LIVER UK

The new name for the British Liver Trust and Children's Liver Disease Foundation

Alagille syndrome

Help, support and guidance for children and families

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Contents

Welcome

Welcome to your guide to understanding Alagille syndrome. It provides information on causes, diagnosis, symptoms, treatment and living with Alagille syndrome.

This information has been written for:
Parents and carers of children and young people with Alagille syndrome

Others who may also find this information useful:

- young people with Alagille syndrome
- adults with Alagille syndrome
- healthcare professionals

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

- Introduction to liver disease
- Pruritus
- Portal hypertension and ascites
- Nutrition
- Liver transplantation

Use this QR code to view our resources or visit **liveruk.org/alagille-syndrome**

How to say it:
Alagille syndrome
A-luh-JEEL
SIN-drome

Key facts about Alagille syndrome

1. Alagille syndrome is a rare genetic condition.
2. It mainly affects the liver, but can also affect other parts of the body.
3. It happens in around 1 in 30,000 to 1 in 50,000 births.
4. Some children have a mild form of the condition. Other children have a more severe form and may be very unwell early in life.
5. Tests may include blood tests, scans and biopsies.
6. Liver symptoms may include itching, yellow bumps on the skin, jaundice, pale poo, dark wee and faltering growth.
7. Treatments include dietary support and medicines.
8. A liver transplant will only be considered if your child has cirrhosis, liver failure or severe symptoms that cannot be controlled.
9. A small number of people are diagnosed as adults.

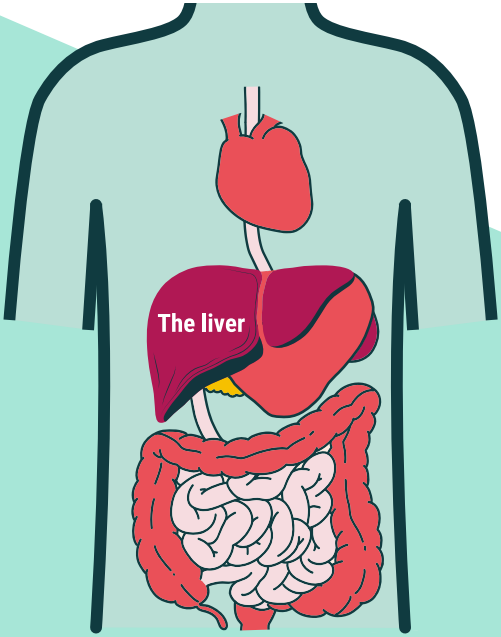
About the liver

The liver is one of the most important organs in the body. It is on the right side of the tummy, just under the ribs. It works like the body's factory and carries out hundreds of important jobs every day.

The liver is a dark reddish-brown colour.

It is divided into two main sections called "lobes". There is a right lobe and left lobe. The right lobe is a bit bigger.

The liver is joined up to some important arteries and veins that bring blood into and out of the liver.



The liver has over 500 jobs. These include:

- digesting food
- producing and storing energy
- storing vitamins, iron and other nutrients
- fighting infections
- breaking down toxins and other harmful substances
- helping you heal

About Alagille syndrome

Most people have never heard of Alagille syndrome unless someone in their family has been affected by it. This section explains what Alagille syndrome is, what causes it, and how it may affect your child.

What is Alagille syndrome?

Alagille syndrome (ALGS) is a rare genetic condition. It mainly affects the liver, but can also affect other parts of the body, including the heart, kidneys, eyes, face, skeleton and blood vessels.

Alagille syndrome happens in around 1 in 30,000 to 1 in 50,000 births. It is usually diagnosed early in life and affects boys and girls in equal numbers.

Some children have a mild form of the condition. They may have few symptoms or no symptoms at all. They may even reach adulthood without knowing they have the condition.

Other children have a more severe form and may be very unwell early in life. Sometimes the complications can even be life threatening.

What causes Alagille syndrome?

Alagille syndrome is a genetic condition. This means it happens because of a change in a person's genes.

Genes are like instructions in the body that tell it how to grow and work. They help make proteins, which are the building blocks for our body.
Many people have changes in their genes and most of the time these changes don't cause any problems. But in Alagille syndrome, the change can affect the body and cause health issues.

In Alagille syndrome, more than 9 out of 10 people have a change in a gene called JAG1. A small number of people have a change in a gene called NOTCH2.

