5-16-1929

The Endocrine Glands

Mary Gordon Rule

THE ENDOCRINE GLANDS

A Thesis

Submitted in Partial Fulfillment of the

Requirements for Department Honors

Submitted by Mary G. Rule

Ursinus College,

Collegeville, Pa.

Approved by J. H. Brownback

Department of Biology.

May 16, 1929.

TABLE OF CONTENTS

INTRODUCTION

One of the most interesting and least understood phases of animal physiology is the influence of the endocrine glands on the physical and psychical behavior of the organism. In the olden days the nervous system was thought to have complete control of all bodily processes, but recently another field has been opened, showing the action of another system as complex as the nervous system and closely related to it.

The endocrine glands or ductless glands are those which, obviously, have no ducts. Exocrine glands are furnished with materials from which their secretions are manufactured. These are then poured into the body cavities or on the exterior of the body through definite structures, tubelike in form, called ducts. Endocrine glands, on the other hand, are furnished with raw materials by the arteries. These secretions, elaborated by the glands, are carried away by the veins since there is no communication with the body structure as a whole.

The secretions elaborated by the ductless glands are known as harmones, the name being given by Sterling twenty years ago and derived from the Greek meaning "I stir up or excite". These hormones or chemical activators may initiate changes in the functional state of a distant nerve cell or terminal, or series of chemical changes, or take part in some intermediary chemical reactions in a distant organ.[1]

Not all glands are given solely to sending out their secretions by means of veins. Some are wholly ductless, as the thyroid, parathyroid, pituitary organ and intestinal mucosa. Other glands produce secretions that are eleminated by ducts and others that are carried away by the blood stream. Such are the pancreas and sex glands. These will be treated more fully later in the discussion.

1. Abel, John J., Chemistry in Relation to Biology and Medicine with Especial Reference to Insulin and Other Harmones. Science ns 66:337-46, October 14, 1927, p. 338.

The heart has been shown to elaborate a secretion which influences the rate of its contractions by an action on its regulatory nervous mechanism. The juice from the embryonic heart contains a substance indispensable for the growth of part of the heart. The carbon dioxide, excreted by our tissues as an end product of metabolic activities acts as a hormone or regulator of the external respiratory apparatus. And in addition to the many analogies already made between the plant and animal kingdoms we find an additional similarity in the action of vitamins. These may be called harmones of plant origin and are similar to those produced in the animal organism.[2]

These glands are extremely important for life. If any interference in their proper working caused by disease or removal occurs, death results in some instances, as in the removal of the adrenals. Other glands are not essential for life but if disturbed the proper functioning of the body is interfered with. Other glands may take over their duties to a limited extent but of course cannot entirely replace the missing or diseased structure.

Hence efforts have been made to replace the missing organs and secretion. As early as 600 B.C. we find preparations from testis given in treatment for obesity. Animal derivatives have long been used in medicine though not at all of the same nature or preparation as today. Swines' fat, hair of a goat, and human bone were used by the ancients, apparently to drive away the devils causing the disease by their vile taste and odor. Today we have scientific means of preparing these extracts and some knowledge of the proper means of applying these.[3]

In this paper I shall attempt to describe the structure and locations of the endocrine glands, the chemical nature of their hormones, their applications in medicine, and the relation of the glands to each other.

2. Ibid, p. 339.
3. Parke, Davis and Co., Lectures on Biological Products, p. 154.

The Adrenals or Suprarenal Capsule

The first endocrine gland that we shall consider is the adrenal. There are two of these glands resting in a pad of fat just above the kidneys. They are small flat bodies of yellowish color, in the human varying from $1\frac{1}{4}$ to $1\frac{1}{2}$ inches in length and from $\frac{3}{4}$ to 1 inch in width. Together they weigh less than one-third of an ounce but life is impossible without them. If they are removed the animal appears normal for a day or two, but then the appetite fails, apathy and muscular weakness follow with prostration, fall in temperature, labored respiration, irregular and weak heart action followed by death in three to six days.

