STUDY THE IMMUNOLOGIC DISORDERS IN LIVER DISEASE

THESIS SUBMITTED FOR PARTIAL FULFILMENT OF A MASTER DEGREE OF PEDIATRICS

BY

NADIA MOHAMED MAHMOUD

M.B.B.CH.

SUPERVISED BY

PROF. DR. SAWSAN EL SOKKARY
PROF - OF PEDIATRICS

DR. KARIMA ABED KHALIK
ASSIST. PROF. OF PEDIATRICS

AIN SHAMS UNIVERSITY
FACULTY OF MEDICINE

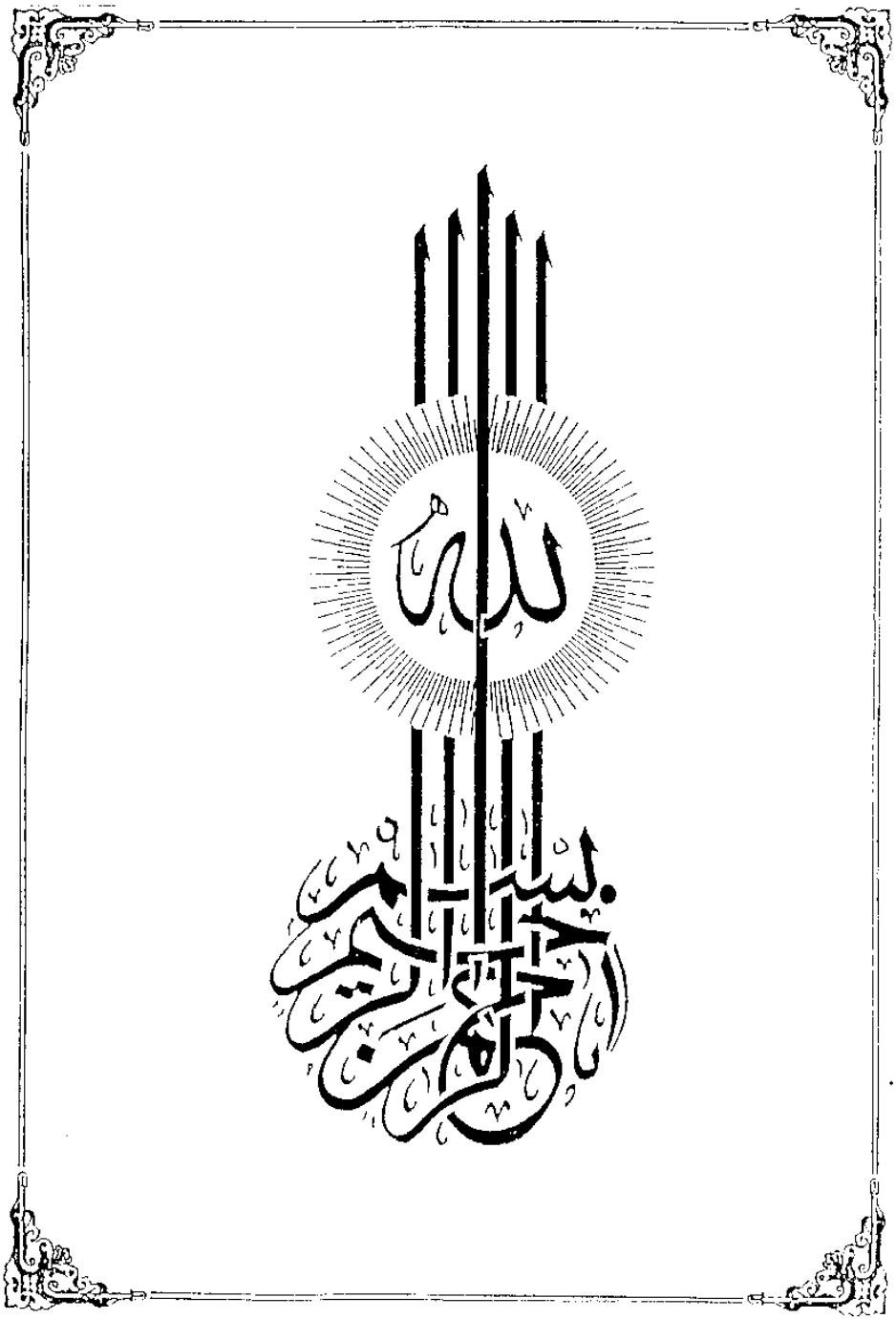
1984

ACKNOWLEDGEMENT

I am deeply indebted to all those without whose aid such a difficult undertaking would have been impossible.

