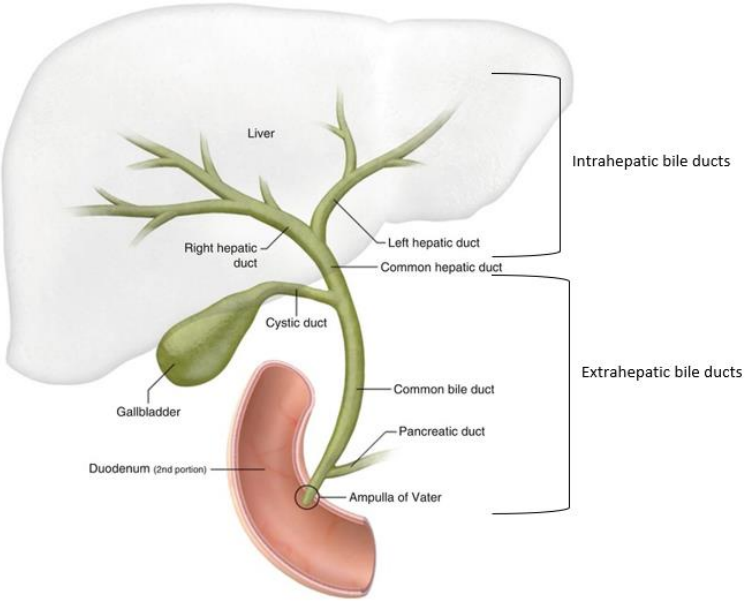
Information about

Primary Sclerosing Cholangitis

What is primary sclerosing cholangitis or PSC?

Primary sclerosing cholangitis (PSC) is a rare liver condition that causes chronic inflammation ('cholangitis') and scarring ('sclerosing') of the bile ducts. The resulting narrowing ('stricture') of the bile ducts interferes with the flow of bile and can lead to symptoms. Over time, PSC may develop into chronic liver disease and cirrhosis, with scarring that spreads throughout the liver. Not everyone with PSC will necessarily develop cirrhosis or complications.



What is bile and what are bile ducts?

Bile is a yellow-green fluid produced in the liver and stored in the gallbladder. It contains various products, including bile salts, bilirubin, toxins, enzymes and cholesterol, as well as waste products that are broken down within the liver. Bile flows from the bile ducts within the liver (intrahepatic ducts) to bile ducts that exit the liver (extrahepatic ducts), which then drain into the small intestine. Bile helps with digesting fat and absorbing fatty acids and certain vitamins. It also helps with excreting waste products from the body. If bile flow is blocked because of narrowed bile ducts, this can lead to the symptoms seen in PSC. Bile ducts (and any strictures) can be seen using various imaging techniques, such as ultrasound and MRI, as well as on a liver biopsy.

What causes PSC?

The exact cause of PSC remains to be determined. Research has suggested that it might be associated with the immune system, about 22 different genes, gut bacteria and other medical conditions, such as inflammatory bowel disease (IBD, which includes ulcerative colitis and Crohn's disease) and autoimmune hepatitis. PSC can be diagnosed at any age, including in childhood, but, on average, people are about 40 years old when they're diagnosed. It is twice as common in men as in women. First-degree relatives of someone with PSC have a slightly increased risk of also having it (around 1% absolute risk).

How is PSC diagnosed?

Tests that lead to a diagnosis of PSC include:

1. **Blood tests related to liver function**

   Elevated levels of the enzyme alkaline phosphatase (ALP) and, in some cases, bilirubin

2. **MRCP (magnetic resonance cholangiopancreatography)**

   This is a specialised imaging test that is done to look for bile duct strictures (narrowing)

3. **Liver biopsy**

   A biopsy may occasionally be needed to diagnose PSC.

PSC is often diagnosed in a patient with IBD who has no symptoms but has elevated liver function test results in their routine blood tests.

After a diagnosis of PSC is confirmed, a colonoscopy is recommended to check if the patient has IBD, if this has not already been diagnosed. Other tests may include a

Fibroscan, which is a bedside test similar to an ultrasound, to assess liver stiffness (from scarring and inflammation).

What are the symptoms of PSC?

Many people with PSC have no symptoms. Symptoms may develop or progress slowly and include itchy skin, fatigue and jaundice (yellowing of the skin). Some people may develop abdominal (belly) pain with fevers or chills, which suggests an underlying infection.

What are bile duct strictures and what is cholangitis?

