A STUDY ON PLASMA GLUCAGON LEVEL IN BILHARZIAL HEPATIC FIBROSIS

A THESIS

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By

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A C K N O W L E D G E M E N T

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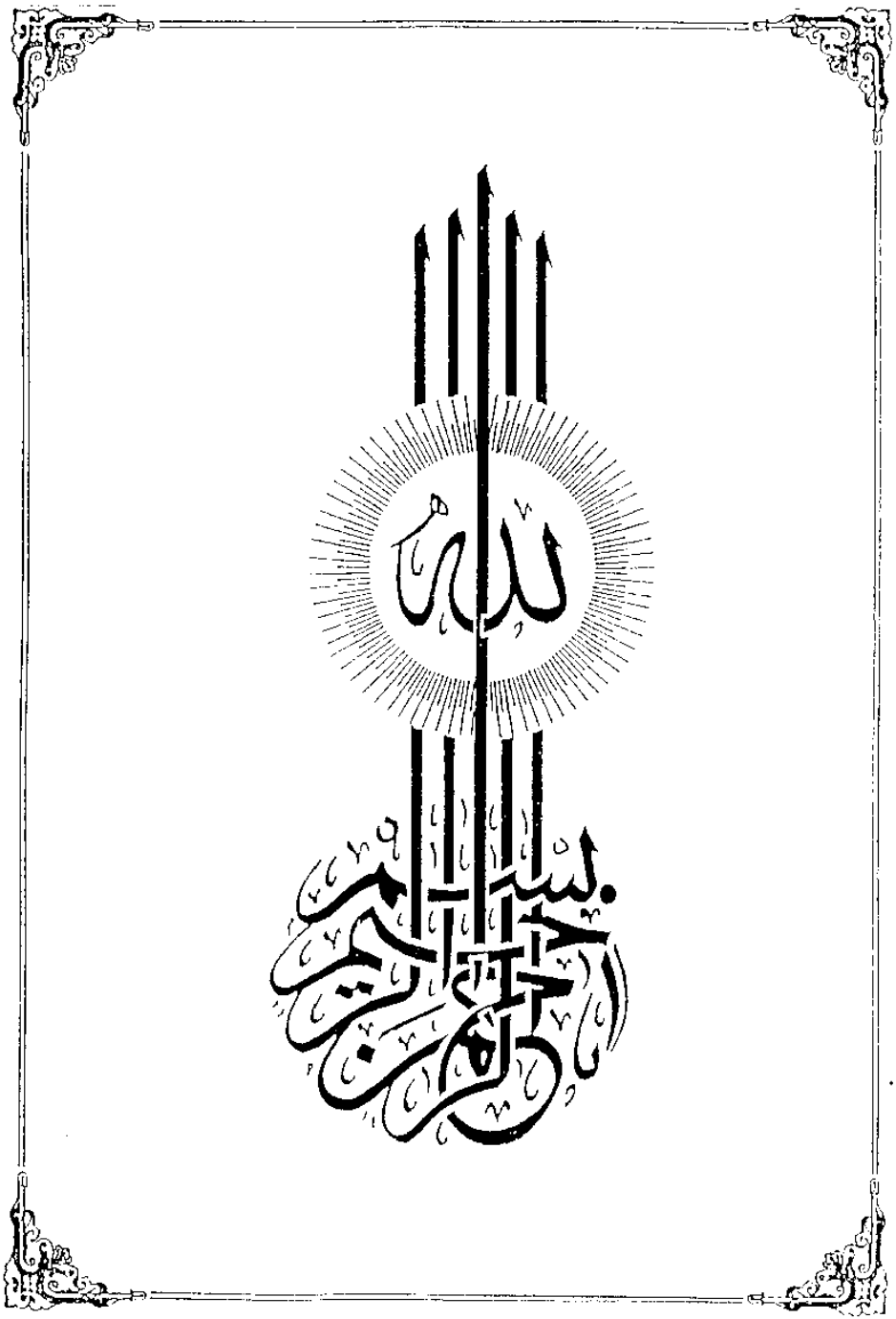

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C O N T E N T S

AIM OF WORK

A I M O F T H E W O R K

The central role of the liver in glucose homeostasis has been recognized since a long time . There was always an increasing interest to study the disturbance in carbohydrate metabolism associated with liver disease .

Recently, many investigators demonstrated the presence of hyperglucagonemia and glucose intolerance as constant features of liver cirrhosis (Megyesi et al., 1967) .

The aim of this work is to determine the basal plasma glucagon level and the glucose tolerance test in patients suffering from bilharzial hepatic fibrosis (B.H.F.), with and without ascites .

REVIEW OF LITERATURE

ANATOMY AND HISTOLOGY OF THE LIVER

The liver, The largest organ in the body ,weighs 1200-1500 gm and comprises one fiftieth of the total adult body weight. It is relatively larger in infancy, comprising one eighteenth of the birth weight (Sherlock, 1975).

Functionally the liver is bilobed organ and each lobe has a separate afferent and efferent blood vessels. (McIndoe and Counseller, 1927 and Healy,1954). The contaguous surfaces of the two lobes are closely applied and lie within a common capsule, so that there is no external evidence of this lober division (Healy, 1954). If the liver is diseased one lobe may be more severely affected than the other .

The liver is of mixed endodermal and mesodermal origin (Sherlock, 1975).

Kiernan (1833) described the anatomy of the pig's liver, and at that time introduced the concept of hepatic lobules as its basic architecture. He described circumscribed pyramidal lobules consisting of a central tributary of the hepatic vein and at the periphery a portal tract containing bile duct, portal vein radicle, hepatic artery branch, few round cells and little connective tissue. Columns of liver cells and blood-containing sinusoids extended between these two systems.

