Liver & Gallbladder Pathology

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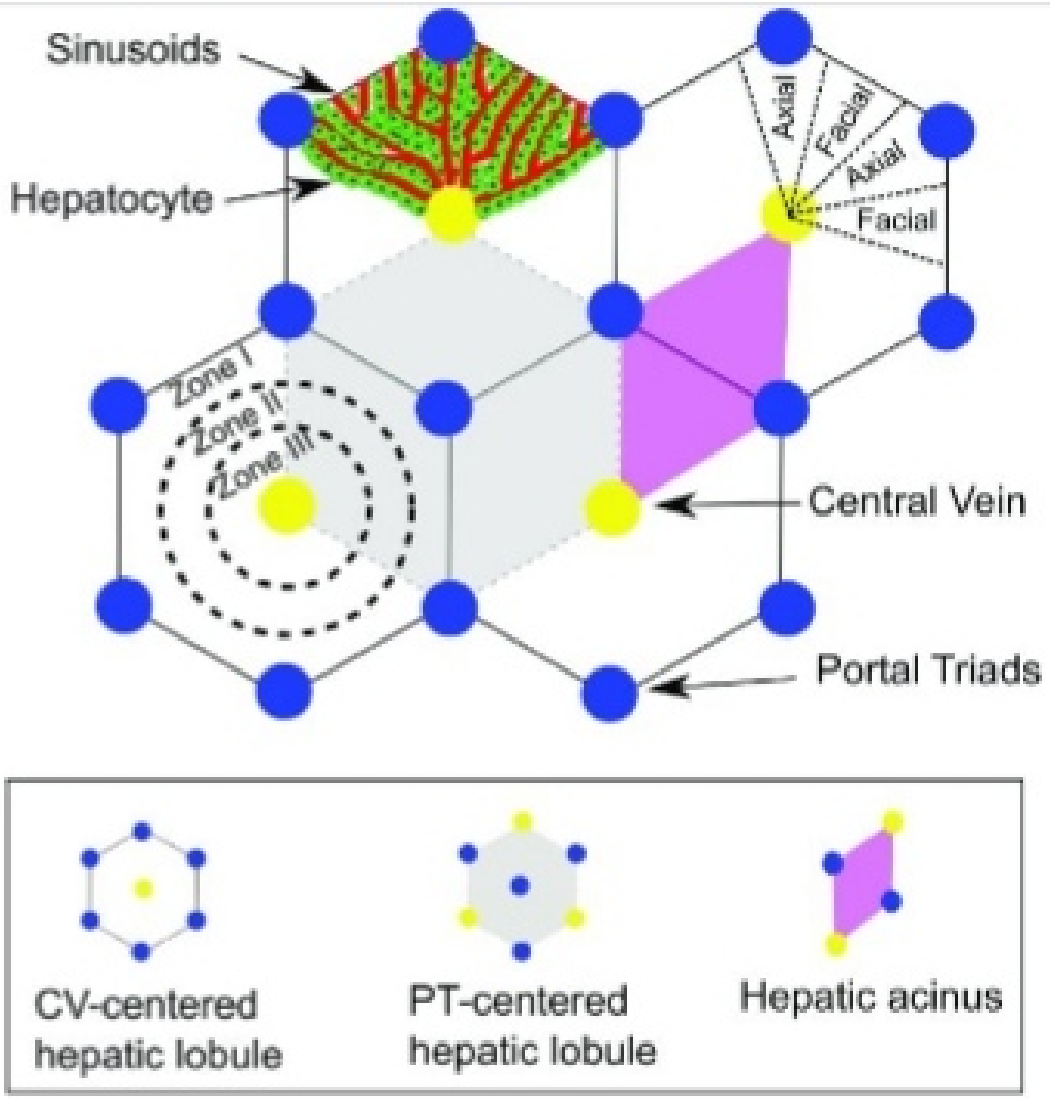
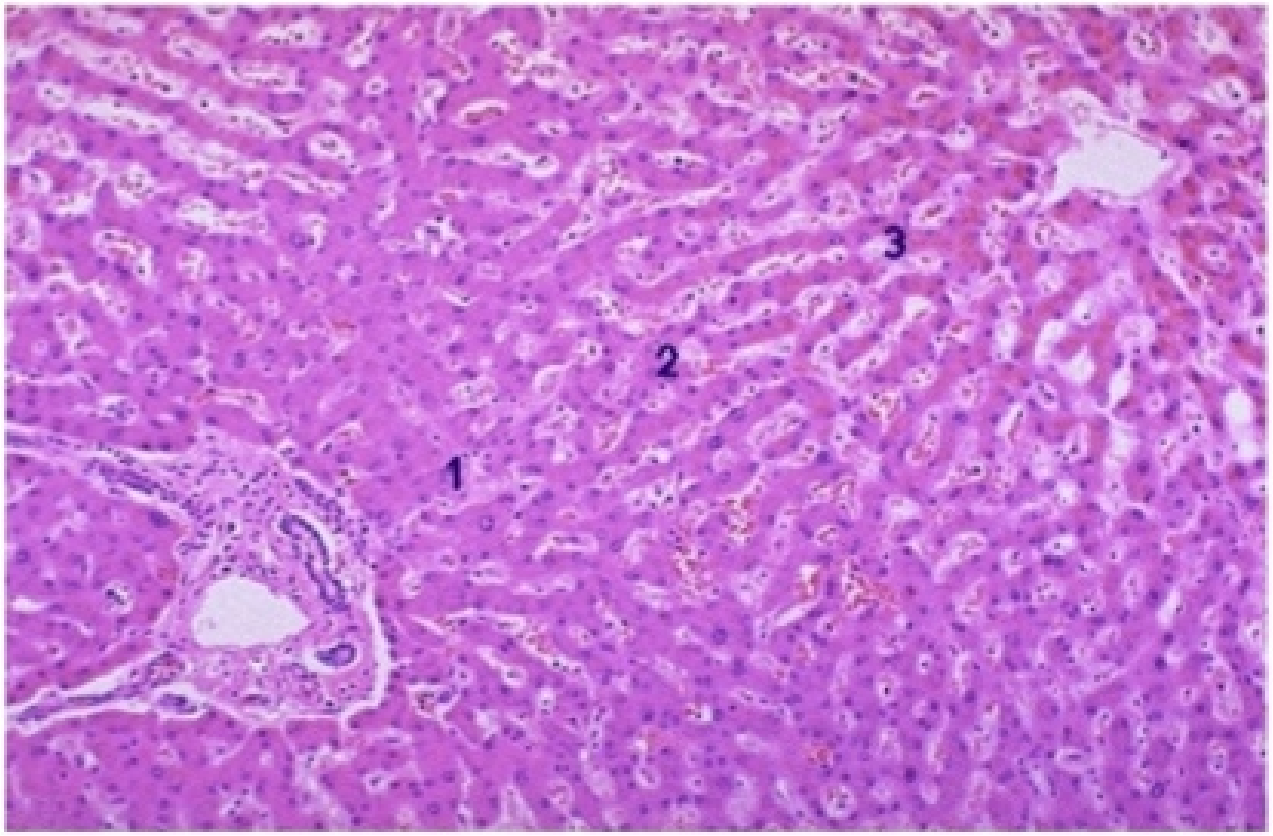
April 6th 2021

Lobule Model

This model divides the liver into lobules 1-2mm in diameter that are centered on a terminal tributary of the hepatic vein & demarcated by portal tracts at their periphery

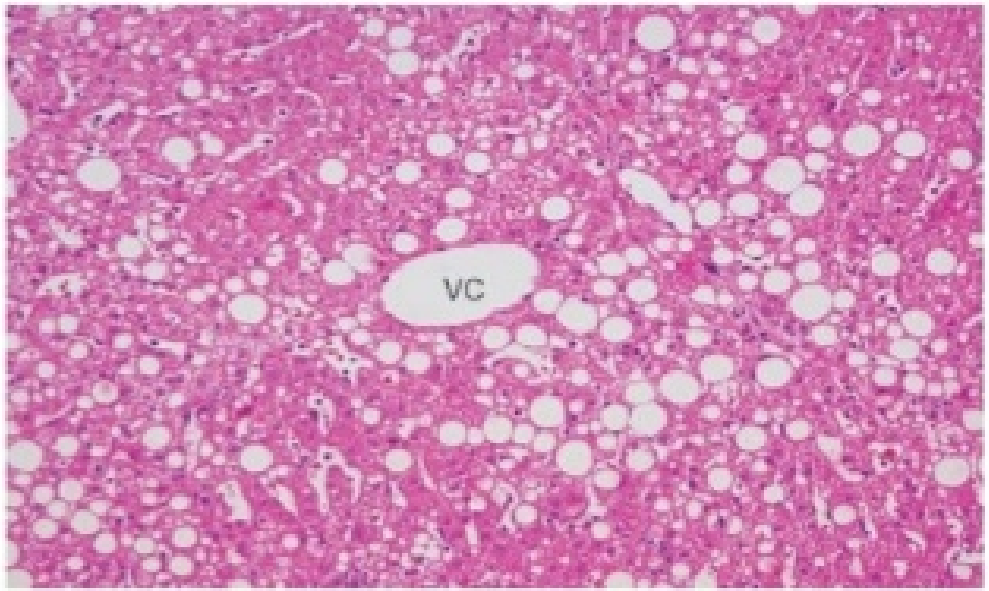




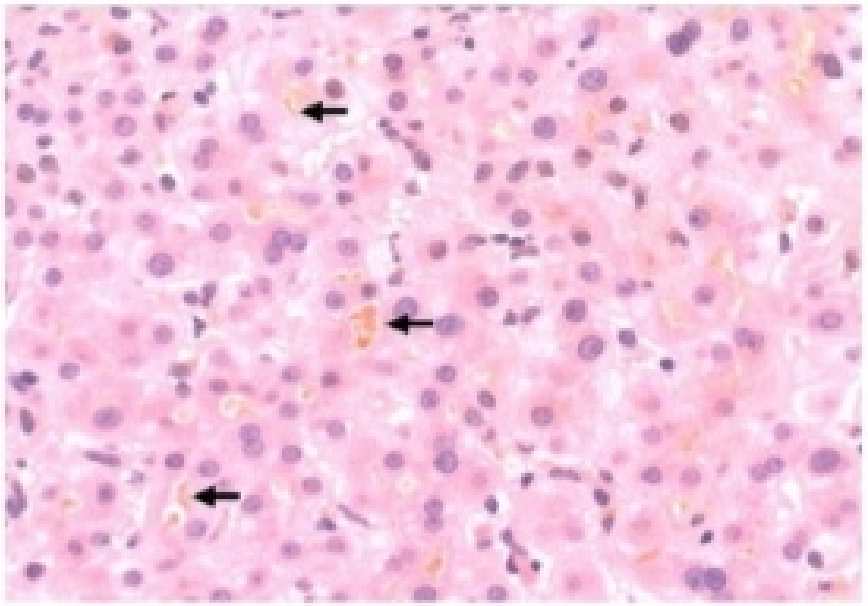
Three Zones

Division of the lobular parenchyma into zones is an important concept because each zone differs in metabolic activities & susceptibility to certain forms of hepatic injury.

