1. Hepatobiliary System Part 1

Hepatobiliary System
Part 1

Basic Human Pathology II, 2008

Michael A. Kahn, DDS
Professor and Chairman
Department of Oral and Maxillofacial Pathology
Tufts University School of Dental Medicine

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2. Liver - Functions

Liver - Functions

- **Metabolic**
  - Glucose homeostasis – glycogenolysis, gluconeogenesis
- **Synthetic**
  - Albumin, blood coagulation factors, complement, specific binding proteins for iron, copper, vitamin A, etc.
- **Storage capacity**
  - Glycogen, triglycerides, iron, copper, lipid soluble vitamins
- **Catabolic processes**
  - Hormones, serum proteins
- **Excretory function**
  - Bile – repository for products of heme catabolism and vital for absorption of fat in the small intestine

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3. Liver Diseases – Overview

Liver Diseases – Overview

- Jaundice
- Hepatic Failure
- Hemodynamics and Vascular Abnormalities
- Hereditary Disorders
- Infections
  - Viruses, bacteria, parasites
- Toxins
  - Alcohol and drug-related
- Tumors
  - Primary - benign and malignant
  - Metastatic

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4. Normal Liver

Normal Liver

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5.

Normal Liver – Histology

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6.

Normal Liver - Histology

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7. Normal Liver - Histology

Normal Liver - Histology

Sinusoids and Kupffer cells

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Bile canaliculi

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8. Five Basic Liver Responses to Injury

Five Basic Liver Responses to Injury

- Fatty change
  - Seen in diabetes mellitus, alcoholism, Reye’s syndrome, pregnancy, obesity

- Cholestasis (flow of bile interrupted)
  - Intra-acinar – viral hepatitis, drug, alcohol, pregnancy
  - Extra-acinar – primary biliary cirrhosis, tumors, polycystic liver disease, sclerosing cholangitis

- Liver cell necrosis
  - Spotty, zonal, piecemeal, bridging, and massive patterns
  - Councilman bodies (dead, shrunken, eosinophilic hepatocytes following apoptosis)

- Fibrosis
  - Scarring between lobules
  - Small and large nodules of cells
  - Disrupted overall architecture

- Storage of abnormal material

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9. Liver Cell Necrosis – Councilman Body

Liver Cell Necrosis – Councilman Body

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10. Fatty Change

Fatty Change

- Alcoholic fatty liver
  - Alcoholism
- Nonalcoholic fatty liver (NAFL)
  - Indolent and under-appreciated
  - Asymptomatic OR
  - Fatigue, malaise OR
  - Symptoms of chronic liver disease due to
    - Obesity
    - Diabetes mellitus, type 2
    - Reye’s syndrome
    - Pregnancy

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11. Jaundice (icterus)

Jaundice (icterus)

- Excess bilirubin accumulation in the skin, oral mucosa, sclerae → yellow discoloration
- Elevated bilirubin → 2.5 mg/dL/hour
- Hyperbilirubinemia
  - Unconjugated bilirubin
    - Tight protein binding in serum → complexed to albumin (lipid soluble; cannot be excreted in urine)
    - Blood to liver [brain damage - kernicterus]
  - Conjugated bilirubin
    - In liver, conjugated to glucouronic acid (water soluble) and excreted in bile → gut → urobilinogen → most in feces, some in urine

12. Normal Bilirubin Metabolism and Excretion

Normal Bilirubin Metabolism and Excretion (elimination)

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13. Jaundice

Jaundice

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Source: Courtesy of Centers for Disease Control and Prevention

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14. Jaundice

Jaundice

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15. Unconjugated Hyperbilirubinemia – Kernicterus Brain

Unconjugated Hyperbilirubinemia – Kernicterus Brain

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16. Causes of Hyperbilirubinemia

Causes of Hyperbilirubinemia

- Hereditary lack of enzyme, protein so abnormal metabolism
  - Gilbert’s syndrome, Dubin-Johnson syndrome, Crigler-Najjar syndrome
- Intrahepatic cholestasis
  - Drugs
  - Pregnancy-associated
- Liver damage
- Obstruction
  - Tumor
  - Stricture
  - Gallstones in bile ducts

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17. Hereditary Disorders of Bilirubin Metabolism

