EFFECT OF VIRAL HEPATITIS ON THE PANCREAS

THESIS

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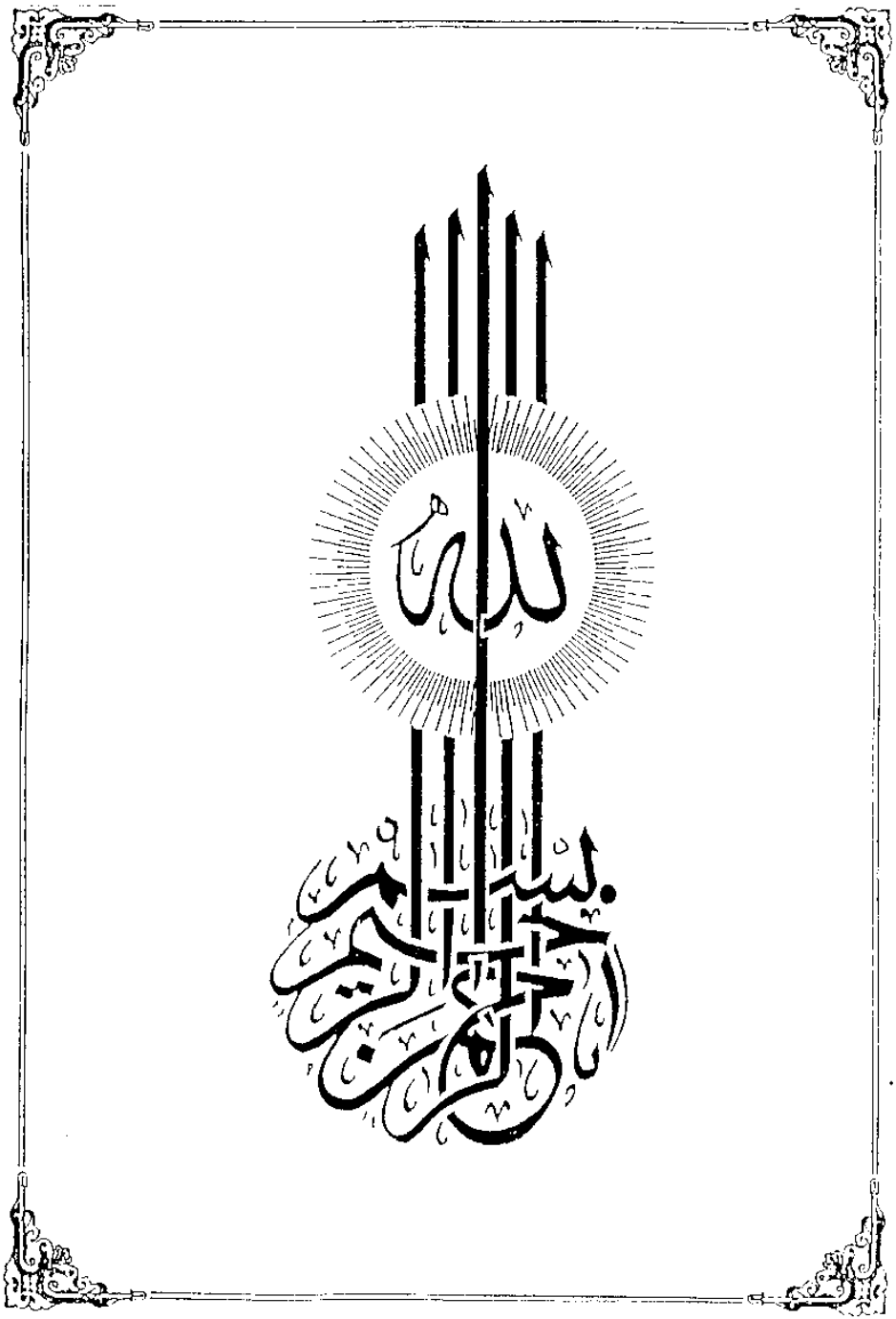

C O N T E N T S

INTRODUCTION

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1. The Liver :

The liver is the largest gland of the body, it is built up of hepatic lobules which are composed of hepatic cells, canaliculi and sinusoids. The hepatic cells are arranged in columns perpendicular to the central vein, the blood sinusoids separate the columns from one another, while the bile canaliculi are found within the cell columns in between the liver cells (Gray, 1967).

