CHAPTER SIX
PATHOLOGY OF THE HEPATO-BILIARY SYSTEM & EXOCRINE PANCREAS

THE LIVER

The dominant primary diseases of the liver are

1. *Viral hepatitis*
2. *Alcoholic liver disease (in the Western world; rare in Iraq)*
3. *Hepatocellular carcinoma*

HEPATIC FAILURE

This is the gravest consequence of liver disease. It should be noted that 80% of hepatic functional capacity must be damaged before failure ensues. In many cases decompensation arises as a result of intercurrent diseases that place further burden on an already sick liver; these include

1. Gastrointestinal bleeding
2. Systemic infection
3. Electrolyte disturbances
4. Severe stress such as major surgery or heart failure.

The morphologic alterations that cause liver failure fall into three categories:

1. Massive hepatic necrosis*;* most often drug-induced, as from paracetamol overdose, halothane & antituberculous drugs (rifampin, isoniazid). Hepatitis A & hepatitis B infection, and other causes (including unknown) account for about one-third of the cases. Hepatitis C infection does not cause massive hepatic necrosis.

2. Chronic liver disease*,* which is the most common road to hepatic failure and is the endpoint of persistent chronic hepatitis ending in cirrhosis.

3. Hepatic dysfunction without overt necrosis*:* hepatocytes may be viable but unable to perform normal metabolic function, as with Reye syndrome, tetracycline toxicity, and acute fatty liver of pregnancy.

Regardless of cause, the clinical signs of hepatic failure are much the same. *Jaundice* is an almost always present. *Hypoalbuminemia*, which predisposes to peripheral edema, and *hyperammonemia*, which may play a role in cerebral dysfunction, are extremely worrying developments. *Fetor hepaticus* (a characteristic musty body odor) occurs occasionally. Impaired estrogen metabolism and consequent hyperestrogenemia are thought to be the causes of

a. palmar erythema and spider angiomas of the skin
b. hypogonadism and gynecomastia in males

Hepatic failure is life-threatening because *with severely impaired liver function, patients are highly susceptible to failure of multiple organ systems*. Thus, respiratory failure with pneumonia and sepsis combine with renal failure to claim the lives of many patients. A *coagulopathy* develops due to impaired hepatic synthesis of blood clotting factors. The resultant bleeding tendency can lead to massive gastrointestinal bleeding as well as petechiae elsewhere (see also esophageal varices). Intestinal absorption of blood places a metabolic load on the liver, which worsens the extent of hepatic failure. The outlook of full-blown hepatic failure is grave: A rapid downhill course is usual, & without liver transplantation, death occurrs within weeks to a few months in about 80% of cases .

Two particular complications signal the gravest stages of hepatic failure

1. Hepatic encephalopathy, which is manifested disturbances of consciousness with rigidity, hyperreflexia, and tremor. It is regarded as a disorder of neurotransmission in the central nervous system and neuromuscular system and appears to be associated with elevated blood ammonia levels, which impair neuronal function and promote generalized brain edema.

2. Hepatorenal syndrome refers to the appearance of renal failure in patients with severe chronic liver disease, in whom there are no intrinsic morphologic or functional causes for the renal failure. Sodium retention, impaired water excretion, and decreased renal perfusion and glomerular filtration rate are the main renal functional abnormalities. There is oliguria associated with rising blood urea nitrogen and creatinine. The prognosis is poor, with a median survival of only 2 weeks in the rapid-onset form and 6 months with the insidious-onset form.

CIRRHOSIS

Cirrhosis is the end-stage of chronic liver disease & is defined by three characteristics:

1. Bridging fibrous septae in the form of delicate or broad bands of fibrosis that link portal tracts with one another and portal tracts with centrilobular veins.

2. *Parenchymal nodules* containing regenerating hepatocytes encircled by fibrosis, with diameters varying from very small micronodules to large macronodules.

3. Disruption of the architecture of the entire liver

Classification of cirrhosis

The only satisfactory classification of cirrhosis is based on the underlying etiology. The descriptive terms "micronodular" and "macronodular" should not be used as primary classifications. Many forms of cirrhosis are initially micronodular (nodules < 3 mm), but there is a tendency for nodules to increase in size; thus converting it to mixed (micro- & macronodular) & eventually to macronodular form (nodules > 3mm).

