The Endocrine Glands

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It is an evident fact that the human body, in truth every living organism, must maintain itself in a relatively steady state (homeostasis). Life can exist only within certain limits of variation in the internal and external environment. Every action or change in the internal environment of the body is normally accompanied or followed by a compensatory action or change. For example, if an increased production of heat occurs in the body a mechanism is initiated for disposing of the heat; or when after a meal containing starches or sugar the blood sugar rises, a corrective process is instituted to decrease the blood sugar. The state of the body at any moment is a sum of the "positive" and "negative" processes going on.

In order to maintain a steady state, the bodily processes must be subject to excitation or inhibition; some way of speeding up or slowing down processes must exist.

The chief agencies through which bodily processes are augmented and retarded, or controlled, are: (1) the nervous system and (2) the hormone secreting cells or organs. The nerves, conducting nerve impulses, are nervous regulators of metabolism and the activities of the body. The hormones are chemical regulators of metabolism and the activities of the body. We are interested in this lecture in the hormonal regulation of the body, although in some instances the nerves regulate the production of hormones.

The hormones are secreted into the blood and/or lymph by glands without ducts, in contrast to such glands as the salivary glands. Hence, the terms "Ductless Glands" and "Glands of Internal Secretion" are applied to the hormone producing glands. The term, "Endocrine Glands" is also used, which means "to separate within." The hormones or internal secretions have been called autacoids, meaning self-remedial substances, because they act much like drugs or remedial agents. It is believed that two sorts of autacoids exist functionally, hormones (to excite) which speed-up bodily processes, and, chalones (to make slack), which slow-down bodily processes.

The endocrine glands concerning which we know most are as follows: The pituitary gland or hypophysis, which is located at the base of the brain almost in the center of the skull. It is divided into three parts, the anterior lobe, the posterior lobe and the intermediate part.

The parathyroids and the thyroid lobes are located in the neck just below the larynx and on each side of the trachea. The thymus, which may or may not produce a hormone is located in the upper part of the chest beneath the sternum or breast bone. The mucous lining of the stomach and upper intestine produce several hormones and a chalone. The "islets of Langerhans," cells located in the pancreas, secrete a hormone, the remainder of the pancreatic cells form the external or digestive secretion of the pancreas. The adrenal glands are located just above the kidneys. The ovaries and testicles, or the gonads, and the placenta secrete hormones. Some think that the liver secretes a hormone or hormones. In fact, there is some evidence which suggests that the endings of some nerves (autonomic nerves) give off hormones which actually cause smooth muscle to contract or relax and glands to secrete.

The Pituitary Gland.—The posterior lobe of the pituitary gland, which receives nerves from the hypothalamus or the base of the brain, controls water metabolism. When it or the appropriate region in the hypothalamus is destroyed or injured, as sometimes occurs in skull fracture, an animal or a human secretes a lot of pale urine (diabetes insipidus) and thirst is excessive. This abnormality may be corrected by injecting an appropriately made extract (pituitrin, antidiuretic principle) of the lobe subcutaneously. An extract of the gland (pituitrin, oxytoxic principle) may be made which causes the uterus to contract and is used rather extensively in obstetric practice.

The anterior lobe secretes a number of hormones, it is believed; some say two, others five, and still others say ten or twelve. When the anterior lobe is removed in a young animal, the animal does not grow and the gonads do not develop and the thyroid and adrenals atrophy (pituitary infantilism). In the adult slow cachexia (Simond's disease) and death may result. The following extracts may be made from the anterior lobe: (1) An extract, phyone or somototropin, that causes growth in hypophysectomized animals; (2) gonadotropin, follicle stimulating and lutein stimulating, that causes development of the testicles and ovaries, and certain changes in the ovary such as development of the follicle, corpus luteum, and ovulation; (3) prolactin, that causes development of the mammary gland and the secretion of milk; (4) thyreotropin, that causes growth of the thyroid; (5) adrenotropin that causes growth of the adrenals. There is also a relation between the anterior lobe and pancreatic or sugar diabetes. If the pancreas is removed from an animal it develops diabetes, the blood sugar rises abnormally and sugar is excreted in the urine. Now, if the anterior lobe is removed, the sugar usually disappears from the urine. Because of the diversified influences of the anterior lobe it has been referred to as "governor of the endocrines," the "motor of the ovaries," etc. If the anterior lobe does not produce adequate growth hormone, a pituitary dwarfism results. Such dwarfs may have normal gonads, and

