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Studies on the Intermediary Metabolism of Purines and Pyrimidines.

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Previous experiments¹ indicated that in the metabolism of uracil in the dog we are dealing with the following sequence of reactions: Uracil \rightarrow Isobarbituric Acid \rightarrow Isodialuric Acid \rightarrow Urea + an unknown carbon compound. Offe² has shown that formyloxaluric and oxaluric acids are intermediate products in the oxidation of isobarbituric acid *in vitro* by means of permanganate. Quite recently, Johnson and Flint³ have found that these compounds are also formed in the course of the oxidation of uracil by ozone.

Formyloxaluric acid and oxaluric acid were fed to dogs maintained in nitrogen equilibrium. In every case there was an increase in the urea output, suggesting that these substances were metabolized. Injection experiments with oxaluric acid yielded the same results. Formyloxaluric acid, on the other hand, when injected, was found to be toxic.

These findings seem to indicate that in the metabolism of uracil in the dog we are dealing with an oxidation resembling that *in vitro* as follows:

Uracil \rightarrow Isobarbituric Acid \rightarrow Oxaluric Acid \rightarrow Urea + Oxalic Acid.

They also suggest that oxaluric acid might be an intermediate product in purine metabolism. The formation of this substance as an end-product of the oxidation of uric acid by various oxidizing agents is a well-known fact.⁴

Experiments were also carried out with alloxan and parabanic acid to determine whether these substances might be intermediary products of purine breakdown in the animal body. Parabanic acid, when fed to dogs in nitrogen equilibrium, is excreted unchanged. The compound was isolated from the urine as the dixanthryl derivative.

Feeding experiments with alloxan show that this substance is

¹ Cerecedo, L. R., *J. Biol. Chem.*, 1930, **88**, 695.

² Offe, G., *Ann. Chem.*, 1907, **353**, 278.

³ Johnson, T. B., and Flint, R. B., *J. Am. Chem. Soc.*, 1931, **53**, 1077.

⁴ Biltz, H., and Schauder, H., *J. f. prakt. Chem. N. F.*, 1923, **106**, 108.

excreted only to a small extent in the urine; the greater part is apparently excreted in the bile. After feeding alloxan we observed a distinct decrease in the output of inorganic sulfur in the urine.

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On the Isolation of Guanidine Compounds from the Urine.

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In an attempt to find a reagent which would enable us to isolate guanidine compounds from urine, experiments were carried out with β -naphthalene-sulfochloride. The substances tested were guanidine, methylguanidine, as-dimethylguanidine and synthalin (diguanidinodecamethylene). We have found that all these compounds react with β -naphthalene-sulfochloride. Except for the methylguanidine derivative, the condensation products are very little soluble in water.

The procedure which we have used to recover the above compounds from the urine is as follows: A certain amount (50-200 mg.) of the substance was added to 50 cc. of human or dog's urine. The urine was evaporated to a volume of less than 10 cc. To the residue water was added, so as to have a total volume of 10 cc. This solution was treated with an equal volume of 4 N-KOH. To this a quantity of β -naphthalene-sulfochloride equivalent to 4 mols, dissolved in 25-35 cc. of ether was added. The mixture was shaken for about 8 hours. The precipitate formed was filtered, washed with water and recrystallized from water.

By means of this method we have been able to recover more than 80% of guanidine and dimethylguanidine added to urine. With methylguanidine the best yield obtained was 66%.