- Gilbert’s syndrome
  (≤ 7% of population)
  - Autosomal dominant
  - **Unconjugated** hyperbilirubinemia
  - Deficiency of glucuronyl transferase and inadequate uptake of bilirubin
  - Result: → mild, no morbidity

- Crigler-Najjar syndrome
  - Autosomal recessive
  - Neonates
  - Complete absence of glucuronyl transferase
  - Result: → ranges from yellow discoloration to death

- Dubin-Johnson syndrome
  - Autosomal recessive
  - **Conjugated** hyperbilirubinemia
  - Lack transport protein
  - Result: → enlarged and pigmented liver

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18. Liver Failure

- **Chronic hepatic disease is the most common cause**
  - Chronic active hepatitis
  - Widespread necrosis from severe damage of hepatocytes (liver cells)
    - Alcohol, carbon tetrachloride, poisonous mushrooms, acetaminophen

- **Acute liver disease less common cause but more deadly (80% die)**
  - Multi-organ failure, adult respiratory distress syndrome (ARDS), acute renal failure, cirrhosis

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19. Liver – Massive Necrosis

Liver – Massive Necrosis

Small, bile stained and soft with wrinkled capsule

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20. Liver - Massive Necrosis

Liver - Massive Necrosis

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Acetaminophen ingestion

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21. Hepatic Failure Consequences

Hepatic Failure Consequences

- Jaundice
- Musty odor of breath and urine
- Encephalopathy
- Renal failure
- Prolonged prothrombin time (impaired hepatic synthesis of coagulation factors)
- Palmar erythema
- Spider angiomas
- Gynecomastia
- Testicular atrophy
- Weight loss
- Muscle wasting
- Pruritis
- Malabsorption
- Hypoalbuminemia
- Hypercholesterolemia
- Anemia
- Coma (hepatic encephalopathy)

22. Hemodynamic and Vascular Abnormalities of the Liver

Hemodynamic and Vascular Abnormalities of the Liver

- Chronic passive congestion
  - Associated with right-sided heart failure
  - Gross
    - Nutmeg liver
    - Enlarged due to back pressure from systemic veins to hepatic veins — accentuation of the lobular pattern; variegated, mottled red
  - Common postmortem finding
- Central hemorrhagic necrosis
  - May be seen in severe heart failure
- Cardiac sclerosis
  - Sequel of chronic passive congestion and central hemorrhagic necrosis
- Infarctions
  - Rare due to liver’s double blood supply (hepatic artery and portal vein) and rich anastomoses of veins in its sinusoids
23. Chronic Passive Congestion - Nutmeg Liver

Chronic Passive Congestion - Nutmeg Liver

Centrilobular Hemorrhagic Necrosis

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Variegated, mottled red

Suffused with RBCs; hepatocytes not readily visible

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24. Liver Infarct

Liver Infarct

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25. Hemodynamic and Vascular Abnormalities of Liver

Hemodynamic and Vascular Abnormalities of Liver

- **Hepatic vein thrombosis (Budd-Chiari syndrome)**
  - Rare, acute or insidious
  - Post-sinusoidal
  - Hepatic vein obstruction resulting in a chronic congested liver, portal hypertension and jaundice
  - May be seen in many unrelated conditions
    - Ex. neoplasms invading hepatic veins, intrahepatic infections
    - All provoke clotting either through platelet activation, abnormal platelet function or activation of the extrinsic clotting system

26. Budd-Chiari Syndrome

Budd-Chiari Syndrome

Thrombosis of the major hepatic vein causing extreme blood retention in the liver (i.e., congestion)
27. Hemodynamic and Vascular Abnormalities of Liver

Hemodynamic and Vascular Abnormalities of Liver

- **Portal vein thrombosis and obstruction**
  - Extrahepatic causes
    * Renal cell carcinoma
    * Pancreatitis
    * Sepsis
  - Intrahepatic causes
    * Cirrhosis
    * Primary or secondary neoplastic invasion
  - Clinical features
    * Portal hypertension and splenomegaly

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28. Hemodynamic and Vascular Abnormalities of Liver