The glands are double structures, consisting of medulla and cortex, the former containing the active principal, adrenalin, also termed suprarenalin, suprarenin, adrenin, and epinephrine.

In looking into the history of this extract we find that about 1903 J. J. Abel of Johns Hopkins University separated the hormone from tissue in the form of a benzoyl derivative which was decomposed with hot sulfuric acid and obtained in the form of a sulfate. A picrate, bisulfate and other salts were prepared besides an acetyl derivative, phenylcarbamic ester and other derivatives. The formula determined was $C_{17}H_{15}NO_4$.

The Japanese chemist, J. Takamine, established a much less laborious process by simply adding ammonia to a more concentrated extract. The native base was obtained in the form of burr-like crystals instead of the amorphous base of Abel. Takamine took the formula $C_{10}H_{15}NO_3$ to represent the substance, the difference in the two formulae being in the retention of a single benzoyl radicle, C_6H_5CO.

The true empirical formula, $C_9H_{13}NO_3$ was finally established by Aldrich, an assistant of Abel, and verified by others abroad. The chemists, Dakin, Jowett, Pauly, Friedmann, Stolz and Flächer, have found that the suprarenal medullary harmone is an aromatic amino-alcohol, dihydroxy-methyl-amino-ethylol-benzene,

$$C_6 H_3(OH)_2 \cdot CHOH \cdot CH_2 \cdot NH \cdot CH_3$$

The cells of the medullary portion of the suprarenal gland are intimately related in origin to the sympathetic nervous system. Hence the secretory product has a pharmacological and quite specific affinity for the sympathetic nervous system--the thoracic-abdominal part of the autonomic nervous apparatus. The changes induced by epinephrine in the activity of various organs enervated by this system are in all respects like those brought about when the sympathetic fibre's controlling these organs are stimulated by an electric current.[4]

The most striking effect of Adrenalin is the rise in blood pressure. The small quantity of less than 1 c.c. of a 1:100,000 solution causes a rapid elevation. This is caused by contraction of the blood vessels and stimulation of the heart. The former is induced by the influence of Adrenalin on the little nerve endings in the vessel walls controlling the contractile action of the muscle fibres, while the quickening of the heart is due to the effect on the nerve endings of the accelerator nerves of the heart muscle.

Adrenalin has the power of causing the contraction of the muscular valves controlling the emptying of the stomach, small intestine, rectum, and bladder. The stomach, intestine and bladder relax and peristalsis ceases. The muscles of the bronchi relax. Adrenalin is applied to the mucous membranes or broken skin causing contraction of the vessels and a resulting blanching of the surface, the effect lasting thirty minutes to two hours. When applied to the surface of the eyeball the blood-vessels of the conjunctiva contract, the pupil is dilated, and the intra-ocular tension is reduced.

Since Adrenalin is so effective in causing contraction of blood vessels we

4. Abel, p. 340-1.

find it used largely in conditions of shock and collapse, as the shock during operation caused by exhaustion, anesthesia, or hemorrhage; in poisoning and the exhaustion of acute infectious disease. Sometimes it is applied directly to the heart muscle, when the muscle is degenerated or in cases of pneumonia and peritonitis.

Adrenalin is also used to cause relaxation of muscular contraction in the uterus and in the Caesarean section. In asthma it is injected subcutaneously controlling the bronchial spasms. For hay fever it is applied directly to the respiratory mucous membranes to relieve catarrhal symptoms. It is used in treatment of diseases of the eye, ear, nose and throat and in surgery in these areas. It intensifies and prolongs the effect of local anesthetics and renders the field of operation practically bloodless. In serum sickness such as that following the injection of antitoxin it is injected subcutaneously in doses of $\frac{1}{4}$ to 1 c.c. and relieves from the intense itching.

