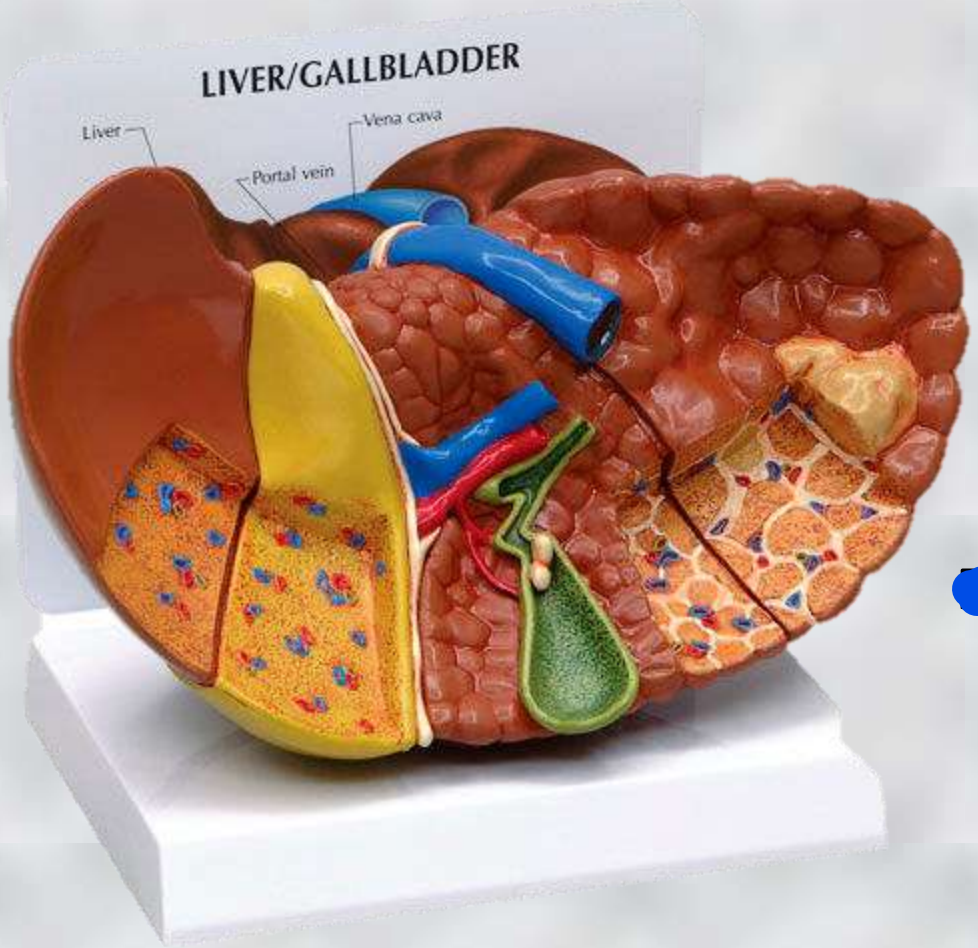
# of Patients with Liver Disease



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What is the liver?

- The liver is a large organ, and occupies the upper right quadrant of the abdomen.
- It develops as an outgrowth of the gut
- Veins returning from the gut come together to form the **portal vein.**
- Hepatic veins join the vena cava.
- The liver will retain normal function until 85% damaged.
- [redacted]

Function of the Liver

Metabolism / Detoxification

- Metabolizes products of digestion
- Glucose regulation
- Vitamin storage
- Metabolizes drugs
  - Some of the common drugs used in Dentistry
  - Ethanol.
- Breaks down bilirubin

Synthesis and Secretion

- Components of clotting factors
- Cholesterol, triglyceride synthesis
- Bile production
- Other proteins and hormones

Storage and Filtration of Blood

- Acts as a blood reservoir
- Contains phagocytic cells
- Part of the reticuloendothelial system.

Liver Function Tests (LFTs)

AST (aspartate aminotransferase) (11 – 47 IU/L)

- AST is an enzyme found throughout the body, but predominantly in heart and liver cells.
- Most useful in detecting liver damage due to hepatitis, drugs toxic to the liver, cirrhosis, and alcoholism.
- Often ordered in conjunction with ALT.

ALT (alanine aminotransferase) (7 – 56 IU/L)

- An enzyme found mostly in the cells of the liver and kidney. When the liver is damaged, ALT is released into the blood stream. ALT is a useful test for detecting liver damage.
- Most useful in detecting damage due to hepatitis and drugs or other substances toxic to the liver.
- Often ordered in conjunction with AST.

AST/ALT Ratio

- The AST/ALT ratio is usually increased in alcoholic hepatitis, cirrhosis, and in the first day or two of acute hepatitis or injury from bile duct obstruction.

ALP (alkaline phosphatase) (30 – 120 IU/L)

- Found in bone and in the cells of bile ducts. ALP can indicate blockage of one or more bile ducts, liver cancer, hepatitis, cirrhosis, or when hepatotoxic drugs are taken.

Liver Function Tests (LFTs)

Total Bilirubin (0.2 – 1.2 mg/dL)

- A breakdown product of hemoglobin (orange-yellow pigmented). Unconjugated (non-water soluble) bilirubin is processed in the liver.
- High unconjugated bilirubin means either hemoglobin is being broken down too fast, or the liver can't process it fast enough.
- High conjugated bilirubin indicates that bilirubin is backing up in the liver.

Albumin (3.5 – 5.3 g/dL)

- A protein made by the liver. Low levels indicate liver disease or nephrotic syndrome.

Prothrombin Time (PT) (10 – 14 seconds)

