Primary biliary cholangitis (PBC)

BRITISH LIVER TRUST

Pioneering Liver Health

Primary biliary cholangitis (PBC)

The British Liver Trust works to:

- support people with, and affected by, liver disease
- improve knowledge and understanding of the liver and related health issues
- encourage and fund research into new treatments
- campaign for greater awareness around liver disease, leading to swifter diagnosis and treatment.

All our publications are reviewed by medical specialists and people living with liver disease. Our website provides information and our Helpline gives advice and support on enquiries about liver health. Call the Helpline on **0800 652 7330**, general enquires on **01425 481320**, or visit **britishlivertrust.org.uk.**

For the latest updates to this information, please refer to our website **britishlivertrust.org.uk.**

This publication explains what primary biliary cholangitis is, how it's diagnosed and treated, and how people living with PBC can best look after themselves.

Contents

The liver

Your liver is the largest organ inside your body and your body's 'factory' carrying out hundreds of jobs that are vital to life. It is very tough and able to continue to function even when most of it is damaged. It can also repair itself, even renewing large sections.

Your liver has around 500 different functions.

Importantly it:

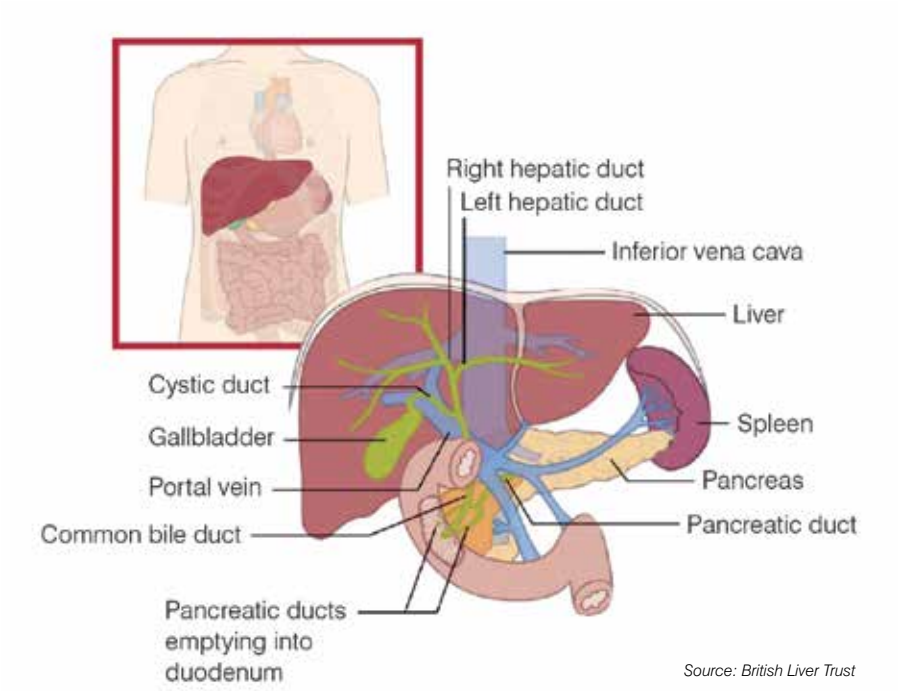
- fights infections and disease
- processes and gets rid of potentially harmful toxins
- filters and cleans the blood
- controls levels of cholesterol in the body
- produces hormones and maintains hormonal balance
- produces chemicals – enzymes and other proteins responsible for most of the chemical reactions in the body, for example, blood clotting and repairing tissue
- processes food once it has been digested
- produces bile to help break down food in the gut
- stores energy that can be used rapidly when the body needs it most
- stores sugars, vitamins and minerals, including iron
- repairs damage and renews itself.

How liver disease develops

Your liver responds to harm by becoming inflamed. Any inflammation of the liver is known as hepatitis, whatever its cause. Sudden inflammation of the liver is known as acute hepatitis. When inflammation of the liver lasts longer than six months, it is known as chronic hepatitis.

Inflammation is part of the process of repairing damaged tissue. In a similar way to a scab forming over a skin wound, a temporary fibrous 'scaffold' forms while new liver cells regenerate. If your liver is repeatedly harmed, new liver cells cannot regenerate fast enough and the fibrous scaffold remains as a scar. This is called fibrosis, and can take a variable amount of time to develop.

When fibrosis is present, your liver may be able to keep functioning quite well. Removing or treating the cause of the inflammation may reverse some, or all, of the fibrosis and prevent further liver damage.

