

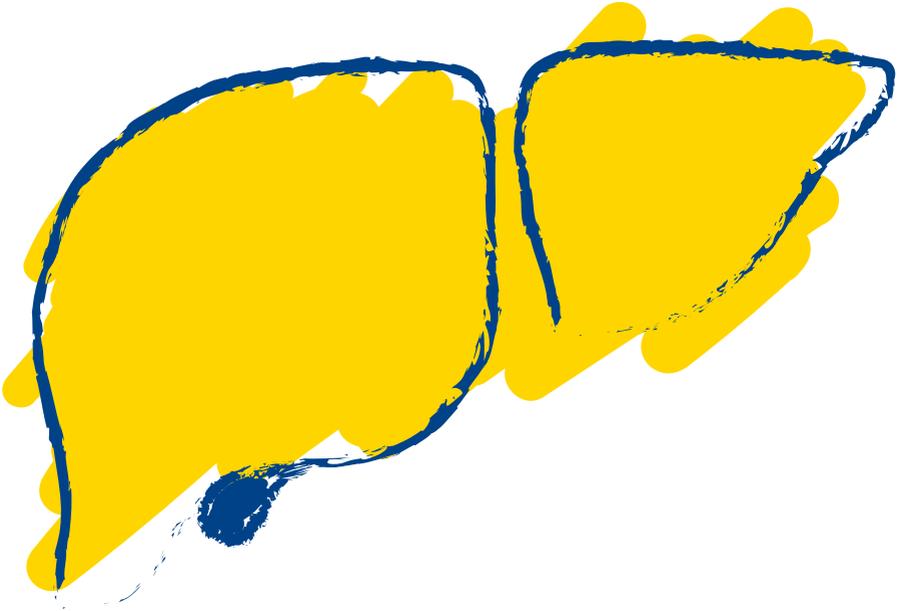


Children's Liver  
Disease Foundation

fighting childhood  
liver disease

# Alagille Syndrome

A Guide



An explanation of what Alagille syndrome is, its  
causes, diagnosis and treatment

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### **This information has primarily been written for:**

- Parents/carers of children with Alagille syndrome

### **Others may also find this information useful:**

- Young people with Alagille syndrome
- Healthcare professionals who would like to find out more about the condition

### **It provides information on:**

- What Alagille syndrome is
- Causes
- Diagnosis
- Treatment

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

- An Introduction to Liver Disease
- Pruritus (itch)
- Portal hypertension and ascites

## **What is Alagille syndrome?**

Alagille syndrome is a rare, genetic condition. It can affect different parts of the body including the liver, heart, kidneys, eyes, face and bones.

## How many children are affected by Alagille syndrome?

Alagille syndrome affects around one in every 30,000 live births.

## What are the features of Alagille syndrome?

There are many different ways Alagille syndrome can affect an individual. It differs from person to person and even two people in the same family with Alagille syndrome can have different features and symptoms.

Some people have a very mild form of the condition and reach adulthood without knowing they have Alagille syndrome. Others can be unwell as babies and may be diagnosed at a very young age.

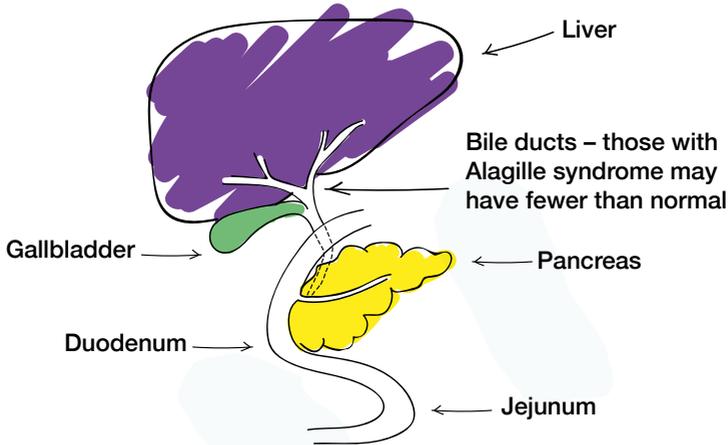
### **The features of Alagille syndrome include:**

#### **Liver abnormalities**

Individuals with Alagille syndrome may have fewer bile ducts than normal. This is known as bile duct paucity.

Bile ducts carry bile from the liver to the gall bladder and small intestine. When there are fewer ducts to carry the bile, the bile can get trapped in the liver and cause damage. This can lead to jaundice which is a yellowing of the skin and eyes.