In each cell there are large number of mitochondriae full up with enzymes. The cytoplasm of the liver cell contains a variety of inclusions as glycogen granules, proteins and others.

The relation which is between the bile canaliculi, the liver cells and the venous sinusoids is reflected in the transformation of blood bilirubin into bile bilirubin. And despite the multiplicity and diversity of the liver functions, there are no groups of cells cytologically specialized for the performance of one function or the other, but some evidence supports the

view that the central cells of the liver lobule are related to storage while the peripheral cells are concerned with the conjugation of bilirubin and for its excretion into the biliary tract which discharges it into the intestines, and this bile being an important agent in the digestion of fats. There is a store of neutral fat in the liver; the bile capillaries or canaliculi are considered as the primary bile channels, they are connected to bile ducts and lined by cells containing cholesterol and fat droplets. So the liver is considered as the centre of metabolic activity of all food stuffs: Sugars and carbon residues from protein and fat, are converted to glycogen which is stored as a carbohydrate reserve, being reconvertible to glucose. Deamination of amino-acids occurs also in the liver, the nitrogen residues are converted to urea. Synthesization of immunoglobulins is completed in the cells of the reticulo-endothelial system (though mainly elsewhere than in the liver), and albumin and the other globulins in the parenchymal cells (Baron, 1973).

When the liver is diseased, one or more but not necessarily all of its functions are impaired, as the

adult liver has considerable functional reserve. An isolated part may be removed or severely damaged by a localized disease (for example by carcinoma), and if the remainder is healthy, liver function may remain apparently normal when tested biochemically in the resting state. On the other hand, in a disease such as infective hepatitis, in which there is diffuse damage to the majority of liver cells, detectable derangement of liver function is always present.

2. Liver Function Tests :

Before describing the individual liver function tests, there are general points which are worthy to mention: No single test can be used to fully evaluate the liver function in health or disease, and no single test is always reliable. In diffuse liver damage the liver function is abnormal and reliable, but in localized damage any single test may be normal despite the other liver function test being abnormal (Joseph, 1976).

These tests are classified according to the specific function of the liver involved; the serum bilirubin which designates the abnormalities of pigment metabolism, the determination of serum enzyme activities as that of aminotransferases and the alkaline phosphatase which are very important in detecting the least damage in some liver diseases as the viral hepatitis. There are other tests which are based on changes in serum albumin and on carbohydrate metabolism (Varley, 1980). All these tests are used in the differential diagnosis of different types of jaundice, to assess the severity of liver damage in known liver disease, to follow the trend of the disease and to assess the residual damage after recovery.

a) Serum bilirubin :

Approximately 75% of bilirubin is a by product of haemoglobin metabolism and is derived from the daily breakdown of 7-8 gm. of haemoglobin from effete red blood cells. The remaining 25% of bilirubin comes from other sources such as myoglobin, cytochromes and catalases. All bilirubin is produced in cells of the reticulo-endothelial system not in hepatocytes (Robinson, 1972).

Unconjugated bilirubin is then transported to the liver bound to albumin and it is nearly insoluble in water. In the hepatocyte, bilirubin is hydroxylated by cytochrome enzyme with uridine diphosphate glucuronic acid to form conjugated (direct) bilirubin glucuronide (Indirebilirubin).

All hepatic cells continually form a small amount of bile; this is secreted into the minute bile canaliculi which are between the hepatic cells. Bile then flows peripherally towards the interlobular septa, then into progressively larger ducts and finally reaching the common bile duct from which the bile either empties directly into the duodenum or diverted into the gall bladder for concentration and storage .

The bile is formed mainly from bile salts and bilirubin but in addition it contains water, cholesterol, lecithin, fatty acids and the usual electrolytes of the plasma.

Reaching the intestine, bilirubin glucuronide is converted by the intestinal bacteria to unconjugated bilirubin and stercobilinogen, this takes place mainly in the colon, where the bacteria are found. In this area the absorption is poor and the enterohepatic circulation of both bilirubin and stercobilinogen is slight. The very small amount of absorbed stercobilinogen which can't be reexcreted by the normal liver (less than 4 mg . daily) is excreted in the urine as urobilinogen. Stercobilinogen and urobilinogen are readily oxidised to similar substances: stercobilin and urobilin (Lester, et al., 1965).

