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AND INTERNAL SECRETIONS. LANE  
MEDICAL LECTURES, 1913**

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**SIR EDWARD SCHÄFER**

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OF THE ENDOCRINE GLANDS AND  
INTERNAL SECRETIONS

LANE MEDICAL LECTURES, 1913

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# An Introduction to the Study of the Endocrine Glands and Internal Secretions

Sir Edward Schäfer

## LECTURE I.

### GENERAL CONSIDERATIONS REGARDING INTERNAL SECRETIONS AND THE ORGANS WHICH FURNISH THEM.

Material which is passed into the blood or lymph from any tissue or cell of the body forms what has been termed its *internal secretion*, and organs which are not known to possess any other function than that of passing such material into the blood or lymph are termed *internally secreting* or *endocrine organs*.\* But this term is not usually extended to organs like the lymphatic glands of which the material production is of a morphological character, although until recently all such organs used to be included along with the true endocrine glands, the functions of which were at that time unknown, in the general expression of *ductless glands*. Under this last term were comprised not only the thyroid (to which must be added the parathyroids), the suprarenal capsules or adrenals, the pituitary body or hypophysis cerebri, and the pineal gland or epiphysis cerebri, to which we now commonly ascribe internally secreting functions, but also the thymus gland, the tonsils, lymph-glands and lymph-follicles, and the spleen; with these the bone-marrow must also be associated. Regarding the thymus gland, although some evidence has been adduced that it may yield an internal secretion to the blood which exercises a specific action upon the functions of growth and development, especially of the generative organs, it appears both developmentally and structurally to present undoubted resemblance to the tonsils, which are universally allowed to be structures of a lymphatic nature, and most of its cells are lymphocytic in character. Some have supposed that the spleen also provides an internal secretion which is destined to affect the quantity of the pancreatic juice. But the proof of the existence of such internally secreting functions in connexion with these lymphoid organs is so inferior to that which we possess regarding the thyroid, parathyroids, adrenals and pituitary, and even the

\*From *endo*, within, and *spiro*, to separate.



pineal gland, that we may, at least provisionally, exclude them from the class of organs which are known to secrete active chemical agents into that fluid for the purpose of influencing other organs. It is to this latter class that I intend to restrict my remarks, and it is to them and them alone that the term "endocrine organ" will be applied in these lectures.

It follows from what has just been said that by the expression "endocrine gland" we imply an organ which is known to form some specific chemical substance within its cells and to pass this directly or indirectly into the blood stream. The substance thus formed is the active material of its secretion, just as ptyalin is the active agent of the salivary secretion. But while in the case of the salivary glands the secretion is conducted by a duct to the exterior, in the case of the ductless glands the secreted material remains within the body and circulates with the blood; hence the term "internal secretion" commonly applied to it.

The expression "internal secretion" was originally applied in a sense somewhat different from that in which it is now used, having been first employed by Claude Bernard to describe the grape sugar which, as he showed, is passed from the liver cells into the blood. It has also similarly been used to designate all materials which are contributed to the blood by the tissues. In this manner the carbon dioxide and other products of metabolism which are taken up by the blood in its passage through the capillaries or are received by it through the medium of the lymph stream would be internal secretions and every tissue would be an internally secreting structure. It is, however, convenient to restrict the term "endocrine" to substances of a specific nature like the active chemical agents which are produced by the ductless glands, and this is the sense in which the expression will be employed in these lectures.

But it is proved that the production of specific chemical agents which are passed into the blood and carried by it to distant structures is not confined to the ductless glands—that an active internal secretion may be produced by other organs than these. A notable example is met with in the case of the pancreas, the obvious and long known function of which is the production and excretion into the intestine of pancreatic juice; which, by virtue of the ferments it contains, is the most active agent in the digestion of food stuffs within the alimentary canal. In 1889, however, it was shown by v. Mering and Minkowski that the pancreas possesses an internal secretory function which is of even greater importance in the economy than its long recognized external secretory activity. For by totally removing the pancreas in animals these observers proved that the presence of the gland and of some material yielded by this gland to the blood is essential to the proper utilisation of carbohydrate material in the tissues, so that if the organ be removed

grape sugar is no longer stored in the liver, and little by little split up by the organism into simple oxidisable substances, but is passed out from the blood in which it is in excess by the kidneys, thus producing glycosuria. It may be added that our present knowledge of the etiology of diabetes is mainly based on these observations.

