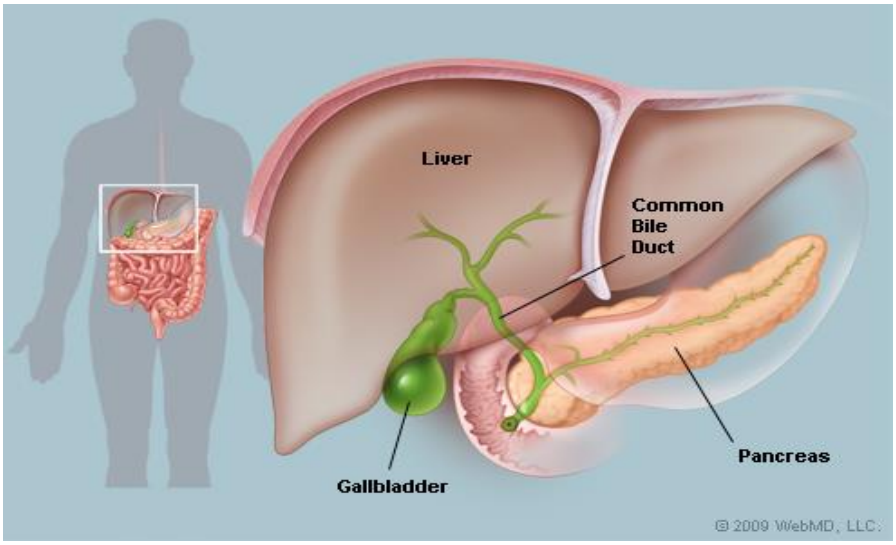
General Pathology

Gall bladder, Liver and Pancreas

Gall bladder

The gallbladder is a sac located under the liver. It stores and concentrates bile produced in the liver. Bile aids in the digestion of fat and is released from the gallbladder into the upper small intestine in response to food (especially fats).



Cholelithiasis (Gallstones)

1. Cholesterol stones

• Most common type

• Composition: cholesterol monohydrate

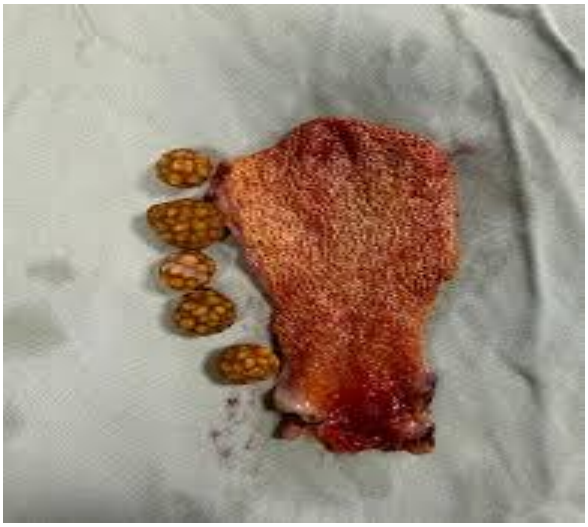
• Risk factors:

1. Female
2. Fat-obesity
3. Fertile-Pregnancy
4. Forty-Increase age

5. Fair-genetic in western countries

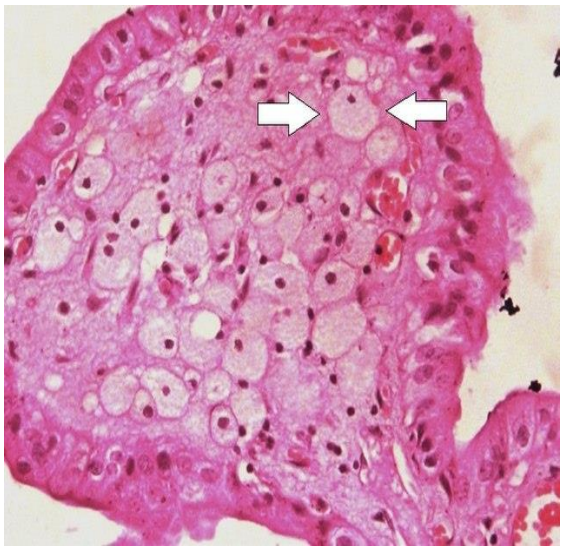
Morphology: hard and pale yellow. 75% are radiolucent

• The supersaturated cholesterol in bile that form cholesterol stones may also diffuse into the mucosa and manifest as cholesterolosis.



