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CLINICAL ASPECTS AND TREATMENT WITH ISOTONIC SODIUM BICARBONATE SOLUTION

By

ESBEN KIRK, M.D.

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To my teacher D. D. Van Slyke
with sincerest gratitude
and admiration

Preface

»There is no reason why every patient should not reap the benefit of the simple methods which are now available for the analysis of blood.«

J. P. Peters and D. D. Van Slyke.

The object of the present book is to spread the knowledge of acidosis and of the treatment of this often dangerous complication with isotonic sodium bicarbonate solution, a therapy which the author had the pleasure of introducing into Denmark in 1934.

In spite of the fact that acidosis is a frequent and serious condition which annually, directly and indirectly, causes numerous deaths, the realisation of the significance of its treatment is not as yet very widespread. The reason why the treatment of acidosis has not become the common property of physicians in the same way as other rational therapies is to be found in several circumstances. The chief reason is no doubt that the clinical symptoms of acidosis, even in its fairly severe degrees, are frequently uncharacteristic, so that often the diagnosis can only be made with certainty by means of laboratory analyses. This renders it necessary to know exactly in what diseases and under what circumstances acidosis may be expected to be found, but here we meet with the difficulty that while several exhaustive theoretical expositions are available the clinical and therapeutic observations as a whole are not easily accessible in the literature. To this must further be added the fact that the form of exposition and the symbols used in the biochemical publications are usually so technical that the comprehension is rendered difficult or impossible to the reader who is not mathematically trained. As a last fact of importance I may finally mention that the clinical laboratory technique and the study of that branch of science is as yet rather undeveloped in this country.

The present book aims at giving a connected exposition for the use of hospital physicians and general practitioners of the clinical aspect and treatment of acidosis, based partly on the available literature, partly on the author's own observations. It is the author's conviction that a rational consistent adherence to the diagnosis and treatment of acidosis may contribute to save the lives of more than a hundred patients in Denmark annually.

Holstebro, Denmark, 1942. ESBEN KIRK.

Preface to the English Edition

After the appearance of the Danish edition of the present book the author has had the pleasure of seeing the treatment of acidosis with isotonic sodium bicarbonate solution widely adopted throughout the Scandinavian countries. The present English edition, the publication af which has been delayed by the war, contains a few new sections necessitated by the development during the last four years.

Holstebro, Denmark, 1946. ESBEN KIRK.

Brief Survey of the History of Acidosis and of its Treatment

The history of acidosis is a fascinating tale of the attainment of clarity in a important field, which constitutes a borderland between medical science and biochemistry. The subject seems especially to have attracted the prominent biochemists of the last generation (Henderson, Sørensen, Hasselbalch, Haldane, Van Slyke, Warburg), with the result that this section of biochemistry has been thoroughly developed theoretically.

The clinical investigation of acidosis dates considerably farther back than the theoretical and chemical study, viz. well over a hundred years, to O'Shaughnessy's researches during the cholera epidemic in London in 1831–32. In a short paper, »Experiments on the Blood in Cholera«, O'Shaughnessy[154] pointed out that on examining the blood of cholera patients he had found the salt and alkali content much reduced, and he added that he had found these salts again, and especially the sodium carbonate, in large quantities in the watery stools of the patients. O'Shaughnessy's findings soon gave rise to the treatment of cholera by intravenous injection of watery salt and soda solutions, a therapy which was first employed by a general practitioner at Leith, Dr. Latta. Latta's[112] reports in The Lancet express enthusiasm for the as a rule excellent results obtained by the new treatment, which was soon adopted in several quarters. With the termination of the epidemic the interest in intravenous treatment again waned, and the therapy seems almost to have been forgotten when the cholera again ravaged London in the fifties.[210]

It was actually Walter's[224] investigations (1877) on experimental acidosis that reawakened the interest in the problem of acidosis. Walter demonstrated the occurrence of a characteristic form of dyspnea following injection of dilute hydrochloric acid into rabbits, and pointed out the possibility