Injured hepatocytes may show reversible changes;



accumulation of fat
(steatosis)

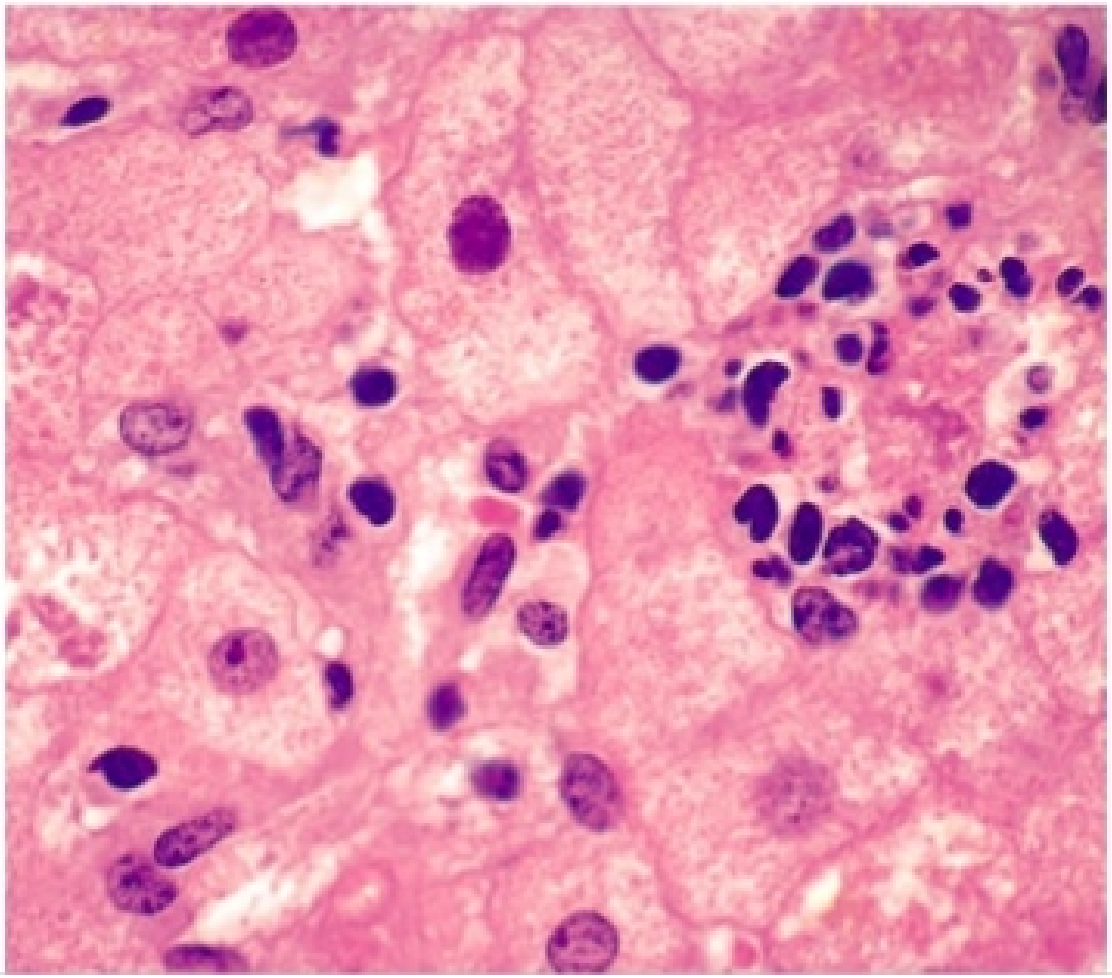


accumulation of bilirubin
(cholestasis)

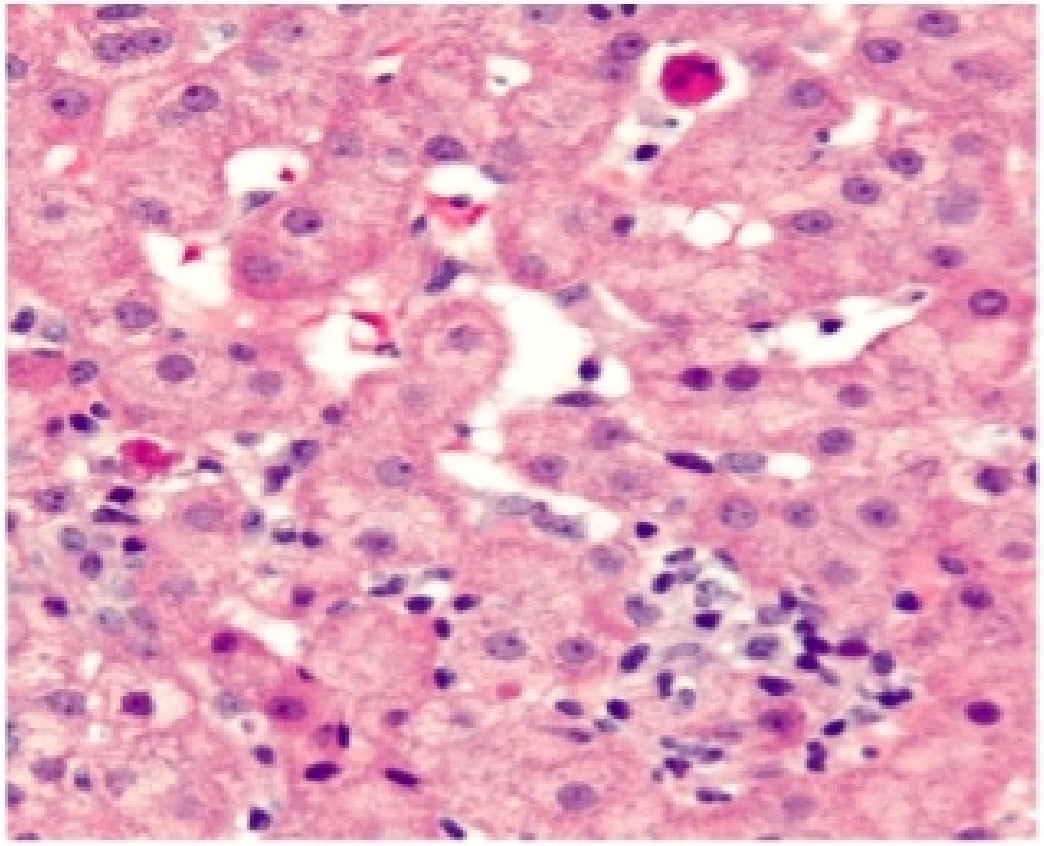
Irreversible injury , hepatocytes die by:

Necrosis

commonly
seen following hepatic
injury caused by
hypoxia & ischemia



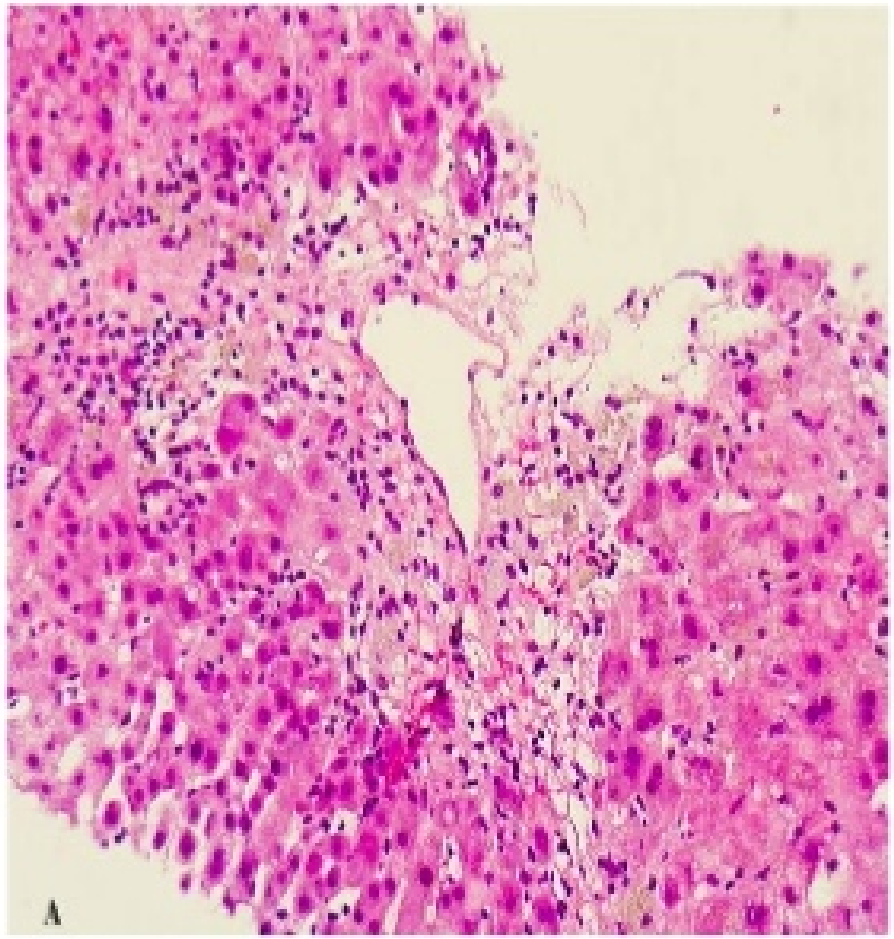
Irreversible injury , hepatocytes die by:



Apoptosis

predominates
in viral,
autoimmune, &
drug/toxin-induced
hepatitides.

Irreversible injury , hepatocytes die by:



Confluent necrosis

may be seen in acute toxic or ischemic injuries or in severe chronic viral or autoimmune hepatitis

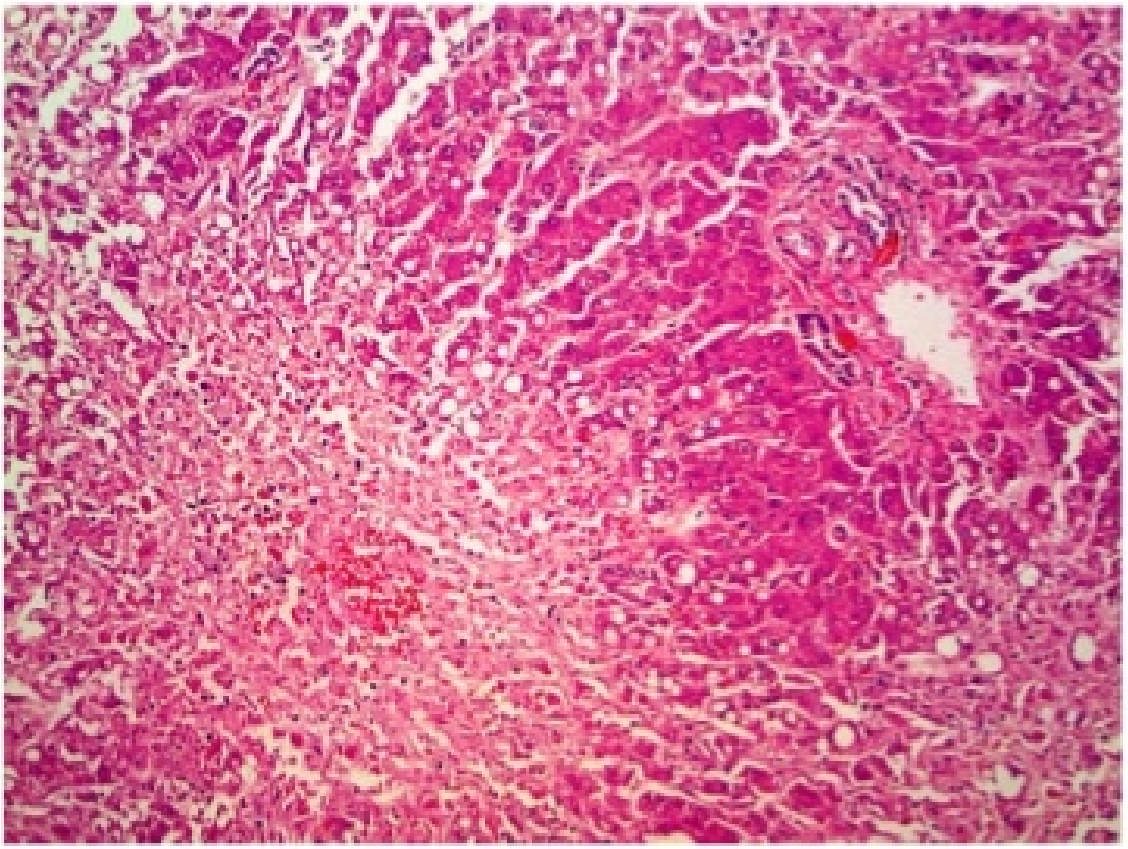
02

Liver Failure

- The most severe clinical consequence of liver disease
- It primarily occurs in three clinical scenarios: acute, chronic, & acute-on-chronic liver failure

