HISTOMORPHOLOGY, INNERVATION AND VASCULATURE OF THE PANCREAS WITH REFERENCE TO THE ISLET OF LANGERHANS

THESIS

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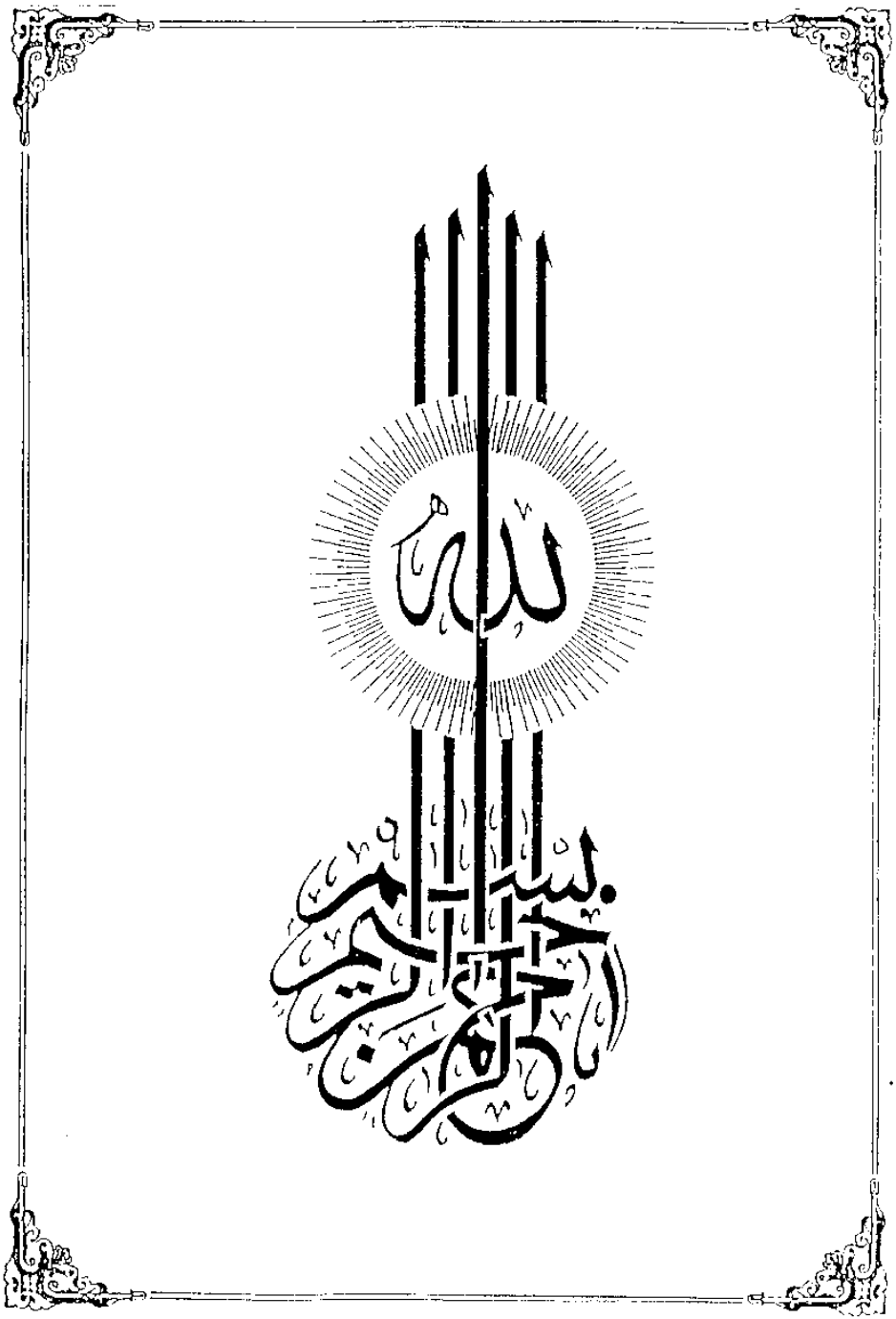
TO MY HUSBAND

AND SON



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INTRODUCTION

INTRODUCTION

The postnatal growth of the pancreatic islets of the rat has been studied, only quantitatively, by several investigators. Overholser (1925) counted the total number of islets in the pancreas of rats at different ages. Hess and Root (1938) and Hellman (1959) studied the relation existing between the number of the developing islets and the weight of the pancreas and body weight of different ages. Sidorova and Babaeva (1968) concentrated on the changes in the weight of the organ, acini and islets.

