Histopathology of Wilson Disease

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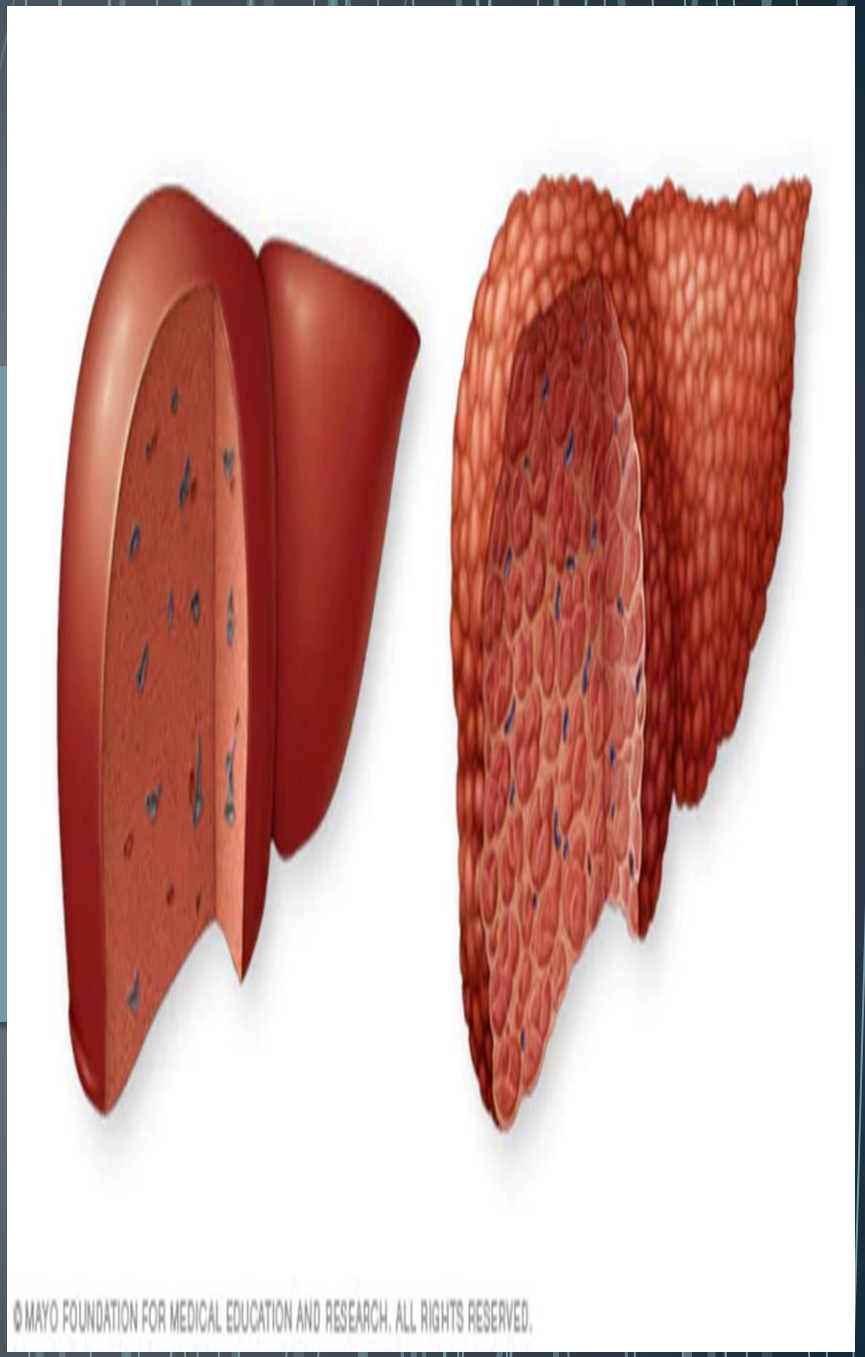
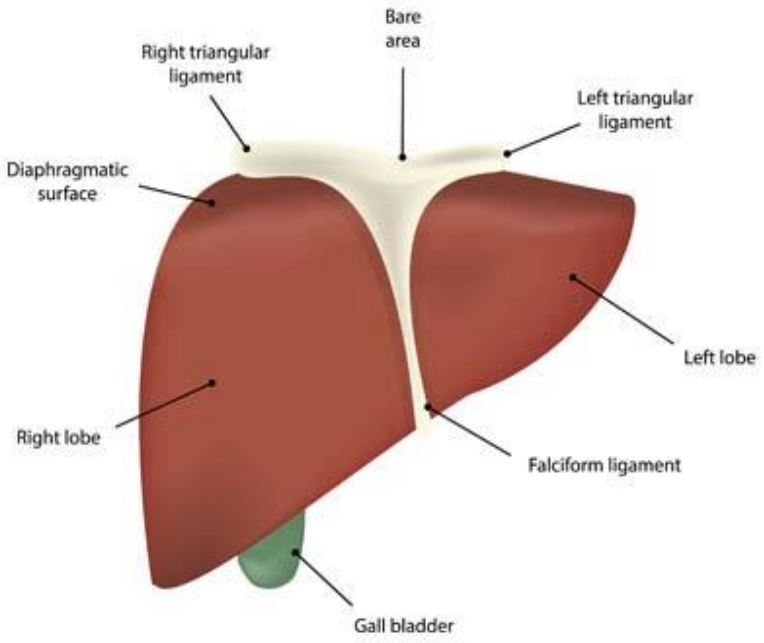