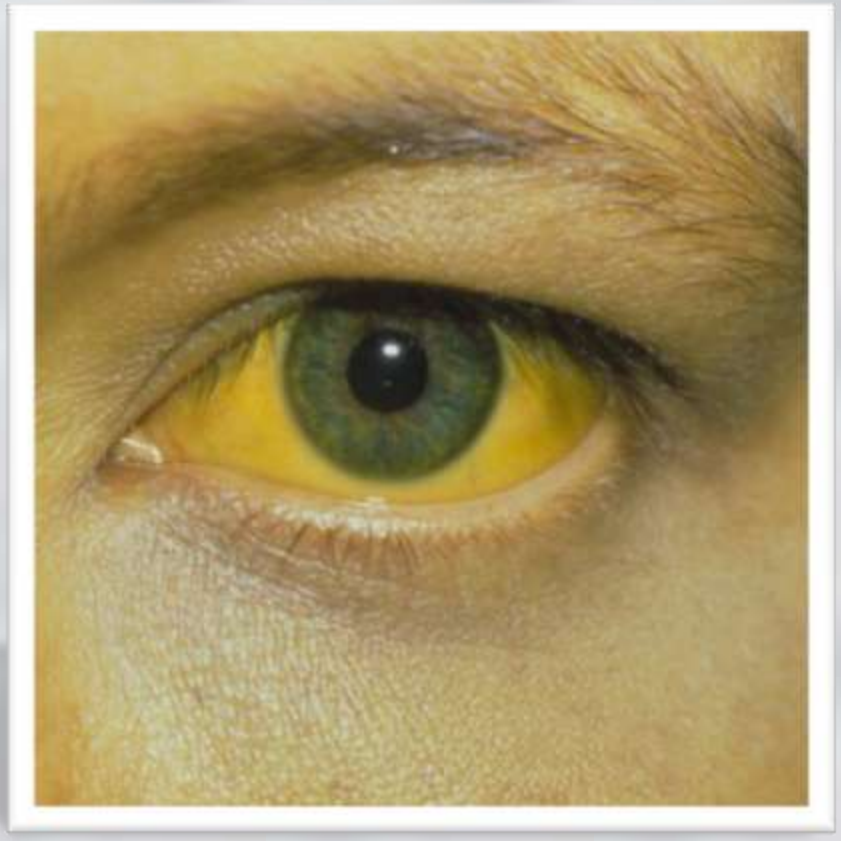
- The prothrombin time (PT) test measures how long it takes for a clot to form in a sample of blood.
- Evaluates the overall ability to produce a clot in a reasonable amount of time.

Platelet Count (150,000 – 450,000 mm3)

- Thrombocytopenia is a decrease in the number of circulating platelets. Platelets are not part of the coagulation cascade, but are essential for the initiation of hemostasis.

Manifestations of Liver Disease

- Jaundice
- Portal hypertension
- Ascites
- Hepatic encephalopathy
- Splenomegaly
- Blood abnormalities
- Light stools/Dark urine
- Peripheral edema
- Pruritus (itching)
- Abdominal pain



Manifestations of Liver Disease

Jaundice

- A yellowing of the skin and eyes from excessive bilirubin in the blood. Also causes itching.
- The diseased liver either cannot processes bilirubin fast enough, or it is backing up from an obstruction to the flow of bile.

Portal Hypertension

- Increased resistance to portal blood flow.
- Leads to the formation of collateral veins that bypass the liver. Enlarged vessels are prone to rupturing causing massive bleeding and often death.

Ascites

- The accumulation of excess fluid in the peritoneal cavity.

Hepatic encephalopathy

- Disturbances in consciousness: subtle to marked confusion and stupor, to deep coma and death.
- Elevated levels of ammonia – brain edema, impaired neural function. Reversible if the underlying hepatic condition can be corrected.

Splenomegaly

- Spleen to enlarges due to increased pressure from the spleen into portal blood vessels. White blood cell count can decrease, platelet count can decrease.

Manifestations of Liver Disease

Blood abnormalities

- Leukopenia and thrombocytopenia due to splenomegaly.
- Clotting abnormalities – decreased ability to synthesize clotting factors.

Light Stools/Dark Urine

- Bilirubin gives stool its characteristic color. In patients with hepatitis or cirrhosis, little bilirubin makes it into the gut, and stool is light in color.
- Dark brown but clear urine is a sign of excess bilirubin in the urine. Light stool and dark urine are generally concurrent with jaundice.

Peripheral edema

- Hypoalbuminemia causes reduced blood osmolarity. Fluid to escapes into the tissues.

Abdominal Pain

- Abdominal pain, discomfort, or “feeling full” due to hepatomegaly or hepatocellular carcinoma.

Types of Liver Disease

- Hepatitis – infectious & non-infectious
- Alcoholic liver disease (ALD)
- Non-alcoholic fatty liver disease (NAFLD)
- Hepatocellular Carcinoma (HCC)
- Cirrhosis

Hepatitis

Non-infectious

Excessive use of toxic substances

- Drugs:
  - Acetaminophen
  - Methotrexate
  - Methyldopa
  - Halothane
  - Ketoconazole
  - Narcotics
- Alcohol