• Cholesterolosis:

Gallbladder mucosa demonstrates lamina propria distended by foamy macrophages.



2. Pigmented stone

• Composition: calcium bilirubin salts

• Risk factors:

1. Hemolytic anemia

2. Biliary infections (e.g., with Escherichia coli, Opisthorchis sinensis)

• Morphology: black stone. 75% are radiopaque

• Clinical features of gall stone

• Usually, asymptomatic

• If symptomatic: Biliary colic-upper right abdomen pain due to impacted stone.

• Complications:

1. Cholecystitis

2. Cholangitis: biliary tree inflammation

3. Fistula and gallstone ileus

Pancreas

Retroperitoneal organ with endocrine part-2% of the pancreas- (islet of Langerhans)-secrete insulin, glucagon and somatostatin with main disease in this part are diabetes mellitus and neoplasm.

The exocrine part (acinar cells that produce the digestive enzymes and the ducts that convey the enzymes to the duodenum) The digestive enzymes secreted as inert inactive proenzyme form except for lipase and amylase which are secreted in active form.

Diseases of the exocrine part are acute and chronic pancreatitis, cystic fibrosis and neoplasms.

Inflammatory conditions (pancreatitis):

By definition, acute pancreatitis is reversible if the inciting stimulus is withdrawn; chronic pancreatitis is defined by irreversible damage to the exocrine parenchyma.

Acute pancreatitis

Acute inflammation of the pancreas

Causes:

1. Gallstone in the biliary tree and alcoholism- 80% of cases

2. Other causes (non gall stone) obstruction e.g., ampullary tumor, Infection e.g., mumps, medications e.g., thiazide diuretics

3. Inherited pancreatitis: autosomal dominant with (serine protease inhibitor, Kazal type-1) SPINK1 mutation. Patient presented with severe recurrent attacks of pancreatitis that begin in childhood

Morphology: Grossly: areas of red-black hemorrhage interspersed with foci of yellow-white, chalky fat necrosis of the pancreas.

Fat saponification:

Grossly visible chalky-white areas composed of fatty acids (from area of fat necrosis) combined with calcium.

Clinical features:

1. Acute stabbing abdominal pain radiating to the back

2. Shock

3. Hypocalcemia

Lab: elevated serum amylase and lipase

Chronic pancreatitis

Inflammation of the pancreas with irreversible destruction of exocrine parenchyma, fibrosis, and, in the late stages, the destruction of endocrine parenchyma Chief distinction between acute and chronic pancreatitis is the irreversible impairment in pancreatic function that is characteristic of chronic pancreatitis.

There is significant overlap in the causes of acute and chronic pancreatitis. By far the Most common cause of chronic pancreatitis is long-term alcohol abuse in male patient.

Morphology:

There is replacement of pancreatic acinar tissue by dense fibrous connective tissue, with relative sparing of the islets of Langerhans, and variable dilation of the pancreatic ducts. The pancreas is hard with focal calcification.

Clinical Features:

Chronic pancreatitis can be silent or can be heralded by recurrent attacks of pain and/or jaundice.

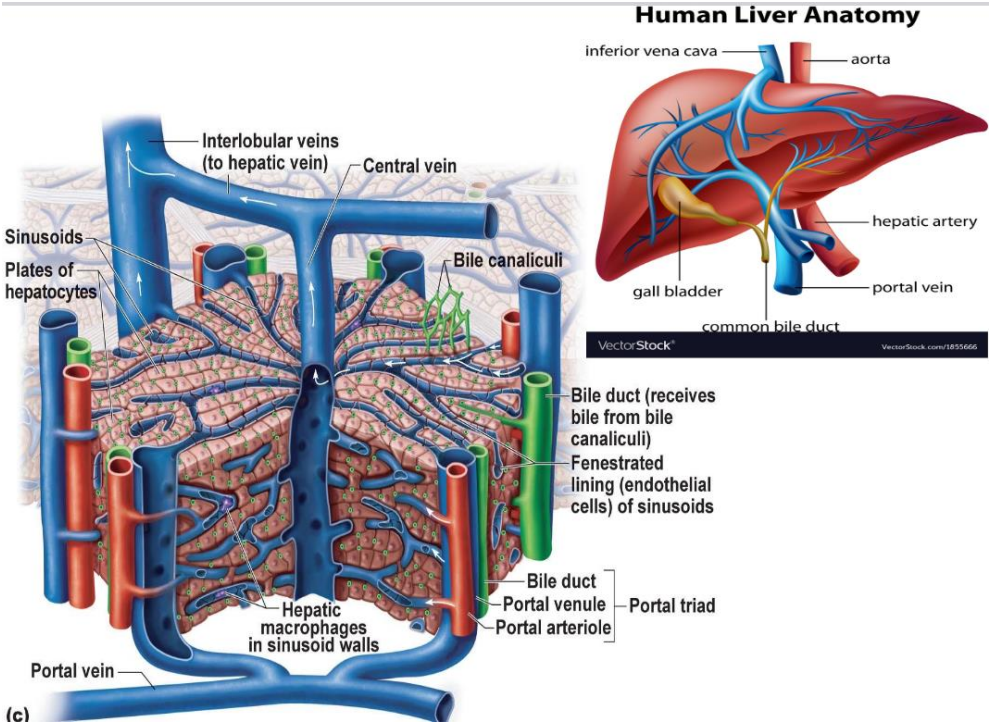
Liver:

• The normal adult liver weighs 1500 gm.

• The liver has a dual blood supply: the portal vein, and the hepatic artery supply. The blood drains the liver through the hepatic vein to the inferior vena cava.

• The microarchitecture of the liver is consisting of: the hepatic lobule (hexagonal) and the portal tract (portal vein, hepatic artery and bile duct) at the corners of the hexagon with the central vein at the center of the hexagon

• In the lobule the parenchyma is divided into three zones, zone 1 being closest to the portal tract, zone 3 closest to central vein, and zone 2 being intermediate



PATTERNS OF HEPATIC INJURY

1. Hepatocyte degeneration

2. Hepatocyte necrosis and apoptosis

3. Regeneration

4. Inflammation

5. Fibrosis: (irreversible)

6. Cirrhosis: (irreversible)

PATTERNS OF HEPATIC INJURY

Hepatocyte degeneration and accumulation

1.Fatty degeneration (Steatosis): fat accumulation inside the hepatocyte. Fortunately, it is a reversible change and can be:

• Microvesicular: multiple tiny droplets of fat do not displace the nucleus. Caused by:

a) alcoholic liver disease

b) Reye syndrome,

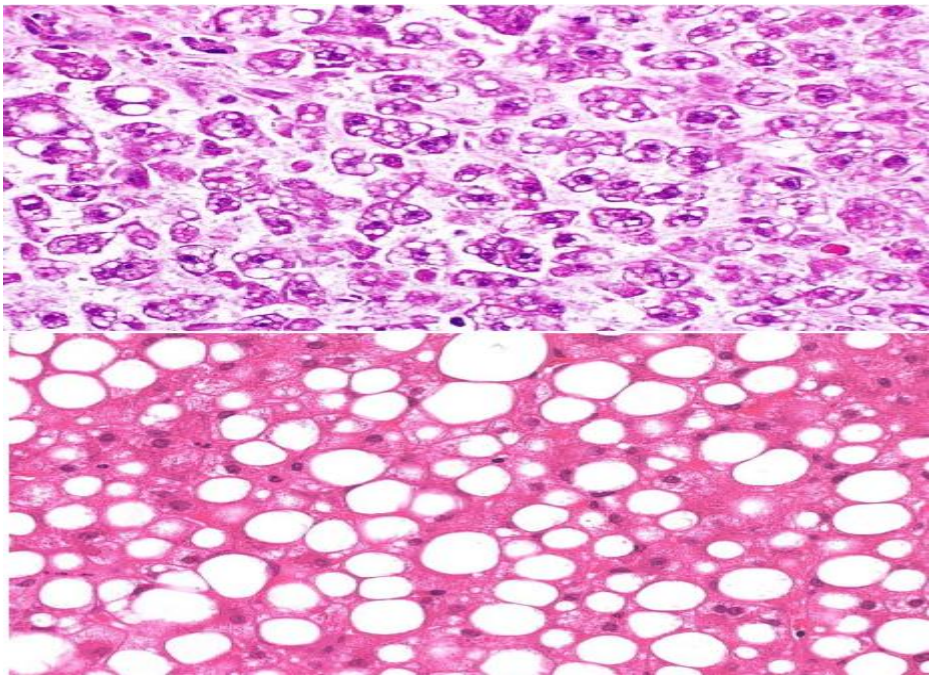
c) fatty liver of pregnancy

• Macrovesicular: single large fat droplet that displace the nucleus caused by:

a) alcoholic liver disease

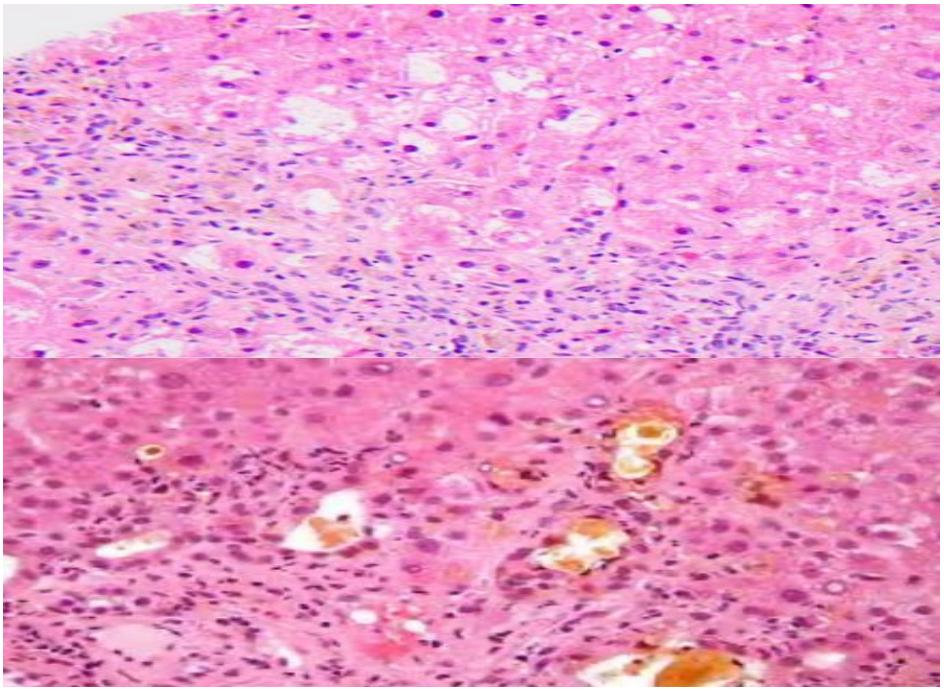
b) obesity

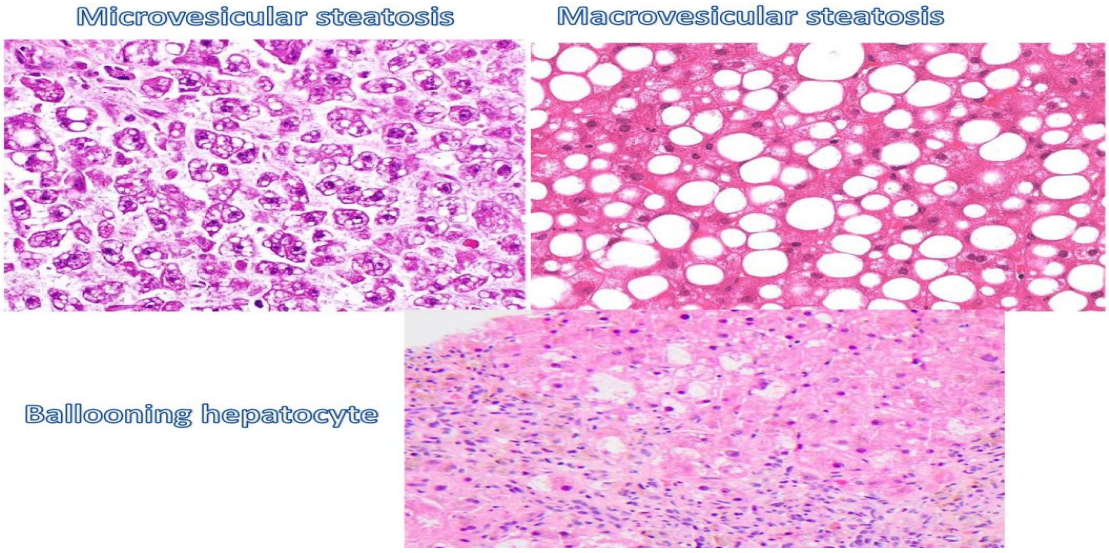
c) diabetes



2. Ballooning degeneration: change marked by cell swelling, cytoplasmic clearing, and clumping of intermediate filaments, which when prominent, may form Mallory hyaline. It is a hallmark of alcohol-induced or nonalcoholic steatohepatitis but also due to severe toxic and immunological insult.

