Remarks

ON

ACIDOSIS FROM THE CLINICIAN'S
POINT OF VIEW *

BY

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I have selected the topic of acidosis because it is a subject which has become in recent years of considerable importance in explaining the pathogenesis of many pathological conditions, especially those occurring in the early years of life. To my mind there has been, and still is, much loose thinking and talking about the matter, because there is little evidence of a definite nature to support many of the opinions expressed.

Broadly speaking, acidosis may be looked upon as a disorder of metabolism accompanying many diseased processes. I would compare it in this respect with fever. In both, the disturbing factor, acid in the one case and heat in the other, is produced under normal conditions, and the abnormal state results from a disturbance of the balance between production and loss. It cannot be too strongly stated that in neither case have we got to the root of matters by merely recognizing an increased accumulation of acid or of heat in the body. We are only detecting the general results of disordered action of the tissues, which is in no way pathognomonic of any particular diseased process, though there may be variations in degree and in type in different diseases. Hence to raise acidosis to the position of a clinical entity, far from being an advance in the classification of disease, as some writers would appear to think, is as retrograde a step as it would be to classify disease according to the presence or absence of fever. Testing for acidosis is, like taking the temperature, of help in deciding if there is any evidence of abnormal action of the tissues, and probably therefore of active disease. Good comparable examples of the value of the thermometer and of the test for acetonuria are tuberculosis and diabetes.

I admit that we may be forced occasionally to a diagnosis of febricula, but it is a confession of our ignorance, and a diagnosis of which, I think, we are always ashamed. In the same way a diagnosis of acidosis should be equally guarded against. It may sometimes be the only abnormality detectable, but that does not mean that we understand what is wrong with the patient. Our predecessors frequently spoke of death from hyperpyrexia when the temperature of the body was above a certain level, but hyperpyrexia as a cause of death is seldom heard of to-day, because it is known that it is not a means of differentiating one type of a particular disease from another, far less different diseases from each other. Nevertheless, it is found advisable in treatment to try to prevent the heat of the body from rising above a certain level, and it is without doubt equally advisable to control the accumulation of the acid elements in the blood and tissue juices, because the tissues have their optimum activity at a certain definite temperature and a certain definite reaction of the blood and of the fluids which bathe them.

Meaning of Acidosis

What do we really mean by the term acidosis? It must be appreciated right away that a true acid state of the blood never occurs in life. The circulation of a free acid (that is, one not combined with its equivalent amount of base) is impossible with the exception of

carbonic acid, which is the only free acid found in blood, whether normal or pathological. Of the total carbonic acid in the blood, only one-twentieth is normally present in the free state, the remainder being combined with alkali. The ratio between the free and combined carbonic acid is the ultimate factor in determining the reaction of the blood. The circulation of free acid (other than carbonic) or a really acid reaction of the blood is incompatible with life. What we understand by acidosis is a tendency to the production of such a state if matters were allowed to go on uncontrolled. The symptoms of the condition, as well as the tests available, are evidence of the means the body adopts to hinder this from coming about.

Acid is always being produced in the body as a result of katabolic activity, but its neutralization and excretion are provided for through the activity of the transport organ (the blood) and the excretory organs (lungs and kidneys). So long as this production of acid remains within normal limits, and the organs engaged in its removal are healthy, there is no evidence of any disturbance. When, however, the production of acid is excessive or pathological in amount, or abnormal or pathological in kind, the efforts of the body must be increased. Further, if the organs employed in the removal of these acids are diseased, not only will the difficulty experienced in their elimination appear earlier, but it will be proportionately greater, as in the case of a diseased heart. It is again a question of balancing the loss with the production, for the body will avoid at all costs the production of a too acid tissue plasma. Signs and symptoms are commensurate with the difficulty encountered in keeping the acid tide under way, and the task may be more than the body can perform. It is probably for this reason that there is the greatest difference between the effects of acidosis arising during the course of a disease and that experimentally or even therapeutically induced. In both, the chemical tests may reveal in equal degree the methods adopted by the body in coping with the rise in the acid tide, but symptoms are noticeably absent when acidosis is experimentally induced and the organs are apparently healthy.

