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)

(Received for publication October 27, 1930)

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 CO_2 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 CO_2 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 CO_2 combining power of 49 volumes per cent. For 10 patients with chronic pellagra the average values given were normal. Ballif, Rennescu and Reznic (4)

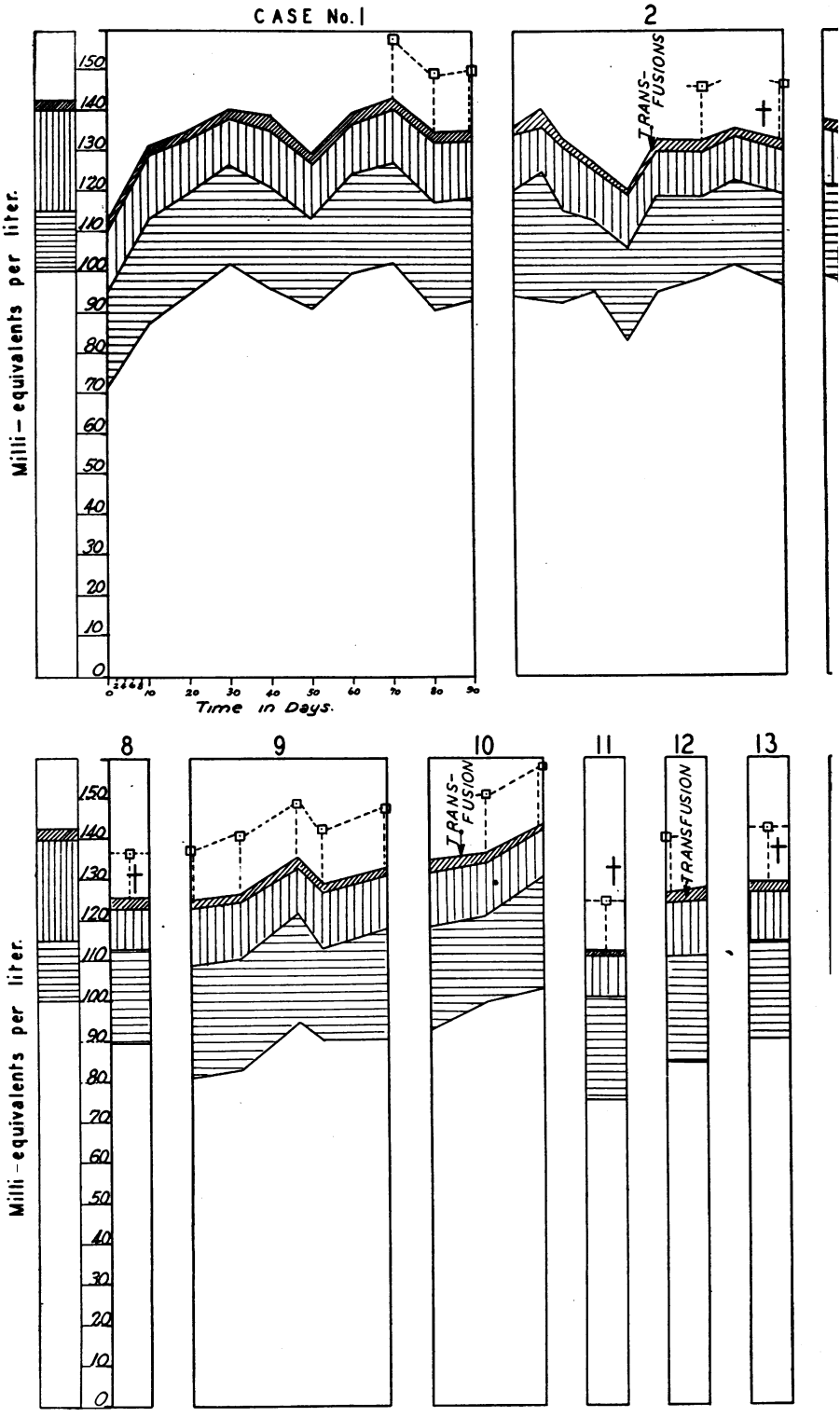
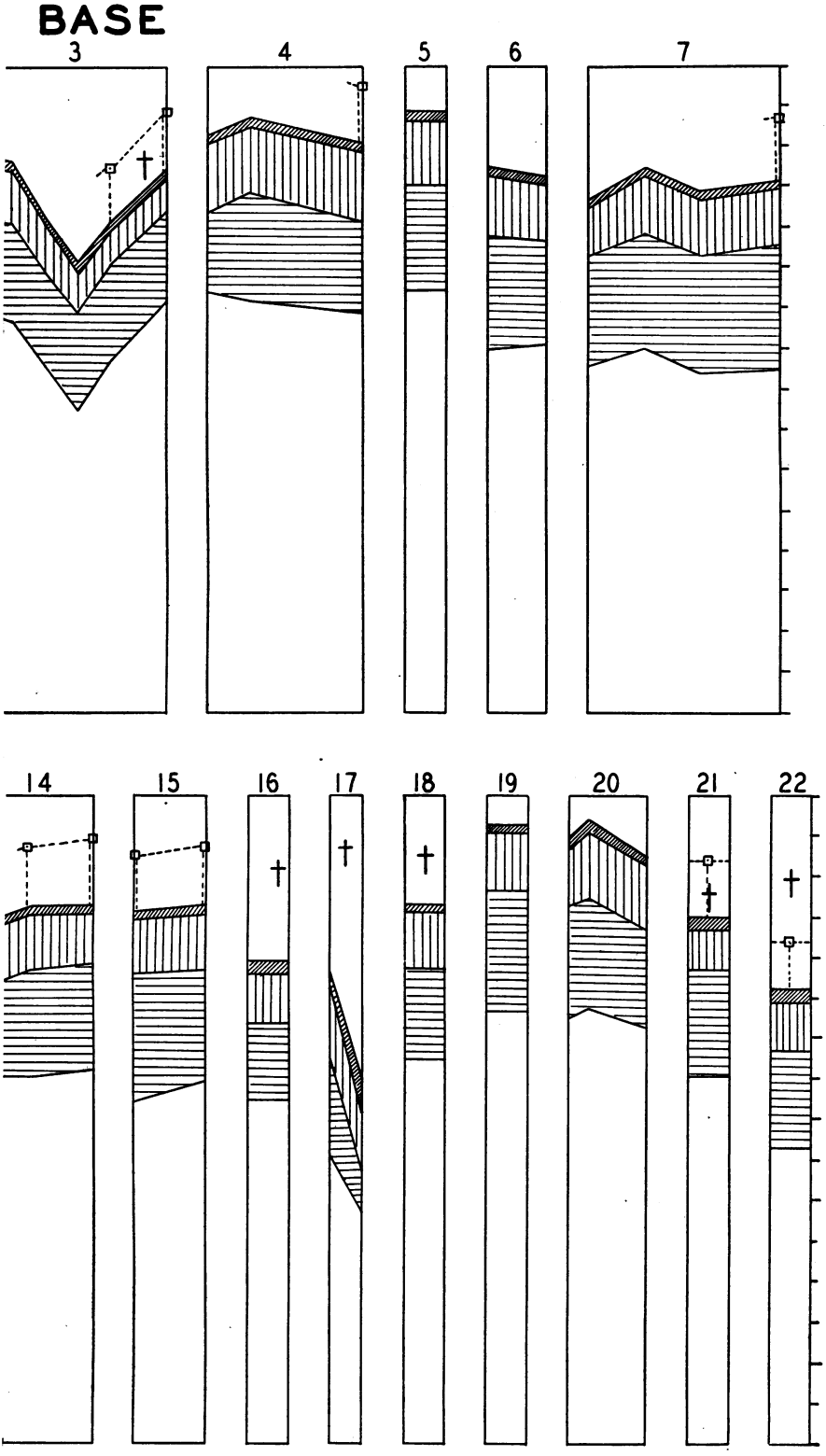