Bile duct strictures are where intrahepatic or extrahepatic ducts have narrowed because of chronic inflammation and scarring. This is important in PSC because bile duct strictures can lead to blockage of the bile fluid and stop bile acids and toxins from being excreted from the body. Jaundice with abdominal pain and fevers may indicate that this has caused an infection (known as 'cholangitis') that needs antibiotic treatment. In some cases, a procedure called 'ERCP' (endoscopic retrograde cholangiopancreatography) may be needed to relieve the blockage.

What are the different types of PSC?

The most common type of PSC is large-duct PSC, which affects the intrahepatic and/or extrahepatic ducts. Large-duct PSC is often just referred to as PSC. About 10% of patients have another type, called 'small-duct PSC'. This affects only the smallest bile ducts in the liver, which cannot be seen on MRCP but can be seen on a liver biopsy. About 25% of patients with small-duct PSC may progress to large-duct PSC over time.

Other medical conditions associated with PSC:

- autoimmune hepatitis with PSC overlap (about 10% of patients)
- IgG4 sclerosing cholangitis (a different condition that mimics PSC)
- IBD – about 70 to 80% of patients with PSC will have or develop IBD; this is most often the type known as ulcerative colitis and less often Crohn's disease.

What are the treatment options for PSC?

Unfortunately, there are no medications that can be used to slow the progression of PSC. However, ursodeoxycholic acid (UDCA) is a bile acid medication sometimes used for people with PSC as it has been shown to lower levels of liver enzymes (ALP), which is thought to lead to a better prognosis. Your doctor can talk to you about whether this is a suitable option for you to consider.

Oral medications like colestyramine and rifampicin can help relieve itchiness. PSC may come with an increased risk of osteopenia and osteoporosis (low bone density), so you may be screened with a bone density (DEXA) scan and given vitamin D supplements.

Liver transplantation may be recommended for people with advanced liver disease caused by PSC. This is a successful treatment option for people with advanced PSC who are medically fit to receive a liver transplant. There is a small risk of the disease coming back after a successful liver transplantation.

Clinical trials of possible new therapies are running around the world, including in Australia, and your treating specialist may recommend you enrol in one of these.

What are the treatment options for complications of advanced liver disease?

Some people with PSC may develop advanced liver disease and cirrhosis. The scarring involved in cirrhosis often causes portal hypertension, which is an increase in blood pressure in the blood vessels within and around the liver. Portal hypertension can lead to other health problems, including hepatic encephalopathy (confusion or an altered state of consciousness because of a build-up of toxins) and bleeding caused by varices (abnormally dilated blood vessels).

Lactulose (to promote regular bowel motions) and rifaximin (an antibiotic) are used to treat hepatic encephalopathy. An endoscopy is needed to check your oesophagus (food pipe) and stomach for varices. Medications (beta-blockers, such as propranolol or carvedilol) are often prescribed to help lower portal hypertension and minimise the risk of bleeding from varices.

I have PSC – am I at risk for cancer?

Unfortunately, people with PSC are at increased risk of developing cancer. The most common type of cancer in people with PSC is cholangiocarcinoma (cancer of the bile ducts). The absolute risk of someone with PSC developing cholangiocarcinoma is uncertain but is up to about 9% over 10 years. Your specialist may perform yearly screening using MRCP, although this is not a proven screening strategy.

The risk of bowel cancer is also higher in patients with both PSC and IBD, and you may need to have surveillance colonoscopies every 1 to 2 years to prevent this.

As there is a slightly increased risk (up to 5% risk) of gall bladder cancer in people with PSC, an annual ultrasound scan of the gallbladder is recommended. Your doctor may suggest having your gall bladder removed if any abnormality is seen on ultrasound.

What is my prognosis?

The prognosis will differ among patients with PSC and depends on the type of PSC they have (e.g. people with small duct-PSC have a better prognosis). Many people with PSC lead normal lives. Reducing or normalising levels of ALP and bilirubin is associated with a better prognosis. If you have a low Fibroscan reading, you also likely have a better prognosis.

Patients who do go on to have complications, such as advanced liver disease or cancer, do so at an average of 10 to 20 years after diagnosis, but all patients need lifelong follow-up by a liver specialist.

General advice to all patients is to follow a healthy lifestyle, with a good diet and regular exercise. Try to limit your alcohol consumption. Some people experience anxiety or depression from having a chronic medical condition, and it is important to look after your mental wellbeing on a regular basis. There are support groups who can help with further information:

PSC Support Australia: www.pscsupport.org.au

PSC Support UK: www.pscsupport.org.uk

Acknowledgements

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