HEPATOTOXIC CHANGES OF VINYL CHLORIDE

THESIS

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BY

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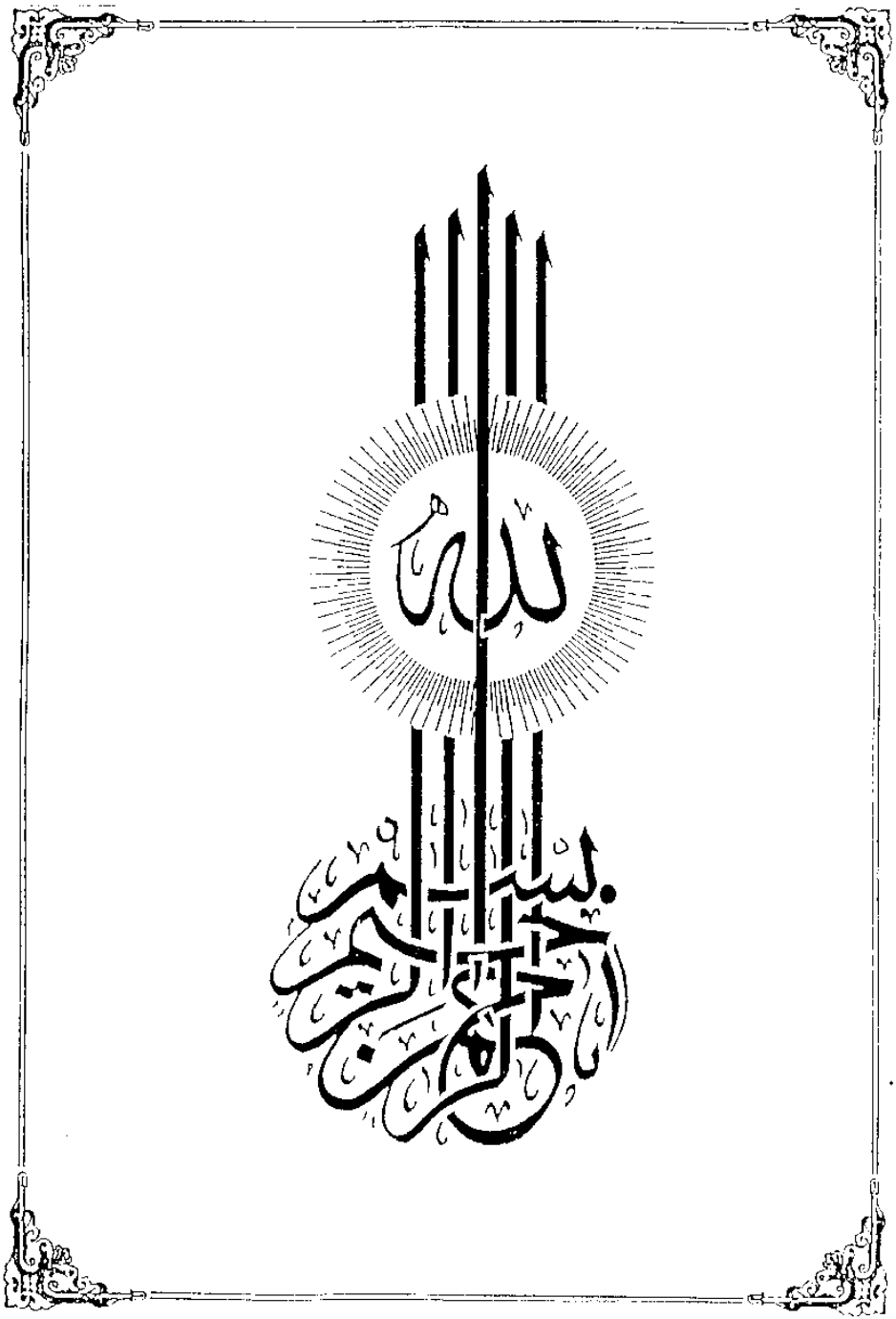

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C O N T E N T S

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I INTRODUCTION AND AIM OF THE WORK

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Workers exposed to vinyl chloride monomer over many years may develop hepatotoxicity. The earliest change is sclerosis of portal venules in the portal zones of the liver with the clinical changes of splenomegaly and portal hypertension. Later associations include angiosarcoma of the liver and peliosis hepatis. Early histological alternations indicative of vinyl chloride monomer exposure are focal hepatocellular hyperplasia and focal mixed (hepatocytes and sinusoidal cells) hyperplasia. This is followed by subcapsular portal and perisinusoidal fibrosis (Tamburro et al., 1984).

The aim of the work is to evaluate the importance of periodic abdominal ultra-sonography and liver function tests in detecting early changes in liver in workers exposed to vinyl chloride.

II REVIEW OF LITERATURE

Microscopic Morphology of the Liver

The hepatic parynchyma is subdivided into hepatic lobules, that are considered as the basic anatomic units of the liver. Kiernan (1833) described the basic architecture of the liver as being made of 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 and hepatic artery branch. Columns of liver cells and blood containing sinusoids extend between these two systems.