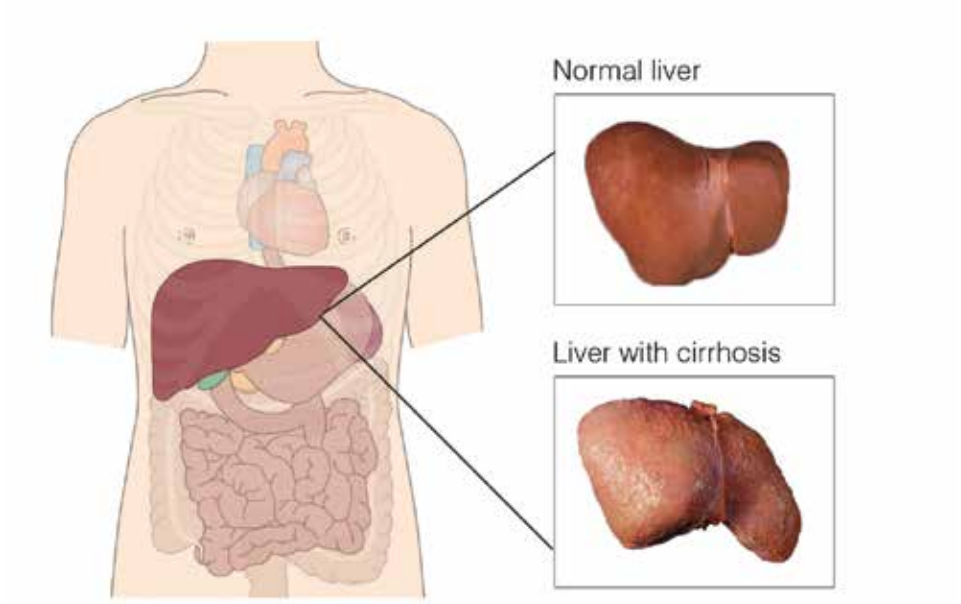


Source: British Liver Trust

If the harm to your liver continues, the inflammation and fibrosis can spread throughout your liver, changing its shape and affecting how well your liver cells work. This is known as **compensated** cirrhosis. Even at this stage, people can have no obvious signs or symptoms.

The scar tissue in cirrhosis interrupts the blood flow through the liver. As a result, the blood pressure in the veins in your abdomen is increased and may result in bleeding. Scar tissue in cirrhosis is difficult to remove and may be permanent. However, further progression can be halted and your cirrhosis stabilised, if the cause of the liver damage is removed.

Cirrhosis increases your risk of liver cancer and can lead to liver failure. If damage to your liver continues, it will become unable to function sufficiently (**decompensated** cirrhosis) and start to fail; this is sometimes referred to as 'end-stage liver disease'. At this stage chemicals and waste products can build up in the body, commonly causing jaundice, ascites (a build-up of fluid in the abdomen) and hepatic encephalopathy (confusion and memory loss). In the final stages of liver disease the build-up of waste products may lead to multiple organ failure and loss of life.



Source: British Liver Trust

What is primary biliary cholangitis (PBC)?

Primary biliary cholangitis is a long-term autoimmune condition which damages the tiny tubes (known as tubules) that drain bile away from the liver and into the small intestine.

Until recently, PBC was known as primary biliary **cirrhosis**, but since not all people with the condition have cirrhosis (see opposite), PBC was renamed to reflect this important fact. The term 'cholangitis' means inflammation of the bile ducts.

When PBC damages the bile tubules, bile can no longer flow through them to bigger tubes called bile ducts, which empty bile into the small intestine. Instead, it builds up in the liver, damaging the liver cells and causing inflammation and scarring. Over the years, this build-up affects more and more of the liver until the damage becomes widespread. The liver is less able to repair itself, which can lead to cirrhosis, although it's important to note that **not everyone with PBC will get cirrhosis**. Over time, cirrhosis can result in the liver being unable to function properly.

What is bile?

Bile is a yellow-green fluid produced by your liver which contains chemicals that aid digestion. It plays a central role in helping the body digest fat by breaking it down so that it can be absorbed from food in your gut. It also makes it possible for your body to take up the fat-soluble vitamins A, D, E and K. A major component of bile includes lots of different bile acids. These are very important for controlling important functions of the liver and bowel. Drugs that change bile acid levels are used frequently to treat liver diseases, including PBC. Bile also contains something called bilirubin, which is naturally produced by the body when red blood cells break down, to be excreted by the liver.

What are the symptoms of PBC?