Originally Wilsons Disease (WD) was described as a neurodegenerative disease associated with cirrhosis of the liver. all related to abnormal copper metabolism ending with systemic accumulation of the copper. Figure 1& 2

- Liver biopsy is typically performed when clinical and laboratory findings are not diagnostic or for evaluation of unexplained liver disease or abnormal liver tests. Another aim is to determine the degree of hepatic inflammation and for hepatic copper quantitation [1].
- Figure 2 show Red –brown cytoplasmic granules are copper deposits in the liver from a patients with Wilsons disease

Wilsons Disease

Healthy Liver



Wilsons Disease

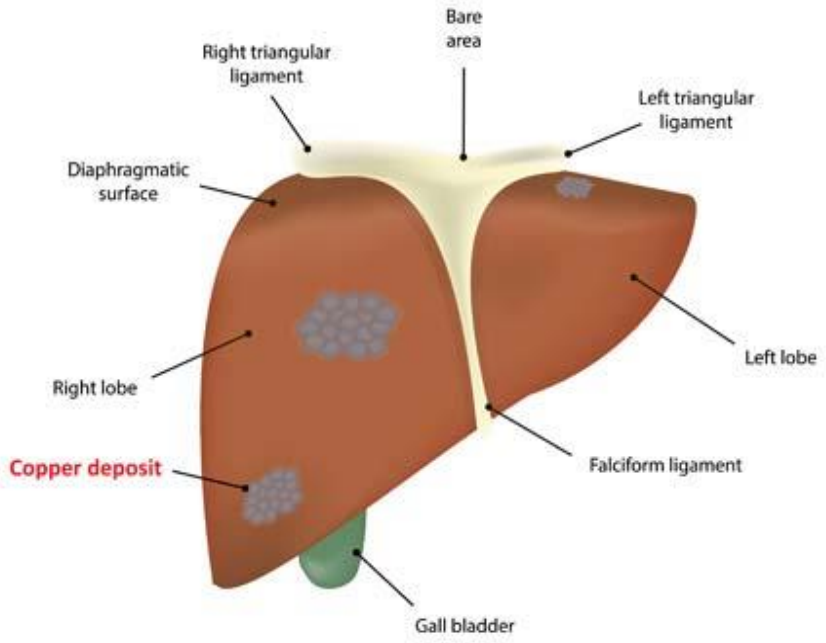
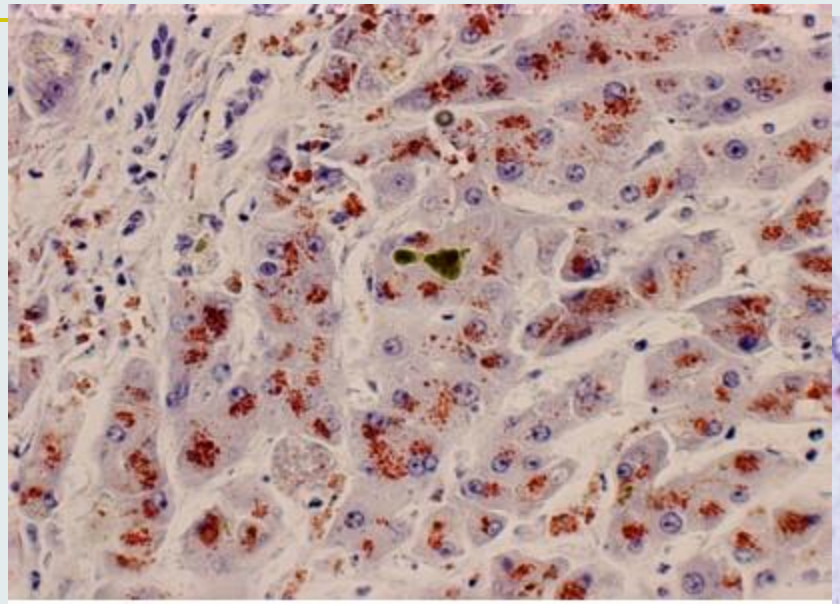
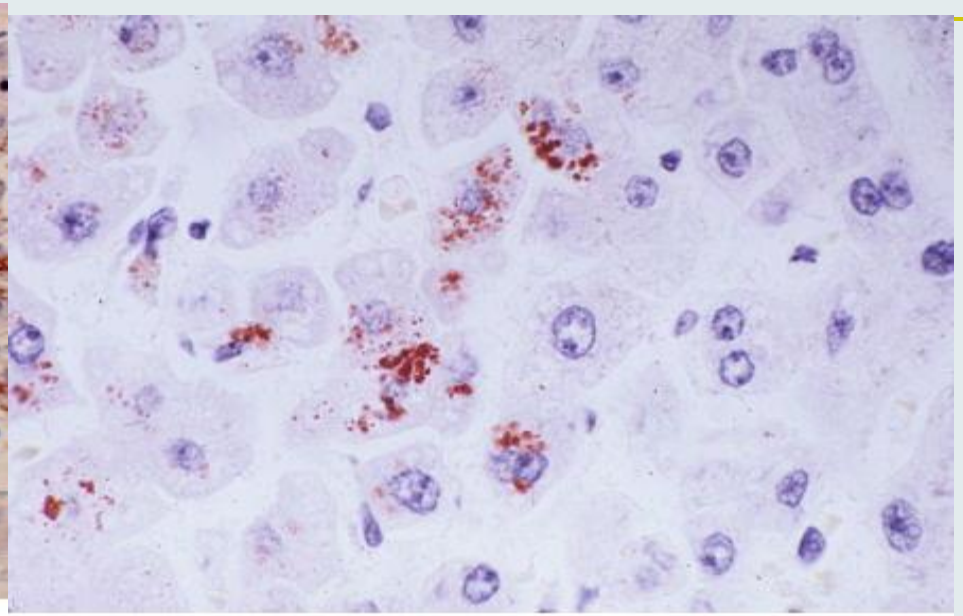
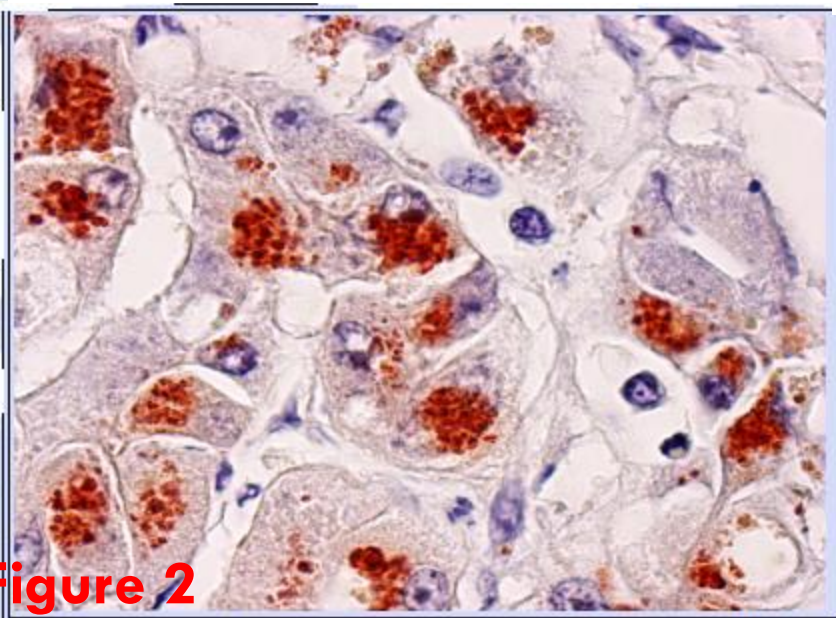


