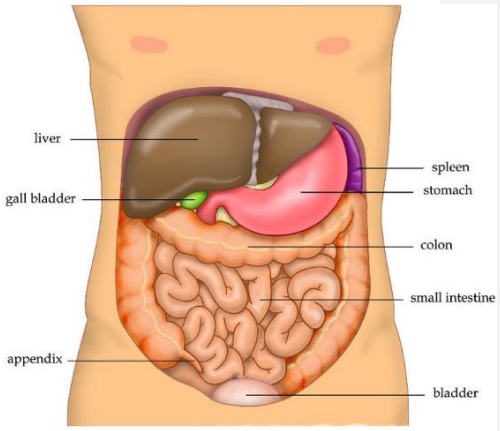
Oral Surgery **د.ياسر رياض الخناق**

LIVER DISEASE



The liver is an essential organ located in the right upper quadrant of the abdomen, below the diaphragm, it has a number of key functions, including metabolism of the byproducts of food, detoxification of drugs, conversion of nitrogenous substances to be excreted by the kidneys, formation of blood clotting factors, metabolism of bilirubin, processing of lipids from the intestines, and storage of glycogen. Obviously then, clinical consequences of liver dysfunction manifest in loss of these functions.

Liver dysfunction may be attributed to a number of causes, including acquired infections and other pathologic conditions, as well as drug use.
Impairment of liver function can lead to abnormalities in many biochemical functions performed by the liver, such as synthesis of coagulation factors and drug metabolism, and dental patients with acute or chronic liver disease may be adversely affected.
Ultimately, serious end-stage liver dysfunction or cirrhosis may result.
Cirrhosis is the consequence of long-term damage to the liver tissues. This condition is irreversible and leads to fibrosis, resulting in jaundice, ascites, and portal hypertension, as well as significant liver dysfunction.
Obviously, liver disorders in persons presenting for treatment are of significant clinical interest to dentists in the context of the proper management of such patients. In this lecture, the two most common liver disorders and main causes of cirrhosis, hepatitis and alcoholic liver disease, are presented.

HEPATITIS

General Description

Hepatitis is inflammation of the liver that may result from infectious or other causes. Examples of hepatitis with infectious causes are viral hepatitis and that associated with infectious mononucleosis, secondary syphilis, and tuberculosis.

Also, noninfectious hepatitis can result from excessive or prolonged use of toxic substances, including drugs (i.e., acetaminophen, halothane, ketoconazole, methyldopa, and methotrexate) or, more commonly, alcohol.

Because the several types of hepatitis have various degrees of impact on dental treatment.

Viral hepatitis

Viral hepatitis is a collective term describing liver inflammation or hepatitis caused by a group of several different viruses.

Is the most common form of infectious hepatitis, there are 5 distinctive types of hepatitis viruses; A, B, C, D and E, they all target the liver.

The clinical manifestations of the five forms of viral hepatitis are quite similar, and the diseases can be distinguished from each other only by serologic assays.

Hepatitis A virus (HAV) and hepatitis E virus (HEV) are forms of *infectious hepatitis*; they are spread largely by the fecal–oral route, are associated with poor sanitary conditions, are highly contagious, occur in outbreaks as well as sporadically, and cause self-limited hepatitis only.

Hepatitis B virus (H BV), hepatitis C virus (HCV), and hepatitis D virus (HDV) are forms of *serum hepatitis*, are spread largely by parenteral routes and less commonly by intimate or sexual exposure, and are not highly contagious. They are capable of leading to chronic infection and, ultimately, to cirrhosis and hepatocellular carcinoma.

Cases of an acute viral hepatitis–like syndrome that cannot be identified as being caused by a known hepatitis virus; this syndrome has been called acute non-A, non-B, non-C, non-D, non-E (non–A-E) hepatitis or acute hepatitis of unknown cause. Despite many attempts, the viral etiology of non–A-E hepatitis remains unproved.