Adrenalin is made in the forms of solutions, tablets, inhalants, ointments, etc. and combined with local anesthetics.[5]

There is a plant principle, ephedrine, related in structure and physiological action to the hormone of the suprarenal medulla. For more than 5000 years the Chinese have used the stems of the Ephedra vulgaris under the name of ma huang, as a medicine famed as a diaphoretic, circulatory stimulant, sedative in a cough, and an anti-pyretic. It is less active physiologically than epinephrine but the effects are more prolonged. In the form of ephedrine sulfate it is of value in nasal operations and in ophthalmology. Its ultimate value is in serious diseases of the heart, hypotension, and other pathological states.[6]

5. Parke, Davis and Co., pp. 162-5.
6. J. J. Abel, pp. 341-2.

The Thyroid Gland

The thyroid gland is a U-shaped structure located in the front and middle part of the neck, very near the trachea. It is shaped somewhat like a butterfly and consists of two lobes with a connecting portion termed the isthmus. It weighs 35 grams or $1\frac{1}{4}$ ounces.[7] This gland is intimately related to growth and development of mind and body. It is also related to sex development and functional activity.[8]

The harmone was isolated and termed thyroxin in 1914 by Kendall. It contains 65% of iodine and is no doubt the active principle to the presence of which the activity of iodothyrin was due. The extract is a colorless odorless crystalline substance, melting at 231°C., insoluble in aqueaus solutions of acids, soluble in caustic alkalies, to form salts. It also yields salts with acids.

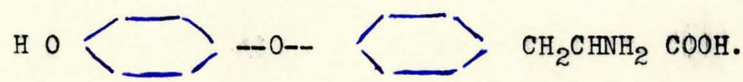
In preparing the extract Harrington has been able to secure larger yields than Kendall. He first employs hydrolysis of the thyroid tissue with 10% baryta, precipitation with acid, and further hydrolysis of the acid-soluble precipitate with 40% crystalline baryta, followed by separation of the throxin, first as the barium, then as the sodium salt, and finally in the free state. The yield was about 0.027% of the weight of the fresh gland and the empirical formula of the pure substance was found to be $C_{15}H_{11}O_4\ NI_4$.

As a step toward the determination of its structure, Harington next removed the iodine from thyroxin by shaking an alkaline with a palladium calcium carbonate catalyst in a hydrogen atmosphere; four atoms of iodine were split of qualitatively and four atoms of hydrogen took their place, the compound which was formed being called "reduced thyroxin".

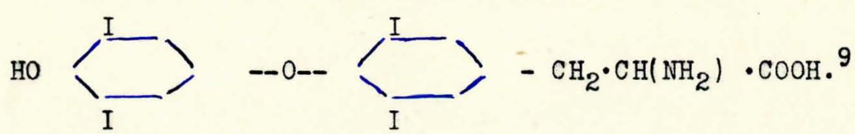
The reduced thyroxin gave the ninhydrin and Millon's reactions, formed acid and basic salts, and contained its nitrogen in the form of an NH_2 group. Fusion

7. D. C. Kimber and C. C. Gray, Text book of Anatomy and Physiology, p. 325.
8. Parke, Davis and Co., pp. 172-3.

with potash gave hydroquinone and p- hydroxybenzoic acid, which indicated the presence of two benzene rings; exhaustive methylation with methyl sulfate gave a betaine which split off trimethylamine to give an unsaturated acid containing one methoxy group, showing that there was **one** phenolic group in reduced thyroxin. The further oxidation products of the unsaturated acid suggested that reduced thyroxin might be a diphenyl ether of the structure



(viz., the p- hydroxyphenyl ether of tyrosine), and this has been confirmed. Thyroxin has been shown by Harington and Barger to be a tetra-iodo substituted derivative of this substance which has the structure:



There are several diseases having to do with the thyroid gland. They may be caused by inadequate secretion or hypothyroidism, too much or hyperthyroidism, and perverted secretion or dysthyroidism. As to the first the most common cases are of simple goitre. Particulary in the Great Lakes basin is this disease prevalent. This is caused by a deficiency in the quantity of iodine taken from food and water. Throid diseases are almost never found near the sea-coast. If there is an insufficient supply more secreting cells are set to work, hence we have quantity but not quality.

