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One Of The Three Monstrous Gorgons , Generally Described As Winged Human Females With Living Venomous Snakes In Place Of Hair

Chronic liver disease and cirrhosis result in about 35,000 deaths each year in the United States.

Cirrhosis is the ninth leading cause of death in the United States and is responsible for 1.2% of all US deaths.

International data

Worldwide, cirrhosis is the 14th most common cause of death, but in Europe, it is the 4th most common cause of death.

NORMAL CIRRHOSIS

Introduction

It is a chronic disease in which there has been diffuse destruction and fibrotic regeneration of hepatic cells.

As necrotic tissue is replaced by fibrotic tissue, normal liver structure and vasculature is altered , impairing blood and lymph flow.

Results in

- Hepatic insufficiency
- Portal hypertension.

Definition

Cirrhosis of liver is a chronic, progressive disease characterized by widespread fibrosis(scarring) and nodule formation.

The progression of liver injury to cirrhosis may occur over weeks to years.

Indeed, patients with hepatitis C may have chronic hepatitis for as long as 40 years before progressing to cirrhosis.

Signs and symptoms

Some patients with cirrhosis are completely asymptomatic and have a reasonably normal life expectancy. Other individuals have a multitude of the most severe symptoms of end-stage liver disease and a limited chance for survival.

Common signs and symptoms may stem from decreased hepatic synthetic function (eg, coagulopathy), portal hypertension (eg, variceal bleeding), or decreased detoxification capabilities of the liver (eg, hepatic encephalopathy).

Signs & Symptoms

Cirrhosis often has no signs or symptoms until liver damage is extensive. When signs and symptoms do occur, they may include:

- Fatigue
- Easily bleeding or bruising
- Loss of appetite
- Nausea
- Swelling in your legs, feet or ankles (edema)
- Weight loss

- Itchy skin
- Yellow discoloration in the skin and eyes (jaundice)
- Fluid accumulation in your abdomen (ascites)
- Spiderlike blood vessels on your skin
- Redness in the palms of the hands
- For women, absent or loss of periods not related to menopause
- For men, loss of sex drive, breast enlargement (gynecomastia) or testicular atrophy
- Confusion, drowsiness and slurred speech (hepatic encephalopathy)

The most common causes of cirrhosis in the United States include the following:

1. **Hepatitis C**
2. **Alcoholic liver disease**
3. **Hepatitis C plus alcoholic liver disease**
4. **Cryptogenic causes - Many cases actually are due to NAFLD**
5. **Hepatitis B - May be coincident with hepatitis D**
6. **Miscellaneous (5%)**

Miscellaneous causes of chronic liver disease and cirrhosis include the following:

- **Autoimmune hepatitis**
- **Primary biliary cholangitis**
- **Secondary biliary cirrhosis - Associated with chronic extrahepatic bile duct obstruction**
- **Primary sclerosing cholangitis**
- **Hemochromatosis**
- **Wilson disease**
- **Alpha-1 antitrypsin deficiency**
- **Granulomatous disease - Eg, sarcoidosis**

- **Type IV glycogen storage disease**
- **Drug-induced liver disease - Eg, methotrexate, alpha methyldopa, amiodarone**
- **Venous outflow obstruction - Eg, Budd-Chiari syndrome, veno-occlusive disease**
- **Chronic right-sided heart failure**
- **Tricuspid regurgitation**

Blood tests

- liver tests that can show abnormal liver enzyme levels, which may be a sign of liver damage.
  - increased levels of the liver enzymes alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP)
  - increased levels of bilirubin
  - decreased levels of blood proteins
- Complete blood count which can show signs of infection and anemia that may be caused by internal bleeding

- Tests for viral infections to see if you have hepatitis B or hepatitis C

- Blood tests for autoimmune liver conditions, which include the antinuclear antibody (ANA), anti-smooth muscle antibody (SMA), and anti-mitochondrial antibody (AMA) tests

- Based on the blood test results, your doctor may be able diagnose certain causes of cirrhosis

Imaging tests

- Imaging tests can show the size, shape, texture, and stiffness of your liver. Measuring the stiffness of the liver can show scarring.
- Magnetic resonance imaging (MRI)
- Ultrasound
- Computerized tomography (CT) scans
- Transient elastography, a special ultrasound that measures the stiffness of your liver and can measure liver fat

Liver biopsy

- Your doctor may perform a liver biopsy to see how much scarring in is your liver. A liver biopsy can diagnose cirrhosis when the results of other tests are uncertain.
- The biopsy may show the cause of cirrhosis. Sometimes your doctor may find that something other than cirrhosis has caused your liver to become damaged or enlarged.
- Can also diagnose liver cancer based on liver biopsy results.