Figure 1







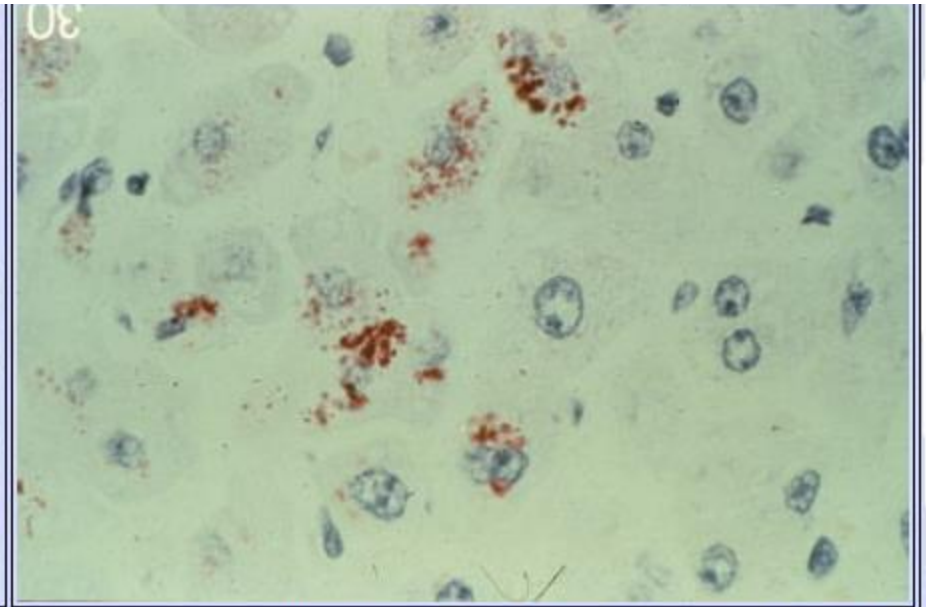
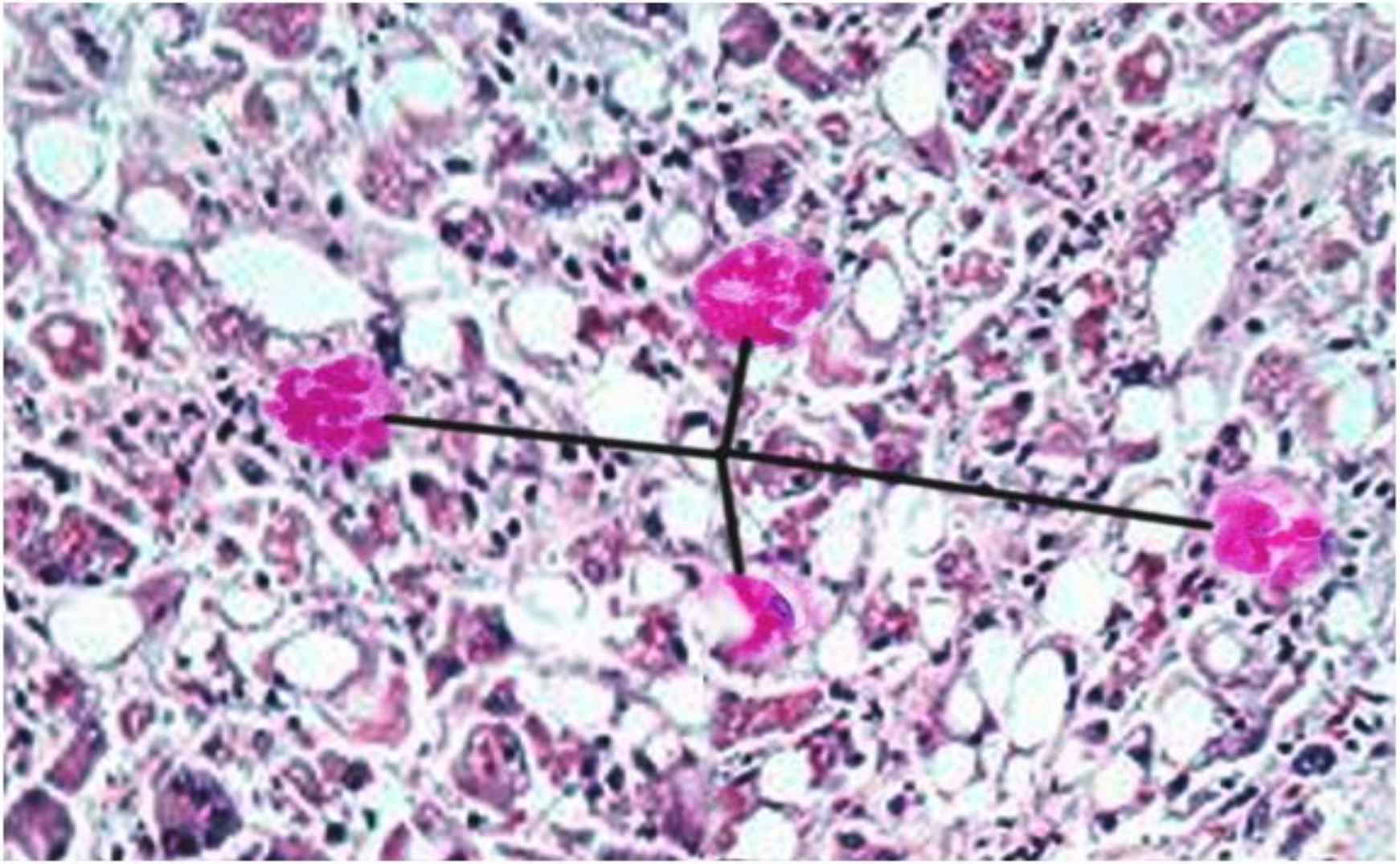


Figure 2

Red-brown cytoplasmic granules are copper deposits in the this liver from a patient with Wilsons disease [top left]. Note the bile (plug) remains green (left panel). Courtesy of Dr. Zhenhong Qu)

- The manifestations of liver involvement :

- Steatosis, Mallory bodies also known as Mallory-Denk bodies (MDB), are cytoplasmic hyaline inclusions of hepatocytes filamentous ranging from a diameter of 3 to 24 nm ,Figure 3 , lipogranulomas and glycogenated nuclei have been represented as characteristic morphologic findings in liver biopsies with WD. [2].
- The distinction from nonalcoholic steatohepatitis (NASH) depends upon the demonstration of accumulated copper in the hepatocytes by histochemical stains.



Mallory bodies. Image courtesy Dr Chaigasame

Figure 3

The distribution of copper is quite variable, with some of the cirrhotic nodules containing a lot and others containing little or none.

Defining widespread copper deposits by histochemistry can help for the diagnosis. It should be noted that the distribution of copper is variable: some nodules with prominent staining, others with minimal or none[3] (Figure 4).

