Children's Liver Disease Foundation

fighting childhood liver disease

Progressive Familial Intrahepatic Cholestasis (PFIC)

A Guide

An overview of PFIC, including the causes, diagnosis, symptoms, complications and treatment

This information has been written for:

- parents/carers of children and young people with PFIC

Others who may also find this information useful:

- young people with PFIC
- healthcare professionals who would like to find out more about the condition

It provides information on:

- causes
- diagnosis
- types of PFIC
- symptoms
- possible complications
- treatment

You may also find it helpful to read the following CLDF leaflets:

- Introduction to Liver Disease
- Pruritus
- Portal Hypertension and Ascites
- Nutrition
- Liver Transplantation

Use this QR code to view our resources

Key facts about PFIC

1. Progressive familial intrahepatic cholestasis (PFIC) is the name given to a group of conditions in which a digestive fluid, called bile, is not released properly from the liver.
2. PFIC is rare and affects around 1 in 50,000 to 1 in 100,000 people.
3. PFIC is a genetic condition. This means it is caused by changes (mutations) in a person's genes.
4. PFIC is usually diagnosed in infants and toddlers, but a diagnosis can take time.
5. Blood tests, scans and biopsies may be used to help with diagnosis.
6. There are different types of PFIC with different levels of severity.
7. The main symptoms of PFIC are itching (pruritus) and yellowing of the whites of the eyes and skin (jaundice).
8. Currently there is no cure for PFIC. However, dietary support, medicines and surgery can reduce the symptoms and complications.
9. Many children with PFIC will need a liver transplant at some point in their life.
10. Support services for children and young people with PFIC and their families are available from Children's Liver Disease Foundation.

How to say it:

Progressive	familial	intrahepatic	cholestasis
pruh-GREH-siv	fuh-MIH-lee-ul	IN-truh-heh-PA-tik	koh-leh-STAY-sis

What is progressive familial intrahepatic cholestasis?

Progressive familial intrahepatic cholestasis (PFIC) is the name given to a group of conditions in which a digestive fluid, called bile, is not released properly from the liver into the gut (gastrointestinal tract).

When the flow of bile reduces or stops, it builds up inside the liver. This is called cholestasis.

Cholestasis can damage the liver. The liver cells can start to die and are replaced with scar tissue (fibrosis). This may eventually lead to severe scarring of the liver, known as cirrhosis.

PFIC is a rare condition which affects around 1 in 50,000 to 1 in 100,000 people. It affects both males and females.

What is bile and why is it important?

Bile is a green/yellow liquid made by the liver. The colour is due to bilirubin, a natural waste product made when old red blood cells break down in the spleen.

Bile is made up of:

- bile acids (which help to digest fat)
- bilirubin (a natural waste product)
- cholesterol (a type of fat made in the liver)

