Liver, Pancreas, Gallbladder

Acute viral hepatitis
Cirrhosis (macronodular and micronodular)
Hepatocellular carcinoma
Chronic pancreatitis
Gallbladder carcinoma

Viral hepatitis

Systemic viral infections (EBV, CMV, herpes, adeno, etc.) can involve the liver but the term **viral hepatitis** is reserved for infection of the liver caused by the group of viruses having a particular affinity for the liver (hepatotropic viruses HAV, HBV, HCV, HDV, HEV, HGV).

Viral hepatitis
Clinicopathologic syndromes

- Asymptomatic acute infection: serologic evidence only
- **Acute hepatitis**: anicteric or icteric
- **Chronic hepatitis**: without or with progression to cirrhosis
- **Chronic carrier state**: asymptomatic without apparent disease
- **Fulminant hepatitis**: submassive to massive hepatic necrosis with acute liver failure

Acute viral hepatitis- histological picture

Irrespective of the kind of viruses – an identical histological changes

- Hypercellularity and disarrangement of liver structure
- The inflammatory infiltrate (mostly lymphocytes) in portal tracts. Sometimes with necrosis of periportal hepatocytes (‘interface hepatitis’)

Acute viral hepatitis- histological picture

Tissue alterations are similar, but a few histologic changes may be indicative of a particular type of viruses

**HBV**
- „Ground-glass“ hepatocytes with a finely granular, eosinophilic cytoplasm- accumulation of HBsAg (chronic hepatitis)

**HCV**
- Steatosis/fatty change of hepatocytes (acute and chronic hepatitis)
- Ductular proliferation in portal tract and lymphoid aggregate formation (chronic hepatitis)

Viral hepatitis (acute and chronic)- histological picture

Hepatitis B viral infection.
A. Liver parenchyma showing hepatocytes with diffuse granular cytoplasm, so-called ground glass hepatocytes. (HE)
B. Immunoperoxidase stain for HBsAg from the same case, showing cytoplasmic inclusions of viral particles.
**Cirrhosis**

The term **cirrhosis** is applied to the end stage of chronic liver injury which is defined by:

- **Bridging fibrous septa** (delicate bands or broad scars)
- **Parenchymal nodules** created by regeneration, varying from small (<3mm, micronodules) to large (macronodules)
- Disruption of the architecture of the entire liver

**Cirrhosis - etiology**

Cirrhosis is the twelfth most common cause of death in the United States, accounting for most liver-related deaths.

The chief worldwide causes of cirrhosis are:

- alcohol abuse,
- viral hepatitis, and
- non-alcoholic steatohepatitis (NASH)

Others:

- Biliary diseases
- Primary hemochromatosis
- Wilson disease
- Alfa1-antitrypsin disease
- Cryptogenic cirrhosis

**Macronodular hepatic cirrhosis**

- Macronodular cirrhosis (formerly named postnecrotic or posthepatitic cirrhosis) is most frequently preceded by chronic viral hepatitis although it is also attributable to the Wilson’s disease

Ma: liver is diminished and composed of nodules of various size and shape surrounded by broad areas of collapsed stroma

**Micronodular hepatic cirrhosis**

- Micronodular cirrhosis (previously „portal”) is caused in most cases by chronic alcohol abuse

- It is characterized by small uniform nodules, which represent fragments of previous hepatic lobules.

- Ma: the liver shows fine, fairly regular yellowish nodularity
Cirrhosis - histological picture

- Hepatocellular nodules vary in size: in macronodular c., the big nodules often contain the axis in the form of portal triads or central veins (axial nodules); in micronodular c., the nodules do not contain either central vein or portal tracts (non-axial nodules).
- The nodules are surrounded by fibrous septa within the fibrous septas we can see elements of portal tracts, proliferated bile ductules and mononuclear infiltration.
- Plates of hepatocytes are irregular; bilayered plates of hepatocytes reflect the tendency of parenchyma to regenerate.
- In macronodular c., hepatocytes are predominantly normal, without the fatty degeneration.
- In micronodular c., hepatocytes are usually in state of steatosis.

Cirrhosis – clinical features

- About 40% of individuals with cirrhosis are asymptomatic until late in the course of the disease.
- When symptomatic, they present with nonspecific clinical manifestations: anorexia, weight loss, weakness, and, in advanced disease, symptoms and signs of hepatic failure.

The ultimate mechanism of deaths in most cirrhotic patients is:
1. progressive liver failure,
2. a complication related to portal hypertension, or
3. the development of hepatocellular carcinoma.

