A CLINICAL METHOD FOR DETERMINING THE ALKALINITY OF THE BLOOD.*

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The desirability of a clinical method for determining the alkalinity of blood—that is to say, the OH and H ionization—has long been recognized. The recent determinations of this ionization by Friedenthal,¹ Höber,² Fraenkel,³ Farkas⁴ and Tangl and his pupils⁵ have shown that the alkalinity is very slight and subject to very little variation. Accordingly a clinical method has seemed difficult to seek. The recent study of indicators by Salm,⁶ however, characterizing with the greatest accuracy a whole series of indicators, has suggested the possibility of devising a method at once certain, accurate and easy of application. The present paper is concerned with experiments to this end.

There are two general methods by which the reaction of a fluid may be quantitatively measured: 1. Titration to an end point. 2. Determination of the H and OH ionization. The former yields information concerning the amount of base or of acid present in a solution, but no direct evidence concerning the nature of the equilibrium. According to such a method, HCl and NaH₂PO₄ in equivalent amounts are equally acid. The latter determination of the H and OH ionization yields no direct information regarding the absolute amounts of base and acid in solution, but gives us direct evidence concerning the intensity of alkalinity, that is, the condition of the equilibrium.

All the methods so far described depend on titration. There are two reasons for this: 1. Investigations of the OH and H ionization of blood have hitherto been possible only with the aid of the concentration cell, involving difficult procedure and expert technic. 2. The indicators which have been in use do not change color within the range of ionization found in blood. Recently, however, Salm has carefully studied the exact point of H and OH ionization at which a number of indicators turn, and accordingly it has been possible to pick out from this list a certain number of these that give sharp color reactions at about the H ion concentration of the blood, in particular two, rosolic acid and neutral red.

Rosolic acid is orange-yellow in the presence of acid and red in the presence of alkali. There is an intermediate pink color at neutrality. According to Salm, it is orange-yellow at 1.10^{-6} n.H.; pink at 1.10^{-7} n.H., and red at 1.10^{-8} n.H. The changes are well marked and intermediate shades were easily distinguished. The variations of H ionization of the blood lies between 0.1×10^{-7} and 3×10^{-7} or less, a variation that falls within the bounds of neutrality as ordinarily conceived. It will be seen, however, that this variation lies at about the

middle of the color change of rosolic acid from yellow to red or, to be more exact, between the pink and the red, and it was to be expected that, if sensitive enough, this variation would be noticeable in a difference in shade of the indicator. In the present investigation rosolic acid was used. The first examinations were made on rabbit's blood. One c.c. of fresh rabbit's blood was caught in a centrifuge tube in which 10 drops of a 1 per cent. solution of NaF had been placed and 10 c.c. normal salt solution added. This was placed in the centrifuge for a few minutes, and the supernatant liquid then removed with a pipette to a clean test tube. Two drops of a 0.1 per cent. alcoholic rosolic acid solution were added and the pink color produced was compared with a standard. The test was repeated with laked blood from which the proteids had been removed by coagulation by heat. The same degree of color was obtained in this case as in the preceding experiment; that is, the reaction was neutral or slightly more than 1×10^{-7} . The objections to the clinical application of this method are that a comparatively large quantity of blood is required, that a standard to compare it with must be at hand, and principally that the color of the blood itself interferes with the color reaction. It was, therefore, determined to exclude, for the time being, the formed elements and to use the serum alone. The test-tube method also seemed cumbersome for clinical work, so ash-free filter paper was prepared with the alcoholic solution of rosolic acid.⁷ The paper was soaked in the solution and then hung up in the air to dry. While still moist, the paper was yellow, but on drying, which occurred rapidly, it became a delicate salmon pink. The serum was obtained in the usual way from the finger or ear of the patient, by capillary tubes, which, after the blood had clotted, were placed in the centrifuge. After the serum had separated, the tubes were opened with a file and a small drop of the serum removed by a capillary pipette and placed on the filter paper. The normal serum produced a strongly marked red color which contrasted well with the unchanged parts of the paper.

