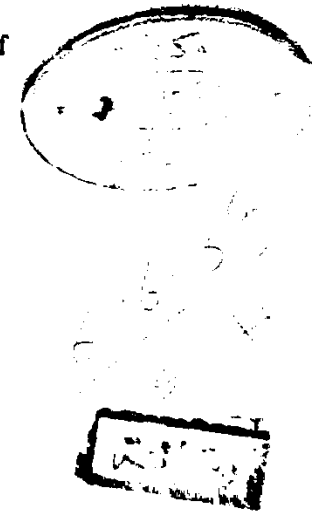
THE ROLE OF THE EXOCRINE AND ENDOCRINE PANCREAS IN SOME COMMON DISEASES

ESSAY

Submitted for Partial Fulfilment of
Master Degree in
(GENERAL MEDICINE)



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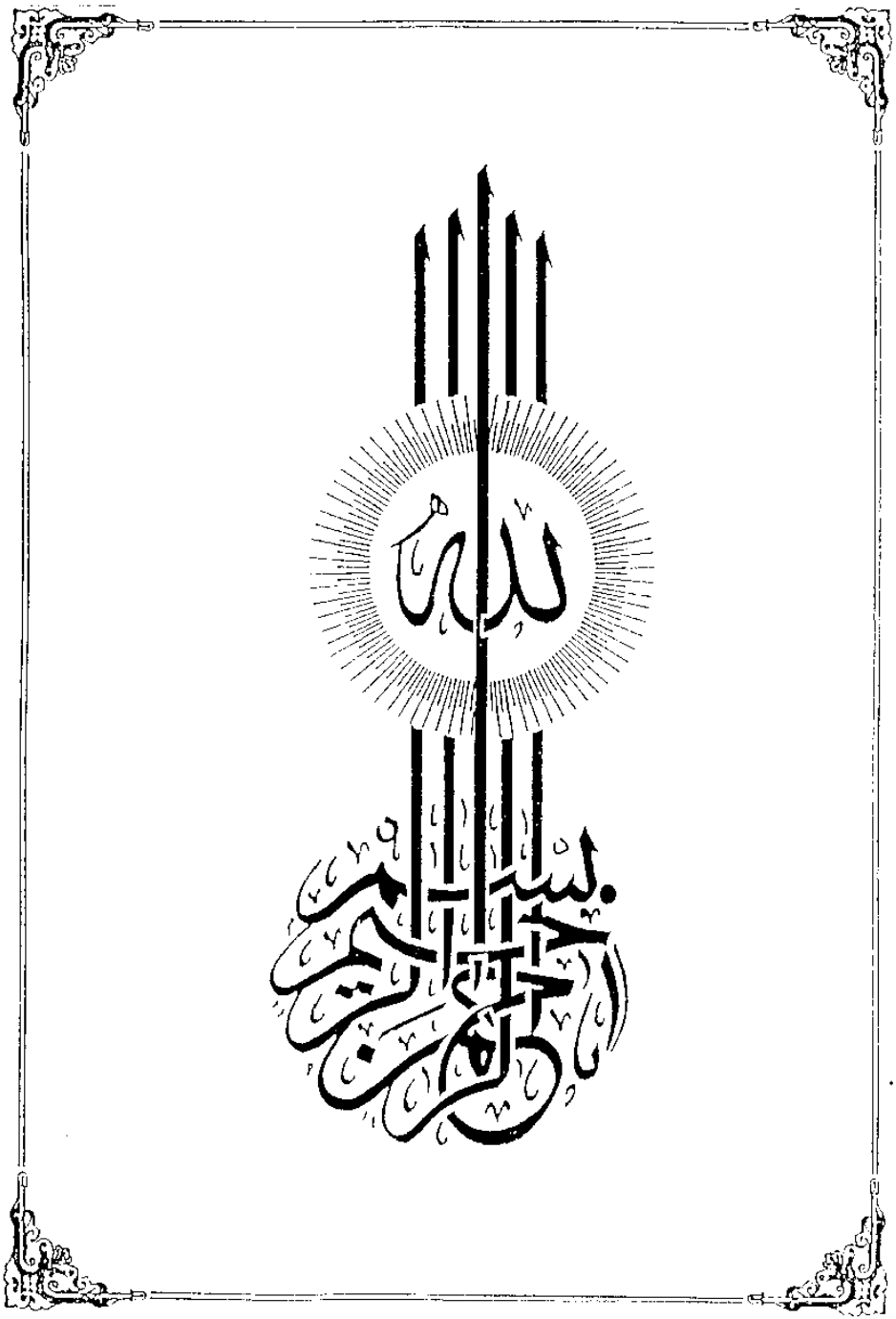
1982

ACKNOWLEDGEMENT

I can not express how to thank Prof. Dr. Ahmed Ghareeb, Chairman of General Medicine Department and Endocrine Unit, Faculty of Medicine, Ain Shams University, for accepting the supervision of this work. This supervision gave me the invaluable opportunity to benefit of his constant help and faithful guidance. I will always remember his unforgetable sincere encouragement and kindness. Any attempt to define my indebtedness will be less than he deserve.