Infectious

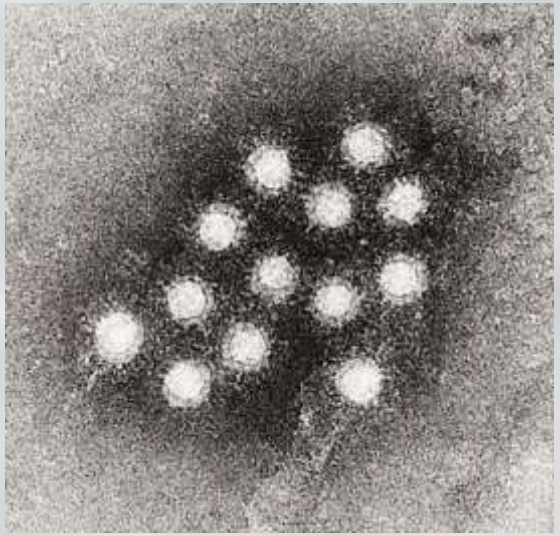
Bacterial

- Tuberculosis
- Secondary syphilis

Viral

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis D, E
- Acute non A-E

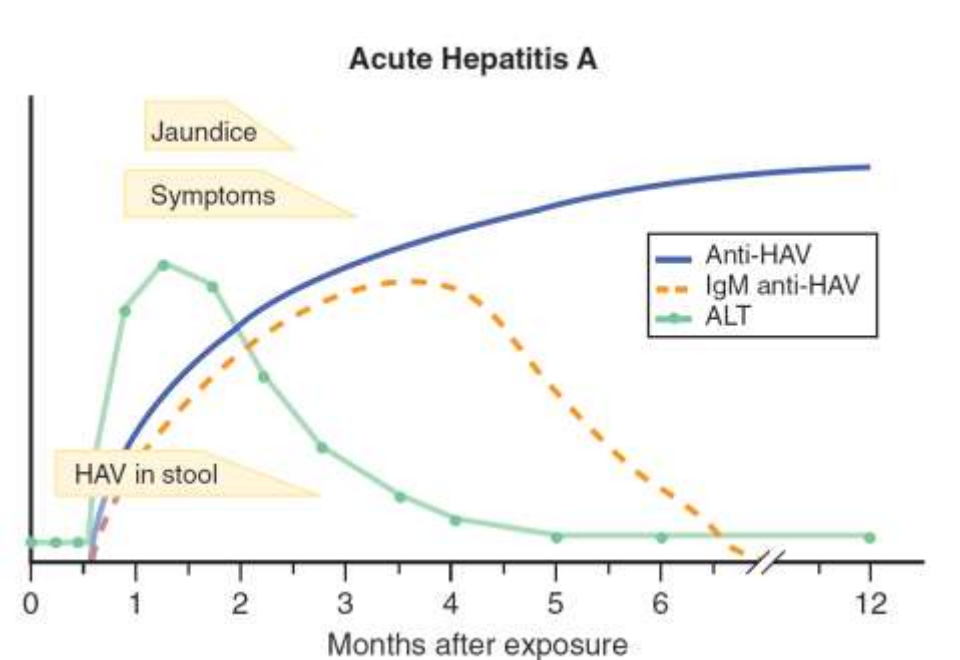
Hepatitis A Virus



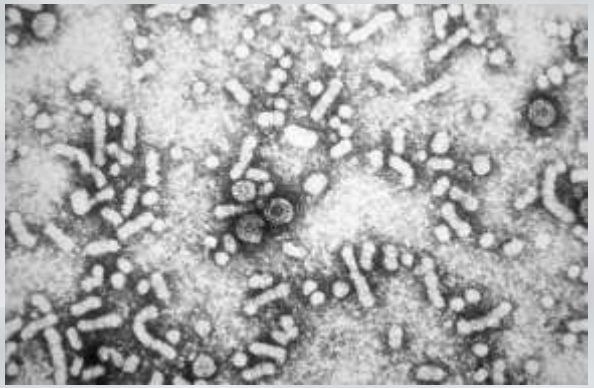
- Food, water borne; heat labile
- Fecal – oral contamination; contagious
- Usually self limited, lasting days to weeks
- 99% spontaneous recovery, no treatment

Diagnosis

- HAV immunoglobulin M (IgM) test (preferred confirmatory test for acute HAV infection)
  - Serum antibodies IgM usually can be detected 5–10 days before symptom onset, and the level remains elevated for 4–6 months.
- Elevated liver enzymes
- Elevated bilirubin levels



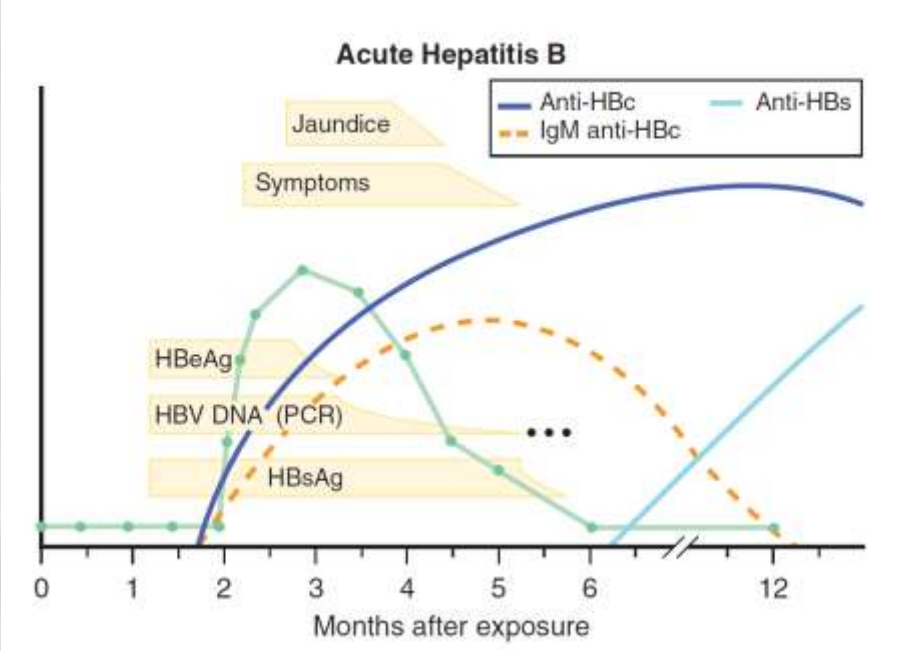
Hepatitis B Virus



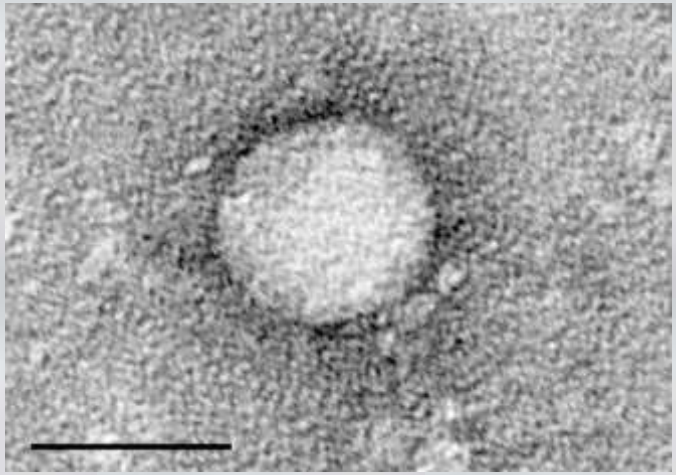
- Blood, semen, saliva, vaginal secretions
- Highly contagious; sexually transmitted
- 90 – 95% self limited over 6 months
- Chronic infection: >6 months
- DNA virus: incorporates into host with chronic infection

<u>Diagnosis</u>

- Hepatitis B surface antigen (HBsAg)
  - Indicates currently infectious, with acute or chronic infection
- Hepatitis B surface antibody (HBsAb)
  - Indicates recovery or successful immunization
- Hepatitis B core antibody (HBcAb)
  - Indicates previous or ongoing infection
- IgM antibody to HBc antigen (IgM anti-HBc)
  - Indicates acute infection, acquired in the last 6 months



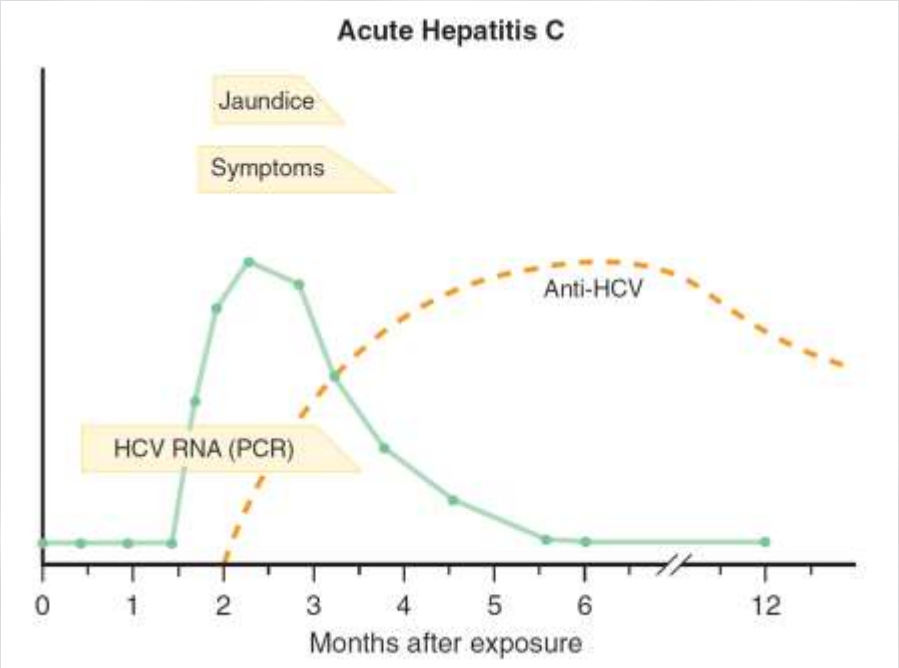
Hepatitis C Virus



- Blood borne, not in food or water; not highly sexually transmitted
- Not highly contagious
- 20% self clearing; 80% chronicity
- RNA virus: does not incorporate into host
- Can cause HCC; #1 cause of transplant