The majority of patients with PBC are now diagnosed while the disease is still in the early stages. In large surveys of patients with PBC, the majority report a good general quality of life. However, some patients do have symptoms that can be troubling. Common symptoms of PBC include itchy skin, dry eyes, dry mouth, bone aches, joint pains, low energy/constant tiredness, and abdominal discomfort.

Itching, also known as pruritus, may be a result of your liver's inability to process bile, although doctors think it's not the bile acids themselves that cause the itching but other chemicals that are retained in the body. As with tiredness, for example, the severity of the itching will vary from person to person, and does not necessarily mean that your liver is not working well. **It's important to remember that even if your symptoms are severe, this does not automatically mean your liver is very damaged. This highlights why PBC treatment guidelines emphasise the importance of both treating the disease AND associated symptoms.**

Other symptoms that patients often report include:

- dry eyes and/or dry mouth (sicca syndrome); some women notice a dry vagina as well
- constant or variable ache or discomfort in the upper right hand side, below your ribs
- indigestion, nausea or poor appetite
- arthritis (inflammation of the joints)
- pain in the bones
- mottled palms with red or pink blotches
- diarrhoea
- dark urine and/or pale stools
- jaundice – yellowing of the skin and whites of the eyes.

It's worth noting that many people with PBC will never get any symptoms. However, tiredness and itching are generally the first symptoms to appear while jaundice is usually associated with the later stages of the disease.

Why is it called PBC?

It is called primary biliary cholangitis because the disease attacks the tiny bile (biliary) ducts inside the liver. This leads to inflammation of the tubes, which is called cholangitis, and scarring, which is called fibrosis. Ongoing scarring can lead to cirrhosis. The word 'primary', in this case, does not mean 'first' but that there is no known reason or 'trigger' for this damage to occur.

As explained above, PBC has been referred to as primary biliary cirrhosis, which is misleading as many people nowadays do not have cirrhosis when they are first diagnosed, or for years afterwards. Many people with PBC never go on to get cirrhosis, but this remains a risk for patients and the reason why having PBC treated efficiently is so important. Because it blocks or stops the flow of bile, PBC is also known as a 'cholestatic' liver disease.

Who is at risk of PBC?

Nine out of ten people who get PBC are women, although there are reports that more men are being diagnosed of late. No one knows why this is. In particular, the following women are most at risk:

- women who are middle aged or older
- women who have a family history of other autoimmune diseases, and PBC in particular.

Large studies have shown that smoking is also a risk factor for developing PBC.

What are the causes of PBC?

Doctors know that PBC is an autoimmune disease that occurs in some people because of a combination of subtle differences in their genetic make-up and environmental factors – so where you live and the environment around you, but also cigarette smoke and other toxins. In an autoimmune disease, the body's defence mechanism (the immune system) wrongly identifies its own cells as 'invaders' and attacks them. In PBC, the immune system attacks the cells lining the bile ducts.

Doctors understand many of the very subtle genetic changes that are associated with developing PBC, and these are the same gene changes that are seen in many other autoimmune conditions. However, experts are still trying to understand more about the environmental factors that play a part in PBC. Smoking is known to be a risk factor, and some doctors believe that an infection or other environmental toxin may act as a trigger.

Very occasionally, PBC is diagnosed during or just after pregnancy. However, it's not clear whether pregnancy itself triggers the condition or simply that pregnant women are under close medical supervision, meaning it's more likely the symptoms of PBC are picked up during this time. Doctors don't know why PBC is nearly only ever seen in adults, or why it's much more common in women than in men.

Drinking alcohol does not cause PBC.

Testing for PBC

Antibody test

When specifically tested, most people with PBC have circulating antimitochondrial antibodies (AMA) in their blood. An antibody is a chemical made by the body to attack an 'invader'; in the case of autoimmune diseases, it is a marker that the immune system is attacking itself. Having AMA present in your blood makes a diagnosis of PBC very likely.

Liver blood tests (previously known as liver functions tests, or LFTs)

This is when a blood sample is taken and tested for different 'markers' to see whether injury or inflammation is present in the liver. The name of this blood test changed because most people with abnormal liver blood test results actually have normal function of the liver, and it was felt the former term led to unnecessary worry and distress.

Enzymes and other indicators

In PBC, doctors will be looking for increased levels of alkaline phosphatase (ALP), which is an enzyme released into the blood by damaged bile ducts. They will also look for raised levels of bilirubin, which indicates reduced liver function, and the amount of immunoglobin IgM, which is one of the first antibodies we produce to fight against disease. The liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are also monitored, although these are a measure of any 'leakiness' or damage relating primarily to liver cells rather than bile duct cells specifically.

