

Disease Name:

BIOTINIDASE DEFICIENCY

BTD DEFICIENCY; MULTIPLE CARBOXYLASE DEFICIENCY, LATE ONSET;
MULTIPLE CARBOXYLASE DEFICIENCY, JUVENILE ONSET

Classification: Organic Acidemia

Genetic Information: **Inheritance:** Autosomal recessive

Population Incidence: 1:60,000

Ethnic Incidence:

Gene & Location: 3p25, Biotinidase gene

Common Mutation: G98:D7/i3 & R538C (52% of alleles)

OMIM # 253260

Disease Information: **Symptom Onset:** Average 3 months, but may present as early as 12 days of age to asymptomatic adults.

Symptoms: Appearance and severity of symptoms are related to the degree of residual enzyme activity. Individuals with profound deficiency (<1%) are more likely to develop early symptoms that include seizures, hypotonia, laryngeal stridor, hearing loss, optic atrophy, skin rash and alopecia. Ketoacidosis and organic aciduria may be severe and death can occur. Individuals with >1% of residual activity may never have symptoms unless stressed, but treatment is recommended nevertheless.

Physical Findings: Alopecia and skin lesions are variable in severity and timing. They are resistant to conventional therapies. No specific dysmorphisms.

Treatment: Biotin (pharmacologic doses) for both partial and profound deficiency. Biotin, sometimes called vitamin H, is an important water-soluble vitamin that aids in the metabolism of fats, carbohydrates and proteins.

Natural History without treatment: Some infants may develop life-threatening ketoacidosis in the perinatal period. In others, damage is more insidious, with hearing loss, optic atrophy, acrodermatitis enteropathica, spastic diplegia and mental retardation rather than acute decompensation and acidosis. Treatment does not reverse neurological damage that has already occurred.

Natural History with treatment: For biotin compliant individuals development remains completely normal. For those who are not compliant varying degrees of damage occur depending on the age of the individual and the severity of the enzyme defect. Individuals with partial deficiencies will probably remain normal even if compliance is an issue.

Metabolic Information:

Missing Enzyme & Location: Biotinidase enzyme cleaves biocytin to form biotin and lysine. Biotin cannot be recycled in the body and for these patients becomes an essential nutrient.

Newborn Screening Profile: Color change occurs, indicating a reduction or absence of the enzyme. Diagnosis is confirmed by biotinidase assay in serum.

Prenatal testing: Cultured amniocytes or DNA mutation analysis.

Miscellaneous Information:

Diagnosis is confirmed by measurement of biotinidase in serum

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