3. Feathery degeneration: bile accumulated in the hepatocytes.





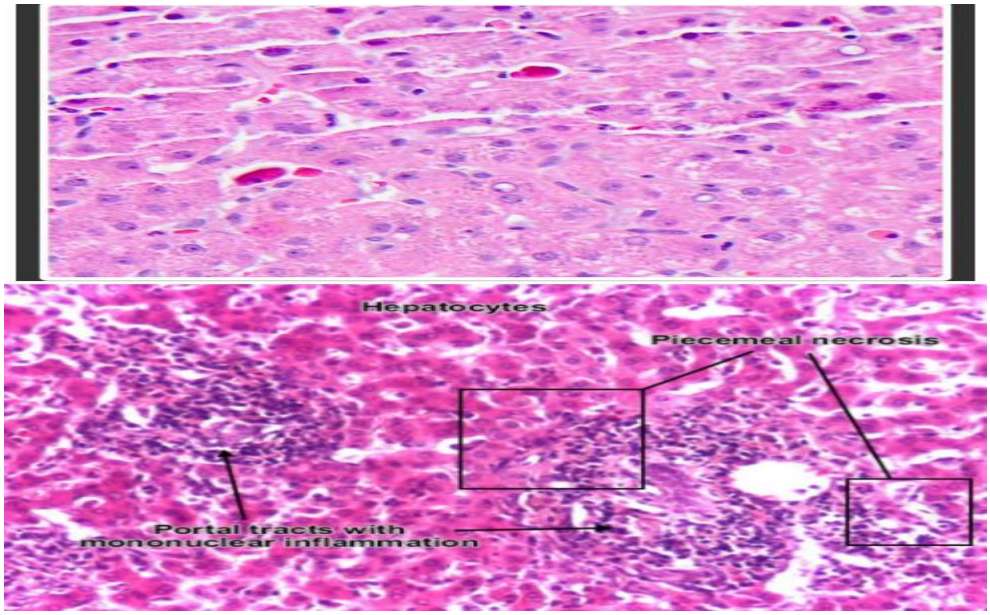
Hepatocyte necrosis and apoptosis

A-Focal apoptosis:(acidophil bodies) (councilman body)

B-Centrilobular necrosis

C-piecemeal necrosis (Interface hepatitis): necrosis of hepatocytes between the periportal parenchyma & inflamed portal tract. D- Bridging necrosis E- Sub massive necrosis: Destruction of entire hepatic lobule. F-

Massive necrosis: Destruction of most of the liver parenchyma & this usually accompanied by hepatic failure.



Regeneration: hepatocyte replication to compensate for the cell or tissue loss.

4. Inflammation: it is injury to hepatocytes associated with Influx of acute & chronic inflammatory cells into the liver (hepatitis).

5. Fibrosis (irreversible): fibrous tissue formed in response to inflammation or toxic insult to the liver

6. Cirrhosis (irreversible): is a destruction of normal liver architecture characterized by nodules of regenerating hepatocytes surrounded by bands of scar tissue due to progressive parenchymal injury and fibrosis.

Liver failure

• The most severe form of liver disease in which 80% to 90% of functional capacity of the liver must be lost. It follows acute injury or

chronic injury, but may also occur as an acute insult superimposed on an otherwise well compensated chronic liver disease (acute on chronic)

Acute liver failure “fulminant liver failure”

• is defined as an acute liver illness due to massive hepatic necrosis, associated with encephalopathy and coagulopathy that occurs within 6 months of the initial liver injury in the absence of preexisting liver disease

• Causes:

• Acetaminophen

• Acute hepatitis B and E.

• Autoimmune hepatitis.

• Clinical Features

• Acute liver failure manifests first with nausea, vomiting, and jaundice, followed by life-threatening encephalopathy, and coagulopathy, portal hypertension, and hepatorenal syndrome.

Chronic Liver Failure and Cirrhosis

• Liver failure in chronic liver disease is most often associated with advanced fibrosis/cirrhosis

• Causes:

• Chronic hepatitis (B and C)

• Fatty liver disease associated with obesity and diabetes.

• Alcoholic abuse (alcohol associated liver disease).