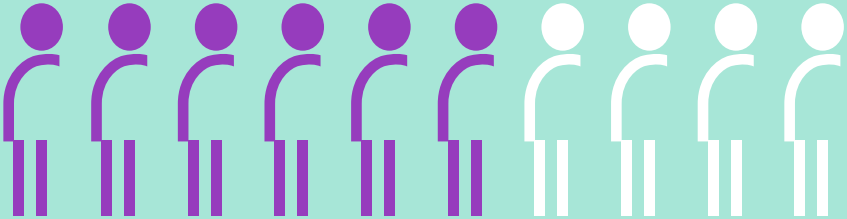
The JAG1 and NOTCH2 genes affect many parts of the body. These genes can change in different ways, which is why Alagille syndrome:

- can be mild in some children and more serious in others
- can affect many different parts of the body

In every 10 people with Alagille syndrome, 9 will have a change in the JAG1 gene

Sometimes we can easily see how a gene change happens, but in Alagille syndrome it's less clear. About 4 out of 10 people inherit the gene change from one parent. About 6 out of 10 people have a change that happens randomly and is said to be "sporadic". This means it is not inherited and happens for unknown reasons.

In every 10 people with Alagille syndrome



6 people will have a sporadic gene change

4 people will have a gene change passed down from one parent

How is Alagille syndrome diagnosed?

If your child shows signs of Alagille syndrome, doctors will do different tests to help confirm the diagnosis. But a diagnosis can be difficult in young babies because the condition looks similar to other types of liver disease.

The tests needed will be different for each child. They may include:

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

A blood sample will be taken and tested in a laboratory. This is a common way to check if the liver is damaged and how well it works. The tests also monitor liver disease over time. They show if your child's liver is getting healthier, getting worse or staying the same.

Ultrasound scans

Ultrasound scans use sound waves to make pictures of the inside of the body. They help check and monitor:

- the size and texture of your child's liver
- the size of your child's spleen
- blood flow to and from your child's liver
- your child's gallbladder and bile ducts
- the size and shape of your child's kidneys

Liver stiffness measurements

The medical team use special scans to check the amount of stiffness in your child's liver. Healthy liver tissue is soft, so stiffness shows that damage has occurred. You may hear this type of scan called a FibroScan or transient elastography.

Genetic tests

Special blood tests will check for changes in your child's DNA. In Alagille syndrome, doctors look for changes in the JAG1 or

NOTCH2 genes. Family members may also be offered genetic testing.

Liver biopsy

Liver biopsies are not always needed, but may be used if there is doubt around the diagnosis. During a liver biopsy a very thin needle goes through the tummy wall and into the liver. The needle collects a small sample of liver tissue. This is sent to a laboratory to be studied under a microscope.

X-rays

An X-ray uses radiation to take a picture of the bones in the body. In Alagille syndrome, it looks for changes in the bones of your child's spine.

Heart tests

An echocardiogram is a type of ultrasound that uses sound waves to make pictures of the heart. It looks at the structure of the heart and blood flow through the heart. It also looks for heart murmurs, which are extra sounds in the heartbeat.

Eye tests

Doctors check for eye problems with a special lamp called a slit lamp. This is a microscope with a bright light that helps the doctor see inside your child's eyes.

Cholangiography

A cholangiogram is an X-ray that uses a special dye to show the bile ducts. It is usually done during surgery when your child is asleep. This test checks for blockages in bile ducts outside the liver. Doctors may use a cholangiogram if a diagnosis in your child is not clear or if genetic test results aren't ready. It can also help rule out other liver conditions.