Ultrasound scan

Ultrasound is the technology used to monitor the health of the growing baby during pregnancy. Gel will be applied to your skin, which may feel slightly cold. A probe, like a microphone, will be moved across your skin to send sound waves into the liver area.

The reflected sound waves, or echoes, are picked up through the probe and used to build a screen image of the liver, so that doctors can get a better idea of its condition. The test is quick and painless, and allows doctors to check the condition of the bile ducts. They can also rule out the possibility that your symptoms could be a sign of a different liver problem. Ultrasound is also useful for examining the spleen. As patients with liver disease develop more scarring, the spleen can get bigger.

Liver biopsy

During a liver biopsy a tiny piece of the liver is taken for study. A fine hollow needle is passed through the skin into the liver and a small sample of tissue is withdrawn.

Most patients diagnosed with PBC do not need a liver biopsy. However, in some cases, doctors may request one to help them assess how serious or advanced the condition is. The circumstances for this may include concern over the presence of another liver disease such as autoimmune hepatitis, or more commonly nowadays, fatty liver.

FibroScan (transient elastography)

This is a non-invasive test, similar to ultrasound, that helps doctors see how 'stiff' the liver is. Healthy liver tissue is soft, so stiffness indicates that scar tissue (fibrosis) has formed as a result of damage to the liver; however it also reflects how much inflammation there is at the same time. You'll be given a FibroScan 'score', which indicates the extent to which scarring is present (results range from 2.5kPa to 75kPa).

Between 90–95% of healthy people without liver disease will have a liver scarring measurement of below 7.0 kPa.

How is PBC treated?

There are a number of treatments for the symptoms of PBC. Some of them help with any side effects, such as dry eyes, and others slow the progress of the disease. Both are important.

Managing difficult symptoms

Symptoms of PBC can be distressing and negatively affect your life day-to-day. One of the main symptoms is itching. Colestyramine (sold as Questran) may be prescribed by your doctor to help ease this. Taken orally, colestyramine works by preventing re-absorption of the chemicals that cause the itching. Unfortunately, it can take days or even weeks before this becomes effective.

Some people taking colestyramine have problems such as changed bowel habits and bloating. Your doctor may prescribe 'Questran light' to reduce these side effects.

If colestyramine doesn't help, your doctor may try other medicines such as rifampicin, naltrexone or gabapentin.

Itching is made worse by dry skin, so make sure you use plenty of moisturiser. When you have a bath or shower, don't run the water too hot, as this dries the skin further. Another common symptom of PBC is dry eye, dry mouth, or dry vagina (known as sicca syndrome). These can be soothed by such treatments as artificial tears, lubricating gels and oestrogen creams. You may find that lozenges from your pharmacist will help with the dryness in your mouth.

Low energy can be a particularly troubling symptom, and doctors don't really know what causes fatigue, brain fog, or the low energy patients suffer with. Itching throughout the night may also lead to broken sleep. It's important to find ways to manage fatigue, as feeling tired all the time can affect many areas of your life. When you feel constantly exhausted, it's easy to break social arrangements with friends and family, leading to feelings of isolation, and it also makes it hard to keep up healthy habits, such as regular exercise.

The following advice may help:

- create a schedule of essential daily or weekly activities so you can prioritise important tasks, delegate others and ensure you still have the energy for social occasions and to see people
- pace your activities so that you don't do too much at once
- take gentle exercise, such as walking and swimming, to increase physical fitness and emotional wellbeing without feeling exhausted
- rethink hobbies and leisure time so that they are fun and enriching without being exhausting.

Treating your condition

To help doctors and patients there are clear guidelines in UK and Europe for the lifelong treatment of patients with PBC. All patients diagnosed with PBC should be offered ursodeoxycholic acid, or UDCA. Made from a naturally occurring bile acid, this medication seems to work in two important ways. Firstly, it protects the liver from the harmful chemicals in the bile. Secondly, it allows bile to be more easily processed by the body. The exact dose you'll be prescribed depends on how much you weigh, so doctors will monitor you regularly and make adjustments if needs be.

Evidence suggests that UDCA may help to extend the lifespan of many people with PBC, and delay the need for liver transplantation. The aim of treatment is to improve liver blood tests results so that doctors are confident of preventing further damage to the liver.