Hemodynamic and Vascular Abnormalities of Liver

- **Portal hypertension** - - - -> continued elevation in portal venous pressure (back pressure) - - - -> splenomegaly and ascites
  - New channels open between portal and systemic veins
    - - - -> varices of lower esophagus, umbilicus (‘caput medusae’) and anus (hemorrhoids)
  - Causes (categorized by location of obstructed flow)
    * Presinusoidal – before the portal tracts
      - Red (Zahn) infarcts (wedge-shaped)
      - Transplant, thrombus, tumors
    * Sinusoidal – most common
      - Cirrhosis; polycystic disease
    * Postsinusoidal
      - Budd-Chiari syndrome, right-side heart failure

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29. Portal Hypertension $\rightarrow$ Caput Medusae

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30. Portal Hypertension $\rightarrow$ Red (Zahn) Infarct

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Clinical Consequences of Portal Hypertension

Most important are:
- Hepatic encephalopathy
- Ascites
- Esophageal varices
- Splenomegaly

Hepatic Circulatory Disorders

Hepatic Circulatory Disorders – Forms and Clinical Manifestations

**Postsinusoidal**
- Hepatic vein outflow obstruction
  - Hepatic vein thrombosis (Budd-Chiari syndrome)
  - Veno-occlusive disease

**Sinusoidal**
- Impaired intrahepatic blood flow
  - Cirrhosis
  - Sinusoid occlusion
  - Systemic circulatory compromise

**Presinusoidal**
- Impaired portal vein inflow
  - Portal vein obstruction by thrombosis or tumor
- Impaired hepatic artery inflow
  - Complications of liver transplantation

Manifestations:
- Ascites
- Hepatomegaly
- Abdominal pain
- Elevated transaminases
- Jaundice
- Ascites (cirrhosis)
- Esophageal varices (cirrhosis)
- Elevated transaminases

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33.

Viral Hepatitis

- Hepatitis = acute or chronic inflammation of the liver caused by
  - Viral infections
  - Autoimmune disorders
  - Drug reactions
  - Alcohol

- Six types of hepatotropic viruses
  - A – fecal-oral contamination
  - E – fecal-oral waterborne
  - B, C, D, & G – parenteral transmission

- Range of clinical symptoms
  - Asymptomatic
  - Acute hepatitis with or without jaundice
  - Massive liver necrosis
  - Acute liver failure
  - Chronic hepatitis
  - Chronic carrier state

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34.

Viral Hepatitis

- Gross specimen
  - Liver is enlarged

- Histology
  - Coagulative necrosis
  - Increased eosinophilia

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35. Hepatitis A (HAV)

Hepatitis A (HAV)

- Self-limited
- Caused by SS RNA virus (2-6 wk. incubation)
  - Picornavirus
- Infection identified by HAV-specific antibodies
  - Confers subsequent immunity
- Usual route of infection is fecal-oral transmission by contaminated food (e.g., mollusks)
- Complete recovery with return to normal liver function tests
- Transient viremia so transmission risk is low
- Does not become chronic hepatitis (only acute)

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36. Sequence of Serological Markers in Hepatitis A

Sequence of Serological Markers in Hepatitis A

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37. Hepatitis B (HBV)

Hepatitis B (HBV)

- Caused by a DS DNA virus
  - Hepadnavirus
  - Virions are called Dane particles
- Incubation 1-6 months (avg. = 2 months)
- Transmission - parenteral
  - Blood
  - Semen
  - Saliva
    - Close physical contact with break in skin or mucous membranes
  - Sexually transmitted diseases
  - Crosses placenta to newborn of infected mother by exposure to maternal blood during the birth process

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38. Hepatitis B

Hepatitis B

Possible Infection Sequelae
- Acute hepatitis
  - Self-limiting
  - Most common
  - Life long immunity
- Carrier state
  - Asymptomatic
- Chronic persistent disease
- Chronic active disease
- Fulminant hepatitis
  - Massive necrosis of liver cells
- Hepatocellular carcinoma

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39. Hepatitis B

Hepatitis B

- Associated antigens
  • Core antigen (HBeAg)
  • Surface antigen (HBsAg) – i.d. in blood for diagnosis and indicates current infection
    - When present 200-fold greater risk of hepatocellular carcinoma
    - Disappears after 6 months in the majority of patients
  • HBeAg-associated with core and indicates infectivity

- Antibodies
  • Antibodies to surface antigen (Anti-HBs)
    - Considered protective, persists for life
  • Antibodies to HBeAg (Anti-HBc) are not protective
  • Antibodies to HBeAg (Anti-HBe)
    - Associated with low risk of infectivity

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40. Sequence of Serologic Markers

Sequence of Serologic Markers in Acute Hepatitis B Infection

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41. Potential Outcomes of Hepatitis B in Adults

Potential Outcomes of Hepatitis B in Adults
(annual frequencies in U.S.)