I would like to express my sincere gratitude to prof. Sawsan El sokkary prof. of Paediatrics, Faculty of Medicine, Ain shams university for her guidance, attention and continuous encouragement throughout this study.

I am also greatly indebted to Dr. Kharima Abed El Khalik Assistant professor of paediatrics for her ready willingness to give advise, help and support on so many occasions while supervising this work.



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Abbreviation

AMA	:	anti-mitochondrial antibody.
ANA	:	Antinuclear antibody.
Anti-HA	:	anti-hepatitis A .
Anti-HBc	:	hepatitis B core antibody.
Anti-HB s	:	hepatitis B surface antibody.
CAH	:	chronic active hepatitis.
CF	:	Complement fixation.
CPH	:	Chronic persistent hepatitis.
H B I G	:	hepatitis B immune globulin.
IC	:	Immunecomplex.
LE	:	lupus erythematosus.
LSP	:	liver specific protien.
PBC	:	primary biliary cirrhosis.
SMA	:	Smooth muscle antibody.
SGOT	:	Serum glutamic oxaloacetic transaminase.
SGPT	:	Serum glutamic pyruvic transaminase.

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INTRODUCTION

Introduction

Immune-mediated liver diseases claimed medical attention just after 1950 with the recognition of the two major categories : Chronic active hepatitis (CAH) and primary biliary cirrhosis (PBC). Recongnition and definition of CAH were facilitated by (1) eletrophoresis which applied to serum, revealed the characteristic hypergammaglobulinemia; (2) liver biopsy which revealed active liver cell destruction accompanied by invasion of the liver by lymphoid cells, (3) measurement of transaminase anzymes in serum which reflected ongoing destruction of the liver, and (4) serological reactions which had high specificity for CAH contrast to various other types of chronic liver disease. When PBC was definitively described in 1951, there were associated autoimmune serological reactions. The introduction of immunoflourescence in the 1960s facilitated general appreciation of CAH and PBC as clinical entities by serum reactivity by immunoflucrescence with nuclei and smooth muscle in CAH, and with mitochondria in PBC.

Next in the investigation of CAH came the discovery of serum particle known as Australia antigen in association with the virus of hepatitis B (serum hepatitis). Certain proportion of patients with CAH were carriers of this particle which is known now as the hepatitis B surface antigen (HBsAg). Application of immunological tests provided evidence for the individuality of CAH

associated with markers of autoimmunity and of CAH with markers of infection with hepatitis B virus (HBV).

AIM OF ESSAY :

The aim of the present essay is to orientate the rapidly expanding mass of data and ideas of present day immunology to the points where they impringe of liver diseases.

REVIEW OF LITERATURE

Review of Literature

Hepatic Morphology

I - Embryology of the liver:

The liver arises from the entodermal lining of the foregut during the fourth week of gestation. The hepatic diverticulum is situated at the venteral side of the foregut, cranial to its opening into the yolk Sac.

The nepatic diverticulum is differentiating cranialy into proliferating hepatic cords and bile ducts, caudally into the gall bladder. The hepatic tubular cords sprout tridiminsionally (cranialy, venteraly, and lateraly), penetrating the septum transversum and passing between the two layers of splanchnic mesoderm. The latter envelop the sprouting lobules, provide their interstitial connective, tissue and form the liver capsule.

Strands of entodermal epithelium growing into the septum transversum enclose islets of proliferating mesenchymal cells that sacculate and are transformed into sinusoids. These groups of cells remain always in contact with the rest of the mesenchyma surrounding the liver analge. In a human embryo of 26 somites, irrigular masses can be observed developing in a frontal plane, Their strand like form might be to the early vascularization of the human septum transversum, between the vessels of which the hepatic cords penetrate. These enlarge at their bases later, fuse and arrange themselves into lamella and plates. Thus the human liver, initially a simple gland, changes into a "composite labyrinthin gland" (Braus,1924) .