## Diagram of the liver and surrounding organs



Liver damage can cause issues such as malabsorption (not properly absorbing fats and nutrients) which can lead to slower growth and development. It can also lead to the formation of harmless xanthomas which are fatty deposits underneath the skin which look like lumps.

### Facial features

Children and adults with Alagille syndrome often share physical features including a prominent forehead, deep-set eyes and a small chin. These features do not make children look abnormal, they are simply common across those with Alagille syndrome.

### Heart or blood vessel (cardiovascular) problems

In addition to liver disease, heart problems are one of the most common features of Alagille syndrome. There may be a narrowing of the pulmonary artery, a blood vessel that carries blood from the heart to the lungs.

This is called pulmonary artery stenosis. If it is mild there may be no symptoms and it may only be picked up due to a heart murmur which can be heard during a chest examination. More severe narrowing of the artery can lead to symptoms including shortness of breath and fatigue. There are treatments available which will be discussed with you by your medical team if necessary. Your child will be referred to a heart specialist for assessment and a treatment plan will be made if required.

### Eye abnormalities

An eye condition called posterior embryotoxon can occur in people with Alagille syndrome.

This occurs when the eye forms in a slightly different way than is usual. This does not affect vision and can only be seen when eyes are examined with a lamp called a slit lamp. Many people without Alagille syndrome will have this but it is more common in those with Alagille syndrome.

### Skeletal shape

An x-ray may show that bones in the spine are shaped abnormally.

This may be a simple notch or sometimes it appears as a 'butterfly-like' shape on the x-ray. This is only visible on an x-ray and does not cause any problems.

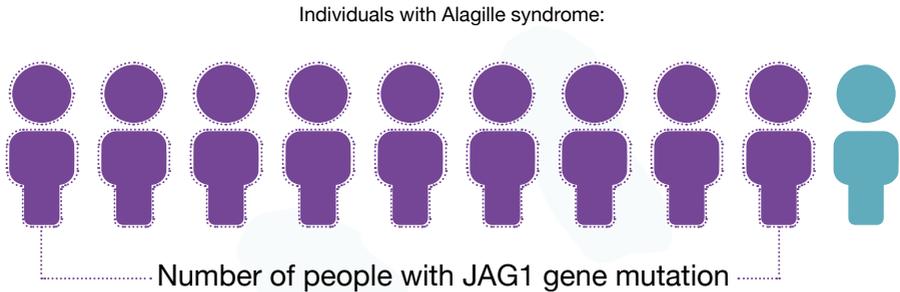
There are also other, less common features such as kidney problems.

## What causes Alagille syndrome?

Alagille syndrome is a genetic disease. Genes are made up of DNA and act as instructions for the body. Genes determine different features such as our hair colour and eye colour.

They also control how different parts of our body develop and function.

More than nine out of ten people with Alagille syndrome have a mutation (change) in a gene called JAG1.



A very small number have a mutation in a gene called NOTCH2. These genes are involved in many different systems in the body, which is why Alagille syndrome can have such a wide variety of effects. We have two copies of each gene in our body but only one of the NOTCH2 or JAG1 genes need to be affected to cause Alagille syndrome.

People can have different mutations in these genes and over 430 different forms of these genes have been identified. This explains why Alagille syndrome can have serious effects in some people and milder effects in others.

In around six out of ten people with Alagille syndrome, the mutation causing the disease is known as 'sporadic'. This means the gene hasn't been passed down from parents but is present for an unknown reason.

In around four out of ten cases, the gene which causes Alagille syndrome has been passed down from a parent to their child.

Individuals with Alagille syndrome:



## How is Alagille syndrome diagnosed?

If your child has some of the features of Alagille syndrome there are a number of tests which can be carried out to find out if Alagille syndrome is the cause.

### These tests include:

- Liver biopsy – to see whether there are fewer bile ducts than normal
- Blood tests – to check whether the liver is working properly
- Heart tests – to check for any heart abnormality or murmur
- Ultrasound of the abdomen
- Eye examination – to check for eye abnormalities
- X-ray – to look for changes in the bones of the spine

Diagnosis can be difficult in young babies because the condition can appear very similar to other forms of liver disease, such as biliary atresia.

## What are the effects of Alagille syndrome?

Although some individuals with Alagille syndrome won't have any issues with their livers, the majority will experience liver problems at some point in their lives.