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42. Hepatitis C

Hepatitis C

Caused by a positive-strand RNA virus
- Flavivirus
- Most cases previously would have been called non-A, non-B hepatitis
- Often cannot recognize source of infection (40-50%)

- Incubation period 2-26 weeks (peak onset 6-8 weeks)
  - Antibody detected by ELISA

- Most often mild and anicteric but occasionally severe with fulminant hepatic failure
  - Asymptomatic OR
  - Fever, malaise, jaundice

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43. Hepatitis C

Hepatitis C

- Transmission parenteral and an important cause of post-transfusion hepatitis
- 15% recover after about 2 months
- 85% develop chronic hepatitis with periods of remission and relapse
  - Most -> chronic active hepatitis -> cirrhosis (20-25%)
- Increased risk of liver cancer (hepatocellular carcinoma)
- By 2008, expected to exceed 22,000 deaths per year
  - Currently about 14,000 per year

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44. Potential Outcomes of Hepatitis C Infection in Adults

Potential Outcomes of Hepatitis C Infection in Adults

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45. Hepatitis D

Hepatitis D

- **Caused by delta agent**
  - Protein capsule surrounding low-molecular weight RNA
  - Defective virus that requires the presence of HBV (antigen coat) for assembly, replication
    - $\rightarrow$ infection
  - Causes disease only in the presence of HBV infection (co-infection vs. superinfection)
    - Can cause quiescent HBV to suddenly appear

- Especially prevalent in drug users and dialysis patients since same mode of transmission as HBV (i.e., parenteral)
  - Chronic HDV seldom resolves
  - $> 60\%$ develop cirrhosis

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46. Differing Clinical Consequences

Differing Clinical Consequences of the Two Patterns of HDV and HBV infection

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47. **Hepatitis E**

Hepatitis E

- Caused by SS RNA virus
  - Calicivirus
- Transmission by fecal-oral route (contaminated water)
  - Most common in India, Nepal, Pakistan, and S.E. Asia
- Acute epidemics of acute, self-limited hepatitis
  - Incubation --- > mild infection with jaundice
  - Does not evolve into chronic hepatitis or carcinoma
  - During pregnancy --- > sometimes acute fulminant hepatitis

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48. **Hepatitis G**

Hepatitis G

- Discovered in 1995
- In plasma of patients with chronic, non A - E hepatitis
- Small minority without a defined viral cause
- Blood transfusion most often
- Note: in 1994 Hepatitis ‘F’ was claimed to be discovered but still not confirmed

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49. Acute Viral Hepatitis

Acute Viral Hepatitis

- Icteric or anicteric
- Gross
  - Enlarged liver with a tense capsule
- Histology
  - Ballooning degeneration of hepatocytes and liver cell necrosis
- Signs and symptoms (last 4 - 6 weeks)
  - Malaise, anorexia, fever, nausea, upper abdominal pain and hepatomegaly => jaundice, putty-colored stools and dark urine
  - In HBV – urticaria, arthralgias, arthritis, vasculitis and glomerulonephritis
  - Elevated transaminases and alkaline phosphatase
    - Elevated serum bilirubin if icteric

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50. Acute Viral Hepatitis

Acute Viral Hepatitis

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Ballooning degeneration of hepatocytes

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51. Chronic Hepatitis

Chronic Hepatitis

- Occurs in 5-10% of HBV infections and > 50% of HCV
- Does not occur in HAV
- More in very old or very young
- More in males, immunocompromised hosts, Down syndrome, and dialysis patients
- Most due to chronic persistent hepatitis

