Liver, Gallbladder, and Pancreas Pathology
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GI Pathology Outline

- Esophagus
- Stomach
- Intestine
- Liver
- Gallbladder
- Pancreas
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><strong>Transmission</strong></td>
<td>Fecal-oral</td>
<td>Body fluids, Needles</td>
<td>Body fluids, Needles</td>
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<tr>
<td><strong>Chronic Hepatitis</strong></td>
<td>None</td>
<td>5%</td>
<td>&gt;85%</td>
</tr>
<tr>
<td><strong>Carcinoma</strong></td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Other stuff</strong></td>
<td>50% of people &gt; 50 are +</td>
<td>Vaccine effective</td>
<td>New drugs are promising</td>
</tr>
<tr>
<td><strong>Bottom line</strong></td>
<td>Benign, self-limited disease</td>
<td>Most recover; small % die</td>
<td>Nasty! Almost 10% die</td>
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</tbody>
</table>
Acute viral hepatitis
Chronic viral hepatitis
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
Conjugated bilirubin = water-soluble (excreted in urine)

Unconjugated bilirubin = insoluble (toxic to tissues!)

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
Jaundice
Icterus
<table>
<thead>
<tr>
<th>Laboratory Tests</th>
</tr>
</thead>
</table>
| Hepatocyte integrity | Serum aspartate aminotransferase (AST)  
|                    | Serum alanine aminotransferase (ALT) |
| Biliary function   | Serum bilirubin (total and direct)  
|                   | Serum alkaline phosphatase |
| Hepatocyte function| Serum albumin  
|                  | Prothrombin time |
Cirrhosis

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

• End point of severe liver disease

• Causes: fulminant hepatitis, cirrhosis, drug overdose

• Symptoms: jaundice, edema, bleeding, hyperammononemia

• Multiple organ-system failure
  • Hepatic encephalopathy
  • Hepatorenal syndrome
Oral Manifestations of Liver Injury

- 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 → reversible steatosis
  - Long-term ingestion of 5 beers/day → severe injury
More youth with irreversible liver disease now
Alcoholic liver disease

STEATOSIS
Fatty change
Perivenular fibrosis

NORMAL LIVER

SEVERE EXPOSURE
Abstinence

HEPATITIS
Liver cell necrosis
Inflammation
Mallory bodies
Fatty change

CIRRHOSIS
Fibrosis
Hyperplastic nodules

CONTINUED EXPOSURE
Abstinence
Repeted attacks
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
Grey-brown skin discoloration in hemochromatosis
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
Hepatocellular carcinoma

Hepatocellular carcinoma
Metastatic 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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- Liver
- 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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- Pancreas
  - Pancreatitits
  - Carcinoma
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
Cell injury (alcohol)

Obstruction (gallstones)

Increased blood amylase and lipase

Acute pancreatitis
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: 5ys <5%
Pancreatic carcinoma
Pancreatic carcinoma