The liver is designed to maintain body’s chemical and metabolic homeostasis
Parenchymal Microcirculation

Hepatic vein

Sinusoid

Hepatocyte

Heptic artery (~30%)

Portal vein (~70%)

Lymphatics

Biliary tree
Parenchymal Microanatomy

Image redrawn based on O’Grady et al., Clinical Hepatology, Mosby, 2000.
Parenchymal Microanatomy
Lobular Microanatomy

Lobular Histology
Portal Tract and Central Vein
Morphological Patterns of Hepatic Injury

• Hepatocellular degeneration and intracellular accumulation
  – *Ballooning and foamy degeneration*
  – *Steatosis*

• Necrosis and apoptosis
  – *Councilman bodies (apoptotic hepatocytes)*
  – *Zonal necrosis*
  – *Massive necrosis*

• Inflammation (hepatitis)

• Regeneration

• Fibrosis
  – *Cirrhosis*
Morphological Patterns of Hepatic Injury: *Hepatocellular Damage*
Morphological Patterns of Hepatic Injury: 
*Hepatitis*
Morphological Patterns of Hepatic Injury: 
Cirrhosis (Regeneration + Fibrosis)
Clinical Signs of Hepatic Injury

Clinical Signs of Hepatic Injury

Portal Hypertension and Venous Collaterals

Portal Hypertension → Varices
Clinical Signs of Hepatic Injury

Bilirubin Metabolism and Elimination

1. Heme oxygenase oxidizes heme to biliverdin

2. Biliverdin reductase reduces biliverdin to *unconjugated*, water-insoluble bilirubin, which is carried in blood bound to serum albumin

3. Carrier-mediated transport of unconjugated bilirubin into hepatocytes

4. Bilirubin is *conjugated* to glucoronic acids by uridine diphosphate glucoronyltransferase (UGT) and conjugated bilirubin is transported into bile canaliculi by MRP2

5. Intestinal bacteria deconjugate and breakdown bilirubin into colorless urobilinogens, which are primarily excreted in feces
Causes of Jaundice

• Disorders of bilirubin production or metabolism
  – Unconjugated:
    • Overproduction (hemolysis, ineffective hematopoiesis)
    • Decreased conjugation (newborns, Crigler-Najjar, Gilbert)
  – Conjugated:
    • Impaired canalicular transport (Dubin-Johnson)

• Liver diseases
  – Acute or chronic hepatocellular injury
  – “Intrahepatic cholestasis”

• Obstruction of bile ducts (“extrahepatic cholestasis”)
  – Gallstones
  – Other masses
  – Inflammation/infection
Intrahepatic Cholestasis
Extrahepatic Cholestasis
Viral Hepatitis
Hepatitis A

• The most common cause of viral hepatitis worldwide.
• Estimated 75,000 clinical cases/yr in the US.

Clinical Characteristics of Hepatitis A

Hepatitis B

• ~300 million infected worldwide, of whom 250,000 die of complications.
• Sexual transmission is the major mode of spread in developed countries.
• Perinatal transmission occurs in 90% of infants born to HBeAg+ mothers.

Clinical Outcomes of HBV Infection

Lifecycle of HBV

Modified from O’Grady et al., Clinical Hepatology, Mosby, 2000.
Hepatitis C

- The global prevalence of *chronic* HCV is ~3%.
- 4 million HCV carriers in US; 5 million in Europe.
- Transmission as a blood-borne pathogen.

Clinical Outcomes of HCV Infection

## Drug and Toxin-Induced Liver Disease

<table>
<thead>
<tr>
<th>Pattern of Damage</th>
<th>Example of Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microvesicular steatosis</td>
<td>Tetracycline, ethanol, aspirin</td>
</tr>
<tr>
<td>Macrovesicular steatosis</td>
<td>Ethanol, methotrexate</td>
</tr>
<tr>
<td>Centrilobular necrosis</td>
<td>Tylenol, rifampin</td>
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<tr>
<td>Massive necrosis</td>
<td>Halothane, isoniazid</td>
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<tr>
<td>Hepatitis</td>
<td>Isoniazid, methyldopa</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>Ethanol, methotrexate</td>
</tr>
<tr>
<td>Granulomas</td>
<td>Sulfonamides, quinine</td>
</tr>
<tr>
<td>Cholestasis</td>
<td>Chlorpromazine, steroids</td>
</tr>
</tbody>
</table>
Drug and Toxin-Induced Liver Disease
Alcoholic Liver Disease
Alcoholic Liver Disease