Liver Cirrhosis and Portal Hypertension

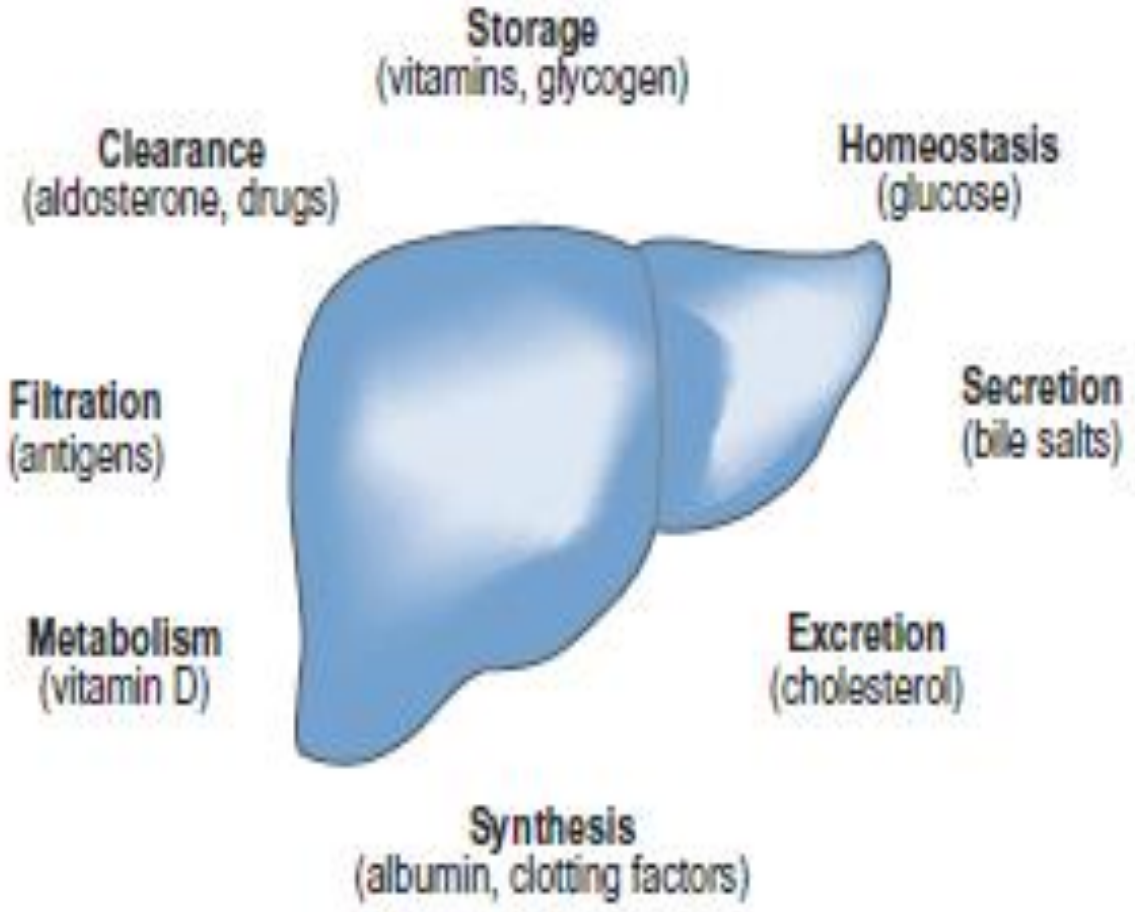
- Cirrhosis is defined as a diffuse process characterized by fibrosis and a conversion of the normal hepatic architecture into structurally abnormal nodules.

