



# CIRRHOSIS & HEPATOCELLULAR CARCINOMA

## CIRRHOSIS

### Definition of cirrhosis

- **Chronic diffuse irreversible progressive liver disease**
- **Characterized by:**
  1. Hepatocellular necrosis
  2. Hyperplasia of the surviving hepatocytes forming regenerating nodules lacking normal lobular architecture
  3. Vascular derangement
  4. Diffuse fibrosis.

### Definition of Regenerating nodule

- **Abnormal mass of liver cells**
  - Without a normal cord pattern nor a central vein
  - Surrounded by fibrous tissue.

## PATHOGENESIS

**Fibrosis is the key feature cirrhosis.**

- ✓ **Collagen deposition:** Collagen is deposited in the lobule, creating delicate or broad septal tracts.
- ✓ **Type:** type I & III collagens
- ✓ **Site:** In the space of Diss
- ✓ **Results:** Accompanied by hepatocytes **hypo**perfusion which **increased** liver damage.
- ✓ **Source of excess collage:** The major source is the peri-sinusoidal stellate cells (which is activated by; **PDGF**, **TNF** & **TGF- $\beta$**  released from activated **Kupffer cell**, **endothelial cells**, **hepatocytes** & **inflammatory cells**)





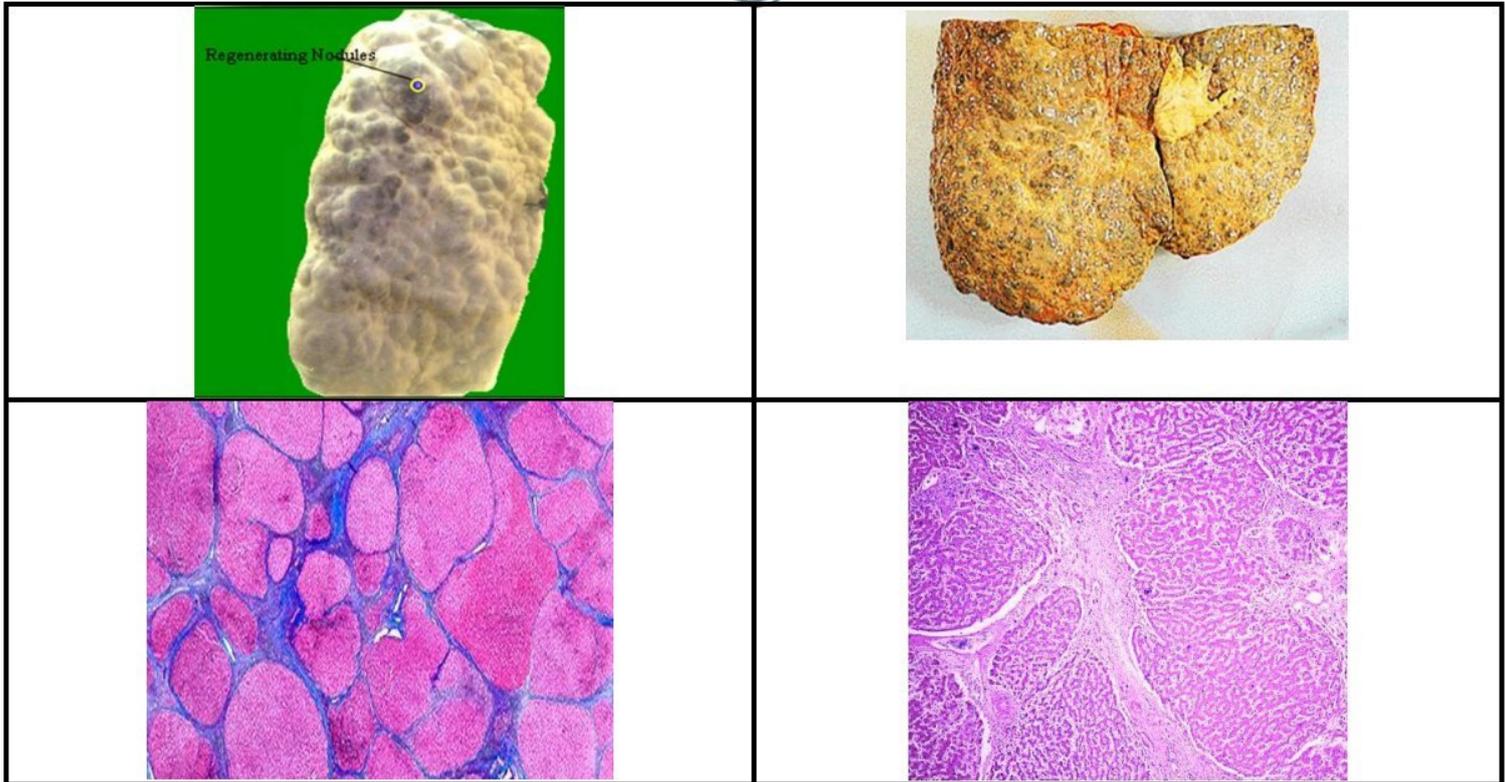
## ETIOLOGICAL TYPES

Congenital cirrhosis	<ol style="list-style-type: none"> <li>1) Congenital syphilis.</li> <li>2) Hemochromatosis</li> <li>3) Glycogen storage disease</li> <li>4) Galactosemia</li> <li>5) Wilson disease</li> <li>6) <math>\alpha</math>1 antitrypsin deficiency</li> </ol>
Acquired cirrhosis	<ol style="list-style-type: none"> <li>1) Post hepatitis (viral) cirrhosis</li> <li>2) Nutritional (alcoholic) cirrhosis</li> <li>3) post-necrotic cirrhosis.</li> <li>4) Biliary cirrhosis (1ry &amp; 2ry).</li> <li>5) Cirrhosis caused by circulatory disorders</li> <li>6) Cryptogenic (idiopathic)</li> </ol>

## MICROSCOPIC EXAM

N/E	<ul style="list-style-type: none"> <li>✓ <b>Size:</b> Usually shrunken (<b>except in biliary cirrhosis</b>).</li> <li>✓ <b>Consistency:</b> Firm.</li> <li>✓ <b>Outer surface &amp; cut surface:</b> Nodular.</li> <li>✓ <b>According to size of the nodules:</b> <ol style="list-style-type: none"> <li>a. <b>Micro</b>nodular cirrhosis: &lt;3 mm.</li> <li>b. <b>Macro</b>nodular cirrhosis: &gt; 3 mm.</li> <li>c. <b>Mixed</b> micro &amp; macronodular cirrhosis.