ALGS FACT SHEET

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UNDERSTANDING ALAGILLE SYNDROME

WHAT IS ALAGILLE SYNDROME?

- Alagille syndrome (ALGS) is an inherited rare genetic disorder that **can affect the liver, heart, brain, blood vessels and bones.**
- Liver damage may result from having fewer, narrowed or malformed bile ducts than normal in the liver which leads to build up of toxic bile acid levels, **which can cause scarring and progressive liver disease**. [1]
- **ALGS is genetic** disorder.
- **Between 30% to 50%** of cases pass to a child from an affected parent with the same diagnosis.[2]

WHAT CAUSES ALGS?

ALGS is caused by a problem with the **JAG1 gene** (usually a mutation in, but sometimes a deletion of it) which causes **more than 90%** of ALGS cases. In **2% to 3% of cases**, a mutation on the **NOTCH2 gene** causes ALGS. In around **3% of people** with ALGS, the genetic cause is not known.

The **JAG1 and NOTCH2 genes** give your cells instructions to make proteins that create a communication pathway between cells, so the cells know when to build certain parts of the body during fetal development. When there is a mutation on either of these genes or a deletion of genetic material on chromosome 20 that includes JAG1, your cells don't have the instructions they need to do their job, which **causes symptoms of the condition like structural heart defects, narrow bile ducts and skeletal abnormalities**.[2]

PREVALENCE, SIGNS & SYMPTOMS OF ALGS

ALGS occurs in about **one of every 50,000 live births**. The disorder affects males and females of all races and geographic locations equally.[3] Approximately 95% of patients with the condition present with chronic cholestasis, usually within the first three months of life, and **as many as 88%** also present with severe, intractable pruritus.[4,5] **Only about 40%** of children with ALGS will reach adulthood with their native liver.[6]

Signs and Symptoms of ALGS?[7,8]

- Severe itching (pruritus)
- Yellowing of the skin or eyes (jaundice)
- Eye abnormalities
- Swishing heartbeat (heart murmurs)
- Changes in size or shape of blood vessels
- Decreased or impaired kidney function
- Enlarged spleen

DIAGNOSIS OF ALGS

While an official diagnosis is confirmed through genetic testing[6], ALGS liver disease is often identified through a physical exam, blood test and ultrasound. A doctor will look for common characteristics including cholestasis, distinctive facial features (triangular or prominent forehead, deeply set eyes), butterfly vertebrae, eye anomalies, heart defects, kidney defects, itching, jaundice, and xanthomas (cholesterol deposits in the skin).

RESOURCES FOR MORE INFORMATION

- **Alagille Syndrome Alliance**
- **Children's Liver Disease Foundation**
- **Childhood Liver Disease Research Network**
- **National Organization for Rare Disorders**

REFERENCES: 1. U.S. Department of Health and Human Services. Alagille syndrome - about the disease. Genetic and Rare Diseases Information Center. https://rarediseases.info.nih.gov/diseases/804/alagille-syndrome **2.** Cleveland Clinic. Alagille Syndrome. https://my.clevelandclinic.org/health/diseases/23540-alagille-syndrome. **3.** American Liver Foundation. Alagille Syndrome. https://liverfoundation.org/liver-diseases/pediatric-liver-disease/alagille-syndrome **4.** Singh SP et al. Euroasian J Hepatogastroenterol, 2018 **5.** Feldman AG and Sokol RJ. Neoreviews 2013 **6.** Vandriel SM, et al. Natural History of Liver Disease in a Large International Cohort of Children with Alagille syndrome: Results from The GALA Study. Hepatology. 2022 Aug 29. doi: 10.1002/hep.32761. Epub ahead of print. PMID: 36036223. **7.** Hopkins Medicine; John Hopkins. Alagille Syndrome. https://www.hopkinsmedicine.org/health/conditions-and-diseases/alagille-syndrome **8.** Childhood Liver Disease Research Network. Alagille syndrome. https://childrennetwork.org/Clinical-Studies/Alagille-Syndrome

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