<u>Diagnosis</u>

- Enzyme immunoassay to detect antibodies to multiple HCV antigens
- Hepatitis C RNA virus by polymerase chain reaction (PCR) detects quantity of the virus itself in the blood (quantification of the virus).



Hepatitis

Clinical Manifestations

Incubation period

- 2 – 20 weeks
- Virus becomes detectable in blood
- Serum aminotransferase, bilirubin levels normal
- Antibody not detected

Pre-Icteric (Prodromal) Phase

- Onset of nonspecific symptoms
- Lasts 3 – 10 days
- Virus specific antibody detectable
- Viral titers at highest point
- Serum aminotransferase levels increase

Icteric Phase

- 1 – 3 weeks
- Jaundice appears
- Fatigue, nausea worsen
- Hepatic tenderness
- Aminotransferase levels are 10x normal limit.
- Levels of virus begin to decrease

Post-Icteric (Recovery) Phase

- Resolution of jaundice
- Usually 6-8 weeks after exposure
- Symptoms diminish
- LFTs usually return to normal

Complications

- Chronic infection
- Fulminant hepatic failure
- Relapsing or cholestatic hepatitis
- Extrahepatic syndromes

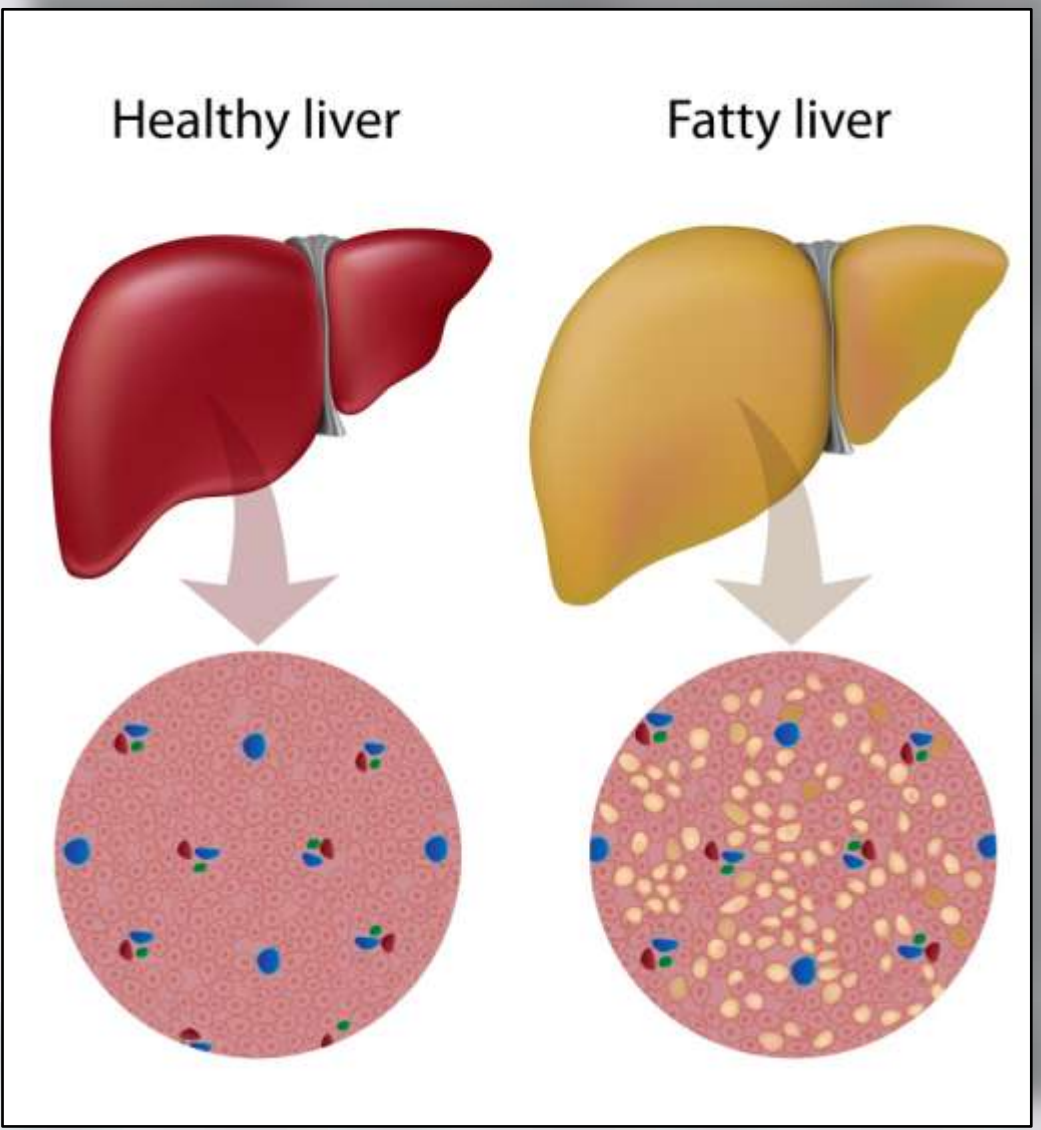
Fulminant Hepatic Failure

- Acute liver failure
- Evidence of hepatic encephalopathy
- Prolongation of PT
- Worsening of jaundice
- Ascites
- Decrease in liver size

Alcoholic Liver Disease (ALD)

- US: 50-70% consume alcohol
- Only 5% have more than 2 drinks/day; 11-15g alcohol/drink
- Maximum recommended daily intake:
  - women: 22-30g alcohol/day
  - men: 33-45g alcohol/day
- Three types of ALD:
  - Hepatic steatosis (fatty liver disease)
  - Alcoholic hepatitis
  - Cirrhosis

Alcoholic Liver Disease (ALD)



