ment (6 dogs) caused a significant increase of the mucopolysaccharide (hexosamine)-level of the blood serum, whereas thyroxine treatment (11 dogs) brought about a significant decrease of the mucopolysaccharide-level of the serum. It may be added that thyroxine still had this effect even after thyroidectomy.

Our previous observations on man on the correlation of the decrease of the hexosamine-level in cases of hyperthyreosis were confirmed by our experiments on dogs. By the administration of thyroxine, the hexosamine-level could be decreased. On elevating the hexosamine-level by previous thyroidectomy or by prolonged administration of methyl thiouracyl, the effect of thyroxine became more manifest. By using the method of thyroidectomy, we were able to confirm the findings of Boas and Foley that thyroidectomy on rats produced a sustained increase in the hexosamine-level of the blood. Our experiments on dogs using thiouracyl and our observations on man regarding myxœdema were supported by the experimental results on hyperthyreosis.

Thus we conclude, as regards dogs and man, that the decrease of thyroid function results in an elevation of the mucopolysaccharide (hexosamine)-level, while the sustained increase of thyroid function results in a decrease of the mucopolysaccharide (hexosamine)-level of the blood.

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Identification of a Compound found during Separation of Purines in Human Urine

The purine bases of normal human urine have been separated, identified and quantitatively estimated[1-3]. During these investigations several additional unknown compounds appeared with the purines; they were separated and designated *E*, *W*, *S* and *Z*.

In our search for abnormal purines in the urine of patients with cancer and leukæmia, compound *Z* was found in high concentration in the urine of one leukæmia patient. From examination of a limited number of urine samples, it appeared that normal subjects and leukæmia patients in remission excreted large amounts of this material when compared with patients with cancer and active leukæmia. Identification of this compound was therefore undertaken.

Compound *Z* was isolated from a urinary concentrate by gradient elution chromatography on a column of 'Dowex 50'[1]. Further purification was accomplished by ascending 2-dimensional paper chromatography. Papergrams containing compound *Z* were sprayed with several reagents, but only the Jaffe reagent gave a positive reaction. The finding of a single red spot with this reagent in the position occupied by spot *Z* (rendered visible by ultra-violet light) suggested that this compound might be creatinine. Overlays of creatinine and *Z* in four different solvents gave no separation of these compounds.

The ultra-violet absorption spectrum of *Z* is unlike that of purines in that it has only end-absorption between *p*H 2 and 5, and above 11. It has, however, an absorption maximum between *p*H 5·8 and 11 at 232 mμ. A pure sample of creatinine exhibits the same ultra-violet absorption characteristics.

The insolubility of a silver–purine complex in acid solution is the basis for Weissmann's[1] separation of purines from creatinine, amino-acids, and pyrimidines. In order to determine whether creatinine could be precipitated with acid silver nitrate, a solution of similar creatinine concentration to that found in the urinary concentrate was prepared; this contained 10 mgm. creatinine/ml. water. Addition of acid silver nitrate gave a precipitate which was filtered, washed, and decomposed with hydrochloric acid under the same conditions as a urinary concentrate. The resulting solution on analysis by the Jaffe reaction contained 0·3 per cent creatinine. From this, it is evident that although 99·7 per cent of the creatinine remains in solution during silver nitrate precipitation, the presence of a high concentration of creatinine in the urinary concentrate is sufficient to exceed the solubility product of the silver–creatinine complex, and therefore the residual 0·3 per cent is carried through the procedure and appears with the purines.

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Muscarinic Receptors

The (+)-isomers of acetyl-α- and acetyl-β-methylcholine are respectively about 10 and 250 times more active as muscarinics than their corresponding enantiomorphs (Table 1). We have recently established the configuration of these (+)-isomers as I and II [1,2]; their configurational identity with (+)-muscarine (III) [3] about C_5 is indicated in Fig. 1.

The muscarinic activity of muscarine is considerably reduced in the isomers in which the CH_3, CH_2NMe_3 or OH groups are inverted[4]. If the quaternary N group and the ether O of (III), lying almost in a plane, form the chief two centres for drug-receptor association (the OH group acting as a secondary association site), then association with receptor must involve the lower surface of (III). Inversion of the methyl group of (III) would then produce a steric barrier against such association. Replacement of this methyl group by a hydrogen atom considerably reduces activity[5], probably because of reduction of