Ambry Genetics®
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Genetic Testing for Inherited Cardiovascular Disease

REFERENCE GUIDE

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More than 1 in 200 people have an inherited cardiovascular condition. Ambry's mission is to provide the most advanced genetic testing information available to help you identity those at risk and determine the best medical management decisions. If we know a patient has a disease-causing genetic change, not only does it mean better disease management, but it also indicates that we can test others in the family and provide them with potentially life-saving information.

Professional Society Guidelines

Heart Rhythm Society/European Heart Rhythm Association

Genetic testing is recommended for patients with a firm clinical diagnosis of hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), long QT syndrome (LQTS), and catecholaminergic polymorphic ventricular tachycardia (CPVT). Genetic testing can be useful for patients with a clinical diagnosis of Brugada syndrome (Brs), arrhythmogenic right ventricular cardiomyopathy (ARVC), left ventricular non-compaction cardiomyopathy (LVNC).

Heart Failure Society of America Guideline #4

Genetic testing is recommended to determine if a pathogenic variant can be identified to facilitate patient management and family screening. The identification of at risk family members is critical because the first presentation may be sudden death. Without genetic testing, all first-degree relatives of a patient with cardiomyopathy need lifetime clinical screening.

Why Is Genetic Testing Important?

KEY BENEFITS

Identifying patients with an inherited cardiovascular disease enables you to:

- Clarify or confirm a diagnosis
- Guide personalized medical management recommendations
- Avoid genotype-specific cardiac event triggers
- Identify at-risk family members

When to Consider Testing for Inherited Cardiovascular Disease

All patients with the following conditions are recommended to be offered genetic testing:

- Hypertrophic cardiomyopathy[1, 2]
- Dilated cardiomyopathy with cardiac conduction disease and/or family history of sudden death[1, 2]
- Long QT syndrome[1]
- Catecholaminergic polymorphic ventricular tachycardia[1]
- Arrhythmogenic right ventricular cardiomyopathy[2]
- Restrictive cardiomyopathy[2]
- Autopsy-negative sudden cardiac death[1]

Recommendations for Familial Hypercholesterolemia (FH)[3]

Genetic testing for FH should be offered to individuals of any age in whom a strong clinical index of suspicion for FH such as:

- Children: LDL-C levels >160 mg/dL and > 1 first-degree relative similarly affected or LDL-C levels >190 mg/dL even in the absence of family history
- Adults: LDL-C levels >190 mg/dL and >1 first-degree relative similarly affected or LDL-C levels >250 mg/dL even in the absence of a positive family history

Recommendations for TAAD[4]

Thoracic aortic aneurysm (>45 mm) or dissection AND one of the following:[4]

- Age at diagnosis <50 years, or
- Age at diagnosis 50-60 years, no hypertension, or
- Positive family history (Section 3.2.), or
- Syndromic features

Genetic testing may be considered for patients with the following conditions:

- Brugada syndrome, type I[1]
- Left ventricular non-compaction[1]
- Peripartum cardiomyopathy[2]

1. *Heart Rhythm Society (HRS)/ European Heart Rhythm Association (EHRA) Guidelines.* Heart Rhythm. 2011 Aug;8(8):1308-39.
2. *Heart Failure Society of America (HFSA) Guideline,* Journal of Cardiac Failure (2018), https://doi.org/10.1016/j.cardfail.2018.03.004.
3. Sturm, Amy C., *et al.*, Clinical Genetic Testing for Familial Hypercholesterolemia. Journal of the American College of Cardiology. 72 (2018) 662-680.
4. Verhagen, Judith M.A., *et al.*, Expert consensus recommendations on the cardiogenetic care for patients with thoracic aortic disease and their first-degree relatives. International Journal of Cardiology. 258 (2018) 243-248.

Please visit ambrygen.com for information about these options

CARDIOMYOPATHY

INDICATIONS FOR TESTING	TEST NAME	GENES
Hypertrophic cardiomyopathy	HCMNext	30 genes
Dilated cardiomyopathy	DCMNext	37 genes
Arrhythmogenic right ventricular cardiomyopathy	ARVCNext	11 genes
Cardiomyopathies (multiple types or complex family history)	CMNext	56 genes

ARRHYTHMIA

INDICATIONS FOR TESTING	TEST NAME	GENES
Long QT syndrome Short QT syndrome Brugada syndrome type 1	LongQTNext	17 genes
Unclear arrhythmia diagnosis	RhythmNext	42 genes
Catecholaminergic polymorphic ventricular tachycardia	CPVTNext	4 genes

OTHER

INDICATIONS FOR TESTING	TEST NAME	GENES
Noonan syndrome and other RASopathies	NoonanNext	18 genes
Thoracic aortic aneurysm/dissection, Marfan, and related disorders	TAADNext	35 genes
Familial transthyretin amyloidosis	TTR	*TTR*

FAMILIAL HYPERCHOLESTEROLEMIA AND LIPID DISORDERS

INDICATIONS FOR TESTING	TEST NAME	GENES
Personal or family history of hypercholesterolemia*	FHNext	*APOB, LDLR, PCSK9, LDLRAP1^*
Familial chylomicronemia syndrome	FCSNext	*APOA5, APOC2, GPIHBP1, LMF1, LPL*
Sitosterolemia	Sitosterolemia	*ABCG5, ABCG8*

COMPREHENSIVE PANELS

INDICATIONS FOR TESTING	TEST NAME	GENES
Cardiomyopathies and arrhythmias	CardioNext	92 genes
Customizable option for hereditary cardiomyopathies, arrhythmias, TAAD, HHT, Noonan, and lipidemias	CustomNext-*Cardio*	up to 167 genes

ALL PANELS HAVE A TURNAROUND TIME OF 2-3 WEEKS

** Adults (20 yrs of age or older): LDL cholesterol >190 mg/dL or non-HDL cholesterol > 220 mg/dL*
Children, adolescents and young adults (under 20 yrs of age): LDL cholesterol > 160 mg/dL or non-HDL cholesterol > 190 mg/dL

^ + pharmacogenetic c.521T>C SNP in SLCO1B1

Over 1 Million Tests Completed

MOVING SCIENCE FORWARD

Free Family Member Testing

Free testing for ALL family members is now available within 90 days of the original report if the proband was tested at Ambry. Family testing is done via specific site analysis for pathogenic or likely pathogenic variants. (Excludes SNP array and applies to single gene, panel or exome testing.)

Purposeful Confirmatory Testing

Many labs validate their tests based on certain limited studies. That's why we led the largest study of its kind (20,000 cases) guiding us to utilize confirmatory testing when we see specific well-defined thresholds. Our mission is to get it right the first time.

Flexible Sample Options

Ambry accepts blood, saliva and other sample types to perform genetic testing.

Sample for Life

We periodically review variants and let you know when there is updated information, such as a reclassification. This is part of our commitment to finding answers.

About Ambry

Just as no two fingerprints are alike, the way disease presents itself in every individual is different. Since 1999, our mission has always been about understanding disease better, so treatments and cures can be found faster. Every sample that arrives in our lab is viewed as a person with a life and a story that is unique to only them. By providing advanced confirmation genetic testing for inherited and non-inherited diseases, we can help you make more informed and responsible medical management decisions with your patients.

Visit ambrygen.com for more information.

15 Argonaut, Aliso Viejo, CA 92656 USA Toll Free +1 866 262 7943 Fax +1 949 900 5501 ambrygen.com