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LIPOPROTEINS PATTERN IN CASES OF FATTY LIVER

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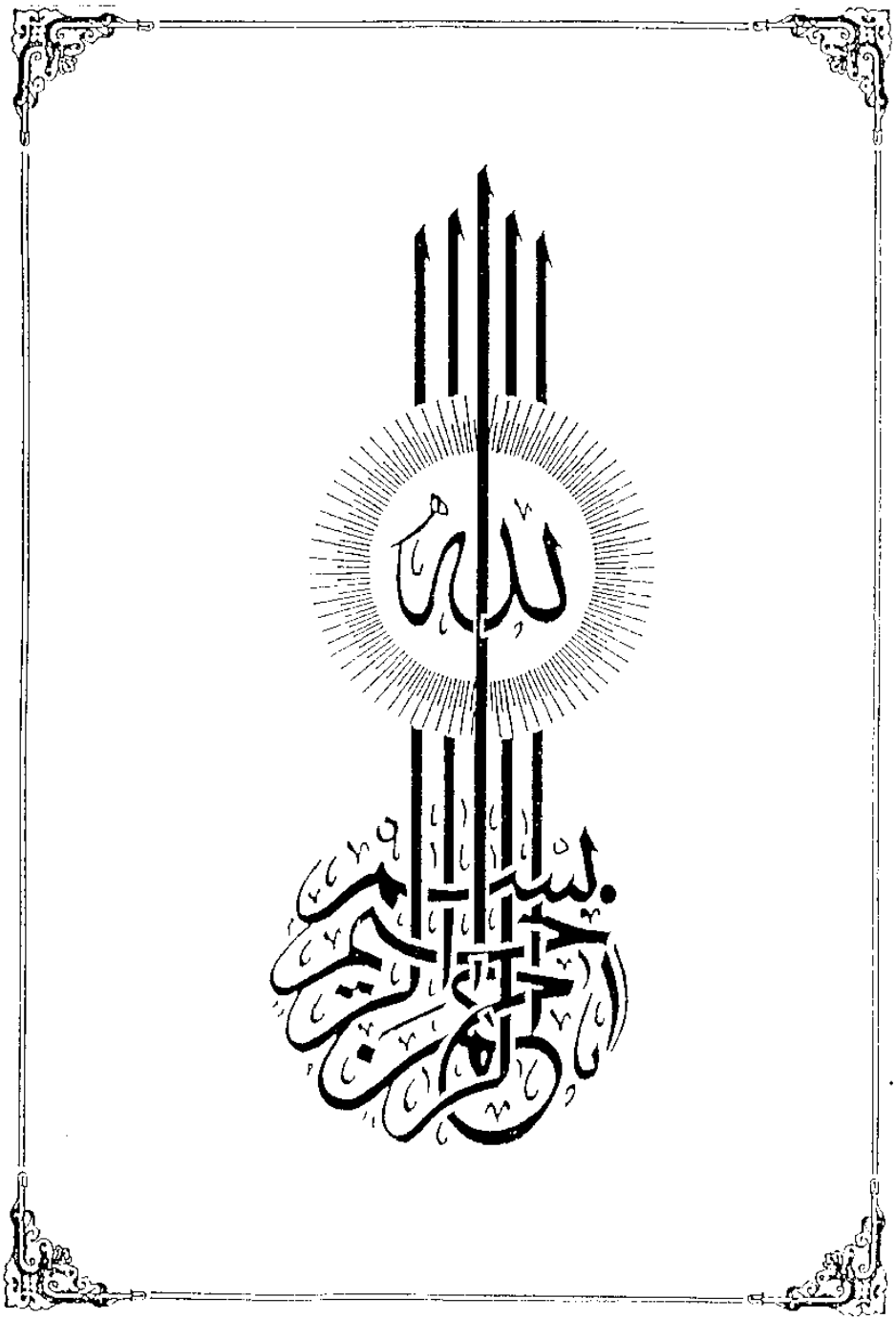

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(3)

FATTY LIVER

Definition

Fatty liver is defined as liver fat contents exceeding 5% of the liver weight (largely triglycerides). It is caused by failure of normal hepatic fat metabolism either due to defect within the hepatocyte or due to delivery of excess fat, fatty acids or carbohydrates beyond the capacity of the liver **(Sherlock, 1997)**.