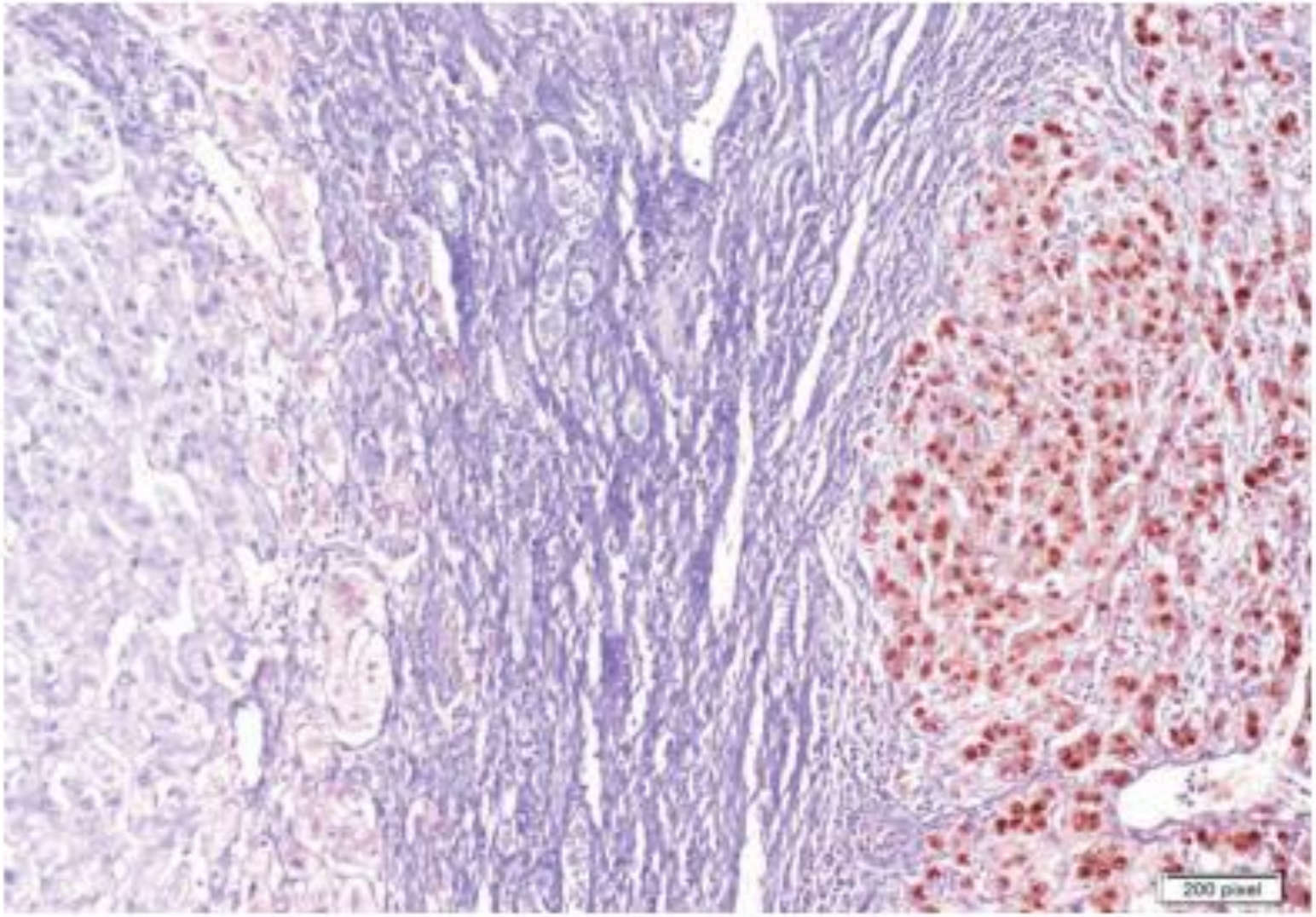


Figure 4

Heterogenous copper accumulation in a hepatectomy specimen (Rhodanine).

hepatic pathological changes occurring in WD

- **The spectrum of hepatic pathological changes occurring in WD is very broad, ranging from elementary changes typical of a toxic pathology, to inflammatory changes typical of viral or autoimmune etiology [4]. The main features are microvesicular and macrovesicular steatosis, inflammation, and variable hepatocellular anisonucleosis Figure 5 [5, 6].**
- Ultrastructural findings of WD have also been studied. The mitochondrial changes are the most distinctive and pathogenetically significant and include heterogeneity of size and shape, increased matrix density, separation of inner from outer membranes, enlarged intercristal spaces and various types of inclusions. [7, 8].

