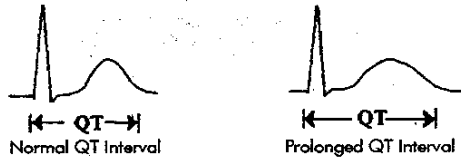


## WHAT IS THE LONG QT SYNDROME?

The inherited long QT syndrome (LQTS) is a genetic abnormality of the heart electrical system due to defects in cardiac ion channels.

These electrical defects predispose affected persons to a very fast heart rhythm (arrhythmia) called torsade de pointes which, at times leads to sudden loss of consciousness (syncope) and, in some cases sudden cardiac death. QT refers to a time interval measured on the electrocardiogram (ECG). The figure below shows the difference between a normal and an LQTS ECG.



The syndrome may be inherited (the generic form) or acquired.

**INHERITED:** There are two variants of LQTS. The Romano-Ward syndrome with normal hearing and the Jervell, Lange-Nielson syndrome which is associated with congenital deafness.

**ACQUIRED:** Acquired LQT is most often due to the administration of medications. These medications are contraindicated in patients with the long QT syndrome, and a subsequent section will identify these drugs.

## HOW COMMON IS LQTS?

The frequency is unknown but it appears to be a common cause of sudden and unexplained death in children and young adults. It is certainly much more common than previously thought. It may be as frequent as 1 in 5,000.

The Jervell, Lange-Nielson form is rare, but the Romano-Ward variant is being recognised with increasing frequency.

## WHAT ARE THE SYMPTOMS?

The usual symptoms are syncope or sudden death, typically occurring during physical activity or emotional upset. These most commonly begin in pre-teen to teen-age years, but may present from a few days of life to middle age. The syncopal episodes are often misdiagnosed as the common faint (vasovagal event) or a seizure. The syncope and sudden death usually occur during physical exertion or emotional upset, but may occur during sleep. A family history of unexplained syncope or sudden death in young people should raise suspicion of LQTS. **Importantly, about one third of individuals who have the long QT syndrome never exhibit symptoms, and therefore, the lack of symptoms does not exclude a person or family from having LQTS. Any young person that has an unexplained cardiac arrest should be considered for LQTS, as well as those with unexplained syncope.**

## COMMON TRIGGERS OR SYMPTOMS:

Swimming, running or startling from an alarm clock may trigger a symptom as well as a loud horn, or a ringing telephone. A symptom may also be precipitated by emotional stresses such as anger, crying or test taking.

## HOW IS THE SYNDROME DIAGNOSED?

The diagnosis is commonly suspected by the occurrence of syncope, cardiac arrest or sudden death in a young person. The diagnosis may be suspected or confirmed from an ECG. All children and young adults with unexplained syncope should have an ECG as part of their evaluation. It may be necessary to request the ECG be done. In about 12% of LQTS patients the QT interval on the initial ECG is normal, and in about 40% the QT interval is borderline- not prolonged enough to clearly make the diagnosis. In these cases, an exercise ECG or "holter" ECG will usually assist in clarifying the diagnosis. 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 much in excess of 150-160 beats per minute. The principal abnormality to be identified is a prolonged QT interval relative to the heart rate, and the appearance of abnormal T-waves. Genetic testing will likely become the primary means for diagnosing LQTS in the future. It is available now on a limited basis in certain research laboratories. A negative result does not exclude LQTS since not all of the genes have been identified.

## HOW IS THE SYNDROME INHERITED?

It is inherited by autosomal dominant transmission. This means that it affects boys and girls equally, and that each child of an affected parent has an independent 50/50 chance of inheriting the gene and having LQTS. The Jervell, Lange-Nielson syndrome occurs when both parents have an abnormal gene and a child receives the abnormal gene from each parent, thus they receive a "double dose". Those children who receive one normal gene and one abnormal gene have Romano-Ward syndrome. It is extremely important that all members of the family, including the extended family, be tested for LQTS once a family member is identified with the syndrome. (See Pedigree). All affected persons must be identified and treated early in order to prevent the tragic and unnecessary sudden deaths that may occur.

## GENETICS OF THE LONG QT SYNDROME.

**LQT 1:** This gene KVLQT1, on chromosome 11 encodes potassium channel proteins.

**LQT 2:** The HERG gene, on chromosome 7 also encodes potassium channel proteins.

**LQT 3:** SCN5A, located on chromosome 3 encodes a sodium channel gene.

**LQT 4:** A fourth locus was mapped to chromosome 4q 25-27.

**LQT 5:** A fifth locus is associated to the KCNE 1 gene.

**LQT 6:** The LQT 6 gene was identified on chromosome 21, by Abbott GW, et al, Cell 1999; 97 175-187. It was named MiRP 1 for Min K related protein 1. It resides next to LQT 5 (min K gene). MiRP 1 is a small protein, which coassembles with HERG (LQT 2) gene to form the 1Kr potassium channel. Three mutations of this gene were described.

## WHAT IS THE TREATMENT?

Beta blocker medication is the mainstay of therapy for most patients with LQTS. These medications are effective in about 80-90% of affected subjects. New information regarding the genetics of LQTS suggests that a subset of patients might be treated with other drugs, either instead of or in addition to, the beta blocker medication. This can be discussed with your physician and it depends upon the gene type which you have.