Acute Liver Failure - *Histologically*

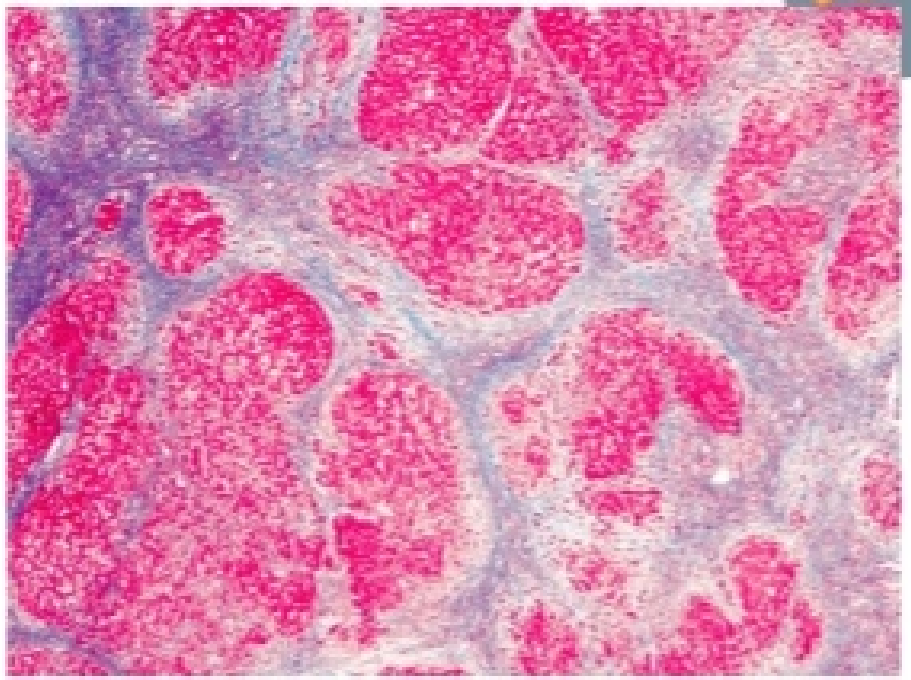
Massive hepatic necrosis: Large zones of destruction surrounding occasional islands of regenerating hepatocytes.



Chronic Liver Failure & Cirrhosis - *Morphology*

Chronic Liver Failure & Cirrhosis - *Morphology*

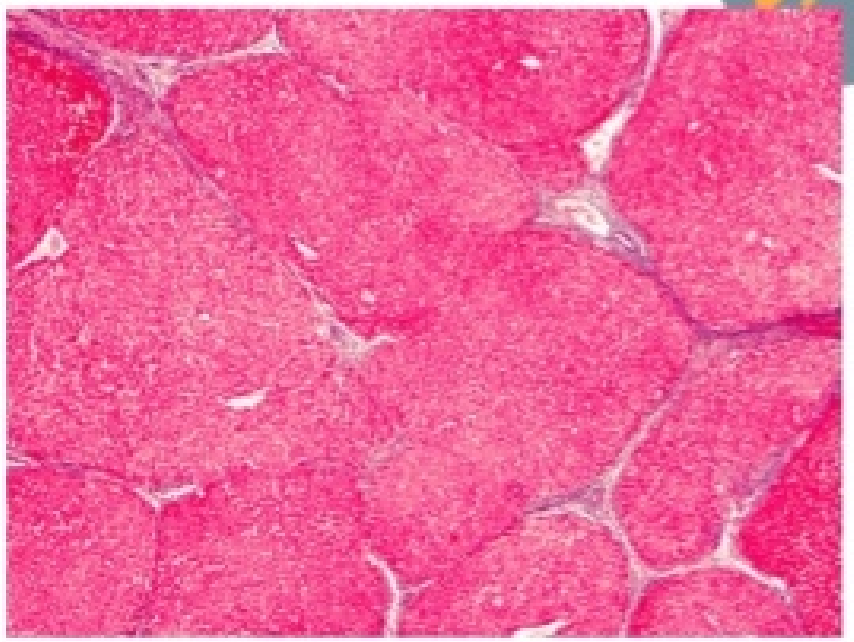
Size of the nodules, the pattern of scarring (linking of portal tracts to each other vs. linking of portal tracts to central veins), the degree of parenchymal loss all vary between diseases



Chronic Liver Failure & Cirrhosis - *Morphology*

Regression of fibrosis may follow disease remission or cure;

- Scars become thinner, more densely compacted, & eventually start to fragments.
- All cirrhotic livers show elements of both progression & regression balance being dictated by the severity & persistence of the underlying disease.

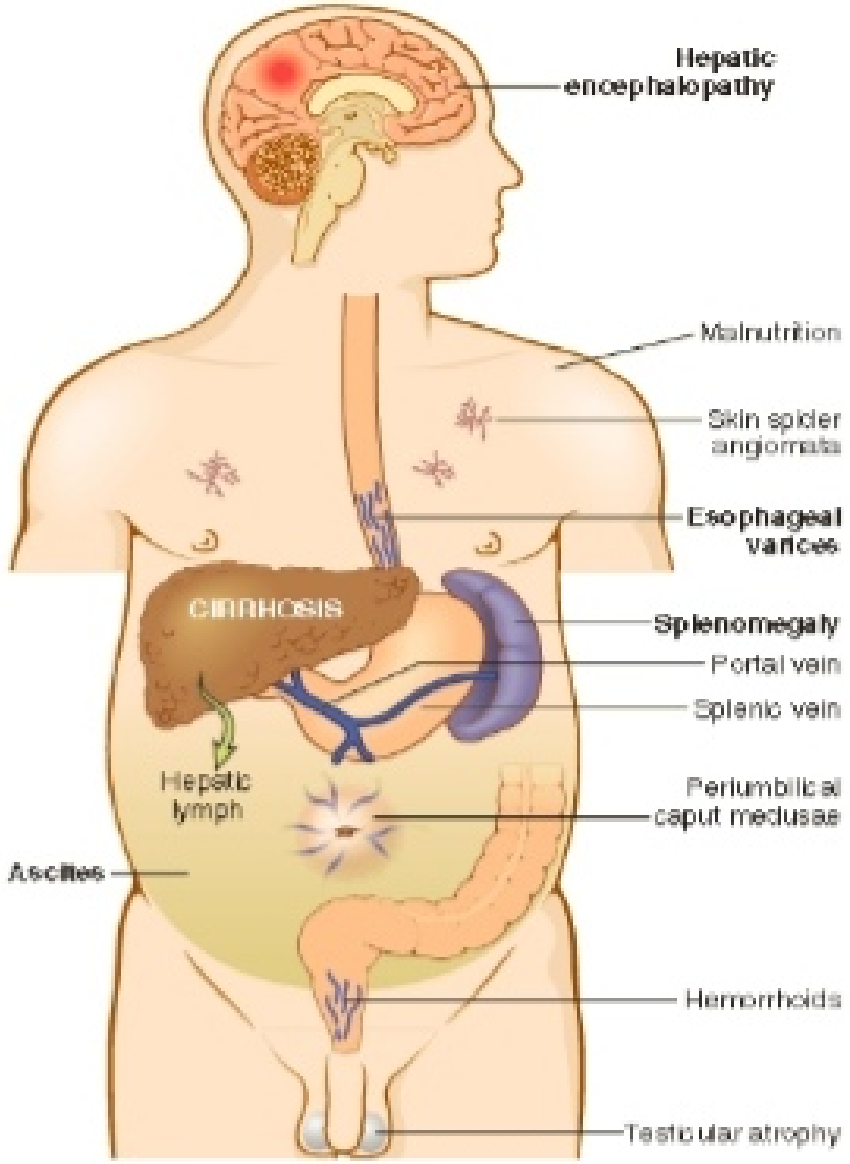


Chronic Liver Failure – *Clinically*

- **Hyperestrogenemia** due to impaired estrogen metabolism in male patients with chronic liver failure can give rise to palmar erythema (local vasodilatation) & spider angiomas of the skin. Such male hyperestrogenemia also leads to hypogonadism & gynecomastia.

Portal Hypertension

- Portosystemic shunts:
  - develop when blood flow is reversed from the portal to systemic circulation.
  - principally produced by dilation of collateral vessels.
- Venous bypasses develop wherever the systemic & the portal circulations share common capillary beds.



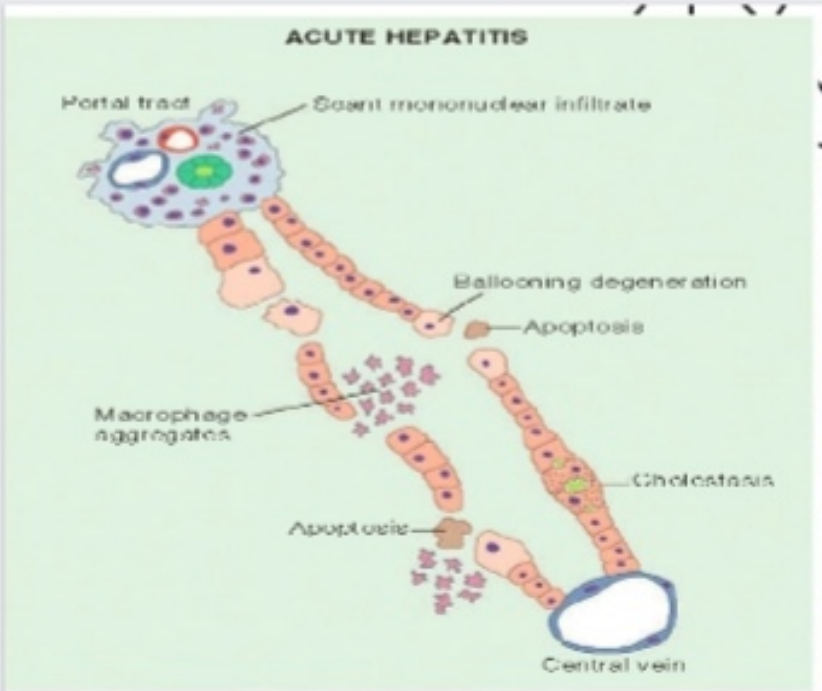
03

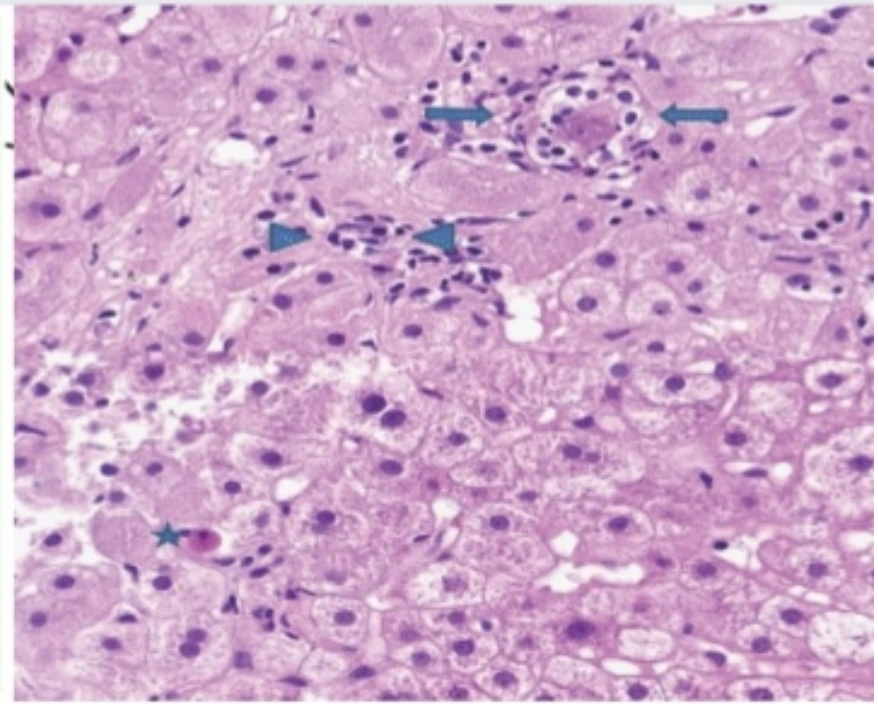
Hepatitis

- *A group of hepatotropic viruses ; have a specific affinity for the liver.*
- *other viruses such as EBV, CMV , & yellow fever*
- *Autoimmune reactions*
- *Drugs*
- *Toxins.*