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52. Chronic Hepatitis

Chronic Hepatitis

- Chronic persistent hepatitis
  - Benign, self-limited; prolonged recovery
  - Asymptomatic except elevated transaminases
- Chronic active (aggressive) hepatitis
  - Chronic inflammation with hepatocyte destruction
  - Cirrhosis and liver failure (portal tract areas)
  - Caused by HBV, HCV, HDV, drug toxicity, Wilson’s disease, alcohol, \( \alpha_1 \)-antitrypsin deficiency and autoimmune hepatitis
  - Fatigue, fever, malaise, anorexia, elevated liver function tests
  - Diagnosis by liver biopsy
  - Histology is aggressive in appearance

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53. Chronic Active Hepatitis

Chronic Active Hepatitis

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Piecemeal (periportal) necrosis – scattered liver cell death immediately next to portal tract c.t.

54. Chronic Hepatitis

Chronic Hepatitis

➢ Carrier state
  – HBV and HCV
  – Asymptomatic or with liver disease (elevated transaminases)
  – Most common in immunodeficient, drug-addicted, Down syndrome and dialysis
  – Histology
    • Asymptomatic carriers have “ground glass” hepatocytes with finely granular eosinophilic cytoplasm

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55. Chronic Carrier Hepatitis

Chronic Carrier Hepatitis

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Ground glass hepatocytes

55

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56. Chronic Hepatitis

Chronic Hepatitis

Fulminant hepatitis

- Leads to submassive and massive hepatic necrosis – bridging necrosis
- HAV, HBV, HCV, HDV superinfection, HEV, chloroform, carbon tetrachloride, isoniazid, halothane and acetaminophen overdose
- Progressive hepatic dysfunction with mortality of 25-90%
- Gross
  - Progressive shrinkage of the liver as parenchyma destroyed

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57. Acute vs. Chronic Hepatitis

Acute vs. Chronic Hepatitis

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58. Cholangitis, Pericholangitis and Liver Abscesses

Cholangitis, Pericholangitis and Liver Abscesses

- **Cholangitis**
  - Inflammation of the bile ducts; *concentric fibrosis*
  - Usually associated with biliary duct obstruction by gallstones or carcinoma - - - - infection with enteric organisms - - - - purulent exudation within the bile ducts and bile stasis (*cholestasis*)
  - Jaundice, fever, chills, leukocytosis and right upper quadrant pain

- **Pyogenic liver abscess**
  - Caused by E. coli, Klebsiella, Strep, Staph, Bacteroides, Pseudomonas, and fungi

- **Pericholangitis**
  - Inflammation around the bile ducts without intraductal involvement

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59. Cholangitis – Concentric Fibrosis

Cholangitis – Concentric Fibrosis

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60. Liver Parasitic Infections

Liver Parasitic Infections

- **Amebiasis**
  - Caused by Entamoeba histolytica
  - Bloody diarrhea, pain, fever, jaundice, and hepatomegaly

- **Schistosomiasis**
  - Caused by different organisms depending upon geographic area
  - Splenomegaly, portal hypertension, ascites
  - Lesions caused by immune response to ova (egg) of organism
    - Granulomatous inflammation

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61. Liver Amebiasis - Abscess

Liver Amebiasis - Abscess

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62. Schistosomiasis Ova – Liver

Schistosomiasis Ova – Liver

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63. Drug-induced Liver Damage

Drug-induced Liver Damage

- **Direct hepatotoxins**
  - Carbon tetrachloride
  - Acetaminophen
  - Methotrexate
  - Anabolic steroids
  - Oral contraceptive pills

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64. Cirrhosis

Cirrhosis

- Diffuse involvement of the whole liver by fibrosis due to hepatocellular injury by toxins, drugs, viruses, or deposition of metabolites or minerals (e.g., glycogen, copper)
- The normal architecture of the liver is diffusely replaced by regenerated nodules of liver cells, separated by bands of collagenous fibrosis
  - Lack usual architecture of ordered sinusoids and central vein
    - **Micronodular vs. macronodular patterns**
    - Irreversible
    - End stage of many processes

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65. Normal Liver Architecture

Normal Liver Architecture

Key:
1. Right lobe of liver
2. Left lobe of liver
3. Quadrate
4. Round ligament
5. Falciform
6. Caudate lobe of liver
7. Inferior vena cava
8. Common bile duct
9. Hepatic artery
10. Portal vein
11. Cystic duct
12. Hepatic duct
13. Gallbladder