The reduced number of bile ducts can mean bile doesn't easily flow from the liver to the bowel. This means the normal roles of the liver can be affected which causes different symptoms in different people. These can include:

### Jaundice

The level of jaundice can differ from person to person.

### Pale Stools (Poo)

Bile gives normal stools their dark colour. If there is less bile flow then this can result in pale stools.

### Poor absorption of nutrients

Bile contains substances that help the food to be broken down and digested. With less bile, nutrients and vitamins aren't absorbed properly from the gut. This can lead to slower growth and development, bone weakness and rickets.

### Pruritus (itch)

Bile carries bile salts out of the body in stools (poo). If there is less bile flow, bile salts build up in the body which can lead to itchiness. Itching can occur with or without jaundice being present.

To find out more CLDF has a separate leaflet on pruritus available.

### Xanthomas

These look like warts and are normally found around joints such as the elbows and knees. They are made of extra cholesterol which builds up under the skin. The liver is responsible for producing and removing cholesterol from the body but when it is damaged this doesn't work properly.

### Nose bleeds/bleeding gums

The liver plays an important role in producing and storing substances that control bleeding (e.g. vitamin K). If the liver is not working properly then bleeding is more likely.

The following are less common:

### Hepatomegaly and cirrhosis

Hepatomegaly means your child's liver is larger than usual. Cirrhosis is scarring in the liver. Both of these are signs that the liver is damaged.

When normal liver cells are replaced by scar tissue this can affect the blood pressure in the blood vessels in and around the liver. This is called portal hypertension.

To find out more see the CLDF leaflet on portal hypertension.

## Splenomegaly

Splenomegaly is an enlarged spleen. This can happen due to the increased blood pressure which occurs in portal hypertension.

If splenomegaly develops your child's medical team may advise your child to avoid sports where a hard direct blow to the abdomen could occur, e.g. martial arts.

## How is Alagille syndrome treated?

There is no cure for Alagille syndrome but there are treatments that can deal with the symptoms of the disease. The main treatments manage the liver problems which occur due to the reduced number of bile ducts in and around the liver.

Some of the more common ways to manage Alagille syndrome are detailed here. They include taking vitamin supplements and medications, assessing nutrition and, in rare cases, liver transplantation or other surgery.

### Vitamins

When the liver is damaged, some vitamins (A, D, E and K) may not be absorbed properly from the diet.

**Vitamin A** is needed for good eyesight, particularly to see in the dark and for the eyes to adapt to changing light conditions.

**Vitamin D** is needed for strong and healthy bones and teeth.

**Vitamin E** is needed for a healthy nervous system and the development of co-ordination.

**Vitamin K** is needed to make clotting factors that help control bleeding.

When the liver is damaged these vitamins may be given as supplements to make sure healthy levels are maintained. Usually these are given orally but sometimes they may need to be given by injection.

### Medication

A number of medications may be given to increase bile flow and reduce itching. It may be necessary to try a combination of different medicines to see what works best for your child. Sometimes these medications will only work for a short time.

Medications which could be prescribed include:

#### Ursodeoxycholic acid (Urso)

Urso is an artificial bile salt which also aims to increase bile flow, and therefore can help reduce itching.

#### Cholestyramine (Questran)

This medicine combines with bile acids in the small intestine and reduces their reabsorption. The medicine can also bind with fat-soluble vitamins (A, D, E and K) which can reduce their absorption, therefore some vitamins (and some medicines) shouldn't be taken within two hours of taking cholestyramine.

This medicine has an unusual taste and texture. If your child is having difficulty taking it then ask your hospital team for advice.

Questran can be given by mixing it well with liquids, but NOT with milk, to make a drink. For babies you will be advised to mix it with smaller quantities of liquid. For older children the dry powder can be mixed with foods such as fruit purées.

#### Rifampicin

Rifampicin is an antibiotic. Normally a low dose is given at the start of the treatment and is gradually increased to stop the itch. It can cause urine, saliva and tears to turn an orange-red colour.

### Naltrexone

Naltrexone is another medication which may be given to reduce the level of itch. Similarly to rifampicin, a low dose is normally given at the start of treatment and it is gradually increased to stop the itch.

### Sedatives

A sedative is a medication which can help your child to sleep. This may be given if the itch is affecting your child's sleep. Antihistamines such as chlorpheniramine (Piriton) and alimemazine act as sedatives and may be prescribed for use at night.