Pathophysiology and Complications

The pathogenesis of the liver injury in viral hepatitis is not well understood. None of the five primary agents seems to be directly cytopathic. The hepatocyte injury in viral hepatitis suggest that **immune responses**, particularly cytotoxic T-cell responses to viral antigens expressed may be the major effectors of injury. Other proinflammatory cytokines, natural killer cell activity, and antibody dependent cellular cytotoxicity also may play roles in cell injury and inflammation during acute hepatitis virus infection.

Recovery from hepatitis virus infection usually is accompanied by the appearance of rising titers of antibody against viral envelope antigens, such as anti-HAV, anti-HBs, anti-HCV-E1 and anti-HCV-E2, and anti-HEV; these antibodies may provide at least partial immunity to reinfection.

Clinical Presentation

Acute hepatitis

is highly variable and ranges in severity from a transient, asymptomatic infection to severe or fulminant disease. The disease may be self-limited with complete resolution, run a relapsing course, or lead to chronic infection. The **incubation period** ranges from 2 to 20 weeks. During this phase, virus becomes detectable in blood, but serum aminotransferase and bilirubin levels are normal, and antibody is not detected.

Patients classically exhibit three phases of acute viral hepatitis:

1. **Prodromal (preicteric) phase** is usually precedes the onset of jaundice by 1 or 2 weeks and consists of nonspecific anorexia, intermittent nausea, vomiting, fatigue, myalgia, malaise, fever, and vague right upper quadrant pain. Virus specific antibody first appears during this phase. Viral titers generally are highest at this point, and serum aminotransferase levels start to increase.
2. **Icteric phase** is heralded by the onset of clinical jaundice, manifested by a yellow-brown cast to the conjunctivae, skin, oral mucosa, and urine (dark urine). Many of the nonspecific prodromal symptoms may subside, but gastrointestinal (GI) manifestations (e.g., anorexia, nausea, vomiting, right upper quadrant pain) may increase, especially early in this phase. In more severe cases Hepatomegaly and splenomegaly (HSM)frequently are noted. This phase lasts 2 to 8 weeks and is part of the clinical course in at least 70% of patients infected with HAV, 30% of those acutely infected with HBV, and 25% to 30% of patients acutely infected with HCV.

   Serum bilirubin levels (total and direct) rise, and aminotransferase levels generally are higher than10 times the upper limit of normal, at least at the onset.
3. **Convalescence or recovery (posticteric) phase** symptoms disappear, but hepatomegaly and abnormal liver function values may persist for a variable period. This phase can last for weeks or months, with longer recovery times for HBV and HCV with usual recovery (clinical and biochemical) within approximately 4 months after the onset of jaundice. Neutralizing antibodies usually appear during the icteric phase and rise to high levels during convalescence.

Complications of acute viral hepatitis include chronic infection, fulminant hepatic failure, and Cirrhosis.

Commented [WU1]: **Incubation period** is the time elapsed between exposure to a pathogenic organism, a chemical, or radiation, and when symptoms and signs are first apparent

Commented [WU2]: Bilirubin is a degradation product of hemoglobin and one of the major constituents of bile, to which it confers the characteristic yellowish color. Bilirubin normally is transported to the liver by way of the plasma. In the liver, it conjugates with glucuronic acid, and then it is excreted into the intestine, where it aids in the emulsification of fats and stimulates peristalsis.1,3a In the presence of liver disease, bilirubin tends to accumulate in the plasma as a consequence of decreased liver metabolism and transport.

Chronic hepatitis, generally defined as illness of at least 6 months' duration, develops in approximately 2% to 7% of adults with hepatitis B and in 50% to 85% of adults with hepatitis C.

Acute liver failure or fulminant hepatitis

serious complication of acute viral hepatitis occurs in 1% to 2% of patients with symptomatic acute hepatitis, perhaps most commonly with hepatitis B and hepatitis D and least commonly with hepatitis C.

It characterized by massive hepatocellular destruction and a mortality rate of approximately 80%. The condition occurs more commonly among older adults and patients with chronic liver disease. Coinfection or superinfection with HBV and HDV or infection by a single hepatitis virus can cause fulminant disease.

