ERN RARE-LIVER
European Reference Network on Hepatological Diseases

Primary biliary cholangitis (PBC)

What is PBC?

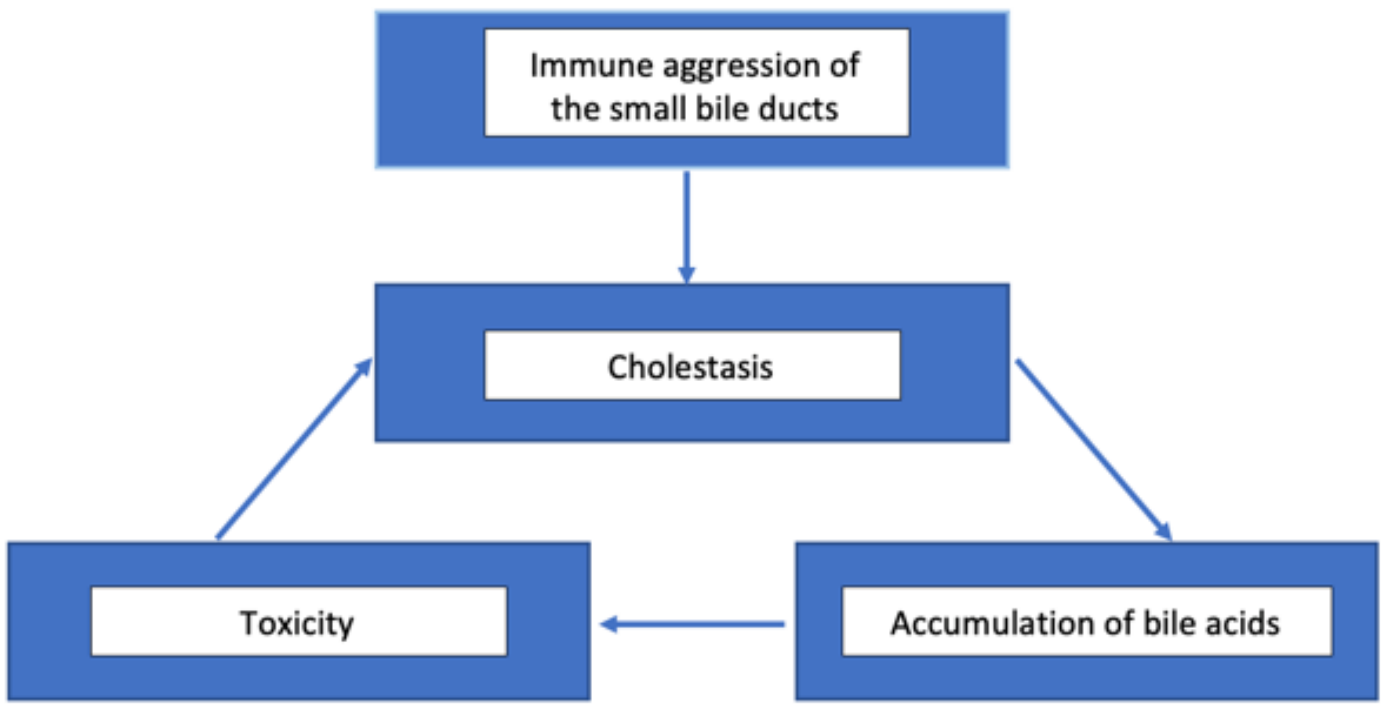
Primary biliary cholangitis (PBC), formerly called primary biliary cirrhosis, is a chronic inflammatory autoimmune liver disease, affecting the small intra-hepatic bile ducts. Over time, PBC can lead to fibrosis and eventually to cirrhosis.

The term fibrosis refers to the presence of scar tissue on analysis of a liver biopsy. Other methods of detecting fibrosis include blood tests and elastography measurement.

A chronic inflammation of the liver destroys the liver cells, leading to liver fibrosis. This fibrous tissue surrounds abnormal nodules formed by the anarchic regeneration of destroyed liver cells. The consequence is to have progressively a liver function reduction as far as fibrosis becomes cirrhosis. It is possible to live with cirrhosis, but it is important to have a strict and correct follow up.

The immune system produces antibodies to defend your body against external aggressors (viruses, bacteria). In the case of an autoimmune disease, your immune system attacks components of your own body and in the case of PBC, the antibodies are directed to the small bile ducts causing cholestasis.