The normal serum contains 0.2 mg . or less per 100 ml. of conjugated bilirubin and the total serum bilirubin level is not more than 1.0 mg per 100 ml. (Wootton, 1964).

Serum bilirubin determination is one of the most frequently utilized laboratory tests for diagnosis of acute viral hepatitis. With the onset of the icteric phase, serum bilirubin concentrations usually rise and the high levels are maintained for ten to fourteen days in the average adult. The levels vary widely, but total serum bilirubin levels above 20 mg. per 100 ml. are infrequent. In most patients the maximum concentration of total bilirubin is less than 10 mg. per 100 ml.(Swift, 1950). An increase in conjugated (direct) pigment is early, even when the total bilirubin level is still normal (Sherlock, 1970).

The rate of decline from the peak level is more gradual, and often requires two to four weeks to return to the normal value. The raised levels reflect a disturbance of all the usual pathways of bilirubin excretion.

b) Serum glutamic-pyruvic transaminase (Alanine aminotransferase: S.G.P.T.:-

The alanine aminotransferase catalyzes the reaction:
Alanine + oc ketoglutarate $\xrightarrow{GPT}$ pyruvate + glutarate.

Although it is widely distributed in the body, its concentration in tissues other than the liver is low (Sherlock, 1970). The normal S.G.P.T. value is 2-15 I.U/L (Wootton , 1964) . It increases in most disorders that produce hepatic dysfunction (Pryse Davies, 1958; Wroblewski, 1959; Zimmerman, 1963; and De Ritis; et al., 1965), especially in acute cases being 10-100 times the normal, and it is among the first laboratory sensitive indicators of abnormalities detected in the preicteric phase of hepatitis (Krugman;et al., 1960), its raised value may precede the onset of symptoms by seven to ten days (Goldberg, 1962; and Le Bouvier; et al., 1972). Or it may coincide with the onset of symptoms (Boggs, 1970). The maximum increase occurs five days after the onset of the jaundice. The peak of enzyme activity and the peak of bilirubin concentrations are usually ten days apart, the former preceding the later. Return of enzyme activity to normal occurs within fourty to fifty days after the onset of symptoms. If the enzyme activity remains elevated and has not returned to normal after fifty days; the possibility of chronic course should be expected. Relapses are associated with secondary

rise of the enzyme activity (Wroblewski, 1957; Schoen, 1961; and Amelung, 1959).

The assay of enzyme levels can detect those individuals who are suffering from asymptomatic form of the disease.

c) Serum alkaline phosphatase :

In (1924, Martland), and his associates, were able to demonstrate the existence of this enzyme in human blood and serum. The alkaline phosphatase is widely distributed in human body, it is derived from four sources: liver, bone, intestine and in pregnant women's placenta, and there is no evidence that other tissues contribute.

Most of the normal serum alkaline phosphatase activity originates in the bones probably from the osteoblasts which actively secrete the enzyme and much smaller fraction may be of hepatic origin (Gutman, 1959).

The catabolism of alkaline phosphatase in serum has been studied by measuring the disappearance of infused, heat stable placental alkaline phosphatase in normal subjects and in patients with parenchymal liver

cell disease and bile duct obstruction. Placental alkaline phosphatase infused into all groups having half life in serum approximately seven days (Clubb, 1963). Using the king method, normal serum alkaline phosphatase level is 3-13 king-Armstrong units, The level is higher in infants and growing children than in adults varying from 10-20 K.A.U.

This higher concentration is due to the osteoblastic stimulation for bone formation, then subsides to the adult level rapidly. Using the method of king, (Dent; and Harper, 1962), found that there is clear sex difference; males having definitely higher levels than females.

The sex difference was thought to be an indication of the smaller skeletal mass in the female, but this possibility was rejected by (Dent;et al., 1962), because they did not find any relation between height and weight and the enzyme.

The highest serum elevations of alkaline phosphatase occurred in patients with obstructive jaundice which may reach 100 times greater than normal; and is associated with marked bilirubinemia. The obstruction