The disease is called fulminant if evidence of hepatic encephalopathy appears; however, the initial symptoms (changes in personality, aggressive behavior, or abnormal sleep patterns) may be subtle or misunderstood.

Commented [WU3]: **Encephalopathy** is a general term that means brain disease, damage, or malfunction.

Cirrhosis

Liver cell necrosis and inflammation followed by fibrosis, regeneration and vascular derangement. Liver function deteriorates and blood flow through the organ is obstructed.

It is a common sequel to hepatitis C and alcohol related damage.

Clinical features include; jaundice, ascites, anemia, gastrointestinal hemorrhage, HSM, spider nevi, opaque nails, gynecomastia, liver failure, bleeding tendencies, portal hypertension and hepatic encephalopathy.

Laboratory findings

- **Serum Transaminases** including; Alanine aminotransferase (ALT) (formerly serum glutamatepyruvate transaminase [SGPT]) {Normal range 7-56 IU/L} and Aspartate aminotransferase (AST) (formerly serum glutamate-oxaloacetate transaminase [SGOT]) {Normal range 0-35 IU/L}, these enzymes are released from damaged hepatocytes. ALT is more sensitive indicator of liver damage because it is found only in liver cells. AST is also found in heart, skeletal muscle, pancreas, kidney and RBCs.
- **Plasma bilirubin** level; normal value is less than 1 mg/100ml. jaundice is evident when bilirubin level approaches 2.5mg/100ml.
- **Serum alkaline phosphatase**; it is non-specific test may be normal or slightly elevated. Normal value is 9 to 85 IU/L.
- **WBC count** is increased.
- **Prothrombin time** may be elevated.

- **Diagnosis** is through **serological tests**:

Hepatitis A→ IgM-specific anti-HAV arises early in the disease and persists for only 4 to 12 months

→IgG anti-HAV develops in all patients infected with the virus, is first detectable shortly before the onset of symptoms; titers then rise to high levels, which persist for life.

Hepatitis B→ HBsAg (infectious). Anti-HBsAg (recovery)
Anti-HBcAg (acute infection and Previous infection).
HBeAg (infectious). Anti-HBeAg (clearing\cleared infection).

Hepatitis C→ HCV RNA (infectivity). Anti-HCV (previous infection).

Hepatitis D→ Anti-HDV and HDAg.
Hepatitis E→ Anti-HEV

PREVENTION

Prevention Through Active Immunization

The risk of viral hepatitis is reduced by receiving active immunization. At present, vaccines are available for HAV, for HBV and for combination hepatitis A and B. The HAV vaccines are safe, highly immunogenic, and recommended for patients 2 years of age and older.

The vaccines for prevention of HBV infection are administered in three doses over a 6-month period and produce an effective antibody response in more than 90% of adults and 95% of infants, children, and adolescents.

Vaccination are advocated for persons at high risk for contracting HBV infection table No.1. At the top of the list are health care workers, including dentists, for whom inoculation with the vaccine is strongly recommended.

A current strategy to interrupt HBV transmission in all age groups includes
(1) Prevention of perinatal HBV infection,
(2) Routine vaccination of all infants, and
(3) v Vaccination of selected adolescents and adults not vaccinated as infants.

Table No.1

Persons at Substantial Risk for Hepatitis B Who Should Receive Vaccine
Individuals with occupational risk
Health care workers
Public safety workers
Clients and staff of institutions for developmentally disabled individuals
Hemodialysis patients
Recipients of certain blood products
Household contacts and sex partners of HBV carriers
Adoptees from countries where HBV infection is endemic
International travelers
Illicit drug users
Sexually active homosexual and bisexual men (men who have sex with men)
Sexually active heterosexual men and women (who have multiple partners)
Inmates of long-term correctional facilities

Commented [WU4]: The duration of immunity and the need for booster doses remain controversial. Current information based on experience with the plasma-derived HBV indicates that immunity remains effective for more than 10 years. Current guidelines published by the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices recommend booster doses only for persons who did not respond to the primary vaccine series.

