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Comparative Diuretic Actions of Bismuth, Digitalis and Theophylline; Changes in Blood and Urinary Metabolites in Edema.

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The diuretic action of bismuth has now been demonstrated in a total of 21 patients with edema, thus confirming the results previously reported.[1] Attempts are being made to determine, if possible, the mechanism of the diuretic action from comparisons with the well-known diuretics, digitalis and theophylline, and chemical analyses of blood and urine. The results on 10 patients with edema are definite enough to warrant a report at this time.

The edemas represented were mostly anasarca of cardiac origin, nephrosis, and ascites due to hepatic cirrhosis. The patients were at complete rest in bed on constant fluid and salt intakes throughout. Urine was collected during 24-hour periods and samples of blood were removed daily, or as often as necessary, for analysis. Urea of the blood and urine was estimated by Folin's method[2]; chlorides of the blood by Austin and Van Slyke's method[3]; chloride of the urine by the Seelman-Volhard method,[4] and hemoglobin by Palmer's method.[5] After suitable control periods, at least 2 and sometimes all 3 of the following drugs were administered successively with intervening periods without medication; bismuth sodium tartrate (Searle), 0.03 to 0.06 gm. intramuscularly; powdered (standardized) digitalis in capsules, 0.4 to 2.5 gm. orally; and theophylline sodium acetate, 1.2 gm. orally, total doses. Generally, the bismuth was used after the other diuretics had been tried.

Briefly summarized, the results obtained in 8 patients showing definite diuretic action were as follows: The maximum increase in daily urine output after digitalis was from 100% to 190% of the control output; after theophylline, from 30% to 280%; and after bismuth from 10% to 360%. The duration of the diuresis after digitalis was about 4 days, after theophylline 1 day, and after bis-

[1] Hanzlik, P. J., Bloomfield, A. L., Stockton, A. B., and Wood, D. A., *J. Am. Med. Assn.*, 1929, xcii, 1413.

[2] Folin, O., *Z. f. Physiol. Chem.*, 1901, xxxii, 504.

[3] Austin, J. H., and Van Slyke, D. D., *J. Biol. Chem.*, 1920, xli, 345.

[4] Seelman, J. J., *J. Lab. Clin. Med.*, 1916, i, 444.

[5] Palmer, W. W., PROC. SOC. EXP. BIOL. AND MED., 1914, xii, 175.

muth 4 days (medians). The removal of edema fluid was estimated to be from 930 to 3300 cc. after digitalis, from 70 to 1750 cc. after theophylline, and from 200 to 3900 cc. after bismuth. Thus, the diuretic and antiedemic efficiencies of bismuth compared favorably with, or were superior to, those of the other drugs. Bismuth was more efficient when compared with digitalis and theophylline used individually, but less efficient when compared with the latter two drugs used together.

Bismuth and theophylline (digitalis not being as extensively investigated) caused concurrent, definite, and sometimes marked, increases in blood- and urinary-chlorides and an increase in urine-urea with a simultaneous decrease in blood-urea, when increases in diuresis resulted. These correlations failed of demonstration in 2 moribund patients who did not respond to bismuth and theophylline. Accordingly, the results as a whole fit in with modern conceptions of the mechanism of action of purine and certain metallic diuretics, namely, that the diuretic action is mediated through the tissues as a whole. The well-sustained diuretic and antiedemic actions of bismuth are more consistent with a tissue than with a purely renal action.

Final conclusions are reserved, however, until other possibilities are explored, and the diuretic and antiedemic efficiencies of various diuretics are tested in different clinical edemas.

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A Receiver Unit for the Determination of Lactic Acid.

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The analytical methods for determination of lactic acid have been greatly improved in the last few years, notably by Clausen[1]; Friedmann, Cotonio and Shaffer[2]; Davenport and Davenport[3]; and Friedemann and Kendall.[4]

The receiver unit here described was designed for use with the

[1] Clausen, S. W., *J. Biol. Chem.*, 1922, lii, 263.

[2] Friedemann, T. E., Cotonio, M., and Shaffer, P. A., *J. Biol. Chem.*, 1927, lxxiii, 335.

[3] Davenport, H. A., and Davenport, H. K., *J. Biol. Chem.*, 1928, lxxvi, 651.

[4] Friedemann, T. E., and Kendall, A. I., *J. Biol. Chem.*, 1929, lxxxii, 23.