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.[2]

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.

[1] Hunter, Andrew, *Physiol. Rev.*, 1922, ii, 586.

[2] 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[1] 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[2] and of Bull,[3] who note the overwhelming predominance of gram negative organ-

isms, among which, members of the *B. lepisepticum* group are almost a constant finding. Webster has shown[4] that this group is responsible for snuffles and most of the other chronic respiratory infections in the rabbit. It seems reasonable to assume that in this animal the rôle played by *B. lepisepticum* is quite analogous to that of the streptococcus in man, and that the rabbit should show allergic reactions to antigens prepared from these organisms. Antigens were prepared from a number of strains of *B. lepisepticum* and *B. bronchisepticus*, isolated from the naso-pharynx of rabbits in our laboratory, among which sporadic cases of snuffles had appeared. Also from the virulent Rockefeller strain (R.D.) kindly furnished us by Dr. Webster. The method consisted of preparing Berkefeld filtrates of 72 hour plain broth cultures and preserving in sterile stoppered bottles in the ice box. Adult rabbits were shaved over the flanks and abdomen, and 0.2 mls. of the undiluted filtrate injected into the skin. Within 5 hours a slightly raised area of erythema appeared, which reached greatest intensity in about 24 hours, and usually faded within 60 hours, leaving a scaling, slightly pigmented spot. The animals varied much in the intensity of the reaction. In the strong reactors, the area was 5 to 7 cm. in diameter with considerable swelling and even ecchymosis. Most of the animals showed an erythema 3 to 4 cm. in diameter, while a small proportion showed no reaction, although they were found to harbor *B. lepisepticum* in the naso-pharynx. Striking immunological differences were noted between the "Strong" and "Weak Reactors," which will be recorded elsewhere.

Similar tests were carried out in guinea pigs, and the skin reactions were irregular or negative. These animals are quite free of chronic upper respiratory lesions and show a most inconstant bacterial flora.

Many factors influenced the intensity of the reaction though it remained strikingly constant for the same rabbit. In the young under 3 weeks of age, it was absent, but usually appeared by the 6th week. During pregnancy and lactation, wasting disease and severe acute infections, it was markedly diminished. Intravenous injections of the filtrate or of bacterial suspensions or even of India ink caused it to disappear for several days, or permanently, if the animal became ill from the injection. There was a diminishing effect of successive intravenous injections on the intensity of the skin reactions.

Repeated injections of the filtrate had but little effect. Animals which received 20 or more mills during the course of an experiment showed no change in their reactivity. It was also impossible

permanently to alter the reactivity of a section of skin. When repeated injections were made into an area already inflamed, there was less effect than usual, apparently because the endothelium was incapable of taking up more of the antigen. After healing, however, the reactions resumed their former intensity. The potency of the filtrates was somewhat diminished by boiling for one hour. We were unable to neutralize it with immune serum of an agglutinin titer 1:40. No deterioration has been noted in filtrates kept at ice box temperatures for 6 months.

The skin test is not limited to any strain of organism. Filtrates of most of the gram negatives from the pharynx of the rabbit will produce it, though certain of the avirulent ones lost this capacity after cultivation for several months on artificial media. Antigens from the virulent Rockefeller strain (R.D.) were active for all groups tested; however, the intensity of skin reaction is not a criterion of virulence, since strains of relatively harmless *B. lepisepticum* isolated from a certain group of rabbits, produced filtrates even more potent for those particular animals than those obtained from the more invasive organism. Broth controls were uniformly negative.

There is apparently considerable antigenic relationship between many gram negatives of different biological groups, inasmuch as rabbits react to filtrates of *B. influenzae, B. coli* and meningococcus organisms, to which they could not have been directly sensitized. Likewise, humans who react to filtrates of these organisms also react to those of *B. lepisepticum.*

[1] Mackenzie, G. M., and Hanger, F. M., *J. Immunol.*, 1927, xiii, 41.
[2] Webster, L. T., *J. Exp. Med.*, 1924, xxxix, 843.
[3] Bull, C. G., and McKee, C. M., *Am. J. of Hyg.*, 1927, vii, 110.
[4] Webster, L. T., *J. Exp. Med.*, 1926, xlviii, 573.

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Phagocytic Activity of Capillary Endothelium of Skin and Probable Relation to Focal Immunity.

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Bacteria and many colloidal substances injected intravenously rapidly disappear from the blood stream. This is due chiefly to the phagocytic activity of the reticulo-endothelial system of the liver,