Biotinidase Deficiency

Biotinidase Deficiency is an inherited metabolic disorder of biotin (Vitamin B complex) recycling that leads to multiple carboxylase deficiencies. Biotinidase is an important enzyme in the biotin cycle, the chain of biochemical reactions involved in the use and reuse of the vitamin biotin. One important role of biotinidase is to separate, or free, biotin from proteins to which it is bound in foods. Free biotin is required to allow a group of enzymes called carboxylases to function properly. Carboxylases are important in the production of certain fats and carbohydrates, and for the breakdown of proteins. Without biotinidase to release free biotin, the ability of the body to alter fats and to metabolize proteins and carbohydrates is impaired. Additionally, biotinidase lets the body recycle or reuse the biotin over and over again so that we do not need to consume large amounts of this vitamin in our diets.

Infants with Biotinidase Deficiency appear normal at birth, but develop one or more of the following symptoms between three to six months of age. These symptoms may occur as early as 1 week of age or as late as 10 years of age. Symptoms may include: ataxia, hypotonia, respiratory problems, seizures, hearing loss, cutaneous abnormalities (e.g., alopecia, skin rash, candidiasis), developmental delay, vision problems, or metabolic acidosis, which can result in coma and death. Individuals with partial deficiency (a variant form) are associated with an increased risk of developing the same symptoms that affect children with profound deficiency. However, the appearance of symptoms seems to be associated with metabolic stressors (e.g., illness, fever, fasting) and children may not be symptomatic until such time.

Prevalence for Profound and Partial Biotinidase Deficiency in Missouri: 1:40,000

Analyte: Biotinidase

Feeding Effect and Early Collection:

Biotinidase: The Biotinidase screening results should be abnormal in all profound (enzyme absent) or partial deficiency infants even if the specimen is obtained before formula or milk feeds or collected before 24 hours of age, **unless the infant has been transfused**.

Timing Effect: Infants who need a transfusion or antibiotics should be screened prior to instating these therapies.

- **Pre-transfusion:** at any hour of age results are valid
- **Post-transfusion:** ≥30 days post transfusion results are valid

Reporting Results:

- **Normal:** Normal Biotinidase. The final newborn screening reports are mailed to the submitter and physician of record.
- **Abnormal:** Biotinidase is decreased or absent. Final results are phoned and faxed to physician/health care provider and appropriate follow up center. Follow up centers are contracted by the Department of Health and Senior Services for follow up tracking, testing, diagnosis, and counseling. Final newborn screening report is mailed to the submitter and physician of record.

Interpretation of Newborn Screening Results:

Final Result	Test Results	Likely Causes
	Biotinidase	
Normal	Normal	No indication of a defect in Biotin metabolism.
Abnormal	Abnormal (reduced or absent enzyme activity)	-Profound Biotinidase Deficiency - Variant form of Biotinidase deficiency - Other enzyme defects in red blood cells - Improperly handled sample (heat damage or transit delay) -impaired liver function, prematurity, severe jaundice
No Result	No Result	-Transfusion -Possible transfusion

Follow Up Testing:

Follow up testing usually includes a quantitative Biotinidase serum assay and mutation testing that determines the genotype of the baby. Other tests may be ordered for diagnosis.

Decreased Biotinidase levels require prompt diagnostic testing to determine if the baby has Biotinidase Deficiency or is a carrier for the disease. It is highly recommended that the baby's physician/health care provider contact one of the **Newborn Screening Follow Up Centers** (see below) for consultation, diagnosis, and treatment. Early detection for Biotinidase Deficiency is crucial. Treatment is simple, inexpensive, and highly effective.

Newborn Screening Follow Up Centers:

- St. Louis Children's Hospital 314-454-6093
- Cardinal Glennon Hospital For Children 314-577-5639
- Children's Mercy Hospital 816-234-3290
- University of Missouri 573-882-6991

Variant Forms of Biotinidase Deficiency:

There are several genetic variants characterized by less severe reduction in the enzyme activity. Although most of these individuals are asymptomatic, all should be evaluated, as some will require management and monitoring.

Treatment:

All individuals with profound Biotinidase Deficiency and even those who have some residual enzymatic activity should have lifelong treatment with biotin. Biotinidase Deficiency is treated by Biotin therapy and should be done in consultation with a pediatric metabolic specialist. Siblings of an individual with Biotinidase Deficiency should be tested for the deficiency even if they do not exhibit symptoms.

This genetic disorder is transmitted in an autosomal recessive manner, which means both parents are carriers of a mutation for the gene. Carrier testing for at-risk family members by targeted mutation analysis using the panel of common BTD mutations are available. Families with Biotinidase Deficiency should be referred for genetic counseling.

Avoiding False Positive and False Negative Results:

False negative Biotinidase Deficiency results may occur in infants if they:

- are being treated with antibiotics
- have been recently transfused

Infants who need a transfusion or antibiotics should be screened prior to instituting these therapies.

False positive results may be caused by:

- improper collection
- improper drying
- samples placed in plastic prior to drying
- delayed transit
- impaired liver function
- prematurity
- infants with severe jaundice

Proper collection, drying techniques and reducing transit delays can help to reduce false positive results.