Long QT Syndrome

A Guide for Patients

GeneDx
DNA DIAGNOSTIC EXPERTS

Long QT Syndrome

What is long QT syndrome?

Long QT syndrome (LQTS) is a condition that affects the ability of the heart to beat (contract) regularly and efficiently. An electrocardiogram (ECG) helps determine if you have this condition. When the part of the heartbeat known as the QT interval is longer than normal, you are considered to have LQTS. In LQTS, the system controlling the heartbeat does not work normally due to problems with electrical signals within the heart muscle cells. LQTS affects 1 in 3,000–5,000 individuals, with men and women of all ethnic backgrounds equally at risk. Every year 4,000 deaths in the U.S. are the result of LQTS.

What are the symptoms of LQTS?

Symptoms of LQTS usually develop before age 40. Sometimes symptoms occur in infancy, but most usually show up by the time you are in your 20s. Approximately half of the time, you may have LQTS and not show any signs of the disease. However, if you do have symptoms, you may experience one or both of the following:

- Fainting (syncope)
- Rapid heartbeat (arrhythmia)

In many cases these symptoms are triggered by events such as loud noises during sleep, strong emotions, or intense physical activity–especially swimming. Sometimes LQTS may be misdiagnosed as a seizure disorder. Sudden death is the first and only symptom in 10%–15% of fatal LQTS events.

What causes LQTS?

LQTS is primarily caused by an abnormality (mutation) in one of your genes. Mutations in the 12 genes that are important in the function of your heart's electrical conduction system have been associated with LQTS. LQTS is inherited in an autosomal dominant manner, so if you have the genetic form of LQTS there is a 50% chance of passing the genetic defect on to each of your children. Based on the specific gene affected and type of mutation found, LQTS is categorized as LQT1 to LQT12 as shown in Table 1 on the following page.

TABLE 1

GENOTYPE	AFFECTED GENE	GENE NAME
LQT1	KCNQ1	KQT-like voltage-gated potassium channel-1
LQT2	KCNH2	Potassium channel, voltage gated, H2
LQT3	SCN5A	Alpha polypeptide of voltage-gated sodium channel type V
LQT4	ANK2	Ankyrin-B
LQT5	KCNE1	Voltage-gated potassium channel, Isk-related subfamily, member 1
LQT6	KCNE2	Voltage-gated potassium channel, Isk-related subfamily, member 2
LQT7	KCNJ2	Inwardly rectifying potassium channel
LQT8	CACNA1C	Calcium channel, L type, alpha 1 polypeptide isoform
LQT9	CAV3	Caveolin-3
LQT10	SCN4B	Sodium channel, voltage-gated, type IV beta subunit
LQT11	AKAP9	A-kinase anchor protein-9
LQT12	SNTA1	Alpha 1 Syntrophin

How is LQTS diagnosed?

LQTS is usually diagnosed by an electrocardiogram (ECG). The ECG in Figure A shows an abnormally long QT interval. Your ECG, medical history and family history are essential in evaluating the likelihood of a genetic cause for your LQTS. Genetic testing can be used to confirm your doctor's clinical diagnosis.

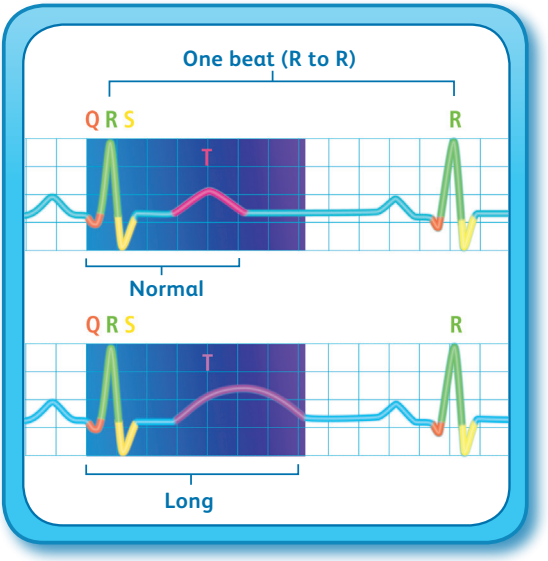

Figure A: *Illustration showing prolonged QT interval on an electrocardiogram (ECG)*

How is LQTS treated?