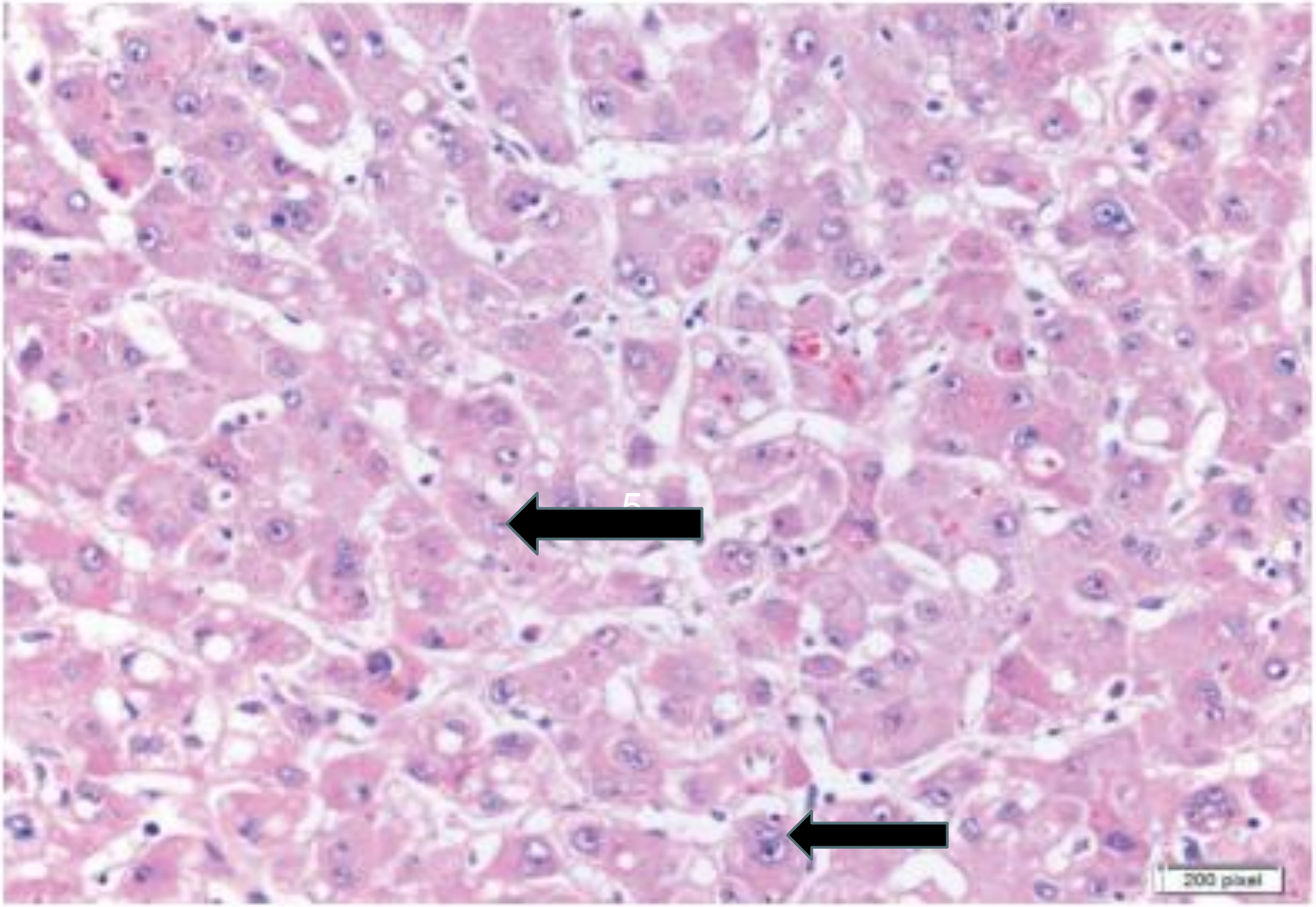


Figure 5
Steatosis and anisonucleosis in a hepatectomy specimen (H&E).

hepatic pathological changes occurring in WD

Steatosis

Definition: Conditions characterized by abnormal storage of fat due to a mismatch between the supply of and demand for fat.

Causes of Steatosis (Fatty Liver)

2 major causes of steatosis

Alcohol is a hepatotoxin that leads to **increased synthesis and reduced breakdown of lipids.**

Nonalcoholic fatty liver disease is associated with **diabetes and obesity.**

this is becoming more common, though the mechanism remains unknown. It also leads to cirrhosis and liver failure

dry cleaning

less common

CCl_4 and **protein malnutrition** cause **reduced synthesis of apoproteins.**

apoproteins are required for lipid metabolisms

Hypoxia inhibits fatty acid oxidation.

important in fatty deposition in myocardium too

Starvation increases mobilization of fatty acids from peripheral stores.