The etiology of cirrhosis varies both geographically and socially. The following are established causes of cirrhosis:

1. Alcoholic liver disease (70% in Western countries)
2. Viral hepatitis (a very common cause in our country)
3. Biliary diseases
4. Primary hemochromatosis
5. Wilson disease
6. α1-Antitrypsin deficiency
7. Cryptogenic cirrhosis

Infrequent types of cirrhosis also include those complicating galactosemia and tyrosinosis in infants and children, and drug-induced cirrhosis, as with α-methyldopa (aldomet). After all the categories of cirrhosis of known causation have been excluded, a substantial number of cases remain (15%) & is referred to as *cryptogenic cirrhosis*. It is possible that many of these cases are due to undiagnosed *nonalcoholic fatty liver disease*. *Once cirrhosis is established, it is usually impossible to establish an etiologic diagnosis on morphologic grounds alone.*

Pathogenesis of cirrhosis

The central pathogenetic processes in cirrhosis are progressive fibrosis and reorganization of the vascular microarchitecture of the liver. In cirrhosis, types I and III collagen are deposited in the lobule, creating delicate or broad septal tracts. New vascular channels in the septae connect the vascular structures in the portal region (hepatic arteries and portal

veins) and terminal hepatic veins (centrilobulat & larger veins), shunting blood around the parenchyma. Continued deposition of collagen in the space of Disse is accompanied by the loss of fenestrations in the sinusoidal endothelial cells. As a result hepatocellular secretion of proteins (e.g., albumin, clotting factors, and lipoproteins) is greatly impaired.
The major source of excess collagen in cirrhosis is the perisinusoidal stellate cells, which lie in the space of Disse. Although normally functioning as vitamin A fat-storing cells, during the development of cirrhosis they become activated. It is predominantly the cytokines secreted by activated Kupffer cells and other inflammatory cells that stimulate perisinusoidal stellate cells to divide and to produce large amounts of extracellular matrix.
Throughout the process of liver cell damage and fibrosis, remaining hepatocytes are stimulated to regenerate and proliferate as spherical regenerative nodules within the confines of the fibrous septae. The net outcome is a fibrotic, nodular liver in which delivery of blood to hepatocytes is severely impaired, as is the ability of hepatocytes to secrete substances into plasma. Disruption of the interface between the parenchyma and portal tracts obliterates biliary channels as well. Thus, the cirrhotic patient may develop jaundice and even hepatic failure, despite having a liver of normal mass.

In cirrhosis death is usually due to one or more of the following

1. Progressive liver failure
2. Portal hypertension related complications
3. The development of hepatocellular carcinoma.

PORTAL HYPERTENSION

Increased resistance to portal blood flow may develop in a variety of circumstances, which can be divided into *prehepatic, intrahepatic, and posthepatic causes*.

Prehepatic conditions include

1. Portal vein thrombosis & narrowing
2. Massive splenomegaly through shunting excessive blood into the splenic vein.

Posthepatic causes are

1. Severe right-sided heart failure
2. Constrictive pericarditis
3. Hepatic vein outflow obstruction.

Intrahepatic causes:

1. Cirrhosis is the dominant cause accounting for most cases of portal hypertension.
2. Schistosomiasis
3. Massive fatty change
4. Diffuse fibrosing granulomatous disease such as sarcoidosis and miliary tuberculosis
5. Diseases affecting the portal microcirculation, exemplified by nodular regenerative hyperplasia

Portal hypertension in cirrhosis results from increased resistance to portal flow at the level of the sinusoids, and compression of terminal hepatic veins by perivenular scarring and expansile parenchymal nodules. Anastomoses between the arterial and portal systems in the fibrous septa also contribute to portal hypertension by imposing arterial pressure on the low-pressure hepatic venous system.