of calling even almost moribund animals to life again by the injection af sodium carbonate; this in connection with Kussmaul's[108] description in 1874 of a pronounced air-hunger in diabetic coma, »die grosse Athmung«, formed the background for Stadelmann's[202] demonstration of the fact that an acid poisoning occurs in diabetic coma (1883). For the treatment of fully developed diabetic coma Stadelmann suggested intravenous injection of a 2–3 p. c. solution of sodium carbonate and was thus the first to adopt the injection of unmixed alkaline solutions to combat acidosis. During the next 25 years the interest in alkaline treatment of this form of coma was lively. Even though it is approximately correct that, as pointed out by Hanssen[62] in 1910, the number of patients with fully developed diabetic coma whose lives had been saved by a bicarbonate therapy, could still at that period be written with one figure, these few cures of a form of coma previously regarded as hopeless, have been of signal importance for the understanding of the problem and the therapy of acidosis. At about the same time it was realised that in infantile diarrhea[33] and in uremic coma, too, serious acid poisoning was often present. Owing to the usually unfavourable prognosis for the chronic renal disease the renal form of acidosis never attracted the attention of physicians as much as the diabetic acidosis.

In the decade 1910–1920 the clinical investigation of acidosis attained a wider recognition. From this period date Sellards'[195, 198] brilliant results in his treatment of cholera on the Philippines by intravenous injection of bicarbonate solutions, and from the same time we have Marriott and Howland's[79, 80] significant publications on acidosis in infantile diarrhea. Sellards' treatment was later carried on by Rogers[177] in India, which resulted in a considerable reduction in the mortality from cholera. A very considerable advance followed the publication by Van Slyke and Cullen[219] in 1917 of a practical clinical method for the determination of carbon dioxide in the plasma. It is hardly too much to say that this method, which put the analysis into the hands of hospital physicians, has been of decisive importance for the more detailed clinical elaboration of the acidosis problem. There was still, in the years that followed, much uncertainty concerning the optimal concentration of the bicarbonate solutions employed. There seems to have been a marked tendency to use comparatively concentrated solutions as it was not yet understood that it

was necessary to treat at the same time the dehydration which was present. Even though the momentary effect of the treatment was often indubitable, the final results were in many cases less satisfactory.

In 1922 insulin treatment of diabetes was introduced by Banting and Best and medical science was enriched by one of the most important means of fighting acidosis. Even though it is hardly possible to overrate the value of insulin treatment, it should nevertheless be pointed out in this connection that the impressive efficiency of the insulin therapy has caused too great a loss of interest in the alkali treatment of diabetic coma. The striking clinical picture of that affection, and the usually excellent effect of insulin treatment, have impressed most students and physicians to such an extent that their attention has been diverted from other less conspicuous but frequent and often very grave conditions of acidosis. The period after 1922 has therefore in the main been marked by the insulin therapy in its various forms. In American pediatry, however, clinical investigations on the alkali treatment of infantile diarrhea have been carried on, though with varying intensity, and the treatment with sodium lactate introduced by Hartmann[70] in 1930 seems lately to have gained an increasing number of adherents. It is especially Van Slyke (1934)[216] who has emphasised the value of using an *isotonic* sodium bicarbonate solution, a therapy which has been adopted quite extensively by Cullen[32] in Cincinnati. As was pointed out in the preface, the parenteral alkali therapy in spite of its excellent effects is still as a whole very little known. In 1934 the author introduced the treatment with isotonic sodium bicarbonate solution into European clinical medicine.

I

Introduction

1. Definition of the Term Acidosis.

By the term acidosis is meant a condition in which the degree of acidity of the blood and the tissue fluids is increased. Acidosis never occurs as a separate disease but only as a complication. Its deleterious effects are due to the fact that the increase in the degree of acidity in the tissue fluids brings about changes in the function of the cells and eventually destruction of the same. These changes may be of so grave a nature that acidosis becomes the actual cause of death, probably owing to paralysis of the cells of the respiratory centre.

The term acidosis was first used by Naunyn (1906)[147] in a discussion of diabetic ketonemia. The concept has later quite correctly been extended to include other forms of the accumulation of acid in the body and such cases in which, owing to loss of alkali (e.g. in severe diarrhea and intestinal fistulas), an increase in the acidity of the blood occurs. It is of historical interest that it was the latter form of acidosis which first attracted the attention of clinicians and gave rise to the introduction of the intravenous alkali therapy (O'Shaughnessy and Latta 1831–32).

The determination of the degree of acidosis can be made by direct measurement of the degree of acidity of the plasma (the hydrogen ion concentration), a quantity which, at the suggestion of the Dane S. P. L. Sørensen, is usually expressed by the sign pH*). This measurement, with the simplified methods now available, can be made in any well equipped hospital laboratory.

