7411 P

Recent Observations on Thyroxine and Allied Compounds.

W. O. THOMPSON, S. B. NADLER, S. G. TAYLOR, III, AND P. K. THOMPSON. (Introduced by A. B. Hastings.)

From the Department of Medicine, Rush Medical College, the Presbyterian and Cook County Hospitals, Chicago, and the Department of Biochemistry, Tulane University, New Orleans.*

In an effort to determine whether the formation of the comparatively soluble disodium salt accounts for the well-marked increase in basal metabolism recently observed by Thompson *et al*[1] following the oral administration of thyroxine in alkaline solution, we have prepared a disodium salt of thyroxine according to the method of Kendall[2] and have determined its calorigenic action in patients with myxedema. In one patient a single oral dose in distilled water of 15.1 mg. of the product containing 6.5 mg. of iodine, produced an increase in basal metabolism only from —29% to —21%, and in another patient the same dose produced an increase only from —26% to —20%. These increases are about the same as those produced by single doses of the monosodium salt containing the same amount of iodine and only about ⅓ as great as those produced by thyroxine in alkaline solution. This small effect may be explained in at least 2 ways: (1) The method as used by us may not actually yield the disodium salt. (2) A large part of the disodium salt may hydrolyze when treated with distilled water to form sodium hydroxide and thyroxine. Although the disodium salt is said to be soluble to the extent of 4% and the monosodium salt only slightly soluble, the well-marked effect of thyroxine in alkaline solution by mouth must not be attributed to the formation of the disodium salt without more evidence.

N-acetyl thyroxine, prepared according to the method of Kendall and Osterberg,[3] has been given intravenously in alkaline solution to 3 patients with myxedema in doses of from 10.5 mg. to 31.5 mg., containing from 6.5 mg. to 19.5 mg. of iodine; subcutaneously, suspended in 10% glucose, to 2 patients with myxedema in doses of 10.5

* We are greatly indebted to Dr. Frederick Tice and Dr. Karl A. Meyer for the privilege of making some of these observations in the Cook County Hospital.

1 Thompson, W. O., Thompson, P. K., Dickie, L. F. N., and Alper, J., *Arch. Int. Med.*, 1933, **52**, 809.

2 Kendall, E. C., "Thyroxine." New York, The Chemical Catalog Company, Inc., 1929.

3 Kendall, E. C., and Osterberg, A. E., *J. Biol. Chem.*, 1919, **40**, 265.

and 21.0 mg. respectively; and orally to one patient with myxedema in a dose of 10.5 mg. The patient who received 31.5 mg. intravenously showed a slight but fairly prolonged increase in basal metabolism of from —41% to —35%. If this slight increase may be considered definite, then this compound when administered intravenously in alkaline solution produces only about 1/16 of the effect of thyroxine. When given subcutaneously in suspension, the effect was greater and amounted in one patient to about ¼ and in another to about 1/6 of the effect of thyroxine given intravenously. These data suggest that the amino group is important for the calorigenic action of thyroxine.

By proteolytic digestion of desiccated thyroid according to the method of Harington and Salter,[4] we have prepared a peptide of thyroxine containing 2.5% nitrogen and 48% iodine, with a nitrogen:iodine ratio of 0.48:1. This peptide was insoluble in distilled water but soluble in sodium hydroxide. When suspended in distilled water and administered by mouth to patients with myxedema, it produced only a slight increase in basal metabolism, which was about the same as that produced by the monosodium salt in doses containing the same amount of iodine. When administered by mouth in alkaline solution it produced 3½ times as much effect as when given suspended in distilled water. In an alkaline solution its effect was about 4/5 as great as that of thyroxine injected intravenously in an alkaline solution, and slightly greater than those of oral administration of desiccated thyroid and an alkaline solution of thyroxine in doses containing the same amount of iodine.

7412 P

Antistreptolysin Content of Blood Serum of Children. Its Significance in Rheumatic Fever.

MAY G. WILSON, G. W. WHEELER AND M. M. LEASK. (Introduced by O. M. Schloss.)

From the Department of Pediatrics, Cornell University Medical College and the New York Hospital.

Todd[1a] described a method of titrating antistreptolysin in blood serum by which a diagnosis of a preceding hemolytic streptococcus

[4] Harington, C. R., and Salter, W. T., *Biochem. J.*, 1930, **24**, 456.

[1] (a) Todd, E. W., *J. Exp. Med.*, 1932, **55**, 267. (b) Todd, E. W., *Brit. J. Exp. Path.*, 1932, **13**, 248.