DOPAMINE
SCIENTIFIC TEAM

GI PATHOLOGY

Final | Lecture 1-3

LIVER DISEASES

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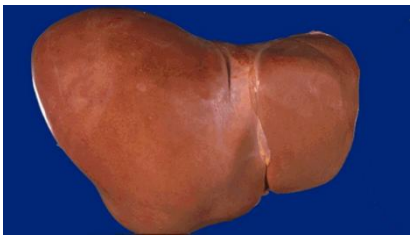
Color code: **Black** = slides, **Gold** = from doctor or book, Silver = additional from us.

Note: Some images are not explained here, instead there's a file for every picture with its explanation: click here.

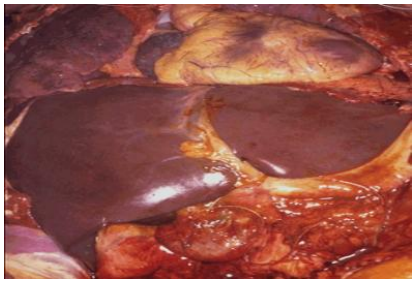
Liver Diseases 1

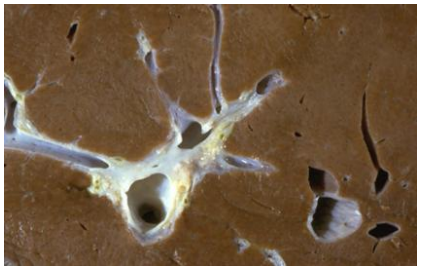
Liver:

- Due to multiple functions, manifestations are variable.
- Liver diseases manifestations are not only confined to the liver, sometimes they can have extrahepatic manifestations.



Normal liver





1. Functions:

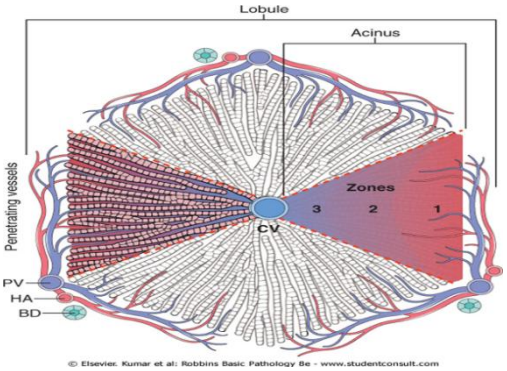
- Metabolic: Glucose
- Synthetic: Albumin, clotting factors …
- Detoxification: Drugs, hormones, NH3
- Storage: Glycogen, TG, Fe, Cu, vit
- Excretory: Bile

2. Net weight:

- 1400 – 1600gm (2.5% of body wt.)

3. Blood supply:

- Portal vein: **60 – 70%**
- Hepatic artery: **30 - 40%**



4. Microstructure: (structure fits function)

- Hexagonal lobules → 6 acini
  - **Acinus is divided into 3 zones:**
  - Some diseases prefer certain zones.

1- Zone 1

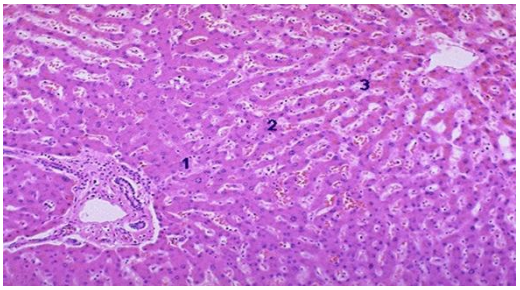
- Periportal areas – close to the vascular supply

2- Zone 3

- Pericentral area

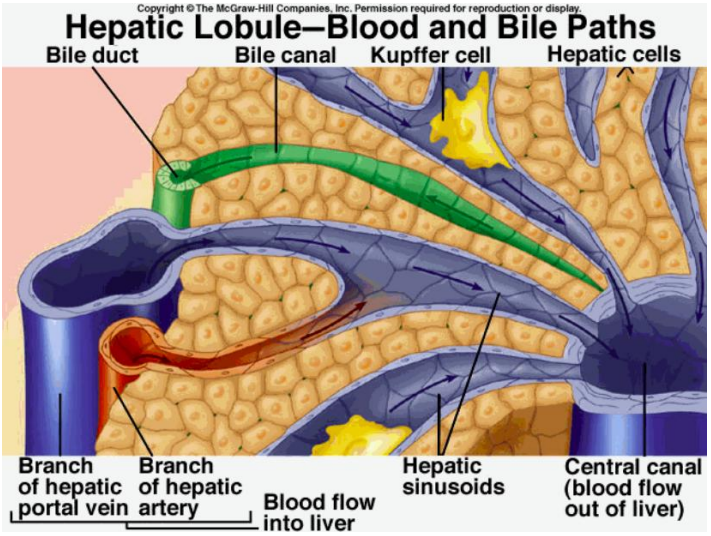
3- Zone 2

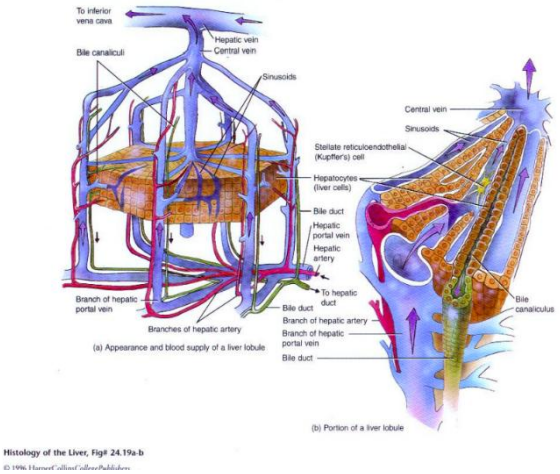
- Intermediate between Zones 1&2



5. The liver parenchyma:

- The parenchyma is organized into plates of hepatocytes.
- Hepatocytes are radially oriented around terminal hepatic vein (central v.)
- Hepatocytes show only minimal variation in the overall size, but nuclei may vary in size, number & ploidy esp. with advancing age
- Vascular sinusoids (bigger capillaries) present between cords of hepatocytes



