LABupdate

CHARGE Syndrome

CHARGE is an acronym for the hallmark characteristics of a congenital syndrome that affects about 1 in 10,000 births worldwide.[1] Those characteristics include: coloboma of the eye, heart defects, choanal atresia, growth and developmental retardation, genital abnormalities, and ear anomalies. Affected individuals are usually diagnosed during the neonatal period, and feeding difficulties are a common cause of death in affected individuals of all ages.[2]

A clinical diagnosis of CHARGE syndrome may be made on the basis of the presence of 4 major features or 3 major and 3 minor features as presented in the table below.[1,2]

Major Features	Minor Features
• Ocular coloboma	• Genital hypoplasia
• Choanal atresia or stenosis	• Delayed developmental milestones
• Cranial nerve dysfunction or anomaly	• Cardiovascular malformation
• Ear abnormalities typical of CHARGE, including helical anomalies, inner or middle ear malformations, or temporal bone abnormalities	• Orofacial cleft
	• Tracheoesophageal fistula
	• Facial dysmorphisms

Some manifestations of CHARGE overlap with other congenital syndromes, including VACTERL association (vertebral defects, anal atresia, cardiac defects, trachea-esophogeal fistula, renal anomalies, and limb abnormalities), and 22q11.2 deletion syndrome.[1,2] These conditions are often considered in the differential diagnosis of a child with multiple congenital anomalies and facial dysmorphisms.

Inheritance of CHARGE syndrome is autosomal dominant[2,3], and penetrance is high.[2] Most cases are attributed to de novo mutations.[2] There is a recurrence risk of 1% to 2% in siblings, most likely due to germline mosaicism in a parent.[2]

Management of CHARGE syndrome may include tracheostomy and surgical correction of choanal atresia, feeding therapy, hearing aids, psychological and school evaluations, and surgery and/or routine heart defect care.[2]

Given the complexities of CHARGE syndrome, genetic testing may help to[2]:
- Confirm a diagnosis.
- Differentiate CHARGE syndrome from other multiple malformation syndromes, such as 22q11.2 deletion syndrome, and VACTERL association.

Relevant Assays*

Test Name	Test No.
GeneSeq®: Cardio Familial Congenital Heart Disease Profile	451402
GeneSeq®: Cardio Gene Specific Sequencing, NGS**	452053
Mutation-specific Sequencing, Whole Blood†	451382

* Visit the online Test Menu at **www.LabCorp.com** for more information, including a current list of included genes, test methodology, and specimen requirements. To request a sample shipping kit, please call 866-647-0735.
**Full Gene Sequencing for any gene(s) on any of the GeneSeq: Cardio panels
†Known mutation testing for any gene(s) on any of the GeneSeq: Cardio panels

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References
1. Blake KD, Davenport SL, Hall BD, et al. CHARGE association: an update and review for the primary pediatrician. *Clin Pediatr (Phila).* 1998; 37: 159–173.
2. Lalani SR, Hefner MA, Belmont JW, Davenport SLH. CHARGE syndrome. GeneReviews Web site. http://www.ncbi.nlm.nih.gov/books/NBK1117. Updated February 2, 2012. Accessed June 8, 2016.
3. Pauli S, Pieper L, Häberle J, et al. Proven germline mosaicism in a father of two children with CHARGE syndrome. *Clin Genet.* 2009; 75: 473–479.