The clinical management of LQTS depends on the severity of your disease and symptoms. Beta-blockers are the main medications prescribed to LQTS patients. Some high-risk patients may need surgery to have a defibrillator placed. Less frequently, surgery to block some of the nerves of the heart may help. Your physician also usually recommends lifestyle adjustments such as avoiding activities that may trigger your LQTS symptoms, including competitive sports, alarm clocks and other loud noises in the home. Additionally, certain medications can prolong the QT interval and should be avoided.

Genetic Testing for Long QT Syndrome

How is genetic testing for LQTS performed?

The LQTS genetic test is a blood test ordered by your physician. GeneDx will extract your DNA and analyze it by specifically searching for mutations in the genes that are associated with LQTS. After the test is complete (in approximately eight weeks), the results are sent to your physician, who will explain them to you.

What makes the GeneDx test different from others?

GeneDx offers the most comprehensive genetic test for LQTS. Identifying the genetic cause of your LQTS is important, as the recommended treatment for LQTS may differ depending on the genetic cause identified in you. If GeneDx finds a variation, but cannot determine if it is the cause of your disease, another family member with LQTS will be tested at no additional cost. In such circumstances, GeneDx will also evaluate a large panel of clinically normal individuals to determine if the genetic variant is seen in individuals who do not have LQTS.

Who should have genetic testing for LQTS?

- Anyone with a clinical diagnosis of LQTS
- Family members of the person who has a disease-causing mutation (although these individuals need only targeted testing for the mutation found in their relative)

How is genetic testing for LQTS helpful?

- Confirms your clinical diagnosis of LQTS, especially if the diagnosis is not clear.
- Identifies your family members who are at risk of developing LQTS.
- Allows for informed personal and family health decisions to be made.

How long does it take to complete the genetic test?

It usually takes approximately eight weeks to complete the test (from the time the lab receives the blood sample to the time your physician receives the results). It can take longer if GeneDx has to study clinically normal individuals or test family members to interpret results.

What type of test results can I expect?

Three types of results are possible:

- **A positive result** indicates that we identified a disease-causing mutation in one of your genes associated with LQTS. This finding confirms the diagnosis of LQTS and provides valuable information to family members. Knowledge of your specific genetic mutation can help your physician identify activities and behaviors to avoid and may be useful in determining your risk of experiencing a life-threatening cardiac event. All first-degree relatives (children, siblings, parents) may then be offered

diagnostic or predictive genetic testing to clarify their risk for LQTS. If a family member is found to be positive for the familial mutation, this individual is considered to be at risk for LQTS and should be referred for cardiac evaluation including an ECG. Mutation-positive family members should have a baseline electrocardiogram, clinical evaluation by a cardiologist, and annual evaluations with a cardiologist. It is important to note that there is variability in symptoms–even within families.

- **A negative result** indicates that we did not identify a disease-causing mutation in one of your genes associated with LQTS. **However, this does not rule out LQTS or a genetic cause of LQTS, and you should be managed according to your clinical symptoms.** Possible reasons for a negative result could be: (1) you may have a mutation in a gene not covered in the testing panel, (2) you may have a mutation in a part of a LQTS gene that was not covered in the test, or (3) you do not have a heritable form of LQTS. When a genetic test result is negative, predictive genetic testing of family members will not be informative and therefore not helpful. Careful review of your family history may help determine if your disease is hereditary, so that other family members can have their hearts monitored by their doctor(s). In addition, a heart health evaluation prior to participation in competitive sports is recommended.

- **A variant of unknown significance (VOUS) result** indicates an inconclusive finding. This happens when we find a new DNA abnormality (i.e., one that has never been seen before), but it is unclear if that change causes LQTS. A VOUS report is sent only after GeneDx has confirmed that no individual in a large panel of normal controls carries the variant. To further clarify the clinical significance of the VOUS, it may be helpful to test other family members. If an affected relative also has the variant, it is more likely that the variant causes LQTS. The more affected family members who carry the VOUS, the greater the likelihood that the VOUS is responsible for LQTS in your family.

How will I learn my test results?

Your physician will share your results with you and discuss them in the context of your health care.

Will my insurance cover this test?

