Lecture 10:

Pathology of Liver Cirrhosis

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Objectives

- Define Cirrhosis.
- Recognize the types of cirrhosis.
- Recognize the major causes and the pathological mechanisms leading to cirrhosis.
- Describe the pathological findings in cirrhotic livers

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Liver Cirrhosis by Armando Hasudungan

Cirrhosis

Definition: the end-stage of chronic liver disease

Classification of cirrhosis: based on the etiology:

- Alcoholic liver disease "Most common cause"	60% to 70%
- Chronic Viral hepatitis	10%
- Biliary diseases "like obstruction by gall stones"	5% to 10%
- Primary hemochromatosis "accumulation of iron"	5%
- Wilson disease "accumulation of copper"	Rare
- α1-Antitrypsin deficiency	Rare
- Cryptogenic cirrhosis "cryptogenic means idiopathic"	10% to 15%

- galactosemia and tyrosinosis "in infants and children"
- drug-induced cirrhosis.
- Cardiac cirrhosis " cardiac disease cause stasis in the blood for long time will cause stimulation of Fibroblast"

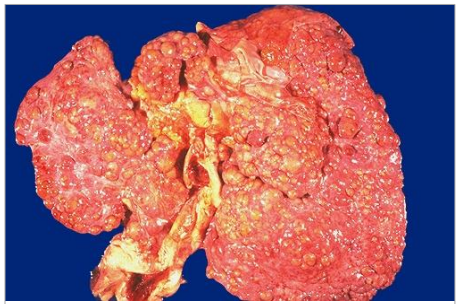
Fate of liver cirrhosis: irreversible

Treatment: Liver transplantation

Features of cirrhosis

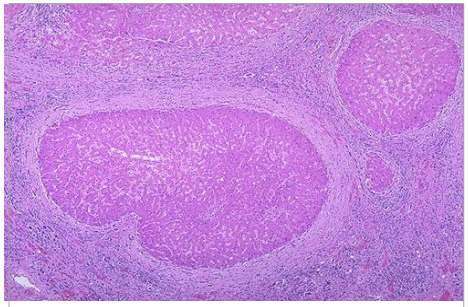
Cirrhosis is defined by three characteristics:

1) Diffused Fibrosis (key feature) in the form of delicate bands or broad scars/septa
2) Nodules containing regenerating hepatocytes encircled by fibrosis
3) Disruption of the vascular architecture* of the entire liver



Macronodular cirrhosis: The nodules seen here are larger than 3 mm.

Micronodular cirrhosis: The nodules are quite small, averaging less than 3 mm in size. Usually in Chronic alcoholism.



Regenerative nodules of hepatocytes are surrounded by fibrous connective tissue that bridges between portal tracts.

* (the parenchymal damage and scarring, with the formation of abnormal interconnections between vascular inflow and hepatic vein outflow channels).

Pathogenesis of cirrhosis

First we have to know that normally liver contains:

- I and III collagens are concentrated in portal tracts and around central vein
-IV collagen (reticulin) is in the space of Disse*.

Then due to damage of liver that will lead to stimulation of collagen synthesis by:

1- the perisinusoidal stellate cells * (Ito cells) activate and become myofibroblast-like cells. "major cause"

2- Cytokine production by activated endogenous cells (Kupffer cells, endothelial cells, hepatocytes, and bile duct epithelial cells).

3- Disruption of the normal extracellular matrix.

Finally loss of fenestrations in the sinusoidal endothelial cells (capillarization of sinusoids, that is the sinusoidal space comes to resemble a capillary rather than a channel for exchange of solutes between hepatocytes and plasma).

* The space separating sinusoids from hepatocytes.