The four major consequences of portal hypertension in the setting of cirrhosis are

1. Ascites

2. The formation of portosystemic venous shunts leading to esophageal varices & hemorrhoids
3. Congestive splenomegaly
4. Hepatic encephalopathy

Ascites *refers to the collection of excess fluid in the peritoneal cavity.* It usually becomes clinically detectable when at least 500 mL has accumulated, but many liters may collect and cause massive abdominal distention. It is generally a serous fluid having less than 3 gm/dL of protein (largely albumin) as well as the same concentrations of solutes such as glucose, sodium, and potassium as in the blood. Influx of neutrophils suggests secondary infection, whereas red cells point to possible disseminated intra-abdominal cancer. With long-standing ascites, seepage of peritoneal fluid through transdiaphragmatic lymphatics may produce hydrothorax, more often on the right side.

The pathogenesis of ascites

This is complex, involving the following mechanisms:

1. Sinusoidal hypertension, altering Starling's forces and driving fluid into the space of Disse, which is then removed by hepatic lymphatics; this movement of fluid is also promoted by hypoalbuminemia.

2. *Percolation of hepatic lymph into the peritoneal cavity*: normal thoracic duct lymph flow approximates 800 to 1000 mL/day. With cirrhosis, hepatic lymphatic flow may approach 20 L/day, exceeding thoracic duct capacity.

3. Intestinal fluid leakage: portal hypertension also causes increased perfusion pressure in intestinal capillaries. This promotes movement of additional fluid out of intestinal capillaries into the abdomen.

4. Renal retention of sodium and water due to secondary hyperaldosteronism

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). *Never the less 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)

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 and only rarely causes fulminant hepatitis.* Nevertheless, most viral hepatitis epidemics are attributed to HAV. 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 of 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 hepatocytes, and is shed in the bile and feces. It appears that the liver cell injury is not directly related to the virus but results from T cell-mediated damage of infected hepatocytes. *Detection of anti-HAV IgM antibody is the best diagnostic marker for the disease.*

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
    a. Non-progressive or
    b. 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.* Liver disease caused by HBV is a real worldwide problem, with an *estimated carrier rate of 400 million*. HBV remains in blood during the last stages of a long incubation period (4-26 weeks) 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. Whereas blood and body fluids are the primary vehicles of transmission, virus may also be spread by contact with body secretions such as semen, saliva, sweat, tears, breast milk, and pathologic effusions. *In endemic regions, vertical transmission from mother to child during birth constitutes the main mode of transmission*. HBV infection in adults is mostly cleared, but vertical transmission produces a high rate of chronic infection.

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), which may be followed by acute disease lasting weeks to months. The natural course of acute disease can be followed by serum markers. ***HBsAg*** appears before the onset of symptoms, peaks during overt disease, and then declines to undetectable levels in 3 to 6 months. ***Anti-HBs*** persists for life, conferring protection; this is the basis for current vaccination policy using noninfectious HBsAg. *HBeAg appears in serum shortly after HBsAg to signify active viral replication. Persistence of HBeAg is an important indicator of*

1. Continued viral replication
2. Infectivity
3. Probable progression to chronic hepatitis

IgM anti-HBc (c for core Ag) is detectable with the onset of elevated serum aminotransferase levels and thus indicative of hepatocyte destruction. Later this IgM is replaced by IgG anti-HBc.

The host immune response to the virus is the main determinant of the outcome of the infection. A strong response by virus-specific CD4+ and CD8+ interferon γ-producing cells are associated with the resolution of acute infection. HBV, (like HAV) does not seem to cause direct hepatocyte injury as many chronic carriers have virions in their hepatocytes without any evidence of cell injury. Hepatocyte injury and damage seem to be mediated by CD8+ cytotoxic T cells of the virus-infected hepatocytes.

Hepatitis C Virus (HCV) is another major cause of liver disease. The worldwide carrier rate is estimated at 175 million persons. A decrease in the incidence has resulted from the marked reduction in transfusion-associated hepatitis C (as a result of screening

procedures). *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.