Rappaport (1963) accepted the hepatic lobule to be the basic anatomic unit, and considered the acinus as the basic functional unit of the liver. The acinus is composed of a portal tract and that mass of parynchyma dependent on the blood flow arriving through these vessels within the tract. The blood flows from the artery and portal vein of this terminal portal tract into the sinusoids, supplies the intervenning parynchyma and then drains into two or three peripheral efferent veins (the central vein of the lobule). Each efferent vein recieves blood from several

acini. The hepatocytes of the acinus are zoned or garded relative to the terminal portal tract. Those nearest the tract form zone 1 and those farthest away are called zone 3. This grading cannot be defined anatomically without injection studies.

It has been customary to consider the hepatic lobule as consisting of cords of liver cells radiating from a central vein, each cord consisting of two rows of liver cells with a bile capillary between them, and radiating venous sinusoids lying between adjacent cords in such a way that the bile capillary is separated from the sinusoids by the sinusoids by the thickness of a liver cell (Elias, 1969). However, recent studies indicate that liver cells really arranged as plates or sheets (hepatic laminae) mostly of one cell thick mass which form a continuous system throughout the liver, except at regions of branching or union (Arey, 1974).

The cell plates on standard microscopy appear as anastomosing Indian file cords of plygonal hepatocytes, which pass in radial manner from portal tract to central vein. Around the portal tract is a concentric but

discontinuous layer of heptocytes from which these cords arise. This layer forms the limiting plate of the lobule. Communications between portal vessels and the sinusoids by necessity breach the plate and so produce discontinuity (Schiff, 1963).

The Idian file arrangement of hepatocytes between portal tracts and central veins is only a two dimensional representation of the architecture. The constancy of this arrangement in histological sections, despite the plane of the liver in which they are examined, indicated a symmetrical meshwork of hepatocytes. This is formed by a fenestrated series of cell plates thatare both anastomosing and continually curving. In babies and small children, the cell plates are double, and the adult single cell plate pattern is acquired, usually by the age of five years. Over this age, twinning of cell plates is generally regarded as evidence of regeneration (Millward-Salder and Jezequel, 1979).

The hepatocytes are large cells 20-30 Mm, when isolated from a fresh piece of liver, they are more or

less rounded. After fixation, they acquire a polyhydral form, with a single or less often multiple nuclei with one or more prominent nucleoli (Elias, 1969).

A clear, homogeneous layer of ectoplasm comprises the periphery of the cell. The granular endoplasm contains cell organelles and stored substances. Many of the granules are glycogen droplets, specifically stainable. There are also protein granules, fat droplets salts and pigments. The hepatocyte has three surfaces, each of which bears microvilli. The first of these surfaces faces the sinusoid and the space of Disse, whereas the second faces a bile canaliculus, while the third surface facing the neighbouring hepatocyte (Sherlock, 1981).

The sinusoids are tortuous channels that are 9 to 12M wide. They recieve blood from vessels at the periphery of the lobule and discharge it into a central venule in the axis of the lobule. A sinusoid is lined by two types of cells,with tiny gaps in it. The first of these cells is a thin "endotheial cell" that lies close to the hepatic cells.

It has a dark, flattened nucleus and a thin film of cytoplasm. The other cell type, is a large one with a large, vesicular, bulging nucleus. It has an irregular shape and prominent cytoplasmic processes and is known as the stellate of Von Kupffer. Such cells overlie the microvilli that project from hepatic cells. A space and a network of reticular fibres, occur between lining and hepatic cells. There is no basement membrane underlying the sinuosidal lining (Arey, 1974). The space of Disse is the tissue space between hepatocytes and sinusoids (Sherlock, 1981). At the periphery of the lobule, the space of Disse is continous with another space designated the space of Mall around the vessels and bile ductules in the portal canals. In this space of Mall, lympho vessels of the liver commence by blind ends (Elias, 1969).

The bile canaliculus is a tubule coursing between the opposed faces of hepatic cells. At the periphery of a lobule the bile canaleucli open into tributaries of bile ducts. The smallest of -these are known as cholangioles or canals of Hearing, which are present at the periphery

of lobule and continue directly into branches of inter-lobular ducts which form a characteristic component of a portal canal. Its epithelial lining varies according to the size of the duct. They rang from low cuboidal to low columnar epith. The component cells are distinct and have a clear cytoplasm. The ducts are embaded in fibrous tissue; the larger ones become ensheethed (Arey, 1974).

The branches of the portal vein contained in the portal vein contained in the portal canals, are usually the largest blood containing, endothelial-lined spaces with the tract. They give off branches, called inlet venules, which pass through holes in the limiting plate surrounding the portal canal in order to enter the hepatic loubles, where they become continuous with the sinusoids. The latter conveys blood from the enterlobular branches of the portal vein (in the portal canal) central vein (Elias, 1969).

Branches of the hepatic artery are intimately related to the corresponding branches of the portal vein. The terminal interlobular arteries are small, they lack the

internal elastic lamina and have intima surrounded by a single layer of smooth muscle. They produce a leach of capillaries that encircles the accompanying bile duct and is termed the peribiliary plexus (Mitra, 1966). This is thought to regulate the concentration of bile excreted (Millward-Sadler and Jezequal, 1979). Drainage of the plexus is directly into the sinusoids (Nakata and Kanbe, 1966). Another leach of capillaries from the arteriole supplies other portal tract structures and drains either directly into the sinusoidal network or may join the terminal portal venule immediately before it enters this network. A smooth muscle sphincter has been described around these latter capillaries, so that the volume and pressure of arterial blood can be controlled (Rhodin, 1967).