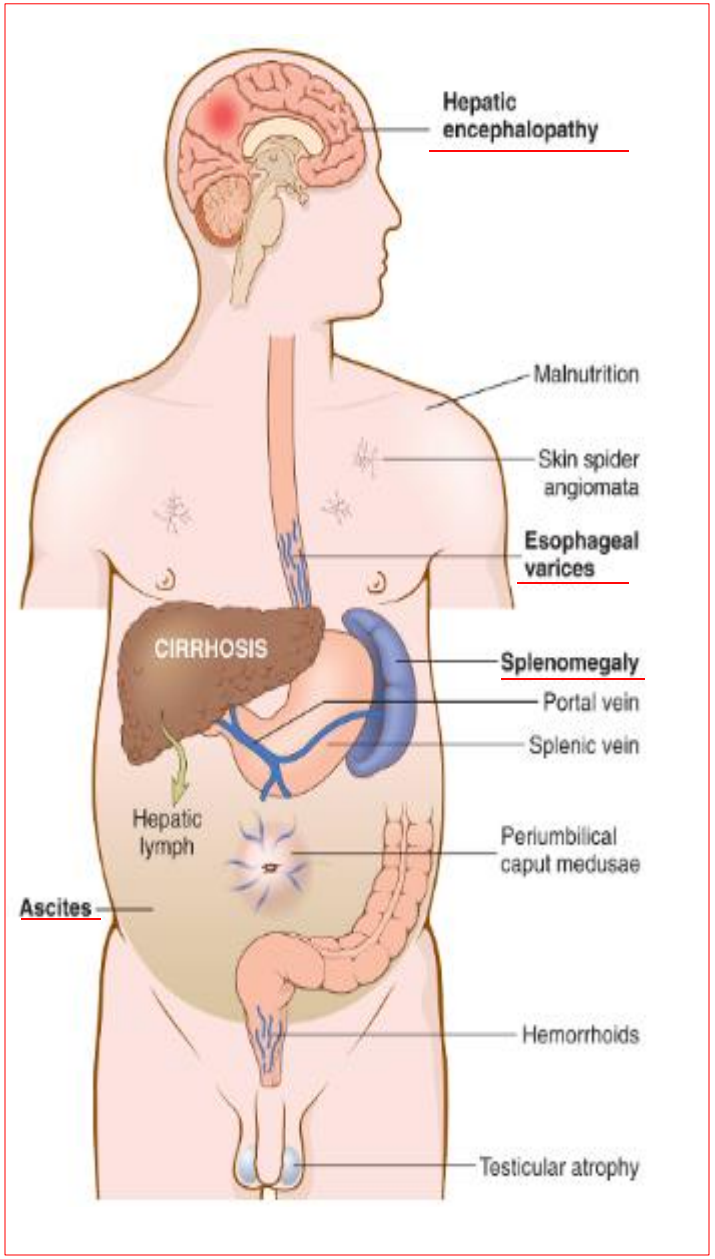
* Stellate cells lie in the space of Disse. Although normally functioning as vitamin A fat-storing cells.

Clinical features of cirrhosis

- All forms of cirrhosis may be clinically silent.
- nonspecific clinical manifestations: anorexia, weight loss, osteoporosis, and in advanced disease, frank debilitation "general weakness".
- Jaundice.

* The ultimate mechanism of most cirrhotic deaths is:

1. progressive liver failure ,
2. complication related to portal hypertension "most common"
3. development of hepatocellular carcinoma "rare"



Chronic Hepatitis

Staging and grading help to know the prognosis and severity of the disease:

- Portal tract Inflammation (grading):

Grade I: in portal tracts

Grade II: in parenchyma, with necrosis of hepatocytes ("interface hepatitis")

- Fibrosis (staging):

Continued loss of hepatocytes results in fibrous septa formation which ultimately leads to cirrhosis