An expression for the degree of acidosis still simpler than the pH of the plasma is, however, as pointed out by Van Slyke and Cullen[219] in 1917, the total carbon dioxide content of the

*) Normal value 7. 35—7. 51.

plasma, since this value will be reduced in all cases of acidosis which are of practical clinical importance).* The content of carbon dioxide in the plasma closely follows the variations in the total content in the organism of acid-binding factors and thus becomes a reliable measure for the degree of acidosis. For a staff not specially trained the analysis has fewer possibilities of error than the measurement of the pH and forms a more convenient foundation than the pH value for the calculation of the amount of alkali needed for the treatment of the acidosis. In the analysis for carbon dioxide which is made by shaking the sample with lactic acid in vacuum, besides the amount of carbon dioxide derived from bicarbonate, the so-called »bound« carbon dioxide, the determination will also include the amount of carbon dioxide physically dissolved in the plasma, the so-called »free« carbon dioxide. The amount of free carbon dioxide is, however, so small, c. 5 p. c. of the total amount of carbon dioxide, that in practice no great error is committed by regarding the whole as bicarbonate. *From the above statement it will appear that acidosis in a clinical sense may be defined as a condition in which the bicarbonate content of the plasma is reduced, and that the only laboratory analysis necessary for the determination of the presence and degree of the acidosis is the analysis of the bicarbonate of the plasma.* In our exposition the term »plasma bicarbonate« will be used to denote the total carbon dioxide content of the plasma, this term being preferable to the frequently employed but less accurate expression »alkali reserve«.

The determination of the total carbon dioxide content of the blood as an expression of its content of alkali was first employed by Walter[224] in 1877 in his famous work on experimental acid poisoning. Before the introduction by Van Slyke and Cullen of the determination of the plasma bicarbonate into the clinic in 1917, the determination of the carbon dioxide content in the exhaled air was a frequently

*) In lung diseases with difficult respiration and in other conditions with reduced pulmonary function (e. g. under premortal conditions) an accumulation of carbon dioxide in the blood, a carbonic acid acidosis, is sometimes seen, which is not accompanied by any reduction in the content of bicarbonate, but is frequently associated with a considerable increase of the hydrogen ion concentration, expressed by a reduction of the pH value. Conversely, in hyperventilation the removal of large amounts of carbon dioxide by the lungs may cause a reduction in the total carbon dioxide content of the plasma which is not indicative of an acid poisoning.

used method for the diagnosis of the presence and degree of acidosis. The determination is based on the fact that the carbon dioxide content of the exhaled air varies approximately as the bicarbonate content of the plasma. In the practical developments of Fridericia[50] and Marriott[128] the method was widely adopted and has been of great value in the early clinical elaboration of the acidosis problem. Since, however, the collection of the gas samples requires no little collaboration on the part of the patient, a collaboration which it is difficult to obtain from very exhausted patients, and since, further, the results give a much less accurate picture of the bicarbonate content of the plasma than the direct determination, the method has now in the main been abandoned. The historical significance of the analysis, is, however, incontestable.

The normal bicarbonate concentration in the plasma (and the serum) is 22–30 millimols or milliequivalents*) per litre. The bicarbonate content of total blood is lower than that of plasma, the bicarbonate concentration of the red blood cells being only six-tenths of that of the plasma. The term millimol has to a great extent superseded the earlier much employed expression of the bicarbonate content in volume per cent (vol %) of carbon dioxide. The use of the term millimol is, however, more convenient, for in investigations on the acid-base equilibrium it is an advantage to be able to express the acid and basic elements in the same and thus comparable values. A recalculation of millimol carbon dioxide per litre of plasma to vol % can, however, easily be made, since vol % carbon dioxide = millimol · 2.3.

Bicarbonate (carbonic acid) is a weak acid, the amount of which normally constitutes about $^1/_6$ of the acid constituents (total acid) of the plasma (see Fig. 1). *It possesses the conspicuous property that it can neutralise stronger acids, bicarbonate being thus split into carbon dioxide and water.* The neutralisation takes place almost instantly. The separated carbon dioxide is removed by the lungs while the invading acids replace the bicarbonate. The greater the amounts of invading acids are, the less will be the amount of bicarbonate remaining in the plasma (see Fig. 1, accumulation of acid).

*) One millimol is 1/1000 part of a gram molecule, i. e. the molecular weight expressed in mg. 1 millimol of carbon dioxide (CO_2) is thus 44 mg of carbon dioxide. By a milliequivalent is meant the millimol value divided by the valency. Carbonic acid being monovalent, 1 millimol of bicarbonate = 1 milliequivalent.