FIG. 1A. GRAPHS SHOWING ELECTROLYTE CC



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 CO_2 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 CO_2 combining power instead of CO_2 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 CO_2 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.

ACKNOWLEDGMENTS

Our thanks are due Mr. J. H. Arrington for the determinations of total base.

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 CO_2 combining power

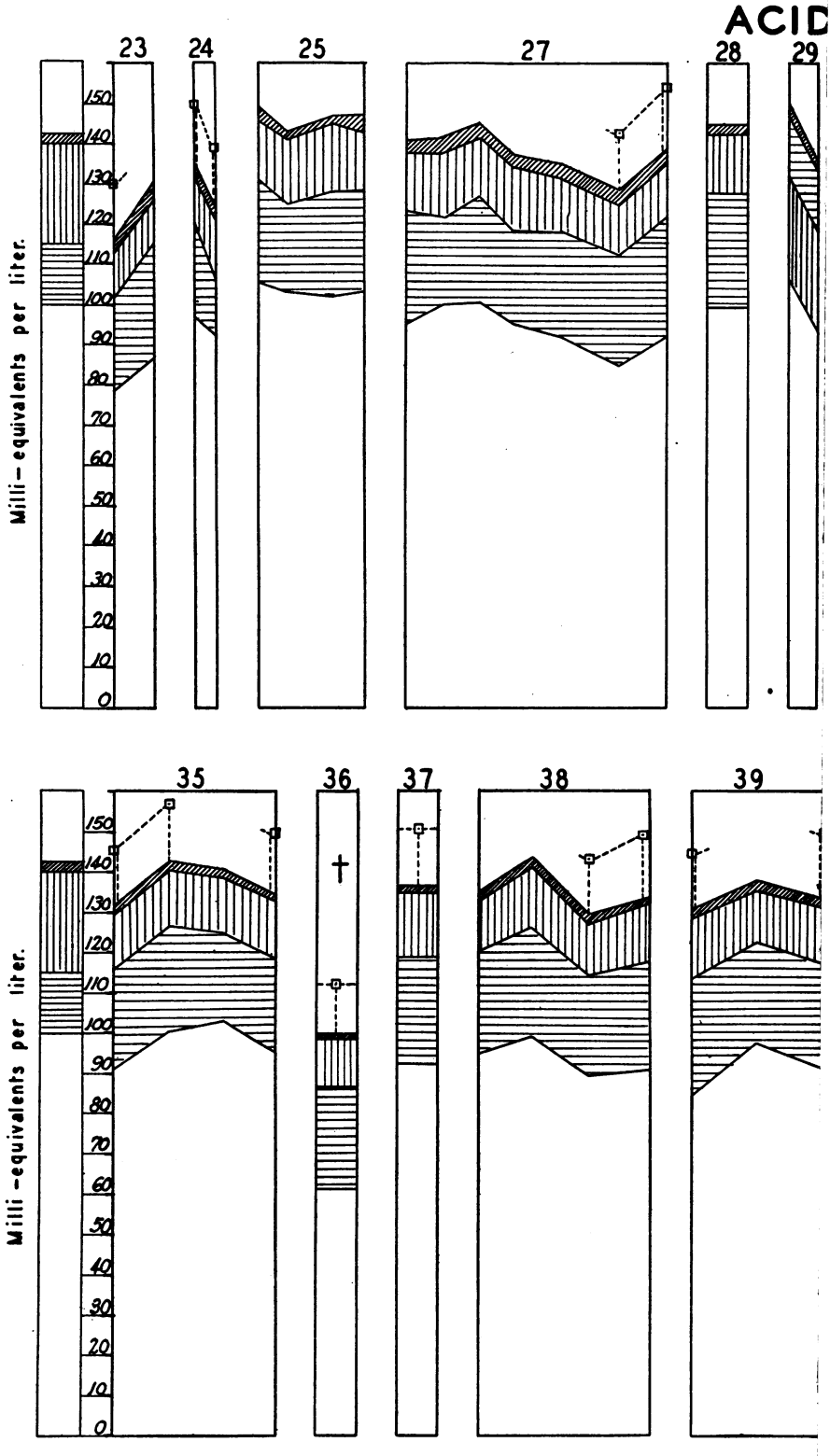
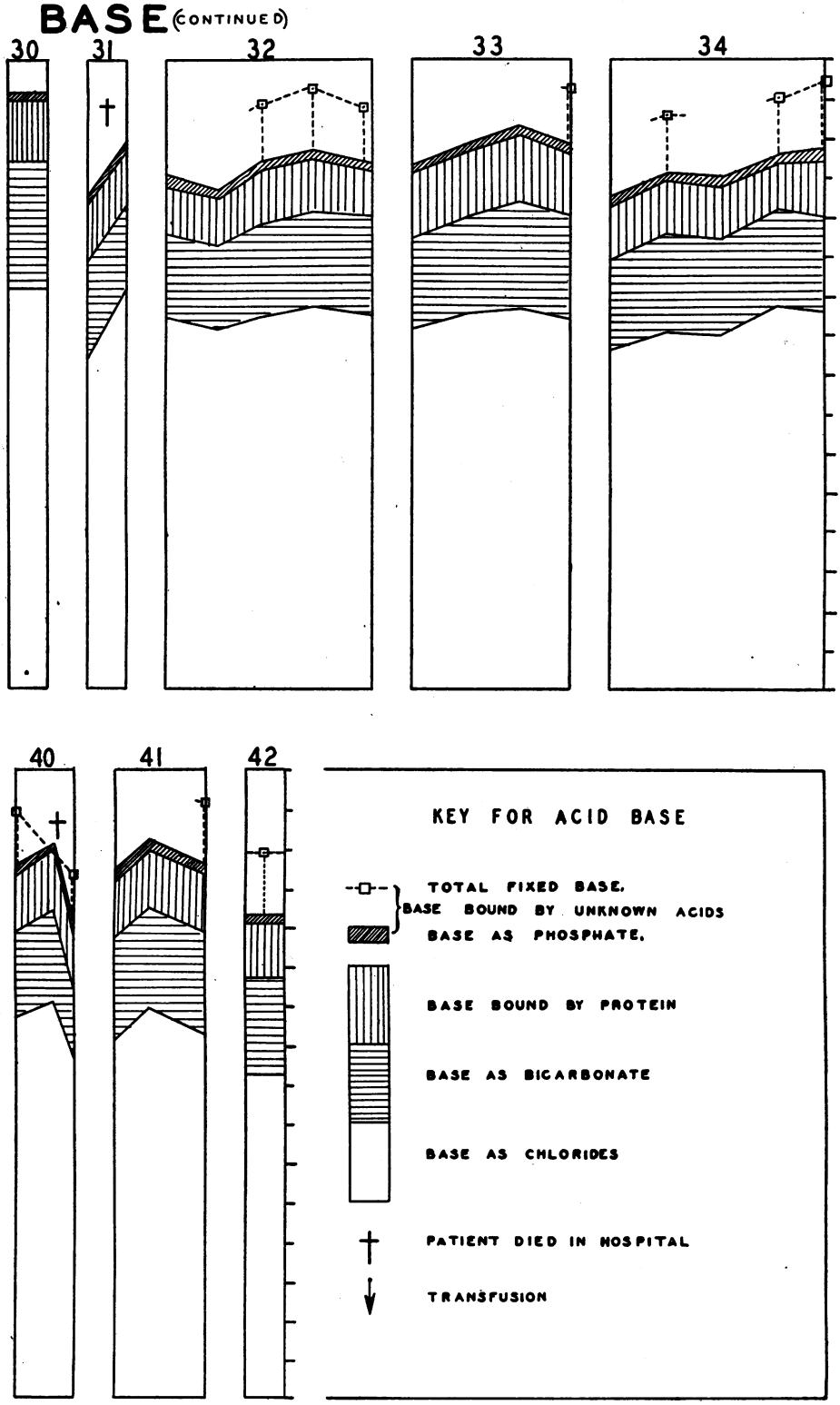