More serious conditions of deficiency are known as cretinism and myxedema. Cretinism is a condition common to children in which there is marked under-development of mind and body.[10] This class of people is found particularly in the Swiss Alps. The features are misshapen and flabby, the brow low, the bridge of the nose depressed and the nostrils wide, the tongue is too large for the coarsely moulded

9. C. L. Evans, Recent Advances in Physiology, pp. 265-6.
10. Parke, Davis and Co., pp. 174-5.

mouth. The skin is thick and the hair sparse. Dr. George Murray has succeeded in treating several cretins and restoring them to a practically normal state. The success depends on the progress of the disease.[11] Myxedema is a similar condition developing in adults.

Other conditions may also be recognized. Children who show more than peculiar reticence, cannot read or study long, show fatigue with little exertion, and are indifferent to food may be victims of thyroid deficiency. Swelling of the joints, puffiness of the eyelids, lips and checks, and poor circulation in the extremities may be due to the same cause. Thyroid preparations have been used in anemia, chlorosis, scleroderma, arthritis, chronic types of rheumatism, delayed mending of fractures and mental disturbances. Thyroid extract may be used as a fat reducer but may also damage the heart and nerve tissues.

Exophthalmic goitre or Grave's disease is due to perverted activity of the gland. It enlarges, the eyeballs protrude, the action of the heart is rapid and irregular, there are tremors and nervousness. The treatment is largely surgical though milk, blood, or serum from animals from which the thyroids have been removed have been administered.[12]

11. N. B. Taylor, The Physiology of the Ductless Glands. The Scientific Monthly, 27:385-97. November 1928.
12. Parke, Davis and Co., p. 177-9.

The Parathyroid Gland

The Parathyroid glands are very small structures, each about $\frac{1}{4}$ in. in diameter (6.25mm.) two of which are imbedded in each lobe of the thyroid. They are solid accumulations of epithelial cells, invested with a tunic of areolar tissue and supplied with many blood vessels. It was formerly believed that their function was similar to that of the thyroid but today we know that after removal of these glands tetany is produced, resulting in death in a few days. Their function seems to be principally to connteract poinsonous substances resulting from interference with the metabolism of nuecoproteins. Some authorities also state that they disintegrate the mucin absorbed from mucous membranes.[13]

The condition of tetany is associated with increased excitability of the central and peripheral motor nerve system and is combined with a low calcium content of the blood. Hence it can temporarily be relieved by the administration of calcium salts.

There are two principal theories to explain these symptoms. Noel Paton and his colleagues believe they are due to the accumulation of guanidine or its derivatives, which are normally removed by the parathyroids. Injection of these substances produce similar conditions. The second theory regard the parathyroids as responsible for producing a harmone regulating the blood calcium level. Hence tetany is due to reduced calcium. The parathyroid tetany is modified by various conditions.

In preparation the fresh glands are heated on the water bath with an equal volume of 5% HCL for one hour. The layer of fat is removed, the extract cooled and brought to p H 8 by addition of sodium hydroxide. Hydrochloric acid is then slowly added until maximal precipitation of proteins occurs. This precipitate is

13. Kimber and Gray, p. 327.

removed and may be re-extracted. The filtrate is subjected to further purification by being made acid to Congo Red and then saturated with sodium chloride. The precipitate thus formed is dissolved in water containing dilute HCl and again reprecipitated by sodium chloride. This precipitation may be repeated several times, the precipitate finally being dissolved in weak alkali, which then has its p H adjusted to 4.8, at which reaction an isoelectric precipitate forms. This is removed, re-dissolved, and the isoelectric precipitation repeated. Finally the precipitate is dissolved in weak acid at p H 4, or may be obtained as a powder by suspending in absolute alcohol and adding an equal volume of ether. The resulting precipitate is washed in ether and dried over sulfuric acid.