Hepatitis D Virus (HDV) (Hepatitis delta virus) is a unique RNA virus in that it is *replication defective, causing infection only when it is encapsulated by HBsAg* i.e. *HDV is absolutely dependent on HBV co-infection for multiplication.* Delta hepatitis arises in two settings:

1. Acute coinfection after exposure to serum containing both HDV and HBV and

2. Superinfection of a chronic carrier of HBV with a new inoculum of HDV. In the first case, most coinfected individuals can clear the viruses and recover completely. The course is different in superinfected individuals in that most cases show acceleration of hepatitis, progressing to more severe chronic hepatitis. Infection by HDV is worldwide, with the highest prevalence rates (40%) in Africa & the Middle East. *IgM anti-HDV antibody is the most reliable indicator of recent HDV exposure,* but its appearance is transient.

Hepatitis E Virus (HEV)

HEV hepatitis is a single-stranded RNA virus that is fecally transmitted. HEV is endemic in India (where it was first documented). Epidemics have been reported from Asia and Africa. HEV is not associated with chronic liver disease or persistent viremia. *A characteristic feature of the infection is the high mortality rate among pregnant women, approaching 20%*. A specific antigen (HEV Ag) can be identified in the cytoplasm of hepatocytes during active infection. Virus can be detected in stools, and anti-HEV IgG and IgM antibodies are detectable in serum.

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)
3. Acute hepatitis (anicteric or icteric)
3. Chronic hepatitis (with or without progression to cirrhosis)
4. Chronic carrier state (asymptomatic)
5. Fulminant hepatitis (submassive to massive hepatic necrosis with acute liver failure)

With rare exceptions, HAV, HCV, and HEV do not generate a carrier state, and HAV and HEV infections do not progress to chronic hepatitis. Viral persistence and development of chronic disease is much more common after HCV infection than HBV infection. *Because other infectious or noninfectious causes (such as drugs and toxins), can lead to essentially identical syndromes, serologic studies are decisive for the diagnosis of viral hepatitis and identification of virus types.*

Asymptomatic Infection:
The patients are identified only on the basis of minimally elevated serum aminotransferases or the presence of antiviral antibodies.

Acute viral hepatitis
Any one of the hepatotropic viruses can cause acute viral hepatitis. Acute infections are easily detected for HBV infections but only rarely diagnosed for HCV. A hepatitis virus etiology is suggested by elevated serum aminotransferase levels. As jaundice appears (icteric phase), symptoms begin to fade away. To begin with there is predominantly conjugated hyperbilirubinemia but later hepatocellular injury interferes with bilirubin conjugation, thus, unconjugated hyperbilirubinemia can also occur. An icteric phase is usual especially in adults infected with HAV, but is absent in about 50% of the cases infected with HBV and in most cases of HCV infection. Within weeks, the jaundice and most systemic symptoms clear as convalescence begins.

Chronic Hepatitis *is defined as "the presence of clinical, biochemical, or serologic evidence of continuing hepatic disease for more than 6 months, with histological documentation of inflammation and necrosis."*

Although chronic hepatitis is mostly caused by hepatitis viruses, there are other causes of this condition, these include

- *Drugs (isoniazide, α-methyldopa, methotrexate),*
- *Auto-immune damage (autoimmune hepatitis)*
- *Wilson disease, α_1-antitrypsin deficiency, chronic alcoholism.*

In chronic hepatitis, it is the etiology that determines the likelihood of progression. In particular, HCV is notorious for causing a chronic hepatitis evolving to cirrhosis in a significant percentage of patients. Chronic hepatitides are highly variable in their clinical features. The most common signs are spider angiomas, palmar erythema, & mild tender hepatomegaly. Laboratory studies may show prolongation of the prothrombin time, hypergammaglobulinemia, hyperbilirubinemia, and mild elevations in alkaline phosphatase levels. The course is again highly variable. Persons with hepatitis C may have indolent disease without progression for years. Conversely, others have rapidly progressive disease and develop cirrhosis within a few years. *Causes of death in chronic hepatitis are related to the complicating cirrhosis* e.g. liver failure, hepatic encephalopathy, massive hematemesis from esophageal varices, and hepatocellular carcinoma.

