

Primary Biliary Cirrhosis (PBC)

- **Basics**

Overview

- **What is PBC?**

Primary Biliary Cirrhosis (PBC) is a chronic liver disease that is characterized by inflammation and progressive destruction of the bile ducts. PBC is usually diagnosed in patients between the ages of 35 to 60 years. About 90 to 95 percent of patients are women. Liver inflammation over a long period of time may cause scarring which leads to cirrhosis. The cause of PBC is unknown, but it is most likely an autoimmune disease. An autoimmune disease is a process where the immune system attacks a specific tissue in the body. In PBC, it is thought that the immune system attacks and destroys small bile duct cells in the liver. It is not uncommon for patients with PBC to have other associated autoimmune diseases including pernicious anemia, scleroderma, or thyroid disorders. In addition, there are environmental factors such as infections, which may trigger the disease. Due to widespread laboratory screening, the number of patients being diagnosed early in the asymptomatic stage has risen dramatically over the past decade. More than 60 percent of newly diagnosed PBC patients now are asymptomatic.

- **What are the signs and symptoms of PBC?**

Many patients may not have symptoms for years, and some may never have complaints relating to their disease. Because of the varying and sometimes subtle symptoms, doctors may have difficulty initially making the diagnosis. Signs and symptoms may include the following:

- Hypercholesterolemia (elevated cholesterol levels)
- Intense itching of the skin (pruritus)
- Dry eyes and mouth (sicca syndrome)

Most patients however are asymptomatic, and the diagnosis is made on the basis of an elevated alkaline phosphatase level in the blood.

- **What type of tests are needed to evaluate PBC?**

Many patients are now diagnosed before symptoms are present. Typically, screening level blood tests show a higher than normal alkaline phosphatase (AP) level with a normal bilirubin. Usually, the bilirubin does not increase until a late stage of the disease. Your doctor may decide to conduct one or more of the following tests.

- *Anti-mitochondrial antibody (AMA) blood test* - Up to 95% of patients with PBC will have a positive AMA test. This test is used to help confirm a diagnosis of PBC. However the AMA tends to remain stable, and has no value in following disease progression, or in monitoring the response to treatment.
- *Liver function tests* - Blood tests that are specific for liver disease are total bilirubin, alkaline phosphatase, aminotransferase levels (ALT, AST), albumin and prothrombin time.
- *Cholesterol and triglyceride levels* - These blood tests are often increased.
- *Ultrasound exam of the liver* - Images of the liver and bile ducts are taken to assess for liver abnormalities. These imaging studies are usually normal in PBC.

Liver biopsy - A small sample of liver tissue helps to confirm the diagnosis and determines the severity of the liver damage. A liver biopsy is not always necessary, especially if the AMA is positive, the alkaline phosphatase is 3-4 times normal, and the imaging studies are normal.

- **Treatment of complications of PBC**

Some patients have complications of PBC that require therapy. In many cases, doctors find that symptoms can be controlled by lifestyle modifications and medications.

- Itching

Itching can be a very troublesome symptom of PBC. Itching may range from mild to severe, where a patient's lifestyle may be impaired. Itching may be worse with fatty meals or at night, interfering with sleep. The initial medications typically used by doctors include diphenhydramine, cholestyramine and colestipol. Rifampin is used in patients who fail or are intolerant to cholestyramine and colestipol. In resistant cases, opioid antagonists such as nalmefene, naloxone and naltrexone are used. Plasmapheresis and ultraviolet light have been utilized in extreme cases. Liver transplantation is indicated for patients with uncontrolled itching.

- Osteoporosis

When the diagnosis of PBC is made, a bone mineral density scan (DEXA scan) should be performed to determine if a patient has osteoporosis or bone thinning. In many cases, doctors may suggest that their patients start exercising if possible, stop smoking and take calcium 1500 mg/day with vitamin D 1,000 IU/day. Hormone replacement therapy (estrogen) is safe in PBC and is recommended where appropriate. When osteoporosis is evident, therapy with medications such as Fosamax® (alendronate) and Actonel® may be helpful in PBC.

- Fat-soluble vitamin deficiencies

As PBC progresses, some patients lose the ability to absorb fat-soluble vitamins A, D, E and K. Measurement and replacement of these vitamins is recommended.

- Esophageal varices

Varices are swollen veins which form in the esophagus and stomach. When blood is returning to the heart, it must pass through the liver. In PBC, the pressures encountered in the liver may be so high that the blood flow will shunt through the esophagus or stomach. The dilated veins that form as a result are called varices, and can potentially result in serious bleeding. Patients with PBC should undergo regular endoscopies for variceal surveillance and treatment if necessary.

- [Treatment of underlying disease](#)

- Ursodiol

Ursodiol is currently the only drug approved by the FDA for the treatment of PBC and it is often the initial therapy for patients. The drug is a "gentler" bile acid than those normally made by the body and is well tolerated. Studies have shown that ursodiol, given in a dose of 13 to 15 mg/kg daily up to four years, delays the time to liver transplantation. In addition to improving blood tests, there are some patients with PBC whose disease appears to become inactive (remission) on ursodiol. Repeat or even serial liver biopsies may be required in order to document remission.

- Colchicine

Colchicine is associated with improvement of liver tests in some patients with PBC and improved itching in two recent studies. However, there was no improvement in liver biopsy findings and therefore this medication is not commonly used to treat PBC.

- Methotrexate

In early studies, methotrexate had appeared to be associated with improvement in symptoms, liver function tests and liver biopsies. However, an 8-year multicenter NIH trial has clearly documented that the use of Methotrexate is not associated with improvements in liver disease and the development of complications of cirrhosis.

- [Liver Transplantation](#)

Many people with PBC may never develop cirrhosis or liver failure. However, as can be seen in PSC, a late stage of PBC can be liver failure. For those people who reach the late stages of PBC, liver transplantation may be considered. The signs and symptoms of liver failure, which may or (depending on

the specific aspects of the symptoms / disease) may not prompt consideration of any potential role for liver transplant, are the following:

- Persistent jaundice
- Fluid retention with swelling of hands, feet and abdomen
- Variceal bleeding (internal bleeding from swollen intestinal blood vessels, commonly in upper stomach and esophagus)
- Bone thinning and/or fractures
- Hepatic coma or encephalopathy

The survival for PBC patients after liver transplantation is excellent although some patients may develop recurrent PBC over time. With better understanding of the nature of PBC and its complications, many patients will have improved outcomes.

Author(s) and Publication Date(s)

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