



Classical Galactosemia Information for Healthcare Professionals

Galactosemia is an inherited disorder resulting from the inability to digest galactose. Galactose-1-phosphate uridylyltransferase (GALT) deficiency is the cause of classical galactosemia and its milder variants. Infants with classical galactosemia, or severe GALT deficiency, generally present within the first weeks after birth with a life-threatening illness. Milder variants of galactosemia, such as Duarte, are not associated with such serious complications.

✓ Clinical Symptoms

The signs and symptoms of classical galactosemia typically appear within the first few days of life. Children with classical galactosemia may present with feeding problems, vomiting, diarrhea, jaundice and lethargy. Excessive bleeding may occur when blood is drawn. Hepatomegaly and cataracts are common findings on physical examination. Septicemia due to *E. coli* infection is a major cause of morbidity/mortality in infants with untreated galactosemia. A less common picture of classic galactosemia may be of an older infant with failure to thrive, developmental delay and feeding problems.

Variant galactosemia is a milder form of galactosemia. Many of these individuals will be asymptomatic, however, a metabolic disease specialist should evaluate all newborns with an abnormal screen.

✓ Incidence

Classical galactosemia occurs in approximately 1 in 50,000 newborns.

✓ Genetics of Galactosemia

Mutations in the *GALT* gene cause classical galactosemia and its variants. The *GALT* gene encodes galactose-1-phosphate uridylyltransferase. Galactose, as a component of lactose, is a sugar found in large quantities in milk. Because milk is the major source of nutrition for infants, babies with galactosemia must have all foods containing lactose and galactose removed from their diet immediately.

✓ Inheritance Pattern

Galactosemia is inherited in an autosomal recessive pattern. The parents of a child diagnosed with galactosemia deficiency are unaffected. Parents are carriers of the condition and have one normal *GALT* gene and one abnormal *GALT* gene. Each pregnancy between carrier parents has a 25% chance of producing a child affected with galactosemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Treatment consists of complete removal of lactose-containing foods from the diet. Most newborns do well on a soy-based formula. Complete restriction of lactose-containing foods usually is required for at least the first year of life.

For those babies with variant galactosemia, a lactose “challenge” may be done (under the supervision of a metabolic specialist) at approximately one year of age, or when daily intake of lactose-containing foods diminishes. Because brain growth is greatest within the first year of life, many of these children can tolerate a limited amount of galactose in the diet once out of the infant stage, and can go on to eat a largely standard diet.

Children with classical galactosemia are at risk for brain damage and permanent neurological/developmental problems when dietary galactose is not strictly limited. The prognosis for individuals with galactosemia is very good when treatment is initiated before symptoms appear. However, even when treatment is promptly initiated, some individuals with classical galactosemia are at risk for growth retardation and developmental delays (in particular, speech delays). Females with classical galactosemia are at risk for premature ovarian failure.

✓ **Screening Methodology**

Beutler assay of the specimen is performed to measure GALT enzyme activity. The enzyme evaluated in screening is prone to damage if the sample is delayed in the mail or exposed to high temperatures. Because GALT analysis is performed using red blood cells, there may be a false-negative result for up to 3 months if the infant has received a blood transfusion.

✓ **What to do After Receiving Presumptive Positive Galactosemia Screening Results**

- 1) The clinician should *immediately* check on the clinical status of the baby. Findings may include jaundice, vomiting, diarrhea, lethargy, excessive bleeding, hepatomegaly, and cataracts.
- 2) Refer the infant to a metabolic disease specialist.
- 3) *Remove all breast milk and/or cow milk-based formula from newborn's diet.* Initiate feedings with soy-based formula.
- 4) Molecular and/or biochemical testing to determine genotype (classic or variant) may be indicated.
- 5) Call KS Newborn Screening Program at 785-291-3363 with questions.
- 6) Report Clinical Findings to Newborn Screening Program at 785-291-3363.

✓ **Confirmation of Diagnosis**

An abnormal newborn screening result requires immediate suspension of breast milk or cow milk-based formula. A metabolic specialist should promptly evaluate the newborn and initiate diagnostic testing.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive galactosemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to initiate consultations or obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with galactosemia, the following points should be conveyed to parents:

- ***Compliance with treatment is necessary for the best outcome.***
- ***Parents who have a child with galactosemia have a 25% chance with each pregnancy of having another affected child.***
- ***Prenatal diagnosis by molecular genetic testing may be available when parental mutations are known.***

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