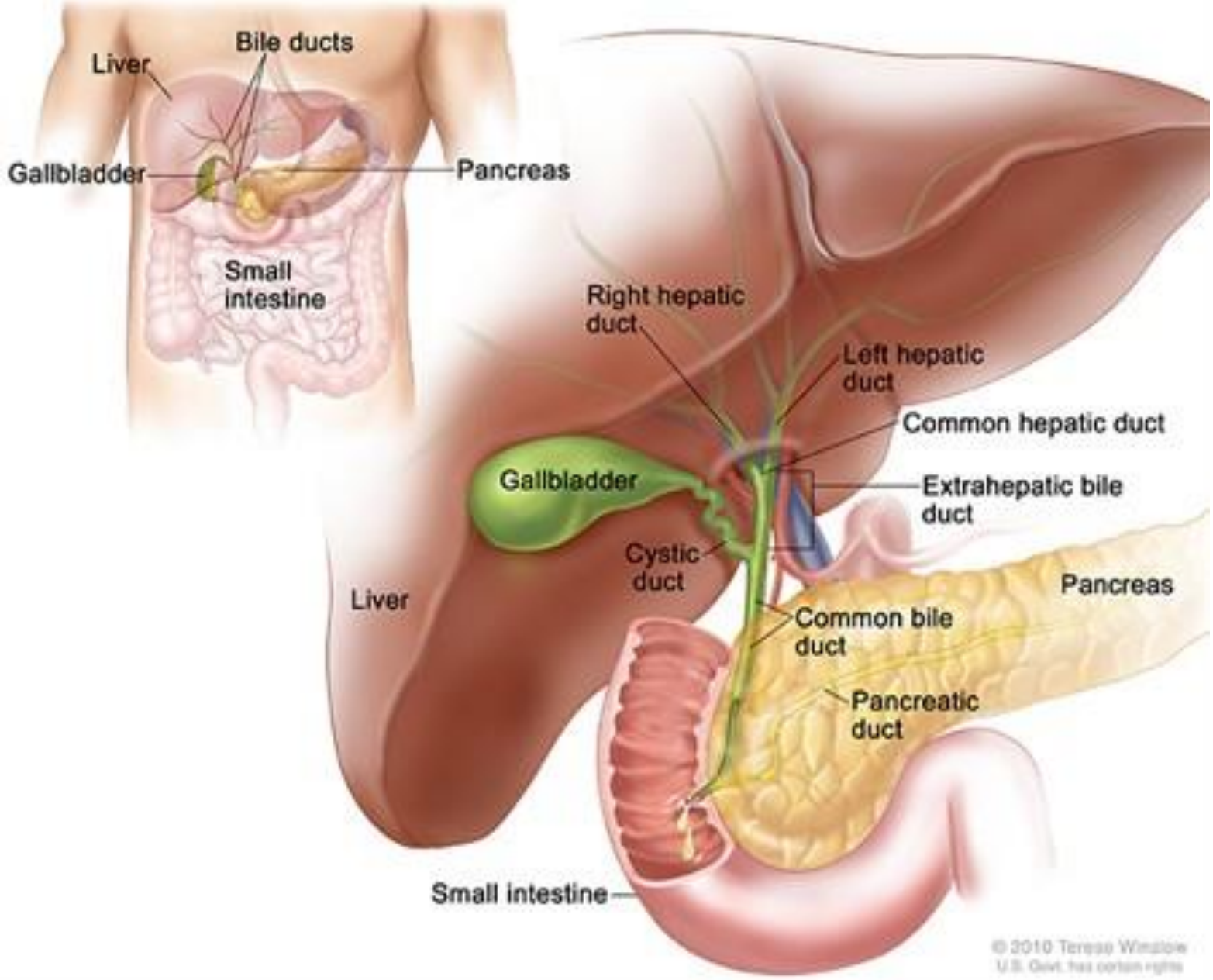
- The end result is destruction of hepatocytes and their replacement by fibrous tissue.

- The resulting resistance to blood flow results in portal hypertension and the development of varices and ascites.

- Hepatocyte loss and intrahepatic shunting of blood results in diminished metabolic and synthetic function, which leads to hepatic encephalopathy (HE) and coagulopathy.