The serum in two cases of diabetic coma did not produce this change in color. The same observation was made in the case of a patient suffering with acute meningitis, and at the time of examination, in a comatose condition. The urine of this patient contained acetone, but no sugar. At autopsy the case proved to be one of basillar meningitis. The serum from a large number of cases of coma due to meningitis, without acetonuria, showed the normal alkaline reaction to rosolic acid.

The serum from a case of acute jaundice showed the same reduction in alkalinity that was observed in the diabetic coma. The serum in this case was yellower than normal and left a yellow stain on the paper quite distinct from the pale color of the diabetic reaction.

The blood from a number of athletes was examined in a similar way to determine if a variation in the alkalinity of the blood could be shown to occur after extreme physical exertion. For this purpose the blood was taken from members of the senior class crew immediately after a hard four-mile race, when all the crew were in a state of considerable exhaustion. The reaction was normal. No variation from the normal was observed also in the serum of a runner who had just completed a two-mile race and who was completely exhausted, fainting immediately after the blood had been obtained.

* Read in the Section on Pathology and Physiology of the American Medical Association, at the Fifty-eighth Annual Session, held at Atlantic City, June, 1907.

* From the Laboratories of Clinical Pathology and Biological Chemistry of the Harvard Medical School and the Boston City Hospital.

1. Friedenthal: *Ztschr. für allgem. Physiologie*, 1902, i, 56; 1904, iv, 44.

2. Höber: *Archiv für die gesammte Physiologie*, 1900, lxxxi, 522; 1903, xcix, 572. Also Hofmeister's *Beiträge*, 1903, iii, 525.

3. Fränkel: *Archiv für die gesammte Physiologie*, 1903, xcvi, 601.

4. Farkas: *Archiv für die gesammte Physiologie*, 1903, xcvi, 531.

5. Other articles on the subject which may be consulted are: Benedict, H.: *Archiv für die gesammte Physiologie*, 1906, cxv, 106-117. Szili, Alex.: *Ibid.*, pp. 72 and 82.

6. Salm, Eduard: *Ztschr. für physikalische Chemie*, 1906, lvi, 471.

7. The rosolic acid paper mentioned above may be obtained from Dr. R. L. Emerson, 739 Boylston St., Boston.

A number of cases of marked diabetes, with large quantities of acetone and diacetic acid and high sugar percentages, gave perfectly normal reaction. In all these cases there was no disturbance of consciousness, some of the patients being up and attending to their affairs.

A second experiment was carried out to verify these clinical observations. A rabbit was fed 25 c.c. of a 0.9 per cent. solution of HCl daily for two weeks. The serum showed no variation during this time. An increase in alkalinity above the normal has so far not been observed in any case.

At times, in cases of diabetes, an intermediate reaction between the normal and the marked reaction of the diabetic coma has been observed. It appears as a delayed reaction. The paper remains unchanged by the serum at first, but after a few seconds the red color gradually appears and attains its full normal intensity in a minute or two. This appears to be due to the loss of CO₂ by the serum on exposure to the air, and interferes with the use of the intermediate color reactions for quantitative estimation in the present form of the method.

From these observations it appears probable that the reaction of the blood is maintained at the normal point of ionization even in cases of marked acidosis. When, in extreme cases, the entire reserve of alkali is exhausted and the concentration of H ions increases, the result is coma. That this variation is extremely small, probably not more than $1.5^{-1} \times 10^{-7}$ n.H., is in full accord with the accepted views on the delicacy of the equilibrium that is constantly maintained in the body and the sensitiveness of living protoplasm in general to variations in reaction.

Henderson and Black⁸ have shown that in a system containing both free and combined carbonic acid in which there is not great variation in the tension of carbonic acid, the H and OH ionization correspond to those of blood serum and that enormous variation in NaHCO₃ results from slight variation (corresponding to that found in blood) in H and OH ionization. Therefore, it follows that variations in reaction to rosolic acid indicate not only H and OH ionization, but also NaHCO₃ content of blood, perhaps the most important factor in acidosis.

