**Pathology 4th class / قسم المختبرات الطبية / lecture: 11**

**Viral hepatitis**

**Definition**: Viral hepatitis may be defined as viral infection of hepatocytes that producesnecrosis and inflammation of the liver.

**Cause**

Most cases of hepatitis are caused by a group of five separate, unrelated viruses that have a particular affinity for the liver known as hepatotropic virus (hepatitis viruses A, B, C, D, andE). All except HBV are RNA viruses.

- Hepatitis A and E cause infectious hepatitis and transmitted mainly by the fecal-oral route or ingestion of contaminated water.

- Hepatitis B, C, and D cause serum hepatitis. They are transmitted mainly by parenteral routes and less commonly by intimate or sexual exposure. They canproduce chronichepatitis, which may progress to cirrhosis and hepatocellularcarcinoma.

**Hepatitis A Virus**

-Source of infection: Only source of infection is acutely infected person.

– Virus is excreted in bile then excreted in stool/feces of infectedpersons for about 2 weeks before the onset of symptoms and then for a further 2 weeks or so.

– Disease is maximally infectious just before the onset of jaundice.

**Mode of Transmission**

-Fecal-oral route by ingestion of contaminated water and foods. HAV viremia is transient. Hence, blood-borne transmission does not occur.

Incubation period: 3 to 6 weeks (mean ~ 4 weeks).

**Hepatitis B Virus (HBV)**

Mode of Transmission

-Vertical/congenital transmission: From mother to child may occur in utero, during parturition or soonafter birth.

-Horizontal transmission: It is the dominant mode of transmission.

◆ By percutaneous and mucous membrane: Exposure to infectious body fluids. HBV can survivefor long periods on household articles, e.g. toys, toothbrushes and maytransmit theinfection.

◆Intravenous route: Through transfusion of unscreened infected blood or blood products.

– Close personal contact: Unprotected heterosexual or homosexual intercourse. The virus can be found in semen and saliva.

Incubation period: It ranges from 4 to 26 weeks

**Outcome of HBV Infection:-**

1. Acute hepatitis with recovery and clearance of the virus.

2. Chronic hepatitis.

3. Progressive chronic disease ending in cirrhosis.

4. Fulminant hepatitis with massive liver necrosis.

5. Asymptomatic carrier state.

6. Hepatocellular carcinoma.

**Hepatitis C Virus**

Mode of spread: It mainly spreads by the parenteral route as a blood-borne infection. It may also spread by sexual contact.

Incubation period: 2 to 26 weeks (mean 6 to 12 weeks).

**Outcome of HCV Infection**:-

1. Acute hepatitis.

2. Chronic hepatitis: It occurs in the majority of individuals infected by HCV.

3. Cirrhosis: It develops over 5 to 20 years in 20% to 30% ofpatients.

4. Fulminant hepatic failure is rare.

**Hepatitis D Virus**

Mode of spread: Parenteral route and sexual contact.

**Hepatitis E Virus**

Source of infection: HEV is a zoonotic disease with animalreservoirs, such as monkeys, cats, pigs, and dogs.

Mode of transmission: It is an enterically transmitted, water-borne infection.

Incubation period:~6 weeks.

**Outcome of HCV Infection**

It causes self-limiting acute hepatitis. It does not cause chronic liver disease. But it has a high mortality rate (about 20%) among pregnant women.

**Acute Hepatitis**

It can be caused by any one of four hepatotropic viruses. This can be divided into four phases:

i. Incubation period (varies depending on the type of virus).

ii. Symptomatic preicteric phase: It presents with nonspecific symptoms such as malaise, nausea, poor appetite, and abdominal pain.

iii. Symptomatic icteric phase: Jaundice and yellow sclera, dark colored urine (conjugated hyperbilirubinemia), light-colored stool, and pruritis (bile saltretention).

**Chronic hepatitis**

**Definition**: Chronic hepatitis is defined as symptomatic, biochemical, or serologic evidence of hepatic disease for more than 6 months. Microscopically, thereshould be inflammationand necrosis in the liver.