Liver biopsy and imaging procedures such as ultra-sound and CT are resulting in increasing number of patients being identified with excess fat in the liver **(Sherlock, 1997)**.

Clinical Presentation

Fatty liver results from fat accumulation (triglycerides, fatty acids, phospholipids, cholesterol and cholesterol esters). When fat accumulates the lipid is stored primarily as triglycerides but may also be phospholipids. The clinical importance of fatty liver is highly variable *e.g.* steatosis during prednisone therapy may have minimal consequences but fatty liver of pregnancy may be life threatening. The liver serves as pivotal biochemical role in lipoprotein metabolism and neutral lipid clearance, specially free fatty acids, triglycerides, cholesterol and cholesterol esters. Disease states or medications may alter these biochemical processes resulting in clinical expression of

fatty liver, the spectrum of disease includes steatosis, steatohepatitis and cirrhosis **(Schiff, 1993)**.

Signs and Symptoms

Most patients with fatty liver have no symptoms and fatty liver is usually suggested by abnormal laboratory tests and ultrasonographic findings. The most common complaint of these patients is right upper quadrant fullness or discomfort **(Thaler, 1988)**.

Individual causes of fatty liver, however, characteristic of the underlying disease may be associated with systemic symptoms. These signs and symptoms are correlating to each disorder. Physical findings include palpable hepatomegaly in 90% of cases **(Schaffiner, 1986)**.

Differential Diagnosis

Numerous disease states are associated with fatty liver, the major subgroups of these various states are alcoholic and non alcoholic fatty liver disease as well as with a number of systemic diseases associated with fatty liver (Table 1) **(Schiff, 1993)**.

Pathogenesis

Sherlock (1997) stated that, theoretically fatty liver could occur through four mechanisms at least (Fig. 1):- 2

(1) Increased delivery of dietary fat to the liver as dietary fat is transported in the circulation mainly as chylomicrons.

(2) Increased mitochondrial synthesis of fatty acids or reduced oxidation, both of them augment triglycerides production.

(3) Impaired export of triglycerides out of the liver cell. Export of triglycerides from hepatocytes depends up on packing with apoproteins, phospholipids and cholesterol to form very low density lipoproteins. The out-pouring of hepatic VLDL into the plasma may prevent fatty liver.

(4) Excess carbohydrates delivered to the liver which may be converted to fatty acids.

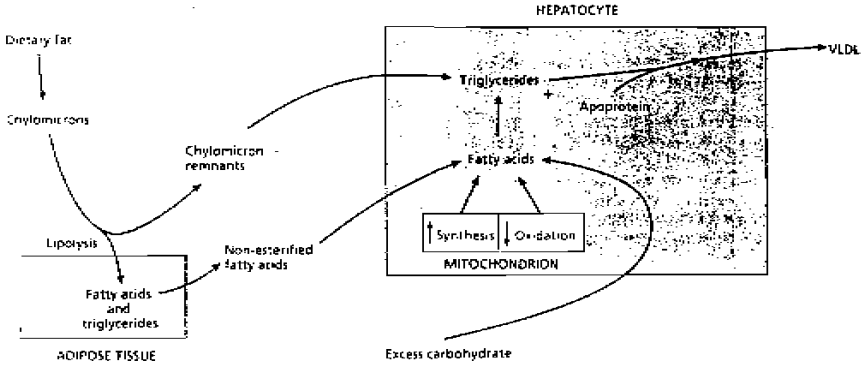

Fig. (1) Factors in fatty liver ***(Sherlock, 1997).***

Pathology

Macroscopic

Macroscopically the liver is usually large and may weigh up to 6000 grams the bulk of fat is triglycerides and may comprise up to one fourth of the liver net weight. A notable exception is found in acute fatty liver of pregnancy (AFLP), where the liver is frequently small, weighing from 800 to 1200 gm. On cut section, the fatty liver is yellow as a result of accumulation of carotenes and other lipochromes **(Rolfe and Ishak, 1985)**.