Now it is known that the pancreas possesses, besides the secreting alveoli which form the enlarged and blind terminations of its ducts, a special kind of secreting cells which are massed together into islets of irregular shape and variable number and size, having a special kind of blood supply. These islets, which were first described as a distinct element of pancreatic tissue by Langerhans, have been originally developed from and may retain a connexion with the ducts of the organ, in this respect resembling the ordinary alveoli. But in the course of growth they have lost all open connexion with the ducts; their cells have acquired specific properties; and their function is without doubt different from the ordinary cells of the gland. With some show of reason the special internal secreting function which has been above mentioned has been ascribed to them, and in support of this it may be stated that in many if not most cases of diabetes these cells are found to have undergone degeneration. They in fact form an organ within an organ, and may be collectively regarded as belonging to the group of internally secreting or endocrine organs.

An example of a tissue which is devoted to the formation of both an external and an internal secretion is found in the epithelium which lines the duodenum. The functions of this epithelium which have been longest known are those of aiding in the absorption of digested food materials and of helping to furnish the material known as the intestinal juice. But in 1902 it was discovered by Bayliss and Starling that if an extract of the duodenal epithelium is boiled with dilute hydrochloric acid and after neutralization is injected into the blood stream of an animal a rapid flow of pancreatic juice is determined. It had already been known that the gush of acid gastric juice through the pylorus or the painting of the mucous membrane of the duodenum with dilute acid would determine a flow of pancreatic juice, but this flow had been supposed to be brought about as a reflex act by excitation of a local nervous mechanism by the acid. The observations of Bayliss and Starling rendered it clear, however, that this is not the correct explanation of the phenomenon; but that the flow must rather be regarded as due to the absorption of some internal secretion into the blood: the material of this internal secretion being produced in an inactive form by the epithelium cells and becoming so altered by the dilute acid as to be converted into an agent which, after

absorption into the blood stream, excites the secreting cells of the pancreas to activity.

To the active substance which is yielded by the epithelium cells of the duodenal mucosa the name *secretine* was given by Bayliss and Starling, whilst they termed *pro-secretine* the inactive material contained within the cells before the action of dilute acid upon them. The active material is obviously of the nature of an internal secretion; it appears, however, not to be produced by a special structure, certainly not by a special organ; but so far as one can tell, by the ordinary cells which line the mucosa and extend into its glands.

A similar but not identical internal secretion has been shown by Edkins to be produced by the cells of the mucous membrane of the pyloric end of the stomach. When rendered active and absorbed into the blood this secretion, which is termed *gastrine* by Edkins, stimulates not the cells of the pancreas but those of the fundic glands of the stomach itself.

A yet more remarkable example of the coincidence of external and internal secretory functions in the same organ is supplied by the generative glands (ovary and testicle). It has been known from time immemorial—the experiment is repeated daily for commercial purposes in thousands of animals, and is still practiced upon man for domestic reasons in certain Oriental countries—that the removal of the generative glands in the young male animal usually entirely prevents the development of the accessory generative organs, such as the prostate, and of the features which characterize the male sex externally. These changes may be prevented by successfully grafting a testicle in the castrated animal.

Again, removal of the ovaries in the young female exerts a profound influence over the organism and prevents the development of many female characteristics. In some cases, even in the adult, removal or atrophy of the ovaries has been noticed to lead to the development of male characters. Instances of this have been often recorded in birds. In young mammals removal of the ovaries is followed by arrest of development of the uterus. This may be prevented by successfully transplanting the ovaries or by grafting an ovary from another animal of the same species into the peritoneum or elsewhere. It seems clear, therefore, that the result of removal is due in both male and female to the absence of the internal secretion of the generative gland.

#### THE NATURE AND MODE OF ACTION OF THE ACTIVE PRINCIPLES OF THE INTERNAL SECRECTIONS.

We have compared the active materials of the internal secretions, which are formed within cells and passed out into the blood, to the active