Cholestasis is when the liver is not able to adequately secrete bile to the intestine, being this the main consequence of the bile duct damage induced by autoimmunity in PBC. The accumulation of bile into the liver is toxic and results in persistent inflammation and development of fibrotic scares, which in turn aggravate cholestasis in a vicious circle, as shown below.



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One of the objectives of treatments in PBC is to avoid the aggravation of cholestasis, thereby interrupting the vicious circle causing progressive liver damage.

An early diagnosis is essential to enable treatment to prevent or slow down the progression of the disease. Patients who are diagnosed early and who show a good response to treatment have a life expectancy comparable to individuals without the disease. Fortunately, this is the case of a large majority of patients.

Who is affected?

90 percent of PBC patients are women, and most patients are diagnosed between the ages of 35 and 55. The prevalence of the disease (number of cases in a given population) for women above the age of 40 is estimated to be ~ 1 / 1000. PBC should thus be considered a rare disease.

Why do I have PBC?

The cause of this liver disease is unknown. A genetic predisposition in combination with environmental factors may be responsible for the autoimmune dysfunction triggering the development of PBC.

What are possible symptoms?

Many patients are asymptomatic at the time of diagnosis. Fatigue and itching are frequently reported throughout the course of the disease. Additional symptoms can include difficulty in concentration, joint pain, and pain in the upper right quadrant of the abdomen. Dryness of the eyes or mouth are also reported, and can sometimes be linked to other autoimmune diseases or syndromes accompanying PBC.

As symptoms are often subtle, and do not necessarily occur, they rarely lead to the diagnosis of PBC. These symptoms, mainly fatigue, are generally independent from the severity of the disease.

In some cases, patients can suffer from other autoimmune diseases and/or syndromes including Sjogren's syndrome or thyroiditis Hashimoto. These conditions require separate attention from various experts, resulting in the need to coordinate between medical specialists.

How is PBC diagnosed?

Nowadays, PBC is mostly detected following routine blood tests. Abnormal liver-related blood tests, which can indicate cholestasis, motivate physicians to assess for the cause of liver disease. PBC is usually easily diagnosed based on the combination of chronic cholestasis and detectable anti-mitochondrial antibodies (AMA) or antinuclear antibodies specific to PBC. The AMAs can be detected in over 90 percent of patients.

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The main abnormal blood tests in PBC are elevated levels of alkaline phosphatase (AP) and/or gamma-GT, associated with inflammation of the bile ducts, and elevated immunoglobulin M (IgM). Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are frequently above the upper limit of normal as well, without necessarily meaning that there is co-existent Autoimmune Hepatitis (AIH).

Only in certain situations, a liver biopsy will be considered. Liver biopsy is not part of the routine diagnostics to diagnose PBC, but can be useful in case PBC is suspected but the autoantibodies are not detectable. In addition, liver biopsy may be required to determine the extent of duct bile loss or to exclude other associated liver diseases like AIH or Non-Alcoholic Fatty Liver Disease (NAFLD).

Following the diagnosis of PBC, the treating physician needs to assess the stage of the disease (degree of liver fibrosis, up to cirrhosis). A liver elastography can be used for this purpose. The final stage of disease is frequently based on a combination of blood tests, elastrography results, imaging of the liver and clinical symptoms.

What can your doctor (hepatologist) do?

A rapid and precise diagnosis is essential to determine the appropriate treatment. As PBC is a rare liver disease, it is important that PBC is monitored by hepatologists (experts in diseases of the liver).

Your doctor will examine your case and prescribe you the treatment(s) that are needed, also according to your response to the treatment(s) as measured by blood tests. In addition, he/she will assess possible problems which may occur during the course of the disease, including other conditions related to PBC.

The standard firstline treatment for PBC is ursodeoxycholic acid (UDCA), which is usually very well tolerated. The preferred dosage is between 13 and 15 mg per kilogram of body weight per day. Your hepatologist will calculate the correct dosage for you, which may change over time in case of significant weight changes. As adequate dosages of UDCA are associated with prolonged life expectancy and lower rate of liver transplantation in PBC, it can be considered essential to protect your liver. Indeed, in most patients, the progressive damage to the liver can be effectively stopped/slowed down by UDCA.