THE ROLE OF THE BLOOD IN CONTROLLING ACIDOSIS

It has already been stated that no free acid can circulate in the blood except CO_2 . All other acids must be combined with base. It is also a fundamental law that the total acid and basic elements which go to form the reaction of the blood are practically constant and perfectly balanced with each other. So far as the acid elements are concerned, therefore, a certain definite amount only can be carried; if some abnormal acid is present, or if one of those normally present is increased in amount, it will only be at the expense of and by replacing so much of one of the others—usually CO_2 , since it is the most volatile acid: hence the indication of an increased formation of acid in the body, and of a tendency to the production of a more acid reaction of the blood and tissue juices, is a low CO_2 blood content. It is on account of the lessened power of the blood to carry CO_2 , and the consequence that a larger proportion is free, that the respiratory centre is stimulated to a greater activity, with the resulting characteristic symptom of hyperpnoea. It must be appreciated, however, that a low CO_2 blood content does not always indicate a tendency to the production of a more acid state of the blood. It depends entirely on how the diminished CO_2 content is produced. In the above example the reason for the low CO_2 content is that some other acid has in part replaced it. If, however, the diminished CO_2 content results from a more rapid loss of CO_2 than normal, if it is, as it were, pulled out and not pushed out—for example, by forced

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respiration, which may be performed voluntarily, or as the result of high altitudes (mountain sickness), or in consequence of the hyperpnoea, which is at times a manifestation of encephalitis lethargica—then the primary change is a loss of normal acid, and the tendency will be towards the production of a more alkaline blood—the state of so-called alkalosis. This will tend to be rectified by an increase in some of the other acid elements in the body, the chlorine or organic acids. In fact, we know that in alkalosis produced at high altitudes from the loss of CO_2 , and in the alkalosis found in pyloric stenosis due to a diminution of the chlorine, acetonuria does occur, this being significant of an increased formation of the organic acids of the oxybutyric series. Surely this should give the death blow to the current opinion that the presence of acetonuria indicates acidosis. Acetone in the urine simply results from incomplete combustion of fats, and may be present both in acidosis and in alkalosis. In the former it is the primary change producing a rise in the total acids, whereas in the latter the formation of excess of ketone acids, probably the result of defective oxidation, makes up for a deficiency of acid, and so helps to bring the reaction from the alkaline side back to normal.

Thus we are studying by our tests the different directions in which these abnormal changes in the blood are brought about, and the methods of the body in rectifying or compensating for a loss or an increase in the acid elements, rather than the true reaction so far as acidity and alkalinity are concerned. It is apparent, too, that for a true reading of the condition a knowledge of the factors leading up to the change—that is, the clinical history—is essential.

EXCRETORY FUNCTION OF LUNGS AND KIDNEYS

This so-called "buffer action" of the blood, which comprises a complex physico-chemical mechanism involving practically all the constituents of the blood, is not the sole means of the body's protection, since the excretory functions of the lungs and kidneys, and probably intestines also, play an important part. Excessive amounts of CO_2 are got rid of by the lungs; this may be revealed by the characteristic hyperpnoea of acidosis. The volatile acids of the oxybutyric series are also in part expelled by the lungs, and consequently we have another characteristic symptom, the smell of acetone in the breath. By the kidneys there is increased acid excretion, increase in ammonia formation to aid in the excretion of acids and to neutralize tissue juices, increase in fixed base excretion—for example, Ca from the bones and Na and K from the tissues generally—and, as it is the salts of the body which in great part retain fluid, this resulting diminution in their amount allows of the escape of fluid. In view of this function of the lungs and kidneys in rectifying any tendency towards the production of a hyperacid blood and plasma fluid, the importance of the health of these organs is apparent.

EXAMPLES OF ACIDOSIS IN DISEASE

I shall now attempt to explain how acidosis is produced in several clinical states with which we are familiar. This will be helpful, not only in fixing in our minds the more or less theoretical considerations outlined above, but in applying a sane therapy.

Gastro-enteritis

In fatal cases of gastro-enteritis a state of acidosis is often observed. This arises both from the increased production of acid in the body and an increased loss of base available for its neutralization. The former is due to the necessary concomitant starvation in consequence of the vomiting and defective absorption from the gut, apart altogether from any therapeutic deprivation

of food; the latter accompanies the loss of fluid by vomiting and diarrhoea. The acidosis in gastro-enteritis is merely an indication of the severity of the lesion, and is in no way concerned with an explanation of the etiology of the condition. Nevertheless, it shows how the fatal termination may be contributed to, and it certainly suggests that the rational treatment is to replace the loss of fluid and to hinder the production of acetone bodies by the administration of water, salts, and glucose. This should be done at all costs; if they cannot be retained in the usual way, they must be administered either by the venous or the peritoneal route.