The present investigation shows that the slight variation in H and OH ionization heretofore detected only by the aid of the concentration cell can quite certainly be observed with the aid of properly chosen indicators, thus making possible the clinical investigation of the subject. It remains to determine which the best method of application may be, and then to proceed to a quantitative clinical study.

8. Henderson and Black: *Am. Jour. of Physiol.*, April, 1907.

Diagnosis of Suppurative Labyrinthitis.—W. P. Eagleton has tested the value of v. Stein's symptom in diagnosing supuration of the labyrinth and gives his conclusions in the *Archives of Otolaryngology*, June, 1907. He believes that the symptom has a value in chronic non-suppurative aural disease in which the labyrinth has become affected and that it is a very valuable aid in diagnosing the chronic suppurations of the semicircular canals. The symptom is probably more marked in cases of early involvement of the labyrinth, and may persist in some cases after drainage. The symptom described by v. Stein consists in "a peculiar inability of patients suffering from labyrinthine disturbances to execute delicate co-ordinate movements."

THE VESSEL CHANGES AND OTHER HISTOLOGIC FEATURES OF CUTANEOUS SYPHILIS.*

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While the literature covering the pathologic anatomy of syphilitic lesions is very extensive, it contains little which tends to elucidate the manner in which the process develops and spreads, many of the descriptions applying equally well to the other infectious granulomata. In order to arrive at any satisfactory conclusion or obtain a proper conception of the reaction the syphilitic organism produces it is necessary to examine an enormous amount of material, not only in different stages of evolution of a given lesion, but also in series. The present article is an endeavor, not by any means to cover the entire histopathology of cutaneous syphilis, but rather to point out some features in the histologic picture of the early and late lesions which are more or less pathognomonic and which perhaps offer some data on which to base a microscopic diagnosis.

Aside from the presence of the spirochætæ in the tissues, the reaction which they excite is more or less peculiar to this condition and should enable one to make a diagnosis in the majority of instances. It is a not infrequent experience of dermatologists to meet with cases where surgeons have excised initial lesions on extragenital parts under the mistaken diagnosis of malignant growths. To the expert the clinical features of such lesions should be sufficiently distinctive to exclude the latter, and where there is a doubt it is often a simple matter to examine histologically and differentiate the growth from carcinoma, which is about the most common condition which comes into question.

Hoffmann¹ believes the spirochætæ enter the lymph spaces of the rete where they are protected against phagocytosis or immediately make their way into the lymph vessels of the papillæ. Only after about three weeks, when multiplication has taken place, does a reaction appear. The first changes then would be an endo- and perilymphangitis, followed by budding of capillaries, infiltration and connective tissue hyperplasia. According to the findings of Ehrmann² the lymph vessels are involved secondarily, the earliest change taking place in the connective tissue interstices, followed by new capillary formation and perivascular infiltration. He based his deductions on gelatin injection experiments with initial lesions immediately after their excision. Unless special technic is observed the vessels can not readily be differentiated. In a general way, however, the arteries are distinguished from the accompanying veins and lymphatics by their thicker coats and greater abundance of elastic fibers. In an infiltration the media is relatively free and appears as a band separating the intima from the exudate. The walls of the lymphatics are thinner than those of the veins. The lymphatic capillaries are apt to have a more irregular lumen than the blood capillaries and a less complete lining. Their lumina often contain infarctions of a homogenous substance and sometimes a few lymphocytes.

In practice, as a rule, patients do not present them-

* Read in the Section on Cutaneous Medicine and Surgery of the American Medical Association, at the Fifty-eighth Annual Session, held at Atlantic City, June, 1907.

1. Die Ätiologie der Syphilis: monograph, 1906.

2. *Archiv. f. Derm. u. Syph.*, 1904, lxxviii, 1.