- other fats
- water
- other waste products

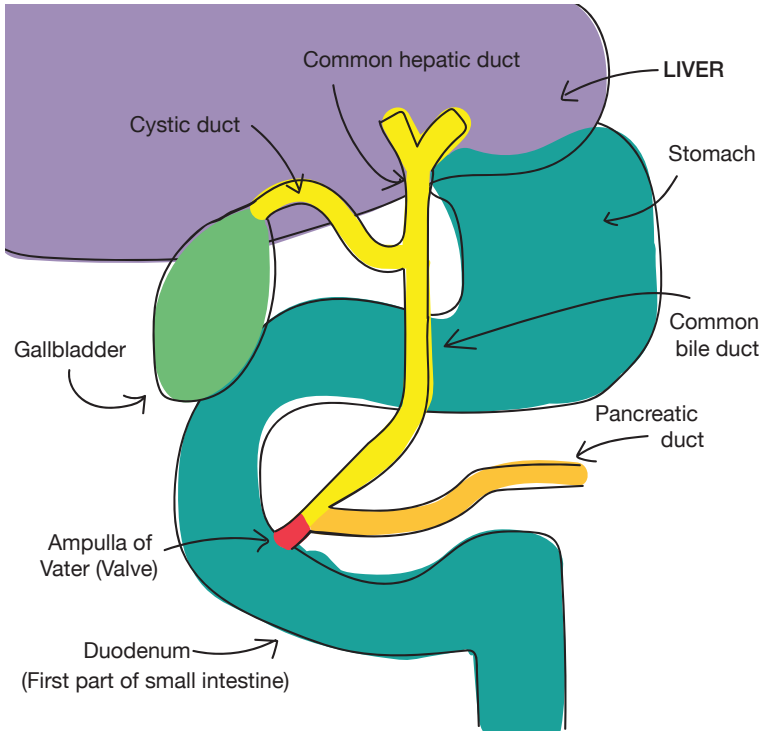

Figure 1: The bile duct system or 'biliary tree'

Bile is made by the liver and stored in the gallbladder. When you eat food, the gallbladder releases bile through the bile ducts. It moves into a part of the small intestine called the duodenum. The bile helps your body break down food and remove waste products.

Bile has several important jobs:

- It helps the body digest food by breaking down fats
- It helps the body absorb vitamins A, D, E & K
- It helps the body get rid of waste products such as bilirubin and leftover cholesterol. Both pass out in the poo (stool).

PFIC happens when there are problems in the system which makes and releases bile. Retention of bile in the liver or bile ducts causes waste products to remain in the body. This damages liver cells.

What causes PFIC?

PFIC is a genetic condition. This means it is caused by changes (mutations) in a person's genes.

Genes are sections of DNA that contain the instructions for making proteins. These proteins are the building blocks for everything in the body. They control how it grows and works.

Many of us will have some changes in our genes. Usually, these do not have any impact. Sometimes, however, these changes can cause diseases and other problems.

There are different types of PFIC. Each type is caused by changes in a different gene.

What are the chances of a child inheriting PFIC from their parents?

PFIC usually only happens when both parents are carriers of the change (mutation) that causes PFIC.

A carrier of the condition has one copy of the mutated gene. They do not have the disease themselves and will probably not know they are at risk of passing on the mutated gene. This is why conditions like PFIC can come 'out of the blue' for families. It is only when a child receives two mutated genes (one from each parent) that they develop the disease.

Getting a diagnosis of PFIC2 left us with feelings of guilt, knowing that she had inherited this from us. With time, those feelings lessened.

- Parent

If both parents are carriers, the chance of a child receiving a mutated gene from both parents (and therefore having PFIC) is one in four (25%). If the child only receives one copy of the mutated gene, they won't have PFIC, but will be a carrier. This pattern is called "autosomal recessive" and is shown in figure 2.

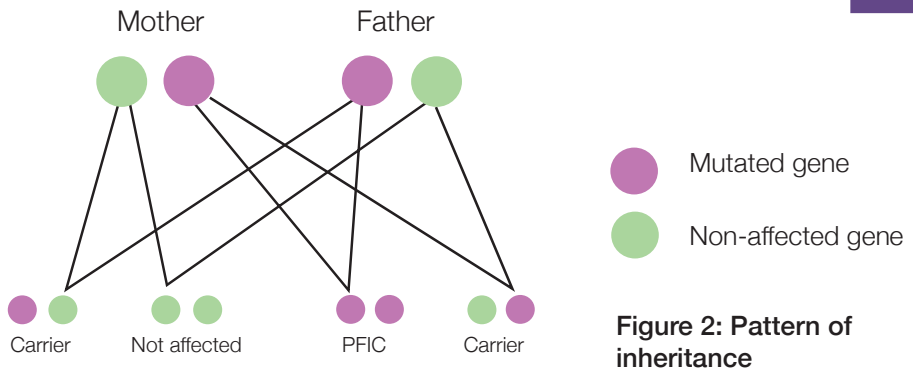

Figure 2: Pattern of inheritance

How is PFIC diagnosed?

PFIC is usually diagnosed in infants and toddlers. It can take time for a PFIC diagnosis to be made because the condition is rare and your child may need different tests.

Tests used to help diagnose PFIC:

Liver blood tests (also known as liver function tests/LFTs)

To do these tests, a blood sample will be taken and tested in a laboratory. They are a common way of seeing if the liver is injured and how well it is working. The tests are also used to monitor liver disease over time. They can help to see if the liver is getting healthier, getting worse or staying the same.