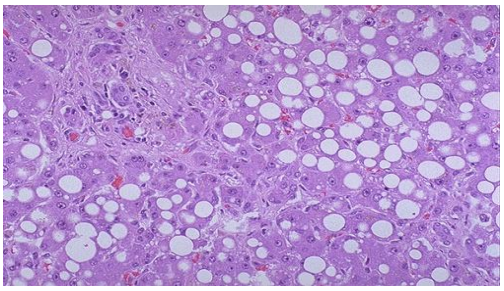


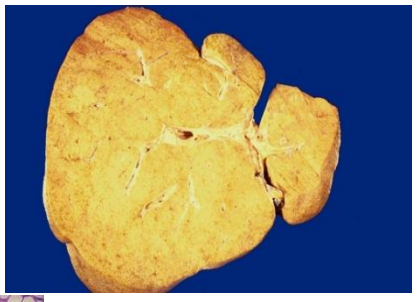
Extra images showing the parenchyma (the main functional tissue of the liver) that is divided into plates of hepatocytes, hepatocytes are arranged into 2 layers (or into Cords), each layer is facing a vessel, one is facing the sinusoid which drains into a central structure called the central vein, eventually toward the IVC. While the other is facing a bile canaliculus.

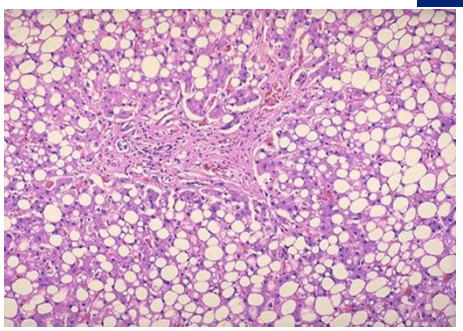
6. Liver injury:

1. Can be due to **Inflammation (Hepatitis).**
2. **Ballooning degeneration:**
    - Irregularly clumped cytoplasm showing large, with clear spaces.
    - Many Substances may accumulate in viable hepatocytes, including fat, iron, copper, and retained biliary material

3. **Steatosis (Fatty change) -** (steato always refers to fat)
    - Microvesicular: Alcoholic liver disease (ALD), Reye syndrome, acute fatty change of pregnancy.
    - Macrovesicular: Diabetes mellitus (DM), obese.







4. **Necrosis**

Depending on the type	Depending on the cause	Depending on location
Coagulative necrosis: around central v.	Ischemic: caused by ischemia (maybe due to low blood supply).	Zonal necrosis: ▪ Centrilobular necrosis: around central vein (zone 3) ▪ Mid zonal: in zone 2 ▪ Periportal: involves zone 1 and linked to interface hepatitis.
Councilman bodies	Toxic: caused by toxins (ex. acetaminophen overdose).	Focal: ▪ Piece meal necrosis. ▪ bridging necrosis.
Lytic necrosis **(liquefactive)**		Diffuse: ▪ Massive necrosis. ▪ Submassive necrosis.

5. **Regeneration**
    - evidenced by increased mitosis or cell cycle markers.
    - the cells of the canal of Hering are the progenitor for hepatocytes & bile duct cells (oval cells).
6. **Fibrosis**
    - portal or periportal fibrosis
    - pericentral- around the central vein.
    - pericellular fibrosis or fibrous tissue may be deposited directly within the sinusoids around single or multiple hepatocytes
    - bridging fibrosis

➢ 5 and 6 are related to injury, but not hepatic injuries themselves, they're repair mechanisms in response to injury.

7. **Cirrhosis (تشمع الكبد)**
    - Micronodular.
    - Macronodular.
8. **Ductular proliferation**.

7. Hepatic Failure: (فشل الكبد)

✓ Results when the hepatic functional capacity is **almost totally** lost (80 – 90%).

- **Causes**:
    1. **Massive hepatic necrosis:** (To be explained in p.7)
        - Fulminant viral hepatitis
        - Drugs & chemicals:
            - Acetaminophen. - Halothane. - Anti TB drugs.
            - CCL4 poisoning. - Mushroom poisoning.
    2. **Chronic liver disease.**
    3. **Hepatic dysfunction without overt cirrhosis**
        - Reye's syndrome. - Tetracycline toxicity.

- Acute fatty liver of pregnancy.

✓ Clinical features:

1. **Jaundice** (yellowing of the skin and eyes) - (Remember bilirubin metabolism in liver)
2. **Hypoalbuminemia → edema**. (Remember, liver makes albumin (maintains water in BVs), so low osmotic pressure of blood forces water to move toward the interstitial space (high osmotic pressure), causing edema).
3. **Hyperammonemia.**
4. **Fetor hepaticus** (musty or sweet & sour).
   - A **musty or sweet-sour smell** on the breath, due to volatile substances like dimethyl sulfide accumulating.
5. **Palmar erythema** linked to **hyperestrogenemia.** (redness of the palm)
6. **Spider angiomas.**
7. **Hypogonadism** (dec. testosterone) **& gynecomastia** (breast enlargement in men).

✓ Consequences:

1. **Multiple organ failure: kidneys & lung.**
2. **Coagulopathy → bleeding due to defective coagulative factors.**
   - **II, VII, IX, X**
3. **Hepatic encephalopathy** (The liver fails to detoxify substances like **ammonia**, which accumulate and affect the brain, remember the clinical feature hyperammonemia.)
   - Leads to (associated signs):
     - **↓level of consciousness.** – **Rigidity.** – **Hyperreflexia.**
     - **EEG changes.** – **Seizures.** – **Asterixis.**
4. **Hepatorenal syndrome** **(if the multiple organ failure(1) includes kidneys)**
   - **Renal failure in patients with severe liver disease with no morphologic or functional causes for renal failure.**

[Quiz on this lecture]

8. Massive hepatic necrosis:

- ✓ Fulminant hepatic failure from the onset of symptoms to hepatic encephalopathy (within 2 -3 wks.) or subfulminant (within 3 months).
- ✓ **Causes:**

1. Viral hepatitis 50 – 65% (B, B-D, A, C hepatitis).
2. Drugs & chemicals 20 – 30%
3. Heat stroke.
4. Hepatic vein obstruction.
5. Wilson disease.
6. Acute fatty liver of pregnancy.
7. Massive malignant infiltration.
8. Reactivation of chronic HBV hepatitis on HDV superimposed infection.
9. Autoimmune hepatitis.

