

CHARGE SYNDROME

CHARGE syndrome is an autosomal dominant condition involving many organ systems. The four major common characteristics of CHARGE syndrome are coloboma of the eye, choanal atresia or stenosis, cranial nerve dysfunction or anomaly and characteristic CHARGE ear with inner, middle and outer ear malformations. Minor characteristics are congenital heart defects, hypoplastic genitals, cleft palate and/or lip and a characteristic CHARGE face and hand. Patients with CHARGE syndrome can vary in which of the features they have and the degree of severity of each feature.

GENETICS

CHARGE syndrome is caused in 60-65% of patients by mutations in the *CHD7* gene found on chromosome 8 at a location designated 8q12.1. CHARGE is an autosomal dominant condition and so individuals are affected with CHARGE when a mutation is present on one of their two copies of the *CHD7* gene.

An individual with a *CHD7* mutation has a 50% chance of transmitting the *CHD7* gene mutation to a child. Most patients with CHARGE syndrome are new occurrences (i.e. *CHD7* mutation is not inherited) although parents may be more mildly affected and so should also be tested.

MAJOR CHARGE FEATURES

Coloboma

Choanal atresia or stenosis

Cranial nerve dysfunction or anomaly

Characteristic CHARGE ear and absent/missing/malformed semi-circular canals

WHO SHOULD BE TESTED?

- Individuals clinically suspected of being affected with CHARGE syndrome
- Relative of probands with identified *CHD7* mutations
- Pregnancies at increased risk of being affected with CHARGE syndrome

TEST METHODS

- Complete sequencing of the 38 exon coding region and flanking exon/intron boundaries of the *CHD7* gene to identify point mutations
- Quantitative testing of the *CHD7* region on 8q12.1 to test for deletions, using Multiplex Ligation-dependent Probe Amplification (MLPA).

TEST SENSITIVITY

Approximately 60-65% of patients with clinically diagnosed CHARGE syndrome will have a mutation in *CHD7*

For More Information

Online Mendelian Inheritance in Man: <http://www.ncbi.nlm.nih.gov/omim/> Item # 214800

GeneReviews online clinical information resource <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=charge#charge>

Charge Syndrome Canada: <http://www.chargesyndrome.ca>

To locate a genetics center near you, please visit the National Society of Genetic Counselors web-site at www.nsgc.org or the Canadian Association of Genetic Counsellors web-site at www.cagc-accg.ca



1. Current molecular testing may not detect all possible mutations for this disease. A negative test does not rule out the diagnosis of CHARGE syndrome.
2. The clinical course or severity of symptoms cannot be predicted by molecular analysis.
3. Test results should be interpreted in the context of clinical findings, family history, and other laboratory data.
4. If molecular analysis is negative, chromosome analysis should be performed on all patients clinically suspected of being affected with CHARGE syndrome. These studies may identify patients with a translocation involving chromosome 8 and another chromosome.
5. This test was developed and its performance characteristics validated by the Genome Diagnostics Laboratory at the Hospital for Sick Children. It has not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes.

POTENTIAL OUTCOMES & INTERPRETATION OF TEST RESULTS

Reason for referral	<i>CHD7</i> Mutation Testing	Explanation
Diagnosis	None detected	This result does not support a diagnosis of CHARGE syndrome
Diagnosis	Mutation detected	This result supports a diagnosis of CHARGE syndrome