Diabetes Mellitus

Diabetes mellitus is of course the classical example of a disease in which a state of acidosis results. Owing to disease of the pancreas the patient is unable to utilize or combust sugar, and so fats are incompletely burned with the production of ketones (the acetone series). These bodies accumulate and compete with the CO_2 for the available alkali of the blood. This results not only in a diminished amount of CO_2 per unit of blood, but in a relatively increased proportion being in the free state—hence the hyperpnoea. In diabetes there is another factor working in the same direction. In consequence of the diuresis there is a washing out of the fixed alkali (Na, K, and Ca) available in the body for neutralizing the increased formation of acid. The kidney itself, however, plays an important part in minimizing this loss of base by a great increase in the formation of ammonia, which to a large extent takes the place of the fixed alkali. It is well known that renal disease increases the gravity of diabetes mellitus, and it is probable that the impaired formation of ammonia is the serious factor.

Nephritis

It is appropriate that nephritis should be considered as a disease contributing towards acidosis, since it is an example of interference with the normal excretion of the acid products formed during the processes of metabolism rather than of the production within the body itself of increased or abnormal acid. In importance or in degree, however, the acidosis produced in this way falls far behind that mentioned above.

IMPORTANCE OF HEALTH OF THE TISSUES

To illustrate the importance of the excretory organs in hindering a progressive acidosis, and to indicate the complexity of the whole problem, it is interesting to consider acidosis artificially induced, as not infrequently happens for therapeutic purposes. A state of acidosis may be induced by adding to the body one of its acid elements—chlorine—or by encouraging the incomplete combustion of fat with the production of ketones.

1. The first type of acidosis may be produced by the administration of either CaCl_2 or NH_4Cl . In the case of the former drug the Ca is split off in the gut and the Cl alone is to all intents and purposes absorbed. In the case of NH_4Cl the ammonia factor is converted into urea and leaves the Cl free. In both instances the chlorine content of the blood rises and competes with the CO_2 for the available base. Thus in both instances there is a fall in the CO_2 content of the blood, which, with certain provisos, is not only our evidence, but also our measure of the degree of acidosis.

2. In the second type of induced acidosis the incomplete combustion of fat with the production of ketones is brought about by the withdrawal of food (starvation), or by disturbing the balance of fat and carbohydrate in the diet (poor carbohydrate and rich fat). In this case the acetone bodies (ketones) compete with the CO_2 for the alkali of the blood and tissue juices, and again the CO_2 content of the blood is diminished.

It is a striking fact, however, that although by estimation of the CO₂ content of the blood in either of these two types of acidosis there might appear to be a degree equal to that met with when the condition arises spontaneously, yet no symptoms are apparent. It is admitted, of course, that if the doses of the salts of chlorine are enormous, symptoms do arise, but I have seen as severe an acidosis, at least as revealed by CO₂ content of the blood and the amount of acetone in the blood and urine, induced by a ketogenic diet as in many an example of gastro-enteritis or of cyclical vomiting, but I have never seen vomiting and hyperpnoea. Moreover, almost always within a day or two, in spite of a continuation of the ketogenic diet or administration of the drugs (CaCl₂ and NH₄Cl), the degree of the blood changes becomes modified. This brings home to us the remarkable powers of the body in accommodating itself to new conditions, and the completeness of these powers so long as the tissues are healthy. It also demonstrates that the symptoms of acidosis, and the progressive and cumulative nature of the condition as met with clinically, are not so much due to any peculiar pathological process as to the inability of the tissues, in consequence of the effect of disease in general on the cells, to exert their inherent regulating mechanism.