One particularly useful test is gamma GT (GGT). This measures the amount of an enzyme called gamma-glutamyl transferase (GGT) in the blood. The results can help find out which type of PFIC your child has.

Find more information in CLDF's leaflet: An Introduction to Liver Disease.

Bile acid tests

These are blood and urine tests which measure the level of bile acids in the body. Children with PFIC usually have much higher levels of bile acids than normal.

Genetic tests

These are special blood tests used to find changes (mutations) in a child's DNA. Blood will be taken from the child and both parents, if possible.

Ultrasound scans

An ultrasound scan uses sound waves to create a picture of the inside of the body. It may be used to check and monitor:

- The size and texture of the liver
- The size of the spleen
- The blood flow into and out of the liver
- The gallbladder, bile ducts and the flow of bile

Bone X-rays

A bone X-ray uses a type of radiation to create a picture of the bones inside the body. It may be used to look for the early stages of bone weakness (rickets). This can be caused by a lack of vitamin D in the body (vitamin D deficiency) due to PFIC.

Liver biopsy

During this test a very thin needle is inserted through the tummy (abdominal) wall and into the liver. The needle takes a small sample of liver tissue. This is sent to a laboratory to be studied under a microscope.

The biopsy results may help with the PFIC diagnosis. They can also help find out if your child is responding to medical treatment.

Magnetic resonance imaging (MRI)/ magnetic resonance cholangiopancreatography (MRCP)

These scans use strong magnets and radio waves to make pictures of the internal organs. The results may be used to help with the PFIC diagnosis. They can also help plan treatments and monitor liver disease over time.

Radionuclide (isotope) scan

This type of scan uses a small amount of a radioactive chemical called an isotope to make pictures of parts of the body. A small amount of the isotope will be injected into a vein, and this will travel in the bloodstream to the liver, bile ducts and gallbladder. The isotope is detected and imaged using a special scanner called a gamma camera.

The first year after diagnosis was about finding our "new normal". We adapted and realised our daughter was still our beautiful baby girl. She taught us so much about what is important in life.

- Parent

What are the different types of PFIC?

There are three main types of PFIC:

- F1C1 deficiency (previously known as PFIC1)
- BSEP deficiency (previously known as PFIC2)
- MDR3 deficiency (previously known as PFIC3)

Other types of PFIC are also being discovered as we learn more about the gene mutations.

Each type of PFIC is caused by a change (mutation) in a different gene. These changes can be more or less severe in different children. This leads to differences in the disease, its severity, symptoms and the treatments available.

F1C1 deficiency

This type is caused by changes (mutations) in the ATP8B1 gene, which leads to a shortage of the FIC1 protein.

F1C1 deficiency has been divided into:

- PFIC
- benign recurrent intrahepatic cholestasis (BRIC)

PFIC and BRIC are the same condition, but they have different levels of severity.

BSEP deficiency

BSEP deficiency is the most common type of PFIC. It is caused by changes (mutations) in the ABCB11 gene. This gene tells the body to make a protein called the bile salt export pump (BSEP). Changes in this gene cause bile acids to build up in liver cells. This leads to liver damage.

MDR3 deficiency

MDR3 deficiency is caused by changes (mutations) in the ABCB4 gene. This gene tells the body to make a protein which moves fats across the outer layer (membrane) of cells. When there is a change in this gene, bile acids can build up outside the liver cells. This can cause damage to the bile ducts and liver.

Other types of PFIC

Doctors have identified other types of PFIC, but they are very rare:

- TJP2 deficiency
- FXR deficiency
- MY05B deficiency
- USP53 deficiency
- FXR deficiency

Researchers think they will be able to identify more genetic causes of PFIC as testing gets better.

What are the symptoms of PFIC?

Symptoms in children with PFIC often begin in infancy or early childhood. The severity of symptoms will vary from child to child and will depend on the type of PFIC they have.

Itching (pruritus)

One of the serious effects of PFIC is itching (pruritus). The level of itch can vary from child to child. It can range from being mild to being very disruptive and causing severe discomfort.