Reviewing the literature, it was evident that the histomorphologic changes of the developing acini and islets received a little attention.

The aim of this study was to describe the morphology of the exocrine and endocrine portions of the pancreas of the rat from birth up to the age of 3 weeks, using the light and electron microscopy. The fine structure of pancreatic innervation and vasculature would be also studied.

The morphological changes of the endocrine pancreas following alloxan treatment was studied in different

animals e.g. rabbit (Williamson and Lacy, 1959; Wellmann, Volk and Lazarus, 1967), Cottus scorpius (Falkmer and Olsson, 1962), mice and Mongolian Gerbil (Boquist, 1977). Cats were described to be resistant to the diabetogenic effect of alloxan (Hatchell, Reiser, Bresnahan and Whitworth, 1986).

Reviewing the literature, it was noticed that the morphological changes of the endocrine pancreas of alloxan treated rats received a little attention and was only limited to the light microscopic level. Therefore, the present study aimed at describing the ultrastructural changes of the endocrine pancreas of rats treated with different doses of alloxan.

Pregnancy in a diabetic patient was considered to be hazardous to both the mother and fetus. Macrosomia, fetal distress, increased morbidity and mortality were the major complications in the outcome of diabetic pregnancy (Fleischman and Finberg, 1983).

Since the discovery of the diabetogenic effect of alloxan, animal models had been widely used to study the effect of diabetes on pregnancy (Miller, 1947; Frye, 1957 and Kim, Runge, Wells and Lazarow, 1960); however decreased fertility and increased mortality complicated this approach

(Miller, Hurwitz and Kuder, 1944; Hultquist, 1950).

Although macrosomia was observed in the human (Cardell, 1953), conflicting reports on birth weights of offspring of diabetic rats had been reported. Hultquist (1950), Angerwall (1959), Solomon (1959) and Lazarow, Kim, and Wells (1960) reported increased birth weight of the offspring. While Kim et al. (1960), Lawrence and Contopoulos (1960) and Eriksson, Andersson, Efendic, Elde and Hellerstrom (1980) reported a decrease in the rat offspring birth weight. In the meantime, unchanged weight of the young was reported by Sinden and Longwell (1949).

The light microscopic changes of the islets in the fetuses of diabetic rats during the prenatal period was described by Frye (1957) and Angerwall (1959). Aerts and Van Assche (1981) described the ultrastructural changes in the endocrine pancreas in neonates of diabetic rat, where diabetes was induced on the first day of gestation by the intravenous injection of streptozotocin. However, the injection of B-cytotoxins had been declared to be injurious to both conceptus and placenta, therefore in an animal model an interval should elapse between the administration of the cytotoxic drug and the occurrence of pregnancy (Deuchar, 1978; Eriksson et al., 1980).

REVIEW OF LITERATURE

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HISTORICAL REVIEW

The history of diabetes was cited by Lazarus and Volk (1962) and Chang and Diani (1985). They mentioned that the first reference on this disease was contained in the papyrus Ebers (1500 B.C.), found at Luxor in Egypt at 1872. A medical prescription on how to stop polyurea was included. The Greek term "Diabetes" meant "to run through a siphon" was first introduced by Aretaeus of Cappadocia (81-138 A.C.). During the tenth century, diabetes was thoroughly studied by the Arabian physician Ibn-Sina (980-1037). He noticed the abnormal appetite, sweetness of urine, gangrene and loss of sexual function among diabetics. The adjective "Mellitus" was introduced by Cullen (1709-1790). Cawley (1778) was the first to associate diabetes with the pancreas. He described multiple calculi and marked destruction of pancreatic tissue at autopsy in a patient, who had died from diabetes. Hedon (1893) observed that diabetes was absent in pancreatectomized dog following transplantation of partially resected pancreas. This finding suggested the presence of internal rather than external secretion of the pancreas. Langerhans (1869) described yellow areas of 0.1 to 0.2 mm in the