FIG. 1B. GRAPHS SHOWING ELECTROLYTE



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

1. Sullivan, M. X., Stanton, R. E., and Dawson, P. R., Arch. Int. Med., 1921, xxvii, 387. Metabolism in Pellagra: A Study of the Urine.
2. Ballif, L., and Gherscovici, I., Compt. rend. Soc. de Biol., 1928, xcviii, 393. La réserve alcaline et la calcémie dans la Pellagre.
3. Ballif, L., and Gherscovici, I., Compt. rend. Soc. de Biol., 1928, xcix, 1187. Le pH du plasma sanguin et du liquide céphalorachidien dans le pellagre.
4. Ballif, L., Rennescu, N., and Reznic, A., Compt. rend. Soc. de Biol., 1926, xcv, 1565. Contribution a l'Étude du Sang dans la Pellagre.
5. Van Slyke, D. D., J. Biol. Chem., 1917, xxx, 347. Studies of Acidosis. II. A Method for the Determination of Carbon Dioxide and Carbonates in Solution.

   Van Slyke, D. D., and Cullen, G. E., J. Biol. Chem., 1917, xxx, 289. Studies of Acidosis. I. The Bicarbonate Concentration of the Blood Plasma; Its Significance, and Its Determination as a Measure of Acidosis.
6. Whitehorn, J. C., J. Biol. Chem., 1921, xlv, 449. A System of Blood Analysis. Supplement II. Simplified Method for the Determination of Chlorides in Blood or Plasma.
7. Stadie, W. C., and Ross, E. C., J. Biol. Chem., 1925, lxv, 735. A Micro Method for the Determination of Base in Blood and Serum and Other Biological Materials.
8. Turner, R. H., J. Clin. Invest., 1931, x, 87. The Pathologic Physiology of Pellagra. III. The Serum Calcium and Phosphorus with Special Reference to Nervous Symptoms.
9. Van Slyke, D. D., Hastings, A. B., Hiller, A., and Sendroy, J., Jr.: Studies of Gas and Electrolyte Equilibria in Blood. XIV. The Amount of Alkali Bound by Serum Albumin and Globulin. J. Biol. Chem., 1928, 79, 769.
10. Peters, J. P., Bulger, H. A., and Eisenman, A. J., J. Clin. Invest., 1927, iii, 497. Total Acid-Base Equilibrium of Plasma in Health and Disease. VIII. Bicarbonate and Chloride in the Serum of Patients with Heart Failure.
11. Turner, Roy H., J. Clin. Invest., 1931, x, 61. The Pathologic Physiology of Pellagra. I. Tabulated Clinical and Physiologic Data.
12. Van Slyke, D. D., Wu, H., and MacLean, F. C., J. Biol. Chem., 1923, lvi, 804. Studies of Gas and Electrolyte Equilibria in the Blood. V. Factors Controlling the Electrolyte and Water Distribution in the Blood.
13. Gamble, J. L., Ross, G. S., and Tisdall, F. F., J. Biol. Chem., 1923, lvii, 633. The Metabolism of Fixed Base During Fasting.