reproduce normal offspring; yet, in many instances when growth hormone is not produced in adequate amounts, the gonad stimulating hormone is also inadequately produced. In such a case, of course, reproduction cannot occur. Sometimes boys or girls grow normally, but do not develop sexually, and become excessively fat (Froelich's syndrome, Dicken's fat-boy type). In such instances, a tumor of the anterior lobe may be found on X-ray examination. Although the failure of sexual development is generally ascribed to deficiency of the anterior lobe, the cause of the obesity is ascribed to a disturbance of the hypothalamus because it is claimed that with a normal anterior lobe an injury of the hypothalamus in the rat causes very marked obesity. In this connection it must be kept in mind that defective thyroid secretion may also cause obesity, but the type of obesity or the places at which excessive fat is deposited differs in the two conditions. In a few human patients anterior lobe extracts have been given with apparent improvement in the presence of stunted growth, stunted sexual development, and excessive obesity. Unfortunately, in many cases no improvement results; but it may be hoped that in the future more potent extracts for the human will be made and patients will be treated earlier when the possibility of success is greater.

When too much growth hormone is produced prior to or during pubertal growth, a pituitary giant (7-8 ft.) is said to result. When too much growth hormone is produced after 21 years of age, or after the period during which growth of the long bones occurs, then acromegaly occurs, in which condition the tip (acro) parts enlarge or continue to grow. The head, mandible, nose, lips, hands and feet enlarge. In acromegaly a tumor of the hypophysis is frequently found, which may be removed by operation. By giving growth hormone to hereditary dwarf-mice, mice of normal size have been produced; also, very large (giant) rats have been produced. When the growth hormone is given to young English bull dogs, an animal resembling an acromegalic human in certain particulars results.

The Thyroid.—The thyroid gland secretes thyroglobulin, a protein (globulin) plus a substance called thyroxin, according to present knowledge. It regulates the rate at which oxidation or combustion occurs in the body and in a specific manner. If too little is secreted, oxidation is abnormally low; if too much, oxidation is abnormally elevated. When the thyroid gland is removed from a young animal (e.g. rabbit, sheep) the mental and physical growth is stunted. This condition is called Cretinism and occurs in human babies or children. If desiccated thyroid is fed in proper amounts to Cretin animals or children, normal growth ensues. To obtain normal mental development thyroid should be fed early in the disease. A crystaline substance, thyroxin, has been isolated from the thyroid, which has the same effect as desiccated thyroid. Thyroxin contains idodine, the presence of which is necessary for potency. Iodine not only activates thyroxin, but it also apparently makes

it easier for the gland to secrete thyroxin and when present in an amount above that required for normal bodily needs, it causes the gland to store secretion ("colloid") in spaces within the gland. When the thyroid secretes hyponormally in the adult, the condition is called adult hypothyroidism. Hypothyroidism, of course, also occurs in childhood, but may not be sufficiently severe to cause obvious Cretinism, causing only lethargy, dullness, easy fatiguability, and a tendency toward obesity (hypothyroid obesity). The adult hypothyroid has similar symptoms, and then severe myxoedema of the skin occurs, in which condition the skin is thick and dry, the hair falls out, and the face appears to be "bloated." Like Cretinism, hypothyroidism with or without myxoedema responds to thyroid administration. Sometimes the thyroid is said to hypersecrete; the rate of oxidation is augmented, the heart beats rapidly, breathing is increased; the patient sweats easily, is irritable and the fingers are tremulous. That is, the patient is said to be suffering from hyperthyroidism, thyrotoxicosis, or a toxic goiter, if the thyroid is enlarged. In some exopthalmus (exopthalmic hyperthyroidism or goiter) occurs. The administration of iodine helps such patients; it sometimes controls the condition, but unfortunately it may rarely make the condition worse. In many cases the thyroid must be removed by a surgeon; it is occasionally treated with X-rays.

Goiter (enlarged thyroid) is believed to be due to a relative or absolute iodine deficiency. If iodine is given in proper doses to young sheep or to children who live in goiter regions, the occurrence of goiter is markedly reduced. Peculiarly goiter may be present without disturbing bodily processes or it may be associated with either hyper or hypothyroidism. The "situation" is very complicated.

The Parathyroids control calcium or lime metabolism chiefly, although phosphorus metabolism is frequently disturbed also. When the parathyroids are removed the calcium in the blood decreases, the muscles and nerves become more and more irritable, until finally the muscles begin to twitch violently and convulsions ensue. These symptoms may be controlled by the proper administration of calcium, or by the injection of parathyroid extract (parathormone or parathyrin). However, if too much extract is injected the blood calcium may become so high that death from calcium poisoning results.

