Understanding the genetics of Long QT syndrome

Long QT syndrome (LQTS) is a condition that affects the ability of the heart to beat correctly. At the end of one heart beat, the heart muscles have to re-set (repolarize) so an electrical signal can trigger the next heart beat. The time it takes the heart muscles to re-set is called the “QT interval”. In long QT syndrome the heart muscles take longer than usual to re-set for the next heart beat. Individuals with LQTS have a much higher chance to experience abnormal heart beats (cardiac arrhythmia).

Symptoms of long QT syndrome include:
- Palpitations (rapid heart beat)
- Fainting
- Seizure
- Cardiac arrest

These symptoms can occur during exercise, at rest, or as a result of being startled or stressed. In rare cases, an arrhythmia can lead to sudden death. Most deaths associated with LQTS can be prevented with early diagnosis and treatment.

How is long QT syndrome diagnosed?
LQTS is diagnosed by a doctor who reviews your medical history, asks about your family history, performs a physical exam, and orders an electrocardiogram (ECG), which measures the rhythm of your heart beat. There are specific findings on the ECG that lead to a diagnosis of long QT syndrome. Most people with LQTS have hearts that look and sound normal but have an ECG that shows abnormal electrical activity. Some people with LQTS have a normal ECG at rest, and only experience abnormal heart beats when exercising or taking certain medications.

What causes long QT syndrome?
LQTS is genetic, which means that it is caused by a change in a gene (gene mutation). Many different genes are known to cause LQTS. These genes are important in the function of the heart’s electrical system, which controls the rhythm of the heart beat. When there is a mutation in any one of the LQTS genes, the gene does not work correctly, sometimes causing an abnormal heart beat. Individuals with a gene mutation have it from birth and it cannot be corrected.

SCREENING FOR LONG QT SYNDROME
The main screening recommendation for those at risk for long QT syndrome is regular electrocardiogram (ECG or EKG) exams. The frequency of screening depends on your age and medical history.

Electrocardiogram (ECG) is a heart beat rhythm tracing. It records the electrical activity of your heart as it beats. An ECG can detect abnormal electrical signals, including differences in the QT interval. Normally an ECG is only done for a few minutes at a time.

Special ECGs may be done to test for irregular heart beats that may not be present all the time:
- A stress test is an ECG done while you exercise on a treadmill or stationary bike.
- A chemical or pharmacological stress test is an ECG done after taking a medication that makes the heart work harder.
- A Holter monitor is a portable form of EKG that records your heart beat for a much longer period of time. A Holter monitor is usually worn on the body for 24 to 48 hours.
How is long QT syndrome inherited?
The genes that cause LQTS can be passed from one family member to the next. In most families this condition is inherited in an autosomal dominant manner. This means that both men and women can have LQTS. It also means that if a person has a gene mutation that causes LQTS, there is a 50% chance to pass the gene mutation to each child.

How is a gene mutation identified?
A blood test can be done to look for mutations in a select group of LQTS genes. Hundreds of mutations in many different genes have been reported, but genetic testing is available for only some of these genes. Current genetic testing is able to find a mutation in about 70% of families suspected to have inherited LQTS. Genetic testing is most likely to be informative when your medical history and family history shows a clear diagnosis of LQTS. Your genetics consultation will help determine whether or not testing is appropriate.

What are the benefits of genetic testing?
Genetic testing for LQTS can be helpful in two ways: clinical management and identification of at risk family members. When a mutation is identified in a person with LQTS, cardiologists use that information to guide that person’s medical care and management. Additionally, once a mutation is identified in a person with LQTS, we can offer genetic testing to family members. Testing can determine if family members without cardiac symptoms are at increased risk to have this condition. LQTS often has no noticeable symptoms. Healthy individuals who carry a gene mutation can potentially lower the chance for serious heart problems by having regular cardiac screening. Relatives without the family mutation can be reassured that they are not at risk for heart problems related to LQTS.

What if genetic testing doesn't find a mutation?
Genetic testing is not always able to find a mutation. This may be due to limitations in the current testing methods or the mutation may not be on any of the genes included in the current testing panel. If the family history is suspicious for inherited LQTS, cardiac screening may still be recommended for family members, even when genetic testing is negative (no mutation is found).

Will I have heart problems if I inherit mutation for Long QT syndrome?
A person who inherits a LQTS mutation has a much higher chance than usual to develop long QT syndrome during his or her lifetime. However, some people who inherit a mutation have a normal heart beat and never develop any of the related heart symptoms. Regular cardiac screening is recommended for mutation carriers.

What happens if I develop Long QT syndrome?
Even when a long QT interval is found on ECG, many people never have severe heart problems and are able to live a normal life. However, some people with LQTS have symptoms from the abnormal heart beat, such as fainting, dizziness, fatigue, and heart palpitations. Less often the irregular heart rhythm caused by LQTS can lead to sudden cardiac death. Treatment is available to minimize or prevent symptoms and reduce the risk of complications. Treatment includes regular follow-up, lifestyle changes, medications, and surgical procedures, as needed.