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Suffolk District Medical Society.

MEETING OF APRIL 26, 1922.

SUBJECT OF THE EVENING: ENDOCRINE THERAPY.

A CRITICAL CONSIDERATION OF ENDOCRINE THERAPY.

BY W. B. CANNON, M.D., BOSTON.

NOEL PATON entitled his little book on the endocrine glands "The Regulators of Metabolism." But these glands have other functions than that; they regulate growth, they determine the development of intelligence; they fix the appearance of the secondary sexual characteristics and the regular sequences in reproduction, and they control the nature and rate of the chemical changes which take place in the body. There is no question of the importance of these glands and of their capacity to cause very profound disturbances in all the above-mentioned processes. It is only fair to ourselves, however, and to a satisfactory development of the knowledge of the functions of these glands, that we recognize the present limitations of our ability to control these "controllers" and see clearly the dangers of using careless methods and of making hasty inferences.

In justification of these strictures it may be said, first of all, that we lack reliable clinical tests of the defective functioning of the endocrine glands. We have a good clinical test for the over-functioning of the thyroid gland,—the increased metabolism. This increase in cases of "hyperthyroidism" is not paralleled by any other pathological state. But we have no similarly trustworthy way of judging the operations of other glands. It is very common to attribute low blood pressure to hypoadrenalism, and to attribute high blood pressure to hyperadrenalism. There is no evidence whatever that the blood pressure is maintained by the secretion of adrenalin. In many different kinds of animals a small amount of adrenalin causes a fall of blood pressure rather than a rise. Furthermore, it has been shown that an amount of adrenalin which is necessary to induce a rise of blood pressure will stop the whole process of digestion. Dr. Aub has shown that after removal of the adrenal glands an animal may have no fall of blood pressure for two or three days. Stuart and Rogoff have removed one adrenal gland and severed the nerves to the other so that there was no secretion, and kept the animals thus operated upon in normal condition, for months. In the face of such evidence, to attribute a low blood pressure to absence of adrenal secretion is wholly unjustified. Similar remarks could be made about such conditions as adiposity or short stature in relation to these glands. These

conditions may be due to a variety of widely different causes. Furthermore, it is necessary to discriminate between what may be an immediate sequence of disturbance in the functioning of an endocrine gland and the results of secondary changes in other glands before we can decide what is the rational course to pursue.

We are largely ignorant of the ways in which agents are effective when they are administered. In literature which is widely distributed at the present time and in medical writings the giving of adrenalin by mouth is commonly advocated. There is clear evidence that relative to the physiological output enormous amounts of adrenalin can be given by mouth with no effect whatever. Either the substance is destroyed in the alimentary tract or it is absorbed so slowly that it has no influence. Recently it has been found that after an animal is deprived of the pancreas, the high blood sugar can be brought down sharply to normal by intravenous injections of an extract of the pancreas, but that the extract has no effect if given by mouth.

There is a danger in the misuse of endocrine products which is shared by all other therapeutic agents. For example, the misuse of adrenalin and pituitary extract in the treatment of shock. In a state of shock there is evidence that the individual is suffering from diminished blood volume, which fails to fill the circulatory system even though the blood vessels are greatly contracted. After the giving of pituitrin or adrenalin arterial pressure may be increased, but the circulation has not been improved in the essentially important capillary area. The action of these drugs is to constrict the arterioles. This dams up the blood in the arteries and, if anything, checks the circulation in the capillaries.

Certain fallacies ought to be borne in mind in dealing with these substances. They are frequently given in the belief that there is a deficiency of one gland or another. For example, because pituitrin will cause contraction of the uterus in labor it has been supposed that it is the natural function of the pituitary to stimulate the uterus during labor. That is a fallacy dependent upon the failure to recognize that pituitrin is a drug with a pharmacodynamic action. There is no evidence that pituitrin acts in the body as it does when given as a drug. We are not at all justified in drawing inferences from the therapeutic effect of a drug made from these glands as to their physiological rôle in the body.

A second fallacy is dependent on the use of polyglandular therapy. There is a tendency to believe that all the substances included in the mixture are effective. All the agents may get credit for a single one contained in the mixture. An analysis of a number of cases in which such a compounded preparation had been used with extraordinary effect showed that they could all be reasonably regarded as cases of hypothyroidism and that the thyroid substance in the mixture

had wrought its usual changes in such conditions.

Another fallacy lies in the claim that there is a condition of the body known as "hormone hunger," that is, that when a gland is absent or deficient and a mixture of gland substances is given the body will take from the mixture what it needs and will neglect the rest. That is pure theory. It is not commonly true of therapeutic agencies. It is not true of thyroid substances, for example, for thyroid can be given until it produces a very distressing condition. The body does not neglect it, but suffers from it.

I believe as we make progress in our knowledge of endocrine therapy we shall get greater and greater control of the bodily processes. Most of the original progress in endocrinology was made by clinical observers. That fact deserves emphasis. The clinics receive varieties of disturbances that are very difficult to reproduce in the laboratory. What is needed for progress is not this confusing, misleading use of mixtures of all sorts, but a careful use of single agents, rationally chosen, so that when results are obtained they may be attributed to the agent used. My plea is for a critical attitude in the presence of the present wave of enthusiasm for endocrine interpretations of medical disorders and for endocrine treatment of all sorts of complaints. Throughout the history of medicine advance has been made by critical study and not by simple faith. Furthermore, silliness on the part of the credulous has a tendency to repel the more sober-minded, so that persons who are most needed for the development of new knowledge in endocrinology are not encouraged to undertake the task.

THE USE AND ABUSE OF THYROID.*

By J. H. MEANS, M.D., BOSTON.

Although little enough is known of the function of any of the endocrine glands, I am inclined to believe perhaps that little is greater in the case of the thyroid than in that of any of the others. There are definite syndromes which we associate clinically with over or underactivity of the thyroid which can be closely paralleled artificially through thyroid feeding in the one case or thyroidectomy in the other. Furthermore, in the case of the thyroid a substance has been isolated in pure chemical form, which in many respects behaves as though it were the active principle, or perhaps better one of the active principles of the gland. This substance has been called thyroxin by its discoverer, Kendall.¹

The functions of all the endocrine glands are unquestionably closely interrelated, but the manner of these interrelationships is very imperfectly understood. Many of the hypotheses

*Such original work of the author and his associates as is referred to in this paper has been aided in part by a gift from Dr. William Norton Bullard.