The Thymus chiefly because it involutes or atrophies in most mammals at puberty and for other minor reasons is generally considered in a discussion of the endocrine glands. That it produces an internal secretion has never been proved. However, a very interesting observation has been made recently. If successive generations of rats are injected with an appropriately made extract of the thymus, the new-born rats of the 5th to 7th generation are much more precocious in regard to hair, body, and eye growth. For example, eight days after birth the rats whose ancestors received thymus have a heavy fur, their eyes are open,

and their weight may be as much as 37 gm., whereas the control rats have little or no fur, their eyes are closed, and they weigh only 11 gm. Just what this remarkable phenomenon means has not been determined.

The Islets of Langerhans in the pancreas produce insulin, which plays a very important role in sugar metabolism. I shall not repeat the remarkable story of this hormone, since I believe most of you are familiar with it. The use of the hormone, insulin, in the treatment of diabetes mellitus has saved and prolonged the lives of thousands of diabetic patients. There are at least one million people living in the United States today who, according to statistical studies, have or will develop diabetes and will benefit from the use of insulin.

The ovaries produce at least two hormones, one called theelin and the other progestin. Theelin or estrin has been crystalized. It is responsible for the development of the secondary female characters. In addition it causes certain specific premenstrual changes in the lining of the uterus and in the ducts of the mammary gland. Progestin is formed by the corpus luteum, which grows at the site of the follicle ruptured in the course of ovulation. It completes the preparation of the lining of the uterus for the implantation of the fertilized egg. If the egg is not fertilized and hence does not imbed in the uterus, the corpus luteum degenerates and menstruation results. The exact cause of menstruation, however, is still unsettled. Progestin or the corpus luteum is necessary for the maintenance of early pregnancy, because if removed in early pregnancy, abortion or death of the embryo occurs. In some animals progestin also acts on the mammary gland. Estrin increases and progestin decreases the irritability of the uterine muscle. The anterior lobe of the pituitary is concerned in the periodicity of the menstrual cycle. Relaxin is a hormone produced by the ovary. Together with theelin it causes softening and relaxation of the pelvic ligaments, thus increasing the size of the birth canal. In the pocket gopher estrin even causes a resorption of the symphysis pubis, thus enlarging the birth canal. Estrin also prevents or tends to prevent lactation.

The placenta produces estrin in large quantities and probably progestin also. In addition it produces emmenin (placental hormone) and a substance that is like, but not identical with, the gonad stimulating hormone of the anterior lobe of the pituitary.

All of these active principles have been and are being employed for certain female disorders, but it is too early to evaluate the results in a scientific manner.

The testes produce a hormone called androitin (crystalized), which causes the development of the secondary male characters. Some claim that a second hormone, or chalone, is produced, inhibin, which prevents excessive enlargment of the prostate gland.

The adrenals consist of two parts, the medulla and the cortex. The medulla produces epinephrine, or adrenin, which is thought to be given off during emotional excitement to assist the body in meeting the bodily emergencies associated with fight or flight. Hence, the so-called emergency function of the medulla of the adrenals. The medulla of the adrenals is not a vital structure. However, if the cortex is destroyed in animals, death results in a few days. In man it is sometimes destroyed slowly and Addison's disease, or chronic adrenal insufficiency, results which terminates in death. The active principle or hormone of the cortex may be extracted and is called cortin. Cortin keeps adrenalectomized animals alive and preserves the lives of patients with Addison's disease. In adrenal insufficiency the metabolism of sodium and potassium is deranged. The sodium in the blood decreases and the potassium increases to the extent that potassium poisoning results. Such animals are benefited markedly by giving sodium chloride. In fact, adrenalectomized animals may be maintained for months without cortin on a high sodium (sodium chloride and citrate) and low potassium diet.

The gastrointestinal hormones.—If extracts of the lining of the stomach are made and injected, gastric secretion is stimulated. The active principle has been called *gastrin.* It is apparently a chemical substance known as histamine. *Secretin* is a hormone produced by the lining of the upper intestine which causes the pancreas to secrete its very important digestive secretion. Cholecystokinin is a hormone produced by the upper intestinal lining, when acids and fats are eaten, which causes the gall bladder to contract and evacuate. Enterogastrone is a chalone which is produced chiefly by the intestinal lining when considerable fat and sugar is eaten. This chalone depresses gastric secretion and motility, i. e. it slows down gastric digestion apparently so that fat and sugar will not be delivered to the intestine at too rapid a rate.

It should be obvious from this very brief review that the endocrine glands play a very important and essential role, a vital role in many instances, in regulating the processes occurring in the internal environment of our body. We know considerable about the subject at present, but more is to be learned. In numerous instances we can produce, prevent and control defects of the endocrine glands in animals, and much of this knowledge has been, and more in the future, may be applied successfully to human beings afflicted with grave disturbances of endocrine function. Many lives have been saved, prolonged, and made happier. The future outlook is even brighter.

(This lecture was illustrated with sixty lantern slides.)