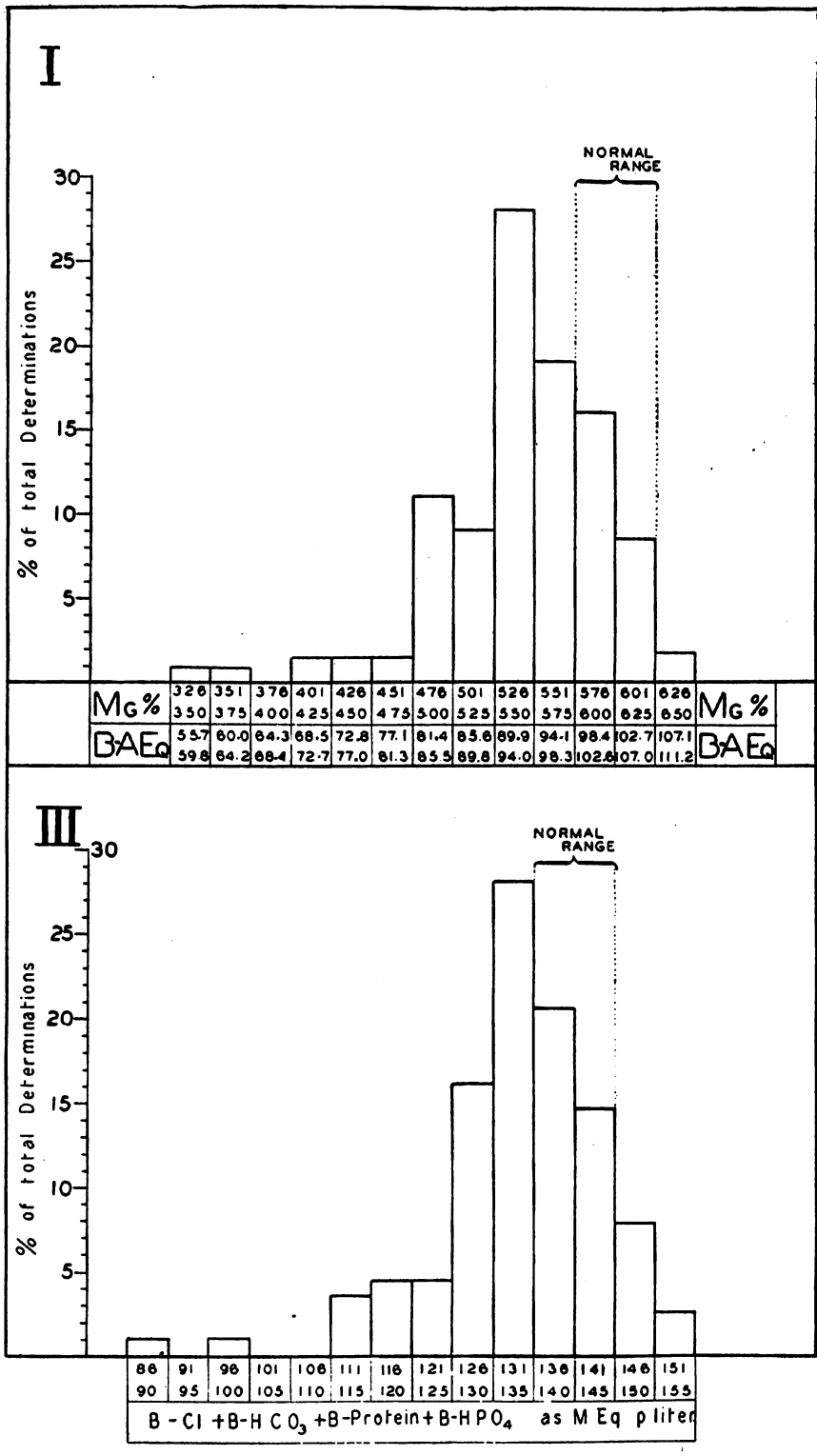
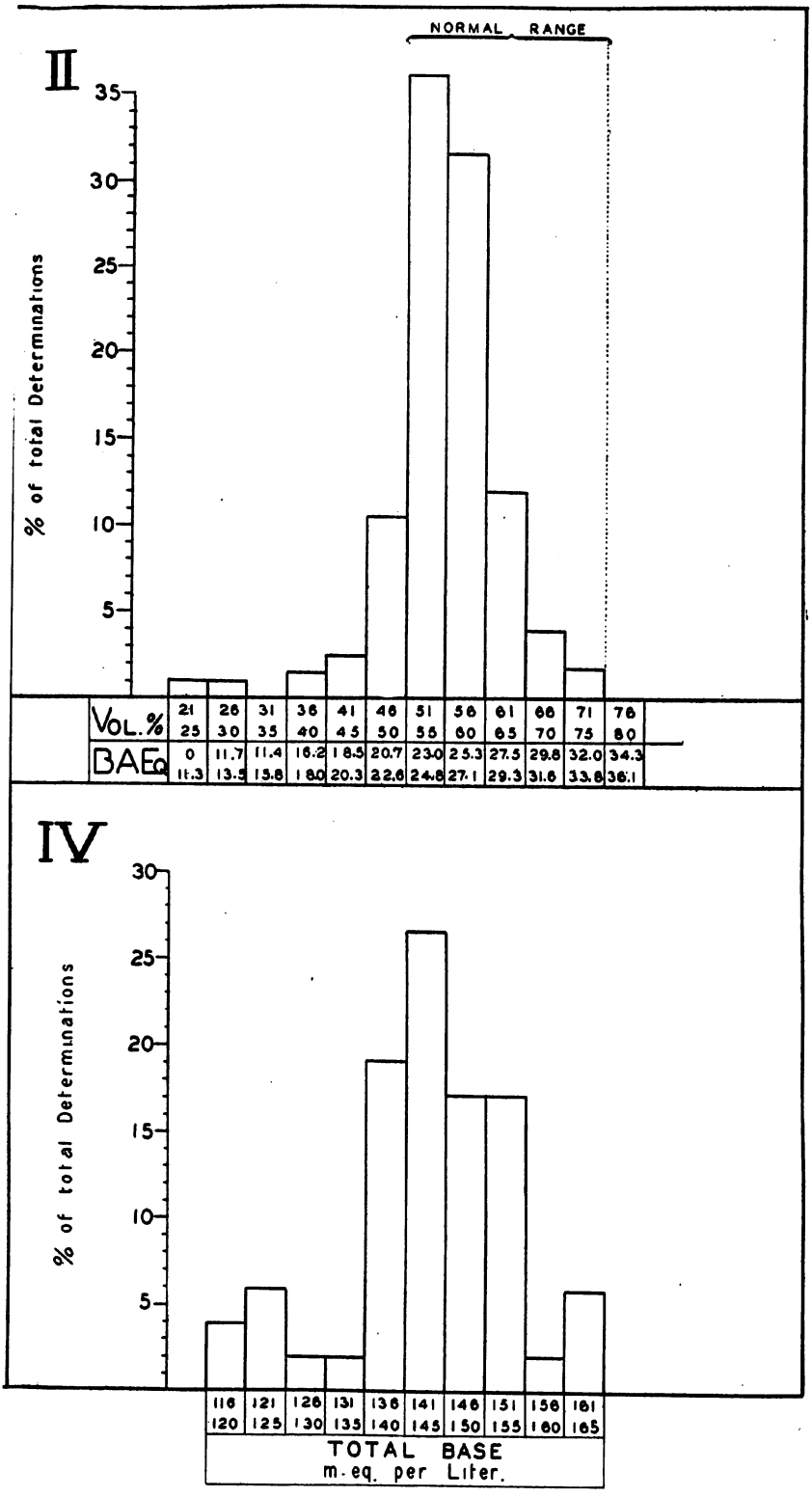