Prevention Through Passive Immunization

Treatment of viral hepatitis can be accomplished by administering early postexposure immune globulins or postexposure hepatitis B vaccine. Immune serum globulin is derived from a pool of antibodies collected from human plasma that is free of HBsAg, HCV, and HIV. This sterile solution contains antibodies against both hepatitis A and hepatitis B. Another type of immune globulin is called hepatitis B immune globulin (HBIG).

It is specially prepared from preselected plasma that is high in titers of anti-HBs. Administration of both immune globulin and HBIG is safe, but they interact adversely with live attenuated vaccines (i.e., measles, mumps, rubella [MMR] vaccine) if given within 5 months of each other.

TREATMENT

- As with many viral diseases, therapy basically is **palliative and supportive**. Bedrest and fluids may be prescribed, especially during the acute phase. A nutritious and high calorie diet is advised.
- Alcohol and drugs **metabolized by the liver** are not to be ingested.
- Viral **antigen and ALT** levels should be monitored for 6 months to determine whether the hepatitis is resolving.
- Chronic hepatitis is treated by administration of **interferon (alfa-2b)** (3–10 million units given three times weekly for 6 months to 1 year).
- **Corticosteroids** usually are reserved for patients with fulminant hepatitis.
- **Liver transplantation** is a last resort for patients who develop cirrhosis.

Dental management

1. **Identification of potential or actual carriers** of HBV, HCV and HDV is very difficult through history.
2. **All patients with viral hepatitis** must be managed as though they are **potentially infectious**, so standard precautions for infection control should be implemented.
3. It is recommended that all dental health care workers should receive **vaccination against HBV** and implement **standard precautions** during the care of all dental patients.
4. Patients with **active hepatitis**:
    - Should be referred for medical treatment, only urgent dental treatment should be provided with strict adherence to standard precautions of infection control and preferably in isolated operatory.
    - Aerosols should be minimized.
    - Drugs that are metabolized in liver should be avoided.
    - If surgery is necessary prothrombin time (PT) and bleeding time should be obtained.

5. Patients with **history of hepatitis**:
   - Since most patients are unaware that they have had hepatitis, identification of carriers is very difficult, and requesting screening tests for every patient is not practical. The only method for providing protection is to adopt a strict program of clinical asepsis for all patients.
   - If knowing the type of hepatitis virus through history is not possible, screening test can be ordered for the presence of HBsAg or Anti-HCV.
6. Patients at **high risk of HBV or HCV infection**:
   - Patients are at high risk of hepatitis B or hepatitis C are listed in table No.1.
   - **Screening** is recommended for HBsAg and Anti-HCV.
   - Patients who are carriers might have chronic active hepatitis leading to bleeding problems or metabolism problems that require treatment modification.
   - If **accidental needle stick occurs**, knowing if the patient is HBsAg positive or HCV positive is very important to determine the need for immunoglobulin, vaccine and follow up medical care.
7. Patients who are **hepatitis carriers:**
   - Standard precautions of infection control should be followed.
   - Such patients may have chronic active hepatitis with compromise liver function. Liver function tests can be ordered and consultation with physician may be needed.
8. Patients with **signs and symptoms of hepatitis**
   - Only emergency dental care should be provided in isolated operatory with adherence to the standard precautions of infection control.
   - Routine dental care should be postponed and the patient referred to the physician.
9. **Dentists who are hepatitis** virus carriers:
   - If the dentist is found to be positive for blood transmissible virus, exposure-prone procedures should not be performed, or strict adherence to aseptic technique should be followed to prevent transmission.
   - Periodic retesting is necessary.
10. **Postexposure protocols for percutaneous or permucosal exposures to blood.:**
   - In case of percutaneous or permucosal exposure through needle stick or puncture wound contaminated with blood from an individual who is HBsAg, the risk of infection may approach 30%.
   - ❖ If the exposed is **vaccinated;** a test to evaluate Anti-HBsAg should be done:
   - If inadequate levels→ HB immunoglobulin + vaccine booster should be administered.
   - If adequate levels→ nothing further is required.
   - ❖ If the exposed is **not vaccinated**→ HB immunoglobulin + initiation of vaccination is recommended.
   - For HCV; no postexposure protocol or vaccine is available.