Morphology of Acute viral hepatitis

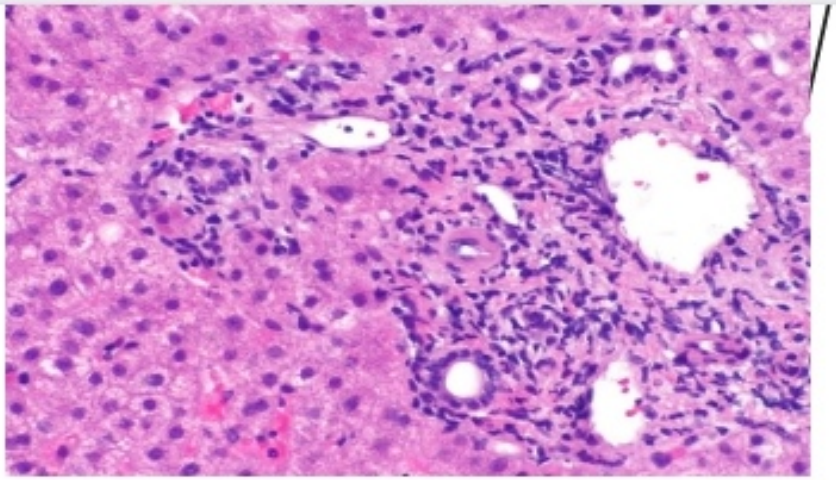
- Grossly, livers normal or slightly mottled.
- Mononuclear cells predominate in all phases (T-cells mainly)
- Parenchymal injury is scattered as "spotty necrosis" or **lobular hepatitis**.
- Portal inflammation is <u>minimal or absent.</u>
- **Ballooning degeneration**

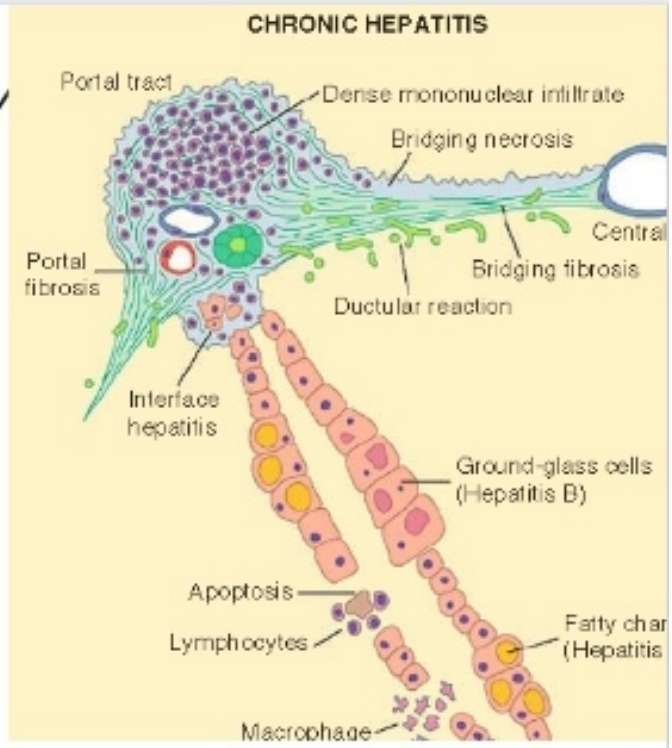


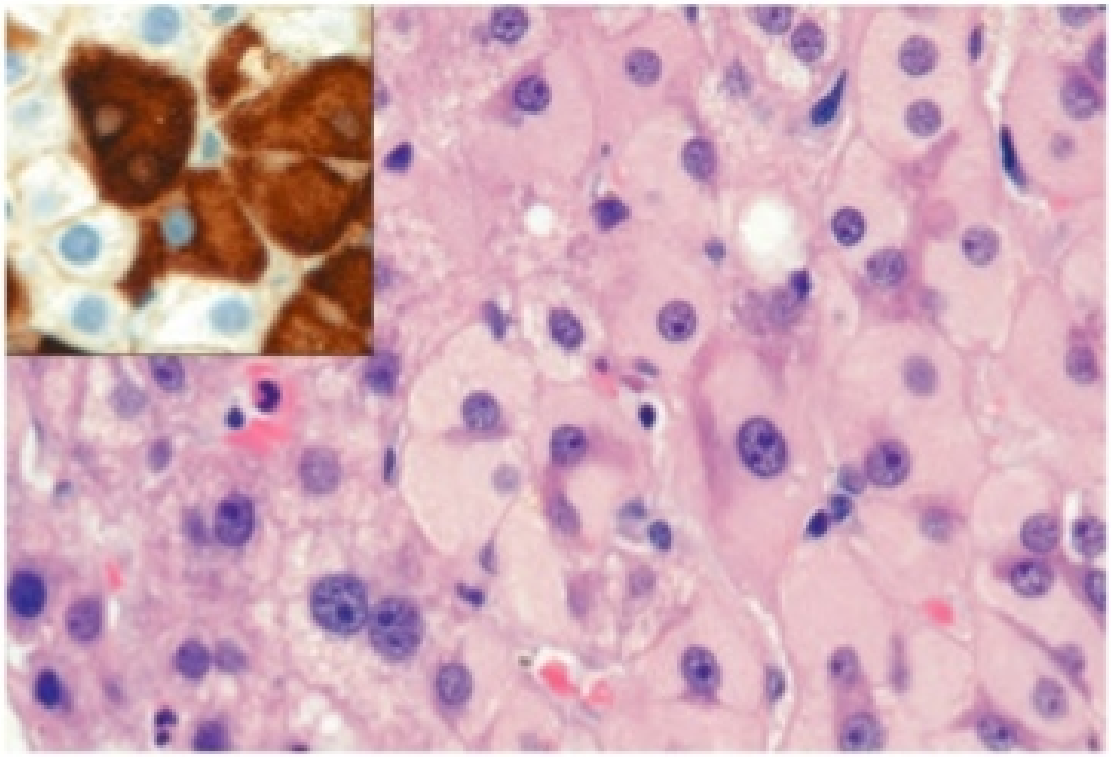


Morphology of chronic viral hepatitis

- Mononuclear portal infiltration
- **Interface hepatitis** & lobular hepatitis
- The hallmark of progressive chronic liver damage is scarring. At first, only portal tracts exhibit fibrosis, but with time, fibrous septa (bands of dense scar) may extend between portal tracts □ continued scarring and nodule formation □ cirrhosis (severe cases)

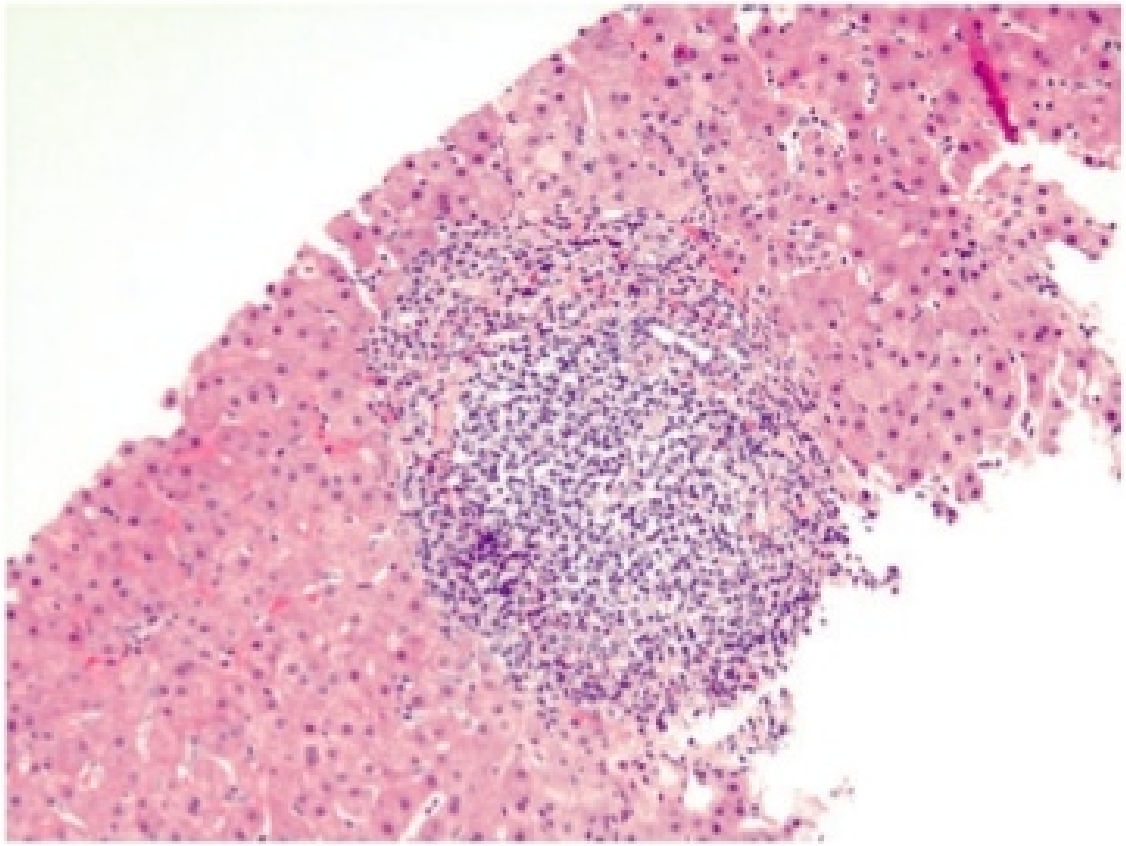






Microscopy :

- Certain histologic features point to specific viral etiologies:
- Chronic hepatitis. In HBV, **"ground-glass" hepatocytes**(cells with endoplasmic reticulum swollen by HBsAg)are a diagnostic hallmark,



Microscopy :

- Liver biopsies involved by chronic hepatitis C quite commonly show large lymphoid aggregates.
- HCV is associated with fatty change in scattered hepatocytes.