Alcoholic fatty liver disease

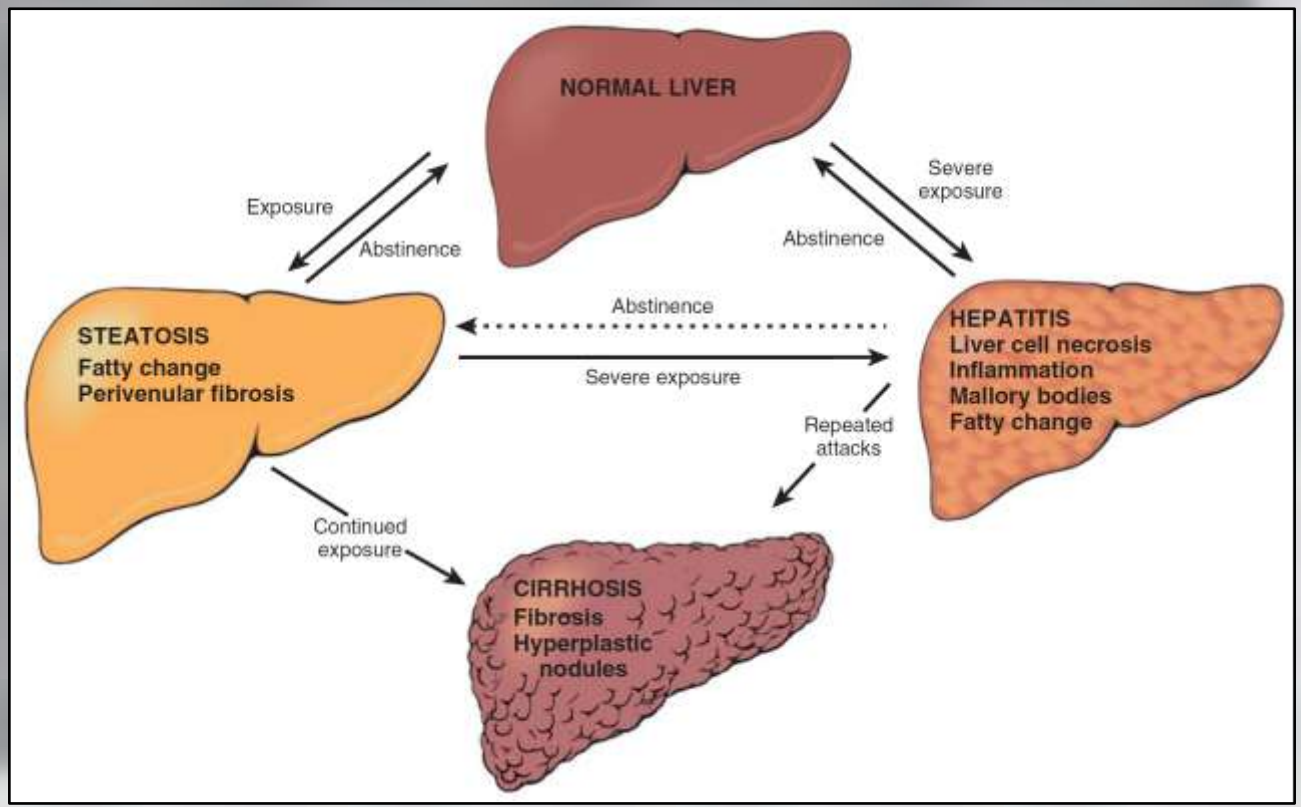
- Hepatic steatosis
- Micro-vesicular lipid droplets in hepatocytes, become macro-vesicular globules
- Large, soft, yellow, greasy liver
- Non-fibrous initially
- Severe liver dysfuncion unusual
- Reversible with abstinence

Alcoholic Liver Disease (ALD)

Alcoholic hepatitis

- Hepatocyte swelling and necrosis
- Neutrophilic reaction
- Fibrosis
- Non-specific symptoms

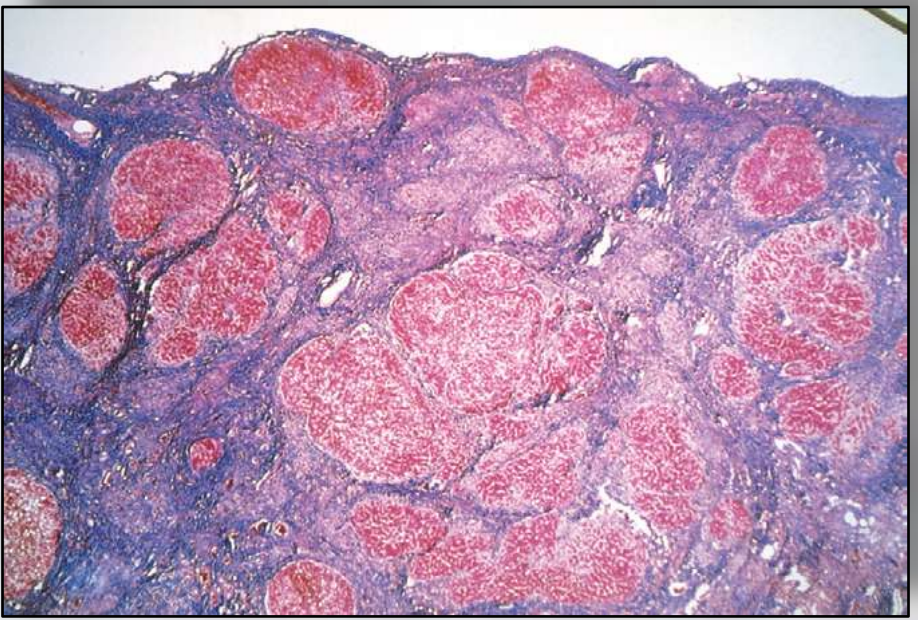
- Appears acutely after drinking
- 10-20% risk of death
- May resolve, or may progress to cirrhosis