11.Drug administration:

- Patients who are completely recovered from viral hepatitis, no special considerations are needed.
- In patients with *chronic active hepatitis with impaired liver function*; drugs that are metabolized in the liver should be avoided if possible or reduced doses used (Aspirin, Acetaminophen, Lidocaine, Ibuprofen, Ampicillin, Tetracycline, Metronidazol) table No.2. A quantity of 3 cartridges of 2% Lidocaine (120mg) is considered limited.

Table No.1

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§

Oral manifestations and complications

- **Abnormal bleeding**; results from abnormal synthesis of blood clotting factors, abnormal polymerization of fibrin, inadequate fibrin stabilization, excessive fibrinolysis, or thrombocytopenia associated with splenomegaly that accompanies chronic liver disease. Before surgery platelet count, PT and INR should be evaluated.
- Hepatocellular carcinoma rarely metastasize to the jaws.

Alcoholic liver disease

Alcoholism is a chronic addiction to ethanol in which a person craves and uncontrollably consumes ethanol and becomes tolerant to its intoxicating effect. It is the most common drug of abuse.

Alcohol is CNS depressant and it impairs the capacity to reason, it eventually interferes with cerebellar function causing ataxia, motor incoordination and unconsciousness.

Excessive alcohol consumption causes alcoholic liver disease and ultimately cirrhosis of the liver and worsens other liver disorders such as viral hepatitis.

The lack of treatment of alcohol abuse leads to significant morbidity and mortality rates.

An alcoholic is a man who drinks regularly 30 units/week or a woman who drinks 20 units/week.

Alcohol is hepatotoxic and its metabolite, acetyl aldehyde, is fibrinogenic.

Clinical presentation Pathophysiology and Complications

Alcohol has a deleterious effect on neural development, the corticotropin-releasing hormone system, metabolism of neurotransmitters, and the function of neurotransmitter receptors causing sensory and motor disturbances.

Prolonged abuse of alcohol contributes to malnutrition (folic acid deficiency), anemias, and decreased immune function.

The pathologic effects of alcohol on the liver are expressed as one of three disease entities. These conditions may exist alone but commonly appear in combination.

1. **Fatty liver** is the earliest change seen in alcoholic liver disease, characterized by presence of a fatty infiltrate with no visible manifestations except liver enlargement; it is considered completely reversible,
2. **Alcoholic hepatitis** is diffuse inflammatory condition of the liver is characterized by destructive cellular changes, some of which may be irreversible. For the most part, alcoholic hepatitis is considered a reversible condition. The clinical presentation of alcoholic hepatitis often is **nonspecific** and may include features such as nausea, vomiting, anorexia, malaise, weight loss, and fever. More **specific** findings include hepatomegaly, splenomegaly, jaundice, ascites, ankle edema, and spider angiomas.
3. **Cirrhosis** most serious form of alcoholic liver disease, which generally is considered an irreversible condition characterized by progressive fibrosis and abnormal regeneration of liver architecture in response to chronic injury or insult (i.e., prolonged and heavy use of ethanol).

It may remain asymptomatic for many years until sufficient destruction of the liver parenchyma has occurred to produce clinical evidence of hepatic failure.Ascites, spider angiomas, ankle edema, and jaundice may be the earliest manifestations, but frequently hemorrhage from esophageal varices is the initial sign with rapid progression to hepatic encephalopathy, coma, and death.

Laboratory findings

Laboratory findings in alcoholic liver disease range in significance from minimal abnormalities caused by a fatty liver to manifestations of alcoholic hepatitis and cirrhosis.

- Increased bilirubin, AST, ALT, gamma-glutamyl transpeptidase, amylase, uric acid, triglycerides and cholesterol.
- Leukopenia (or Leukocytosis) and anemia.
- Thrombocytopenia (due to splenomegaly).
- Increased prothrombin time (PT), partial thromboplastin time (PTT) and thrombin time.