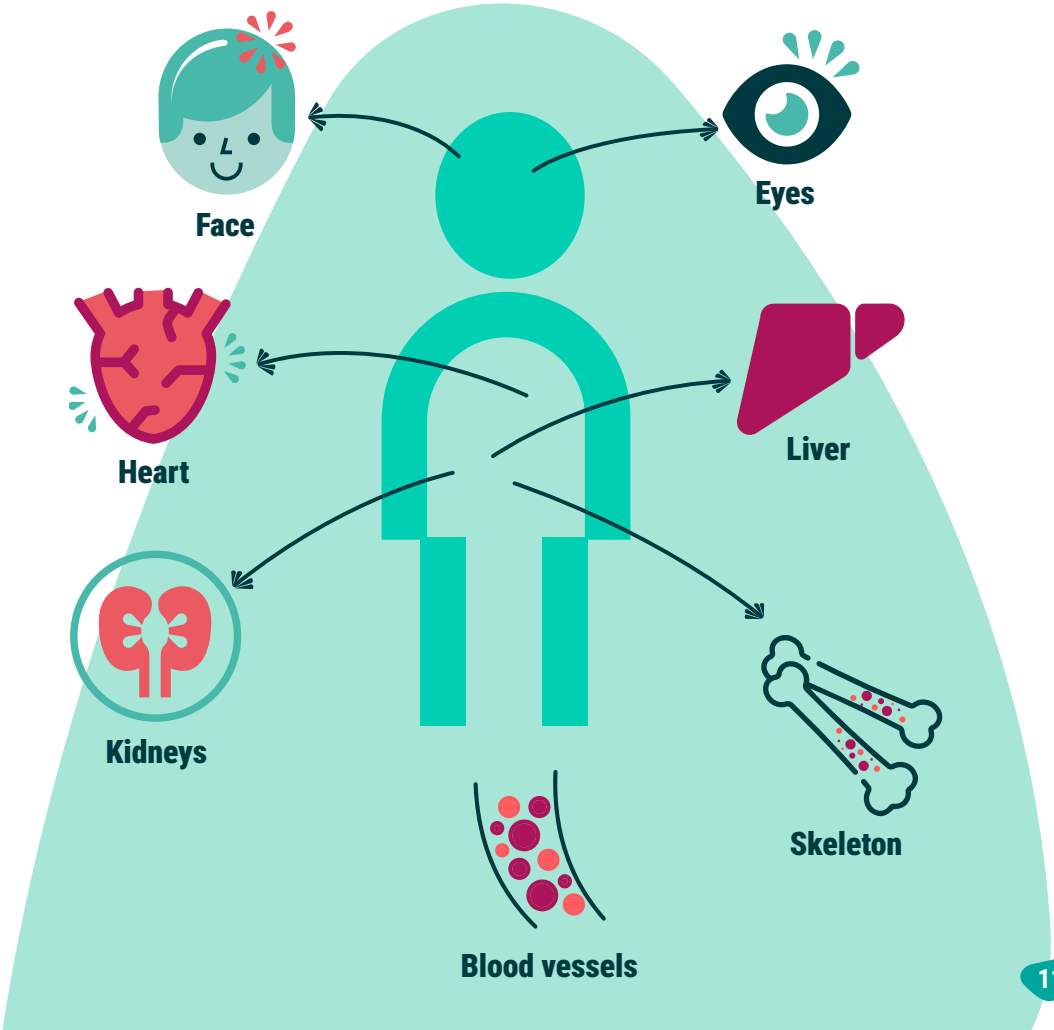
Magnetic resonance imaging (MRI) / magnetic resonance angiography (MRA)

These tests use strong magnets and radio waves to create images of the body. They can only be used when children are old enough to sit very still. In Alagille syndrome, they help doctors see the blood vessels in the head.

What are the features of Alagille syndrome?

Alagille syndrome is different for every child. Even two members of the same family can have very different experiences of it. Some children have lots of symptoms, while others have only a few – or none at all.

The main parts of the body that can be affected by Alagille syndrome are the liver, heart, kidneys, eyes, face, skeleton and blood vessels.



Liver problems

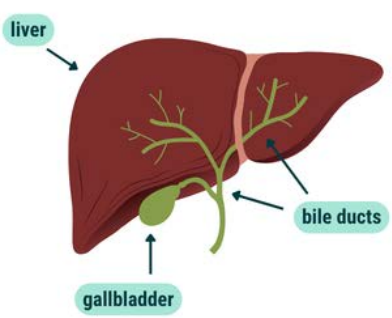
Liver problems are common in children with Alagille syndrome and are often the first sign of the condition. In Alagille syndrome, the liver has fewer bile ducts than normal.

Bile ducts are tiny tubes that carry bile from the liver to the gallbladder and small intestine. When there are fewer bile ducts, bile can build up in the liver. This is called cholestasis. It usually starts in the first three months of life.

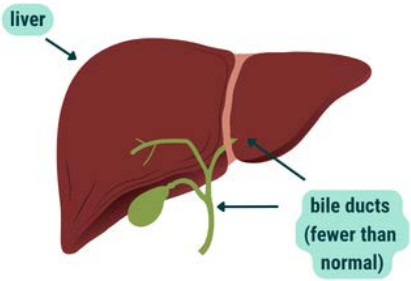
Some children have mild cholestasis and do not have major problems. In other children, cholestasis can be more severe, causing symptoms, complications and damage to the liver over time.