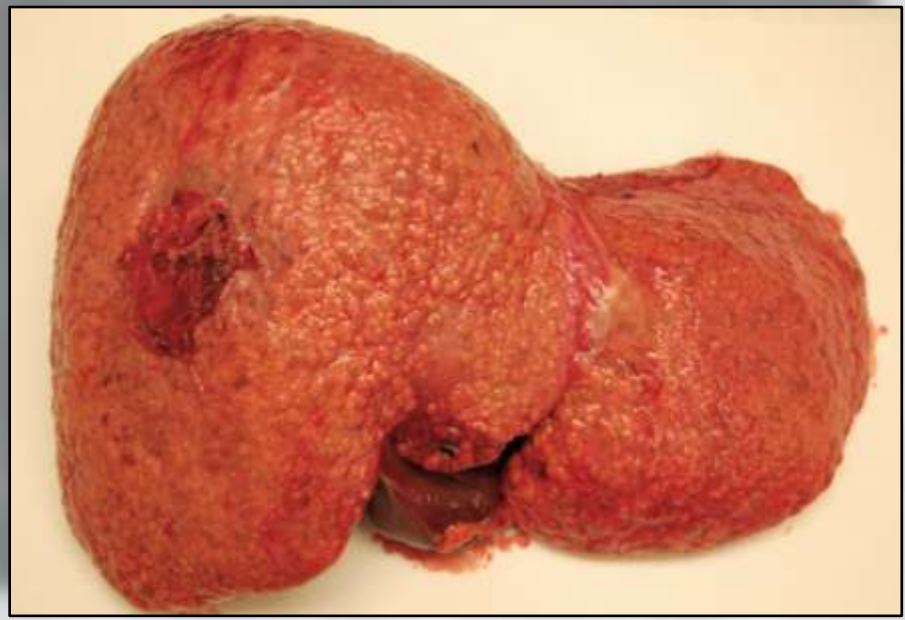


Alcoholic Liver Disease (ALD)

Alcoholic cirrhosis

- Usually develops slowly
- Progression from large, tan, fatty to shrunken, brown, non-fatty
- Fibrous septa form around nodules of hepatocytes
- Eventual ischemic necrosis and fibrous obliteration of nodules
- Tough, pale scar tissue
- Similar appearance to other forms of cirrhosis





Non-Alcoholic Fatty Liver Disease (NAFLD)

- NAFLD includes simple hepatic steatosis; steatosis w/ minor, non-specific inflammation; nonalcoholic steatohepatitis (NASH)
- Develops in patients who are not alcoholic
- Causes liver damage that is histologically indistinguishable from alcoholic hepatitis
- Risk factors: obesity, dyslipidemia, glucose intolerance
- Pathogenesis poorly understood but seems to be linked to insulin resistance
- Most patients are asymptomatic (except NASH)
- Elevations in aminotransferase levels
- Biopsy is required to confirm the diagnosis
- Treatment includes elimination of causes and risk factors

Hepatocellular Carcinoma

- Hepatocellular carcinoma accounts for the vast majority of liver cancers. Globally, HCC is the 3rd most frequent cause of cancer death.
- 78% of HCC cases caused by chronic HBV and HCV infections
- Three types of gross morphology
  1. Unifocal large mass
  2. Multifocal and widely distributed nodules
  3. Diffusely infiltrative, permeating widely
- Strong propensity for invasion of vascular structures
  - If venous invasion is identified during transplant, recurrence of HCC is likely
- Clinical manifestations often masked by underlying cirrhosis or chronic hepatitis
- Causes death by:
  - Wasting syndrome (cachexia)
  - Esophageal or gastric variceal bleeding
  - Liver failure with hepatic coma

Cirrhosis of the Liver

- Irreversible damage to liver
- Fibrosis with areas of nodular regeneration
- Primary causes:
  - Alcoholic liver disease
  - Chronic infection with hepatitis B virus and hepatitis C virus
- Less common causes:
  - Primary biliary cirrhosis, hemochromatosis, Budd–Chiari syndrome, Wilson's disease and alpha 1- antitrypsin deficiency
  - Medication such as amiodarone and methotrexate can also cause cirrhosis
- In just under 1/3 of cases, cause is unknown – referred to as *cryptogenic cirrhosis*
- Decompensation – Infection, alcohol consumption, imbalance of urea and electrolytes, GI bleeds or progression of the underlying disorder – can cause mortality rates without liver transplantation can be as high as 85% within 5 years
- Classification: Child-Turcotte-Pugh Classification of Cirrhosis is helpful in determining prognosis of disease

Major Clinical Manifestations of Cirrhosis

- Hepatic encephalopathy
- Ascites
- Esophageal, gastric varicies
- Portal hypertension
- Jaundice
- Splenomegaly
- Blood abnormalities

Child-Turcotte-Pugh Classification of Cirrhosis

Risk (grade) is based on the total number of points:
Low (A): 5–6; Moderate (B): 7–9; High (C): 10–15

Factor	Units	1	2	3
Serum bilirubin	mol/L mg/dL	<34 <2.0	34–51 2.0–3.0	>51 >3.0
Serum albumin	g/L g/dL	>35 >3.5	30–35 3.0–3.5	<30 <3.0
Prothrombin time	seconds prolonged INR	0–4 <1.7	4–6 1.7–2.3	>6 >2.3
Ascites		None	Easily controlled	Poorly controlled
Hepatic encephalopathy		None	Minimal	Advanced

