ULTRASTRUCTURAL ASPECT OF THE LIVER IN CERTAIN HUMAN HEPATIC DISEASES WITH SPECIAL REFERENCE TO BILHARZIASIS

THESIS

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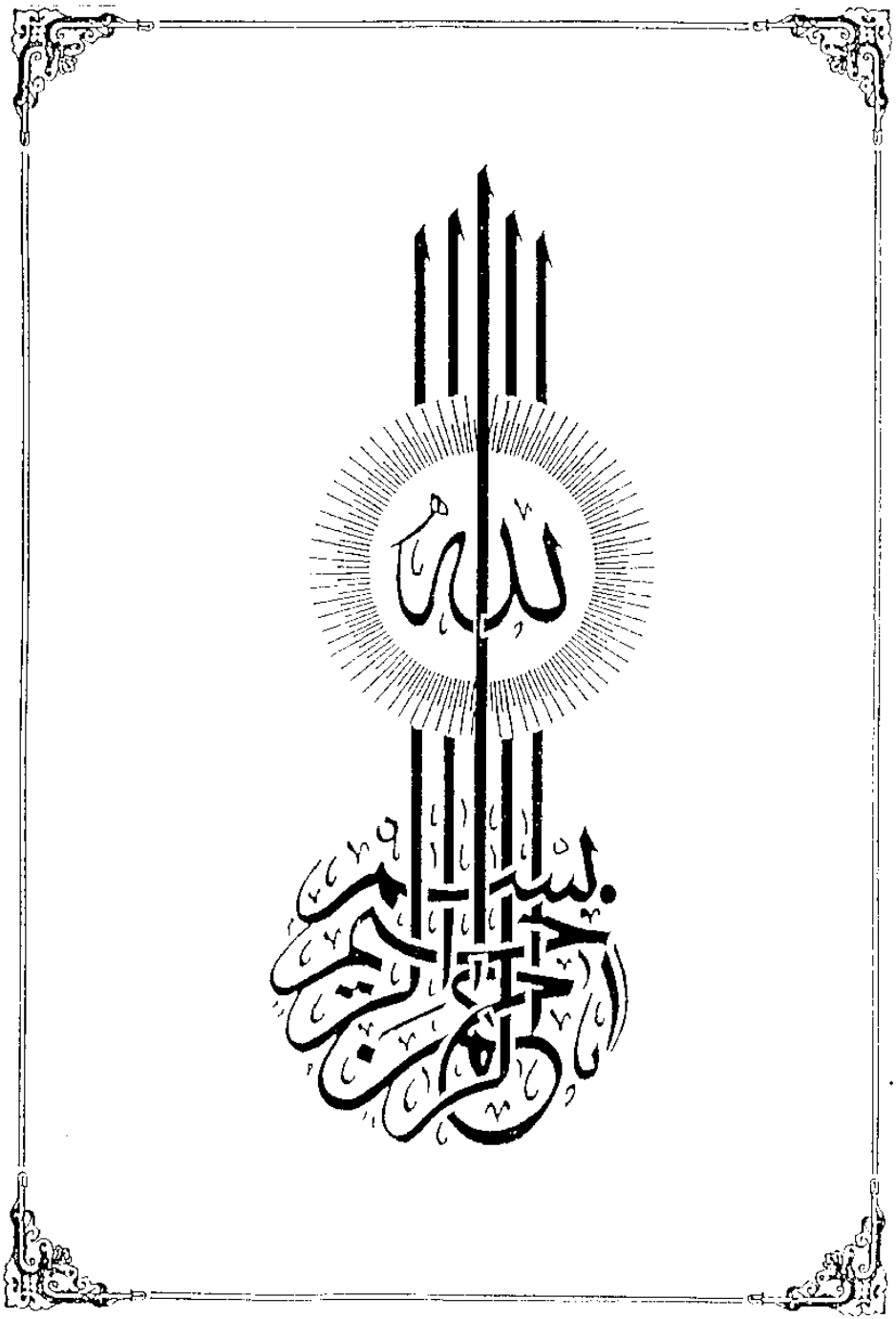

Aim of Work

The hepatocyte is a cell which is vulnerable to various pathological conditions: infections, intoxication, inadequately or poorly balanced diet and congenital diseases

Inspite of the fact that the hepatocytic changes had been described under a variety of pathological conditions, the ultrastructural changes of the hepatic cells in some endemic diseases in Egypt e.g. Schistosomiasis mansoni and its association with chronic hepatitis, had not thoroughly investigated.