The chemical nature of the parathyroid harmone is unknown. Collip and Clark found their purest material to contain 15.5% of nitrogen and traces of iron and sulfur, but no phosphorus. It gives no Molisch reaction, and according to Berman, no biuret action. Collip and Clark's product gives the common protein reaction, the Pauli reaction, and is destroyed by pepsin and trypsin, thus bearing a strong resemblance to insulin. According to Davies, Dickens and Dodd, the active principal also forms an insoluble picrate and hydrochloride when treated by Dudley's method for the purification of insulin.[14]

14. Evans, pp. 29307.

The Thymus Gland

The thymus is an irregular-shaped body containing glandular and lymphatic tissue. It is surrounded by a fibrous capsule, strands from which enter the organ dividing it into lobes, and serving as support for blood and lymph-vessels and nerves. It is in the center of the lower part of the neck and the upper part of the mediastinum.[15] It is largest during the first few years of life increasing in size from birth till the end of the second year, receding following this period especially after puberty.

The function of this gland is not clear. Some believe it to be merely a lymph gland; others think it is related to early development, especially of the bones. It is certain that it is not necessary to life although its removal in very young animals makes the skin soft and pasty, retards the development and ossification of bones. There is a steady increase in weight, the blood is impoverished, and the animals die in a state of coma. The thymus may also be involved in thyroid diseases.

Thymus therapy has been applied in treatment of rickets, softening of the bones, rheumatic involvement of the joints, and certain types of goitre. Enlargement of the gland is usually associated with a general overgrowth of the lymphatic tissues, status lymphaticus, causing death from slight operations, nervous excitement, or relatively non-toxic drugs.[16]

15. Kimber and Gray, p. 327.
16. Parke, Davis and Co., pp. 187-190.

The Pancreas

In addition to its digestive function the pancreas is known to elaborate an internal secretion influencing carbohydrate metabolism.[17] This secretion is produced by small masses of modified glandular tissue known as the islets of Langerhans or the interalvealar cell-groups. They are about 3 mm. in diameter, lying between the tubular alveoli from which they are separated by delicate envelopes of fibrous tissue. The total number is said to vary from 200,000 to 1,760,000. The bodies are most numerous at the splenic end and consist of anastomosing solid cords of small polyhedral cells, of which there are two types, the a and B islet-cells.[18]

The preparation of the extract by Collip's method consists in extraction of the pancreas with alcohol. The extract is evaporated in vacuo to a small bulk, and the fat separating removed. Alcohol is added to bring up the percentage to about 80 and a precipitate of protein is separated. More alcohol is added and insulin is precipitated when the alcohol content is 92%. Dudley and W. W. Starling improved this method by extracting with alcohol to which sodium bicarbonate has been added to render it slightly alkaline. The filtrate is acidified with acetic acid, and then treated much as in Collip's method. The yield of crude insulin is about five times as great as by the original method.

The crude insulin is further purified by Dudley's method, in which it is precipitated from solution by picric acid, and the resulting insulin picrate then converted into a hydrochloride by treatment with alcoholic HCl, and finally with acetone, in which the hydrochloride is insoluble. The hydrochloride is filtered off and washed with acetone and then with ether, and dried. It forms a white amorphous powder readily soluble in water.

17. Parke, Davis, and Co., p. 192.
18. Wm. H. F. Addison - Piersol, Normal Histology, p. 215,233.

Substances resembling insulin in their effects have also been prepared from clams, from yeast, and from plant tissue of the most varied description by Collip. The insulin-like substance of vegetable origin has been called "glucokinin" by Collip who says it acts more slowly and for a longer time. Other workers have prepared from animal tissues other than the pancreas a substance apparently identical with insulin.[19]

Insulin is given by hypodermic injection of the solution and is ineffective if given by the mouth. The blood-sugar level falls rapidly and then follow the effects of this hypoglycaemia: the animal shows signs of extreme hunger. When the blood-sugar has fallen to 0.045% violent convulsions result, between which the animal is comatose. After a series of convulsive attacks, the convulsions become feebler, the body temperature falls and the animal dies of respiratory failure. Rigor mortis sets in at once.

