



**NEWBORN SCREENING  
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## **Biotinidase Deficiency**

### **Information for Physicians and Other Health Care Professionals**

**Definition** Biotinidase deficiency is an inherited metabolic disorder of biotin (vitamin B) recycling that leads to multiple carboxylase deficiencies.

**Clinical Symptoms** Symptoms of untreated biotinidase deficiency may appear at any time from 1 week to 10 years of age. The most common early symptoms include seizure activity of various types (myoclonic, grand mal, and focal or infantile spasms) and hypotonia. Other early symptoms include breathing problems (tachypnea, hyperventilation, stridor, apnea), skin rashes and alopecia. Later developmental delays, speech problems, ataxia, and vision and hearing problems may occur. Less frequent findings include feeding difficulties, vomiting/diarrhea, fungal infections, hepatomegaly and splenomegaly.

**Newborn Screening and Definitive Diagnosis** In Illinois, the testing methodology used to detect biotinidase deficiency is colorimetric assay, and results are reported as either “normal” (enzyme present) or “abnormal” (reduced or absent enzyme activity). False positive results may occur with specimens drawn from pre-term infants, or with improper handling of the specimen. Improper drying, delayed submission or exposure to excess heat are all factors that can destroy the enzyme. Transfusions may cause false negative results. **Confirmation of any initial abnormal newborn screening result requires an immediate repeat filter paper specimen. If the second test also is abnormal, the infant should be referred to a metabolic disease specialist.** Individuals discovered to have less than 10 percent biotinidase activity have profound deficiency. Through newborn screening, followed by definitive diagnostic testing, a milder form of biotinidase deficiency, in which there is 10 percent to 30 percent biotinidase activity, also has been identified.

**Treatment** Biotin therapy is initiated in **prescription doses** of 5 mg-20 mg per day (10-20 times that of RDA requirements). This provides the body with sufficient free biotin for all metabolic needs. Therapy is lifelong, and no dietary restrictions are necessary. The prognosis for individuals diagnosed with biotinidase deficiency is very good, especially for those who were treated before symptoms occurred. No serious side effects of biotin treatment have been recognized.

**Incidence** The incidence of biotinidase deficiency is estimated at one of every 110,000 births. Incidence in Illinois is approximately one in 150,000 births.

**Inheritance Pattern** This disorder is inherited in an autosomal recessive pattern. As an autosomal recessive disorder, the parents of a child with biotinidase deficiency are unaffected, healthy carriers of the condition and have one normal gene and one abnormal gene. With each pregnancy, carrier parents have a 25 percent chance of having a child with two copies of the abnormal gene, which results in biotinidase deficiency. Carrier parents have a 50 percent chance of having a child who is an unaffected carrier and a 25 percent chance of having an unaffected, non-carrier child. These risks hold true for each pregnancy. All siblings of infants diagnosed with biotinidase deficiency should be tested; genetic counseling services should be offered to the family.

**Physiology** Biotinidase is an essential enzyme that liberates biotin from proteins in foods for utilization by the body. It also enables the body to recycle biotin, which is necessary for proper functioning of carboxylase enzymes. Without biotinidase to release free biotin, the ability of the body to alter fats and to metabolize proteins and carbohydrates is impaired. Complications including metabolic acidosis, coma and death can occur unless supplements of biotin are provided.

**Key Points for Parents** Avoid overly alarming the child’s parents if the diagnosis has not yet been confirmed. If the child needs additional testing or diagnostic evaluation, make certain the parents understand the importance of following the pediatrician’s and/or specialist’s recommendations for additional testing and/or referrals.

**Follow-up After Confirmation of Diagnosis** These guidelines should be followed after a diagnosis of biotinidase deficiency has been confirmed:

1. Parents should understand that treatment is lifelong and that compliance with the daily medication regimen is imperative to the child's health, growth and development.
2. Infants and children with biotinidase deficiency should have regular follow-up appointments with a metabolic disease specialist.
3. Parents should understand that treatment is not curative and that long-term management, monitoring and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics and genetics. Evaluations for eye problems, such as optic atrophy, and hearing loss also may be recommended.
4. Genetic counseling services are recommended. A list of genetic counselors and geneticists, whose services are available through the Illinois Department of Public Health, should be given to the parents if they have not already seen a geneticist.
5. Provide a list of available support services in the community, such as the local health department, Early Intervention service providers and the University of Illinois at Chicago, Division of Specialized Care for Children (DSCC).
6. Parents may find beneficial support groups that give them the opportunity to talk with parents of other children with biotinidase deficiency.
7. Additional information about newborn screening can be found at:
  - Baby's First Test: <http://www.babysfirsttest.org/>  
Health Resource and Service Administration (HRSA), Grant no. U36MC16509, Quality Assessment of the Newborn Screening System.
  - National Center for Biotechnology Information: <http://www.ncbi.nlm.nih.gov/gtr/>  
National Center for Biotechnology Information, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.