Stage I: Begin at portal tracts

Stage II: Bridging between portal tracts only

Stage III: Bridging between portal tracts and central vein

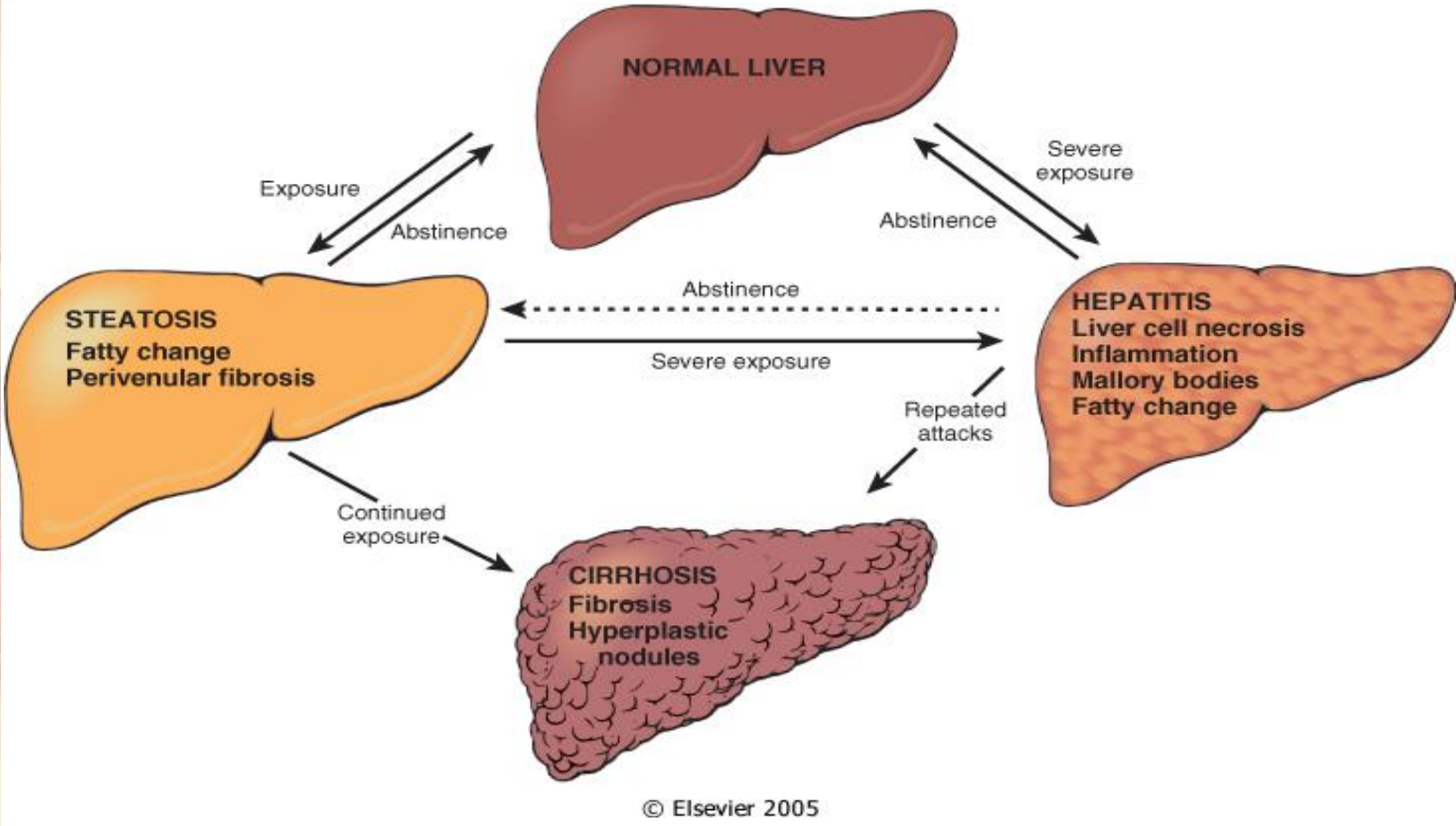
Stage IV: Nodules formation

In Hepatitis B: "ground-glass" hepatocytes, "sanded" nuclei

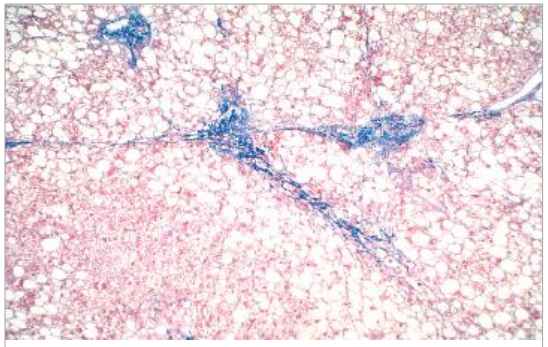
In Hepatitis C: bile duct damage, lymphoid aggregate formation

Alcoholic liver disease

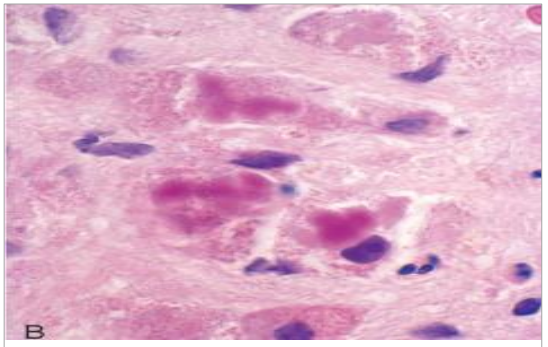
- Exposure of alcohol may leads to steatosis first then with Continues exposure of alcohol may end-up with cirrhosis.
- Severe exposure of alcohol may leads to hepatitis first then with repeated attacks of hepatitis it will cause liver cirrhosis



Morphology



Macrovesicular steatosis. The intracytoplasmic fat is seen as clear vacuoles (classical feature of alcoholism)



Eosinophilic Mallory bodies are seen in hepatocytes

Note: collagen can be seen as blue-stained under microscope by (Masson trichrome stain)

Summary from Robbins

SUMMARY

Cirrhosis

- The three main characteristics of cirrhosis are (1) involvement of most or all of the liver, (2) bridging fibrous septa, and (3) parenchymal nodules containing a mix of senescent and replicating (often stem/progenitor cell-derived) hepatocytes.
- Cirrhosis usually is an end-stage process that may have multiple causes. The most frequent are chronic hepatitis B and C and alcoholic and nonalcoholic steatohepatitis. Less frequent causes are autoimmune and biliary diseases and metabolic conditions such as hemochromatosis.
- The main complications of cirrhosis are related to decreased liver function, portal hypertension, and increased risk for development of hepatocellular carcinoma.