Although the differenetiation of the liver analge is conditioned by the interrelation of both entodermal and

mesenchymal elements, the primary factor, remains the proliferation of the epithelium in tubular cords that communicate with the bile ductules(Bloom, 1925).

II- Anatomy of the liver:

The normal liver is the largest organ in the body. During the first year of life it constitutes approximately 5 percent of body weight. It is composed of 4 incompletely separated lobes, each containing structural units termed lobules. The upper border is at the level of 5th or 6the rib in the mammary line and extends nearly horizontally.

The lower border in the newborn is usually less than 2cm belw the costal margin in the right mid clavicular line.

(1) Blood supply

The liver has a double blood supply. The portal vein carries venous blood and its terminal branches discharge their blood into the sinusoids. The direction of flow is determined by the higher pressure in the portal vein than in the central vein. The hepatic artery carries arterial blood and empties into the sinusoidal network at different levels. There are no direct hepatic arteriolar portal venous anastmosis.

The hepatic sinusoids run in between the liver cells.

The central veins join to form the sublobular veins which join to form the hepatic veins. Generally one from the left lobe and two from the right lobe.

The blood supply to the liver is about 1000-1200ml/m^2, About 20% of which comes through the hepatic artery which provides about 30% of o_2 supply.

III- Histology of The liver:

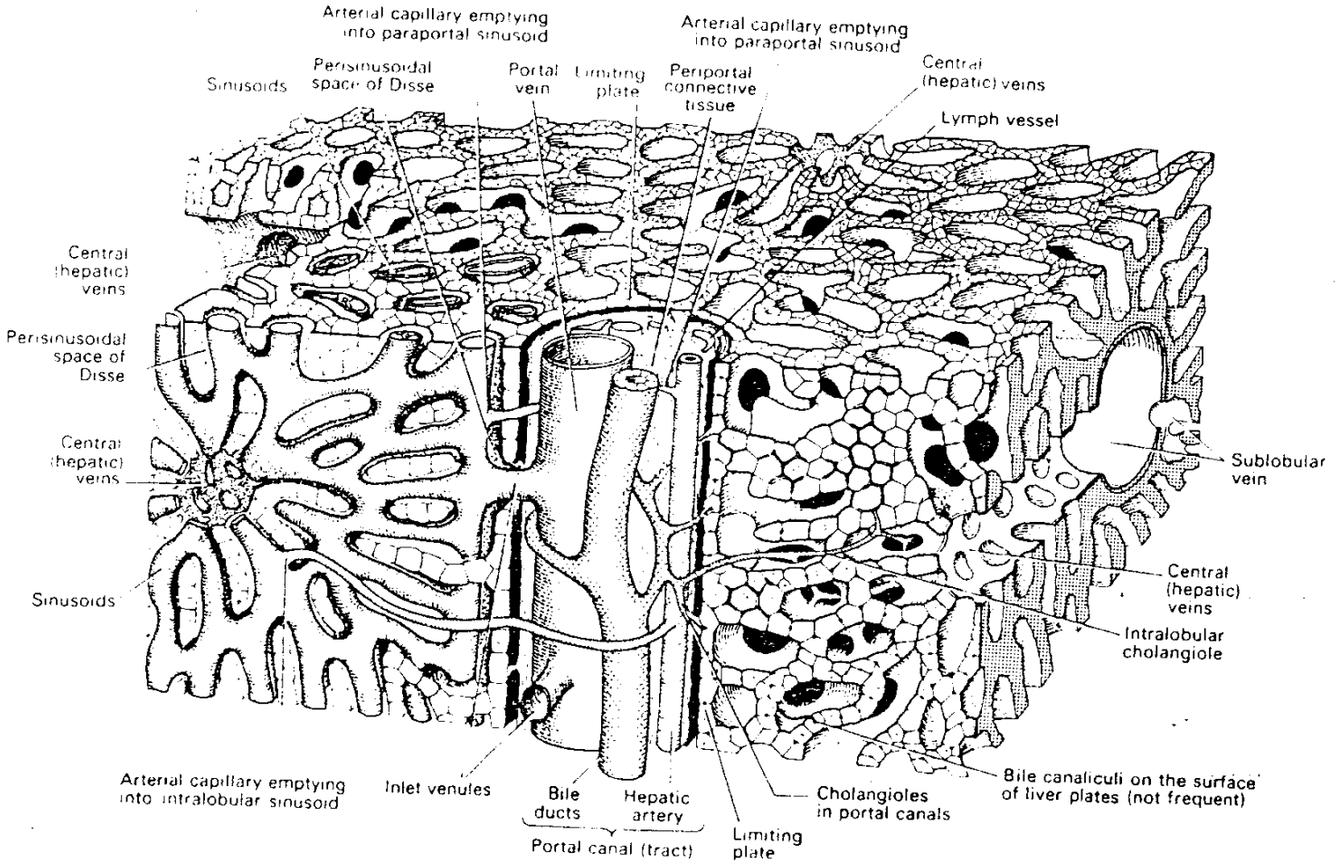
Hepatic lobules are the basic architecture of the liver. Kiernan (1833) described them as pyramidal lobules consisting of a central tributary of the hepatic vein and at the periphery a portal tract containing bile duct, portal vein and hepatic artery branch with a few round cells and a little connective tissue as shown in figure 1. Columns of liver cells and blood containing sinusoids extended between these two systems.