GeneDx accepts all commercial insurance. GeneDx will bill your insurance company and appeal for payment. GeneDx is a Medicare provider and therefore is able to accept Medicare patient samples. A completed Advance Beneficiary Notice (ABN) is required for Medicare patients. In most cases, Medicaid will not cover genetic testing for these conditions, as Medicaid coverage varies by state. For more information, please visit our website at: **www.genedx.com/cardiology** or call us at 301-519-2100.

What if I do not have insurance?

If you do not have health insurance or cannot afford to pay the full cost of testing, GeneDx provides a generous financial assistance program including a significantly discounted price. For more information, call us at 301-519-2100.

Do my family members need to be tested?

If you have a disease-causing mutation in one of the LQTS genes, your family members can be tested for that specific mutation. If you have a VOUS, GeneDx may ask to test your family members at no additional cost if it is necessary to interpret your test results.

Does GeneDx test family members?

Yes, GeneDx offers mutation-specific testing (for a known mutation) for family members of anyone who has been shown by GeneDx to have a genetic mutation. For more information, please call one of our genetic counselors at 301-519-2100. If a family member has been tested at another lab, we can still test you or other family members, but we require blood from the previously tested relative to be sent along with your sample for confirmation.

How does testing of family members differ from full LQTS panel testing in a patient?

The first LQTS patient in a family to be tested typically requires analysis of all 12 genes in the LQTS panel. Once a disease-causing mutation is identified in a specific gene, family members are tested only for that specific mutation. The cost and turnaround time are significantly reduced when family members get tested for a specific mutation only, instead of the full gene panel.

Does GeneDx perform prenatal testing?

Yes, GeneDx can provide prenatal testing for a known familial mutation in any gene for families who have had previous testing at GeneDx. For more information, please call one of our genetic counselors at 301-519-2100.

Can my health insurer or employer discriminate against me based on my test results?

No, The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, is a federal law that protects Americans from discrimination by health insurance companies and employers based on their genetic information. The President signed the act into federal law on May 21, 2008. The parts of the law relating to health insurers took effect on May 2009, and those relating to employers took effect on November 2009. **However, this law does not cover life insurance, disability insurance, or long-term care insurance.** For more information, please visit **http://www.genome.gov/10002328**.

How can I order this test?

Your physician can order this test by taking the following steps:

- Download cardiology requisition forms from the GeneDx website: www.genedx.com/cardiology
- Complete all the forms with the required information
- Ship completed forms along with 2mL–5mL whole blood in EDTA purple/lavender top tube to the following address:

GeneDx
207 Perry Parkway
Gaithersburg, MD 20877

We also provide shipping kits to physicians when requested. To order a cardiology shipping kit, you can call us at 301-519-2100, or email us at zebras@genedx.com.

Where can I find more information?

You can find more information at the following Web sites:

- GeneDx cardiology page: www.genedx.com/cardiology
- *Gene Reviews*, a database of genetic diseases: www.geneclinics.org
- *National Society of Genetic Counselors*, to help you find a counselor near you: www.nsgc.org
- *Sudden Arrhythmia Death Syndrome (SADS) Foundation*, a patient support organization: www.sads.org
- *The Canadian Sudden Arrhythmia Death Syndromes (SADS) Foundation*, a patient support organization in Canada: www.sads.ca
- *Sudden Cardiac Arrest Association*, a patient support organization: www.suddencardiacarrest.org
- *Long QT yahoo group*, an online patient group. Subscribe by emailing: longqt-subscribe@yahoogroups.com
- *LQTS Faceboook support group:* an online support group for anyone affected by LQTS. For details logon to Facebook, and then visit: http://www.facebook.com/groups/193978400681765/

About GeneDx

GeneDx is a highly respected genetic testing company founded in 2000 by two scientists from the National Institutes of Health (NIH) to address the needs of patients and clinicians concerned with rare inherited disorders. GeneDx offers sequencing and deletion/duplication testing for inherited cardiac disorders, mitochondrial disorders, neurological disorders, inherited cancer disorders, and other rare genetic disorders. GeneDx also offers whole exome sequencing, microarray-based testing, targeted mutation testing, and prenatal diagnostic services. At GeneDx, our technical services are matched by our scientific expertise and customer support. Our growing staff includes more than 100 geneticists and genetic counselors specializing in clinical genetics, molecular genetics, metabolic genetics, and cytogenetics who are just a phone call or email away. We invite you to visit our website www.genedx.com to learn more about us and the services we offer.

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