Microscopic

Microscopically a variety of pathological lesions can be seen, including: lipids, Mallory's bodies, cellular inflammatory infiltrates, fibrosis and cirrhosis.

A. Lipids

Hepatic lipids or steatosis is present primarily as small (microvesicular) (Fig. 2) or large (macrovesicular) droplets (Fig. 3). Although both patterns can coexist, the predominance of one over the other suggests a differential diagnostic list. The affected cells look foamy (microvesicular) or ballooned (macrovesicular) (Fig. 4) depending upon the size and number of fat droplets. Foamy degeneration (microvesicular) is an unusual pathologic finding described in alcoholic liver disease in patients with clinical features of alcoholic hepatitis, this was firstly described in 1983 by Uchida.

Fig. (2) Microvesicular fat. The hepatocyte has a foamy appearance. The nucleus is central with a dense nucleolus ***(Sherlock, 1997).***

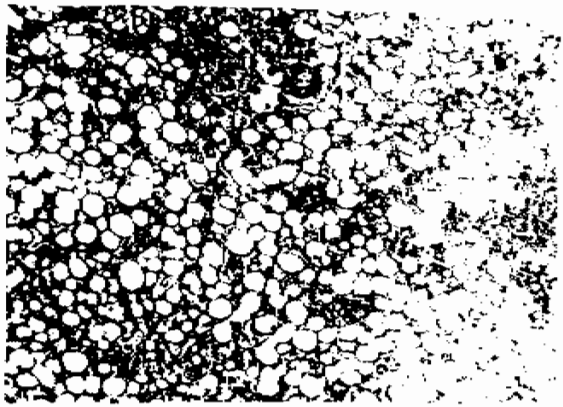

Fig. (3) Macrovesicular fat. The liver cells appear empty. The change is maximal in zone 1 ("portal"). Stained B & F x 135 ***(Sherlock, 1997).***

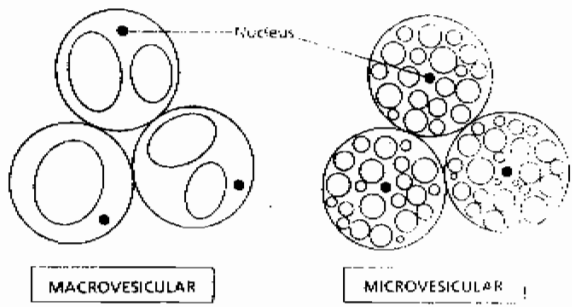

Fig. (4) Fatty liver may be classified into macrovesicular (large droplet) and microvesicular (small droplet) types ***(Sherlock, 1997).***

In 4% of subjects who had alcoholic associated hepatic failure the lesion was characterized as occurring in first episode of hepatic decompensation. The biopsy specimens showed swelling of perivenular hepatocytes, with micro vesicular steatosis producing foamy appearance **(Uchida, 1983)**.

In addition to fatty hepatocytes, there may be an accumulation of lipid and lipofuscin containing macrophages in fatty liver. These macrophages may be included in lipogranules along with lymphocytes and eosinophils **(Christofferson, 1971)**. When the severe fatty accumulation subsides, the lipid droplets in the macrophages diminish, and the lipogranules may be difficult to be distinguished from other granules. Usually, however, the fat in the peripheral granules persists along after the hepatocellular steatosis and may raise the suspicion of preceding steatosis **(Christofferson, 1971)**.

B. Mallory's Hyaline

Mallory's hyaline (is also called Mallory's bodies) is most commonly seen in alcoholic liver disease but it is not specific for that condition, with or without fat. By light microscopy the bodies are eosinophilic, coarsely granular, usually perinuclear and always intracellular. The loss of Mallory's bodies typically takes 6 to 12 weeks if the precipitating substance (*e.g.* alcohol) is removed **(Schaffiner, 1986)**.