



Biotinidase Deficiency Information for Healthcare Professionals

Biotinidase deficiency is an inherited metabolic disorder that results from the inability to recycle biotin, leading to multiple carboxylase deficiencies. Complete or partial enzyme deficiency causes a variety of neurological and cutaneous symptoms. **Early diagnosis and treatment can prevent or reverse many or all of the clinical manifestations.**

✓ **Clinical Symptoms**

The signs and symptoms of biotinidase deficiency typically appear within the first few months of life, but the age of onset varies. Children with profound biotinidase deficiency (less than 10% of normal biotinidase activity), often have seizures and hypotonia. Additional early symptoms can include breathing problems, skin rashes, and hair loss. Later problems that may occur include developmental delays, speech problems, vision and hearing loss, and ataxia.

Partial biotinidase deficiency (10-30% of normal biotinidase activity), is a milder form of this condition. Symptoms in these individuals may only appear during times of metabolic stress including infection, illness, and fasting.

✓ **Incidence**

Profound or partial biotinidase deficiency occurs in approximately 1 in 75,000 newborns.

✓ **Genetics of biotinidase deficiency**

Mutations in the BTD gene cause biotinidase deficiency. The BTD gene encodes an enzyme called biotinidase. This enzyme helps the body release biotin, a B vitamin found in foods such as liver, egg yolks, and milk. Biotinidase also recycles biotin from enzymes involved in metabolism. Biotin deficiency then inhibits several carboxylases that are responsible for processing fats, proteins, or carbohydrates.

✓ **Inheritance Patterns**

Biotinidase deficiency is inherited in an autosomal recessive pattern. Typically, parents of a child diagnosed with biotinidase deficiency are unaffected. These individuals are carriers of the condition and have one normal BTD gene and one abnormal BTD gene. Each pregnancy between carrier parents has a 25% chance of producing a child affected with biotinidase deficiency, 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. In some families, asymptomatic parents and siblings were found to have either partial or complete BTD deficiency.

✓ **Treatment**

Treatment is life long and consists of daily biotin therapy in the form of oral biotin. No dietary restrictions are necessary. The prognosis for individuals is very good, particularly if they are treated before symptoms appear.

✓ **Screening Methodology**

Testing methodology used in newborn screening to detect biotinidase deficiency is a colorimetric assay. A positive newborn screen indicates absent biotinidase enzyme activity.

False positives are possible and may occur if the specimen is drawn from pre-term infants, submission is delayed, or if the specimen has been exposed to heat. False negatives can result if an infant has had a blood transfusion. The newborn screen should be performed 90 days post-transfusion. In such babies, if clinically indicated, DNA analysis can help confirm biotinidase deficiency.

✓ **What to do After Receiving Presumptive Biotinidase Deficiency Screening Results**

- 1) **Clinical Evaluation: Common findings include seizures, hypotonia, and skin rashes.**
- 2) **Immediately consult a metabolic specialist.**
- 3) **Laboratory: Order enzymatic testing for biotinidase activity unless told otherwise by metabolic specialist.**
- 4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
- 5) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**

✓ **Communication of Results to Parents**

If a baby has a presumptive biotinidase deficiency 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 obtain repeat specimens when needed to complete the screening process.

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

- ***Treatment is life-long. While very effective, it does not prevent all medical problems.***
- ***Compliance with treatment is necessary for the best outcome.***
- ***Parents who have a child with biotinidase deficiency have a 25% chance with each pregnancy of having another affected child.***
- ***Prenatal testing for pregnancies at 25% risk is available through measurement of biotinidase activity in cultured amniotic fluid cells.***
- ***Prenatal diagnosis by molecular genetic testing may be available from laboratories offering custom prenatal genetic testing.***

For consultation, contact:

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