The Burden of Alagille Syndrome

What is Alagille syndrome?

Alagille syndrome (ALGS) is a rare autosomal dominant disease caused by mutations in the *JAG1* or *NOTCH2* genes[1]

- Approximately 70% of mutations occur *de novo* without being inherited[2]

ALGS affects approximately one in 50,000 children[a]

Key clinical features of ALGS include cholestasis, characteristic facial features, cardiovascular complications, vertebral abnormalities, and posterior embryotoxon[3]

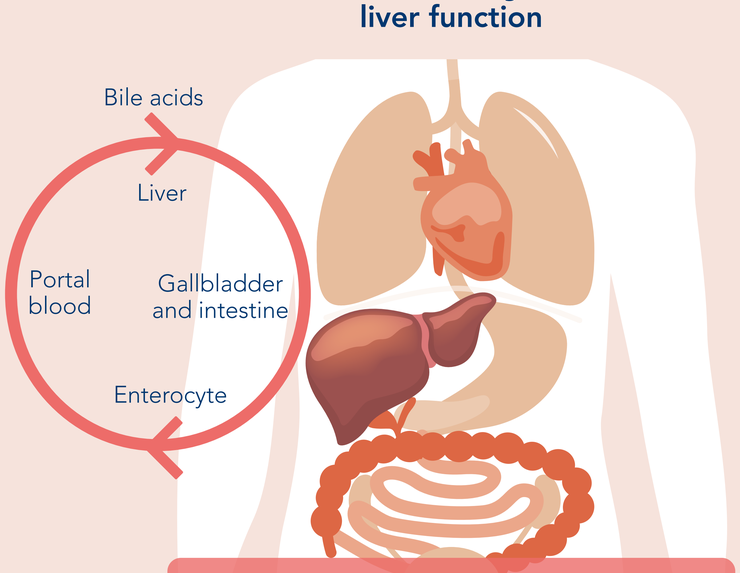
ALGS diagnosis may be complicated or delayed due to variability in clinical presentation, absence of family history of disease, or similarities with other conditions[3]

Misdiagnosis may impact course of treatment and worsen patient outcomes[3]

- For example, patients may be misdiagnosed with biliary atresia and undergo Kasai portoenterostomy, resulting in liver transplantation and increased mortality

Liver function

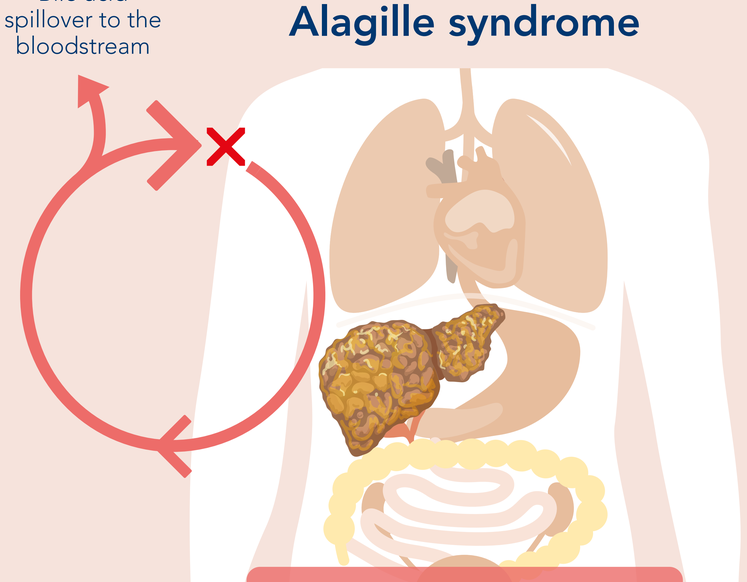
Healthy liver function



Bile acids are produced in hepatocytes before entering enterohepatic circulation,[4,5] with up to 95% being reabsorbed via the ileal bile acid transporter (IBAT) and transported back to the liver, while the remainder are excreted in feces[4,5]

Bile acid spillover to the bloodstream

Liver function in Alagille syndrome



In ALGS, bile duct paucity impairs bile flow, which can cause biliary components to accumulate in the liver and spill over into systemic circulation[4]

Disease progression and burden

ALGS can be a burdensome, lifelong disease that may impact the emotional, physical, and financial well-being of patients and caregivers[6,7]

Patients may experience diminished physical functioning and have problems with self-esteem and mental health[6]

Caregivers may encounter limitations to their time, interruption of family activities, and increased stress and worry[6]

More than 80% of patients with ALGS have cholestasis,[8] and associated clinical features may include elevated levels of serum bile acids, total bilirubin, and cholesterol; impaired growth; xanthomas; severe intractable pruritus; and progressive liver disease[3]

Up to 80% of patients with ALGS experience pruritus,[9] a debilitating symptom of the disease that can lead to skin damage, considerable sleep disruption, and mood disturbances[1]

Approximately 60% of patients with ALGS may need liver transplantation before they reach 18 years of age[2]

Indications for liver transplantation may include intractable pruritus, disfiguring xanthomas, bone fractures, and signs of end-stage liver disease[1]

The consequences of cholestasis on the health and quality of life in patients with ALGS and their caregivers are a continuing unmet need

[a]Determined using data from the Global ALagille Alliance (GALA) Study, literature reviews, and marketing research by Albireo Pharma, Inc., and presented at Albireo Commercial Day, February 11, 2021.

1. Kamath BM, et al. *J Pediatr Gastroenterol Nutr.* 2018;67(2):148–156; 2. Vandriel SM, et al. *J Hepatol.* 2020;73(suppl 1):S554–S555; 3. Ayoub MD, Kamath BM. *Diagnostics* (Basel, Switzerland). 2020;10(11):907; 4. Kamath BM, et al. *Liver Int.* 2020;40(8):1812–1822; 5. Karpen SJ, et al. *Hepatol Int.* 2020;14(5):677–689; 6. Elisofon SA, et al. *J Pediatr Gastroenterol Nutr.* 2010;51(6):759–765; 7. Ebel NH, et al. Presented at: Annual Meeting of the American Association for the Study of Liver Diseases; November 12–15, 2021; 8. Kamath BM. Presented at: Quadrennial World Congress of Pediatric Gastroenterology, Hepatology and Nutrition; June 2–5, 2021; 9. Kamath BM, et al. *Hepatol Commun.* 2020;4(3):387–398.

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