratory, but even so the results are apt to be uncertain, because the total amount of proteins consumed by the patient is unknown.

Rothera's test is the simplest one to apply to urine for the recognition of the presence of the acetone bodies. A mixture of one thousand part of pure solid ammonium sulphate, and one part of solid sodium nitroprusside is prepared by grinding and intimate mixing. The test can be performed as follows: in a test tube place the solid for a depth of two inches. In another similar tube place a like depth of the urine. Pour the urine on to the solid, and mix by repeatedly pouring from tube to tube. Add 2 c.c. of strong ammonia, mix and allow to stand. The/

The development of a permangate colour indicates the presence of acetone bodies in the urine.

Hurtly has recently described the following test, which is specific for aceto-acetic acid. To 10 c.c. of urine add 2.5 c.c. of concentrated hydrochloric acid, and 1 c.c. of a freshly prepared 1% solution of sodium nitrite. Shake and allow to stand for two minutes. Now add 15 c.c. of strong ammonia and 5 c.c. of a 10% solution of ferrous sulphate. Shake, pour into a large boiling tube and allow to stand undisturbed. A violet or purple colour develops if aceto-acetic acid be present. The speed at which the colour develops depends on the concentration of aceto-acetic acid. With small amounts the colour may not develop for about five hours. The test shows in a solution of one in 50,000.

The estimation of ammonia in urine until 1902 was a matter of considerable trouble on account of the length of time required to perform an analysis, but in that year Folin introduced his aeration method for removing the ammonia from urine made alkaline with sodium carbonate.

In 1908 Malfatti showed that the ammonia in the urine could be rapidly estimated by titrating neutralized urine after the addition of formaldehyde. The method depends upon the fact that when a neutral solution/

solution of an ammonium salt is treated with formaldehyde, combination occurs with the formation of hexamethylenetetramine, with the liberation of a corresponding amount of acid which can be titrated with N/10 NaOH.

The amount so obtained is higher than the value obtained by the Folin method, and is due to the presence in the urine of small amounts of amino-acids, which also react with formaldehyde. The result is therefore the amount of ammonia and amino-acid. Since the amino-acids are present in only very small amounts, the value can be used as an expression of the ammonia content. This method is particularly useful for clinical work.

Test for ammonia.- Take 25 c.c. of urine and dilute it with about the same amount of water, add 15 gms. of potassium oxalate and five drops of 1% solution of phenolphthalein and shake it well in a beaker. In another beaker place 10 c.c. of formalin (40% formaldehyde) and same quantity of water, add five drops of phenolphthalein. From a burette run in N/10 NaOH until neutralized, both beakers are now pink. Pour the contents of one beaker into the other, the pink colour will disappear. Again run in the N/10 NaOH until the pink colour reappears. Take the difference in reading before and after the last/

last titration and multiply it by .0014 and this gives you the number of gms. ammonia nitrogen in 25 c.c. urine; knowing the total urine passed in the 24 hours you find the number of gms. ammonia nitrogen. Next find the urea nitrogen, and you have the normal ratio of the ammonia nitrogen to the urea nitrogen is 1 in 20.

Take an example, the difference in the reading shows 3.05 c.c.

3.05 x .0014 = .00427 gms. ammonia nitrogen in 25 c.c. urine.

Total volume of urine = 2556 c.c.

2556 x .00427 and divided by 25 = .4326 gms. ammonia nitrogen.

Urea = .5 gms. per litre, i.e. 21.7 per diem.

Urea nitrogen = 21.7 x 28 and divided by 60 = 10.12 gms. nitrogen.

$$\text{Therefore } \frac{\text{ammonia nitrogen}}{\text{urea nitrogen}} = \frac{.04326}{10.12} = \frac{1}{23}$$

The normal is 1/20.

Other observers approach the subject in another direction. They estimate the tension of the carbon dioxide in the expired air. The estimation of the alveolar pressure of carbon dioxide by Haldane's method at present is the best guide to the prognosis and treatment of diabetes, a value of twenty-five mm. is of/

of grave significance, and one below twenty mm. indicates that coma is present.

Barcroft introduced an apparatus, it consists of a manometer of 0.5 mm. bore glass tubing. He used it for the analysis of oxygen in 0.1 cc. of blood. Two methods are advisable for this calibration, (1) a direct comparison of the oxygen given out by blood with that given out by the same blood in the larger form of apparatus, the constant of which is known; (2) the hydrogen peroxide method.

Fridericia has introduced a modification, called carbon dioxide tensimeter, which is a glass bent tube through which the patient blows. Caustic potash is used to absorb the carbon dioxide. A graduated marking enables the observer to read off the percentage of carbon dioxide in the expired air.

