

The New Jersey Department of Health and Senior Services

Galactosemia

Information for Health Professionals

Description

Galactosemia is a group of inherited metabolic disorders in which an enzyme deficiency affects the normal metabolism of the sugar galactose. The most common (and most severe) form, results from a disruption of the galactose-1-phosphate uridyl transferase (GALT) gene on chromosome 9. This results in an almost total deficiency of that enzyme's activity in all cells of the body.

Galactosemia is inherited as an autosomal recessive disorder and it can be caused by over one hundred mutations. The most common mutation, Q188R, causes complete loss of the body's ability to process galactose. Other mutations only diminish the body's ability to process galactose. The Duarte variant (N314D) has enzyme activity at about 50% of the normal level and usually produces no clinical manifestations. Other variant forms have less than normal activity, and in some cases there may be clinical manifestations.

Incidence

Galactosemia results from a recessive gene being passed on by both parents. In New Jersey the incidence of classical galactosemia is one in 60,000 births. The incidence of the less severe compound heterozygote form, Duarte galactosemia, is 1:4,000-5,000 births.

Prevalence of the various mutations differs by ethnic group. For example, Caucasians are much more likely than African-Americans to carry the Q188R mutation. Galactosemia is not a sex-linked disorder, so it occurs equally in males and females.

Clinical Features

Infants with galactosemia appear normal at birth, however symptoms usually appear a few days to two weeks after initiating milk feedings. The early clinical features of severe galactosemia include liver dysfunction, manifested by jaundice and hypoglycemia; neurological findings of irritability and seizures; and gastrointestinal findings of poor feeding, vomiting and diarrhea. Proteins and elevated levels of amino acids are found in the urine.

Galactosemia can kill quickly; it should be considered in any infant with non-glucose reducing substances in the urine. It is important to emphasize that testing of urine with glucose oxidase (Clinistix, Tes-tape) will not detect galactose. This is a strong argument for continued use of the older methods for the screening of urine for reducing substance (Benedict or Fehling test, Clinitest). There is a high frequency of neonatal death due to E. coli sepsis. If the infant is untreated and survives the neonatal period, mental retardation, cataracts and renal Fanconi syndrome are common.

Parents should understand that treatment is not curative, and that all morbidity cannot necessarily be prevented. Affected individuals may have problems such as speech disorders, learning disabilities and behavioral problems. Females are at risk for ovarian atrophy and infertility as they grow older.

Screening

The screening test for galactosemia is done as part of the standard newborn biochemical screening program in New Jersey. The test result is based on determination of enzyme (galactose-1-phosphate uridylyl transferase or GALT) activity, using the enzyme level as the indicator. The IEM laboratory also tests for galactose based on total blood galactose levels. Prompt confirmatory testing should be done even if there is evidence to suggest that one of the situations associated with false positive screens is present. These circumstances include prematurity, hyperalimentation, heat-damaged specimen or antibiotic therapy. The presence of any of these does not exclude the possibility of disease.

Confirmatory testing

The diagnosis of galactosemia is generally made by assay of the enzyme. The screening assay is followed by quantification of activity in freshly obtained erythrocytes.

Treatment

Treatment is based on the exclusion of galactose from the diet, accomplished by the elimination of milk and milk products. Galactose is a non-essential nutrient, and individuals diagnosed with classical galactosemia require lactose-restricted diets for life. Casein hydrolysate or soybean preparations are substituted for milk formulas and breast milk. When a lactose-restricted diet is provided within the first 10 days of life, presenting symptoms may be reversed.

Early diagnosis and treatment of classical galactosemia is crucial to prevent life-threatening complications of sepsis and liver failure. In addition, early detection will help prevent or limit developmental delays and mental retardation.

Implications for genetic counseling

Parents who have had a child with galactosemia are considered obligate carriers and have a 25% chance of having another affected child in each future pregnancy. Unaffected siblings have a 66% chance of being carriers. Carriers are asymptomatic but can often be identified through enzymatic or genetic testing.

Results/Recommendations

Initial Specimens:

- **Expected Results:** GALT level (enzyme activity) >3.5 u/gHb and <5.7 mg/dL galactose
- **Equivocal Results:** GALT level normal (>3.5 u/gHb) with $\geq 5.7 - \leq 7.8$ mg/dL galactose
Recommend: Repeat filter paper specimen within 2 days
- **Borderline Results:** a normal GALT (>3.5 u/gHb) with an increased galactose >7.8 mg/dL
Recommend: Within 2 days of contact: immediate assessment of baby's health status, collect a repeat filter paper specimen, and THEN place baby on soy or other non-lactose formula. **COLLECT SPECIMEN BEFORE PLACING ON SOY TO ASSURE A VALID GALACTOSE LEVEL.**
- **Borderline Results:** a reduced GALT level (3.2 – 3.5u/gHb) with a normal (<5.7 mg/dL) or equivocal ($\geq 5.7-7.8$ mg/dL) or elevated (> 7.8 mg/dL) galactose
Recommend: Within 2 days of contact, immediate assessment of baby's health status, place baby on soy or other non-lactose formula and collect a repeat filter paper specimen.

Presumptive-Positive Results: a low GALT level (≤ 3.1 u/gHb) with a normal or equivocal or elevated galactose

Recommend: Immediate assessment of baby's health status, place baby on soy or other non-lactose formula, and consultation with metabolic specialist/geneticist.

Results/Recommendations (cont.)

Repeat Specimens:

- **Presumptive-Positive Results:** Any repeat equivocal or borderline results
Recommend: Immediate reassessment of baby's health status and consultation with metabolic specialist/geneticist.

Note: Newborn screening is an adjunct to clinical assessment, which is paramount. Galactosemia should be considered in infants with any of the signs/symptoms.

Additional information:

Texas Department of State Health Services Newborn Screening
http://www.tdh.state.tx.us/newborn/galac_1.htm

Illinois Department of Public Health Newborn Screening Program
<http://www.idph.state.il.us/HealthWellness/fs/galactosemia.htm>

Washington State Department of Health
<http://www.doh.wa.gov/search.htm>

For questions, contact:

Newborn Screening and Genetic Services at (609) 292-1582
Inborn Errors of Metabolism Laboratory at (609) 292-3090

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