We provide this information with the hope that informing physicians, other health care providers, and the public will encourage early and correct diagnosis and proper therapy, resulting in the reduction and ultimately elimination of cardiac arrest and sudden death from inherited LQTS.

Why do I need to know about the Inherited Long QT syndrome?

We estimate as many as 2-3,000 children and young adults die each year in the United States due to LQTS. Now, because of early diagnosis and treatment, those deaths may be decreasing. Still, this condition is often undetected prior to death and not recognized as the cause of death. Family members of individuals with unexplained death should be evaluated for LQTS and other genetic arrhythmias. LQTS is a treatable disorder and, with correct diagnosis and common treatments, most deaths are preventable.

Physicians need to know:
- When to consider LQTS as a possible diagnosis.
- When to refer patients for diagnosis & treatment.
- How to develop a family pedigree and screen family members for LQTS.

Patients need to know:
- The signs and symptoms of LQTS.
- Who to see for proper evaluation.
- How to protect themselves.
- When to contact other family members regarding a diagnosis of LQTS in the family.

What is LQTS?

LQTS is a disturbance of the heart’s electrical system. It is caused by abnormalities of microscopic pores, or holes, in the heart cells called ion channels. Ions such as potassium, sodium, calcium and chloride pass back and forth across the cell membrane through ion channels. As they do, they generate the electrical activity that controls the heart’s beating. These electrical signals are recorded on the body as the electrocardiogram (EKG or ECG). Potassium and sodium ion channels are two of the sites affected in LQTS. The abnormal channels prolong the repolarization process and the QT interval, thus predisposing patients to certain cardiac arrhythmias.

What is the QT interval?

The QT is a time interval on an ECG. It represents the time from the electrical stimulation (depolarization) of the heart’s pumping chambers (ventricles), to the end of the recharging of the electrical system (repolarization). It is measured in seconds and closely approximates the time from the beginning of the ventricles contraction until the end of relaxation.

The QT interval varies in each person and between persons—like most physiologic parameters, such as blood pressure or heart rate. In particular, the QT varies with the heart rate. It shortens as the rate increases and lengthens as the rate decreases. Therefore, there is no single QT interval that is normal or abnormal.

To determine if a given QT is normal for a given heart rate, the QT is corrected for the heart rate using a simple mathematical formula, and the resultant quantity is called the QTc. The QTc is the value that doctors generally use when assessing for LQTS.

The normal QTc interval varies from 0.35 to 0.46 seconds (350-460 milliseconds). About 95% of people have a value between 0.38 and 0.44 seconds, which is the range doctors generally consider as the normal range. The diagram below provides an example of a normal and a prolonged QTc interval. The RR interval determines the heart rate.

I n this diagram, since the heart rate (RR) is the same for both examples but the QT interval is longer for the lower panel, the QTc is larger in the lower panel example.

What are the symptoms of LQTS?

Sudden, temporary, loss of consciousness (syncope) is the most common event. About 1/2 of LQTS patients never experience syncpe. Others have one or many syncopal events or cardiac arrest possibly resulting in sudden death. These events usually occur without warning. They are caused by a very fast cardiac arrhythmia known as torsade de points. Typically, the onset of symptoms is earlier in boys than in girls. Events may occur in the twenties, not often in the thirties, and rarely past 40 years of age. When events do occur later, QT prolonging drugs and low potassium are often the cause.

In patients who experience syncope or the same type of rhythm spontaneously returns to normal, usually within about one minute, and the patient quickly regains consciousness, without disorientation or confusion. Some patients experience fatigue afterwards, others feel fine and resume their regular activities. On the other hand, in a minority of patients, the torsade rhythm persists, then degenerates into the heart rhythm known as ventricular fibrillation, which rarely reverts back to a normal rhythm without medical intervention. If the ventricular fibrillation is not converted, usually by electrical defibrillation, the outcome is death.

When should the diagnosis be suspected?

In any young person with unexplained syncope (fainting), cardiac arrest or sudden death.

Usually, a careful history of the events surrounding the syncpe differentiates LQTS induced syncope from the common faint, known as vasovagal or neurocardiogenic syncope. The LQTS syncope is usually precipitous and without warning. In other words, during or just after physical exertion, emotional excitement or sudden auditory arousal (such as a doorbell or alarm clock), but may occur during sleep or at rest. Conversely, in vasovagal syncope, most times there are warning symptoms, such as dizziness, blurring or blackening of vision, tingling or sweating, for seconds to even minutes prior to the syncope. Also, a precipitating event is usually present, commonly pain, injury, nausea, or an unpleasant or stressful experience.

When there is a family history of unexplained syncope or sudden death.

As noted above, about one-half of LQTS patients never exhibit symptoms, and, therefore the lack of prior symptoms does not exclude a person or family from having LQTS.

How is the diagnosis made?

