THE PATHOLOGIC PHYSIOLOGY OF PELLAGRA

IV. SERUM ELECTROLYTES AND ACID-BASE EQUILIBRIUM

By ROY H. TURNER

With the Technical Assistance of VIRGINIA BLANCHARD

(From the Department of Medicine, Tulane University of Louisiana School of Medicine, and the Medical Services of the Charity Hospital, New Orleans)

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Many clinical observers have considered acidosis to be a common and important feature of pellagra, an impression due chiefly to the acid reaction of the urine. An elaborate theory, based largely on an active imagination, explained the pathogenesis of the disease as an acidosis due to taking acid silicates in the drinking water. The first clear indication that a disturbance in acid-base equilibrium occurred in pellagra was furnished by Sullivan and Stanton (1), who showed that for some pellagrins an abnormally high proportion of the urinary nitrogen was bound as ammonia.

Ballif and Gherscovici, in Roumania, are the only workers who have used modern methods in the study of acid-base equilibrium in pellagra. Their reports are characterized by a distressing scarcity of clinical and chemical detail. They report (2) determinations of CO₂ combining power for 80 pellagrins by stating that for 59 per cent it was less than 65 volumes per cent, for 27 per cent less than 50 volumes per cent, for 6 per cent less than 40 volumes per cent, and for 8 per cent greater than 65 volumes per cent. They also found that the administration by mouth of 10 grams of sodium bicarbonate had little effect on the urinary pH and the CO₂ combining power of the plasma. In a later study (3) they determined plasma pH by a colorimetric method, and for 20 patients with grave acute pellagra they found an average pH of 7.27, and for the same patients an average CO₂ combining power of 49 volumes per cent. For 10 patients with chronic pellagra the average values given were normal. Ballif, Rennescu and Reznic (4)
ACID CASE No. 1

Milli-equivalents per liter.

Time in Days.

T R A N S - F U S I O N S

Fig. 1a. Graphs showing electrolyte Cc
ENTRATION FOR 41 PATIENTS WITH PELLAGRA
mention finding high chloride concentration along with diminished protein concentration in their patients with severe acute pellagra but normal chloride concentrations in the other types of the disease.

METHODS AND MATERIAL

Venous blood was collected after an over night fast, without stasis and protected from air. The CO₂ combining power of oxalated plasma was measured by the method of Van Slyke (5). Plasma chlorides were determined by the method of Whitehorn (6). For total fixed base of serum the method of Stadie and Ross (7) was used. Methods for determining serum calcium and phosphorus have been given in a preceding article (8).

In determining the acid value of serum proteins use was made of the formula of Van Slyke, Hastings, Hiller, and Sendroy (9). The acid value of phosphorus was obtained by multiplying milligrams of inorganic phosphorus by the factor \( \frac{1.8}{3.1} \) as adopted by Peters, Bulger and Eisenman (10). For calculating the base bound as bicarbonate we used our values for CO₂ combining power instead of CO₂ content. The error thus introduced is probably small.

The patients studied were 42 pellagrins. Detailed clinical and chemical data have been recorded in tabular form in article I of the present series (11). As a rule no attempt was made to supply electrolyte by means other than in the diet previously described (11).

RESULTS

The results are presented in tabular form elsewhere (11) and graphically in figures 1a-b, and 2. The outstanding features of the results are also outlined in the summary.

COMMENT

Our data would seem to indicate that low serum electrolyte concentration occurs more frequently than does marked disturbance of acid-base equilibrium as indicated by the CO₂ combining power of the plasma. This does not indicate that some of the mechanisms which may produce severe acidosis or alkalosis may not play a major rôle in the disease processes. In recent years leading workers (12, 13, 14) in
this field have stressed the importance of total electrolyte concentration, and Hartmann (15), Marriott and Hartmann (16), Hartmann and Darrow (17), and Hartmann and Elman (18) have brought forth strong evidence to show that abnormal serum osmotic pressure was of greater importance in some of the clinical conditions, which were formerly considered due chiefly to acidosis or alkalosis, than is the actual disturbance of acid-base equilibrium. One is justified in suspecting that disturbed serum osmotic pressure may be responsible, in severe pellagra, for the production of generalized cellular injury and death. We are now studying pellagra from this viewpoint.