Complications

- **High blood pressure in the veins that supply the liver (portal hypertension).** Cirrhosis slows the normal flow of blood through the liver, thus increasing pressure in the vein that brings blood to the liver from the intestines and spleen.

- **Swelling in the legs and abdomen.** The increased pressure in the portal vein can cause fluid to accumulate in the legs (edema) and in the abdomen (ascites). Edema and ascites also may result from the inability of the liver to make enough of certain blood proteins, such as albumin.

- **Enlargement of the spleen (splenomegaly).** Portal hypertension can also cause changes to and swelling of the spleen, and trapping of white blood cells and platelets. Decreased white blood cells and platelets in your blood can be the first sign of cirrhosis.

- **Bleeding.** Portal hypertension can cause blood to be redirected to smaller veins. Strained by the extra pressure, these smaller veins can burst, causing serious bleeding. Portal hypertension may cause enlarged veins (varices) in the esophagus (esophageal varices) or the stomach (gastric varices) and lead to life-threatening bleeding. If the liver can't make enough clotting factors, this also can contribute to continued bleeding.

- **Infections.** If you have cirrhosis, your body may have difficulty fighting infections. Ascites can lead to bacterial peritonitis, a serious infection.

- **Malnutrition.** Cirrhosis may make it more difficult for your body to process nutrients, leading to weakness and weight loss.

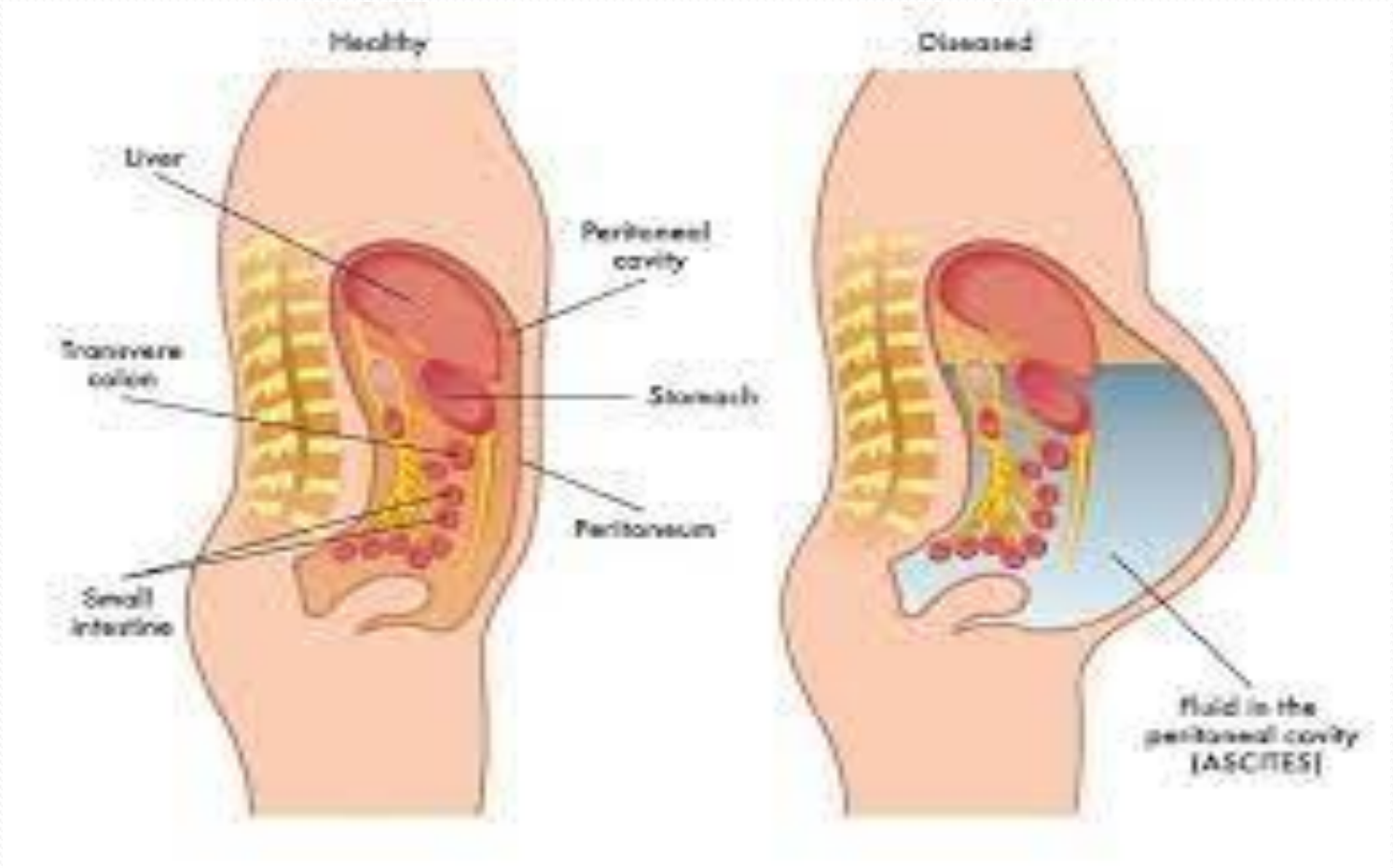
- **Buildup of toxins in the brain (hepatic encephalopathy).** A liver damaged by cirrhosis isn't able to clear toxins from the blood as well as a healthy liver can. These toxins can then build up in the brain and cause mental confusion and difficulty concentrating. With time, hepatic encephalopathy can progress to unresponsiveness or coma.