Itching is usually felt all over the body. It often most severely affects the palms of the hands, the soles of the feet and the upper part of the body (the trunk). The itching may come and go in phases or in different seasons.

I remember the itch felt like it was under the skin. Having to scratch myself felt like a reflex and I just couldn't ignore it. It was worse at night because I had nothing to distract me.

- Child

Severe itching can lead to:

- skin damage (due to scratching)
- disturbed sleep
- fatigue (tiredness)
- irritability
- poor attention
- loss of appetite
- feeling sick (nausea)
- being sick (vomiting)

Find more information in CLDF's leaflet: Pruritus. This gives details of the treatments available and includes advice from other parents on how to deal with severe itching.

Jaundice

This happens when bilirubin trapped in the liver passes back into the bloodstream. It moves around the body and causes yellowing of the whites of the eyes (sclera) and skin.

I used to be jaundiced some days and I even came up with a yellow superhero called Banana Girl to describe myself!

- Child

Darker wee (urine)

A type of bilirubin called conjugated bilirubin passes out in the wee (urine) and can make it appear darker than normal.

Staining or darkening of teeth

This can happen when jaundice is present while the teeth are forming and growing. It can also be caused by the high calorie diet and/or medicines used to manage PFIC.

Pale, smelly, greasy poo (stools)

Poo (stools) will often be watery and loose (diarrhoea). They may float in the toilet and be more difficult to flush away. This is because they contain more undigested fat. This is due to less bile flowing from the liver into the intestine.

Faltering growth (also known as failure to thrive)

This refers to poor weight gain and slower growth. In PFIC this can be caused by a lower absorption of fats and other important nutrients.

Lack of vitamins in the body (vitamin deficiencies)

The vitamins A, D, E and K need good fat absorption to be taken into the body. In PFIC, fat absorption is poor, leading to a lack of these vitamins. This can cause problems, because the vitamins each play an important role in the body.

Enlarged liver (hepatomegaly)

This is a larger than normal swelling of the liver. It may cause tummy (abdominal) discomfort or lead to your child “feeling full”.

Enlarged spleen (splenomegaly)

This is a larger than normal swelling of the spleen. It may happen as a result of a condition called portal hypertension. It can cause tummy (abdominal) discomfort or lead to your child “feeling full”.

Gallstones (cholelithiasis)

These are small stones that form in the gallbladder or bile ducts. In most cases gallstones are present but cause no problems. However, if a stone blocks a bile duct this can cause severe pain and jaundice. Gallstones also increase the risk of infection in the bile ducts (cholangitis).

What are the possible complications of PFIC?

In children with PFIC, there are some possible complications. Bile trapped in the liver may cause damage that gets worse over time. This can cause the liver to become stiff and scarred (fibrosis). It may also lead to severe scarring, known as cirrhosis. The effects of severe scarring (cirrhosis) of the liver include:

Portal hypertension

When damage happens inside the liver, it stiffens. This makes it more difficult for blood to flow through it. This can cause high pressure in the portal vein. This is the blood vessel that carries blood from many organs in the tummy (abdomen) to the liver. This pressure is known as portal hypertension.

Portal hypertension can make the spleen get bigger. It can also cause swollen blood vessels in the food pipe (oesophageal varices). These blood vessels have thin walls and may bleed. This may cause your child to vomit blood or pass black tarry poo (stools). Both symptoms need urgent medical attention.

Portal hypertension can also cause fluid to build up in the tummy (abdomen). This is known as ascites.

Find more information in CLDF's leaflet: Portal Hypertension and Ascites.

Fluid in the tummy (abdomen) (ascites)

Ascites is the term for a build-up of fluid in the tummy (abdomen). It is caused by:

- increased pressure in some of the blood vessels.
- the reduced ability of the liver to make an important protein called albumin.

The main symptom of ascites is swelling of the tummy (abdomen).

Find more information in CLDF's leaflet: Portal Hypertension and Ascites.

Liver failure

Liver failure happens when large parts of the liver become damaged and scarred. The liver can no longer do its job and is said to be failing. This is a late stage of liver disease.