Source: http://training.seer.cancer.gov

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66. Cirrhotic Liver

Cirrhotic Liver

Source: http://digestive.niddk.nih.gov

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67. Micronodular Cirrhosis

Micronodular Cirrhosis

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68. Micronodular Cirrhosis

Micronodular Cirrhosis

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69. Macronodular Cirrhosis

![Image of Macronodular Cirrhosis](image1)

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70. Cirrhosis

![Image of Cirrhosis](image2)

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71. Cirrhosis

Cirrhosis

- Third leading cause of death in 25-65-years-old age group
- Types
  - Alcoholic
  - Postnecrotic
  - Biliary
  - Hemochromatosis-related

72. Alcoholic Cirrhosis

Alcoholic Cirrhosis

Diffuse nodularity of the surfaced induced by underlying fibrous scarring; avg. nodule size = 3 mm

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73. Cirrhosis – Clinical Features

Cirrhosis – Clinical Features

- Portal hypertension
  - Most common cause of portal hypertension is cirrhosis
- Impaired estrogen metabolism
- Dupuytren’s contractures
- Hypoalbuminemia
- Peripheral edema
- Low levels of vitamin K-dependent clotting factors - - - > bleeding diathesis
- Rare hepatorenal syndromes
- Hepatic encephalopathy

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74. Cirrhosis

Cirrhosis

- Etiologies
  - Chronic hepatidites (HBV, HCV)
  - Chronic drug reactions
  - Postnecrotic cirrhosis
  - Biliary cirrhosis
  - Hemochromatosis
  - Wilson’s disease
  - α₁-antitrypsin deficiency
    - Deficiency of a protease inhibitor - - - > pulmonary emphysema and hepatic damage
  - Syphilitic cirrhosis

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Hemochromatosis

- Autosomal recessive
- Excessive iron accumulation in the liver from the gut due to abnormal absorption of normal iron intake resulting in organ dysfunction
  - Iron also deposited in pancreas, heart, adrenal, thyroid, parathyroid, and anterior pituitary
- Liver turns a rusty brown color (hepatocytes dying)
- Increased risk of hepatocellular carcinoma
- Not to be confused with hemosiderosis
  - Iron overload from any other cause such as frequent transfusions or dietary overconsumption

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Hemochromatosis – Rusty Brown

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77. Hemochromatosis

Hemochromatosis

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Hepatocellular iron deposition (Prussian blue stain) in the cytoplasm of periportal hepatocytes

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78. Wilson’s Disease

Wilson’s Disease

• Autosomal recessive
  ➢ Inadequate hepatic excretion of copper
    – Excess copper accumulates in liver and brain due to low concentration of copper binding enzyme ceruloplasmin in the serum
• In addition to cirrhosis it causes:
  • Degenerative changes in the lenticular nuclei of the brain
    • Psychiatric disorders
    • Movement disorders
    • Abnormal eye movements
  ➢ Kayser-Fleisher rings
    • Pathognomonic
    • Deposition of copper in the corneal limbus

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79. Kayser-Fleischer Rings

![Kayser-Fleischer Rings](source: http://cogancollection.nib.nih.gov)

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80. Toxic Liver Disease

Toxic Liver Disease

- **Alcohol – most common cause**
  - Aldehyde is the metabolic product from alcohol that actually damages the liver

- **Drugs**
  - Intrinsic and idiosyncratic hepatotoxins
  - Methotrexate, tetracyclines, sulphonamides, isoniazid, corticosteroids, chlorpromazine, oral contraceptives, anabolic steroids, acetaminophen

- **Hepatitis**
Alcoholic Liver Disease

- **Results in fatty liver, alcoholic hepatitis and alcoholic cirrhosis - overview**
  - Fatty change is asymptomatic
  - **Alcoholic hepatitis** – fever, hepatomegaly, jaundice, elevated AST, alkaline phosphatase and ALT
  - **Alcoholic cirrhosis** – often presents with portal hypertension
- Accounts for 60-70% of cirrhosis in Western Hemisphere
- Male : female ratio is 2:1
- Patients die from liver failure, infection, upper GI bleeds, hepatocellular carcinoma, encephalopathy, and renal failure

