

**The New Jersey Department of Health and Senior Services  
Newborn Screening and Genetic Services**

## **Biotinidase Deficiency**

### **Information for Health Professionals**

#### **Description**

The enzyme biotinidase releases the essential vitamin cofactor biotin from a protein-bound form so it can be utilized by the body. Deficiency of the enzyme results in improper functioning of several other enzyme systems dependent on biotin, leading to neurological damage.

#### **Incidence**

The incidence rate is estimated to be 1:72,000 to 1:126,000 live births.

#### **Clinical Features**

The symptoms are variable with respect to age of onset, frequency and severity. Infants with biotinidase deficiency appear to be normal at birth, but develop hypotonia, seizures, and rash, often accompanied by hyperventilation, laryngeal stridor, and apnea. Older children may also have alopecia, ataxia, developmental delay, neurosensory hearing loss, optic atrophy, and recurrent infections. Some affected children may have episodes of life-threatening metabolic acidosis. Individuals with partial deficiency (a variant form) may also be at risk for development of symptoms.

#### **Screening**

Testing for Biotinidase Deficiency is part of the standard newborn screening. A quantitative colorimetric assay determines enzyme activity. Detection of the deficiency does not depend on timing or type of feeding because it is an enzyme test. It should therefore be detected on the first specimen unless the infant has been transfused with whole blood, plasma, or serum. Newborn screening specimens should always be obtained prior to a transfusion. False positive results may occur in premature infants (who can have reduced biotinidase activity due to functional immaturity of the liver) and in samples placed in plastic prior to drying. The enzyme is prone to damage if the specimen is delayed in the mail or exposed to high temperatures, resulting in a potentially false negative test.

## **Confirmatory Testing**

Upon receiving a positive filter result, confirmatory testing using a serum sample should be done (0.5 ml of serum should be collected). The specimen must be frozen (sent on dry ice) and tested for biotinidase enzyme activity. Prompt confirmatory testing is required even if there is evidence to suggest that one of the situations associated with false positive screens is present. These situations can include prematurity, heat-damaged specimen, or hyperalimentation. The presence of any of these does not preclude the possibility of disease.

## **Treatment**

The acute symptoms of biotinidase deficiency will completely disappear with administration of pharmacological doses of biotin. If given early enough in an infant's life, the prognosis for normal growth and development is good.

Lifelong treatment consists of prescribed daily biotin supplements that clear the skin rash and alopecia and improve the neurological status in children diagnosed outside the newborn period (not identified by newborn screening). With early diagnosis and treatment, signs and symptoms can be prevented.

If the disorder is not detected until neurological damage has occurred, treatment with biotin can reduce further damage but not reverse damage already done. Untreated children with partial deficiency are usually healthy, although signs may appear if the child's body is stressed from an infection or poor diet. Currently, some children with partial deficiency are being treated with prescribed doses of biotin, whereas others remain untreated and are carefully watched for the development of signs.

## **Implications for genetic counseling**

Biotinidase deficiency is inherited in an autosomal recessive manner. Family studies are indicated when an affected newborn is identified. With each pregnancy, a couple who has had one affected child has a 25% chance of having an affected child, a 50% chance of having an unaffected child who is a carrier, and a 25% chance of having an unaffected child who is not a carrier. Siblings of an individual with biotinidase deficiency should be tested for the deficiency, even if they are not symptomatic. Prenatal testing for pregnancies carrying a 25% risk can be done by measuring biotinidase activity in cultured amniotic fluid cells.

## **Interpretations/Recommendations:**

### **Expected Results**

- **Within Acceptable Limits**

### **Initial Borderline Results**

- **Reduced enzyme activity**
- **Recommend: Repeat filter paper sample within 2 days and assessment of the baby's health status.**

### **Repeat Borderline Results**

- **Reduced enzyme activity**
- **Recommend: Immediate assessment of the baby's health status and consult with a metabolic/genetic specialist for confirmatory/diagnostic testing and treatment.**

### **Presumptive-Positive Results**

- **Low enzyme activity**
- **Recommend: Immediate assessment of the baby's health status and consult with metabolic/genetic specialist for confirmatory/diagnostic testing and treatment.**

**Note: Newborn screening tests are an adjunct to clinical assessment, which is paramount. Biotinidase Deficiency should be considered in infants with any of the signs.**

### **Sources:**

Gene Tests/Gene Clinics  
[www.geneclinics.org/profiles/biotin](http://www.geneclinics.org/profiles/biotin)

eMedicine  
[www.emedicine.com](http://www.emedicine.com)

Illinois Department of Public Health Newborn Screening Program  
[www.idph.state.il.us/HealthWellness/fs/biotinidase.htm](http://www.idph.state.il.us/HealthWellness/fs/biotinidase.htm)

For questions, contact:

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

March 2005