In some people, UDCA may not work and/or they may not be able to tolerate it, due to side effects. These include diarrhoea, thinning of the hair, nausea and vomiting. A recently introduced medication called obeticholic acid (OCALIVA), which helps to reduce the build-up of bile and increase the flow of bile acids out of the liver, is now being used along with UDCA, or on its own if patients can't tolerate UDCA, to help these people. It was the first new drug officially approved for patients with PBC in many years, and a sign that there is real hope in the future that patients will have more choices for their treatments. Doctors can tell whether UDCA on its own is working or not by looking at a patient's ALP levels. For example, if they are not reduced to around 200 after one year of UDCA treatment, doctors may decide to add obeticholic acid to a treatment plan. Therefore, it's worth knowing what your ALP 'value' is when starting UDCA and ensuring it is monitored after one year and at regular intervals thereafter to see whether additional medication is needed.

A number of other medicines are also now being tried and your medical team may ask whether you'd like to take part in clinical trials to help. Inclusion in the trials would be on the basis of ALP not being sufficiently reduced after a year of treatment with UDCA - again, it's important for both patients and doctors to know what their UDCA response has been for any of these options to be available. (Please note you are not under any obligation to take part in clinical trials and your care won't be affected if you choose not to.)

At present, a liver transplant is the only option for people who have advanced PBC, but, pleasingly with better treatment approaches, including earlier and more prompt diagnosis as well as increased use of medicines such as UDCA and obeticholic acid, rates of transplant are falling.

How do I know if I need a liver transplant?

A liver transplant is usually only recommended if other treatments are no longer helpful and there is a risk to life from end-stage liver disease. Liver transplantation is a major operation and you will need to plan it carefully with your medical team, family and friends. However, liver transplantation has an excellent rate of success, and works very well for the few people with PBC who need a new liver. It is possible that PBC will return in your new liver, but it may take up to 15 years before damage from the disease becomes significant. Fatigue does not get better after transplant, so patients must be aware of this.

Taking care of yourself

PBC affects everyone differently. Some people with PBC experience very few problems, while for others PBC may have a major impact on daily life, with symptoms such as itchy skin being unpleasant to live with.

If your liver has become damaged it can have a broader impact on your health.

For example:

- it may reduce your body's ability to digest food properly, including fats
- you may feel lacking in energy, tired all the time or extreme fatigue
- you may find you're very sensitive to alcohol and some medications.

Diet

A healthy, well-balanced diet is good for everyone, but is even more important if you have a liver condition. This means eating plenty of fruit and vegetables (at least five portions a day), lean protein (such as chicken, fish, beans and lentils), healthy fats such as those found in nuts, avocado and oily fish, and slow-release carbohydrate foods. Choose wholemeal bread, rice and pasta, which are also higher in fibre than the refined (white) versions. Cut down on sugary drinks, processed foods such as cakes, biscuits and crisps, and save high calorie foods such as chocolate for treats only.

Some people with cirrhosis may need to eat a special diet. If you have any questions about what you should (or shouldn't) eat or drink, talk to your GP, who can refer you to a registered dietician.

You should also see a registered dietician if you have:

- fluid building up in your abdomen (ascites) or leg (oedema)
- mental slowness or confusion (encephalopathy)
- diarrhoea where the stools are pale, bulky and difficult to flush away (steatorrhoea).

Alcohol

Alcohol is something many of us enjoy in the UK, and for most people, drinking alcohol in moderation causes no problems. However, alcohol is a toxin, which is cleared from the body by the liver. If your liver is damaged it may mean that you have difficulty coping with alcohol and some people with PBC may find they can no longer drink it. Others find they can tolerate a little bit every now and again.

Current Government guidelines for UK adults recommend drinking no more than 14 units of alcohol a week, spread over seven days, with two or three consecutive alcohol-free days to give your liver a chance to recover. **For people living with liver disease, be sure to speak to your doctor about alcohol use, so you get personal advice; alcohol can be dangerous, depending on the nature of your liver condition and your general health**. If your liver disease is still in the early stages, your doctor may advise that it's OK to drink in moderation, perhaps on a special occasion.

Be careful with medicines

Talk to your doctor before taking medication for advice on the safest option that puts the liver under the least amount of stress (most medicines are processed by the liver). For example, it's better to take paracetamol (but never more than four 500mg tablets in any day) rather than aspirin or ibuprofen for day-to-day aches and pains.

Thinning bones (osteoporosis)

As we get older, our bones can lose density – that is, they become thinner and weaker. This is more common among women, especially after the menopause. PBC may make this worse but there are things you can do to preserve and build bone strength, such as weight-bearing exercise and including the right things in your diet. Weight-bearing exercise is any activity that increases bone strength by putting your bones under a healthy amount of stress, such as running or high intensity aerobics.