- **Jaundice.** Jaundice occurs when the diseased liver doesn't remove enough bilirubin, a blood waste product, from your blood. Jaundice causes yellowing of the skin and whites of the eyes and darkening of urine.

- **Bone disease.** Some people with cirrhosis lose bone strength and are at greater risk of fractures.

- **Increased risk of liver cancer.** A large proportion of people who develop liver cancer have pre-existing cirrhosis.

- **Acute-on-chronic cirrhosis.** Some people end up experiencing multiorgan failure. Researchers now believe this is a distinct complication in some people who have cirrhosis, but they don't fully understand its causes.


Healthy
Diseased
Liver
Peritoneal cavity
Transvere colon
Stomach
Peritoneum
Small intestine
Fluid in the peritoneal cavity (ASCITES)

Ascites

Ascites. which is an accumulation of excessive fluid within the peritoneal cavity, can be a complication of either hepatic or nonhepatic disease. The four most common causes of ascites in North America and Europe are cirrhosis, neoplasm, congestive heart failure, and tuberculous peritonitis.

Spontaneous bacterial peritonitis

SBP is observed in 15-26% of patients hospitalized with ascites. The syndrome arises most commonly in patients whose low-protein ascites (< 1 g/dL) contains low levels of complement, resulting in decreased opsonic activity.

SBP appears to be caused by the translocation of gastrointestinal (GI) tract bacteria across the gut wall and also by the hematogenous spread of bacteria.

The most common causative organisms are *Escherichia coli, Streptococcus pneumoniae, Klebsiella* species, and other gram-negative enteric organisms.

Classic SBP is diagnosed by the presence of neutrocytosis, which is defined as greater than 250 polymorphonuclear cells (PMNs) per mm^3 of ascites, in the setting of a positive ascites culture.

Culture-negative neutrocytic ascites is observed more commonly. Both conditions represent serious infections that carry a 20-30% mortality rate.

Hepatorenal Syndrome

This syndrome represents a continuum of renal dysfunction that may be observed in patients with a combination of cirrhosis and ascites.

Hepatorenal syndrome is caused by the vasoconstriction of large and small renal arteries and the impaired renal perfusion that results.

Hepatic Encephalopathy

Hepatic Encephalopathy , a syndrome observed in some patients with cirrhosis, is marked by personality changes, intellectual impairment, and a depressed level of consciousness.

The diversion of portal blood into the systemic circulation appears to be a prerequisite for the syndrome. Indeed, hepatic encephalopathy may develop in patients without cirrhosis who undergo portocaval shunt surgery.

Hematologic manifestations

Anemia may result from folate deficiency, hemolysis, or hypersplenism.

Thrombocytopenia usually is secondary to hypersplenism and decreased levels of thrombopoietin.

Coagulopathy results from decreased hepatic production of coagulation factors.

If cholestasis is present, decreased micelle entry into the small intestine leads to decreased vitamin K absorption, with resulting reduction in hepatic production of factors II, VII, IX, and X. Patients with cirrhosis also may experience fibrinolysis and disseminated intravascular coagulation.

Hepatocellular Carcinoma

Multiple masses in the liver seen on a CT scan, consistent with hepatocellular carcinoma.

Assessment of the Severity of Cirrhosis

Child-Turcotte-Pugh Classification for Severity of Cirrhosis			
Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3
*Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)			
Class A = 5 to 6 points (least severe liver disease)			
Class B = 7 to 9 points (moderately severe liver disease)			
Class C = 10 to 15 points (most severe liver disease)			

Pharmacologic Treatment

Specific medical therapies may be applied to many liver diseases in an effort to diminish symptoms and to prevent or forestall the development of cirrhosis.

Examples include prednisone and azathioprine for autoimmune hepatitis, interferon and other antiviral agents for hepatitis B and C, phlebotomy for hemochromatosis, ursodeoxycholic acid for primary biliary cholangitis, and trientine and zinc for Wilson disease.

Liver Transplantation

Liver transplantation has emerged as an important strategy in the management of patients with decompensated cirrhosis. Patients should be referred for consideration of liver transplantation after the first signs of hepatic decompensation.