Normal physiological functions of the liver,

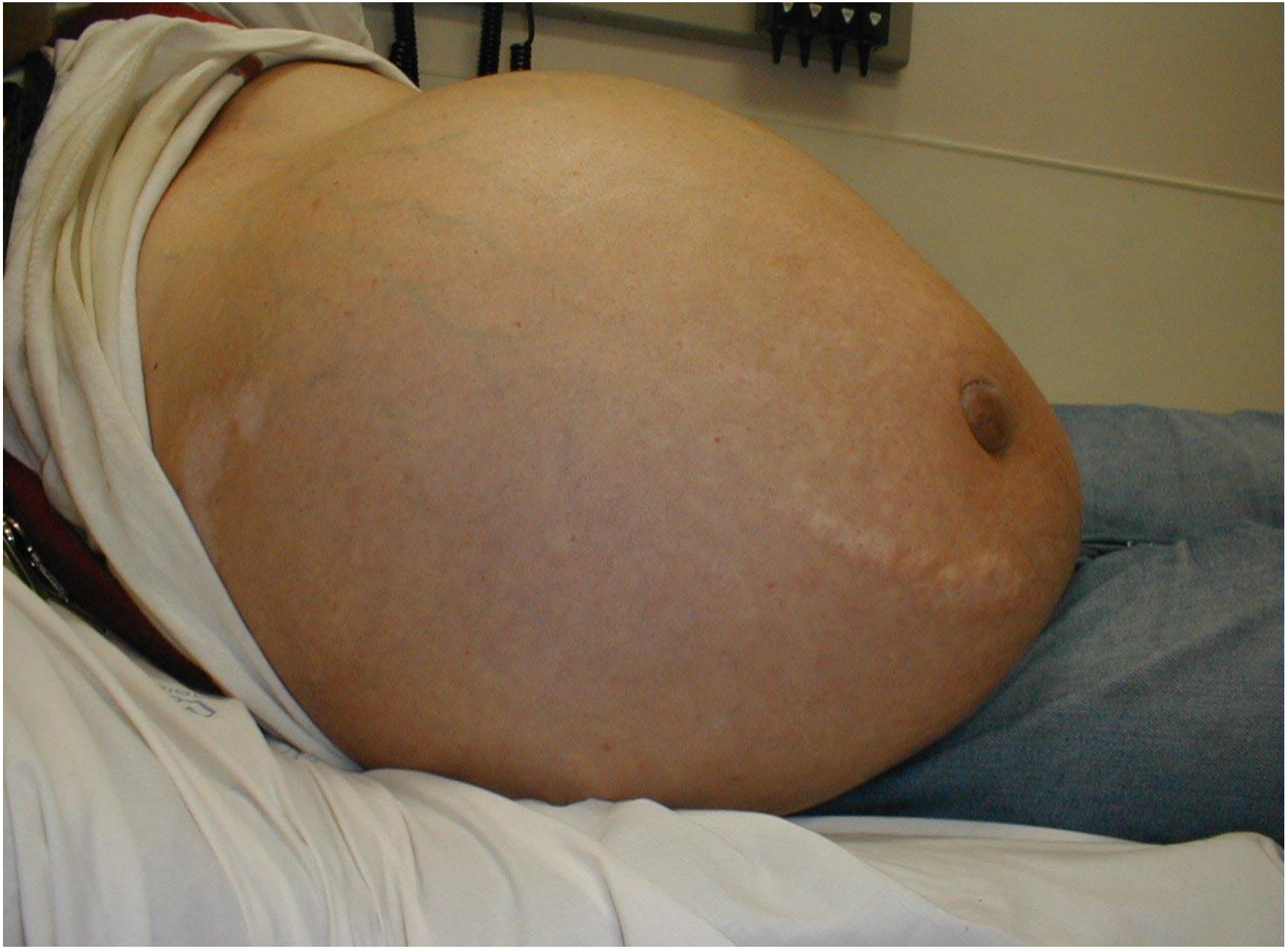


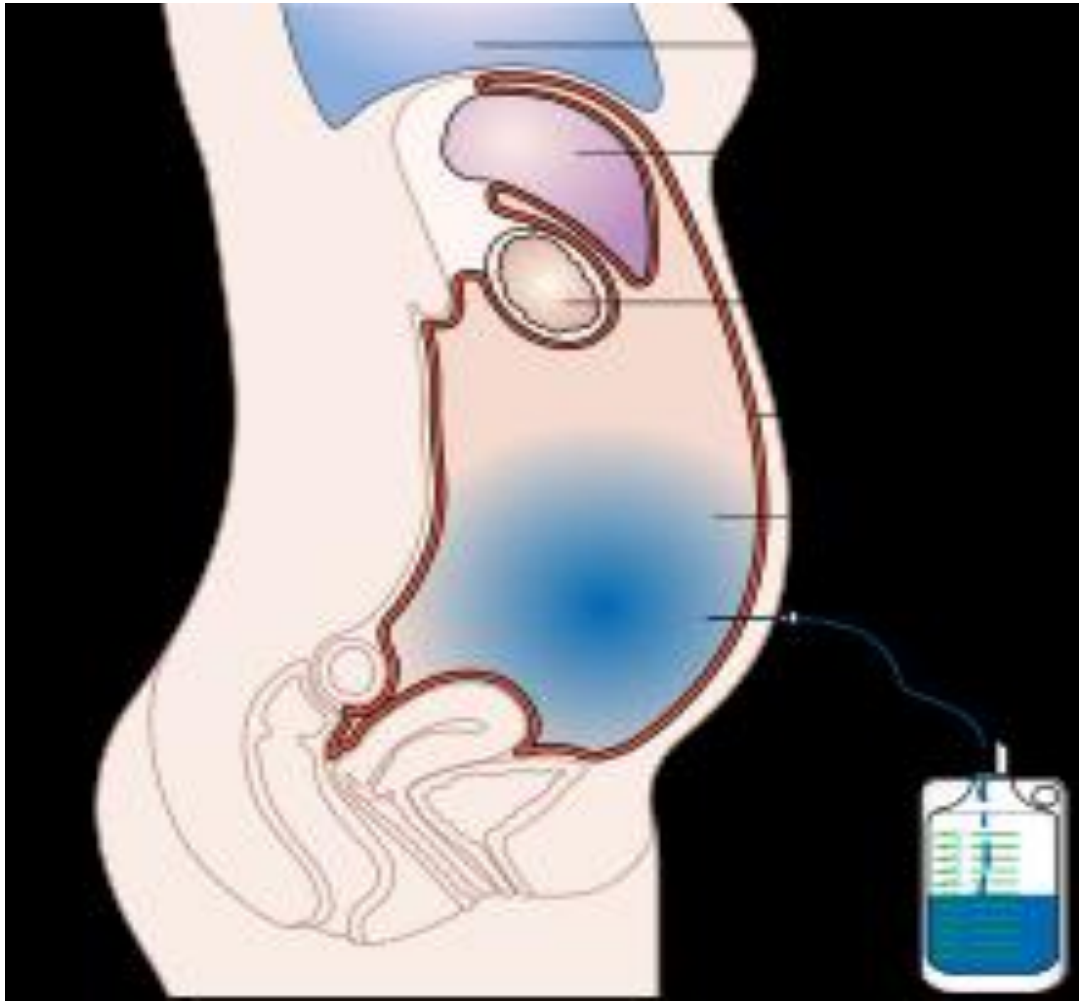


- The pathophysiologic abnormalities that cause cirrhosis result in the commonly encountered problems of ascites, portal hypertension