FIG. 2. HISTOGRAMS SHOWING DISTRIBUTION OF VARIOU

The height of the columns expresses per cent of the total number of determinations wh on patients during convalescence. *I.* Plasma chlorides. *II.* CO_2 combining power or inorganic phosphorus. *IV.* Total base.



US SERUM ELECTROLYTES AND COMBINATIONS THEREOF

hich 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

14. Bulger, H. A., Peters, J. P., Eisenman, A. J., and Lee, C., J. Clin. Invest., 1926, ii, 213. Total Acid-Base Equilibrium of Plasma in Health and Disease; VII. Factors Causing Acidosis in Chronic Nephritis.
15. Hartmann, A. F., Am. J. Dis. Child., 1928, xxxv, 557. Chemical Changes Occurring in the Body as the Result of Certain Diseases. I. The Effects of Diarrhea, Vomiting, Dehydration and Oliguria on the Acid-Base Balance of the Plasma of Infants with Mastoiditis.
16. Marriott, McK., and Hartmann, A. F., J. Am. Med. Assoc., 1928, xci, 1675. Newer Aspects of Acidosis.
17. Hartmann, A. F., and Darrow, D. C., J. Clin. Invest., 1928–9, vi, 127. Chemical Changes Occurring in the Body as a Result of Certain Diseases in Infants and Children. II. Acute Hemorrhagic Nephritis; Sub-acute Nephritis; Severe Chronic Nephritis.
Hartmann, A. F., and Darrow, D. C., J. Clin. Invest., 1928–9, vi, 257. Chemical Changes Occurring in the Body as the Result of Certain Diseases. III. The Composition of the Plasma in Severe Diabetic Acidosis and the Changes Taking Place During Recovery.
18. Hartmann, A. F., and Elman, R., J. Exp. Med., 1929, l, 387. The Effects of Loss of Gastric and Pancreatic Secretions and the Methods for Restoration of Normal Conditions in the Body.