</li> </ol> </li> <li>✓ <b>Color:</b> <ul style="list-style-type: none"> <li>▪ Sometimes indicate a specific etiology <ul style="list-style-type: none"> <li>- <b>Yellow</b> → Nutritional cirrhosis</li> <li>- <b>Green</b> → Biliary cirrhosis</li> <li>- <b>Red</b> → Congestion</li> <li>- <b>Dark brown</b> → Hemochromatosis</li> </ul> </li> </ul> </li> </ul>
M/E	<ul style="list-style-type: none"> <li>✓ <b>Loss of the normal hepatic architecture</b> &amp; replacement by <b>regenerative nodules</b> (<b>Which is surrounded by fibrous tissue septa</b>).</li> <li>✓ <b>The regenerative nodules:</b> <ul style="list-style-type: none"> <li>▪ <b>Consist of:</b> Proliferating hepatocytes arranged in thick plates &amp; separated by sinusoidal spaces.</li> <li>▪ <b>The central veins:</b> Eccentric or Absent.</li> <li>▪ <b>The regenerating hepatocytes may be:</b> Small – Large – Uni or Binucleated.</li> </ul> </li> <li>✓ <b>The fibrous tissue septa:</b> <ul style="list-style-type: none"> <li>▪ <b>The fibrous tissue:</b> Replace the damaged hepatocytes &amp; develops at certain sites e.g. <b>perivenular – persinusoidal - pericellular - in relation to portal tracts</b>.</li> <li>▪ <b>Contains:</b> Proliferating bile ductules &amp; chronic inflammatory cells.</li> </ul> </li> </ul>





### EFFECTS

- ① **Asymptomatic** in 40% of case (early)
- ② **Symptoms** of complications

### COMPLICATIONS

- ① **Portal hypertension** → Splenomegaly – Ascites – Esophageal varices
- ② **Liver cell failure** → Jaundice – Hypoproteinemia – Ascites – Encephalopathy
- ③ **Hepatocellular carcinoma**

## HEPATOCELLULAR CARCINOMA

### Definition

- **Primary carcinoma** formed of cells resembling hepatocytes.

### INCIDENCE

- ✓ **Percent:** 80-85% of primary malignant liver tumors
- ✓ **Sex:** Males > females





### PREDISPOSING FACTORS

- ① **Cirrhosis:** ~ 80% of hepatocellular carcinoma cases arise in cirrhosis
- ② **Infectious:** Hepatitis B & C virus
- ③ **Metabolic causes:**
  - a. Nonalcoholic fatty liver disease
  - b. alpha 1 antitrypsin deficiency
  - c. Hemochromatosis.
- ④ **Environmental exposure:**
  - a. Aflatoxins contaminate badly stored cereals.
  - b. Azo dyes.
  - c. Nitrosamines.
- ⑤ **Hormones:** Estrogen & Progesterone.