**Causes**

Hepatitis may be caused by viruses as well as other etiological agents. The virusesinclude:

-**HCV**: It is the most common cause of chronic viral hepatitis and mostly asymptomatic.

-**HBV**: Chances of chronic hepatitis is high if the infection occurs at a younger age. Maternalto-infant transmission is a major riskfactor.

**Fulminant Hepatic Failure**

**Definition**: Hepatic insufficiency progresses within 2 to 3 weeks from onset of symptoms to hepatic encephalopathy, in patients who do not have chronic liverdisease.

**Causes**

- Viral hepatitis: HBV and HAV. Occasionally, HCV and others

- Noninfectious causes: Acetaminophen toxicity.

- Unknown

**Cirrhosis**

**Definition**: Cirrhosis is an end stage of any chronic liver disease. It is a diff use process (entire liver is involved) characterized by fibrosis and conversion of normalarchitecture to structurally abnormal regenerating nodules of liver cells.

**Morphological Characteristics**

The three main morphologic characteristics of cirrhosis are:

1. Fibrosis

- It is the characteristic feature of progressive liver damage.

2. Regenerating Nodules

3. Loss of Architecture

**Clinical features**

The clinical features of cirrhosis range widely:

-**Initial phase**: It is termed as “compensated” cirrhosis, the patient may be asymptomatic.

-**Later phase**: It is termed as “decompensated” cirrhosis, presents with complications ofportal hypertension or liver dysfunction (or both).

**Malignant tumors of liver**

Malignant tumors of liver can be primary or metastatic. Most primary cancers of liver arise from hepatocytes and are termed hepatocellular carcinoma (HCC).Less common are cancersthat arisefrom bile duct known as cholangiocarcinomas.Two rare primary liver cancers are: hepatoblastomas andangiosarcomas.

**Hepatoblastoma**

- Most common liver tumor arising in young childhood.

-Malignant tumor and usually fatal

**Hepatocellular Carcinoma (HCC)**

-Hepatocellular carcinoma (HCC) is a malignant tumor derived from hepatocytes or their precursors.

- Predominantly in males with a M:F ratio of 2.4:1

**Etiopathogenesis**

It is multifactorial disease and complex in pathogenesis. It is probably a multistep processthat involves various risk factors. Three major and several minorrisk factors are associatedwith HCC .

**A. Major risk factors**

1. Chronic hepatitis: The risk of liver cancer in individuals infected with both HCV and HBV is three times higher than with either alone.

2. Cirrhosis: Strong association between HCC and cirrhosis and both frequently coexists.

- Alcoholic cirrhosis predisposes to HCC.

- Male gender, age, and duration of cirrhosis are the major risk factors for HCC in patients with cirrhosis.

3. Aflatoxin B1 (chemical carcinogen): It isatoxin produced by the fungus Aspergillusflavus. This fungus contaminates improperly stored peanuts and grains.Dietary exposure to aflatoxin B1 is an important risk factor for hepatocellular carcinoma.

4. Non-alcoholic steatohepatitis (NASH)

**B. Minor Risk Factors**

-These include: genetic factors, age, gender, chemicals, hormones, and nutrition.

- Hemochromatosis: Excessive free iron may be carcinogenic and generates mutagenic reactive oxygen species.

- Wilson's disease: It is characterized by accumulation of copper in the liver.

-Metabolic disorders:

**Spread**

-**Local spread**: HCC may first spread within the liver itself and develop satellite nodules. Local invasion of the diaphragm is common.

-Lymphatic spread: HCC may spread to portal lymph nodes, peripancreatic, and para-aortic nodes.

**- Blood spread**:

– All patterns of HCCs have a strong tendency for invasion of vessels.

– It may metastasize to the lungs.

**Cholangiocarcinoma (CCA)**

- It is the second most common hepatic malignant tumor of liver.