The Carrier State
With hepatotropic viruses, carriers are those who harbor one of the viruses & may have nonprogressive liver damage, but are essentially free of symptoms. They constitute reservoirs of infection. HBV infection early in life, particularly through vertical transmission during childbirth, produces a carrier state in 90% to 95% of the cases. In contrast, less than 10% of HBV infections acquired in adulthood yield a carrier state. Individuals with impaired immunity are particularly likely to become carriers. HCV can induce a carrier state, which is estimated to affect 0.2% to 0.6% of the general population.

Fulminant Hepatitis
A very small proportion of patients with *acute viral hepatitis A, B, or E* may develop acute liver failure, resulting from massive hepatic necrosis. Cases with a more prolonged course of several weeks or months are usually referred to as *subacute hepatic necrosis*;

livers of these individuals show both massive necrosis and regenerative hyperplasia. It should be remembered that drugs and chemicals can also cause massive hepatic necrosis.

Pathological features of viral heaptitis

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 **(Fig. 6-1)**

- The normal radial array of the lobules is lost.
- There is *diffuse ballooning degeneration* of hepatocytes; the cells are swollen with clear, wispy cytoplasm.
- *Hepatocytes necrosis* assume one of 3 morphologic types
  1. Cytolysis i.e. dissolution of the hepatocytes. The necrotic cells vanish (cell dropped out). This is detected indirectly as macrophage aggregation
  2. Apoptosis i.e. hepatocytes shrink, become intensely eosinophilic, and have fragmented nuclei. Apoptotic cells are phagocytosed within hours by macrophages and hence may be difficult to find despite extensive apoptosis.
  3. Confluent necrosis of hepatocytes, seen in severe cases & may lead to *bridging necrosis* that extends through portal-portal, central-central, or portal-central areas. (**Fig. 6-2**)
- *Hepatocyte regeneration* as evidenced by irregularly thickened plates with occasional rosettes & and multinucleation.
- *Inflammation* is usually a prominent feature of acute hepatitis. The portal tracts are infiltrated predominantly by lymphocytes. The inflammatory infiltrate may spill over into the parenchyma to cause necrosis of periportal hepatocytes (*interface hepatitis*) and may also infiltrate the sinusoids.
- *Hypertrophy & hyperplasia of Kuppfer cells*
- *Cholestasis* may be present**,** both intracellular (brown pigmentation of hepatocytes) & canalicular (bile plugs in canaliculi).
- *HBV* infection, acute or chronic, may produce two distinctive features of the infected hepatocytes.
  a. *Ground-glass*" *hepatocytes*: a finely granular, eosinophilic cytoplasm due to massive quantities of HBsAg (as seen by electron microscopy).
  b. *Sanded nuclei***,** resulting from abundant intranuclear HBcAg.

Chronic hepatitis **(Fig. 6-3)**

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

- *Hepatocyte necrosis* may occur in all forms of chronic hepatitis.
- *The inflammatory component* consists mainly of lymphocytes, macrophages, and occasional plasma cells. In the mildest forms, significant inflammation is limited to portal tracts. *Lymphoid aggregates* in the portal tract are often seen in HCV infection.
- The liver *architecture is usually well preserved*
- Continued *periportal necrosis (interface hepatitis) and bridging necrosis* are forerunners of progressive liver damage.
- *The hallmark of serious liver damage is the deposition of fibrous tissue*. At first, at the portal tracts, but with time *periportal fibrosis* occurs. This is followed by *bridging fibrosis* that links fibrous septa between lobules**.**
- Continued loss of hepatocytes with fibrosis results in *cirrhosis, with fibrous septa and hepatocyte regenerative nodules.* This pattern of cirrhosis is characterized by

irregularly sized nodules separated by variable but mostly broad bands of fibrosis. The nodules are typically greater than 0.3 cm in diameter; accordingly, *the cirrhosis is by definition macronodular*.

Autoimmune Hepatitis is microscopically indistinguishable from chronic viral hepatitis but is associated with a set of immunologic abnormalities. This disease may run an indolent or severe course. Salient features include:

- Female predominance
- Absence of viral infection serologic markers
- Immunological abnormalities
  a. Elevated serum IgG (>2.5 g/dl)
  b. High titers of autoantibodies (80% of cases)
  c. Presence of other autoimmune diseases (in 2/3 of the patients), including rheumatoid arthritis, thyroiditis, Sjögren syndrome, and ulcerative colitis.