Increased risk of liver cancer

All types of liver disease increase the risk of liver cancer, but the risk is particularly raised in BSEP deficiency.

To help spot any problems at an early stage, your child will be offered screening for a type of liver cancer known as hepatocellular carcinoma.

How is PFIC treated?

There is no cure for PFIC. However, dietary support and medicines can help reduce the symptoms and complications. Surgery may also be an option in a small number of cases.

The medical team will recommend treatments. These may differ from child to child depending on the severity of the symptoms.

Dietary support

Children who have liver disease are likely to need extra calories and nutrition. Eating and drinking normally doesn't always provide this. Extra support for your child may include:

- **MCT (medium chain triglyceride) formulas and diets**
  MCT is a type of fat. It is more easily absorbed and is a good source of energy. Your child's dietitian will prescribe special milk formulas and supplements containing MCT. They will also provide a list of suitable foods for older children.

- **Fat soluble vitamins (vitamins A, D, E and K)**
  These vitamins are usually given by mouth (orally). In some cases, they have to be given by injection.

- **Nasogastric feeding**
  Nasogastric feeding may be used if your child needs more calories or is not growing well. This involves passing a very thin, soft tube up the nose, down the back of the throat and into the stomach. A special milk formula will be given overnight using a pump. Parents/carers can be taught how to do this at home.

I was petrified of needing an NG tube for feeding but was really well supported when that day came. It gave her the energy to enjoy things again.

- Parent

Find more information in CLDF's leaflet: Nutrition.

Medicines

The choice of medication for children with PFIC will depend on the PFIC type and the severity. The main purpose of the medicines is to reduce symptoms. In particular, doctors try to reduce the severe itching (pruritus). Medicines are also used to try and help slow down the disease.

- **Ileal bile acid transporter (IBAT) inhibitors**
  This type of drug works by blocking a protein called the ileal bile acid transporter (IBAT). This protein is present in the intestines and transports bile acids back into the liver. By blocking the protein, the drug reduces the amount of bile acids that build up in the liver. Clinical trials show that this may help limit liver damage and reduce pruritus (itching).

I used to love some of my medications when I was little. I used to give it to myself from when I was a baby. I actually miss the taste of some of them now!

- Child

- **Cholestyramine**
  This drug mixes with bile acids in the small intestine. It then stops them being reabsorbed into the blood stream. In some cases, it may help to reduce itching (pruritus), but the results vary. It will not be given at the same time as vitamin supplements as it can stop them being absorbed properly.

- **Ursodeoxycholic acid**
  This is a bile salt that occurs naturally in small amounts in bile. Taking it as a medicine can help improve bile flow out of the liver. This can reduce jaundice and/or itching (pruritus) and can help improve liver function. It has been found to be particularly useful in MDR3 deficiency.

- **Rifampicin**
  This is an antibiotic used to treat various conditions. It is not licensed to treat itch (pruritus) but is often used by liver doctors to help with this symptom. It is used very carefully in severe liver disease because it can cause a rise in liver function tests. Rifampicin is a red colour and it can make wee (urine), spit (saliva) and tears turn orange/red. This side-effect is harmless.

Other medicines which have been used to treat itch (pruritus) in some children include:

- Phenobarbital
- Naltrexone
- Ondansetron

Some medicines in PFIC are used “off-label”. This means they were developed for other diseases, but sometimes work in PFIC. The response to off-label medicines can vary. There is currently no strong evidence to show that they are effective in children with PFIC.

Potential operations

Not all children and young people respond well to dietary support and medicines. Sometimes they do not give enough relief from itching (pruritus). In a small number of children, the medical team may consider surgery. They will carefully assess your child’s condition before recommending any of these operations. Not all operations will be suitable for all children.

- **Partial external biliary diversion (PEBD)**
  This is only suitable for children who do not have advanced liver disease. During the operation, the surgeon opens the end of the gallbladder. They bring it out through the skin to form an opening known as a stoma. This sits on the surface of the tummy (abdomen). Your child would need to wear a bag over the stoma to collect bile. In some cases, the surgeon uses a short section of small intestine to connect the gallbladder to the surface of the tummy (abdomen).