In man there are the same hunger pains, followed by a feeling of faintness, fatigue, tremor and anxiety, sometimes with loss of emotional control or even temporary delirium, pallor or flushing and profuse sweating, and in extreme cases deep coma. These symptoms may be removed by the administration of glucose.[20]

Experiments have also been made on two groups of fish. The first have a blood sugar average above 0.040% and are the blue mackerel, common mackerel, bonito, menhaden, butterfish, etc. Group II is below 0.040% and is composed of the toadfish, goosefish, puffer, sea robin etc. The first group reacts similar to mammals with the symptoms described above while the second group seems to have no visible reactions and are similar to toads and snakes. Perhaps animals with low metabolic activity have a different mechanism of controlling sugar metabolism. In many fishes insulin is manufactured not in the pancreas but in

19. Evans, pp. 276-8.
20. Evans, pp. 280-1.

other islets for production outside the pancreas in the body cavity. This is particularly true of the more sluggish fish.[21]

The pancreatic islets seem rather closely related to the other endocrine organs since the hyperglycaemia produced by adrenaline can be insulin and vice versa. Cannon, McIver, and Bliss have shown that when insulin is administered there is excitation of the sympathetic system and a discharge of adrenalin from the suprarenals as soon as the blood sugar falls below 0.07%, checking the further fall of blood sugar. The converse is probably also true. Feeding with thyroid reduces the glycogen store of the liver and makes the liver glycogen more easily available.

Insulin is stable in solutions of acid or neutral reaction, even at $100^{\circ}C$, but in alkaline solution is rapidly destroyed when at bodily temperature. It is destroyed by trypsin, and by pepsin even in acid solutions. Purified insulin gives the ninhydrin reaction, contains an iminazole ring compound, and sulfur.[22]

21. Irving E. Gray, The Effect of Insulin on Fishes, The Scientific Monthly, pp. 271-4. March 1929.
22. Evans, pp. 291-3.

The Pituitary Gland

The pituitary gland or hypophysis cerebri is a small mass of reddish-brown tissue located at the base of the brain. It consists of four parts: the anterior and posterior lobes, pars intermedia and pars tuberalis, the first two being of most importance.[23]

The anterior lobe may be over-active or deficient in activity. In the second case we have gigantism usually developing in early life, during the growing period. There is a general overgrowth of the body and the individual may be seven or eight feet tall. People with this disease are below par mentally, are indolent and apathetic, and have muscles poor in development and quality. They usually die early in life because of lack of vital resistance.

Acromegaly is associated with over-activity of the pituitary in adult life. The first symptoms show in the nervous system--lassitude, apathy, sleepiness, pain in the muscles, and severe headache. Striking changes take place in the face, hands, and feet since the bony and soft parts undergo change. The disease is usually chronic and finally terminates in death.[24]

If there is deficient secretion the person is apparently normal but built on a small scale.[25]

The posterior lobe is related to the contraction of involuntary muscles and the metabolism of starches and sugars. If there is decreased activity of the posterior lobe low blood-pressure results and the body develops the capacity to digest and absorb immense amounts of starches and sugars; hence obesity often results.

If there is increased activity of the posterior pituitary there is an increase of the blood-pressure and a decreased tolerance of starches and sugars.

23. Kimber and Gray, p. 329.
24. Parke, Davis and Co., pp. 167-8.
25. Taylor, p. 292.

The over secretion of the posterior lobe cannot be neutralized but the condition is not common. However, treatment with the posterior lobe or whole gland has proved to be valuable in cases showing deficiency. Pituitrin, the extract of the posterior lobe, as a drug is more efficient, causing contraction of muscular tissues. Hence it is used in treatment of shocks and other conditions in which the vascular tension is low, but particularly in obstetrics and surgical operations.[26]

26. Parke, Davis and Co., p. 169-71.

The Pineal Gland

The Epiphysis cerebri or pineal body is a cone-shaped organ, 8-10mm. long and attached to the posterior extremity of the roof of the third ventricle.[27]

This gland is most important during early life. Changes in its structure occur as early as the seventh year and by maturity there is only a little of the glandular tissue left. This however remains and may still be an active secretory organ.

Growth and sexual maturity are brought about prematurely by pineal tumors which seem to take over the functional characteristics of the glandular tissue. They may also be hastened by administering pineal gland substance. The animal rapidly reaches maturity but does not go beyond it, indicating that this gland furnishes normal growth stimuli.