04

ALCOHOLIC AND NONALCOHOLIC FATTY LIVER DISEASE

Fatty liver disease: **Steatohepatitis.**

Alcohol vs NAFLD

More pronounced with alcohol use than in NAFLD, seen in either

Hepatocyte ballooning

Single or scattered foci of cells undergo swelling & necrosis. Most prominent in the centrilobular region

Mallory-Denk bodies

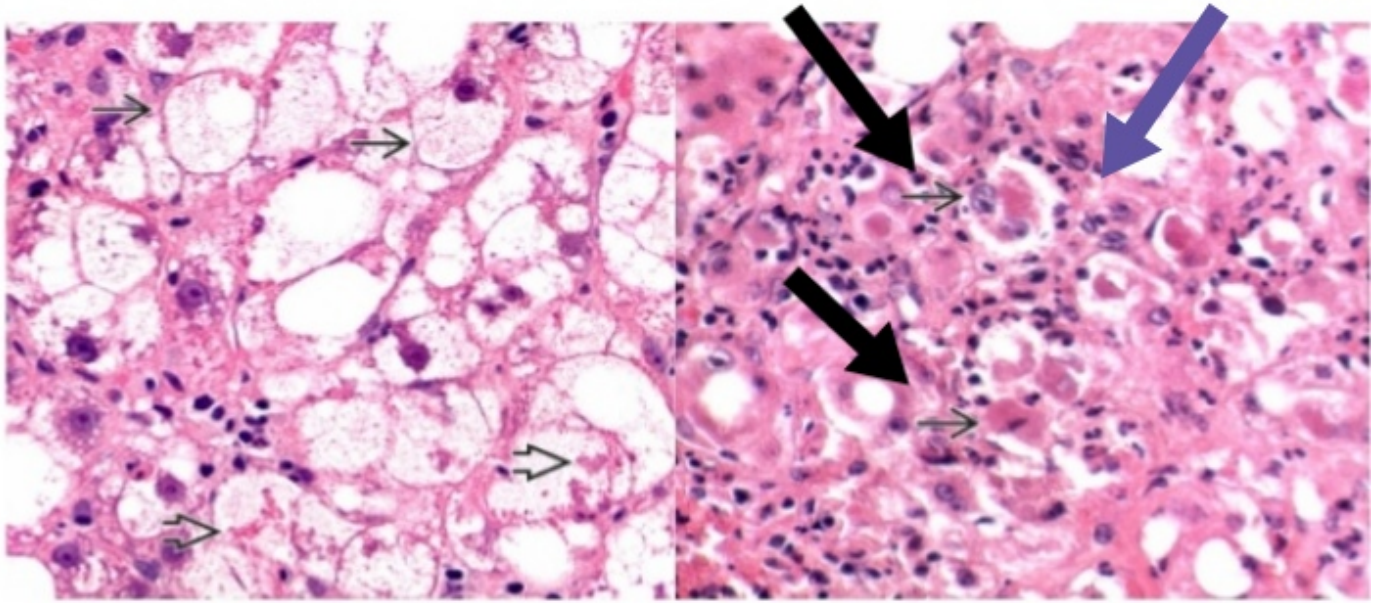
Tangled skeins of intermediate filaments.
Visible eosinophilic cytoplasmic inclusions in degenerating hepatocytes

Neutrophil infiltration

May permeate the lobule and accumulate around degenerating hepatocytes

Mallory denk bodies

neutrophils infiltration



in early stage it starts by fat accumulation in the cells, followed by injury & ballooning.
the injury is associated with becoming large cells (ballon swallowed cells) undergo degeneration so the mallory denk bodies appear

Mallory denk bodies: intermediate filaments (keratin), normally present in the cells, but become more prominent in hepatic injury

Fatty liver disease: **Steatofibrosis**

fibrosis appears first in the centrilobular region

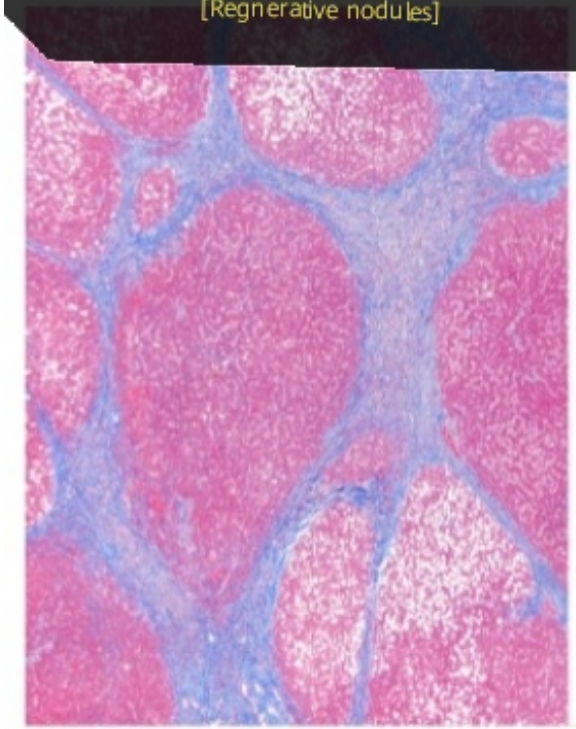
encircling individual or small clusters of hepatocytes

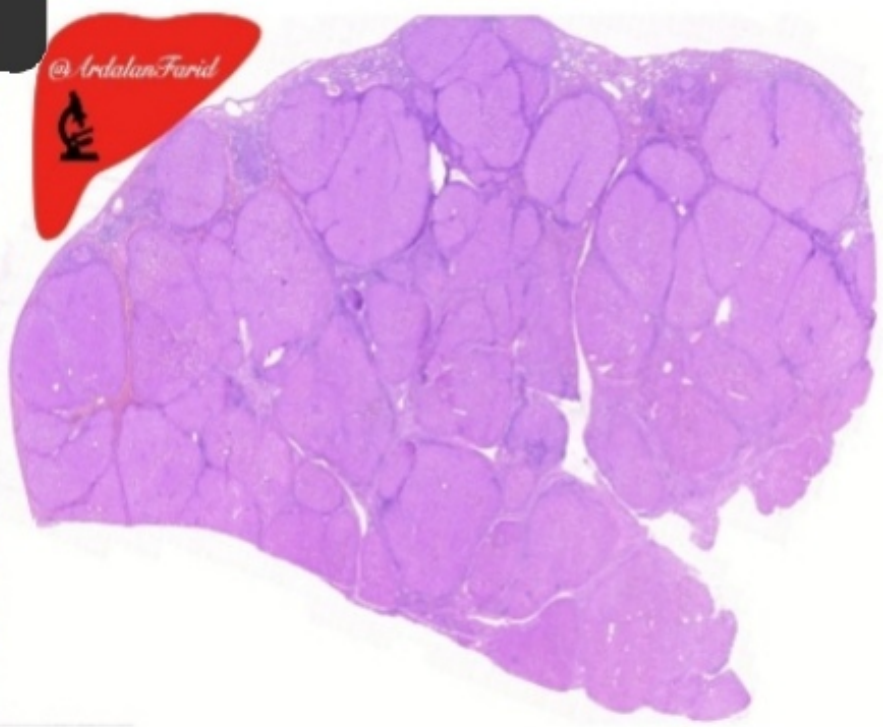
portal tracts & then condense to create central portal fibrous septa.

As Septa become more prominent liver takes on a nodular, cirrhotic appearance

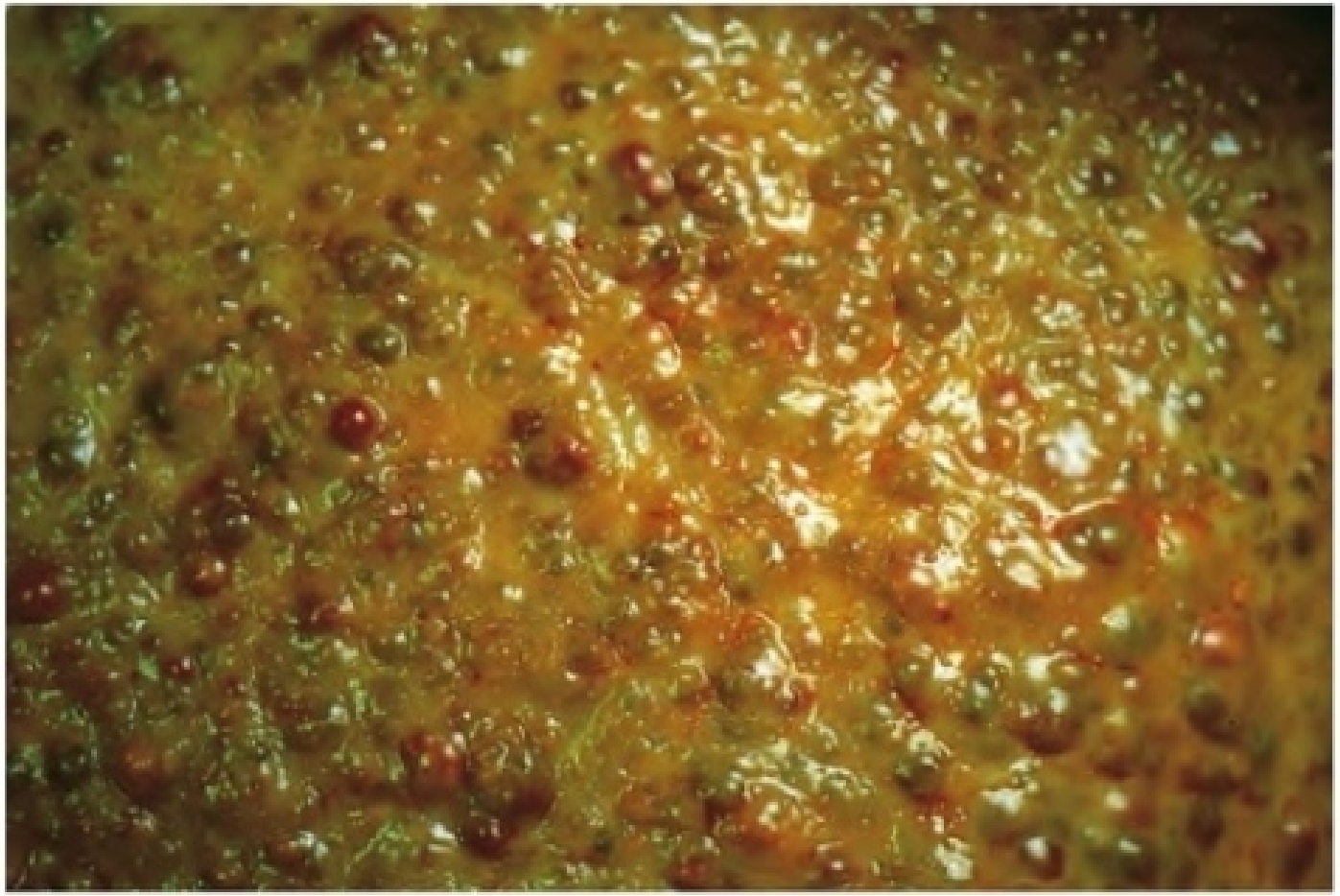
H&E stain

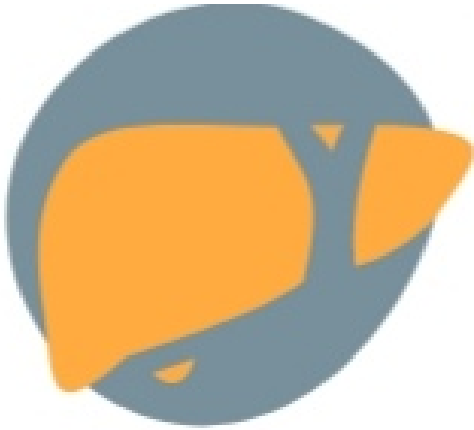
the necrotic area appear in pinkish color between the nodules [Regnerative nodules]





