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## The Effect of Iodine on Creatinuria in Hyperthyroidism.

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The urine of normal human adults taking a diet free from meat, fish, peas and beans, contains no creatine. The only known exception to this is in women during the menstrual period when small amounts of creatine may appear in the urine. A very high creatine-free protein diet may produce creatinuria in women but has not been obtained in men. Creatinuria has been observed in starvation, wasting diseases generally, during carbohydrate deprivation, diabetes mellitus, Graves' disease, fevers and the muscular atrophies and dystrophies.<sup>1</sup> Studies made on 21 cases of Graves' disease with or without a nodular thyroid gland confirm in general previous observations regarding the appearance of creatine in urine of individuals with hyperthyroidism.

In observing the effect of iodine on creatinuria in hyperthyroidism the cases have been studied in a specially organized metabolism ward under rigid metabolic conditions. Each patient was given a creatine-free diet with a caloric value equivalent to 100% above the actually determined basal requirement, with a protein intake of 1½ gm. per kilo and the carbohydrate and fat distributed according to the likes and dislikes of the individual. Usually, however, the carbohydrates were taken more freely than fats. Such a diet brings the patient into nitrogen equilibrium within a few days. After three days to a week Lugol's solution, 1 to 3 cc., is given, in most instances as part of the program in preparation for operation.

Out of 16 cases of true Graves' disease all except one have shown a daily excretion of creatine varying from 200 to 1000 mg. On the exhibition of iodine in the form of Lugol's there is a striking diminution of creatine excretion to less than 100 mg. This is usually accompanied by an improvement in symptoms and a fall in the basal metabolism rate. In one case there was no improvement in symptoms or fall in basal but a remarkable drop in creatine excretion occurred. Of the 5 cases with nodular thyroid glands, the so-called toxic adenomas, relatively small amounts of creatine in the urine were observed although the basal metabolism was high in some of the patients. Iodine in the cases of toxic adenoma studied seems to have only a slight influence on the general condition and almost no

effect on the creatinuria. While the observations are by no means extensive, the creatinuria occurring in fever (pneumonia, sepsis) and experimental hyperthyroidism are uninfluenced by iodine. The result so far as it concerns experimental hyperthyroidism might be anticipated, since the symptoms, pulse rate, and basal metabolism produced by intravenous injections of thyroxine in rabbits are not modified by the administration of iodine by mouth.<sup>2</sup>

The significance of the observations reported in many respects is not clear. The fact that iodine diminishes the excretion of creatine in Graves' disease and has no effect on experimentally produced hyperthyroidism lends further support to the idea that the effect of iodine is due to a congestion within the thyroid gland mechanically interfering with discharge of thyroxine into the general circulation.

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<sup>1</sup> Hunter, Andrew, *Physiol. Rev.*, 1922, ii, 586.

<sup>2</sup> Sturgis, C. C., Zubiran, Salvador, Wells, Guy W., and Badger, Theodore, *J. Clin. Invest.*, 1926, ii, 289.

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#### Allergic Reactions in Rabbits to Bacterial Antigens.

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In January, 1927, Mackenzie and Hanger<sup>1</sup> described reactions in the human, following intradermal injections of antigens prepared from streptococci obtained from throats of rheumatic patients and normal individuals. These antigens were thermostable and non-neutralizable by immune serum. Like tuberculin, they gave a negative reaction during most acute infections, and in very young children. It was assumed by us that the chronic lesions, produced in the nasopharynx and tonsils of even normal individuals by the streptococcus, render such persons allergic to the bacterial protein as is manifested by these skin reactions. When these same streptococcus antigens, strongly active for the human, are injected into the skin of normal rabbits, the animals seldom show a local response. Cultures were therefore made of the naso-pharynx of rabbits to determine the presence or absence of the streptococcus, and also to establish the general character of the bacterial flora in these animals.

Our results agree essentially with those of Webster<sup>2</sup> and of Bull,<sup>3</sup> who note the overwhelming predominance of gram negative organ-