- **Partial internal biliary diversion (PIBD)**
  During this operation the surgeon connects the gallbladder to the large intestine. This is done using a piece of small intestine. There is no need for a bag on the outside of the body.

- **Ileal exclusion (IE)**
  During this operation the surgeon creates a bypass around a part of the bowel called the distal ileum. The aim is to reduce the amount of bile salts re-entering the bloodstream. There is no need for a bag on the outside of the body.

Liver transplant

Many children with PFIC will need a liver transplant at some point in their life. This may be during childhood or when they are an adult. This is because the treatments available may only give some relief from symptoms. They are not a cure and can only slow down liver disease.

A liver transplant is an operation to remove a liver that does not work. It is replaced with a healthy liver from another person (donor). Children with PFIC may receive a whole, split or reduced liver from a deceased donor. It is also possible that they may receive part of a liver from a living donor.

A successful liver transplant will help a child survive when the liver is failing. It will also significantly improve a child's quality of life. It is currently the only definitive treatment for PFIC.

It is important to remember that a liver transplant is a major operation. It will only be done after the benefits and risks have been carefully weighed up. Following a successful liver transplant children will need lifelong medication and follow up.

The year before transplant was tough but we never felt alone and the incredible medical team around our child literally carried us through.

- Parent

Find more information in CLDF's leaflet: Liver Transplantation.

Useful resources

Glossary of liver terms

Many medical terms may be used by those caring for children and young people with liver disease. Follow this QR code for a list of terms.

Other CLDF resources

CLDF produces a wide range of information for children and young people up to the age of 25 with liver disease, their families and the healthcare professionals who look after them.

Information can be downloaded or ordered from:
Website: **www.childliverdisease.org**
Email: **info@childliverdisease.org**
Tel: **0121 212 3839**
Follow this QR code to see our resources.

Information from other organisations

Genetic Alliance UK
www.geneticalliance.org.uk
A national charity providing support for people with genetic, rare and undiagnosed conditions.

PFIC Advocacy and Research Network
www.pfic.org
A US-based charity run by PFIC patients and families. They aim to improve the lives of those affected by PFIC through support, education, advocacy and research.

Rare Disease UK
www.raredisease.org.uk
A national campaign for people living with rare conditions.

How we produce information

Our information resources are written, edited and reviewed with the help of medical experts and families living with liver disease.

Thanks

We would like to thank staff at each of the specialist paediatric liver centres: Birmingham Children's Hospital, King's College Hospital and Leeds Children's Hospital. We would also like to thank the families who helped us produce this information.

PIF TICK accreditation

We have gained PIF TICK accreditation for our information production process. Follow this QR code for more details.

Disclaimer

This resource provides general information but does not replace medical advice. It is important to contact the medical team if you have any worries or concerns.

Feedback and information sources

Your feedback is important to us and will help us improve our information. To provide feedback, or for more information on how it was developed, email info@childliverdisease.org.

This leaflet was reviewed in March 2024

It is due to be reviewed by March 2027

Notes

Children's Liver Disease Foundation

Children's Liver Disease Foundation (CLDF) is the UK's leading organisation dedicated to fighting all childhood liver diseases.

CLDF provides information and support services to young people up to the age of 25 with liver conditions and their families and is a voice for everyone affected.

CLDF is here for you, whether you want to talk, meet and share with others, or just belong to a group which cares, knows what it's like and is fighting to make a difference.

Are you a young person up to the age of 25?

Contact the Young People's Team:

Phone: 0121 212 6024 **Email:** youngpeople@childliverdisease.org

Are you the parent or carer of a child or young person with a liver condition?

Contact the Families Team:

Phone: 0121 212 6023 **Email:** families@childliverdisease.org

Would you like to help us support the fight against childhood liver disease? Please help us to continue to support children, young people and families now and in the future.

Contact the Fundraising Team:

Email: fundraising@childliverdisease.org

Tel: 0121 212 3839
Email: info@childliverdisease.org
Website: www.childliverdisease.org

Registered Charity Number: 298858
Charity registered in Scotland: SC042140

Trusted Information Creator
Patient Information Forum

Children's Liver Disease Foundation
fighting childhood liver disease