Again other observers have taken the alkalinity of the blood as their test for measuring the degree of acidosis present.

Sellards says, the reaction of the blood depends upon the physico-chemical balance between the hydrogen and the hydroxyl ions which it contains. In this sense the blood is hardly more alkaline than water. More loosely the reaction of the blood was formerly stated in terms of its behaviour towards indicators, and its ability to neutralize acids or bases.

Although/

Although normal blood serum reacts as an acid towards a few indicators, notably phenol-phthalein, yet it is definitely alkaline towards the majority of the common indicators used. Since the alkaline reaction to these indicators can be maintained even after the addition of small amounts of acids, the blood is commonly spoken of as an alkaline fluid.

Walpole goes into this question very fully in the Biochemical Journal, vol. V., where he also gives a chart illustrating the relation between the composition of certain mixtures, the logarithms of their hydrogen ionic concentration, and the related colour changes of certain indicators. This chart was constructed from the various tables published by Sörensen.

Boycott and Chisholm in the same Journal quoted above, writes.- Apart from the question whether the blood is really alkaline in the sense that it contains such an excess of hydroxyl ions as can be determined by the available physical method, there is no doubt that the amount of acid which must be added to blood to produce a certain effect with a given indicator varies under different circumstances, and it seems clear that these variations are the expressions of phenomena which cannot be neglected. The current methods of determining the alkalinity of the blood/

blood involve the use of varied coloured indicators, - litmus, dimethylamidoazobenzol, and the like. To get a colour effect it is almost necessary to apply the method to plasma or serum. This is no disadvantage, but the ordinary coloured indicators do not give a sharp end point when used in the titration of proteid solutions. In the first place the actual colour of the indicator may vary materially with the presence or absence of proteid. The result is that the determination of the end point is essentially subjective. That this does not necessarily vitiate the methods is of course clearly shown by the concordant data which have been obtained by their use.

The possibility of doing without added indicators was suggested by the method of Dave, in which acid is added to diluted laked blood, until the absorption bands of oxyhaemoglobin are no longer visible on spectroscopic examination.

In the cases recorded below the method called "The Flocculent Precipitate reaction", as given by Boycott and Chisholm, was used. They based their determinations on the quantity of N/1000 Sulphuric acid required to precipitate the haemoglobin in one hundred grammes of blood.

The method is as follows.- A series of test tubes containing gradually increasing concentrations of /

of sulphuric acid is set up. When the syringe and needle are small the tubes were filled in the following way.- Twelve tubes are used, numbered one to twelve. In the first tube 0.1 cc. N/1000 sulphuric acid is placed, increasing 0.1 cc. right up to tube 12, and water added to the tubes to bring the volume of liquid in each up to 2 cc. When the syringe and needle are larger we placed in the first tube 0.5 cc. N/1000 sulphuric acid, increasing 0.1 cc. in each tube as before. The syringe and needle are sterilized and dried with alcohol and ether. A trace of neutral potassium oxalate is placed on the piston of the syringe to delay coagulation of the blood. When the blood is withdrawn a small quantity is allowed to drop from the needle to ensure evenness of flow, and then five drops are dropped into a weighed weighing bottle and the stopper immediately replaced. A single drop of blood is now allowed to fall into each test tube of the series, and at the end of the experiment five drops are again added to those in the weighing bottle, the stopper is replaced and the bottle and its contents weighed. By this means the average weight of a drop of blood is determined. The test tubes containing the acid and the blood are shaken to ensure mixing, and incubated in a water bath at 45°C. for an hour. They are then removed from the water bath, wiped/

wiped and examined. The lowest in the series show no turbidity, those higher show a gradually increasing turbidity, and then one tube shows a well marked flocculent precipitate and all the tubes above this show a similar flocculent precipitate. The average of the quantity of acid in the tube which first shows the flocculent precipitate and of that in the tube immediately before, gives a measure of the alkalinity of the blood. For example, suppose the syringe drops a drop of blood weighing .045 gms. and the first tube which shows a flocculent precipitate is that containing 1.4 cc. of acid, then the quantity of acid required to precipitate .045 gms. of blood is 1.35 cc. From this we ascertain that 100 gms. of blood require 30 cc. N/1000 sulphuric acid to precipitate it.

