General features Of Hepatic Disease

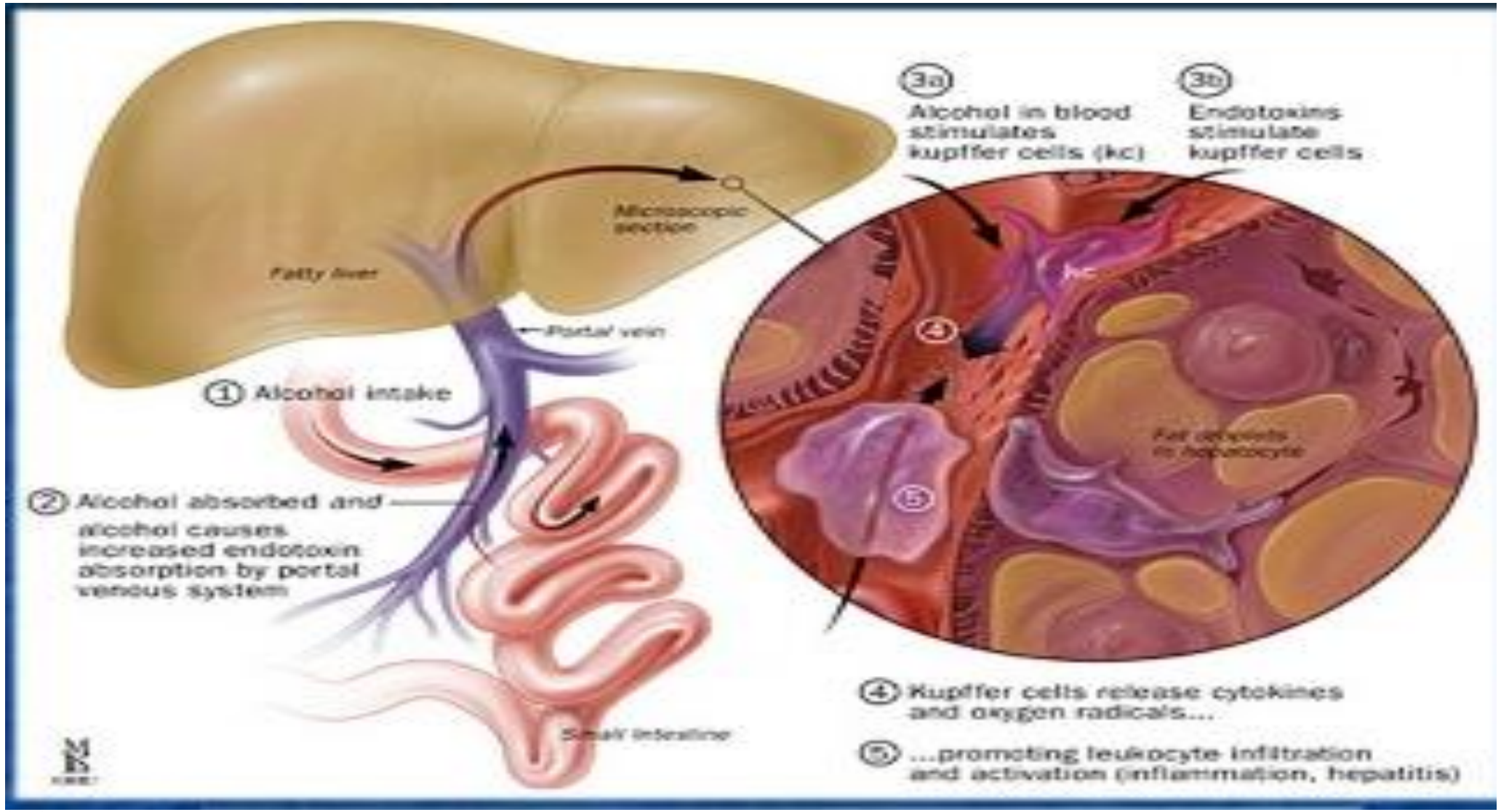
- The liver is vulnerable to a variety of metabolic, toxic, microbial, circulatory, and neoplastic insults.

- The major primary disease of the liver are viral hepatitis, alcoholic liver disease, nonalcoholic fatty acid disease (NAFLD), and hepatocellular carcinoma (HCC).

- Hepatic damage also occurs secondary to some of the most common diseases in human, such as cardiac decompensation, disseminated cancer, and extrahepatic infection, that may become life threatening.

- liver disease is an insidious process in which clinical detection and symptoms of hepatic decompensation may occur weeks, months and even years after the onset of injury.

- The ebb and flow of hepatic injury may be imperceptible to the patient and detectable only by abnormal laboratory tests, and liver injury and healing may also with out clinical detection.