Pineal preparations are given in the treatment of mentally backward children of the borderline group. However, the condition may also be due to pituitary or thyroid disorder. Research does not at the present justify any definite conclusions.[28]

27. Piersol (Addison), p. 229.
28. Parke, Davis and Co., p. 190-2.

The Sex Glands

The matter of sex differentiation has long been a matter of interest to scientists. The older view has been and remains in the present that sex differences are caused by the Y chromosome or absence of one chromosome in the fertilized egg. Another view is now put forth by Lipschütz, the German scientist, that these differences are due to the action of the sex glands. He says that the somatic basis of mammals and birds is probably sexually undifferentiated and is changed during embryonic life by the sexual gland.

We know that the formation and persistence of sexual characters in mammals, birds, amphibians, and some invertebrates depend upon the sexual glands. These are "secondary" characteristics. Not only are the sexual characters involved in the sexual function concerned, but also such characteristics as plumage, bodily proportions, voice, mental outlook, growth and metabolism. This influence may also relate to some of the organs of internal secretion. These harmones are produced by the testes in the male and by the ovary in the female.[29]

The framework of the testis is made up of dense fibro-elastic tissue. However the interstitial connective tissue between the seminiferous tubules is composed of delicate bundles of white fibrous tissue with few elastic fibres. Herein by groups of interstial cells. These are rounded, polygonal, possess small eccentric nuclii and granular cytoplasm containing fat droplets, pigment granules, crystalloids, and mitochondria.[30]

It has been shown by experiments recorded by Dr. Lipschütz that in mammals the interstitial cells are a necessary part of the endocrine apparatus of the testicle. Furthermore, no proof exists of a direct harmonic action by the cells of Sertoli or by other constituents of the wall of the tubules independently of the interstitial cells.[31]

29. Alexander Lipschütz, The Internal Secretions of the Sex Glands, p. 71.
30. Piersol, p. 267.
31. Lipschütz, p. 185.

The ovary in the female is thought to secrete a specific harmone also. It is composed of cortex and medulla, the cortex alone containing the Graafian, or egg follicles, and the ova, while the medulla is distinguished by the number of blood vessels, especially veins.

The cortex is made up of modified connective tissue composed of spindle-shaped cells and fibrous tissue. Beneath the germinal epithelium covering the free surface is the tunica albuginea where the ova are absent, and within the subjacent looser stroma lie the Graafian or egg-follicles. The wall of the ripe follicle consists of a well-developed capsule or theca, a delicate membrane propria, stratum granulosum, surrounding the space filled with the liquor folliculi. After the liberation of the ovum the follicle becomes filled with a new growth of cells and is called a corpus luteum.[32]

Lipschütz says, "It is highly probable that the internal secretion of the ovary of the mammal is elaborated by cells of the membrane granulosa, and partly by cells of the theca interna, and that these cells originate from follicles undergoing atresia or from ripe follicles rupturing and transforming themselves into corpora lutea. It is difficult to decide whether the increased internal secretion of the ovary is caused by a proliferation or only by an activation of the endocrine cells.... It is very probable that in man and many other species the endocrine cells of the ovary become transformed, when they are not undergoing degeneration, into common connective tissue cells or into fibrous connective tissue."[33]

The fluid within the follicle, supporting the egg, liquor folliculi, is also said to contain a hormone. This is also present in large amounts in the human placenta and in smaller amounts in the placenta of lower animals. Both corpora lutea and dessicated ovarian glands have been used in the treatment of cases in which there

32. Piersol, pp. 284-7.
33. Lipschütz, pp. 270-1.

is not enough ovarian tissue left to supply the demands of the body.[34]

In preparation from the liquor folliculi Ralls, Jordan and Doisy use a process in which the alcoholic extract of the proteins is distilled to dryness, the residue dissolved in dilute alkali and the aqueaus solution extracted with ether. The ether is distilled off and the solids fractionated between 70% ethyl alcohol and petroleum ether (B.P. 40°- 60°). The hormone remains in the alcohol and the impurities pass into the petroleum. The composition is said to be 80.7% C, 10.4% H, 0.93% N, and no P.[35]

