Journal of the Minnesota Academy of Science

Volume 5
Number 7 *Volume 4 (1936)*

Article 10

1936

Studies On The Interrelationship Of The Thyroid And The Suprarenal Cortex

Roy Alfred Waggener
Carleton College

"STUDIES ON THE INTERRELATIONSHIP OF THE THYROID AND THE SUPRARENAL CORTEX"

ROY ALFRED WAGGENER, PH. D.
Carleton College

Recent experimental work in the field of endocrinology suggests that the activities of certain of the endocrine glands are controlled, in part at least, by the secretions from other glands of the endocrine system. This regulatory function is perhaps best typified by the pituitary, since it appears to elaborate a number of substances which are specific incitants to other glands, including: thyrotropic hormones for the regulation of thyroid function, adrenatropic hormones for the control of the suprarenal cortex, parathyrotropic hormones for the control of the parathyroid, insulin antagonist for the control of blood sugar concentration, gonadotropic hormones for the regulation of the growth and function of the ovary and testis, prolactin for the stimulation of the mammary glands, and perhaps others. In addition to the specific incitants just enumerated, the pituitary exerts a profound effect upon body growth and function by liberating additional hormones which act upon the soma. These include a growth factor, a possible fat controller (lipoitrin), and alpha-hypophamine and beta-hypophamine. Lest this extensive array of chemical compounds synthesized by a single organ no larger than the end of one's finger fail to confound the most obstinate investigator, at least some of the glands under the influence of pituitary hormones in turn regulate pituitary activity through the presence of their secretions in the blood stream.

In addition to the elaborate interstimulation of the glands of the endocrine system by hormones, as suggested by the example just cited, there is increasing evidence to support the contention that certain glands are capable of liberating anti-hormones which counteract excesses of a particular hormone. Collip, Anderson, Thomson, Zondek, Blum and others have reported results which suggest the presence of anti-hormones in the normal circulation and also that these immunizing substances may be produced more freely in the presence of pathological excesses of the hormone concerned. It is quite clear that the endocrinologist is confronted with a difficult task as he endeavors to unravel the intricate interrelationships which play an all-important role in the maintenance of a normal hormone balance.

The pituitary probably presents the greatest chemical extravaganza of all of the glands of the system and, because of the wide range of its stimulating influence, it has often been regarded as the master gland of the body. Yet other glands of the endocrine system show evidence of interrelational complicity. We shall direct our attention for the next few minutes to the portion of this evidence which has a bearing upon the interaction between the thyroid and

the adrenal cortex. It will be recalled that the thyroid is responsible for the production of a hormone (thyroxine) which has been shown to influence the rate of tissue oxidation within limits. It is to be expected that substance which materially alters a process as fundamental as the metabolic rate would exert a profound and rather general influence upon the organism. Such is the effect of either subminimal or excessive amounts of thyroxine, if long continued, the time required for deleterious effects being somewhat greater in the case of the adult than in the growing individual. Prolonged administration of excessive doses of the thyroid principle to otherwise normal animals has been shown to cause a gradual destruction of the tissues of most organs until death ensues. The response of the adrenal gland is a noticeable exception. An enlargement of the adrenal has been repeatedly reported to accompany marked hyperthyroidism, whereas, thyroidectomy produces adrenal involution. In a study conducted on 40 thyroid-fed guinea pigs the writer found the weight of the adrenal glands to vary from 12 to 85% above normal, with the increment varying in most instances with the duration of the experiment. The increase in size is due to cell hypertrophy of the cortical layer with little or no perceptible increase in the medulla.

The evidence at the present time would indicate that thyroxine and some cortical principle (possibly cortin) are antagonistic and that the maintenance of a correct balance is a matter of prime importance. In this connection a contrast of deficiency symptoms in the two glands may or may not be significant; however, it will be recalled that hypothyroidism is followed by myxoedema, whereas, cortical deficiency is followed by dehydration, vascular collapse, and the loss of certain electrolytes (notably sodium and chlorine). A theory of balanced antagonists favors a plausible explanation of the cortical hypertrophy following thyroid feeding, in that it may be interpreted as the natural response of an organ to a shortage of its own secretion. An excess of thyroxine would be the equivalent of a shortage of its antagonist, namely, the cortical principle.