Hepatocellular carcinoma (HCC)

- Worldwide, HCC constitutes approximately 5.4% of all cancers, but the incidence varies widely in different areas of the world.
- More than 85% of cases occur in countries with high rates of chronic HBV infection. The highest incidences are found in Asian countries (Southeast China, Korea, Taiwan) and African countries.
- In Western countries HCC incidence is rapidly increasing. It tripled in the United States during the last 25 years, but it is still much lower (8- to 30-fold) than the incidence in some Asian countries.
- In Western populations HCC is rarely present before age 60, and in almost 90% of cases tumors develop in persons with cirrhosis.
- There is a pronounced male preponderance of HCC throughout the world, about 3 : 1 in low-incidence areas and as high as 8 : 1 in high-incidence areas.
- Risk factors: infection HBV, HCV, alcohol.

Hepatocellular carcinoma - pathogenesis

Three major etiologic associations have been established:
- infection with HBV or HCV.
- chronic alcoholism
- aflatoxin exposure

(high exposure to dietary aflatoxins derived from the fungus Aspergillus flavus. These carcinogenic toxins are found in "moldy" grains and peanuts)

Other conditions include:
- hemochromatosis
- tyrosinemia (extremely rare in which almost 40% of patients develop this tumor despite adequate dietary control).

Hepatocellular carcinoma – conventional variant

Histologically, HCCs range from well-differentiated lesions that reproduce hepatocytes arranged in cords, trabeculae or pseudoglandular patterns, to poorly differentiated lesions. In the better differentiated variants, globules of bile may be found within the cytoplasm of cells and in pseudocanaliculi between cells. There is surprisingly scant stroma in most HCCs, explaining the soft consistency of these tumors.

In this microscopic view of a well-differentiated lesion, tumor cells are arranged in nests, sometimes with a central lumen, one of which contains bile (arrow).
A distinctive clinicopathologic variant of HCC is the **fibrolamellar variant**. It occurs in young male and female adults (20-40 years of age) with equal incidence, has no association with cirrhosis or other risk factors. The prognosis is better than the conventional HCC.

**MA:** It usually consists of a single large, hard "scirrhous" tumor with fibrous bands coursing through it. **Histologically** it is composed of well-differentiated polygonal cells growing in nests or cords and separated by parallel lamellae of dense collagen bundles.

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**CHRONIC PANCREATITIS**

The prevalence of chronic pancreatitis is hard to determine, but it probably ranges between 0.04% and 5%.

There is significant overlap in the causes of acute and chronic pancreatitis (80% of cases of a.p. gallstones and alcoholism).

By far the most common cause of chronic pancreatitis is **long-term alcohol abuse**.

And these patients are usually **middle-aged males**.

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**CHRONIC PANCREATITIS - MORPHOLOGY**

Chronic pancreatitis is characterized by:
- **parenchymal fibrosis**,
- reduced number and size of acini with relative sparing of the islets of Langerhans, and
- variable dilation of the pancreatic ducts.

These changes are usually accompanied by:
- chronic inflammatory infiltrate around lobules and ducts.
- the ductal epithelium may be atrophied or hyperplastic or may show squamous metaplasia.
- the remaining islets of Langerhans become embedded in the sclerotic tissue and may fuse and appear enlarged.

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**PANCREATITIS**

Pancreatitis encompasses a group of disorders characterized by inflammation of the pancreas with injury to the exocrine pancreas.

By definition, **acute pancreatitis**, the gland can return to normal if the underlying cause of the pancreatitis is removed.

By contrast, **chronic pancreatitis** is defined by the presence of irreversible destruction of exocrine pancreatic parenchyma.

**Chronic pancreatitis** is characterized by inflammation of the pancreas with destruction of exocrine parenchyma, fibrosis, and, in the late stages, the destruction of endocrine parenchyma.

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**CHRONIC PANCREATITIS - MORPHOLOGY**

Grossly, the gland is hard, sometimes with extremely dilated ducts and visible calcified concretions.

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**CHRONIC PANCREATITIS - MORPHOLOGY**

Chronic pancreatitis, **A**, Extensive fibrosis and atrophy has left only residual islets (left) and ducts (right), with a sprinkling of chronic inflammatory cells and scar tissue.

**B**, A higher power view demonstrating dilated ducts with inspissated eosinophilic ductal concretions in a person with alcoholic chronic pancreatitis.
**Gallbladder carcinoma**

- the most common malignancy of the extrahepatic biliary tract
- slightly more common in women
- it occurs most frequently in the seventh decade of life.
- For unknown reasons carcinoma of the gallbladder is more frequent in Mexico and Chile. In the United States the incidence is highest in Hispanics and Native Americans.
- The most important risk factor associated with gc. is gallstones (cholelithiasis), which are present in 60-95% of cases. However, it should be noted that only 0.5% of patients with gallstones develop gallbladder cancer after twenty or more years.

**Prognosis.** Only rarely is it discovered at a resectable stage, and the mean 5-year survival rate has remained for many years at about 5% despite surgical intervention.

**M**ost carcinomas of the gallbladder are adenocarcinomas. They may be papillary, poorly differentiated, or undifferentiated infiltrating tumors. About 5% are squamous cell carcinomas or have adenosquamous differentiation. A minority are neuroendocrine tumors.