and esophageal varices, HE, and coagulation disorders.

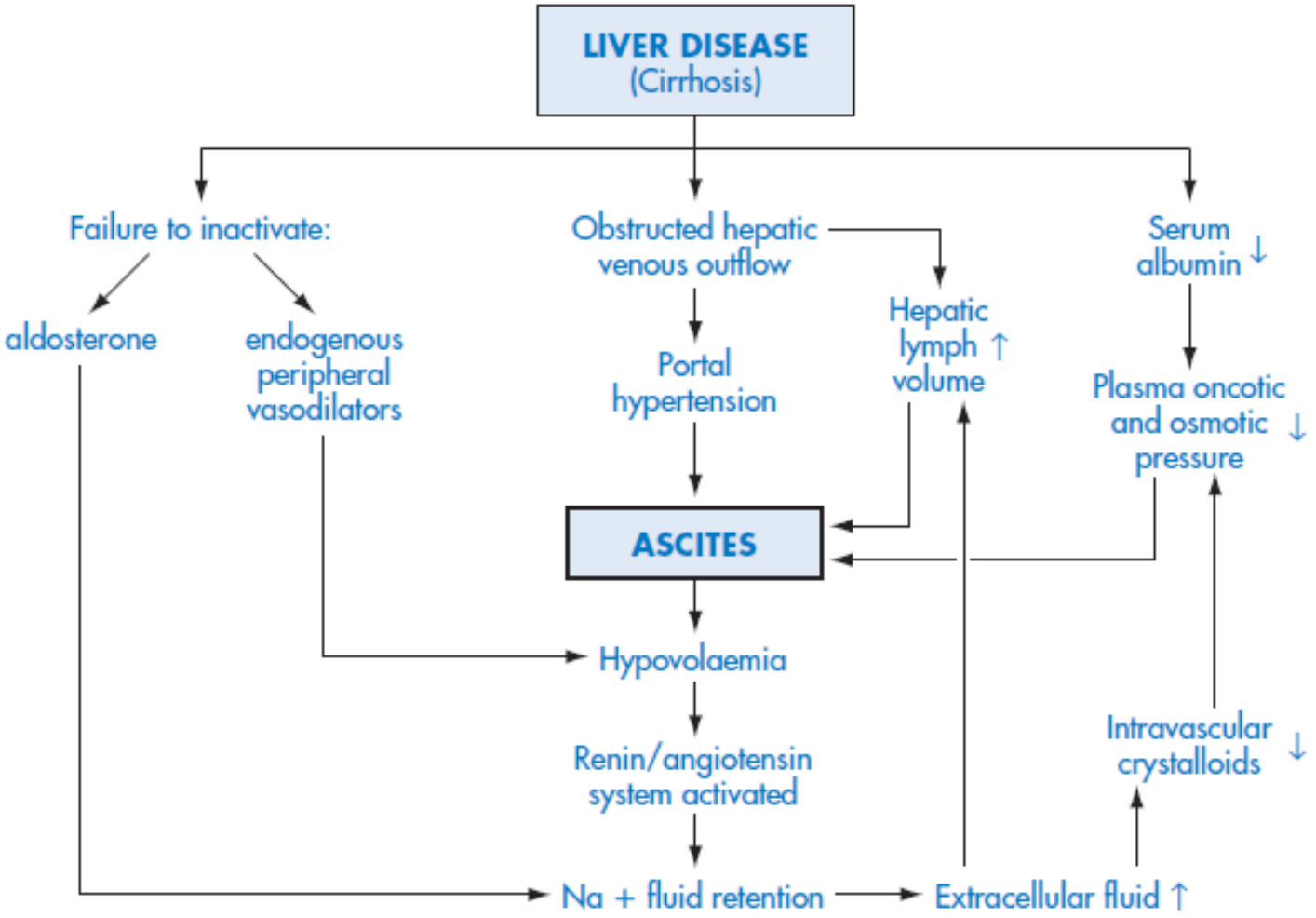
- Ascites is the pathologic accumulation of lymph fluid within the peritoneal cavity. It is one of the earliest and most common presentations of cirrhosis.

