**Lecture 18 General pathology Dr. Ali H. Murad**

***SYSTEMIC PATHOLOGY***

***PATHOLOGY OF LIVER AND BILIARY TRACT***

## PATTERNS OF HEPATIC INJURY

***Degeneration:***

Ballooning, “feathery” degeneration, fat, pigment (hemosiderin, bile, both intrinsic) ***Inflammation***: Viral or Toxic

* Regeneration
* Fibrosis

***Neoplasia*:** 99% metastatic, 1% primary

### *INFLAMMATORY & INFECTIOUS DISORDERS*

The liver is almost always involved in blood-borne infections such as bacterial (pyogenic abscesses, miliary tuberculosis, salmonelloses), parasitic (malaria, amebiasis), fungal (candidiasis), & viral (infectious mononucleosis, cytomegalovirus & herpes virus). *Nevertheless viral hepatitis is the leading primary liver infection.*

### *VIRAL HEPATITIS*

Unless otherwise specified, the term viral hepatitis is reserved for “infection of the liver caused by a group of hepatotropic viruses” i.e. having a particular affinity for the liver.

This group comprises

1. *Hepatitis A virus (HAV)*
2. *Hepatitis B virus (HBV)*
3. *Hepatitis C virus (HCV)*
4. *Hepatitis D virus (HDV)*
5. *Hepatitis E virus (HEV)*

### *1-Hepatitis A Virus (HAV)*

**Acute viral hepatitis A** (**infectious hepatitis**) is a benign, self-limited disease with an average incubation period of 4 weeks. HAV does not cause chronic hepatitis or a carrier state.

In children, where most cases occur, the disease tends to be mild or asymptomatic. HAV spreads by ingestion of contaminated water and foods. The viremia is short-lived, thus, blood-borne transmission occurs rarely; therefore, donated blood is not screened for this virus.

HAV is a small, RNA virus. It reaches the liver from the intestinal tract after ingestion, replicates in hepatocyte, and is shed in the bile and feces.

Detection of anti-HAV IgM antibody is the best diagnostic marker for the disease.

### *2-Hepatitis B Virus (HBV) this can produce*

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

2. Chronic viral hepatitis B, which is either

1. Non-progressive or
2. Progressive ending in cirrhosis
3. Fulminant hepatitis with massive liver necrosis
4. An asymptomatic carrier state.

#### Chronic viral hepatitis B

Is an important precursor of hepatocellular carcinoma**.** HBV remains in blood during the last stages of a long incubation period (4-26weeks) and during active episodes of both acute and chronic hepatitis. It is also present in all physiologic and pathologic body fluids, with the exception of stool. In endemic regions, vertical transmission from mother to child during birth constitutes the main mode of transmission.

HBV is a DNA virus & its replication does not require integration of the virus in the host DNA, however, integrated HBV is frequently found in cells.

After exposure to the virus, there is a long incubation period (average 16 weeks) **HBsAg** appears before the onset of symptoms, peaks during overt disease, and then declines to undetectable levels in 3 to 6 months. **AntiHBs** persist for life, conferring protection; this is the basis for current vaccination.

***Hepatitis C Virus (HCV****)*

is another major cause of liver disease. The major route of transmission is through blood inoculation, with low rates of sexual and vertical transmissions. HCV infection has a much higher rate (than HBV) of progression to chronic liver disease and eventual cirrhosis. It is a single-stranded RNA virus. Based on the genetic sequence, HCV is subclassified into six genotypes. An infected person may carry many HCV variants. This variability seriously hinders efforts to develop an HCV vaccine. The incubation period for hepatitis C has a mean of 6 to 12 weeks. The clinical course of acute viral hepatitis C is usually asymptomatic and is easily missed. Strong immune responses involving CD4+ and CD8+ cells are associated with self-limited HCV infections, but it is not known why only a minority of individuals is capable of clearing HCV infection. Persistent infection is the hallmark of HCV; in 80% of such cases, it complicates subclinical acute infection. Cirrhosis develops in 20% of such patients. Fulminant hepatitis is rare.