Experiments were done according to Boycott and Chisholm in thirty-four instances with the following results:-

No.	Patient.	Date of Experiment	cc. N/10 Acid %	Disease.
1	J. M.	2/9/15	38.6	Gastric Ulcer
2	M. S.	do.	28.4	Epilepsy
3	do.	3/9/15	26.2	do.
4	W. A.	do.	27	Ch. Rheumatism
5	M. S.	6/9/15	29.5	Epilepsy
6	A. F.	7/9/15	32.6	Haematuria
7	M. S.	6/9/15	28.6	Epilepsy
8	do.	7/9/15	29	do.
9	do.	8/9/15	25	do.
10	Mrs B.	8/9/15	20.6	Eclampsia
11	Mrs X.	8/9/15	26	Normal labour
12	Mrs A.	9/9/15	32.6	Puer. Eclampsia
13	Mrs P.	9/9/15	27.5	Normal labour
14	E. F.	10/9/15	24.5	Diabetes
15	A. F.	10/9/15	25.6	Haematuria
16	J. M.	15/9/15	37.5	Acromegaly
17	do.	17/9/15	35.4	do.
18	Mrs F.	21/9/15	28.6	Ch. Rheumatism
19	do.	22/9/15	26.7	do.
20	L. G.	29/9/15	24.5	Diabetes
21	do.	27/12/15	33.3	do.
22	J. F.	3.1.16	15.5	Ch. Brights

23/

No.	Patient.	Date of Experiment	cc. N/10 Acid %	Disease.
23	L. G.	5/1/16	26.74	Diabetes.
24	Mrs T.	10/1/16	21.7	Aortic regurgitation.
25	do.	15/1/16	20.6	do.
26	W. G.	14/6/16	26	Diabetes
27	D. S.	14/7/16	30.4	Rheumatoid Arthritis.
28	Mrs F.	17/7/16	24.5	Tubercular Kidney.
29	Mrs C.	18/7/16	22.9	Constipation
30	Mrs R.	19/7/16	17	Gout
31	W. G.	28/7/16	25.1	Diabetes
32	Mrs C.	28/7/16	27.7	Mediastinal neoplasm.
33	G. M'K.	7/8/16	25.3	Prog. Musc. Atrophy.
34	M. D.	11/8/16	21.46	Diabetes.

NOTES ON CASES.

1. J.M., aged 58, complained of pain and discomfort in stomach. He vomited considerable quantities of undigested food, and had acid eructations. Blood was found in his vomit and faeces. Urine alkaline, with a low specific gravity. Gastric Ulcer was diagnosed. The patient's general condition was good, so that the alkalinity of his blood was not affected.

2, 3, 7, 8, 9. Had two fits previous to my seeing her. The abdomen was very rigid. Phosphates were present in the urine. Epilepsy and mild Tetanus was diagnosed. The alkalinity of the blood was slightly below normal.

6, 15. A.F., aged 45, suffering from Haematuria for two years previous to my seeing him. Patient was a heavy drinker, and had an attack of acute bronchitis six years before, and acute Brights four years before. The urine was acid, and showed blood present in great quantity, also albumin - one gramme per litre. Microscopic examination revealed pieces of papillomatous tumour, which was confirmed by the cystoscope.

16, 17. J. M'K., aged 42, complained of sleeplessness and intermittent pain. This was a well marked case of acromegaly.

18, 19. Mrs F., aged 60, complained of breathlessness, cough, sputum was streaked with blood. She had suffered from rheumatism for thirty-four years, and her hands were showing rheumatoid changes. She had been breathless for a year. Her heart was very irregular and occasionally extra systoles were heard. Pulse varied from 80 to 108. Breathing 36 per minute. Urine showed bile.

20, 21, 23. L.G., aged 17, suffering from excessive thirst and hunger. This was a case of diabetes. The patient was very ill when seen, and although she improved considerably in appearance under treatment, her diabetic condition remained much the same. The urine showed 7% of sugar when first examined, went down to 4.8 and gradually rose to 6%. The urea was 8 gms. per litre at first, increasing gradually to 13.5, and then diminishing to 8.5 gms. Acetone was present in nearly every occasion an examination was made. Diacetic acid was found twice and aceto-acetic acid four times in six of the/

the records kept. The patient was treated with the ordinary diabetic remedies, and in addition took an ounce of sodium bicarbonate daily. After a couple of months of treatment she was feeling very much better, notwithstanding the large amount of sugar she was passing.

22. J.F., aged 70, complained of pain over the region of the heart and breathlessness. Five years previously had been in hospital with dizziness and frequency of micturition. The breathless attacks occurred at night. He suffered from thirst. Right side of heart enlarged, and second sound in aortic area accentuated. Pulse varied from 80 to 124. Breathing 28 per minute. The urine showed urea diminished - 11 gms. per litre. Albumin varied from 1 to 3.5 gms. per litre. The patient could not take alkalies, and his condition became gradually worse.

