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Studies in thyroid activity.

II. THE SPECIFIC PHYSIOLOGICAL ACTIVITY OF CERTAIN CONSTITUENTS OF THE THYROID GLAND.

By **E. C. KENDALL.**

[*From the Pathological Department of St. Luke's Hospital, New York City.*]

Investigations of the physiological activity of the thyroid gland have shown that the internal secretion of the gland serves many different functions. One or more of a series of symptoms accompany cases of thyroid deficiency. These symptoms are relieved by the administration of the thyroid gland of certain animals, as the sheep, hog, and ox. When this treatment is stopped the symptoms return. It would thus appear that the functions of the internal secretion of the thyroid may be fulfilled by furnishing the body with the constituents of the thyroid gland from another animal.

The separation of the various chemical constituents briefly described above suggested the possibility of determining which constituents controlled the various symptoms occurring in cases of thyroid deficiency.

The first step in the method of separation of the constituents results in two solutions. One of these contains about 60 per cent. of the total iodine and 9 per cent. of the nitrogen. This is designated "Solution *A*." The other, called "Solution *B*," contains 40 per cent. of the total iodine and 91 per cent. of the nitrogen. In order to establish the physiological activity of these solutions, experiments were carried out, first upon dogs, and then with cases of thyroid deficiency. The number of cases treated is insufficient to establish completely the physiological properties of these solutions, but the results based upon a series of experiments with two dogs extending over four months, with two typical cases of myxedema, and with three cretins, are as follows:

Solution *A* was found: (1) to affect the nitrogen metabolism and hence the body weight and temperature; (2) to produce tachycardia; (3) to cause nervousness and tremor; (4) to relieve

pain and great weakness felt in the back and certain sensations of cold felt on the head.

Solution *B* was found: (1) to change the dry, scaly, rough skin to a soft and entirely normal condition, which allowed perspiration to take place; (2) to remove the soreness of bones and joints; (3) to prevent cramps and twitching of the muscles; (4) to have a marked effect on the mental activity, especially noticeable in cretins; (5) to relieve the hard, firm condition of the flesh, allowing it to become soft and pliable; (6) to prevent burning sensations which flash over the skin from one part of the body to another.

Solutions *A* and *B* act independently of each other. Furthermore, each of these solutions has been subdivided and the various constituents separated have continued to act independently. It would thus appear that each function of the thyroid gland is due to the specific physiological activity of the separate and distinct chemical constituents of the gland. Baumann claimed that iodothyrin is the active principle of the thyroid gland. It is evident that there is no one active principle of the thyroid gland, but that there are many, each with its own specific action. The separation of the various constituents makes it possible to treat cases of thyroid deficiency with those portions of the gland whose deficiency is indicated by the symptoms. Furthermore, it will be possible to standardize the active principles of the thyroid gland by a method based on chemical analysis.

I wish to thank Dr. F. C. Wood and the attending physicians of St. Luke's Hospital for the opportunity of carrying on this investigation, and Mr. A. W. Thomas for assistance in the chemical laboratory.

Further work is being carried on, both with the chemical separation and identification of the various constituents and with the physiological activity of the same.