A good diet for bone health is one that includes lots of calcium (dairy products, broccoli and almonds are all high in this essential mineral) and ensuring you get enough vitamin D, which helps the body absorb calcium more efficiently. Sometimes, despite your best efforts, you may need to take medication to protect your bones. You may be advised to take calcium supplements, or a type of bisphosphonate, which is a class of drug that helps to prevent loss of bone density. Hormone replacement therapy (HRT) may also help. Bone density loss can be detected with a special type of scan called a densitometry X-ray (DXA). Your doctor can advise on whether you would benefit from this.

Higher risk of bleeding

Some patients with advanced PBC may be more at risk of bleeding because their liver is less able to make the chemicals needed to clot blood. This means that before treatment you need to tell people such as your dentist that you have PBC so they can take special care (albeit this largely only applies to people with advanced PBC).

Complementary and alternative medicines

Many complementary and alternative medicines are available that claim to ease the symptoms of liver disease. At present, healthcare professionals are not clear on the role and place of some therapies in managing liver disease and more research needs to be done. Discuss the use of these therapies with your doctor if you're thinking about using them.

Useful words

ALP – alkaline phosphatase, an enzyme found in certain membranes of the liver. Increases in ALP and another liver enzyme called Gamma GT (GGT) can indicate obstructive or cholestatic liver disease, where bile is not properly transported from the liver because of obstruction (blockage) of the bile duct.

Autoimmune – a type of disease causing the body's immune system to attack another part of the body.

Bile – a yellow/green fluid made by the liver to help digest foods containing fat and cholesterol.

Cholestasis – a condition where the flow of bile from the liver is reduced.

Chronic – an illness that lasts a long time (more than six months; possibly a lifetime).

Cirrhosis – where inflammation and fibrosis have spread to disrupt the shape and function of the liver. Even with no signs or symptoms of liver disease, the working capacity of liver cells has been badly impaired and they are unable to repair the liver. This is usually permanent cell damage and can lead to liver failure or liver cancer.

Encephalopathy – disturbed brain function leading to mental confusion and memory loss. Encephalopathy can follow the development of cirrhosis, for example.

Inflammation – the first response of the immune system to infection, commonly characterised by heat, swelling, pain and tenderness.

Immunoglobulins – also known as Ig, these are large proteins that act as antibodies found in body fluids and cell tissues. They will bind to invading organisms, such as bacteria or viruses, to destroy them.

Steatorrhoea – diarrhoea where the stools (faeces) are pale, bulky and difficult to flush away. This is caused by problems with digesting fat in the diet.

Useful resources

PBC Foundation (UK)

54 Queen St

Edinburgh EH2 3NS

Tel: 0131 225 8586

Email: info@pbcfoundation.org.uk

Web: pbcfoundation.org.uk

The PBC Foundation (UK) Ltd is a charity offering support and information to those living with PBC, and their families and friends.

Royal Osteoporosis Society

Camerton

Bath BA2 0PJ

Tel: 0808 800 0035

Email: info@theros.org.uk

Web: theros.org.uk

The Royal Osteoporosis Society is a national charity dedicated to improving the prevention, diagnosis, and treatment of this condition.

Organ Donation NHS UK

Organ donor line: 0300 123 23 23

Tel: 0117 975 7575

Email: enquiries@nhsbt.nhs.uk

Web: organdonation.nhs.uk

Part of NHS Blood and Transplant and the official NHS transplant site. It provides news, information and resources about organ transplantation, real life stories from those who have benefited from transplants and a facility for potential donors to sign on to the organ donor register.

Special thanks

Professor Gideon Hirschfield, consultant hepatologist with a special interest in PBC, Toronto Centre for Liver Disease, Canada

Dr Imran Patanwala, consultant hepatologist, Royal Liverpool University Hospital

Loo How, lay reviewer living with PBC.

Further information

The British Liver Trust publishes a large range of leaflets about the liver and liver conditions, written for the general public.

Leaflets that you may find particularly helpful include:

- *Cirrhosis of the liver*
- *Diet and liver disease*
- *Liver disease tests explained*
- *Liver transplantation*
- *Life after liver transplant*
- *Living with liver disease.*

We hope you have found this publication helpful

All our publications are reviewed by medical experts and people living with liver disease. If you have any feedback on this publication please email the Trust at info@britishlivertrust.org.uk.

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