LQTS is diagnosed primarily upon recognition of a prolonged QTc interval on the ECG. A QTc of .47 seconds in males and .48 seconds in females appears to be diagnostic of LQTS, in the absence of QT prolonging medications or other forms of heart disease. A QTc of less than .40 in males and .41 in females makes the diagnosis unlikely. The computer generated QTc may be incorrect. So when the diagnosis of LQTS is considered, the physician should verify (hand measure) the computer measurement. Not all LQTS patients have a prolonged QTc on the initial ECG, however. About 12% have a normal QTc of .44 seconds or less, and about 30% have a QTc between .40 and .46 seconds, values which many normal persons have as well. QTcs in the range of 0.41 to 0.46 seconds are, therefore, inconclusive and must be clarified by additional testing. An exercise ECG is the most effective way to clarify these situations. The exercise test is preferably a low level, somewhat protracted exercise test, which allows the individual to exercise for 10 or more minutes without reaching a heart rate in excess of 150-160 beats per minute. A Holter ECG will often assist in clarifying the diagnosis as well. The principal abnormality to be identified during these tests is a prolonged QTc interval. Certain T wave abnormalities occurring during these tests also support the diagnosis of LQTS. Values indicative of LQTS are higher for the Holter test than for the exercise ECG and we use a QTc of .50 or higher on the Holter in order to suspect LQTS.

How is LQTS inherited and which family members should be tested?

LQTS is usually inherited by autosomal dominant transmission. This means that it affects boys and girls equally, and that each child of an affected parent has a 50% chance of inheriting the gene. In a really large family, close to 50% of the children would inherit the gene. In average-sized families it can range from all to none as each child has an independent 50:50 chance of inheriting the gene. Once a family member is identified with LQTS, it is extremely important that other family members know of the diagnosis and the need for screening and possible treatment.
members be tested for the syndrome. It is especially important to know which parent and grandparent has the abnormality, since brothers and sisters, aunts, uncles, nephews, nieces, and cousins on the affected side are potentially at risk.

This prospective screening, by ECG, is extremely important so all affected family members are identified and treated early in order to prevent the tragic and unnecessary sudden deaths that may occur.

What about genetic testing?

Genetic testing is now available as a routine diagnostic test for LQTS—called FAMILION. It tests the five primary genes (over 200 mutations have been found to date) and will find a mutation in 75% of those with Long QT Syndrome who are tested.

Your physician will order the initial test on one family member. Once a family member has a gene mutation identified, testing of other family members for that mutation is also available, and can assist in evaluating other family members with LQTS.

What is the treatment and who should be treated?

All symptomatic patients should receive treatment. All asymptomatic (no symptoms) children and young adults should be treated as well, because some will become symptomatic and sudden death may be the first symptom. At present, it is not possible to tell which child or youth is destined to have symptoms. Thus, preventative treatment is required in all. The usual treatment is beta-blocker medications and these are effective in about 90% of LQT5 patients. The dose needs to be adjusted for each patient, the end point being the relief of symptoms or correction of the exercise induced QT abnormalities. Any patients who continue to have symptoms in spite of appropriate doses of beta-blockers may also require additional medications or devices.

For persons over 40 years of age at the time of diagnosis, who have been asymptomatic all their life (or for many, many years), it may not be necessary to treat them, as their risk of developing symptoms at these later ages is very low. They do, however, need to avoid low blood potassium (caused by diuretic drug use, vomiting or diarrhea) and drugs which lengthen the QT interval which can cause LQTS. For a complete list of drugs that prolong the QTc interval and/or induce torsade de pointes, visit www.sads.org or www.torsade.org.

Medication compliance

It is very important that medication be taken every day and not missed or omitted. The medications are not curative; they only provide protection while being taken and the protecting effect is gone within a day or two of stopping the medication. After that the risk of cardiac events is the same as if the patient had not taken the medication at all. Parents should teach their children about the importance of daily medication and should make sure each daily dose is taken. Physicians need to discuss this directly with all patients, but particularly pre-teens and teenagers. The most common reason for cardiac events while on medication is that the medication has been missed or stopped.

How can parents protect their kids?

Make sure the children take their medication daily, no misses.

See the doctor regularly for follow-up. Growing children need medication dose changes regularly.

Be supportive when the doctor advises no competitive sports for your child. Support this advice, and help the child to understand that usual physical activities are suitable, but that competition may be dangerous. Channel their energies into sports without intense physical demands (golf, for example), or non-physical activities.

Get additional medical advice if you are not comfortable with how things are going. Consult a cardiologist, a cardiac electrophysiologist (rhythm specialist) particularly, or get a second opinion if you have any questions about your child’s treatment.

Have children avoid caffeine and over-the-counter drugs that prolong the QTc interval which can cause LQTS. For a complete list of drugs that prolong the QTc interval and/or induce torsade de pointes, visit www.sads.org or www.torsade.org.