9. Alcoholic liver disease

- ✓ Alcohol is the most widely abused agent.
- ✓ It is the 5th leading cause of death in USA due to:
  1. Accidents
  2. Cirrhosis
- ✓ 80 – 100 mg/dl is the legal definition for driving under the influence of alcohol.
  - ➢ 44 ml of ethanol are required to produce this level in 70kg person.
- ✓ Short term ingestion of 80 gms/d of ethanol is associated with fatty change in liver (steatosis).
- ✓ In **occasional** drinkers, blood Level of 200 mg/dl produces **coma** & **death** & **respiratory failure at 300-400 mg/dl.**
- ✓ **Habitual** drinkers can tolerate levels up to 700 mg/dl without clinical effect due to **metabolic tolerance** explained by 5-10X induction of cytochrome P-450 system that includes enzyme CYP2E1 which increases the metabolism of ethanol as well as other drugs as cocaine & acetaminophen.

✓ Forms of alcoholic liver disease:

- Hepatic steatosis (90-100% of drinkers).
- Alcoholic hepatitis (1- 35% of drinkers).
- Cirrhosis (14% of drinkers).

✓ **Steatosis & hepatitis may develop independently**.

Hepatic steatosis	Alcoholic hepatitis	Alcoholic cirrhosis
▪ This can occur following even moderate intake of alcohol in the form of **microvesicular steatosis.** ▪ **Chronic** intake → **diffuse** steatosis. ▪ Liver is large (4 – 6 kg) soft yellow & greasy ▪ Continued intake → fibrosis ▪ Fatty change is **reversible** with complete absention from further intake of alcohol	**Characteristic findings:** **1- Hepatocyte swelling & necrosis** ▪ Accumulation of fat & water & proteins ▪ Cholestasis ▪ Hemosiderin deposition in hepatocytes & Kupffer cells. **2- Mallory-hyaline bodies** (see next page) ▪ eosinophilic cytoplasmic inclusions in degenerating hepatocytes formed of cytokeratin intermediate filaments & other proteins. **3- Neutrophilic reaction** **4- Fibrosis** • Sinusoidal & perivenular fibrosis • Periportal fibrosis **5- Cholestasis** **6- Mild deposition of hemosiderin in hepatocytes & Kupffer cells**	Usually, it develops slowly. - Initially the liver is enlarged yellow but over years it becomes brown shrunken non-fatty organ s.t < l kg in wt. - Micronodular → mixed micro & macronodular - Laennec cirrhosis = scar tissue - Bile stasis - Mallory bodies are only rarely evident at this stage - **Irreversible** It can develop rapidly in the presence of alcoholic hepatitis (within 1-2 yrs). 

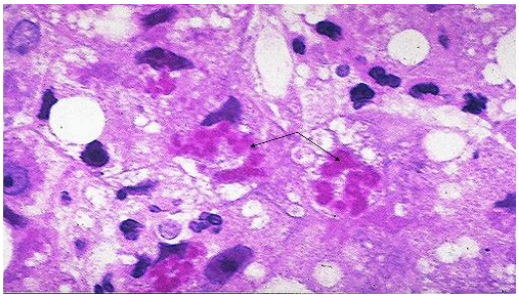
2- Mallory-hyaline inclusions are characteristic but not pathognomonic of alcoholic liver disease, they are also seen in:

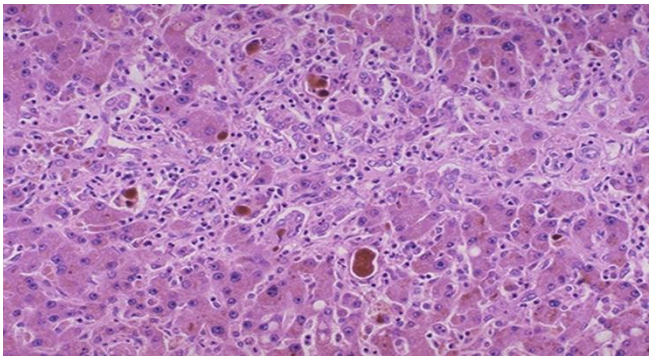
1- Primary biliary cirrhosis

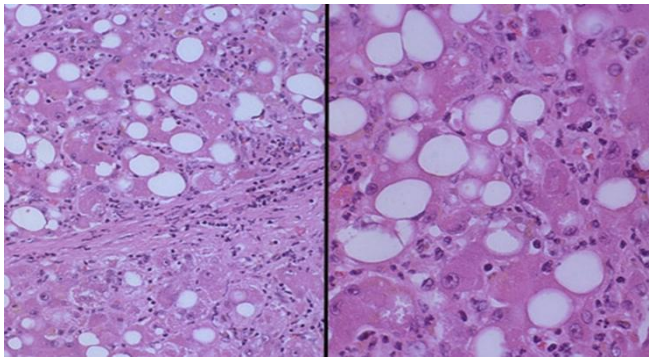
2- Wilson disease

3- Chronic cholestatic syndromes

4- Hepatocellular carcinoma







❖ Pathogenesis of alcoholic liver disease: (refer to toxicity by ethanol in the next seg.)

- **Short term** ingestion of 80gm of ethanol/day (8 beers) → mild **reversible** hepatic changes (fatty liver)
- **Long term** ingestion (10-20yrs) of 160gm of ethanol per day → severe hepatic injury.
  - 50 – 60gm/day → borderline effect
- **Women are more susceptible to hepatic injury due to ↓ gastric metabolism of ethanol.**
- Only 8 – 20% of alcoholics develop cirrhosis.