C O N T E N T S

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I- HISTORICAL REVIEW

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Diabetes mellitus is a disease known to man 3000 B.C. and was described A.D. 1000 by Avicenna, the famous Arab physician, who gave the first complete clinical picture of the disease with all its complications, stressing gangrene, furunculosis and phthisis and commented on the presence of honey-like substance in the urine of his patients. (Ghareeb, 1969).

"Diabetes" is a Greek name used to designate diseases characterized by polyuria and polydypsia. (Ham and Cormack, 1979).

In the 18th century it was proved that the urine in most cases of diabetes contained sugar; hence this kind of diabetes was called diabetes mellitus to distinguish it from (diabetes insipidus) in which polyuria is not associated with glycosuria and urine is tasteless (insipid). It was also realized at this time that it was an ill omen for anyone to begin passing large quantities of sugar - containing urine, for almost invariably, their health would decline steadily from then on. (Ham and Cormack, 1979).

In 1869 Langerhans while still a medical student, discovered "islands" in the pancreas and described

them as lymph nodes. (Ghareeb, 1969). However, Langerhams did not suspect that these islands were little organs of internal secretion. Soon afterwards, it was pointed out that they contained extensive capillary network; this was to help later in leading other investigators to suspect that they had an endocrine function. (Ham and Cormack, 1979).

Although Cowley, an English physician, had suggested a full century before that there was some relation between diabetes and the pancreas, it was not until 1889 that this was established. At this time, Von Mering and Minkowski removed the pancreas from dogs and found that they developed diabetes mellitus. This finding could be interpreted as indicating that a lack of some pancreatic function is responsible for diabetes. But what function? The obvious function known at that time was that of making an external secretion. Nevertheless, the concept of claude Bernard - that certain bodily functions depend on internal secretions - had by this time made a considerable impression on the scientific world, so further work was done in an attempt to discover whether diabetes results from failing to make a proper external or internal secretion. (Ham and Cormack, 1979). To determine this point, Hedon (1892) performed an ingenious experiment. He found that a piece of pancreas

grafted back into a depancreatized animal would keep the animal free from diabetes even though the graft had no duct connections. In other words, he showed that the anti-diabetic principle made by the pancreas was absorped into the blood - that is, it was an internal secretion. At this time, however, it was not all clear whether acinar or islet cells produced this internal secretion. Indeed, it was not even clear whether islet cells were fundamentally different from acinar cells. (Ham and Cormack, 1979). However, this matter was settled soon afterwards by Ssobolew (1902), who tied off the pancreatic ducts of experimental animals and found that after a time the acinar tissue of the pancreas all became atrophied and that only islet tissue was left. Animals so treated, although they suffered from impaired digestion, did not develop diabetes. It remained to prove that diabetes is due to islet cell damage. Evidence was first provided by Opie (1910), who noted that those who died from diabetes in most instances either lacked islets or showed degenerative changes in such islets as were present. So, it became generally believed that diabetes mellitus was due to failure of islets to make a hormone, given the name insulin.

It was established that not only the granules of islet cells had histochemical properties different from those zymogen granules (and hence that islet cells were fundamentally different from acinar cells), but also that two kinds of islet cells could be distinguished. (Lane, 1907). This led to various staining techniques being devised for colouring alpha and beta cells differently. (Ham and Cormack, 1979).

A non-granular C cell in the islet tissue of the ginea pig was described as a precursor of the alpha cell. (Bensley, 1911).

The delta cells were later described. (Bloom; 1931).

The type of fixative and stain is important in identification of the different islet cells. (Ghareeb, 1969).

Allen (1922) showed that if from 80 to 90% of the pancreas was removed from a dog, the remaining portion had enough islets to keep the animal free from diabetes, provided the dog's diet was restricted. He considered that the extra carbohydrate fed the animals placed increased secretory demands on the beta cells, and their degranulation and hydropic

degeneration were evidence of exhaustion through over work. With continued additional food intake the islet lesions became permanent, with no evidence of recovery. (Allen, 1922).