rabbit pancreas. Laguesse (1893) named them the islets of Langerhans and suggested that, they were concerned with the internal pancreatic secretory function involved in carbohydrate metabolism. Bensley (1911) identified two different types of cells in the islets, A and B cells. Banting and Best (1921) demonstrated the extensive lowering of blood and urinary sugar in pancreatectomized dogs given pancreatic extracts. They called the pancreatic hormone causing this effect "insulin".

PRENATAL GROWTH OF THE PANCREAS

Kleitsch (1955) reported that the human pancreas originated as two outpouchings from the primitive foregut. One of these buds extended into the dorsal mesentery, while the other into the ventral mesentery, in close proximity to the hepatic bud. He added that the dorsal rudiment was the largest of the two and situated at a variable distance proximal to the ventral pancreas. Furthermore, he noticed that, with the rotation of the bowel, the two pancreatic rudiments interlocked.

Pictet and Rutter (1972) mentioned that the dorsal pancreatic rudiment gave rise to the splenic portion (i.e. the tail and body) of the pancreas, and the ventral bud

gave rise to the duodenal portion or the head of the pancreas. They suggested that islet cells originated from some protodifferentiated cells at the terminal ends of the budding pancreatic tubules. They added that islet cells first appeared as discrete single cells, then as clusters within the exocrine basement membrane and later separated to form islets. They described a capsule of fibroblasts and collagen fibers partially encircling the islet as a boundary to separate it from the exocrine tissue or interstitial space.

Gomez Dumm, Galeano, Genoro and Gagliardino (1987) described the chronological appearance of the different types of islet cells in rat using the immunocytochemical techniques. They mentioned that A cells were the earliest endocrine colony, appearing on the 12^{th} day of gestation, followed by B cells (14^{th} day), D cells on the 18^{th} day and finally PP cells on the 19^{th} day of gestation.

POSTNATAL GROWTH OF THE PANCREAS

Overholser (1925) determined the relation of age to the total number of islets of Langerhans in the pancreas of albino rat. He reported an increasing number of islets during the first 20 days of life, then reached and

maintained a maximum value during the following 30 days and from this point started decreasing with advancing age until reaching a level which was maintained in animals till 880 days old.

Hess and Root (1938) thoroughly studied the relation between the average number of islet of different age groups and the weight of the pancreas and the body weight of white rats. They also compared between male and female rats in reference to these factors. They reported an increasing number of islets, weight of the pancreas and body weight from the first to the two hundred and fifty-sixth day. Further, the number of islets per unit weight of the pancreas was very large at birth, then decreased very rapidly during the first few days till about the thirty-sixth day when it became nearly constant. They also mentioned an increasing number of islets, larger pancreas and greater body weight of male rats compared to female rats at any given age.

Sidorova and Babaeva (1968) described the postnatal development of the pancreas in albino rats. Their study involved a quantitative and light microscopic examination of the pancreas during the 75 days after birth. They mentioned that the pancreatic weights increased fairly

rapidly after birth and during the first 3 weeks of age mainly due to the high level of proliferative activity of the cells. They reported that the markedly increased pancreatic weight from the 3rd to the 22nd day after birth was associated with little change in the size of the individual acini. They also observed that the relative content of islet tissue continued to fall progressively with the increase of the animal age, and the ratio of the quantity of islet tissue to the quantity of acinar tissue also decreased with age.

THE INNERVATION AND VASCULATURE OF THE PANCREAS

Shorr and Bloom (1970) described 3 types of nerve endings in association with the islet of Langerhans of adult rat. The first type contained agranular vesicles (200-400 A°) and the second contained large granular vesicles (500-800 A°) in addition to the agranular vesicles. They described these nerve endings in relation to A and B cells of the islet. They also described a third type of nerve ending containing electron-lucent vesicles with a slightly darker electron-dense opaque center.

Kamel, Mikhail and Beshir (1979) studied the innervation of the pancreas of the adult rat using the silver