Medical management

1. **Identification through physical examination** to evaluate impaired organ systems, includes a search for evidence of liver failure, GI bleeding, cardiac arrhythmia, and glucose or electrolyte imbalance.
2. **Gradual withdrawal from alcohol**, abrupt withdrawal leads to loss of appetite, tachycardia, anxiety, insomnia, hallucinations, disorientation, impaired memory and attention and agitation.
3. High protein, high calorie and low sodium diet and vitamin supplementation.
4. Management of CNS depression caused by withdrawal.
5. Education of the patient about alcoholism.
6. Management of complications.
7. End stage cirrhosis requires liver transplantation.

Dental management

1. **Detection of such patients** by:
   - History; the patient should be asked about the type, quantity, frequency, pattern and consequences of alcohol use, also family history of alcoholism.
   - Clinical examination for signs and symptoms of alcoholic liver disease.
   - Alcohol odor on breath.
   - Information from family members or friends.
2. A patient with **untreated alcoholic liver disease** is not a candidate for elective, outpatient dental care and should be referred to a physician.
3. In patients with **history of alcohol liver disease or alcohol abuse**, a physician should be consulted to verify the patient's current status, medications, laboratory values (if present) and contraindications for medications and surgery.
4. If signs and symptoms of alcoholic liver disease are present the dentist can request some screening tests before surgical procedures; complete blood count (CBC) with differential, AST, ALT, platelet count, thrombin time, PT and INR. **Abnormal results should be discussed with the physician**.

5. **Treatment considerations**; 3 major dental treatment considerations apply for patients with alcoholic liver disease:
   - **Bleeding tendencies**; can be managed with the assistance of physician, this may entail the use of local hemostatic agents, fresh frozen plasma, vitamin K, platelets and antifibrinolytic agents.
   - The **unpredictable metabolism of drugs**;

The dose of drug in table No.1 may need to be adjusted when treating patients with chronic alcoholism (e.g., half the regular adult dose may be appropriate if cirrhosis or alcoholic hepatitis is present), or a specific agent or class of drugs may be contraindicated as advised by the patient's physician.

In **mild to moderate liver disease**, enzymatic induction is likely to have occurred leading to increased tolerance to LA, sedatives, hypnotics and GA, thus larger doses may be needed to attain the desirable effects of these drugs.

In **cirrhosis or alcoholic hepatitis** avoid drugs that are metabolized in the liver or using half dose particularly if aminotransferases level (AST and ALT) is 4 times more than normal, serum bilirubin is more than 2mg/dl, serum albumin lower than 35g/L, with signs of ascites and encephalopathy or malnutrition.

   - The **risk of infection or spread of infection**; because these patients have reduced reticuloendothelial capacity and altered cell mediated immune function, but antibiotic prophylaxis is not needed unless there is an ongoing infection. Consultation with the physician regarding the use of antibiotic may be considered especially in patients with moderate or severe liver disease.

6. Liver enzyme induction and CNS effects of alcohol in patients with alcoholism can require use of **increased amounts of local anesthetic or additional anxiolytic procedures.**

Oral complications and manifestations

1. Poor oral hygiene and caries which is due to neglect.
2. Impaired gustatory function.
3. Nutritional deficiency can result in anemia causing glossitis, loss of papillae, angular and labial cheilitis.
4. Bleeding tendencies cause spontaneous gingival bleeding, mucosal ecchymoses and petechiae.
5. Alcohol breath odor.
6. Jaundiced mucosal tissues.

7. Sialoadenosis; bilateral painless swelling of the parotid glands, it is attributed to demyelinating polyneuropathy that results in abnormal sympathetic signaling, abnormal acinar protein secretion and acinar cytoplasmic swelling.
8. Oral squamous cell carcinoma, alcohol abuse and smoking are major predisposing factors.
9. Bruxism and dental attrition.
10. Xerostomia