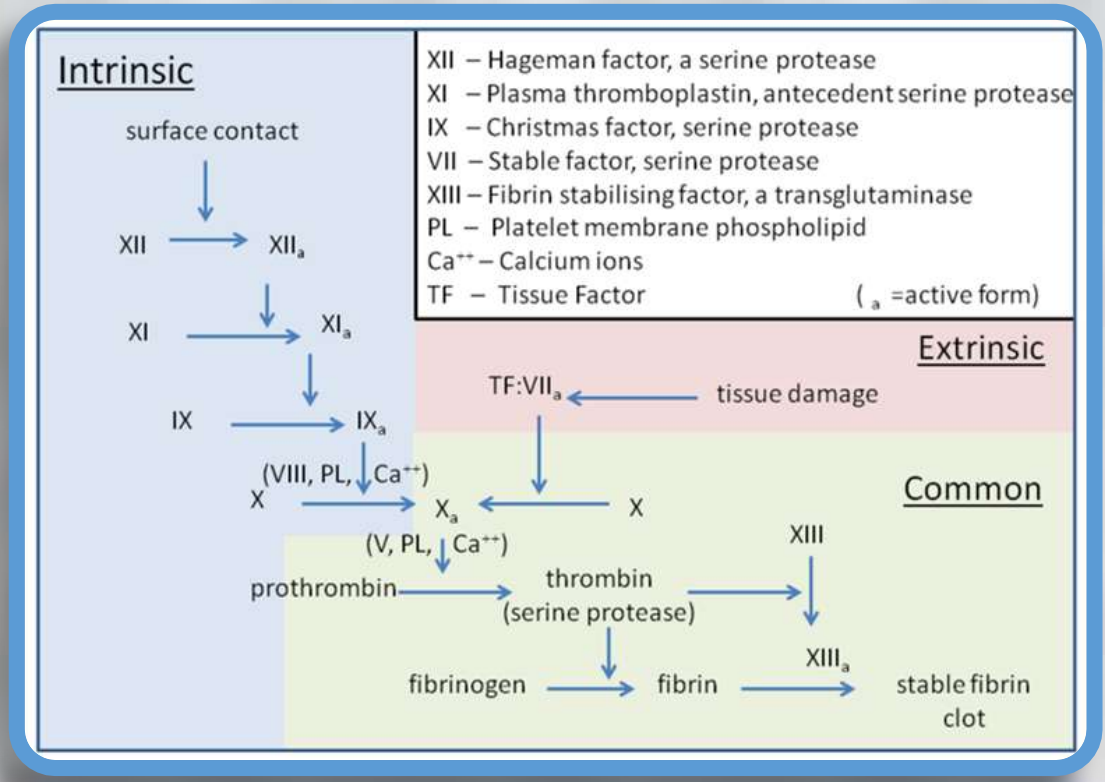
Cirrhosis of the Liver

Management

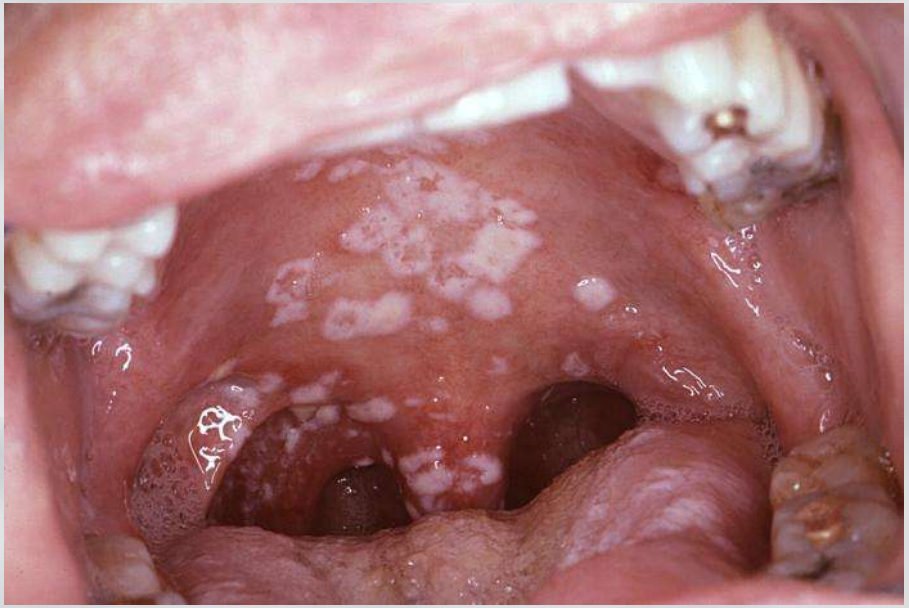
- Nutritional supplements
- Low protein diet if encephalopathy
  - Vegetables as main protein source
  - Lactulose to clear bowels, and reduce absorption of protein.
- Low salt diet if there is ascites
- Avoid alcohol, NSAIDs, sedatives, opiates
- Interferon-α
- Prognosis is relatively poor, with a 5-year survival rate of approximately 50%

Coagulopathy

- Hepatocellular destruction
  - Reduced vitamin K absorption
  - Decreased coagulation factors
- Splenomegaly
  - Thrombocytopenia
- Portal hypertension
  - Esophageal, gastric varices – massive hemorrhaging

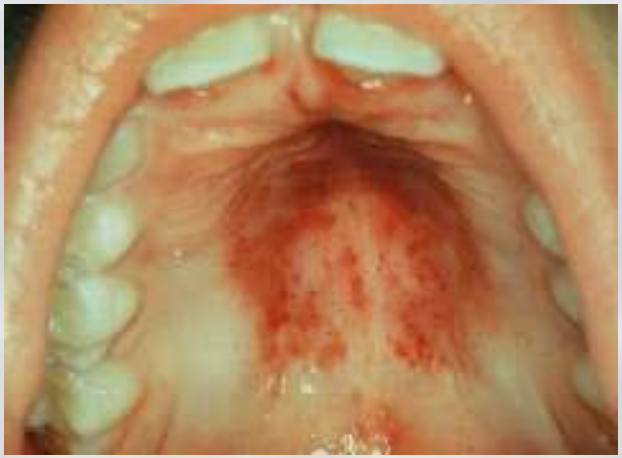


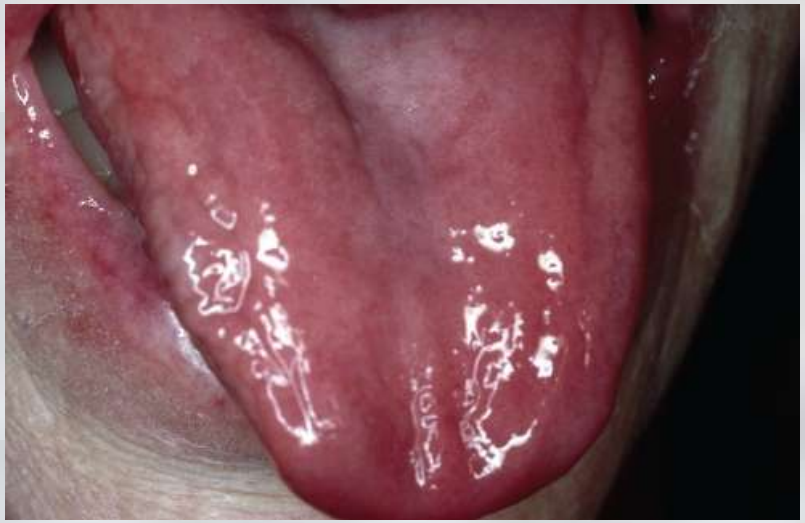
Dental Management of Liver Patients



Oral Manifestations of Liver Disease

- Oral candidiasis – Immunotherapy
- Angular cheilitis – Immunotherapy
- Atrophic glossitis – Anemia
- Petechiae – Thrombocytopenia
- Lichen planus – HCV
- Oral metastases of HCC primarily manifest as hemorrhagic expanding masses located in the premolar and ramus region of the mandible





Dental Management of Liver Patients

Protection for the Practitioner

- Difficult or impossible to identify carriers of HBV, HCV, HDV. Most carriers are unaware that they have had hepatitis
  - Standard precautions
  - HBV vaccination
  - Post exposure prophylaxis

Dental Management of Liver Patients

Dental Drugs

Analgesics/Pain Control
- Aspirin, ibuprofen, and other NSAIDs – use caution
- Acetaminophen – use caution
- Narcotics – increase dose interval, short term
- Morphine – safe

Anesthetics
- Lidocaine, mepivicaine – limit to 300 mg max dosage
- Prilocaine – limit to 400 mg max dosage
- Articaine – safe (metabolized in plasma)

Sedatives/Anxiolytics
- Benzodiazepines – reduce dosage, increase intervals

Antibiotics
- Beta-lactam (penicillins, ampicillin, cephalexin, cefazolin, ceftriaxone) – safe (renal excretion)
- Metronidazole – interaction w/ alcohol
- Clindamycin, aminoglycosides – use caution
- Tetracyclines – reduced dosage, increase intervals