Not every child with Alagille syndrome will have liver problems. However, most will face liver issues at some point in their life.

In some children, liver problems get better on their own between the ages of four and ten - but this doesn't happen for everyone. Unfortunately, doctors can't predict which children will get better, get worse or stay the same.



Normal liver and bile ducts



Bile ducts in Alagille syndrome

Facial features

Children and adults with Alagille syndrome often share similar facial features, including:

- a high, broad forehead
- deep-set, widely spaced eyes
- a small, pointed chin

These features do not make people look unusual. They are simply common among those with Alagille syndrome. These features often become more noticeable as children get older.

Heart problems

Heart problems are common in Alagille syndrome, with most children having some type of heart issue. They range from issues that cause no harm to serious problems that affect the structure and function of the heart. In some children, heart problems can be very serious.

The most common heart problems include:

- Pulmonary artery stenosis: narrowing of the pulmonary artery, which carries blood from the heart to the lungs. Sometimes the only sign is a heart murmur (an extra sound in the heartbeat).
- Tetralogy of Fallot (TOF): a condition where four different problems affect how the heart works.
- Atrial septal defect: a small hole between the two upper chambers of the heart.
- Ventricular septal defect: a small hole between the two lower chambers of the heart.
- Coarctation of the aorta: narrowing of the aorta, the largest artery in the body.

"The first 2 years were really hard after diagnosis but it does get better" - Parent

Eye problems

Alagille syndrome can affect different parts of the eye, including the cornea, iris and retina. One common change is called posterior embryotoxon. This means there is a thicker ring around the clear, front part of the eye. It happens when the eye forms a little differently before birth. Eye differences in Alagille syndrome usually don't affect vision.

Bone and skeletal problems

In Alagille syndrome, the bones of the spine may look a bit different on X-rays. Sometimes they have a small notch or a "butterfly-like" shape. These changes usually don't cause any problems.

Children with Alagille syndrome may have weaker bones, which means they can break more easily. Bone growth can also be affected. Some of these problems are due to Alagille syndrome. Others are caused by problems with nutrition and low levels of vitamin D.

Children with Alagille syndrome are often smaller in height and weight and they are likely to stay smaller as they grow.

Kidney problems

Some children with Alagille syndrome have kidney problems. Their kidneys might be smaller than normal or shaped differently. Sometimes they don't develop properly, or they contain cysts. There can also be problems with how their kidneys work.

Blood vessel problems

Alagille syndrome can affect blood vessels in different parts of the body, including the brain, liver, lungs, heart and kidneys. When blood vessels in the brain are affected, it can cause:

- bleeding in the brain (intracranial bleeding or stroke)
- narrowing of the main blood vessel to the brain (moyamoya disease)

• bulges in blood vessels (aneurysms)

Other problems

Some children with Alagille syndrome also have:

• problems with their pancreas
• delays in reaching development milestones
• trouble with memory, concentration and problem solving

Your healthcare team

Alagille syndrome can affect many parts of the body. This means your child may see different healthcare professionals, such as:

• liver doctors (hepatologists)
• heart doctors (cardiologists)
• kidney doctors (nephrologists)
• eye doctors (ophthalmologists)
• a genetics expert (geneticist)
• specialist nurses
• radiologists
• surgeons
• dietitians

What liver symptoms affect children with Alagille syndrome?

Liver symptoms are different for each child with Alagille syndrome. Some children have no liver problems and others have only mild symptoms. Sadly, some children face more severe liver issues with serious symptoms and complications.

Liver symptoms may include:

Itching (pruritus)

This is a serious symptom of Alagille syndrome that happens when bile salts build up in the body. It often starts in the first two years of life.

The level of itch is different for each child. In some children, the itch is mild, but for others it causes severe discomfort and can have a huge impact on their quality of life.

Itching is usually felt all over the body, but it can come and go in phases or in different seasons. Problems from severe itching may include:

Use this QR code to view our leaflet on pruritus or visit **liveruk.org/pruritus**

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

Itching can be very hard for families to manage.

See our leaflet on pruritus for more information and links to support services.

