Principles of Liver Pathology

1. Review of normal gross and microscopic anatomy

2. Major pathologic pathways in liver disease
   - Acute hepatitis
   - Chronic hepatitis
   - Fatty liver
   - Cholestasis
   - Cirrhosis
Normal microanatomy of the liver

- Portal fibroblast / myofibroblast
- Limiting plate
- Portal tract
- Canal of Hering
- Progenitor / Stem cell
- Stellate cell (Ito cell)
- Space of Disse
- Artery
- Portal Vein
- Bile duct
- Portal
- Vein
- Pit cell (NK cell)
- Kupffer cell
- Sinusoid
- Central Vein
- Sieve plate
- Normal sinusoid
Transporter proteins

**BSEP** (bile salt export pump)

**FIC-1**
(familial intrahepatic cholestasis-1)

**OATP**
(organic anion transport pump)

tight junction
Liver Function Tests (LFT’s)

Cholestatic enzymes
- Total bilirubin/direct bilirubin
- AP (alkaline phosphatase)
- GGT (gamma glutamyl transferase)
- 5’NT (5’ nucleotidase)

Hepatitic enzymes
- AST (aspartate aminotransferase)
- ALT (alanine aminotransferase)

Synthetic proteins
- Total protein
- Albumin
Hepatitis

Inflammation
+
Hepatocyte Apoptosis/Necrosis

Time Course: Acute / Chronic
Causes: Virus / Drugs
Acute Hepatitis
Chronic Hepatitis

Def.: *Inflammation of the liver continuing without improvement for 6 mos. or longer*
Causes of Chronic Hepatitis

1. Hepatitis viruses: HBV, HCV
2. Autoimmune hepatitis
3. Drugs
4. Metabolic diseases:
   - AAT deficiency
   - Wilson’s disease
5. Cryptogenic
Classification of Chronic Hepatitis

- **Etiology**
  - HBV, HCV, HDV
  - autoimmune
  - drug
  - Wilson's
  - AAT def.

- **Grade of necroinflammation**

- **Stage of fibrosis or cirrhosis**
Ground-glass inclusions (HBsAg) in hepatocytes: chronic HBV
Chronic HCV: portal Lymphoid aggregates

Autoimmune chronic hepatitis
Alpha-1-antitrypsin deficiency

Wilson disease: copper overload

copper and copper-binding protein (orcein stain)
Fatty Liver

• Triglyceride vacuoles in hepatocytes
• Fatty liver is the most common cause of increased serum AST & ALT in the U.S.
• MAJOR CAUSES:
  - alcohol—obesity—diabetes—steroids

Types

| Large droplet (common) (macrovesicular) | Small droplet (uncommon) (microvesicular) |
Steatohepatitis

- Ballooned hepatocytes
- Mallory-Denk body
- Fibrosis (pericentral)
- CV
Cholestasis

*Impaired bile secretion
(stagnation of bile flow in the liver)
CHOLESTASIS: impaired bile secretion

Surgical Jaundice: Large bile duct obstruction

Medical Jaundice: Intrahepatic disease (sepsis/drugs/hepatitis/Bile salt transporter dis.)
Cirrhosis

-Def.: 2 components:
  diffuse fibrosis +
  regenerative nodules

-Multifactorial etiology

-Gross types: Micronodular (≤ 3mm)
  Macronodular (≥ 3 mm)

-Complications:
  - portal HTN
  - liver cell failure
  - HCC
Cirrhosis: Diffuse fibrosis + nodules of regenerative liver

- Diffuse fibrosis
- Thickened liver-cell plates (regenerative hyperplasia)
Activated stellate (Ito) cells in cirrhosis: smooth muscle actin immunostain
Causes of Cirrhosis

- Alcoholic liver disease, 60-70%
- Viral hepatitis, 10%
- Biliary diseases, 5-10%
- Hereditary hemochromatosis, 5%
- Wilson’s disease, rare
- Alpha-1-antitrypsin def., rare
- Cryptogenic cirrhosis, 10-15%
Portal Hypertension

Develops when there is obstruction to the portal blood flow anywhere along its course, with:

- increase in portal pressure >7 mm Hg
- development of collateral circulation (varices)
CLASSIFICATION OF PORTAL HYPERTENSION

post-hepatic

intrahepatic
- presinusoidal
- sinusoidal
- post-sinusoidal

prehepatic
Normal splenoportogram
Cirrhotic liver

Enlarged short gastric vein →
gestic + esoph. varices

Splenoportogram in cirrhosis
RECAP

1. Liver gross + lobule / acinus
3. Acute hepatitis: Hepatitis virus A-E, drugs
4. Chronic hepatitis: def. / causes / grading + staging
5. Fatty liver (large/small droplet), steatohepatitis
6. Cholestasis: bile duct obstruct. / intrahepatic— including transporter proteins
7. Cirrhosis: gross types, causes, complications
8. Portal hypertension: pre-hepatic / INTRAHEPATIC / post-hepatic