BOX 10-3 Dental Drugs Metabolized Primarily by the Liver

Local Anesthetics*
Lidocaine (Xylocaine)
Mepivacaine (Carbocaine)
Prilocaine (Citanest)
Bupivacaine (Marcaine)

Analgesics
Aspirin†
Acetaminophen (Tylenol, Datril)†
Codeine‡
Meperidine (Demerol)‡
Ibuprofen (Motrin)†

Sedatives
Diazepam (Valium)§
Barbiturates‡

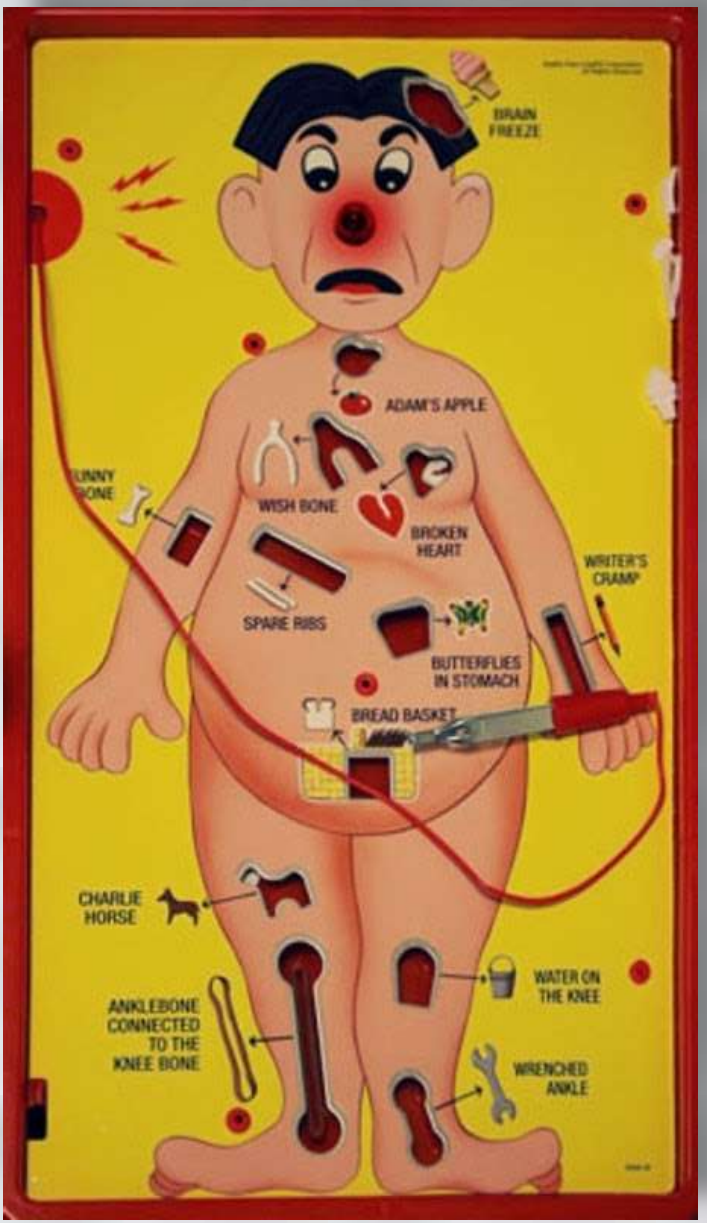
Antibiotics
Ampicillin
Tetracycline
Metronidazole§
Vancomycin§

Dental Management of Liver Patients

Coagulation

- PT/INR, Platelet count requirements for surgery:
  - Maximum INR 3.5
  - Minimum platelets 50,000
- 2 units fresh frozen plasma (FFP) + 6 pack platelets (60,000)

Dental Management of Liver Patients



Liver Transplant

- Pre-transplant
  - Comprehensive dental evaluation
  - Extraction of infected, non-restorable, or periodontally hopeless teeth.
  - Oral hygiene instruction
- Post-transplant
  - No elective dental tx for 3 months following surgery
  - Routine Ab prophylaxis is not recommended
  - Recall program after 3 months
  - Prophylactic care

Dental Management of Liver Patients

P

Patient Evaluation/Risk Assessment (see Box 1-1)

- Evaluation is directed at determining the nature, severity, control, and stability of disease.

Potential Issues/Factors of Concern

	A
Analgesics	Nonsteroidal antiinflammatory drugs (NSAIDs), including aspirin, and acetaminophen, as well as codeine and meperidine, should be avoided or their use very limited in persons who have end-stage liver disease.
Antibiotics	Antibiotic prophylaxis is not recommended; however, patients who have severe liver disease may be more susceptible to infection. Selection of antibiotic agent is based on risk and severity of dental infection. Avoid use of metronidazole and vancomycin
Anesthesia	Higher doses may be required to achieve adequate anesthesia in presence of alcoholic liver disease. Knowledge of current liver function is important to establish proper dosages. Epinephrine (1:100,000, in a dose of no more than two carpules) in local anesthetics generally is not associated with any problems, but patients should be monitored closely.
Anxiety	Use anxiety/stress reduction techniques as needed, but avoid benzodiazepines.
Allergy	No issues.
	B
Breathing	No issues.
Bleeding	Excessive bleeding may occur in the patient with end-stage liver disease. Most such patients will have reductions in coagulation factors and thrombocytopenia, so they are at greater risk for postsurgical bleeding; they may need vitamin K and/or platelet or clotting factor replacement.
Blood pressure	Monitor blood pressure, because it may be significantly increased with portal hypertension in patients with end-stage liver disease.
	C
Chair position	No issues.
Consultation	Once the patient is under good medical management, the dental treatment plan is unaffected. However, consultation with the patient's physician to establish the level of control and to identify bleeding tendencies and altered drug metabolism is recommended as part of the management program.
	D
Devices	No issues.
Drugs	Because many medications are metabolized in the liver, certain drugs may need to be avoided or reduced in dosage. Limit or avoid use of acetaminophen, aspirin, ibuprofen, codeine, meperidine, diazepam, barbiturates, metronidazole, and vancomycin. Refer to a good drug reference. The use of epinephrine or other pressor amines (in gingival retraction cord or to control bleeding) must be limited, especially if portal hypertension is present.
	E
Equipment	No issues.
Emergencies and urgent care	For patient with severe liver disease who requires urgent care, consider treating in special care clinic or hospital. After consulting with physician, provide limited care only for pain control, treatment of acute infection, or control of bleeding until condition improves.
	F
Follow-up	It is important to follow up with the patient post-operatively to be certain that there are no complications.

Thank You

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