The Impact of Alagille syndrome (ALGS)

About ALGS

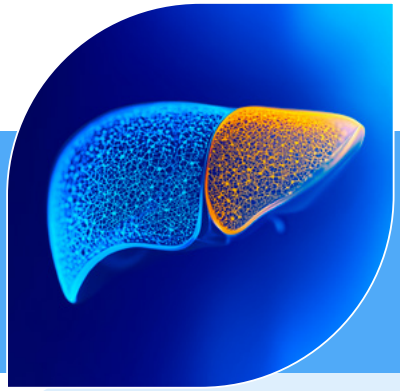
ALGS is an inherited rare genetic condition that can affect multiple organs in the body, including the liver, heart, brain, and eyes.[1]
It can cause severe and even life-threatening complications such as liver failure, heart defects, and bleeding or stroke due to blood vessel problems[2]

Up to **1 in 30,000 babies are born with ALGS** each year.[3] There is a 50% chance of a child inheriting ALGS if one parent has the condition[2]

Symptoms usually appear shortly after birth or in early infancy. For this reason, **ALGS is often diagnosed in children younger than one year of age** and can affect males and females of all races and geographic locations equally[2,4]

The liver is the most commonly affected organ in children with ALGS, where bile can build-up to dangerous levels.[5] In about half of these children, the flow of bile out of the liver improves by age five. In the other half, the build-up of bile gets worse and leads to complications[2]

This build-up in bile usually causes intolerable itching (pruritus) and is the most debilitating symptom for children living with ALGS.[6,7] Due to the impact on the quality of life, pruritus can be a reason for liver transplant[6]



40%

Only about 40% of children with ALGS will reach adulthood with their own (native) liver[3]

What happens in the liver?

- The liver uses cholesterol to make bile acids, which help digest fats and absorb vitamins[8]
- Bile acids are added to a liquid called bile, also made by the liver, which flows through bile ducts from the liver to the small intestine[8]
- Because bile acids don't reach the intestine as they should in children with ALGS, fats are not broken down and vitamins are not absorbed, leading to nutritional deficiencies and reduced growth[10]

Why is bile important, and why do we measure it?

95%

Up to 95% of children with ALGS have fewer than normal bile ducts.[9] This causes bile acids to build-up in the liver (cholestasis), which may cause symptoms like jaundice, pruritus, and long-term liver damage (cirrhosis)[1]

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Symptoms

ALGS doesn't affect everyone in the same way, but common symptoms include:[6]

- Yellowing of skin (jaundice)
- Pruritus
- Failure to thrive (impaired development or growth)
- Certain facial features e.g. deep-set eyes, broad forehead

Healthcare providers may observe the following:

- Swishing heartbeats (heart murmurs)
- Enlarged spleen
- Change in size or shape of blood vessels
- Spinal growth changes
- Decreased or impaired kidney function

One of the most debilitating symptoms is pruritus, which may be so severe that it leads to sleep and mood disturbances and can impact school and social activities[6,7]

What causes the itch?

When bile builds up in the liver and excess bile acids enter the bloodstream, they can irritate nerves near the skin and cause pruritus[13]

Pruritus typically arises within the first 6–14 months of an infant's life and impacts as many as 88% of children with ALGS, with up to 45% experiencing severe pruritus[6]

For some children, the itching is so intense they may scratch through their skin, and some may eventually require surgery, including liver transplant, for relief[6]

Diagnosis and treatment

It is important to diagnose ALGS early to begin a treatment plan. A pediatrician or general practitioner may recommend a care team of specialists, including hepatologists (liver specialists), cardiologists (heart specialists), nephrologists (kidney specialists), and/or ophthalmologists (eye specialists)

In ALGS, where treatment options are limited,[12] the choice of therapy is critical for optimizing patient outcomes and improving everyday life, addressing the diverse needs of children and their families impacted by the condition.

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The impact of ALGS

Families living with ALGS have reported a **negative impact** on **mental health** and **finances** as particularly significant challenges[14]

The *For Everybody Study*, conducted by the Alagille Syndrome Alliance in 2022 amongst families living with ALGS in the U.S., highlighted the following:

100%

of those living with ALGS, including caregivers, suffered from **post-traumatic stress disorder**[15]

75%

of those with ALGS experienced **anxiety**[15]

25%

of families experienced **financial issues** associated with an ALGS diagnosis, attributed to:[15]

- loss of working hours due to time off for hospital appointments
- the cost of traveling to appointments
- job loss to stay home to care for the child and medication costs

96%

Pruritus is not only debilitating for children with ALGS but can also negatively impact their caregivers. 96% of caregivers report **sleep disturbances** due to pruritus[14]

"It was very difficult — you have to manage during the day and then also deal with interrupted nights. Constantly waking up created real exhaustion for me as a mother and a caregiver."

– Celine, parent of Suzanne with ALGS

Looking to the future

The journey towards enhancing the diagnosis and management of ALGS relies on a multifaceted approach that integrates advancements in medical technology, innovation, research, healthcare professional and patient education, and multidisciplinary care. By fostering greater awareness among healthcare providers, leveraging cutting-edge genetic testing and providing comprehensive support to people living with ALGS and their families, we can strive to achieve earlier diagnosis, personalized treatment strategies, and improved outcomes for people living with ALGS.

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Why is bile important, and why do we measure it?

Bile and bile acids have a number of roles in digestion and waste removal:[8,11]

- Removes waste products like bilirubin (made when the body breaks down old red blood cells) and excess cholesterol from the liver
- Neutralizes the acidity of food coming from the stomach, which helps protect the intestine and allows digestion to continue properly
- Travels with food through the intestine to help absorb nutrients
- Helps digest fats, an important source of energy
- Helps absorb fat-soluble vitamins (A, D, E, and K) needed for vision, bone health, immunity, and blood clotting

As bile acids require a lot of energy to produce, when they reach the end of the intestine, most return to the liver to be reused.[8]

In ALGS, the build-up of bile in the liver can cause excess bile acids to enter and circulate in the blood. Measuring the blood serum for elevated bile acids can help to monitor disease severity and treatment efficacy.[12]

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