THE TREATMENT OF GASTRIC AND DUODENAL ULCER

A STATISTICAL INQUIRY

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It is useless to discuss the prognosis and end-results of the treatment of these ailments unless there is a clear understanding of what we mean by the terms in question. There was a time, up to, shall we say, 1910, when it was generally supposed that a patient with haematemesis, with or without other symptoms, had an ulcer, and that many patients with intractable dyspepsia had either ulcer or "gastritis." Needless to say, any conclusions as to the value of medical treatment derived from those days are not trustworthy. Then we learned that haematemesis without pain was seldom, if ever, due to an ulcer, or at any rate to an ulcer that a surgeon could demonstrate, but was the result of bleeding from multiple gastric erosions, or, less often, from a single soft acute ulcer. Haematemesis with pain did not necessarily mean peptic ulcer; it might be associated with a tiny, withered-up appendix. Again, it was thought that hunger-pain meant duodenal ulcer, but many fruitless operations revealed that this was also misleading; hyperchlorhydria, often of reflex origin, might give this symptom without any ulcer. There was an unhappy period—up to 1920, or a little after—during which we were all at sea with regard to the diagnosis of gastric conditions; our methods were inadequate, and we no longer believed, as we had done before surgery taught us otherwise, that gastric or duodenal ulcer could be recognized with certainty. In this period, therefore, we get little or no help towards reading the natural prognosis of peptic ulcer, or the end-results of medical treatment. Shortly after 1920, methods of x-ray examination were worked out, perfected, and came into general use, and the study of symptoms and of chemical analyses made advances, so that now the diagnosis can be made with reasonable accuracy, and often with absolute certainty. The time has come at last, by using the material collected since 1920, to form some conclusions as to the prognosis.

RESULTS OF MEDICAL TREATMENT

That cases of gastric ulcer, even when deeply adherent, can and do heal, either spontaneously or with medical treatment, is certain, partly on clinical, partly on post-mortem evidence, the scars being found at necropsy. According to Stewart, 5 per cent. of the cases examined in the post-mortem room at Leeds showed open or healed gastric ulcers. Simple pyloric stenosis nearly always indicates the presence of an ancient healed duodenal ulcer, just as hour-glass stomach means an ancient healed gastric ulcer. It is also certain that chronic gastric and duodenal ulcers, untreated or treated, may lead to fatal haemorrhage or perforation, and that these catastrophes are not infrequent. They are nearly always the result of chronic, not acute, ulcer. Lord Moynihan and Stewart found over a period of twelve years that of 61 cases of fatal perforated gastric ulcer, 60 were chronic ulcer and 1 was acute; of 14 cases of gastric ulcer with fatal bleeding, 13 were chronic ulcer and 1 was acute; and that of 117 cases of fatal perforated duodenal ulcer, 109 were chronic ulcer and 12 were acute. Acute and chronic ulcers were found in 4 cases.

Of 100 cases of chronic peptic ulcer there is no reliable evidence to indicate how many would heal, or bleed, or perforate. At Leeds, out of 96 cases in which death was attributed to gastric ulcer, 68 had perforated; this had occurred in 178 out of 200 cases due to duodenal ulcer. On the other hand, of 164 patients treated at New Lodge Clinic for gastric or duodenal ulcer between 1921 and 1927, only 3 are known to have perforated. The majority of these 164 cases have a long history; cases of perforated ulcer usually give a history of less than a year, so that the true incidence of perforation must be higher. It is the anterior ulcer that perforates into the general peritoneal cavity, whereas the long-standing ulcer is usually on the lesser curvature or posterior wall. According to Hurst, Moynihan, and Balfour, about 20 to 25 per cent. of cases of gastro-duodenal ulcer bleed. At Guy's Hospital, during the period 1911 to 1920 (Conybeare), 600 cases of haematemesis were admitted, and the mortality was about 2.5 per cent. Crohn of New York gives 94 cases treated medically, with 4 deaths; but Bulmer, at Birmingham, mentions 526 cases with 67 deaths, or 12.7 per cent.

In regard to recent statistical evidence relating to the results of medical treatment for gastric and duodenal ulcer, the following studies are available. The medical treatment adopted was, generally speaking, rest in bed, a milk diet, and alkalization.

Einhorn and Crohn, writing in 1926, present the results of a careful follow-up of 100 cases. One year after treatment, 67.5 per cent. were cured, and 22 per cent. were better; four years after treatment, 27 per cent. were cured, and 23 per cent. were better. Their statistics show very little difference between gastric and duodenal ulcers.

David Smith gives the immediate results in 214 cases treated between 1913 and 1922 as follows: 67 per cent. of the males "cured," 2 per cent. dead; 76 per cent. of the females "cured," 5 per cent. dead. In cases observed five to fifteen years later, 29 per cent. of the males were "cured," 19 per cent. were dead; while the corresponding figures for females were 40 per cent. and 15 per cent. The percentages were calculated on the original number of cases.

Forman, at Guy's Hospital, studying a series of 41 cases five years after treatment, found 22 per cent. of the patients well, 20 per cent. better, and 57 per cent. no better. Franklin White, in a series of 206 private cases followed up from three to five years, reported that 30 per cent. of the gastric patients were well and 24 per cent. better; while 57 per cent. of the duodenal patients were well, and 21 per cent. better. Of the gastric cases,