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Alcoholic Liver Disease

- **Fatty liver (steatosis)**
  - Reversible
  - Yellow, greasy, enlarged liver
  - Fatty vacuoles displace hepatocellular nuclei peripherally
- **Alcoholic cirrhosis**
  - Enlarged liver with micronodular formation
  - End stage resembles postnecrotic cirrhosis

**Alcoholic hepatitis**
- Usually associated with extreme fatty change and sometimes with cirrhosis
- Results from prolonged alcoholic abuse
- Histology:
  - Swelling of hepatocytes
  - Necrosis, PMN inflammation
  - Formation of alcoholic pink hyaline (Mallory bodies) in swollen hepatocytes
  - Not pathognomonic since also seen in Wilson's disease, hepatocellular carcinoma and biliary cirrhosis
  - Cholestasis and beginning fibrosis

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83. Alcoholic Liver Disease – Fatty Liver

Alcoholic Liver Disease – Fatty Liver

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84. Alcoholic Liver Disease

Alcoholic Liver Disease

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Hepatic lobule with fatty liver (steatosis)

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85. Alcoholic Hepatitis

Alcoholic Hepatitis

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86. Alcoholic Hepatitis

Alcoholic Hepatitis

Mallory bodies

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87. Alcoholic Cirrhosis

**Alcoholic Cirrhosis**

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Hepatic micronodules entrapped by fibrous tissue

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88. Chronic Alcohol Exposure

**Chronic Alcohol Exposure**

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89. Benign Tumors of the Liver

Benign Tumors of the Liver

Liver cell (hepatic) adenoma
- True neoplasm mistaken at times for carcinoma
- More common with anabolic steroid use and oral contraceptive use

- Nodular hyperplasia
  - Focal nodular hyperplasia
  - Solitary nodule with fibrous capsule and bile ductules
  - Nodular regenerative hyperplasia
    - Multiple nodules of normal hepatocytes but loss of normal radial architecture

- Cavernous hemangioma
  - Large vascular endothelial-lined spaces filled with RBCs

- Bile duct adenoma
  - Very common; small white nodules

- Cysts

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90. Liver Adenoma

Liver Adenoma

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91. Liver Hemangioma

Liver Hemangioma

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92. Malignant Tumors of the Liver

Malignant Tumors of the Liver

- Metastatic carcinoma is the most common malignant tumor (i.e., not primary)
  - Lung, colon, stomach & breast most often
  - Multiple well circumscribed nodules in markedly enlarged liver

- Cholangiocarcinoma
  - Intrahepatic bile duct
  - 10% of primary liver neoplasms

- Hepatoblastoma
  - Rare; in children

- Angiosarcoma
  - Exposure to vinyl chloride and arsenic

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93. Metastatic Carcinoma to the Liver

94. Malignant Tumors of the Liver

- **Hepatocellular carcinoma (hepatoma)**
  - 90% of primary liver neoplasms
  - Strongly associated with HBV infection, hepatitis, cirrhosis, aflatoxin B (fungal toxin), androgens and oral contraceptives
    - Tender hepatomegaly, ascites, weight loss, fever, polycythemia, and hypoglycemia
    - Alpha-fetoprotein (AFP) present in 50-90% of patient’s serum
    - Death is due to GI bleed and liver failure
95. Hepatocellular Carcinoma

Hepatocellular Carcinoma

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Unifocal, massive, extensive necrosis of right hepatic lobe and a satellite lesion (arrow)

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96. Hepatocellular Carcinoma

Hepatocellular Carcinoma

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Hepatocytes in cords or nests with little intervening stroma

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97. **Hepatocellular Carcinoma**

Hepatocellular Carcinoma

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Well-differentiated nests of tumor cells with some central lumens

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98. **Reye’s Syndrome**

Reye’s Syndrome

- Characterized by fatty change in the liver and edematous encephalopathy following aspirin use, 3-5 days later
  - Usually affects children between 6 months and 15 years of age
  - Etiology uncertain
- Preceded by mild upper respiratory tract infection, varicella, or influenza A or B infection managed with aspirin administration at levels that are not ordinarily toxic but → vomiting, irritability, lethargy, hepatomegaly
  - 25% progress to coma → death or permanent neurologic impairments

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