The aim of the present work is to study the ultrastructural changes in the hepatocytes in Bilharzial infection and in other liver diseases especially chronic- B- hepatitis.

CONTENTS

REVIEW OF LITERATURE

HISTORY OF BILHARZIASIS

In (1851), **Theoder Bilharz** in Kasr-El-Aini Hospital in Cairo had discovered the worms that cause the disease of endemic haematurea in Egypt, in the tributaries of the mesenteric vein

The name "Bilharzia haematobium" had been given for that worms in 1859 by **Cobboled** in honour of Theodor Bilharz. **Sweinland** in the same year had adopted the genetic term Schistosoma.

Belleli in Alexandria (1885) had demonstrated the bilharzia ova in the rectum. In the same year, **Kartulis** in Egypt had described the involvement of the liver in bilharzial patients

In 1902 **Manson** could differentiate between two types of bilharzial parasites, depending on the shape of their eggs. The eggs with a lateral spine for schistosoma Mansoni , while the eggs carried terminal spine for schistosoma haematobium.

Symmer (1904) had given the name " Clay-pipe Stem Cirrhosis " to the extensive scarring and thickening of the large portal tracts that occured in response to bilharzia ova

Ruffer (1910) stated that, schistosomiasis was an endemic disease in Egypt since the time of the ancient pharaos, as he had demonstrated the ova of bilharziasis in mummies of the period of 1220 B.C.

Bogliolo . 1957 . Elwi and Attia. 1962; Warren. 1966; Grimaud and Santos. 1967 had described the light microscopic changes in liver and the presence of bilharzia ova inside the portal venous radicales

The ultrastructural picture of bilharzial granuloma had been described in the experimentally infected mice by Stenger and Johnson (1967).

Bedi and Isseroff (1979) found that proline, which is the major amino acid in bile, was increased by hundred folds in Schistosomal infections and it had been suggested that this is the main factor for fibrotic hyperplasia of the liver

LIFE CYCLE OF SCHISTOSOMIASIS

Prata (1957) showed that the Schistosoma egg had a basophilic cellular content limited by a thin, undulating egg shell While immature they were seen without tissue reaction, unless they died and disintegrated Few macrophages might accumulate around them with a slight condensation of reticulin fibers. Complete resolution of this lesion was to be expected, and only fragments of the egg shell might remain longer within the giant cells. In human infection many eggs were destroyed while still immature, causing negligible tissue damage. The motile embryo or miracidium, in its mature state , had a thick linear chitinous shell and an eosinophilic content with several basophilic granules, some of them forming a rosette-like structure in its center.

Andrade (1965) showed that the miracidial secretions caused tissue irritation and infiltration with eosinophils , this was followed by accumulation of macrophages and granulomatous formation while the miracidium was alive. The cellular granuloma around the egg underwent a progressive fibrous replacement, while giant cells were engulfing the chitinous shell. Following death of the miracidium the disintegrated material was liberated and an area of hyaline or granular necrosis might appear in the center of a granulama already showing peripheral fibrous encapsulation. The lesion might be invaded by eosinophils, later the lesion was replaced by fibrous scar.

Marsden (1975) and Warren (1978) showed that men, animals, birds and mollusks had suffered from infection with many different species of schistosomes. The worms had definitive hosts, usually mammals and birds for sexual reproduction, as well as, intermediate hosts (snails) for asexual multiplications. The worms lived commonly in the portal and mesenteric veins.

According to **Dunn and Kamel (1981)**, the commonest types of human schistosomes are :

-Schistosoma mansoni, presents in middle East, Africa, Central & South America.
affects the liver and colon.

-Schistosoma japonicum, In Far East,
affects the liver, small intestine & colon.

-Schistosoma haemotobium, in Africa and Middle East,
affects urinary bladder and ureters.

-Schistosoma mekongi, South-east Asia.
affects the liver, small intestine & colon.

-Schistosoma intercalatum, in Central Africa,
affects small intestine and colon.

ANATOMY OF THE NORMAL LIVER

According to the reviews of **Copenhaver et al. (1971) and Ham (1974)**, the liver of an adult human ranges from 1.4-1.6 Kgms. comprising one-fiftieth of the body weight. In the newborn, it was about one-twentieth of the body weight due to its blood-forming activity during fetal life

Its exocrine function is the secretion of bile that is conveyed to the intestine by a system of ducts.