Xanthomas

Xanthomas are yellow bumps on the skin caused by fats that build up beneath the surface. They are usually found around joints like the elbows, knees and knuckles. In some children, xanthomas spread across the body, and they may hurt or change how the skin looks. The appearance can be upsetting for some children.

Jaundice

This is when the whites of the eyes and the skin turn yellow. It happens when bilirubin trapped in the liver passes back into the bloodstream.

Pale poo

Bile gives normal poo its dark colour. If there is less bile flow, this can result in pale poo.

Darker wee

A type of bilirubin called conjugated bilirubin passes out in the wee. This can make it look darker than normal.

Faltering growth

Children with Alagille syndrome often struggle to absorb fats and nutrients from food. This can make gaining weight more difficult, and they may grow more slowly than other children. Some children have a poor appetite or struggle with feelings of hunger.

What are the possible liver complications?

When bile gets trapped in the liver, it can damage the liver over time. It can lead to stiffness and scarring, known as fibrosis. It can also lead to severe scarring, known as cirrhosis. This damage can happen in childhood or later in adulthood.

The effects of severe scarring of the liver may include:

Portal hypertension, varices and ascites

When the liver is damaged, it becomes stiff. This stiffness makes it harder for blood to flow through the liver. It causes high pressure in the vein which carries blood from organs in the tummy to the liver. This is called portal hypertension. Portal hypertension can cause several problems:

- the spleen can get bigger
- swollen blood vessels can form in the food pipe
- fluid may build up in the tummy (called ascites)

Liver failure

Liver failure happens when large parts of the liver become damaged and scarred. The liver can't work properly and is said to be failing. This is a late stage of liver disease.

Doctors find it hard to predict who will get liver failure and if this will happen during childhood or later in life.

Use this QR code to view our leaflet on portal hypertension or visit **liveruk.org/portal-hypertension-children**

How are liver problems treated?

There is no cure for Alagille syndrome, but dietary support, medicines and other treatments can help manage liver symptoms and complications. Each child may need a different set of treatments.

Poor bile flow from the liver (cholestasis) is usually worst in the first few years of life. It may improve as your child grows and symptoms like itching and yellow skin patches may improve. But this isn't the case for every child.

Alagille syndrome can be serious, especially if treatments don't work. But it is hard for doctors to predict whose liver disease will respond to treatment.

Your child will be closely monitored with regular clinic appointments, blood tests and scans.

Dietary support

Children with Alagille syndrome often need extra calories and nutrition because normal eating and drinking aren't enough.

Extra support from the medical team may include:

MCT formulas and diets

Medium chain triglycerides (MCT) are types of fat that are easier to absorb and provide good amounts of energy. Your child's dietitian will recommend special milk formulas and MCT supplements. They will also offer a list of suitable foods if your child is older.

Fat-soluble vitamins (vitamins A, D, E and K)

Children with Alagille syndrome may have trouble absorbing vitamins A, D, E and K from food. If your child needs extra vitamins, they are usually given as tablets. If the tablets don't work well, they can be given as injections.

Nasogastric feeding

If your child needs more calories or isn't growing well, they may need extra nutrition through a tube. This means placing a thin, soft tube up their nose and into their stomach. The tube connects to a pump so your child can be fed a special milk formula, often overnight. Parents and carers are often taught how to do this at home.

For long-term feeding, the medical team may suggest a gastrostomy tube, which goes directly into the stomach through the tummy.

Liver medicines

Medicines are used to try and improve bile flow and relieve symptoms. Doctors often focus on reducing severe itching because this can have such an impact on a child's daily life.

Some medicines for Alagille syndrome are used "off-label". This means they were made for other conditions, but can sometimes help in Alagille syndrome. Your child may need to try different medicines or combinations to see what works best. Sometimes, medicines only help for a short time. It's also important to remember that they may have side effects.

Medicines may include:

Urodeoxycholic acid (URSO)

URSO is a bile salt found naturally in small amounts in bile. Taking it as a medicine can help improve bile flow out of the liver. This may help reduce jaundice and itching.

Rifampicin

Rifampicin is not approved for Alagille syndrome, but liver doctors often use it to treat severe itching. It is red in colour and can turn wee, spit, tears and sweat orange/red. This side effect is harmless.

Cholestyramine

Cholestyramine mixes with bile acids in the small intestine and stops them going back into the bloodstream. In some children, this helps reduce itching. Your child should take this medicine at a different time of day to any vitamin supplements. Cholestyramine has an unusual taste and texture. If your child struggles to take it, ask your hospital team for advice.