**Research is being carried out into Alagille syndrome including research into new drugs and treatments which may be available in the future.**

### Nutrition

A dietitian will assess your child's diet. Good bile flow is needed to break down the fat in milk and food. Babies and children who are jaundiced and do not have good bile flow are not able to absorb all the fat they eat. Therefore, children with Alagille syndrome may not gain weight as well as they should.

Babies with Alagille syndrome often need to be given special formula milk that contains a type of fat that is more easily absorbed. Breast feeding can continue but your child may also need a special formula feed. Older children may require extra calories that can be given in the form of high calorie drinks or powders. Your dietitian will advise on any necessary dietary changes and will give specific advice for your child.

Alagille syndrome can be associated with poor appetite and feeding problems. For these children special attention from the dietitian will be necessary. In some cases overnight feeding via a naso-gastric tube may be recommended.

### Liver transplant

Liver transplantation only needs to be considered for a small group of patients with Alagille syndrome. It may be required if there is severe liver disease causing cirrhosis or there are symptoms which cannot be controlled in other ways.

Liver transplantation for children with Alagille syndrome can be more complex than other liver transplants because children with Alagille syndrome may also have problems affecting the heart and/or the kidneys. This requires careful investigation and discussion in each case. A liver transplant will only be considered when it is absolutely necessary. There is plenty of support available if transplantation is considered. Your child's medical team will be there to answer any questions and CLDF's Families Team is here for you to support you through the process.

There is further information available from CLDF about liver transplantation.

### What's next?

Alagille syndrome can be a serious condition but many children and adults with Alagille syndrome respond well to treatment and lead normal, happy lives. Bile flow often improves as your child grows and develops. It's hard to predict whose liver disease will get worse over time and whose liver will respond to treatment.

Advances in understanding and treatments are constantly being made and CLDF is passionate about funding further research across all childhood liver diseases.

CLDF produces a wide variety of information resources for children and young people up to the age of 25 with liver disease, their families and the healthcare professionals who look after them. This information can be downloaded or ordered from CLDF's website [childliverdisease.org](http://childliverdisease.org).

For further enquiries regarding CLDF's information please contact the Information & Research Hub Manager by email at [irhm@childliverdisease.org](mailto:irhm@childliverdisease.org) or call 0121 212 6029.

### Thanks

The booklet has been written, edited and reviewed with the help of staff at each of the specialist paediatric liver centres: Birmingham Children's Hospital, King's College Hospital and Leeds Children's Hospital. Thank you to all the staff involved who have made the production of this leaflet possible.

### Disclaimer

This leaflet provides general information but does not replace medical advice. It is important to contact your/your child's medical team if you have any worries or concerns.

### Feedback and information sources

Information within this leaflet has been produced with input from the three specialist paediatric liver centres in the UK.

To provide feedback on this leaflet, or for more information on the content of this leaflet including references and how it was developed contact Children's Liver Disease Foundation: [info@childliverdisease.org](mailto:info@childliverdisease.org).

This leaflet was reviewed in September 2017. It is due to be reviewed by September 2020.

## What is Children's Liver Disease Foundation (CLDF)?

**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, funds vital research into childhood liver disease and is a voice for everyone affected.

**Are you a young person up to the age of 25 with a liver condition or a family member?** CLDF's Families and Young People's teams are here for you, whether you want to talk about issues affecting you, 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. You are not alone.

**If you are a parent/carer or family member then get in touch with CLDF's Families Team:**

**Phone:** 0121 212 6023 **Email:** [families@childliverdisease.org](mailto:families@childliverdisease.org)

**If you are a young person and want to find out more about CLDF's services you can contact CLDF's Young People's Team:**

**Phone:** 0121 212 6024 **Email:** [youngpeople@childliverdisease.org](mailto:youngpeople@childliverdisease.org)

CLDF have a dedicated Facebook page called HIVE/HIVE+ for 13 – 24 year olds with a liver disease/transplant to make new friends, connect and share stories [childliverdisease.org/young-people/hive](https://www.childliverdisease.org/young-people/hive)

**Would you like to help us support the fight against childhood liver disease?**

CLDF's work rely on voluntary donations. Please help us to continue to support children, young people and families now and in the future. To find out more about fundraising and how you can join the fight against childhood liver disease you can visit [www.childliverdisease.org/get-involved](http://www.childliverdisease.org/get-involved). Alternatively, you can email the Fundraising Team at [fundraising@childliverdisease.org](mailto:fundraising@childliverdisease.org) or call them on **0121 212 6022**.

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