usually seen in patients with other underlying illness, such as cancer

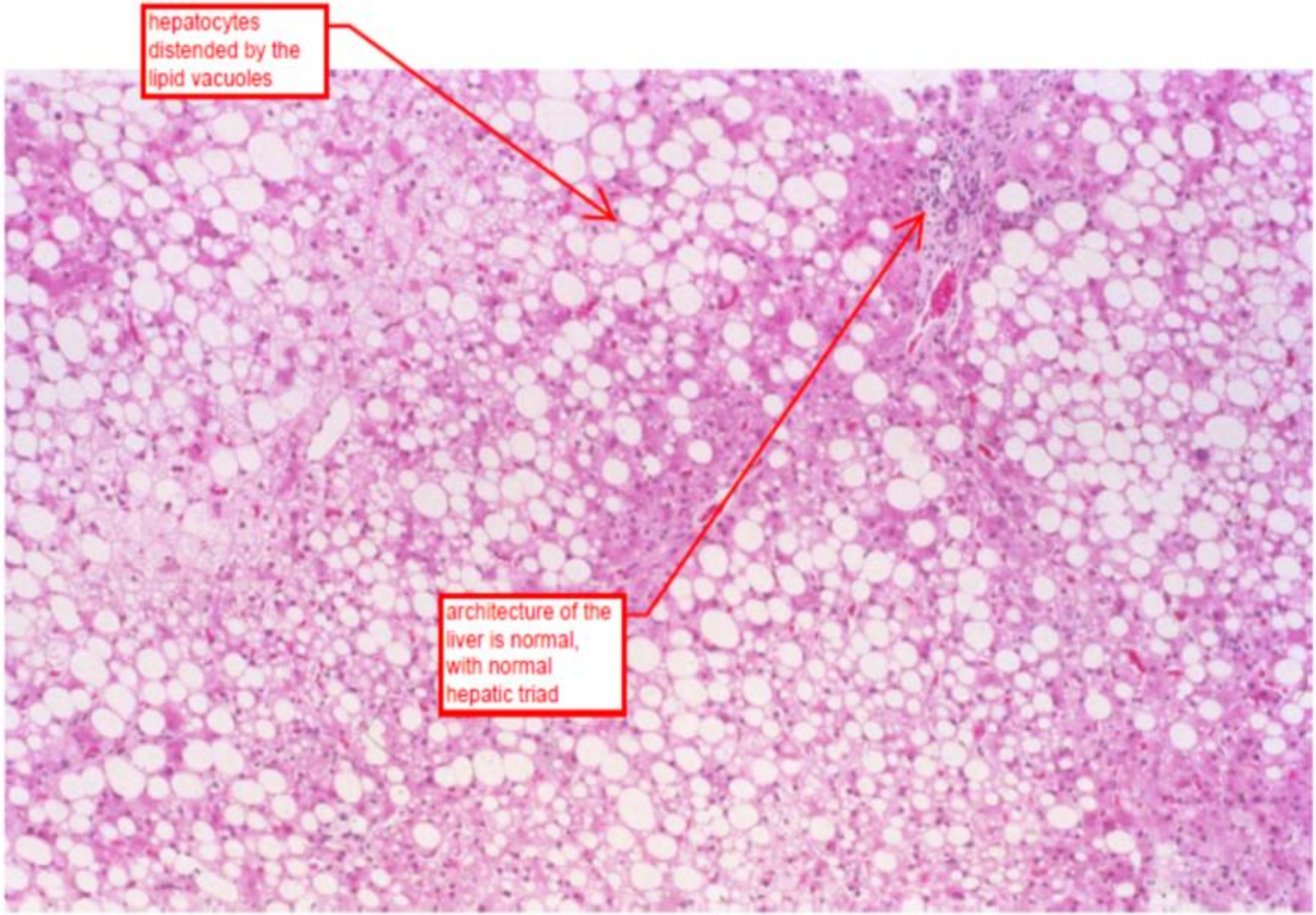


Figure 6 **Liver (Hepatic steatosis) hepatocyte distended by the lipid vacuoles**

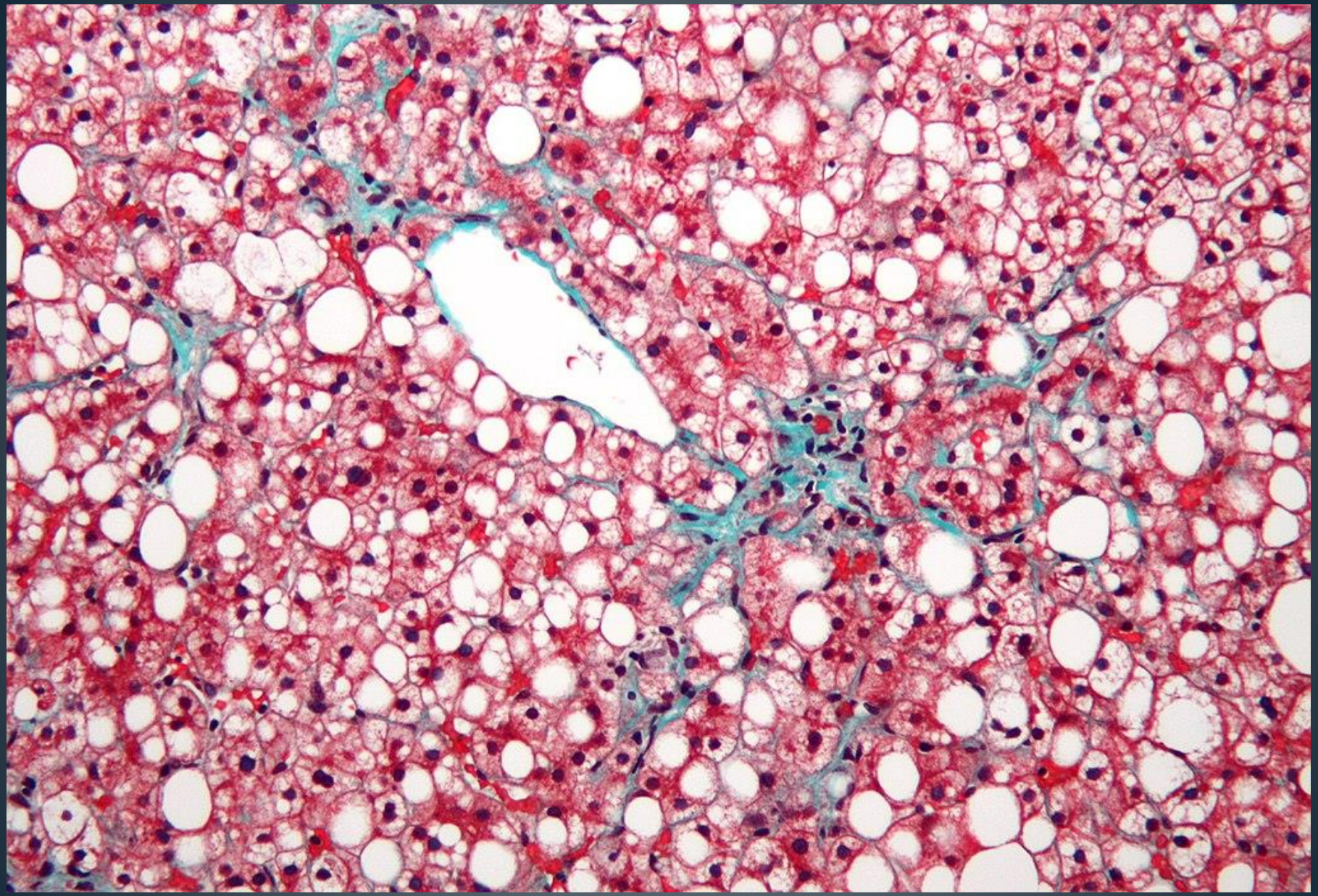


Figure 7 Liver cirrhosis

❖Absorptive Steatosis

Etiologic factors:

— Removal of necrotic tissue: chronic abscess with leukocyte destruction, and fatty tissue necrosis induce histiocytes to phagocytize fats, transforming these cells to foam cells . Figure 8

— Hypercholesteremia) leads to increased phagocytosis of lipids or cholesterol and storage of these substances in vacuoles.