Pathogenesis

Most patients have a variety of auto-antibodies such as antinuclear, anti-smooth muscle, liver kidney microsomal antibody, etc. The best characterized among these antibodies are *smooth muscle antibodies* directed against cytoskeletal proteins that include *actin, and troponin*, and *liver kidney microsomal antibodies*. The main effectors of cell damage are believed to be *CD4+ helper cells*. Response to immunosuppressive therapy is usually dramatic. The overall risk of cirrhosis, the main cause of death, is 5%.

PYOGENIC LIVER ABSCESSES

In developing countries most liver abscesses result from *parasitic infections, such as amebic, echinococcal, etc*. In the Western world, bacterial abscesses are more common, representing a complication of an infection elsewhere. Gram-negative bacteria such as *E. coli* and *Klebsiella* sp. are the usual offenders. *The organisms reach the liver through one of the following pathways:*

1. Ascending cholangitis
2. Vascular seeding, predominantly portal i.e. from the GIT
3. Direct invasion from a nearby focus
4. A penetrating injury.

Debilitating disease with immune deficiency is a common background e.g. extreme old age, immunosuppression, or chemotherapy.

Gross features

- Pyogenic abscesses may be *solitary* or *multiple*, ranging from very small to massive lesions.
- Bacteremic spread through the arterial or portal system tends to produce multiple small abscesses, whereas direct extension and trauma usually cause solitary large abscesses. (**Fig. 6-4 A**)

Microscopic features

- These are identical to pyogenic abscesses elsewhere.

Liver abscesses are associated with fever and right upper quadrant pain and tender hepatomegaly. Jaundice is often the result of extrahepatic biliary obstruction. Surgical drainage is often necessary.

AMEBIC LIVER ABSCESS is usually single, mostly right sided, & close to liver dome, but tends to be multicentric in immunocompromised patients. Adults are mostly affected but can develop in infants & children.

Gross features **(Fig. 6-4 B)**

- The necrotic center contains odorless, pasty, chocolate brown fluid.

Microscopic

- Most of the lesion consists of necrotic debris**.** There few if any neutrophils**.**
- This centre is surrounded by fibrin, macrophages, lymphocytes & a few fibroblasts with clusters of amebic trophozoites (up to 60 microns with small eccentric nucleus and cytoplasmic vacuoles that may contain red blood cells; resemble histiocytes).

Complications

1. Bacterial superinfection
2. Extension or perforation into the following
    1. Pleuro-pulmonary structures
    2. Subphrenic space
    3. Peritoneal cavity, and pericardial sac, bile ducts
    6. Kidney, mediastinum, chest wall, abdominal wall, and flank.

Diagnosis: serology is 90% sensitive

HYDATID DISEASE OF THE LIVER

Three quarters of infected individuals develop one or more hepatic cysts, which grow slowly. The typical hydatid cyst is spherical and may measure up to more than 30 cm in diameter. The majority occur in the right lobe, but they may be multiple, involving all lobes. A characteristic gross feature is the presence of the soft, whitish laminate membrane. (**Fig. 6-4 C**) Histologic examination of the cyst wall shows an outer fibrous layer; a midlle onionskin like laminated membrane, and an inner germinal layer. Calcification in the latter layer signifies that the cyst is dead. The adjacent liver parenchyma often shows pressure atrophy and a portal infiltrate in which eosinophils may be prominent. The viable cyst is filled with colorless fluid, which contains daughter cysts and brood capsules with scolices. Communication with the biliary tract and superimposed infection are frequent. Rupture of the cysts into the peritoneal cavity may result in a fatal anaphylactic reaction or in the formation of innumerable small granulomas grossly resembling peritoneal tuberculosis. Identification of fragments of germinal membrane or scolices in their center points to the diagnosis. Hepatic echinococcus cysts can also rupture inside the gallbladder or through the diaphragm into the pleural space and lung.

The laboratory diagnosis can usually be made by hydatid serology and confirmed or established by ultrasound or computed tomography.