Allen's findings still have great implications with regard to the treatment of diabetes. In particular, they apply to those in danger of developing diabetes, for they show that if an individual overstrains his beta cell capacity, for example by eating too much carbohydrate, beta cells will be destroyed from over work and this, of course, will decrease the individual's beta cell capacity and make those remaining more susceptible to overstrain than before. (Ham and Cormack, 1979).

The Discovery of Insulin:

In 1920, Banting, impressed by the findings of Ssobolew and others who tied the ducts of the pancreas and found that the acinar tissue atrophied after duct ligation, began to suspect that previous attempts to obtain an active extract of islet tissue failed because the digestive enzymes of the acinar tissue destroyed the islet hormone before it could be extracted. He decided to try making extracts from pancreas after duct ligation for 6 to 8 weeks, so that presumably

would contain only islet and not acinar tissue. The events that occured between the inception of the idea and the isolation of insulin, the collaboration of Best and later of Collip, the inevitable succession of encouraging and discouraging results, the lack of funds and above all the persistence of Banting and finally the emergence of insulin as an effective treatment for diabetes make an inspiring story. (Ham and Cormack, 1979).

Houssay and Biasotti (1931) showed that diabetes produced in animals by removing the pancreas could be ameliorated by removing the pituitary gland as well, and that such animals, instead of declining steadily in health like those from which the pancreas is only removed, would live free from diabetes for long periods. Furthermore, Johns, et al., (1927), produced signs of diabetes in dogs by giving them injections of anterior pituitary extract.

Young (1937), showed that sufficiently prolonged course of injections of anterior pituitary extract would make dogs permanently diabetic.

Anterior pituitary extracts injected daily caused progressive degranulation of beta cells; this was followed by hydropic degeneration. (Ham and Haist,1939).

Anterior pituitary extracts containg ACTH stimulate the adrenal cortex to make more cortisol, via its gluconeogenetic effect; viz: conversion of protein into sugar in the liver. The administration of cortisol alone can cause diabetes. However, it seems most probable that the chief diabetogenic factor made by the anterior pituitary gland is growth hormone. (Ham and Cormack, 1979).

Glucagon was identified by Murlin as an insulin contaminant. It was demonstrated that it is a hyperglycaemic glycogenolytic factor secreted by the alpha cells. (De Duve and Stahl , 1953).

The first pancreatic cell tumour was reported in 1902. (Nicholls, 1902). At that time the endocrine function of the islet cell was not recognized. (Ghareeb, 1969).

Beta cell tumours are the commonest group, about 800 such tumours are reported in the literature. (Nicholls, 1902). Such tumours are always associated with the clinical picture of hypoglycaemia due to hyper insulinism; adenomata are found almost equally distributed throughout all portions of the pancreas, but ectopic tumour may be found in the duodenal wall. (Gharreb, 1969). The majority are benign and it was

found that 10 % are malignant, 78 % benign and the rest are questionable. (Howard, et al., 1950).

Zollinger Ellison syndrome was described as a combination of hyperacidity or fulminating ulcer diathesis, frequently accompanied with jejunal ulcers and islet cell tumour. (Zollinger and Ellison, 1955).

Gastrin like activity was first demonstrated in 1964 from islet cell tumour in a patient with Zollinger-Ellison syndrome. (Gregory, and Tracy, 1964).

It was suggested that at least in some cases, the source of tumours is the delta cells. (Cavallero, Solcia, and Sampietro, 1967).

II- ANATOMY OF THE PANCREAS

are the anastomosing superior and inferior pancreaticoduodenal arteries. (Warwick and Williams, 1973).

The head is related anteriorly to the transverse colon and the attachment of the transverse mesocolon. (Snell, 1981). Posteriorly, it is related to the inferior vena cava, which runs upwards behind it and covers nearly the whole of its posterior aspect. In addition it is related to the terminal parts of the renal veins and the right crus of the diaphragm. The uncinate process passes infront of the aorta. The bile duct lies either in a groove on the upper and lateral part of the posterior surface of the head of the pancreas, or in a canal in its substance. (Warwick and Williams, 1973).

The neck is the constricted portion of the pancreas. (Snell, 1981). It is about 2 cm long, extends forwards, upwards and to the left from the head, and merges imperceptibly into the body. Its anterior surface is covered with peritoneum and adjoins the pylorus; the gastroduodenal and the anterior superior pancreaticoduodenal arteries descend in front of the gland at the right side of the junction of the neck with the head; its posterior surface is in relation with the superior mesenteric vein and the beginning of the portal vein. (Warwick and Williams, 1973).