### Clinical Features and Outcomes of Viral Hepatitis

A number of clinical syndromes may develop after exposure to hepatitis viruses:

1. Asymptomatic infection (serologic evidence only)

2. Acute hepatitis.

1. Chronic hepatitis (with or without progression to cirrhosis)
2. Chronic carrier state (asymptomatic)
3. Fulminant hepatitis (sub massive to massive hepatic necrosis with acute liver failure)

### Pathological features of viral hepatitis

The morphologic changes in acute and chronic viral hepatitis are shared among the hepatotropic viruses and can be mimicked by drug reactions.

#### Acute viral hepatitis

1-The normal radial array of the lobules is lost.

2-There is diffuse ballooning degeneration of hepatocytes; the cells are swollen with clear, wispy cytoplasm.

3-Hepatocytes necrosis

4-Inflammation is usually a prominent feature of acute hepatitis.

5-The portal tracts are infiltrated predominantly by lymphocytes.

6-Hypertrophy& hyperplasia of Kuppfer cells

7-Cholestasis may be present

#### Chronic hepatitis

The changes are of variable severity, ranging from very mild to severe.

1-Hepatocyte necrosis may occur in all forms of chronic hepatitis.

2-The inflammatory component consists mainly of lymphocytes, macrophages, and occasional plasma cells. In the mildest forms, significant inflammation is limited to portal tracts.

3-The liver architecture is usually well preserved

4-Continued periportal necrosis (interface hepatitis) and bridging necrosis

5-The hallmark of serious liver damage is the deposition of fibrous tissue. At first, at the portal tracts, but with time periportal fibrosis occurs.

6-This is followed by bridging fibrosis that links fibrous septa between lobules**.**

7-Continued loss of hepatocytes with fibrosis results in cirrhosis, with fibrous septa and hepatocyte regenerative nodules.

## ALCOHOLIC LIVER DISEASE

Excessive ethanol consumption is a common cause of chronic liver disease in Western countries and accounts for up to 50% of deaths due to cirrhosis. Chronic heavy drinkers are predisposed to 3 distinctive forms of alcoholic liver disease; these may overlap.

1. Hepatic steatosis (almost all heavy drinkers)
2. Alcoholic hepatitis (30%)
3. Cirrhosis (15%)

**Alcoholic Cirrhosis:** is the final, irreversible form of alcoholic liver disease.

### *Gross features*

Initially, the liver is yellow, fatty, enlarged, (usually over 2 kg) & finely (micro-) nodular externally and on section.

### *Microscopic features*

1-Initially there are delicate fibrous septa that extend from central veins through the sinusoids to the portal tracts and from portal tracts to portal tracts.

2-Regenerative activity of entrapped hepatocytes generates in the early stages uniform small nodules (< 0.3 cm in diameter). This is by definition a micronodular cirrhosis. The nodules eventually become larger & more prominent and are engulfed by ever wider band of fibrous tissue, and the liver is converted into a mixed micronodular and macronodular cirrhosis.

With alcoholic cirrhosis, the immediate causes of death are

1. Hepatic failure
2. Massive gastrointestinal haemorrhage
3. Intercurrent infection
4. Hepatorenal syndrome
5. Hepatocellular carcinoma (5%of cases).

## Hemochromatosis

1-Hereditary (Primary)

2-Iron Overload (Secondary), e.g., hemolysis, increased Fe intake, chronic liver disease

### Hereditary hemochromatosis

The most common form of this genetic disease is an *autosomal recessive variant* of adult onset caused by mutations in the *HFE* gene.

#### Fully developed cases of hereditary hemochromatosis show

1. Cirrhosis(all patients)
2. Diabetes mellitus(75%)
3. Skin pigmentation(75%).

***Secondary iron overload*** *or (****secondary hemochromatosis****)*

Iron accumulations from known sources of excess iron *,* the most important of these are

1. Multiple transfusions
2. Ineffective erythropoiesis (as in β-thalassemia and sideroblastic anemia)
3. Increased iron intake .

Chronic liver diseases can also cause iron accumulation in the liver e.g. alcoholic liver disease.

#### Gross features

Hemosiderin deposition occurs in several organs & tissues e.g. the myocardium, pituitary, adrenal, thyroid, parathyroid gland, joints, skinThe liver is typically chocolate brown in color.

Fibrous septa develop slowly, leading ultimately to micronodular cirrhosis in an intensely pigmented liver.

#### Microscopic features

The golden-yellow hemosiderin granules accumulate in the cytoplasm of periportal hepatocytes; these stain blue with the Prussian blue stain