The liver has to be divided functionaly into functional acini, each centered on the portal tract and interdigitate mainly prependicularly with terminal hepatic veins of adjecent acini (Rappaport, 1963) as shown in figure 11. The acinus occupies adjacent sectors of neighbouring hexagonal feilds.

The circulatory peripheries of acini (adjacent to terminal hepatic veins) suffer mostly from injury whether viral, toxic or anoxic. Bridging necrosis is located mainly in this area. 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. The contribution of each acinar zone to liver cell regeneration depends on the acinar location of damage.

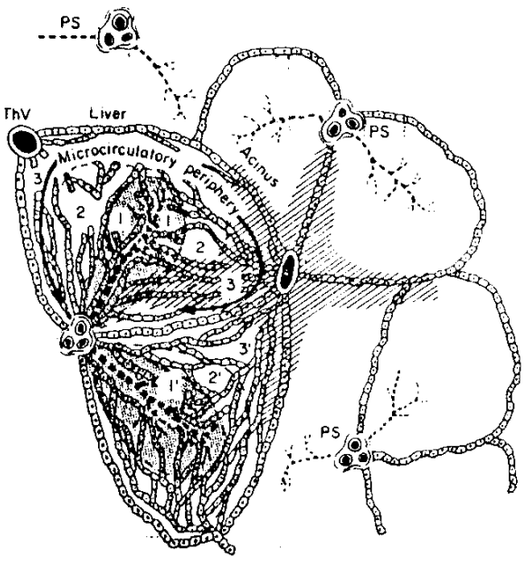
The liver cells (hepatocytes) comprise about 60% of the liver, its life span is about 150 days. The hepatocyte has three suface : one facing the sinusoid and space of Disse, the second facing the canaliculus and the third facing neighbouring hepatocytes. It has no basement membrane.

The walls of the sinusoids consist of endothelial and phagocytic cells of the reticulo-endothelial system. The flat cells are known as kupffer cells.



Hepatic lobules(Shella Sherlock,1981)

Figure I



Blood supply of the simple liver acinus, zonal arrangements of cells and the microcirculatory periphery. The acinus occupies adjacent sectors of neighbouring hexagonal fields. Zones 1, 2 and 3 respectively represent areas supplied with blood of first, second and third quality with regard to oxygen and nutrient contents. These zones centre about the terminal afferent vascular branches, bile ductules, lymph vessels and nerves (PS) and extend into the triangular portal field from which these branches crop out. Zone 3 is the microcirculatory periphery of the acinus since its cells are as remote from their own afferent vessels as from those of adjacent acini. The *perivenular* area is formed by the most peripheral portions of zone 3 of several adjacent acini. In injury progressing along this zone, the damaged area assumes the shape of a seastar (heavy cross-hatching around a ThV in the centre). 1, 2, 3 = microcirculatory zones; 1', 2', 3' = zones of neighbouring acinus; ---- afferent vessels of acini outlining the hexagons (Rappaport 1976).

Functional acini

Figure II