• Clinical features:

• Same as acute failure plus, persistent cholestasis can lead to pruritus (itching). Impaired estrogen metabolism leads to hyperestrogenemia (hypogonadism, gynecomastia)

Hepatitis caused by

1. Hepatotropic Viruses

2. Nonhepatotropic viruses – such as Epstein-Barr virus, cytomegalovirus.

3. Autoimmune hepatitis

4. Alcoholic hepatitis

Viral Hepatitis

Clinical presentation:

• Asymptomatic

• Malaise and weakness, Nausea and anorexia, Jaundice

• Urine maybe dark

• Lab: marked elevated ALT and AST enzymes of the liver

• Viral hepatitis can be

• Asymptomatic acute hepatitis, acute symptomatic, chronic, carrier, or fulminant hepatitis.

• Acute viral hepatitis: characterized by

• Sign and symptoms less than 6 months

• Caused by any of the hepatitis viruses

• Chronic viral hepatitis: characterized by

• Sign and symptoms more than 6 months

• Caused by hepatitis virus B, C, D

Hepatitis A Virus

• It is a single-stranded RNA virus that causes a benign, self-limited disease

• HAV cause acute hepatitis but does not cause chronic hepatitis

• More common in children but it causes more morbidity in older age.

• Transmission: it has a fecal-oral route of spread.

• Diagnosis: detection of anti-HAV immunoglobulin M (IgM) in serum

Hepatitis B virus

• HBV is a circular, partially double-stranded DNA virus with incubation period 4-26 wks

• Hepatitis B virus (HBV) can cause:

1. Acute, self-limited hepatitis, chronic hepatitis disease culminating in cirrhosis with increased risk of hepatocellular carcinoma

2. Fulminant hepatitis with massive liver necrosis

3. Asymptomatic carrier state

• Transmission: vertical transmission from the mother to the baby and parenteral and through body fluids with sexual transmission

• HBV serology

• HBsAg: acute disease and persistent for 6 months is for carrier state

• Anti-HBsAg signifies the end of acute disease and persists for years

• IgM anti-HBcAg is usually the first antibody to appear

• HBeAg: viral replication, persistence suggests progression to chronic disease

• Diagnosis: Detection of HBsAg or antibody to HBcAg in serum

Hepatitis C Virus

• is a single-stranded RNA enveloped virus with incubation period 2-26wks

• Causes: chronic hepatitis, cirrhosis and hepatocellular carcinoma

• Transmission: intravenous drug abusers and individuals with multiple sexual partners Hepatitis D Virus (delta virus)

• **Hepatitis D virus**

(HDV) is a defective RNA virus

• Infection can develop only when there is concomitant HBV infection because it need to be encapsulated by HBsAg.

• so, it arises in two settings:

• Co-infection with HBV • Super-infection of chronic carrier of HBV

• Infection with HDV leads to accelerated hepatitis progressing to more severe chronic hepatitis within 4-8 weeks

• Diagnosis: detection of IgM against both HDV and HBcAg Hepati

Hepatitis E Virus

• Hepatitis E virus (HEV) is a non-enveloped, singlestranded RNA virus;

• it is an entericaly transmitted water-borne infection

• Causes

1. Acute hepatitis

2. Fulminant hepatitis in pregnant women

3. Does not cause chronic hepatitis

• Both HAV and HEV do not cause chronic hepatitis Microscopically acute and chronic hepatitis share the same changes:

1. Lobular disarray

2. Hepatocyte swelling (balloon cells)

3. Apoptotic hepatocytes (councilman body)

4. Lymphocytes in the portal tracts and the lobules

5. Cholestasis

6. inflammation of the portal tract

7. interface hepatitis inflammation spills into the parenchyma

8. Chronic Hepatitis B often has (ground glass hepatocyte -cytoplasmic HBsAg).

9.The characteristic change to chronic hepatitis is fibrosis Chronic HBV infection. A, Showing the diffuse granular cytoplasm, so-called ground-glass hepatocytes with immunostain showing positivity for HBs Ag Autoimmune hepatitis

• Chronic, progressive hepatitis attributed to T-cell–mediated autoimmunity

• Clusters of periportal plasma cells is characteristic.

• There is a female predominance (78% of cases), with elevated serum IgG levels but no serum markers of viral infection

• It is of 2 types:

• Type 1 is more common and is typically characterized by the presence of antinuclear antibodies (ANAs) and anti–smooth muscle actin (SMA) antibodies.

• Type 2 disease is more common in children and is characterized by anti–liver kidney microsome-1 (LKM-1) antibodies.