Stereoscopic reconstruction (Elias, 1952) has shown the human liver as columns of liver cells radiating from a central vein and interlaced in orderly fashion by sinusoids. The liver is regarded as single cell plates tunnelled by a labyrinth of lacunae. The continues liver tissue is prevaded by two systems of tunnels, the portal tracts and the hepatic central canals, which run in planes perpendicular to each other.

The liver cells comprise about 60 percent of the liver. They are polyhydra and are approximately 25-35 u in diameter. The life span of rat liver cells has been measured using tritiated thymidine, and is 191 to 453 days (Mac Donald, 1961).

There are approximately 202 X 10^3 cells in each milligramme of normal human liver of which 171 X 10^3 are parenchymatous and 31 X 10^3 littoral (sinusoidal including kupffer cells) (Gates et al., 1961).

Potential spaces between the hepatic cells and the walls of the sinusoids are called spaces of Disse. They are only seen in necropsy sections (Popper, 1948). They contain tissue fluid which flows outwards into lymphatics in the portal triads.

Rappaport (1963) envisaged a series of acinar units centred on the portal triad of terminal branch of portal vein, hepatic artery and bile duct. These interdigitate, mainly perpendicularly ,with terminal hepatic veins of adjacent fields. The circulatory peripheries of acini(adjacent to central hepatic veins) suffer first from injury. The regions closer to the axis formed by afferent vessels, and bile ducts survive longer and may later form the core from which regeneration will proceed.

BILHARZIASIS

Endemicity of Bilharziasis in Egypt:

Bilharziasis has been found to exist in Egypt since pharaonic era (Wilcocks, 1962). Nowadays Schistosomiasis is the most prevalent disease in Egypt, and next to malaria, the most prevalent disease in the world (Kagan et al., 1962).

Weir et al.,(1952) proved that all inhabitants in rural areas exposed to infection are usually infected. It has been estimated that more than 16 millions amongest the population of Egypt suffer from the infection and/or its complications (Mousa, 1969).

Haematobium infection is present allover the country, while mansoni infection is limited to the Nile Delta (Mousa, 1976).

The maximum age of both bilharziasis haematobium and mansoni infection falls between 10-20 years, females are slightly less affected due to the lower chance of exposure to infection.

In areas heavily infested with mansoni, 50% of the people show hepatosplenic involvement, while in pure urinary bilharziasis the liver is involved in about 15% of cases.

Elwi and Attia (1962) attributed the increase in the endemicity of bilharziasis to both the progressive increase in perenial irrigation and the introduction of large scale antimonial antibilharzial therapy which is known to drive the worms back towards the liver, where they die in bigger portal branches.

Schistosomiasis is a national problem not only because of its endemicity and high incidence, but also because it is intimately connected with our economic resources. The reduction in total economic production has been estimated to be 30 % as a result of incapacitation of a large segment of population (Mousa, 1969), while the annual economic loss has been estimated to be 560 million dollars per year (Farouq, 1968).

Pathology of bilharzial hepatic fibrosis:

Liver involvement in Schistosomiasis is first described in Egypt by Kartulis (1885), but Symmers (1904) was the first to describe the pathology of the disease. He noticed the extensive scaring and thickening of the large portal tracts occured in response to the deposition of schistosoma mansoni ova at these sites. He referred to this type of lesion as clay-pipe stem cirrhosis.

Hashem (1947) introduced the terms fine and coarse types of hepatic fibrosis, instead of diffuse and clay - pipe stem cirrhosis respectively. He restricted the term cirrhosis to chronic disease of liver primarly causing slow degeneration and necrosis of the liver parenchyma with consequent fibrosis of necrotic patchs and regeneration of the spared liver parenchyma, a sequele of events which differ from that occuring in bilharzial hepatic fibrosis which is a consequent of infiltration of bilharzial ova and occasionally worms in and around the fine portal tracts, in which fibrosis is essentially interstitial and rather invasive with no evidence of regeneration occurs, and the enclosed liver tissue frequently presents more or less normal architecture.

Erfan et al.,(1957) analysed the pathological findings in a series of 180 liver biopsies from Egyptian patients with hepatosplenomegaly and found bilharzial hepatic fibrosis in 70%, of these 30% were in the early infiltrative stage, while 70% were in various stages of fibrosis . They came to the following conclusive criteria for early bilharzial hepatic fibrosis: presence of bilharzial ova in and around the small portal tracts, hypertrophy of kupffer cells, engorged sinusoids, absence

of fatty infiltration , degeneration or regeneration of parenchymal cells, and bilharzial pigment engulfed in reticuloendothelial cells. They also considered that thickening of portal tracts with mild swelling and wasting of liver cells at the periphery of the lobule were indicative of advanced pathology.
This description was also confirmed by Abdine (1963) .

Salah (1962) described the bilharzial liver as having the same pathological criteria described by Erfan et al.,(1957) but added two other criteria: diffuse cellular granulometous eosinophilic infiltration ending in diffuse fibrosis, coarse or fine ,of the portal tracts and the lobular pattern is usually preserved until very late in the disease when, in the fine type of fibrosis some distortion may occur as a result of excessively contracting fibrous tissue.

Recent studies suggested that hepatic cellular damage in experimental and human schistosomiasis can indeed occur.
Stenger et al.,(1967) studied the livers of mice infected with schistosoma mansoni by the electron microscope early and late in the course of liver disease. They noticed that in early phases, liver cells displayed subcellular