Antihistamines

Antihistamines are sedatives that can help your child sleep if severe itching keeps them awake at night.

Ileal bile acid transporter (IBAT) inhibitors

IBAT inhibitors are medicines that block a protein called the ileal bile acid transporter (IBAT). This protein usually moves bile acids from the intestines back to the liver. By blocking it, IBAT inhibitors lower the amount of bile acid that builds up in the liver. Clinical trials suggest this may reduce itching, limit liver damage and reduce the need for a liver transplant.

IBAT inhibitors are only considered if other medicines don't work. Access to this type of medicine is only available through specialist services. Access may also be different around the UK. Talk to your medical team for more information.

Other medicines that may sometimes be used include:

- naltrexone
- odansetron
- SSRIs (selective serotonin reuptake inhibitors)

Surgical treatments

Surgical treatments have been used in the past to try and manage the severe symptoms of Alagille syndrome. The surgeries include:

- partial external biliary diversion (PEBD)
- partial internal biliary diversion (PIBD)
- ileal exclusion (IE)

These operations may be used in a small number of children, but are becoming less common. Doctors prefer to use medicines to manage symptoms wherever they can because surgeries are invasive and may not always work well. New medicines now provide alternative treatments for symptoms like itching and xanthomas.

Liver transplant

A liver transplant will only be considered if your child has one of the following:

- cirrhosis
- liver failure
- severe symptoms that lower their quality of life and cannot be managed with other treatments

A liver transplant is an operation to replace a damaged liver with a healthy one from a donor. Children may receive a whole, split or reduced liver from a deceased donor, or part of a liver from a living donor.

For children with Alagille syndrome, a liver transplant can be more complex because they may have other issues with the heart, kidneys or blood vessels.

A successful liver transplant can save a child's life and will greatly improve their quality of life. However, it is important to remember that a liver transplant is a major operation. It is only done after the benefits and risks have been carefully weighed up. Even after a successful transplant, children need lifelong medicines and regular follow-up appointments.

Use this QR code to view our leaflet on liver transplant or visit **liveruk.org/liver-transplant-children**

Alagille syndrome in adults

Alagille syndrome is usually diagnosed early in life, with most children treated in paediatric services.

Thanks to better treatments, many children grow up to be adults and move (transition) to adult health services. They keep having regular check-ups, blood tests and scans throughout their lives.

Some children with Alagille syndrome need a liver transplant before they become adults and others may need one later. After a liver transplant, they no longer have the liver problems caused by Alagille syndrome. But they still need care for other health issues linked with the condition. They also need to take medicines and have regular check-ups to keep their new liver healthy.

A small number of people are not diagnosed with Alagille syndrome until they are adults. This usually happens when there are no clear signs or symptoms during childhood. Adults may be diagnosed if they develop symptoms, or if they are tested for something else. A diagnosis can also happen if they have a child or family member with the condition and undergo genetic testing.

Adults are diagnosed and treated in a similar way to children. A team of specialists will check for issues with different parts of the body, including the liver, heart, eyes, kidneys, skeleton and blood vessels. Support and treatment for liver problems will depend on symptoms and complications and may include dietary support, medicines and surgery.

A small number of people are not diagnosed with Alagille syndrome until they are adults.

Useful resources

Useful websites

Liver UK
www.liveruk.org
Information and support for everyone living with a liver condition.

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

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

How Liver UK can help

A diagnosis of liver disease can be worrying, and you may have a lot of questions. The Liver UK Children's and Families team are here for you and for your family and friends.

Whether you have questions or just need someone to listen, we can help.

Find out how we can help you:
liveruk.org/support

Call our helpline to talk to one of our team: **0800 652 7330**

How we produce information

Feedback and information services

Your feedback is important to us and will help us improve our information. To provide feedback, email **patient-info@liveruk.org**

For more information on how our information was developed, visit our website: **www.liveruk.org**

Trusted Information Creator
Patient Information Forum

We have gained PIF TICK accreditation for our information production process.

Thanks

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Disclaimer
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www.liveruk.org/donate

Liver UK is the UK's leading charity dedicated to supporting adults, children and young people affected by liver disease or liver cancer. Our mission is to transform liver health by raising awareness, promoting prevention, and improving care and support for everyone affected.

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