❖ Clinical features:

- **Hepatic steatosis (reversible with alcohol cessation)**
  - ✦ Enlarged liver (hepatomegaly).
  - ✦ ↑ liver enzymes.
  - ✦ Severe hepatic dysfunction is **unusual**.
- **Alcoholic hepatitis**
  - ✦ Occurs after 15-20 years of excessive drinking.
  - ✦ Non-specific symptoms, malaise, anorexia, wt. loss.
  - ✦ Enlarged liver & Spleen.

- ✦ ↑ liver function test (LFT), increase levels of liver enzymes (AST and ALT, etc.).
- ✦ Each bout (episode) of hepatitis → 10-20% risk of death.

  → cirrhosis in 1/3 in few yrs.

- **Cirrhosis**
  - ✦ Causes **Portal hypertension.**

❖ Causes of death in alcoholic liver disease

1- Hepatic Failure. 2- Massive GI bleeding. 3- Infections.

4- Hepatorenal syndrome. 5- Hepatocellular carcinoma (HCC) in 3-6% of cases.

10. Ethanol metabolism:

- **Ethanol → acetaldehyde → Acetic Acid**

  CH_3CH_2OH $CH_3C{=}OH$

- The first conversion is catalyzed by:
  - ✦ **Alcohol dehydrogenase** (stomach + liver).
  - ✦ **Cytochrome P-450.**
  - ✦ **Catalase (liver).**
- The second conversion is catalyzed by: **Aldehyde dehydrogenase**.

✓ After absorption ethanol is distributed as **Acetic acid** in all tissues & fluid in direct proportion to blood level.

✓ **Women have lower levels of gastric alcohol dehydrogenase activity than men** & they may develop higher blood Levels than men after drinking the same quantity of ethanol.

✓ less than 10% of absorbed ethanol is **excreted unchanged** in urine sweat & breathe.

✓ There is **genetic polymorphism** in aldehyde dehydrogenase that affect ethanol metabolism, for example:

- ✦ 50% of Chinese, Vietnamese & Japanese have lowered enzyme activity due to point mutation of the enzyme → accumulation of acetaldehyde → facial flushing, tachycardia & hyperventilation.

❖ Mechanism of ethanol toxicity:

1. **Fatty change:**

a) Shunting of lipid **catabolism toward** lipid **biosynthesis** due to excess production of NADH over NAD in cytosol & mitochondria.

b) Acetaldehyde forms adduct with tubulin and decrease function of microtubules, therefore a **decrease** in lipoprotein transport from liver.

c) **Increased** peripheral catabolism of fat, thereby **increased** FFA delivery to the liver.

d) **Decreased** secretion of lipoproteins from hepatocytes.

e) **Decreased** oxidation of FFA by mitochondria

2. **Induction of cytochrome P-450 enhances the metabolism of drugs to toxic metabolites (e.g. acetaminophen).**
3. **Increased free radicals production due to (+) of cytochrome P-450, this leads to membrane & protein damage.**
4. **Alcohol directly affects microtubular, mitochondrial function, and membrane fluidity.**
5. **Acetaldehyde causes lipid peroxidation & antigenic alteration of hepatocytes → immune attack**
6. **Superimposed HCV infection causes acceleration of liver injury (HCV hepatitis occurs in 30% of alcoholics)**
7. **Alcohol causes the release of bacterial endotoxins into portal circulation from the gut, thus inflammation of the liver.**
8. **Alcohol causes regional hypoxia in the liver due to the release of endothelins, which are potent vasoconstrictors, causing a decrease in hepatic sinusoidal perfusion.**
9. **Alteration of cytokine regulation**
   - TNF is a major effector of injury.
   - IL6, IL8, IL18.

QUIZ on this lecture

11. Cirrhosis:

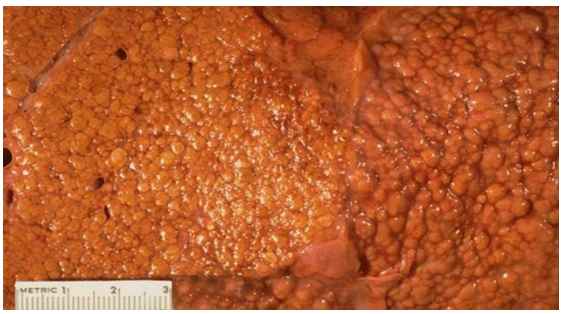
✓ **It is a diffuse process characterized by fibrosis & the conversion of liver parenchyma into nodules.**

✓ **Main characteristics:**

1. Bridging fibrous septae.
2. Parenchymal nodules encircled by fibrotic bands.
3. Diffuse architecture disruption.

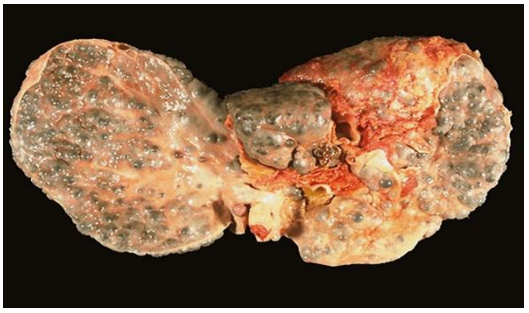
✓ **Types:**

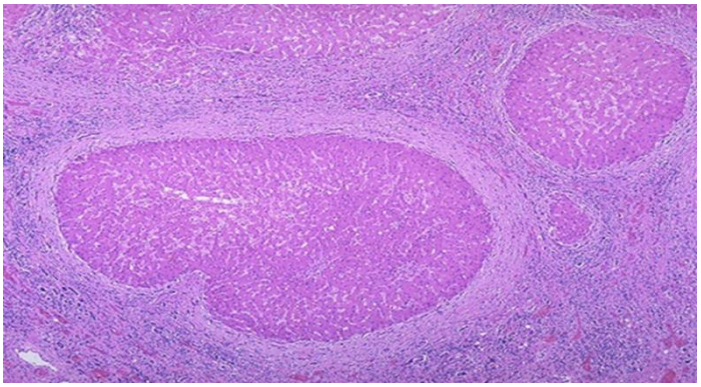
- Micronodules < 3mm in diameter.
- Macronodules > 3 mm in diameter.