- The development of ascites is related to systemic arterial vasodilation that leads to the activation of the baroreceptors in the kidney and an activation of the renin-angiotensin system, with sodium and water retention and vasoconstrictor production.





Mechanisms of ascites formation in hepatic disease



- The most important sequelae of portal hypertension are the development of varices and alternative routes of blood flow.

- Patients with cirrhosis are at risk for varices when portal pressures exceed the vena cava pressure by greater than or equal to 12 mm Hg.

- Hemorrhage from varices occurs in 25% to 40% of patients with cirrhosis, and each episode of bleeding carries a 25% to 30% risk of death.

Etiology of Cirrhosis

- Chronic alcohol consumption
- Chronic viral hepatitis (types B, C, and D)
- Metabolic liver disease
  - Hemochromatosis
  - Wilson's disease
  - α_1-Antitrypsin deficiency
  - Nonalcoholic steatohepatitis ("fatty liver")
- Cholestatic liver diseases
  - Primary biliary cirrhosis
  - Secondary biliary cirrhosis (possible causes: gallstones, strictures, parasitic infection)
  - Primary sclerosing cholangitis (associated with ulcerative colitis and cholangiocarcinoma)
  - Budd-Chiari's syndrome
  - Severe congestive heart failure and constrictive pericarditis
- Drugs and herbals
  - Isoniazid, methyldopa, amiodarone, methotrexate, phenothiazine, estrogen, anabolic steroids, black cohosh, Jamaican bush tea

HEPATIC ENCEPHALOPATHY:

- HE is a central nervous system disturbance with a wide range of neuropsychiatric symptoms associated with hepatic insufficiency and liver failure.

- The symptoms of HE are thought to result from an accumulation of gut derived nitrogenous substances in the systemic circulation as a consequence of shunting through portosystemic collaterals bypassing the liver.

- Altered ammonia, glutamate, benzodiazepine receptor agonists, and manganese are associated with HE. However, serum ammonia levels are poorly correlated with mental status in HE.

- Complex coagulation derangements can occur in cirrhosis.

- These derangements include the reduction in the synthesis of coagulation factors, excessive fibrinolysis, disseminated intravascular coagulation, thrombocytopenia, and platelet dysfunction.

- Vitamin K–dependent clotting factor, including factor VII, is affected early.

- The net effect of these events is the development of bleeding diathesis.

