Liver, Gallbladder, and Pancreas Pathology
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GI Pathology Outline
- Esophagus
- Stomach
- Intestine
- Liver
  - Hepatitis
  - Alcoholic liver disease
  - Hemochromatosis
  - Wilson disease
  - Carcinoma

Viral Hepatitis
- Caused by Hepatitis A, B, or C viruses
- Some cases asymptomatic
- Some cases symptomatic:
  - Acute (jaundice)
  - Chronic (may lead to cirrhosis and liver failure)
  - Fulminant (liver failure)

<table>
<thead>
<tr>
<th></th>
<th>Hepatitis A</th>
<th>Hepatitis B</th>
<th>Hepatitis C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transmission</td>
<td>Fecal-oral</td>
<td>Body fluids</td>
<td>Body fluids</td>
</tr>
<tr>
<td>Chronic Hepatitis</td>
<td>None</td>
<td>5%</td>
<td>&gt;85%</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Other stuff</td>
<td>50% of people &gt; 50 are +</td>
<td>Vaccine effective</td>
<td>New drugs are promising</td>
</tr>
<tr>
<td>Bottom line</td>
<td>Benign, self-limited disease</td>
<td>Most recover; small % die</td>
<td>Nasty! Almost 10% die</td>
</tr>
</tbody>
</table>
Chronic viral hepatitis

• Ground-glass hepatocytes

Bilirubin metabolism and elimination

- Yellow discoloration of the skin due to hyperbilirubinemia (excess bilirubin in the blood)
- The amount of bilirubin in the blood depends on the rate of:
  - bilirubin production (from breakdown of red cells)
  - bilirubin uptake by the liver
  - bilirubin conjugation by the liver
  - bilirubin excretion into bile ducts

Jaundice

- Conjugated bilirubin = water-soluble (excreted in urine)
- Unconjugated bilirubin = insoluble (toxic to tissues!)

Hyperbilirubinemia

- Causes of conjugated hyperbilirubinemia:
  - blockage in bile flow (e.g., tumor near bile duct)
  - congenital disorders affecting bile excretion
- Causes of unconjugated hyperbilirubinemia:
  - excess bilirubin production (e.g., massive hemolysis)
  - impaired bilirubin uptake by liver
  - Impaired bilirubin conjugation
Icterus

Laboratory Tests

<table>
<thead>
<tr>
<th>Hepatocyte integrity</th>
<th>Serum aspartate aminotransferase (AST)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serum alanine aminotransferase (ALT)</td>
</tr>
<tr>
<td>Biliary function</td>
<td>Serum bilirubin (total and direct)</td>
</tr>
<tr>
<td></td>
<td>Serum alkaline phosphatase</td>
</tr>
<tr>
<td>Hepatocyte function</td>
<td>Serum albumin</td>
</tr>
<tr>
<td></td>
<td>Prothrombin time</td>
</tr>
</tbody>
</table>

Cirrhosis

- Fibrotic, nodular liver
- Causes: alcoholism, hepatitis
- Leads to portal hypertension and liver failure
- Increased risk of liver carcinoma

Portal Hypertension

- Impaired flow of blood through liver
- Blood backs up in portal system
- Most common cause: cirrhosis
- Four main clinical consequences
  - ascites (↑ fluid in peritoneal cavity)
  - esophageal varices (dilated esophageal veins)
  - congestive splenomegaly
  - hepatic encephalopathy
Consequences of portal hypertension

- Esophageal varices
- Caput medusae (dilated periumbilical veins)
- Medusa
- End point of severe liver disease
- Causes: fulminant hepatitis, cirrhosis, drug overdose
- Symptoms: jaundice, edema, bleeding, hyperammonemia
- Multiple organ-system failure
  - Hepatic encephalopathy
  - Hepatorenal syndrome

Liver Failure

- Hematomas, gingival bleeding
- Jaundiced mucosa
- Glossitis (in alcoholic hepatitis)
- Reduced healing after surgery
Alcoholic Liver Disease

- 100,000 - 200,000 deaths/year
- Effects on liver: steatosis, hepatitis, cirrhosis
- How much do you need to drink?
  - Short-term ingestion of 8 beers/day \(\rightarrow\) reversible steatosis
  - Long-term ingestion of 5 beers/day \(\rightarrow\) severe injury

More youth with irreversible liver disease now

Alcoholic liver disease

Alcoholic steatosis

Alcoholic hepatitis: inflammation and Mallory bodies

Alcoholic cirrhosis
Alcoholic Liver Disease

- Abstinence: 5ys is 90%
- Continued drinking: 5ys drops to 50-60%
- Causes of death in end-stage alcoholism:
  - Liver failure
  - Massive GI bleed
  - Infection
  - Hepatorenal syndrome
  - Hepatocellular carcinoma

Hereditary Hemochromatosis

- Autosomal recessive disease: ↑ body iron
- Cause: mutations in hemochromatosis gene (regulates iron absorption)
- Cirrhosis, skin discoloration, liver carcinoma
- Early detection and treatment (phlebotomy, iron chelators) = normal life expectancy

Wilson Disease

- Autosomal recessive disease: ↑ body copper
- Cause: mutation in gene regulating copper excretion
- Symptoms: acute and chronic liver disease, neuropsychiatric manifestations, Kayser-Fleisher rings in cornea
- Treatment: copper chelation therapy

Hepatocellular Carcinoma

- Strongly associated with hepatitis B and C, chronic liver disease, and aflatoxins
- Rapid increase in liver size, worsening ascites, fever and pain
- ↑↑↑ alpha fetoprotein level
- Median survival 7 months (death from bleeding, liver failure, cachexia)
Hepatocellular carcinoma

- Most common malignancy in the liver
- Usually multiple lesions
- Most common primaries: colon, lung, breast, pancreas, stomach.

Metastatic Carcinoma

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- Esophagus
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- Gallbladder
  - Cholelithiasis
  - Cholecystitis

Cholelithiasis

- Common! (10% of adults in US)
- Cholesterol stones: Female, Fat, Fertile, Forty
- Pigment (bilirubin) stones: Asian countries, hemolytic anemia and biliary infections
- Symptoms: None, or excruciating pain
- Complications: cholecystitis (inflamed gallbladder), perforation, obstruction, pancreatitis
Cholesterol gallstones

Pigmented gallstones

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Normal Pancreas

- Exocrine pancreas
  - Makes enzymes for digestion
  - Diseases: pancreatitis, cystic fibrosis, tumors
- Endocrine pancreas
  - Makes insulin, glucagon, other hormones
  - Diseases: diabetes, tumors

Acute Pancreatitis

- Acute inflammation and reversible destruction of pancreas
- Symptoms: abdominal pain radiating to back
- Main causes: alcoholism, gallstones
- Labs: elevated serum amylase and lipase
- Prognosis: Most recover, but 5% die in first week
Chronic Pancreatitis

- Longstanding, irreversible pancreatic destruction
- Most are alcohol related, some idiopathic
- Symptoms: silent, or bouts of jaundice and pain
- Prognosis: poor (50% mortality over 20 years)

Pancreatic Carcinoma

- 4th leading cause of cancer death in US
- Biggest risk factor: smoking
- Highly invasive
- Silent until late; then pain, jaundice
- Very high mortality: Sys <5%