←Micronodular cirrhosis.

→ Macronodular cirrhosis.





✓ **Histology of cirrhosis:**

Cirrhosis appears microscopically as regenerating hepatocyte nodules surrounded by fibrous tissue containing blood vessels and inflammatory cells. These regenerative nodules can maintain liver function, which may allow patients to remain asymptomatic for years.

✓ **Causes of cirrhosis:**

1. Chronic alcoholism.
2. Chronic viral infection HBV & HCV.
3. Biliary disease.
4. Hemochromatosis.
5. Autoimmune hepatitis.
6. Wilson disease.
7. α-1- antitrypsin deficiency.
8. **Rare causes**

– Galactosemia. – Tyrosinosis. – Glycogen storage disease III &IV.

– Lipid storage disease. – Hereditary fructose intolerance.

– Drug induced e.g. methyldopa.

9. Cryptogenic cirrhosis 10%

✓ Pathogenesis of cirrhosis:

- **The mechanism of cirrhosis involves:**

1. **Hepatocellular death**.
    - Cell death should occur over a long period of time & accompanied by **fibrosis**[3].
2. Regeneration.
3. Progressive fibrosis.
4. Vascular changes.

✓ **In normal liver the ECM collagen (types I, III, V& XI) is present only in:**

- Liver capsule.
- Portal tracts.
- Around the central vein.

✓ **Delicate framework of type IV collagen & other proteins lies in the space of Disse** (tiny gap found between hepatocytes and sinusoids).

- **In cirrhosis types I & III collagen & others are deposited in the space of Disse.**

✓ The major source of collagen in cirrhosis is the **perisinusoidal** stellate cells (**Ito cells**), which lie in the space of Disse.

- Perisinusoidal stellate cells normally act as storage cells for vitamin A and fat.
- Upon stimulation, they transform into myofibroblast-like cells under the influence of transforming growth factor β (TGF-β).

✓ **The stimuli for the activation of stellate cells & production of collagen are:**

1. reactive oxygen species
2. Growth factors
3. cytokines TNF, IL-I, lymphotoxins

✓ **The vascular changes include:**

1. Loss of sinusoidal endothelial cell fenestration
2. Development of vascular shunts, such as:
   Portal v - hepatic v
   Hepatic a - portal v

✓ **Defect in liver function.**

- ✓ Loss of microvilli from hepatocytes, causes a decrease in the transport capacity of the cells.

- ✓ Collagen deposition converts **sinusoids with fenestrated endothelial channels** that allow free exchange of solutes between plasma and hepatocytes to higher-pressure, fast-flowing vascular channels without such solute exchange.

- ✓ The **movement of proteins** (e.g., albumin, clotting factors, lipoproteins) between hepatocytes and plasma is markedly **impaired**.

- ✓ These functional changes are aggravated by the loss of microvilli from the hepatocyte surface, which diminishes the transport capacity of the cell.

✓ **Clinical features of cirrhosis:**

- Silent
- Anorexia, wt. loss, weakness

✓ **Complications:**

1. Progressive hepatic failure
2. Portal hypertension
3. Hepatocellular carcinoma

12. Portal Hypertension:

- ✓ Increased resistance to portal blood flow at the level of sinusoids and compression of central veins by perivenular fibrosis and parenchymal nodules
- ✓ Arterial–portal anastomosis develops in the fibrous bands → increase in the blood pressure in the portal venous system
  - These changes disrupt the normal low-resistance circulation within the liver, leading to increased pressure in the portal vein. As a result, blood is forced to bypass the liver through alternative vessels, contributing to complications such as varices, splenomegaly, and ascites.
- ✓ Anastomoses between the arterial and portal systems in the fibrous bands also contribute to portal hypertension by imposing arterial pressure on the normally low-pressure portal venous system.

❖ Causes of portal hypertension:

The most common cause of portal hypertension is liver cirrhosis. However, it can also result from other, less common causes divided into three categories:

1. **Prehepatic:**
   - Portal vein thrombosis
   - Massive splenomegaly
2. **Posthepatic:**
   - Severe right-sided heart failure
   - Constrictive pericarditis
   - Hepatic vein outflow obstruction
3. **Hepatic**
   - Cirrhosis
   - Schistosomiasis
   - Massive fatty change
   - Diffuse granulomatosis (e.g., sarcoidosis, TB)
   - Disease of portal microcirculation (e.g., nodular regenerative hyperplasia)

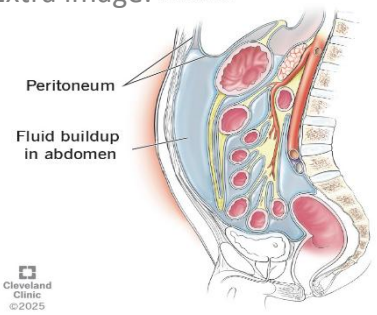
❖ Clinical consequence of portal hypertension:

1. **Ascites**.
2. **Portosystemic shunts**.
3. **Hepatic encephalopathy**.
   - Hepatic encephalopathy, also called portosystemic encephalopathy, happens when your liver isn't filtering toxins as it should. These toxins build up in your blood and affect your brain, causing confusion, disorientation and other changes. Hepatic encephalopathy can get better with treatment, but it can be life-threatening without.
4. **Splenomegaly**

13. Ascites (1st clinical consequence of portal hypertension)

- Collection of excess fluid in the peritoneal cavity
- It becomes clinically detectable when at least 500 mL have accumulated
- **Features:**
  1. Serous fluid
  2. Contains as much as 3 g/mL of protein (albumin)
  3. Has the same concentration as blood of glucose, Na^+, and K^+
  4. Mesothelial cells and lymphocytes (Mesothelial cells are normally lining the cavity)

Extra image: **Ascites**



5. Neutrophils → infection
6. RBCs → disseminated cancer

❖ Pathogenesis:

1. Increased sinusoidal blood pressure.
2. Hypoalbuminemia
3. Leakage of hepatic lymph into the **peritoneal cavity**.
   - ✓ Normal thoracic duct lymph flow is 800–1000 mL/day.
   - ✓ In cirrhosis, it can reach up to **20 L/day.**
4. Renal retention of Na^+ and water due to secondary hyperaldosteronism.