Regeneration has always interested mankind. From the earliest times we find him trying to find a way of prolonging his days or seeking comfort in the thought of another life to follow his present existence. In later years this subject has come more and more to the fore until we find Dr. Serge Voronoff stating that he believes theaverage healthy human being should live 125 years. Deaths due to old age are due to premature weakening or atrophy of the endocrine gland. Death is preventable when caused by unnatural living, by removal of the cause and "regeneration".[36]

The structural integrity and physiological efficiency of a tissue or organ are largely dependant upon the quantity and quality of blood passing thereinto. This is regulated by the bore and elasticity of the vessels. The quality of the blood depends on the efficiency of all tissues especially the endocrine glands. The hormones of these glands invoke harmonious functioning. Microscopic examination reveals the fact that senescence is associated with characteristic and significant changes in their organization.

Occlusion of the vas deferens, implantation of ovary or testis and irradiation of the ovary are followed by degeneration of the reproductive elements in

34. Parke, Davis and Co. pp. 185-6.
35. Edgar Allen and Edward A. Doisy. <u>Ovarian and Placental Harmones</u>, Reprinted from Physiological Reviews, Vol.VII, No.4, Oct. 1927. pp. 622-4.
36. The American Review of Reviews, <u>How to Live 125 Years</u>, Aug. 1927.

the sex-glands and a survival or enlargement of the interstitial tissue regarded as the source of the sex-hormone. Steinach has used vasoligation, invoking forces within the individual's body. Voronoff implants testis-tissue in the aged body. The same result occurs in either case.

In the case of the female, the best way without implantation is proved by Steinach and Holzknecht to be irradiation with carefully graded doses of X-rays. This however causes sterility. The most successful is the transplanting into the aged female the ovary from a vigorous young one.[37]

If these methods of rejuvenation should ever be widely adopted and life prolonged many years, senility will be acute instead of drawn out, and death will be an acute sickness. There must be an end sooner or later for the stimulation of one gland will not renew all others in the chain. However, we can see what an advantage it would be to the world to prolong the lives of men like Edison and the rest who are contributing to human advancement beyond the normal period of years.

37. F. A. E. Crew, On Youth and Old Age. The Nineteenth Century and After, Vol.CI. February 1927, pp. 225-33.

Summary and Conclusion.

The importance of the endocrine glands is now a well-established fact. Sir Arthur Keith states that the skull of the Neanderthal man is quite similar to the acromegalic skulls. Other English scientists believe that differentiation into races may be due to these glands. We know that they play a large part in the proper development of body, features, mentality and temperament. Hence these glands may be related to development and evolution. We have already seen that they have an intimate relation to determination of sex. Chromosomes are now thought to be packets of enzymes which lay down certain centers which proceed to elaborate and influence the growth of other centers. Knowledge of the function and structure of these glands is growing constantly and it is almost impossible to predict where it may lead or what developments may result from it.

BIBLIOGRAPHY

Abel, J. J.	Science ns 66:337-46, October 1928, Vol.LXVI.
Allen, E. & E. A. Doisy,	Physiological Reviews, VII, 4, Oct. 1927.
Crew, F. A. E.	The Nineteenth Century and After, 225-33. Vol.CI.
Evans, C. L.	Recent Advances in Physiology, Blakiston, Philadelphia, 1928.
Gray, I. E.	The Scientific Monthly, 271-4. March 1929.
Kimber, D. C. & C. E. Gray,	Text book of Anatomy and Physiology, Macmillan Co., N. Y., 1925.
Lipschütz, A.	The Internal Secretions of the Sex Glands, Williams and Wilkins Co., Baltimore, 1924.
Parke, Davis and Co.	Lectures and Biological Products, Parke, Davis and Co., Detroit, 1927.
Piersol	Normal Histology, (Ed. by Addison, W. H. F.) Lippincott Co., Phila. and London, 1926.
The American Review of Reviews	76:210-11. August 1927.
Taylor, N. B.	The Scientific Monthly, 27:385-97. November 1928.