Hypothyroidism

HYPOTHYROIDISM

An Essay on Modern Medicine

By

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INTRODUCTION

THE CRITICAL consideration of a clinical condition discloses many simple relationships that are obscure; many assumptions that should be proved; many theories without foundation. One justification for such a lecture is the opportunity to state these gaps in our knowledge.

Another reason for considering hypothyroidism, at this time, is that it is typical of much of the clinical pathology composing the practice of medicine in the present era. We now realize that the degenerative, functional, and malignant diseases that compose such a large part of modern practice have a prolonged initial period in which they are subsymptomatic. If we are to correct these conditions and practice medicine best they must be discovered in this stage.

This is especially true of hypothyroidism which by its very nature reduces the sensitivity of the sensorium. We are dealing with a disease which has no history, which is a disturbing function and which is causing gradual pathologic changes without the victim's knowledge. Diagnosis must be undertaken then as the result of hints, probabilities, and screening tests.

DEFINITION

In this discussion hypothyroidism is taken to mean the state of the body and its functions when insufficient thyroid hormone is present in the cells of the body. The term does not refer to pathology of the thyroid gland, nor to its size

or the rate at which it is producing thyroid hormone. The following elaboration describes the relationships that result in euthyroidism and the etiology of deficient thyroxine in the tissues.

HOMEOSTASIS

It is necessary to set forth the homeostatic mechanism which maintains the euthyroid state in order to study the various forms of hypothyroidism. The generally accepted scheme is that of a (feed back) mechanism in which effective concentration of thyroid hormone around the pituitary cells determines the rate of secretion of TSH. If the concentration is low, increased TSH secretion leads to rising thyroxine level in the environment of the pituitary secreting lobe, this then reduces its rate of TSH production; and as the TSH secretion decreases, the thyroid production of thyroxine falls off, leading to a reduction in concentration of that hormone around the pituitary cells which specifically respond to this diminution again by increased activity.

It seems to the author that this is too restricted a view of the relation between this target organ (thyroid) and the anterior pituitary and, indeed, too limited a view of the relationship of the pituitary to the other target organs and their hormones. It would seem to us that the dynamic biochemical state of the body was the initiating and controlling condition of pituitary activity and that the target organs are stimulated more or less as the tissues need their hormones. This point of view has been well expressed by Perlmutter and Riggs (1) who suggested that "thyroid function may thus be under the control of its end organ, the peripheral tissue, as well as being under the control of its master gland, the pituitary." The difficulty of defending this theory is the unproven connection between the tissues and the pituitary. This theory, however, seems the simplest

explanation of the activation or lack of activation of the thyroid when the animal is placed in a cold atmosphere or a warm one. The experiments of Uotila (2, 3, 4) bear on this specifically and indicate that the anterior pituitary must be connected to the hypothalamus in order that the cold environment may lead to stimulation of the thyroid. If reduction in thyroid hormone in the blood because of increased utilization by the cold tissues led to direct reduction of thyroid hormone in the sella turcica, the pituitary should be activated whether connected to the brain or not.

It would seem then that the need for more thyroxine when the tissues are chilled is transmitted to the brain by the thermo-regulating mechanism and that this in turn discharges stimuli to the anterior pituitary eliciting increased TSH production to raise the level of thyroid hormone supply to the chilled tissues. Hence, the homeostatic mechanism involved in thyroid function is as follows:

1. The need of the tissues for thyroxine, is transmitted to
2. The central nervous system, connecting the tissues to
3. The hypothalamus, which is functionally connected with
4. The anterior pituitary, which secretes TSH into the blood steam to stimulate
5. The thyroid gland which produces
6. The thyroid hormone, thyroxine, which is carried to the tissues
7. The action of thyroxine on the tissues reduces the demand on the hypothalamus.

It is conceivable that tissues might well use thyroxine beyond the rate at which the thyroid could supply it. This might be for a number of reasons involving all six other steps in the chain, but supposing these to be adequate for

ordinary conditions excessive utilization might result in hypothyroidism in the tissues. Such a condition would be extreme environmental cold. Does the person who freezes to death, die because of acute hypothyroidism? Does sustained fever or sustained muscular work require more thyroid hormone than the homeostatic mechanism can provide? There is no evidence.

These seven factors may be simplified into four by saying that thyroid function is governed by 1) the need of the tissues for thyroxine; 2) by the response of the brain (hypothalamus) to this need; and by 3) the anterior pituitary (secretion of TSH) resulting from activation by the brain; and 4) by the production of thyroxine by the thyroid stimulated by TSH. It is possible then to classify hypothyroidism into four etiological types; namely,

CLASSIFICATION

1. That due to *thyroid gland deficiency* in the production of thyroxine.

2. That due to insufficient secretion of TSH by *the anterior pituitary.*

3. That due to disorganization of *the hypothalamus,* in that pituitary activation does not occur, and

4. That due to inhibition, destruction, or diversion of thyroxine from the *tissues* owing to disease.

These may be called thyroid pituitary, hypothalamic, and somatic hypothyroidism. Diagnostic syndromatic, and therapeutic problems in connection with each of these types of hypothyroidism will be considered later.

The homeostatic principle involved for the thyroid may well apply to the adrenal and the gonad. It may be restated as follows: Endocrine homeostasis is maintained by the reflection of the state of the tissues in the central nervous system which expresses its corrective force through its control of the pituitary gland.

SPECIES

It seems that some experiments contain within their protocols deceptions which are accepted for years with the result that false conclusions dominate scientific theory for long periods of time. One of these has been the belief that adult animals, such as sheep (Simpson (5)), monkeys (Fleishman (6)), and dogs (Mayer (7)), do not need the thyroid gland and do not develop hypothyroidism after total thyroidectomy. The protocol indicated a total removal of thyroid tissue from the animals' body; this was the deception. Chaikoff (8) has just shown that when the adult dog is truly totally thyroidectomized by radioactive iodine myxoedema does occur. The surgical and chemical attempts to totally thyroidectomize the dogs were apparently not successful since the repeated use of comparatively large doses of radioactive iodine—10 millicuries given three times at 60-day intervals was necessary to produce total athyreosis. Chaikoff's (8) criterion for myxoedema was the development of alpha cells in the pituitary gland. In this first report, protein bound iodines, excretion of radioactive iodine, TSH stimulation, and conversion to protein bound radioactive iodine were not carried out. It was suggested that the thyroxine of the flesh of animals fed to the dogs might be enough to prevent myxoedema. Not much is required. Complete treatment of a human, weighing 50 kilograms, may be accomplished with 200 micrograms of thyroxine daily; a dog weighing 10 kilograms, therefore, might be completely cured by 40 micrograms and kept above myxoedema by 10 micrograms a day. These dosage levels have not been determined in the human; hence, comparative species sensitivity to thyroxine has not been studied. It may be concluded, however, that these animal species need thyroxine in adult life as much as do humans.