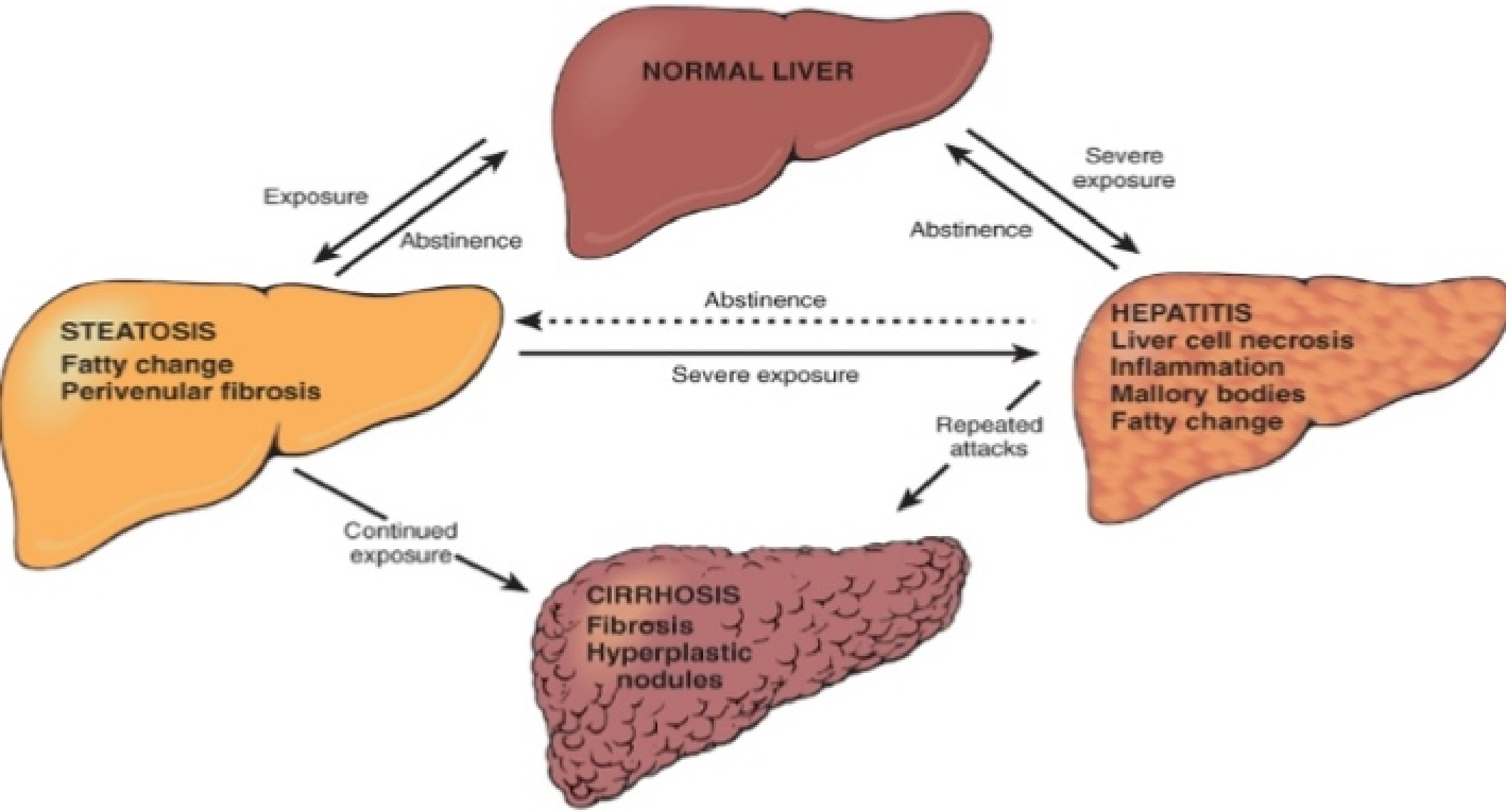
greasy outer surface of the liver





GROSSLY:

- Early: liver is yellow, fatty, & enlarged.
- Persistent damage (years) □ brown, shrunken, nonfatty organ composed of cirrhotic nodules < 0.3 cm in diameter (smaller than is typical for most chronic viral hepatitis


NORMAL LIVER
Exposure
Abstinence
Severe exposure
Abstinence
STEATOSIS
Fatty change
Perivenular fibrosis
Abstinence
Severe exposure
HEPATITIS
Liver cell necrosis
Inflammation
Mallory bodies
Fatty change
Repeated attacks
Continued exposure
CIRRHOSIS
Fibrosis
Hyperplastic nodules

05
CHOLESTATIC SYNDROMES

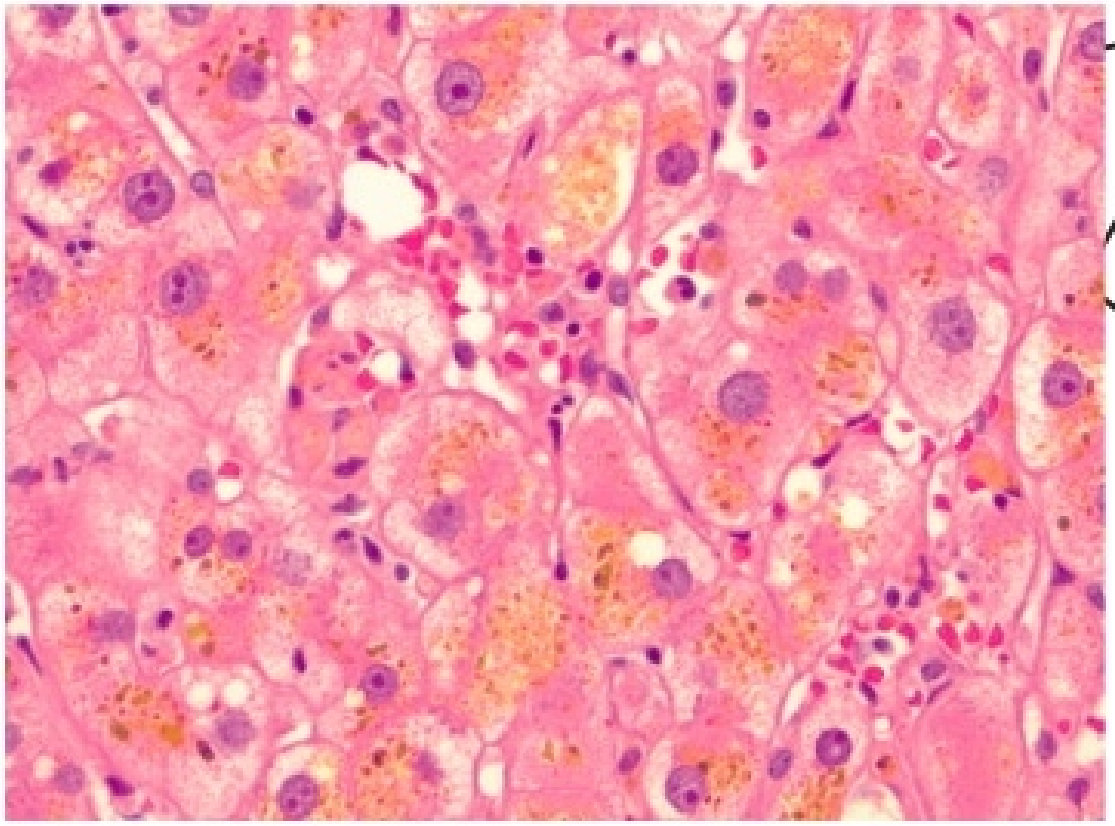
a condition caused by extrahepatic or intrahepatic obstruction of bile channels or by defects in hepatocyte bile secretion.

CHOLESTASIS - Clinically

- Patients may have jaundice, pruritus, skin xanthomas (focal accumulation of cholesterol), or symptoms related to intestinal malabsorption, including nutritional deficiencies of the fat-soluble vitamins A, D, or K. A
- Laboratory finding is elevated serum alkaline phosphatase and γ-glutamyl transpeptidase (GGT), enzymes that are present on the apical membranes of hepatocytes & cholangiocytes.

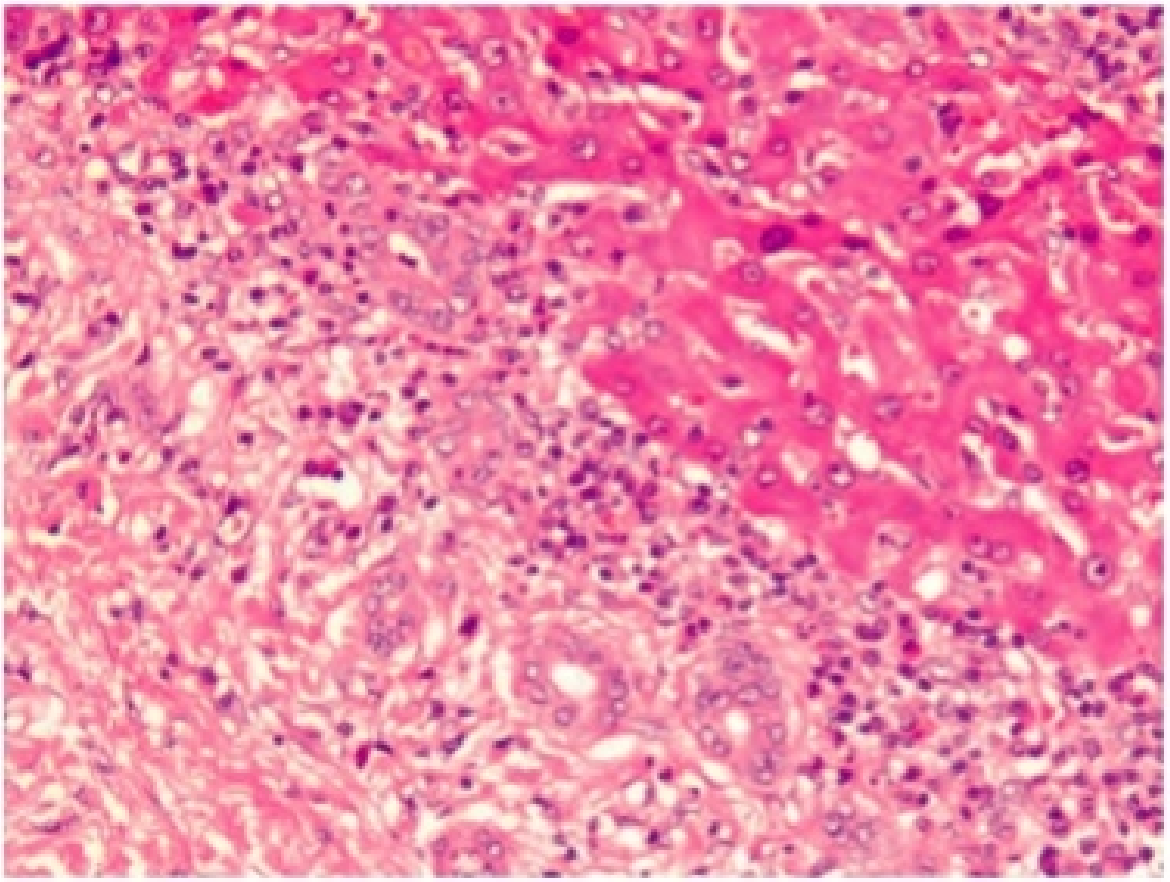
CHOLESTASIS - Morphology

- Depend on its severity, duration, and underlying cause □ accumulation of bile pigment
- Elongated green-brown plugs of bile are visible in dilated bile canaliculi.
- Rupture of canaliculi leads to extravasation of bile, □ quickly phagocytosed by Kupffer cells.
- Apoptotic hepatocytes also may be seen.



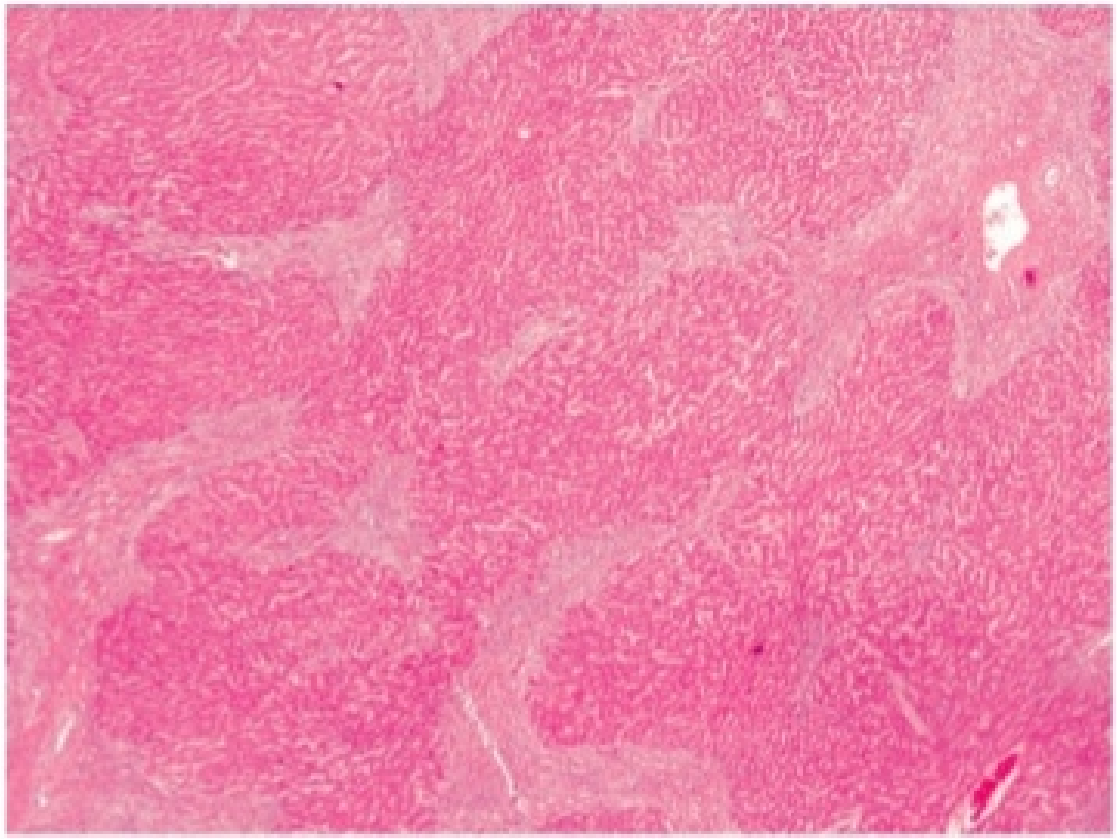
Biliary obstruction - Morphology

- Biliary obstruction, (intrahepatic or extrahepatic) causes distention of upstream bile ducts (dilated).
- Bile ductules proliferate at the portal parenchymal interface, accompanied by stromal edema & infiltrating neutrophils