### SYMPTOMS

- ① **Silent hepatomegaly.**
- ② **Rapid increase** in size of a cirrhotic liver with hemorrhagic ascites.
- ③ **Paraneoplastic syndrome**
- ④ **Increased level of  $\alpha$  fetoprotein (1000 ng/ml)**

### MICROSCOPIC EXAM

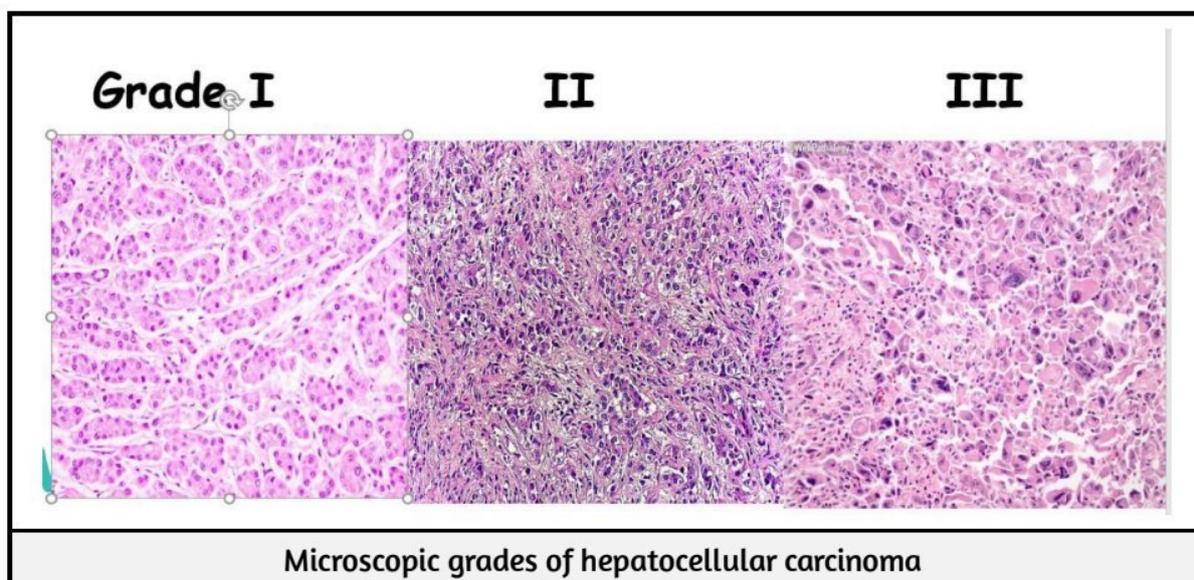
N/E	<ul style="list-style-type: none"> <li>✓ <b>Shape:</b> Well circumscribed mass</li> <li>✓ <b>Colour:</b> Appears tan-yellow to green (color variation depends on proportion of fat &amp; bile content)</li> <li>✓ Areas of <b>hemorrhage &amp; necrosis</b> are common</li> <li>✓ <b>Nodule:</b> Solitary or dominant nodule with multiple satellite nodules or multiple discrete masses.</li> <li>✓ <b>Background liver:</b> Usually cirrhotic</li> </ul>
M/E	<ul style="list-style-type: none"> <li>✓ <b>Malignant hepatocytes:</b> <ul style="list-style-type: none"> <li>▪ Arranged in trabeculae separated by sinusoids &amp; pseudo glandular, Solid &amp; macrotrabecular pattern.</li> </ul> </li> <li>✓ <b>The cells resemble the normal hepatocytes:</b> <ul style="list-style-type: none"> <li>▪ May show intracytoplasmic bile pigment</li> <li>▪ Shows the cytologic criteria of malignancy.</li> </ul> </li> <li>✓ <b>Stroma:</b> Scanty &amp; poorly vascular</li> </ul>





### GRADING SYSTEM

- ① **Well differentiated:**
  - Tumor cells resemble mature hepatocytes
  - Minimal to mild nuclear atypia
- ② **Moderately differentiated:**
- ③ **Poorly differentiated:**
  - Tumor cells show marked nuclear atypia



### SPREAD

- ① **Direct:** In the liver
- ② **Lymphatic:** To L.N of porta hepatis
- ③ **Blood:** Intrahepatic by branches of portal vein & extrahepatic by hepatic vein

### PROGNOSIS

- ☑ **Poor:** Most patients die within one year from liver cell failure or metastasis.
- ☑ **5 years survival rate: 5%.**