3a
Alcohol in blood stimulates kupffer cells (kc)
3b
Endotoxins stimulate kupffer cells
Microscopic section
Fatty liver
Portal vein
1 Alcohol intake
2 Alcohol absorbed and alcohol causes increased endotoxin absorption by portal venous system
Small intestine
4 Kupffer cells release cytokines and oxygen radicals...
5 ...promoting leukocyte infiltration and activation (inflammation, hepatitis)

Patterns of hepatic injury

The liver has a relatively limited range of cellular and tissue responses to injury, regardless of cause.

The most common are:

- Hepatocyte degeneration and intracellular accumulation
- Hepatocyte necrosis and apoptosis
- Inflammation
- Regeneration
- Fibrosis

- Clinically, a few common syndrome occur that are a consequence of many different diseases such as
- **hepatic failure**,
- **cirrhosis**,
- **portal hypertension**
- **jaundice** (disturbance of bilirubin metabolism causing)
- **Cholestasis**.

Hepatic Failure

- It may be result of sudden and massive hepatic destruction and represents the end stage of progressive chronic damage to the liver.
- End stage liver disease may occur by insidious destruction of hepatocytes or by repetitive discrete waves of parenchymal damage.
- In case of severe hepatic dysfunction, hepatic failure is often triggered by intercurrent diseases.
- When the liver can no longer maintain homeostasis, transplantation offers the best way of survival; In case of hepatic failure, mortality is about 80% without liver transplantations

The alteration that cause liver failure fall into three categories:

- Acute Liver failure
- Chronic liver failure
- Hepatic dysfunction without evident necrosis

Acute liver failure

- It is associated with encephalopathy within 6 months after the initial diagnosis.
- fulminant liver failure is the encephalopathy which develop rapidly, within 2 weeks of the onset of jaundice.
- Sub- fulminant liver failure when the encephalopathy develops within 6 months of the onset of jaundice.
- It is caused by massive hepatic necrosis, most often induced by drugs or toxins and hepatitis B and C virus infections.
- The mechanism of hepatocellular necrosis may be direct toxic damage or variable combination of toxicity and immune mediated hepatocyte destruction.

Chronic liver failure

- It is most common route to hepatic failure and is the end point of chronic hepatitis ending in the cirrhosis.

Hepatic dysfunction without clear necrosis

- Hepatocyte may be viable but unable to perform normal metabolic function, as with tetracycline toxicity and acute fatty liver of pregnancy.

Clinical Features

The clinical signs of hepatic failure are the result of hepatocytes failing to perform their homeostasis function.

- **Jaundice**.
- **Hypoalbuminemia** which predispose to peripheral edema
- **Hyperammonemia** which play a major role in cerebral dysfunction.
- Impaired estrogen metabolism and hyperestrogenemia is reflection of local vasodilation and **spider angiomas** of the skin.

- Patients are highly susceptible to encephalopathy and failure of multiple organ systems.

Three Particular complications associated with hepatic failure.

- **Hepatic encephalopathy**
- **Hepatorenal Syndrome**
- **Hepatopulmonary Syndrome**

Hepatic encephalopathy

- It is regarded as a disorder of neurotransmission in the central nervous system and neuromuscular system and seems to be associated with elevated ammonia levels in blood and the central nervous system, which impair neuronal function and promote generalized brain edema.

- In the great majority of instances there are only minor morphologic changes in the brain, such as astrocyte swelling.

- It is reversible if underlying hepatic condition can be corrected.

Hepatorenal syndrome

- It refers to the appearances of renal failure in individuals with severe chronic liver disease. Sodium retention, impaired free water excretion, and decreased renal prefusion and glomerular filtration rate are the main renal function abnormalities.

- Rapid development of renal failure is usually associated with a precipitating stress factor such as infection, gastrointestinal hemorrhage, or a major surgical procedure.

- The treatment of choice is liver transplantation.

Hepatopulmonary Syndrome

- HPS is characterized by the clinical triad of chronic liver disease, hypoxemia, and intrapulmonary vascular dilation (IPVD).
- The possible causes of hypoxemia are: ventilation perfusion mismatch limitation oxygen diffusion.
- Clinically, patient may have decreased arterial oxygen saturation and increase dyspepnea.
- Most patients respond to oxygen therapy, although liver transplantation is the only curative treatment.

- **Cirrhosis, the end stage of chronic liver disease, is defined by three main morphologic characteristics.**

1. Broad scars linking portal tracts with one another and portal tracts with terminal hepatic veins.

2. Parenchymal nodules containing hepatocytes encircled by fibrosis. nodularity results from cycle of hepatocyte regeneration and scarring.

3. Disruption of structure of liver. The parenchymal injury and consequent fibrosis are diffuse, extending throughout liver.

- **Clinical features**; anorexia, weight loss, weakness, incipient or overt hepatic failure, metabolic load on liver, systemic or gastrointestinal infection and impaired oxygenation.

- **Causes** of cirrhosis are alcoholic abuse, viral hepatitis, and non alcoholic steatohepatitis. Other include biliary disease and iron overload.