24, 25. Mrs T., aged 57, complained of fainting fits, a choking sensation, palpitation, and pain over the heart. She had often fainted in the street and after exertion. She was troubled with thirst. Her breathing was rapid, 38 per minute, with rest this came down

to/

to 20. Her pulse was reduced from 118 to 80. The urine showed a trace of albumen, and diminished urea - 6.5 gms. per litre. She was treated with alkalies, and her condition improved very much. The alkalinity of the blood was low. She was suffering from aortic regurgitation.

26, 31. W.G., aged 41, suffering from diabetes millitis for 5 years. He was only 6 stone 11 lbs weight. He suffered from severe diarrhoea. He was constantly thirsty and complained of breathlessness and occasionally palpitation. The sugar in the urine remained at about 8%. Only traces of acetone found. His condition gradually improved under diabetic treatment with the addition of alkalies.

27. D.S., aged 20, complained of acute pain in shoulder, radiating down to elbow. She suffered from thirst. Vomited frequently, and was chronically constipated. She was a case of rheumatoid arthritis.

28. Mrs F., aged 28, complained of pain in left iliac fossa, and diarrhoea. Her pulse kept well over 100. Blood showed a leucocytosis. Temperature occasionally rose to 100°.

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The patient had to get up four or five times at night to pass urine. She was rapidly losing weight. The urine showed large quantities of pus and albumin. Tubercular kidney was diagnosed, which a subsequent operation confirmed.

29. Mrs C., aged 42, a case of pneumonia. Her urine showed albumin. She also suffered from constipation and thirst.

32. Mrs C., aged 27, complaining of sickness and vomiting for three months. There was a stabbing pain between the shoulders. She was very constipated. Urine showed no abnormalities. X-rays revealed a mediastinal tumour.

30. Mrs R., aged 43, complained of a stabbing pain in chest and down the left arm. She had a mitrol systolic murmur. Constipated.

33. G. M'K., aged 38, Atrophy of the muscles of the upper extremities, especially the hands - thenar and hypothenar eminences. This was a case of progressive muscular atrophy.

34. M.D., A severe case of diabetes. He died a short time after the experiment was made on his blood.

C O N C L U S I O N S

Acidosis is present in greater or less degree in every abnormal condition of the body, whose origin can be traced to excessive kinetic activations from any cause, and that the maintenance of the normal potential alkalinity of the body is of vast clinical importance.

The importance of acidosis in connection not only with diabetes, but also with renal, cardiac, and other diseases, is not sufficiently recognised.

The result of the examination of the blood in cases of acidosis does not give one a definite opinion as to the seriousness of the condition, but is a guide to the line of treatment to adopt.

Using Boycott and Chisholm's method, called "The Flocculent Precipitate reaction", the average quantity of N/1000 sulphuric acid required to precipitate 100 gms. of blood would run at about 30 cc.

In the thirty-four experiments recorded, the lowest was that of J.F. (22) a serious case of chronic Brights, with heart complications; his record was as low as 15.5. This patient could not take alkalies, which made his recovery hopeless. The next lowest was that of Mrs R. (30) who while showing a reduced alkalinity to the extent of 17 cc., yet/

yet her general health was not much affected.

Seven experiments on the blood of diabetic patients were made, with results .- E.F. (14) 24.5 cc., L.G. (20) 24.5 cc., L.G. (21) 33.3 cc., L.G. (23) 26.7 cc., W.G. (26) 26 cc., W.G. (31) 25.1 cc., M.D. (34) 21.4 cc. Six of these were below the average, W.G. was seriously ill but gradually recovered, M.D. died, and the others made satisfactory progress under the alkaline treatment.

Another case of low alkalinity was that of Mrs T. (18 & 19), suffering from aortic regurgitation. Her records were 21.7 and 20.6 cc.

The beneficial use of alkalies was demonstrated in the case of L.G. Although her urine showed on an average 7% of sugar, and urea as low as 8 gms. per litre, with acetone nearly always present, yet her general health was good. This could only be accounted for by flooding her system with alkalies.

In the thirty-four experiments tried.-

7 or 20.6% showed an alkalinity of the average (30%) or above.

17 or 50% ranging from 25 cc. to 30 cc.

8 or 23.5% ranging from 20 cc. to 25 cc.

2 or 6% below 20%

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I wish to record my thanks to Dr Rainy. I owe it to him that I have been able to undertake this work. The experimental part of the work was done in the College of Physicians' laboratory.

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