Understanding Type 1 Galactosemia

a rare genetic disease that can be life-threatening for newborns and can cause lifelong cognitive, neurological, speech, and fertility complications.[1]

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Type 1 galactosemia is a rare genetic disease that can be life-threatening for newborns and can cause lifelong cognitive, neurological, speech, and fertility complications.[1] Type 1 galactosemia is **caused by mutations in the *GALT* gene**.[2] The *GALT* gene's job is to tell the body's cells how to make the galactose-1-phosphate uridylyltransferase enzyme, or the **GALT enzyme**.[1, 2]

- Type 1 galactosemia includes classic, clinical variant, and Duarte galactosemia[1]
- Symptoms of Type 1 galactosemia typically occur in classic and clinical variant galactosemia[1]

Why do we need GALT enzymes?

GALT enzymes help the body process galactose, a sugar that is naturally produced in the body and found in dairy, breast milk, and other foods.[2,3]

Genetic mutations in the *GALT* gene means the body is not able to produce enough functional GALT enzyme.[1,2]

Without the GALT enzyme, a buildup of galactose occurs, which results in the accumulation of additional substances including galactose-1 phosphate (Gal-1P) and galactitol. Too much galactose, Gal-1P, and galactitol in the body is toxic and may contribute to lifelong complications.[2,3]

The risk and severity of galactosemia depends on the types of mutations in the *GALT* gene and their resulting level of GALT enzyme activity.[1]

Restricting galactose in people with galactosemia is critical, but not enough.

The current standard of care for galactosemia is a galactose-restricted diet.[3] If galactose is removed from a newborn's diet quickly, severe symptoms, like liver failure and death may be avoided.[2]

However, **the body produces endogenous galactose**, which means it produces galactose naturally, no matter what foods are eaten.[1] So, even when the recommended diet is strictly followed, lifelong complications can still occur.[2]

Lifelong Complications

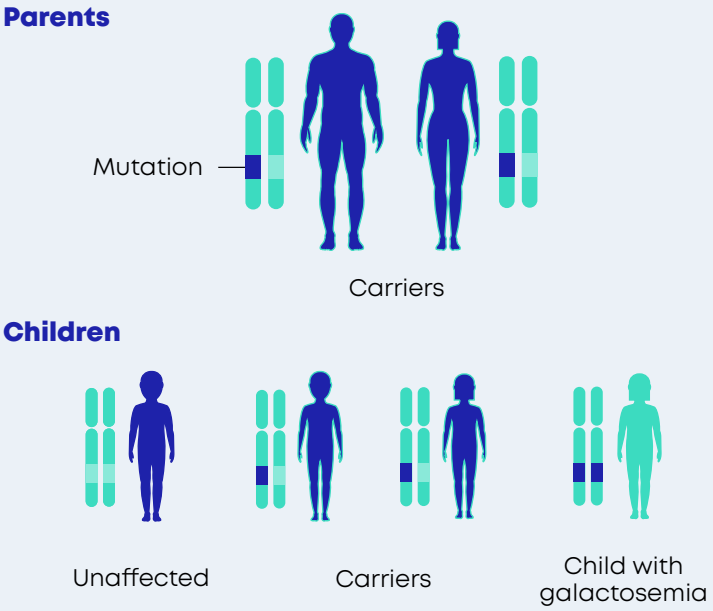
As children with Type 1 galactosemia grow, **the buildup of galactose, Gal-1P and galactitol continues**, which can contribute to lifelong complications.[2,3]

- Cognitive and motor delays **(49.7%)**[4]
- Neurological complications **(52.0%)**, with tremors as the most frequent complication **(31.0%)**[4]
- Language delay **(78.0%)**, and language and speech disorders **(66.4%)**[4]
- Primary ovarian insufficiency **(79.7%)**, which often requires hormone replacement therapy **(83.5%)**[4] and may lead to difficulty in getting pregnant
- Poor growth[5] and delayed puberty for girls **(48.5%)** and boys **(4.8%)**[4]
- Movement and coordination challenges **(27.0%)**[4]
- Cataracts **(25.8%)**[4]

The numbers above represent the percentage of people with Type I galactosemia who reported symptoms in a retropsective obervational study of 509 participants.[4]

How is a child born with galactosemia?

Galactosemia is an autosomal recessive disease. This means the parents of a child with galactosemia are usually carriers of the genetic mutation. Carriers have one dominant working gene and one recessive non-working gene with a mutation. Carriers do not experience symptoms of the disease. **A child is born with galactosemia when they inherit two copies of the gene mutation.**[1,2]



Newborn Screening

Because galactosemia is life-threatening, newborn screening for Type 1 galactosemia is conducted in every state in the United States and several other countries.

Newborn screening is usually done within 48 hours of birth; however, the results may not be available for several days. Since many parents are unaware that they are carriers, a child may be fed breastmilk or infant formula containing galactose, which can cause life-threatening complications.

Because diet is not enough, researchers are developing potential new treatments.

Talk with your doctor about ways to get involved in galactosemia research. You can also visit **Galactosemia.org** or **JaguarGeneTherapy.com** to learn more.

References 1. Berry GT. Classic Galactosemia and Clinical Variant Galactosemia. 2000 Feb 4 [Updated 2021 Mar 11]. In Adam MP, Ardinger HH, Pagon RA, et al., editors GeneReviews®. Seattle (WA): University of Washington. Seattle: 1993-3021. *https://www.ncbi.nlm.nih.gov/books/NBK1518/*. Accessed July 30, 2021. **2.** Galactosemia. NORD (National Organization for Rare Disorders). *https://rarediseases.org/rare-diseases/galactosemia/*. Published May 2019. Accessed July 1, 2021. **3.** Welling L, Bernstein LE, Berry GT, et al. International clinical guideline for the management of classical galactosemia: diagnosis, treatment, and follow-up. *J Inherit Metab Dis*. 2017;40:171-176. *https://onlinelibrary.wiley.com/doi/full/10.1007/s10545-016-9990-5*. **4.** Rubio-Gozalbo ME, Haskovic M, Bosch AM, et al. The natural history of classic galactosemia: lessons from the GalNet registry. *Orphanet J Rare Dis*. 2019; 14:86. *https://doi.org/10.1186/s13023-019-1047-z*. **5.** Panis B, Gerver WJM, Rubio-Gozalbo ME. Growth in treated classical galatcosemia patients. *Eur J Pediatr*. 2007;166:443-446.