The removal of both adrenals from the dog is followed by a complex of symptoms and disturbances somewhat akin to those observed in Addison's Disease. The animal shows no ill effects for the first few days after extirpation and then passes into crisis, which is characterized by extreme muscular weakness, prostration, asthenia, dyspnoea, heart weakness, and finally death. During the early part of the survival period following adrenalectomy small doses of thyroxine are sufficient to precipitate typical adrenal deficiency crisis. The amount of thyroxine required to produce this effect is so small that it would have only a slight effect upon the normal animal, while its effect upon the experimental animal is acute and of the type which indicates an accentuation of the cortical deficiency. Furthermore, the precipitation of crisis by small doses of thyroxine can be prevented by the administration of cortical extract.

There is some evidence to indicate that the adrenal exerts a reciprocal antagonistic effect upon the thyroid and that the defects of thyroid function may be accentuated on the one hand or partially offset on the other by cortical secretion. I have been much interested in this aspect of the problem and have studied several series of experiments which were designed with this glandular interaction in mind. It is known that most animals can survive the removal of one adrenal and continue in apparent good health. While one gland is adequate for an animal that is otherwise normal, it cannot be expected to respond as successfully in an emergency calling for an increased output of cortical principle. In order to determine whether hyperthyroidism constituted such an emergency, a series of normal guinea pigs were fed desiccated thyroid in doses sufficient to produce death in 2½ to 3 months and typical weight charts were thus established, along with the average survival period. A second series of 40 animals was subjected to unilateral adrenalectomy and, after complete recovery, was fed desiccated thyroid equivalent to that given in the first series, equivalence being based on body weight. Weights were charted and the range of the survival periods determined. The second series was subdivided to form a third series which was given daily subcutaneous injections of cortin along with thyroid feeding. The animals ranged from one-fourth to one-half grown at the beginning of the experiment so that weight increase due to growth introduced a complication in the weight charts. In the case of the control series the weights showed an initial drop for a few days following the start of thyroid feeding, and then a gradual increase due to growth. Most animals ceased gaining after five to seven weeks, and, after a temporary hesitancy, would start a second decline in weight which was precipitous and would continue to death.

In the second series the feeding tests were conducted as in the first series except that one adrenal had been previously removed. A study of this group of animals revealed two points worthy of note. First, the survival period for thyroid feeding was noticeably shortened. Second, a plot of weights presented a distinctly different curve from that of series one. Unilateral adrenalectomized animals began to lose weight with thyroid feeding and were unable to gain weight from growth.

The third step in the experiment was an attempt to substitute cortin (Eschatin) injections for the removed gland. A successful completion of this step would definitely connect the increased susceptibility to thyroid feeding with a decrease in cortin, or to state it differently, a normal output of cortin has a protective value in hyperthyroidism. The work with cortin injections has not been carried to a satisfactory conclusion, although some progress has been made and beneficial effects have been demonstrated from its use. To date we have not succeeded in counteracting thyroid feeding to

the extent of establishing weight gains, but have succeeded in obtaining a noticeable prolongation of the survival period.

From the experimental evidence which I have just submitted, it would appear that the adrenal secretions are capable of furnishing a certain degree of protection against hyperthyroidism, although we have not yet been able to determine the possible limits of adrenal protection.

Further evidence of the interaction between adrenal secretion and hyperthyroidism is to be found in the clinical reports. Marine and Shapiro have reported beneficial effects from the administration of whole suprarenal to exophthalmic patients, but found the cortex alone more effective than the whole gland. Rowntree and others have reported the successful treatment of patients suffering from Graves' Disease with the use of cortical extracts. Although clinical reports are quite contradictory, some claiming benefit from Eschatin, others reporting that no benefit is derived from such treatment, the few cases of successful treatment are more significant than a hundred failures; and any claim for beneficial results must rest upon the assumption of interaction. Failure can be attributed to any one of scores of reasons, incorrect dosage, impotent preparation, or pluriglandular defects, just to mention two or three.

In summary we may say: there is an interrelationship between the thyroid gland and the adrenal cortex, and that it appears to be in the nature of a balanced antagonism between the hormones produced by these two glands. In support of this statement the following evidence has been submitted. (1) Hypertrophy of the adrenal cortex in response to excessive thyroid feeding. (2) Increased sensitivity to bilateral adrenalectomy from small doses of thyroxine. (3) Decreased resistance of guinea pigs to large doses of desiccated thyroid when one adrenal is removed. (4) Increased resistance of unilateral adrenalectomized guinea pigs to large doses of desiccated thyroid by subcutaneous injections of the cortical extract, Eschatin. (5) Successful clinical use of Eschatin and similar preparations in the treatment of certain cases of exophthalmic goitre.