Its other products pass to the blood e.g. prothrombin, serum albumin, fibrinogen, $æ_1$- antitrypsin, $æ_1$- fetoprotein and C-reactive protein. The liver stores carbohydrate, fat and vitamins and releases them into the blood at times they are needed by the body.

The liver has an important role in detoxication and removal of waste products from the blood. It has the ability to convert substances into more active forms.

It plays a major role in the intestinal immune system by sequestering dimeric IgA and secreting it into the intestinal lumen via the biliary tree. The presence of abundant phagocytes in the liver makes it one of the principal filters for foreign particulate matter, especially for bacteria coming from the gut.

The liver , like other glands , has a parenchyma that is derived from the endoderm, while the stroma is derived from the mesoderm. The stroma of the liver is formed of the capsule of **Glisson** which is lined with

mesothelial cells and contains regularly arranged collagenic fibres and scattered fibroblasts

From the hilus , the connective tissue extends like the trunk of a tree into the parenchyma of the liver. It surrounds the entering blood vessels and divides the liver into innumerable small lobules.

In man each lobule has no complete investation by connective tissue. The hepatic lobule may be considered the anatomical unit of the structure of the liver and has two main constituents, an epithlial parenchyma and a system of anastomosing blood sinusoids. The parenchyma is made up of hepatic cells arranged in irregular, branching interconnected plates. In sections the sheets of cells give the appearance of cell cords, they have been called the hepatic cords. The plates tend to be arranged in a radiating manner around the central blood vein of the lobule.

The acinar unit was defined **by Rappaport, (1975)** as a functional unit of the liver, it included a small parenchymal mass that surrounded a terminal branch of portal vein accompanied by a hepatic arteriole and a bile ductule. The circulating peripheries of acini, adjacent to central hepatic veins, suffered first from any insult to the liver. The regions closer to the axis supplied by the afferent vessels and bile ducts survived longer and might later form the core from which regeneration would proceed.

FINE STRUCTURE OF HUMAN LIVER CELLS

Previous investigations indicated that the liver consists of four different cell types of which the hepatocytes represent the major component (about 70%). The hepatocytes, all basically, appear similar in their appearance, have a polygonal shape with more than five surfaces and measuring about 20 u in diameter. The hepatocyte surfaces show two distinct regions; the first is exposed to the perivascular Disse's space and the second to the lumen of the bile canaliculi, both had numerous microvilli. In addition to the parencymal cells, there are the lining endothelial cells, the Kupffer cells and the fat storing cells (**Caramia, Frati, 1982 and Anthony Jones, 1983**).

THE HEPATOCYTE

The plasma membrane :

Kyuichi Tanikawa (1968) stated that the plasma membrane had a unit membrane structure about 75 A^0 , composed of two electron dense layers and one electrolucent intermediary layer. The cell membrane facing the Disse's space and along the bile canaliculus had numerous microvilli. The cell membrane bordering the adjacent hepatocyte membrane was more or less straight and smooth. In some places, it might have stud like projections into the concavities that were located between the adjacent hepatocyte. The pinocytic invaginations of the cell membrane at the Disse's space were about 0.1 u in width.

Matter and Rouiller (1969), showed that the intermediate junction and the desmosomes were similar in human and rat livers differing only in the width of the intercellular space separating the two opposing membranes. Fine fibrils appeared to be inserted into the desmosomes. There were amorphous granular material on either side of the plasma membrane to form the intermediate junctions. Another surface specialization called the nexus, composed of two strictly parallel, closely opposed plasma membranes that were separated from each other by a minute distance of about 20 A°. The interhepatocytic plasma membranes were relatively simple, interrupted by an occasional button-like interdigitations.

Popper and Schaffner (1970) showed that the sinusoidal microvilli were commonly tortuous and bifurcating while the bile canalicular microvilli were slender, nonbranching and projecting into the canalicular lumen.

Biempica et al. (1971) showed that the cytochemical activities of the sinusoidal part of the hepatocytic cell membrane stained intensely for alkaline phosphatase but were generally weak for nucleoside di-and triphosphate activities. On the other hand the bile canalicular microvilli exhibited high levels of nucleoside triphosphatase activities and variable alkaline phosphatase activity.

Wisher and Evans (1979) showed that the physiological functions of the hepatocyte plasma membrane were different according to its region,