If the treatment with UDCA is not sufficient to stabilise the disease, additional treatment is wanted to further improve the prognosis. Secondline treatments to consider included obeticholic acid and bezafibrate (or fenofibrate), but the availability differs per country. Together with your hepatologist you can discuss if you need additional treatment next to UDCA, and which second line treatment is most suitable and/or available in your personal case. Several clinical trials evaluating the safety and efficacy of new drugs for PBC are also available worldwide.

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Concerning the main symptoms of PBC, your doctor has several treatments option to try to control itching. Unfortunately, there is not yet a drug, which improves fatigue. Correction of factors that can worsen fatigue, such as unfavourable sleeping disturbances, anaemia, or physical inactivity, is recommended.

What can you do?

Your hepatologist is responsible for the clinical management of your PBC, and the coordination with other specialists in conjunction with your family doctor.

But you, as a patient, have responsibilities as well:
1. to follow the prescribed treatments, as this is fundamental for their success
2. to prepare appointments in advance, which will facilitate the dialogue with your doctor thereby improving your understanding of your own medical situation

With a chronic disease like PBC, there is a long-term relationship between the doctor and patient. This relationship needs to be constructed and maintained from the beginning.

If you decide to use alternative non-prescribed treatments or products, you should discuss this with your doctor first. There may be adverse effects of such ingestions.

How to monitor PBC?

How PBC is monitored is dependent on the severity of the disease. Usually, PBC is monitored by the evaluation of symptoms, blood tests, liver elastography, and, in some cases, abdominal ultrasound and endoscopy.

Blood tests are generally recommended every 6 to 12 months, depending on the severity and stability of the disease. Younger women, male patients and those who have developed cirrhosis may require special attention, including regular abdominal ultrasound examinations.

Patients suffering from PBC can have an increased risk of osteoporosis (reduced bone density). Therefore, bone density tests (osteodensitometry) and preventive measures may be needed.

Liver elastography is also useful to monitor the disease and may be repeated regularly (e.g. every 1-2 years according to the clinical context) over time.

Very rarely a PBC patient will need a liver transplantation. However, if performed, it has good long-term results.

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Do I need a special diet?

There is no special diet for PBC. The recommendation will be to maintain a healthy, well-balanced diet, as for the general population. It is known that a diet with too much sugar and/or too much fat (leading to steatosis or fatty liver overload) can cause liver damage as well. Patients are encouraged to avoid smoking and excessive alcohol consumption.

Avoid any supplements without checking with your doctor first.

Besides these general advises your doctor may have specific recommendations for you personally.

Can I have a family?

Yes. If you are of childbearing age, you can discuss your wish to become pregnant with your doctor. He/she can provide you with recommendations depending on the stage of your disease. Pregnancy and nursing are possible for the large majority of female patients.

Frequently, younger women ask whether they can transmit PBC to their children. PBC is not a hereditary disease as it is not caused by a specific genetic defect which is passed on from parents to their children. However, there does appear to be a genetic suscep

Vaccinations

Vaccinations against hepatitis A and B viruses and pneumococcal infections (bacteria) are recommended, as well for COVID-19. Vaccination against influenza can be considered each autumn, but will depend on your countries recommendations. In general, patients > 65 years and patients with cirrhosis are advised repeated influenza vaccination. If you decide to have other vaccines, you should talk to your doctor to check whether this is possible in your specific case.

Is PBC an infectious disease?

No. PBC is not infectious or contagious.

How can I find a specialist?

PBC is a rare disease and, as such, not every doctor may have sufficient experience to treat patients with PBC. Ideally, patients with PBC are managed by a medical specialist in a hospital with experience in treating PBC.

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Some hospitals are part of a national network for rare liver diseases and/or the Europe-wide network for rare liver diseases, ERN RARE-LIVER. This means that patients seen at hospitals within the network can benefit from the expertise of specialists who work in other hospitals within the network. Case discussions within the network can help very rare and special cases to be solved.

For more information about ERN RARE-LIVER, visit the website: **https://rare-liver.eu/**

Find information and support

Patient organisations are important to help to face the impact of a PBC diagnosis, to share experiences and to facilitate the dialogue with health care providers. With a rare disease it is important to understand what happens to your health. In addition, patient organisations will give you support and make you feel more accompanied to face your condition. You can find patient organisations in your country on the ERN RARE-LIVER website (https://rare-liver.eu/patients/patient-organisations).