Biliary obstruction - Morphology

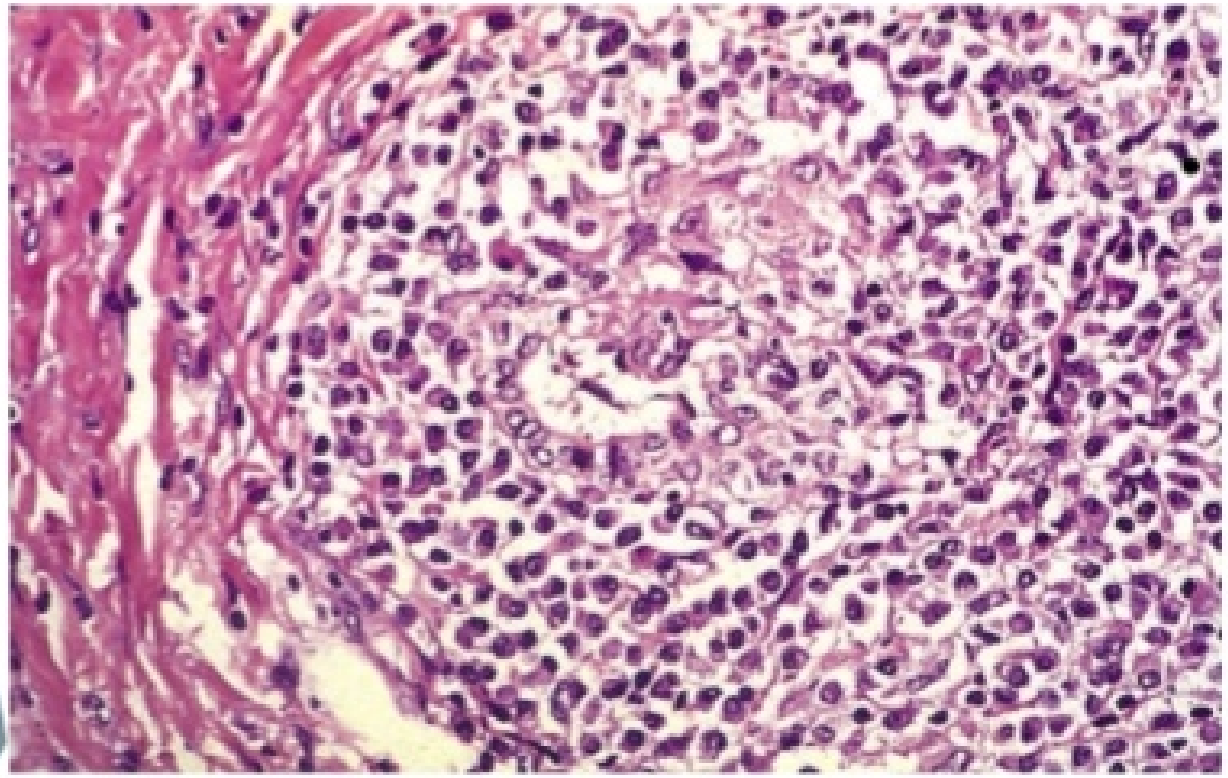
- Left uncorrected, the inflammation and ductular reactions resulting **from chronic biliary obstruction** initiate periportal fibrosis, eventually generating **secondary or obstructive biliary cirrhosis**



06
Autoimmune Cholangiopathies

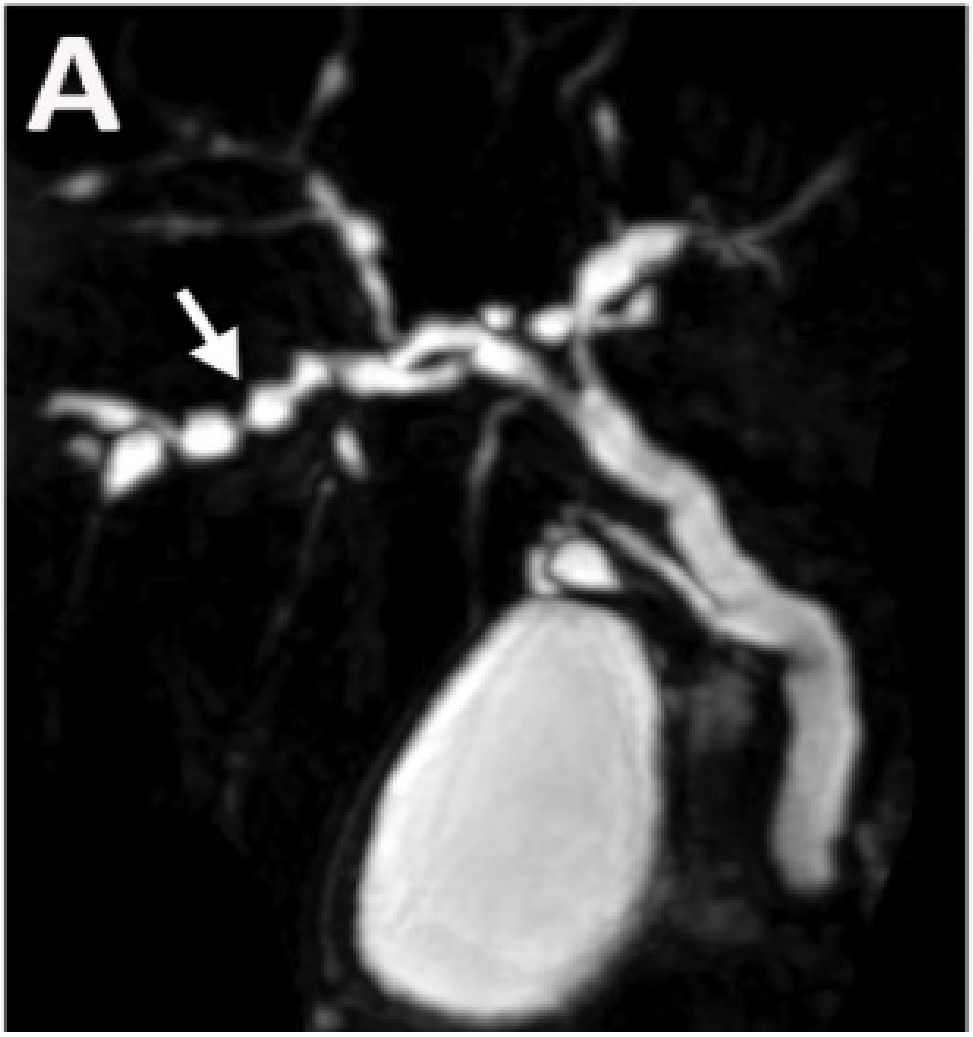
Two distinct immunologically-mediated disorders that involve intrahepatic bile ducts:
Primary biliary cholangitis
Primary sclerosing cholangitis.

PBC – Morphology



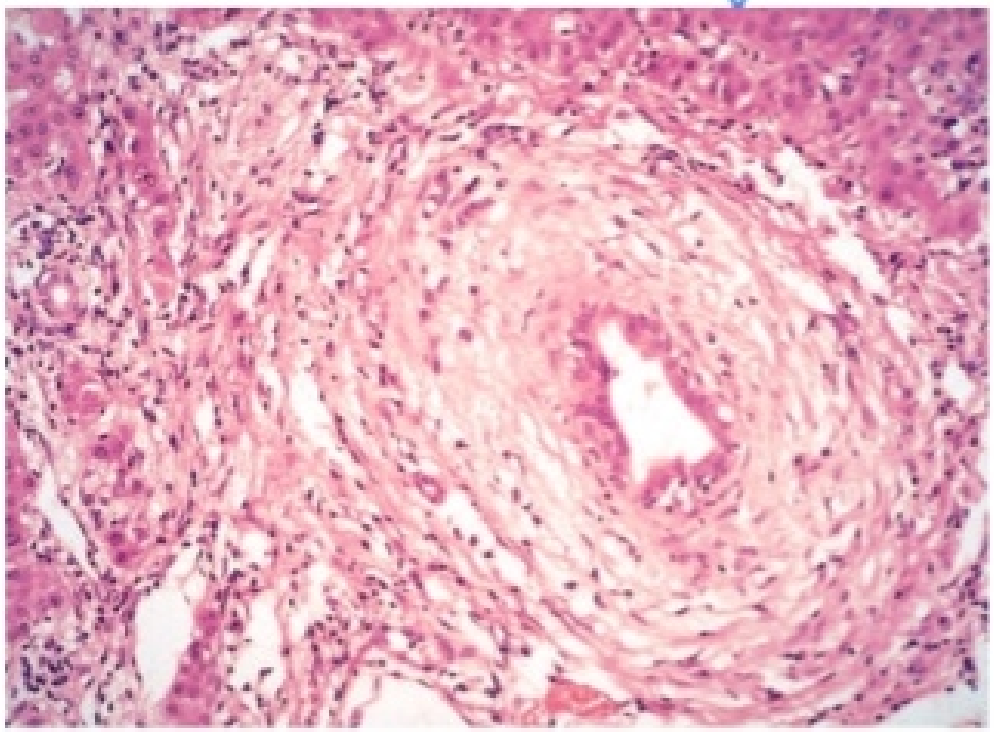
Interlobular bile ducts are actively destroyed by lymphoplasmacytic inflammation with or without granulomas **(the florid duct lesion)**

MRCP:
multiple strictures and a **"string of beads"** appearance of the intrahepatic bile ducts



PSC – Morphology

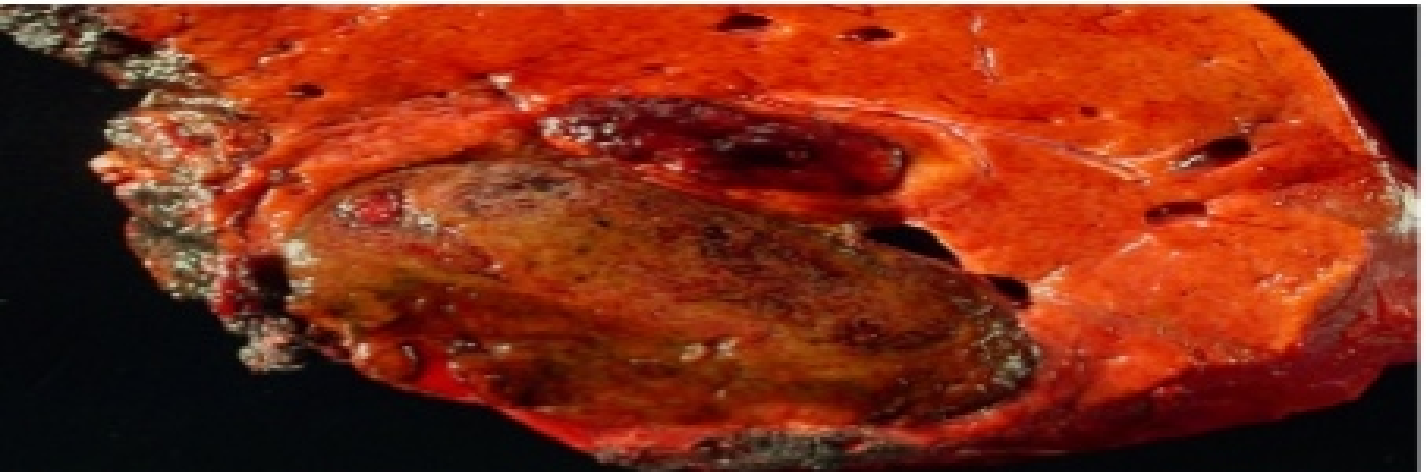
- **Large duct Inflammation:** neutrophils infiltrating into the epithelium superimposed on a chronic inflammatory background.
- Inflamed areas develop strictures as scarring narrows the lumen.
- **Smaller Ducts:** little inflammation & show a striking **circumferential, "onion skin" fibrosis** around an atrophic duct lumen.