❖Foam cells are a type of macrophage that localize to fatty deposits on blood vessel walls, where they ingest low-density lipoproteins and become laden with lipids, foam cells cause atherosclerosis

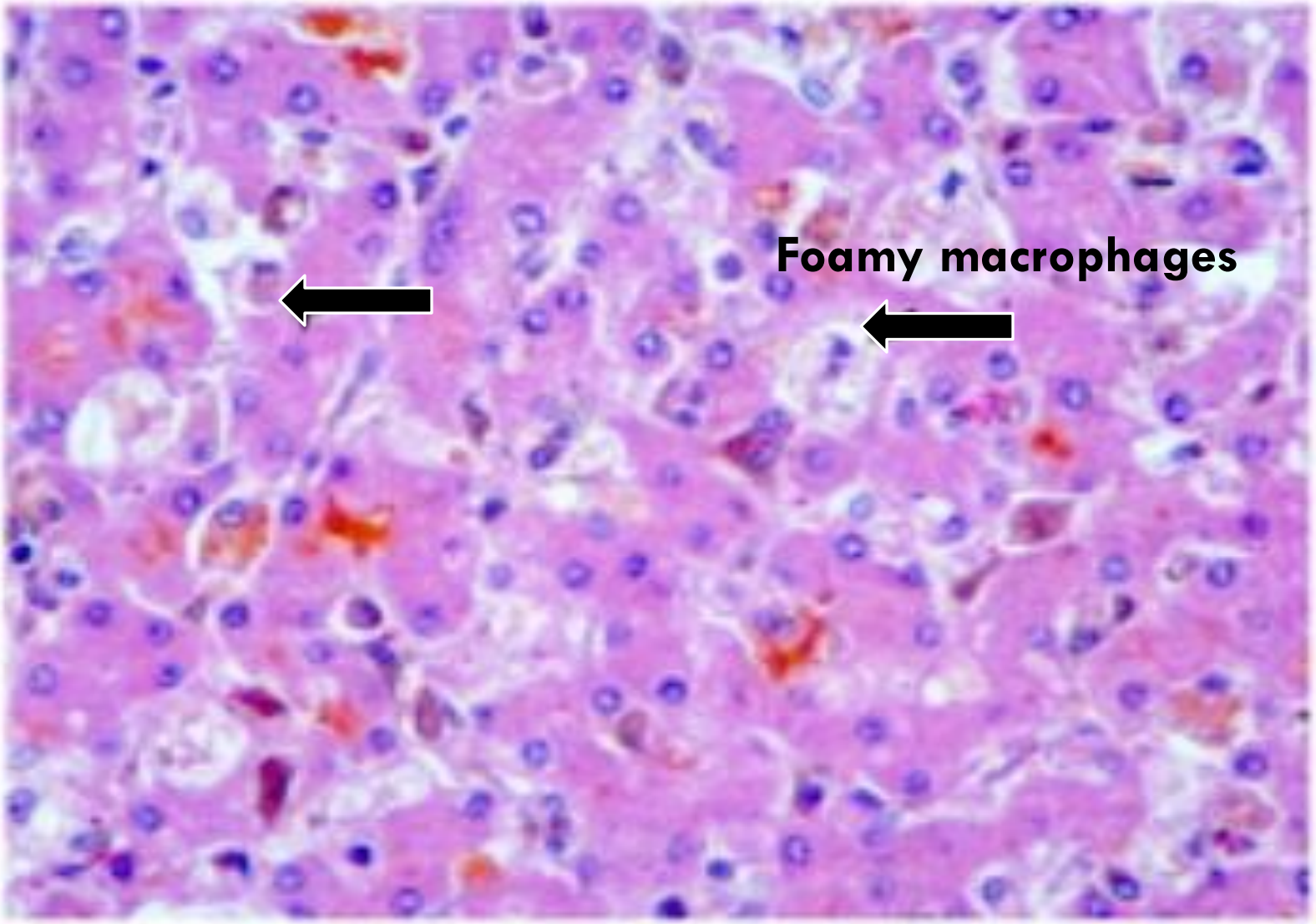


Figure 8 Liver (Hepatic steatosis)

❖ **Dietary Steatosis**

Increased intestinal uptake of fats and carbohydrates overloads the fat transport and catabolism system, resulting in deposit of large droplets of fat in the epithelia of the central portions of the hepatic lobes or the renal tubules

❖ **Retention Steatosis**

Etiologic factors:

— Hypoxia inhibit oxidation of fatty acids. This in turn causes

(a)fatty degeneration in the central portions of the hepatic lobes,

(b)(b) nodular fatty degeneration of the myocardium (

— Enzyme deficiency: Lack of fat-metabolizing enzymes (carnitine deficiency).

— Intoxication: Cell damage (such as from alcohol)

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Thank you