Our findings for plasma chlorides are at variance with those of Ballif, Rennescu and Reznic (4) who mention finding high chlorides in pellagra.

The tendency toward low concentration of serum electrolytes is most likely due to diarrhea and occasionally to vomiting, both well recognized mechanisms for depleting serum electrolyte. One patient (case 36) who had very low plasma chlorides and serum total base did not show either diarrhea or vomiting during the few days of observation, and, according to the best obtainable history, she had been free of both for the preceding two weeks. There is a slight tendency toward low electrolyte content of the serum in other cases without diarrhea.

The mortality among those patients with greatly lowered concentration of serum electrolytes, and the striking relationship, observed in the other patients, between the clinical severity of the disease and the diminished electrolyte content of the serum, suggest an additional basis from which one may estimate the severity of pellagra, the prognosis, and a rational treatment.

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SUMMARY

A study of the acid-base equilibrium in pellagra is reported, based on 129 specimens of blood from 42 pellagrins. The data consist of 119 determinations of plasma chlorides, 125 of the CO₂ combining power
Fig. 1b. Graphs Showing Electrolyte
CONCENTRATION FOR 41 PATIENTS WITH PELLAGRA
of the plasma, 129 determinations each of serum proteins and inorganic phosphorus, and 53 determinations of total fixed base.

The data are presented and analyzed in graphs and histograms.

Plasma chlorides tended to be low. The plasma chlorides in 65 per cent of the observations were less than 576 mgm. per 100 cc. of plasma and in 46 per cent less than 551 mgm. per cent, while in 17 per cent they were less than 526 mgm. per cent. Two patients showed plasma chlorides of less than 400 mgm. per cent.

The maintenance of normal plasma chloride level, by diet alone, even in the absence of vomiting, met with only partial success.

Eighty-four per cent of the determinations for carbon dioxide combining power of the plasma gave results within the normal range, chiefly in the lower portion of the normal range, and 16 per cent were below normal. Marked depletion of plasma bicarbonate was rarely encountered. The observations of Ballif and Gherscovici concerning the carbon dioxide combining power of the blood in pellagra are confirmed.

Marked increase in serum inorganic phosphorus was rarely encountered. Instances seemed to be due to marked oliguria associated with both diarrhea and vomiting.

The sum of the acid values for chloride, carbon dioxide, proteins, and inorganic phosphorus, tended to be low. In 68 per cent of the 118 determinations the sum was less than 136 milliequivalents per liter.

In 32 per cent of the 53 determinations the total fixed base was less than 141; 5 patients showed values of 126 milliequivalents or less. It is probable that the small percentage of low values is misleading, due to the fact that an unduly large proportion of observations were made on convalescent patients.

Four of the five patients in whom the serum total base was less than 126 milliequivalents died soon after study.

The bearing of serum electrolyte concentration upon treatment of pellagra is mentioned.

Diarrhea and occasionally vomiting seem to be chiefly responsible for low electrolyte concentration in the blood serum of pellagrins.
CONCLUSIONS

Diminution in serum electrolyte concentration appears to be of greater importance in pellagra than disturbances of acid-base equilibrium.

BIBLIOGRAPHY

FIG. 2. HISTOGRAMS SHOWING DISTRIBUTION OF VARIOUS COMPOSITIONS

The height of the columns expresses per cent of the total number of determinations with on patients during convalescence. I. Plasma chlorides. II. CO₂ combining power or inorganic phosphorus. IV. Total base.
which fell within that particular range. A large proportion of the observations were made plasma bicarbonate. III. Total acid value for chloride, carbon dioxide, proteins and