07
NODULES AND TUMORS

Benign Neoplasms

- Sex hormone exposure (e.g., oral contraceptive pills, anabolic steroids) markedly increases the frequency of hepatic adenoma, & cessation of exposure leads to tumor regression.

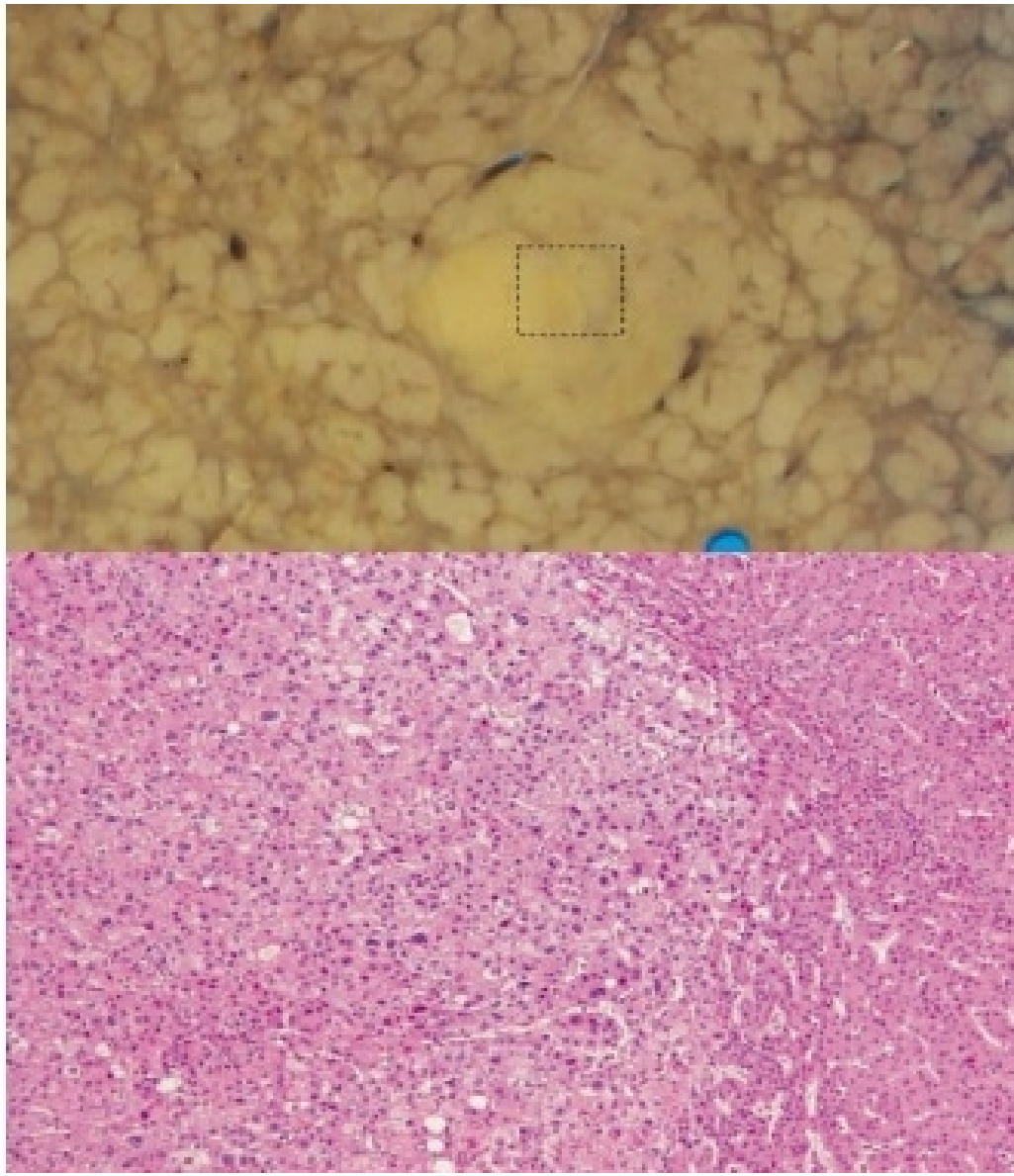


HCC - Morphology

- HCC may appear grossly as:

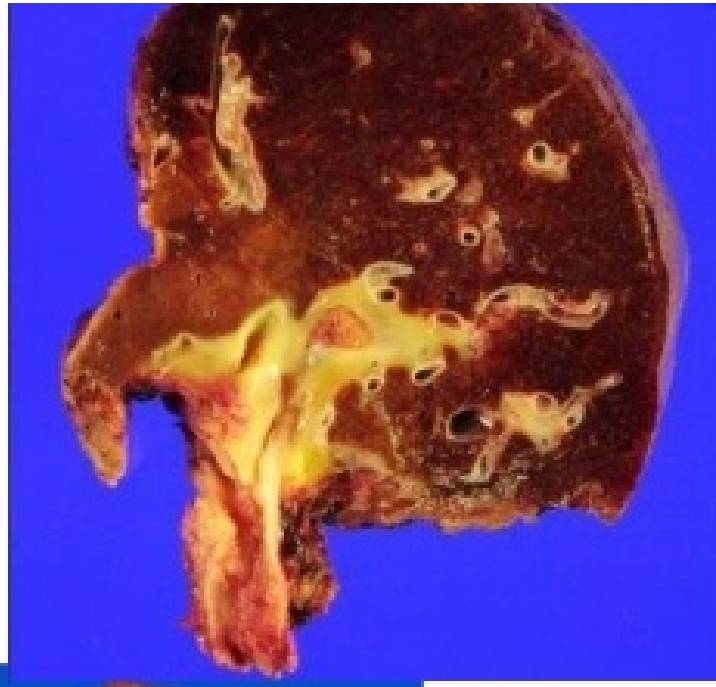
(1) a unifocal (usually large) mass (2) multifocal, widely distributed nodules (3) a diffusely infiltrative cancer

- HCCs range from well differentiated to highly anaplastic lesions.
- Well-differentiatedcells look like normal hepatocytes & grow as thick trabeculae or in pseudoglandular patterns that recapitulate poorly formed, ectatic bile canaliculi.



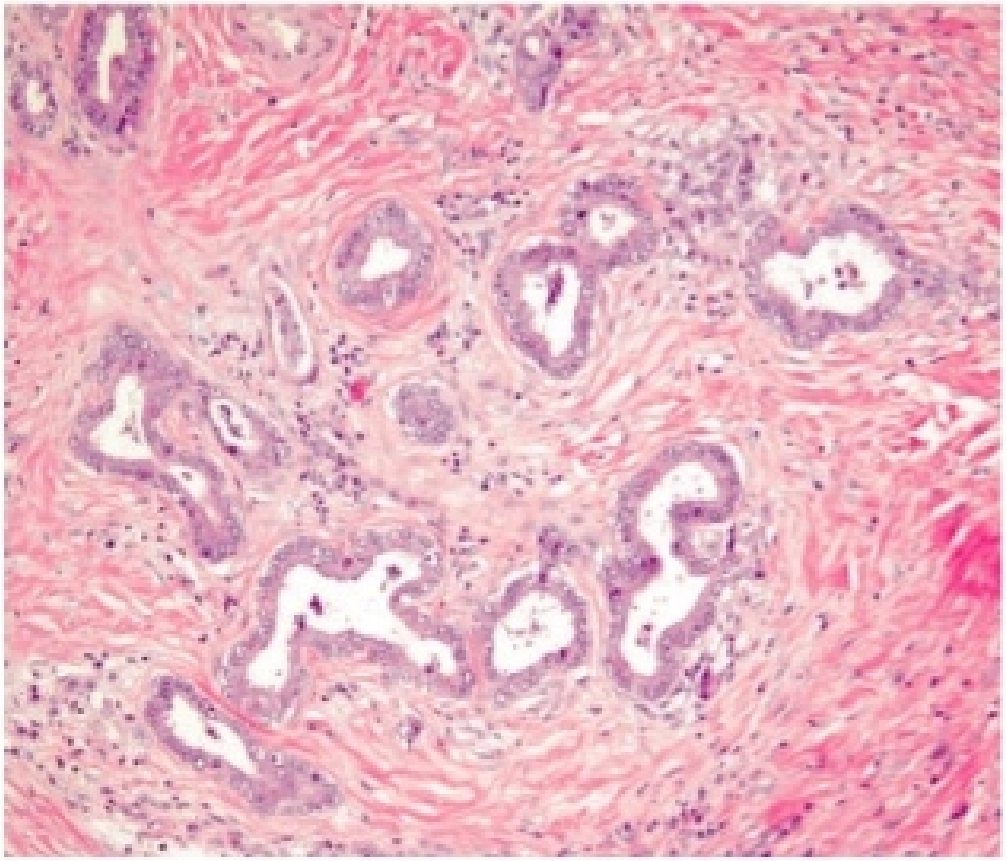
CCA – Morphology and clinical

- Extrahepatic CCA are generally small lesions at diagnosis causing obstruction of the biliary tract early in their course.
- Most firm gray nodules within the bile duct wall; diffusely infiltrative or polypoid.
- Intrahepatic CCA occur in noncirrhotic livers & may track along the intrahepatic portal tract system or produce a single massive tumor.



CCA – Morphology and clinical

- Typical mucin-producing adenocarcinomas glandular/ tubular structures lined by malignant epithelial cells.
- Typically incite marked desmoplasia.
- Lymphovascular invasion & perineural invasion are both common
- Extensive intrahepatic & extrahepatic metastases.

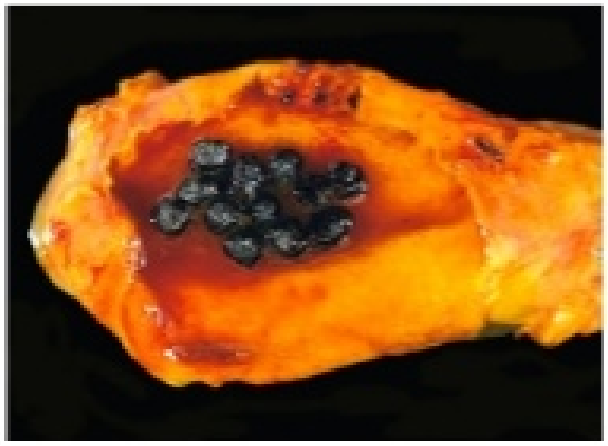


08 Gallbladder Disease

GALLSTONE DISEASE - Stones

- **Cholesterol stones:** exclusively in the gallbladder. Pure cholesterol stones are pale yellow; increasing proportions of calcium carbonate, phosphates, & bilirubin impart gray-white to black discoloration, most often there are several, with faceted surfaces resulting from their apposition.

- **Pigment stones:** arise anywhere in the biliary tree & are classified into black & brown stones. In general, black pigment stones are found in sterile gallbladder bile, while brown stones are found in infected intrahepatic or extrahepatic ducts.



CARCINOMA OF THE GALLBLADDER - Morphology

Two patterns of growth:

- **Infiltrating**: more common & usually appears as a poorly defined area of diffuse wall thickening & induration.
- **Exophytic**: grows into the lumen as an irregular, cauliflower mass, at the same time invades the underlying wall
- Most carcinomas of the gallbladder are adenocarcinomas.