Clinical Presentation of Cirrhosis

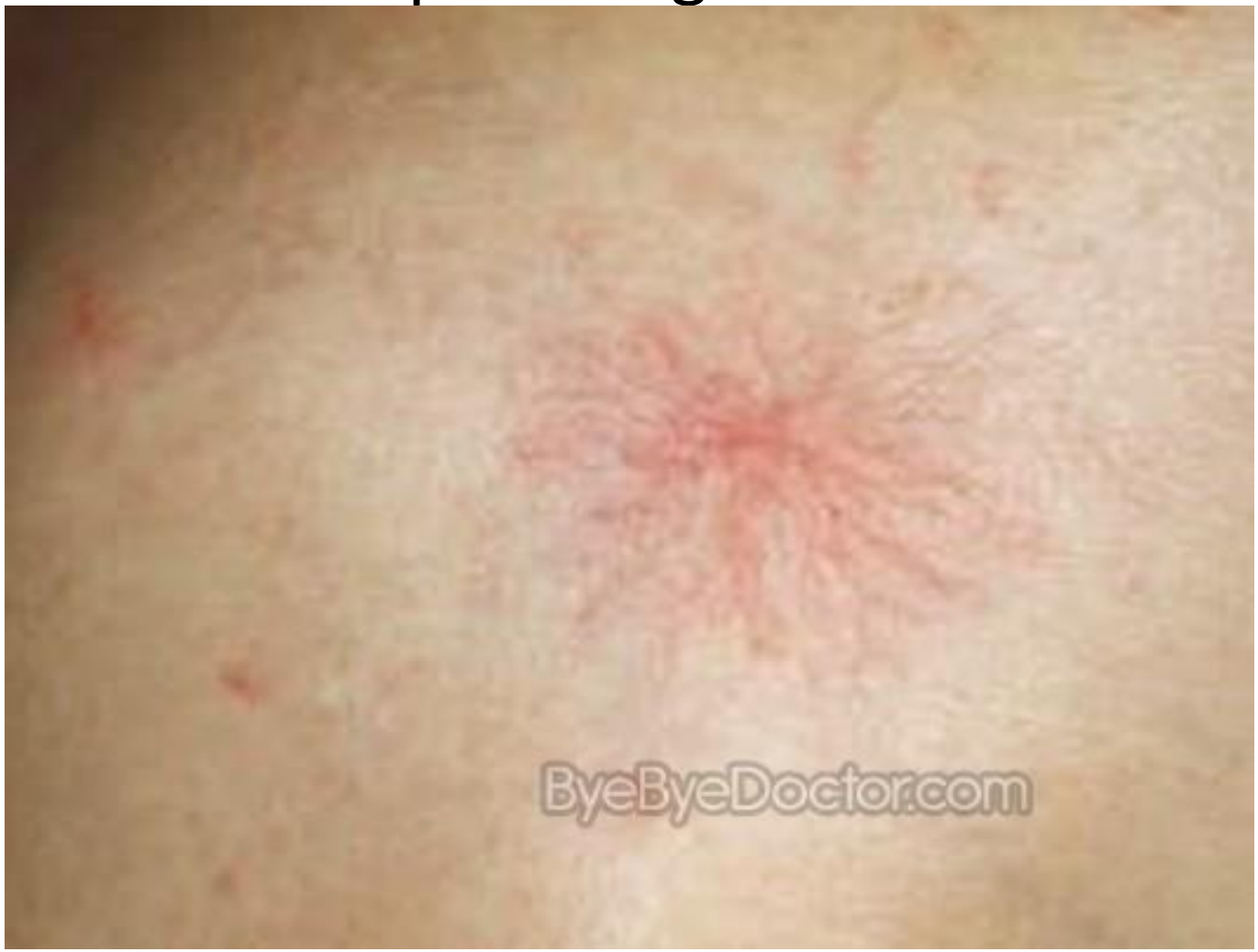
Signs and symptoms

- Asymptomatic
- Hepatomegaly, splenomegaly
- Pruritus, jaundice, palmar erythema, spider angiomata, hyperpigmentation
- Gynecomastia, reduced libido
- Ascites, edema, pleural effusion, and respiratory difficulties
- Malaise, anorexia, and weight loss
- Encephalopathy

Laboratory tests

- Hypoalbuminemia
- Elevated prothrombin time
- Thrombocytopenia
- Elevated alkaline phosphatase
- Elevated aspartate transaminase (AST), alanine transaminase (ALT), and γ-glutamyl transpeptidase (GGT)

Spider angimata



Interpretation of liver function tests