14. Portosystemic Shunt (2nd clinical consequence of portal hypertension)

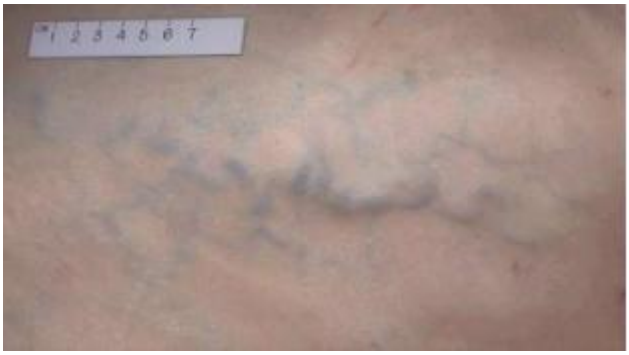
- Because of ↑ portal venous pressure, bypasses develop wherever the systemic and portal circulation share capillary beds

❖ Sites:

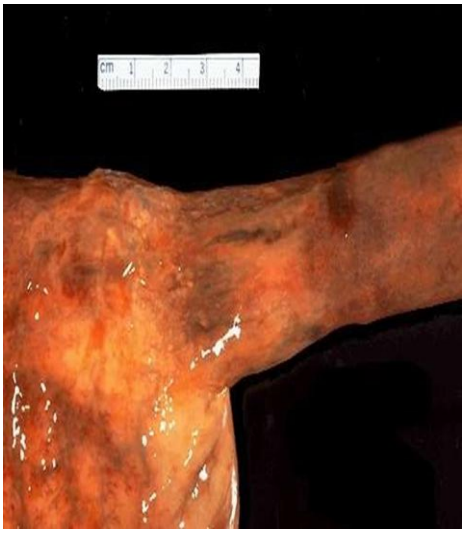
1- Around and within the rectum (hemorrhoids)
2- **Gastroesophageal junction** (varices) – (the most important)
3- Retroperitoneum
4- Falciform ligament of the liver (periumbilical and abdominal wall collaterals) → caput medusae (a cluster of swollen veins in your abdomen.).

- Gastroesophageal varices appear in 65% of patients with advanced cirrhosis and cause death in 50% of them due to upper GI bleeding.

caput medusae (at the anterior abdominal wall**).**



Esophageal varices



15. Splenomegaly (3rd clinical consequence of portal hypertension)

- Usually 500–1000 g (normal < 300 g).
- Not necessarily correlated with other features of increased portal blood pressure.
- May result in hypersplenism.

16. Hepatic Encephalopathy (4th clinical consequence of portal hypertension)

- It is a complication of acute and chronic hepatic failure.
- Disturbance in brain function ranging from behavioral changes to marked confusion and stupor, to deep coma and death.
- The changes may progress over hours or days.

❖ Neurological signs:

1. **Rigidity**
2. **Hyperreflexia**
3. **Non-specific EEG**
    - "Non-specific EEG" means that the electroencephalogram (EEG) findings in hepatic encephalopathy do not show a unique pattern that definitively diagnoses the condition. Instead, the EEG may show generalized slowing of brain activity, which is common in many types of encephalopathy or brain dysfunction.
4. **Seizures.**
5. **Asterixis (non-rhythmic rapid extension-flexion movements of the head and extremities).**
6. **The brain shows edema and astrocytic reaction.**

❖ Pathogenesis

- Physiological factors important in the development of hepatic encephalopathy:
    1. Severe loss of hepatocellular function
    2. Shunting of blood around the damaged liver

    ↓↓

    Exposure of the brain to toxic metabolic products
- Increased NH_3 level in blood, thereby generalized brain edema, impaired neuronal function.

- Alteration in central nervous system amino acid metabolism

17. Drug-Induced Liver Disease:

- **Drug reactions:**
  1. **Predictable (intrinsic)**
     - Predictable drug reactions depend on the dose (**dose-dependent**)
     - **Predictable drugs:**
       – Acetaminophen. –Tetracycline. – Antineoplastic agents.
       – CCl_4. – Alcohol.
  2. **Unpredictable (idiosyncratic)** – (dose independent)
     - Unpredictable drug reactions depend on:
       a. The immune response of the host to the antigenic stimulus.
       b. The rate at which the host metabolizes the agent.
     - **Unpredictable drugs:**
       – Chlorpromazine. – Halothane. – Sulfonamides.
       – Methyldopa. – Allopurinol.
- **The injury may be immediate or take weeks to months.**
- **Drug-induced chronic hepatitis is clinically and histologically indistinguishable from chronic viral or autoimmune hepatitis.**

❖ Mechanism of drug injury:

1. **Direct toxic damage**
   - e.g., acetaminophen, CCl_4, mushroom toxins
2. **Immune-mediated damage**

❖ Patterns of Injury:

1. Hepatocellular necrosis
2. Cholestasis
3. Steatosis
4. Steatohepatitis
5. Fibrosis
6. Vascular lesions
7. Granuloma
8. Neoplasms (benign and malignant)

❖ Drugs that may cause acute liver failure:

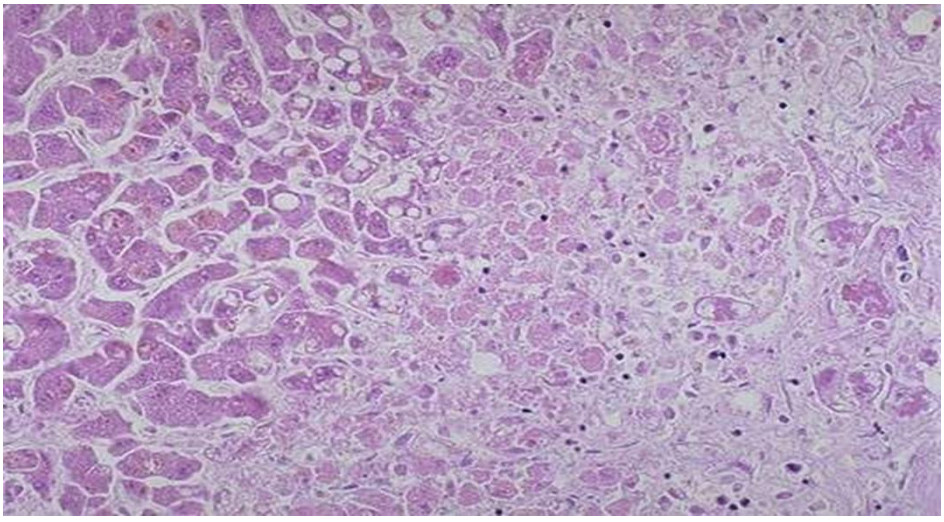
1. Acetaminophen (most common)
2. Halothane
3. Antituberculosis drugs (rifampin, isoniazid)
4. Antidepressant monoamine oxidase inhibitors

5. Toxins such as CCl_4 and mushroom poisoning

❖ Morphology:

- Massive necrosis → 500–700 g liver
- Submassive necrosis
- Patchy necrosis

  - **Left side: shows preserved hepatocytes without necrosis.**
  - **Right side: shows necrosis, pallor, and loss of nuclei.**



18. Fulminant Hepatitis

- Hepatic insufficiency that progresses from the onset of symptoms to hepatic encephalopathy within 2–3 weeks

  Subfulminant: up to 3 months

❖ Causes:

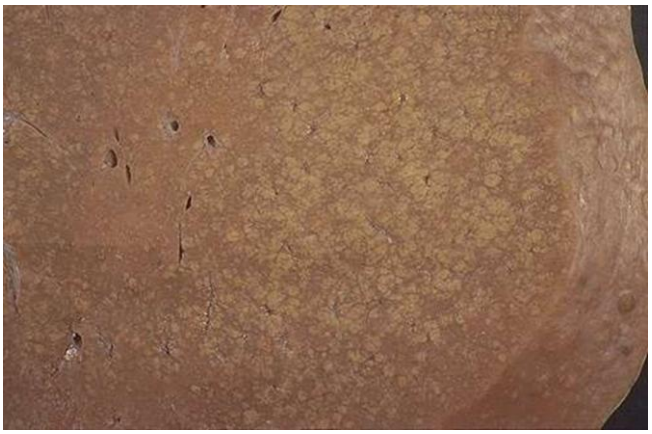
1. **Viral hepatitis** (50–65%)
   HBV is 2x more common than HCV
2. **Drugs and chemicals** (25–50%)
   e.g., isoniazid, halothane, methyldopa, and acetaminophen
3. **Obstruction of the hepatic vein**
4. **Wilson's disease**
5. **Acute fatty change of pregnancy**
6. **Massive tumor infiltration**
7. **Reactivation of chronic hepatitis B**
8. **Acute immune hepatitis**

❖ Morphology:

1. **Decrease in Liver size (500–700 g)**
2. **Necrosis of hepatocytes**

3. **Collapsed reticulin tissue**
4. **Inflammatory infiltrate**
5. **Regenerative activity of hepatocytes**
6. **Fibrosis**

This is the appearance of the liver with necrosis. The pale areas are the necrotic regions. The degree of necrosis is variable; there is also loss of homogeneity. All these are indications of necrosis.



19. Chronic Hepatitis

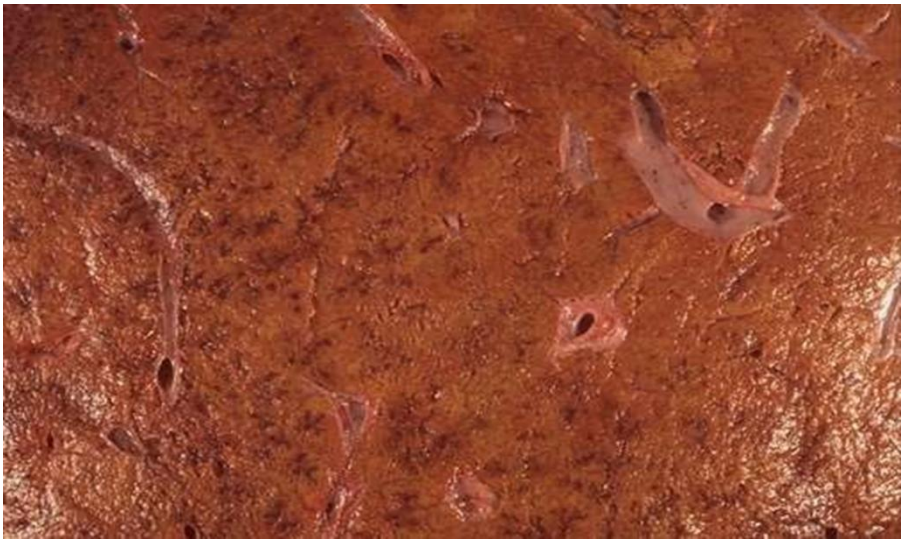
- Symptomatic, biochemical, or serologic evidence of continuing or relapsing hepatic disease for more than 6 months, with histologically documented inflammation and necrosis
- May be progressive or non-progressive
- **Causes**: HBV, HCV, HBV-HDV
- **The other outcome of viral hepatitis, and the most feared one, is chronic hepatitis. It is very important to recognize the causative agent of the viral hepatitis, and we need to follow up with the patient to predict whether they will develop chronic hepatitis.**

❖ Morphology of chronic hepatitis:

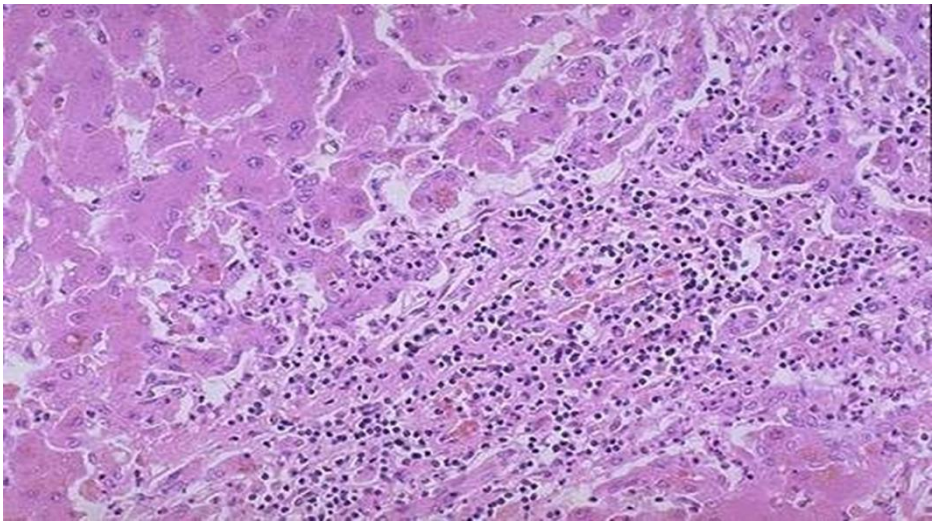
Mild to severe

1. Portal inflammation
2. Lymphoid aggregate
3. Necrosis of hepatocytes-councilman bodies
4. Bile duct damage
5. Steatosis
6. Interface hepatitis
7. Bridging necrosis & fibrosis
8. Fibrosis
9. Ground-glass appearance
10. Sanded nuclei
11. Lobular disarray

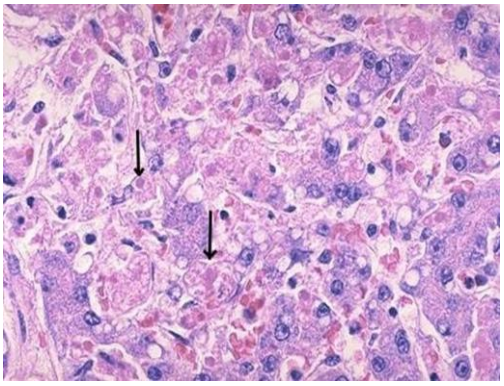
There is loss of homogeneity, as seen by the color changes: pale areas with darker surrounding regions. This is due to the presence of fibrosis. There is also some nodule formation.



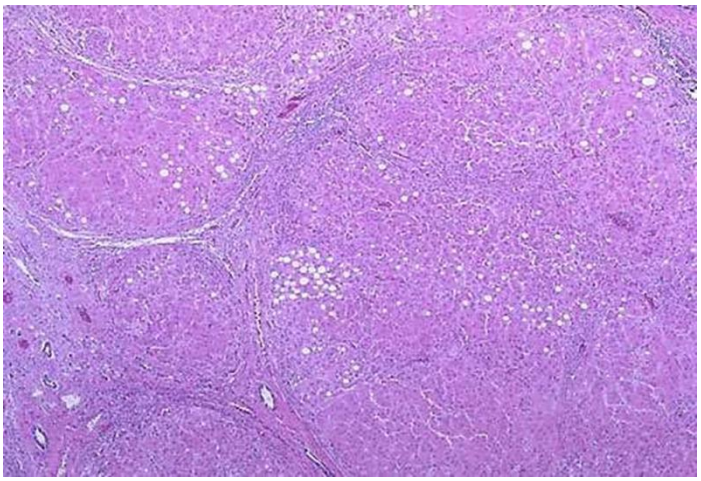
This is the microscopic appearance of a severe form of chronic hepatitis. There are some bridging fibrosis, which is an indication of cirrhosis development, along with extensive lymphocytic infiltration.



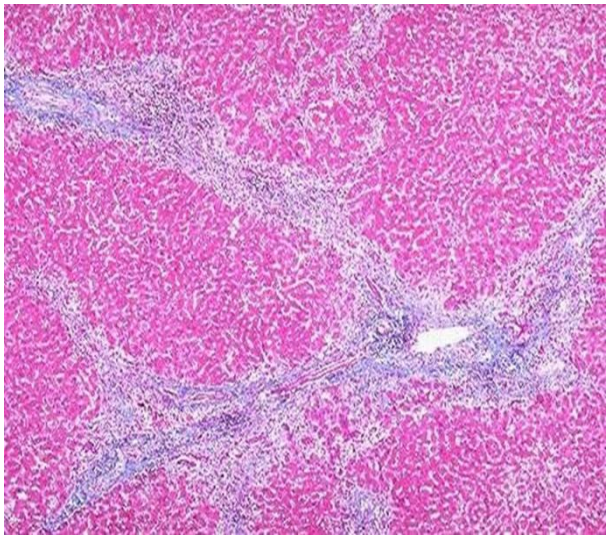
This image displays hepatocyte necrosis, indicated by the presence of Councilman bodies (highlighted by arrows). Additionally, it demonstrates fibrosis and features consistent with chronic hepatitis.

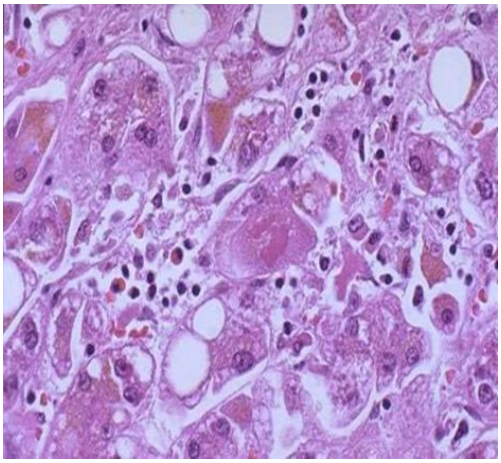


- Fat deposition
- Nodules
- Bridging fibrosis (connecting one structure to another)
- This shows extensive fibrosis, but not cirrhosis, because there is no complete nodule formation



we can see loss of hepatocytes architecture and the collapse of the liver parenchyma with viral hepatitis + fibrous tissue on it.





Quiz on this lecture
Overall quiz
Feedback form

V1	**P4**; adrenoleukodystrophy → alcoholic liver disease **P5**; with E and F it was meant to be 5 and 6.