

CHARGE Syndrome (*CHD7*)

Indications for Ordering

Confirms a clinical diagnosis or suspected diagnosis of CHARGE syndrome

Test Description

Bidirectional sequencing of entire coding region and intron/exon borders of the *CHD7* gene

Tests to Consider

[CHARGE Syndrome \(*CHD7*\) Sequencing 2012609](#)

- Genetic testing to confirm a diagnosis of CHARGE syndrome

[CHARGE Syndrome \(*CHD7*\) Sequencing, Fetal 2012717](#)

- Prenatal test for a fetus with ultrasound findings suggestive of CHARGE syndrome

Disease Overview

Incidence – ~1/10,000

Symptoms

- CHARGE is an acronym for the major features of the condition
 - **C**oloboma
 - **H**ear defects
 - **C**hoanal **a**trisia
 - **R**estricted growth and delayed development
 - **G**enital abnormalities
 - **E**ar anomalies
- Condition is highly variable

Diagnostic criteria

- Diagnosis is based primarily on clinical findings and temporal bone imaging
- Clinical criteria for CHARGE syndrome
 - Four major characteristics, or three major and three minor characteristics
- Clinical criteria for possible/probable CHARGE syndrome
 - Two major and several minor characteristics

Major characteristics

- Ocular coloboma
- Choanal atresia or stenosis
- Cranial nerve dysfunction or anomaly
- Abnormalities of the inner, middle, or external ear characteristic of CHARGE syndrome

Minor characteristics

- Genital hypoplasia
- Developmental delay
- Cardiovascular malformation
- Growth deficiency
- Orofacial cleft
- Tracheoesophageal fistula
- Characteristic facial features

Genetics

Gene – *CHD7*

Inheritance – autosomal dominant

Penetrance – 100%, though severity of the condition is highly variable

De novo mutations

- Almost always de novo
- Rare parent-to-child transmission has been reported

Mutations

- Most mutations are sequence variants
- Partial or full deletions of *CHD7* are rare

Test Interpretation

Sensitivity/specificity

- Clinical sensitivity – ~90% in individuals or fetuses fulfilling clinical criteria for CHARGE syndrome
- Analytical sensitivity/specificity – >99%

Results

- Positive
 - One copy of a pathogenic mutation detected
 - Confirms a diagnosis of CHARGE syndrome
- Negative
 - No mutation detected
 - Likelihood of CHARGE syndrome is reduced, but still possible

Limitations

- Diagnostic errors can occur due to
 - Rare sequence variations
 - Primer- or probe-site mutations
- Not detected
 - Large deletions and duplications
 - Regulatory region mutations
 - Deep intronic mutations

References

- Bergman JE, Janssen N, et al. CHD7 mutations and CHARGE syndrome: the clinical implications of an expanding phenotype. *J Med Genet.* 2011;48:334-342
- Janssen N, Bergman JE, et al. Mutation update on the CHD7 gene involved in CHARGE syndrome. *Hum Mutat.* 2012;33:1149-1160