In patients who do not respond to medication, the insertion of a pacemaker or the automatic defibrillator, or the surgical cutting of certain nerves in the neck, called cervico-thoracic sympathectomy, can be utilised. All patients with symptoms should be treated. Because it is not possible which asymptomatic patients are vulnerable to subsequent syncope and sudden death, and because sudden death may be the first manifestation of the syndrome, we believe asymptomatic, especially children should also be treated.

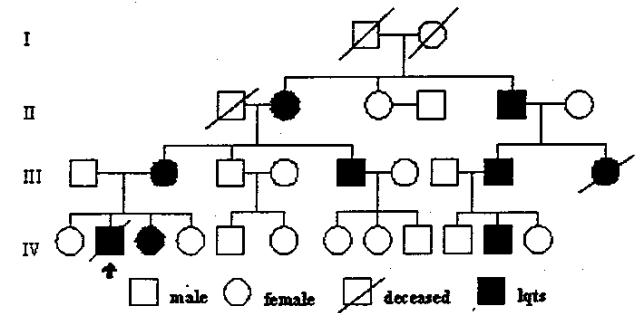
## SHOULD ACTIVITY BE RESTRICTED?

Because the symptoms are often precipitated by physical exertion or emotional upset, it is appropriate to restrict physical activity in symptomatic individuals and reasonable even in those without symptoms. For most, this only requires refraining from competitive and vigorous sports. Recreational activities are often allowable. In individuals with continued symptoms, further restriction of activity may be necessary. Individualised evaluation by a physician based upon past symptoms, ECG findings and medication is appropriate in regards to activity levels and possible restrictions.

## WHAT ABOUT PREGNANCY AND SURGERY?

Although labor and delivery and surgical procedures are stressful and physically exerting events, it is uncommon for LQTS patients to experience symptoms during these times. It is important to be sure that blood potassium is maintained because it may be reduced if diuretic (water) medications are used or if there is sweating, vomiting or diarrhea. Potassium supplementation may be necessary during these times.

## EXAMPLE OF LQTS PEDIGREE.



## DRUGS THAT PROLONG THE QT INTERVAL AND /OR INDUCE TORSADE DE POINTES.

There are a number of drugs which are known to prolong the QT interval and/or induce torsades de pointes, particularly in patients with LQTS. You should always inquire of your physician or other health care provider about the risk of any medication suggested or prescribed for you. Always inform them of your LQTS and make sure they know there are many medications which are contraindicated in this condition.

The following table is a listing of drugs that prolong the QT interval and/or induce torsades de pointes.

Drug (Brand Names)	Drug Class ( Clinical Usage)
Adrenaline (Epinephrine®)	Anesthetic and asthma
Amiodarone (Cordarone®)	Antiarrhythmic (heart rhythm)
Amitriptyline (Elavil®, Endep®) others)	Antidepressant (depression, pain, others)
Amoxapine (Asendin®)	Antidepressant (depression, pain, others)
Ampicillin (Omnipen® Principen®, Polycillin®)	Antibiotic
Astemizole (Hismanal®)	Antihistamine (allergy)
Bepidil (Vascor®)	Antianginal (heart pain)
Chlorpromazine (Thorazine®)	Mental illness & nausea/vomiting
Cisapride (Propulsid®)	Stimulates intestinal motility
Clemastine (Tavist®)	Antihistamine
Clomipramine (Anafranil®)	Mental illness
Desipramine (Norpramin®)	Antidepressant (depression and others)
Diphenhydramine (Benadryl®)	Antihistamine
Disopyramide (Norpace)	Antiarrhythmic (heart rhythm)
Doxepin (Sinequan® Zonalon®)	Antidepressant (depression, pain, and others)
Erythromycin (Akne-Mycin®, E.E.S®, EryDerm®, Ergel®, Ery-Tab®, Erythrocin®, Erythromycin Base Filmstab®, Erythrostatin®, Iliotycin®, PCE®, Statin®)	Antibiotic and intestinal stimulant
Flecainide (Tambacor®)	Antiarrhythmic
Fludrocortisone (Florinf®)	Maintain blood pressure/retain sodium
Fluphenazine (Prolixin®)	Mental illness, Parkinson's Disease
Haloperidol (Haldol®)	Mental illness, agitation
Ibutilide (Corvert®)	Antiarrhythmic
Imipramine (Tofranil®)	Antidepressant (depression, pain others)
Indapamide (Lozol®)	Diuretic (stimulates water and salt loss)
Ipecac	Stimulates vomiting in poisoning
Maprotiline (Ludiomil®)	Antidepressant (depression)
Moricizine (Ethmozine®)	Antiarrhythmic
Nortriptyline (pamelor®)	Antidepressant (depression and others)
Pentamidine (Pantacarinat®, Pentam®, NebuPent®)	Antiinfective (pneumonia and others)

Drug (Brand Names)	Drug Class ( Clinical Usage)
Perphenazine (Trilafon®)	Mental illness
Pimozide (Orap®)	Tourette's Syndrome, seizures
Probucol (Lorelca®)	Lowers cholesterol
Procainamide (Procan®, Procanbid®, Pronestyl®)	Antiarrhythmic
Prochlorperazine (Compazine®)	Nausea
Protriptyline (Vivacil®)	Antidepressant (depression)
Quinidine (Cardioquin®, Duraquin®, Quinidex®, Quinaglute®)	Antiarrhythmic
Risperidone (Risperdal®)	Mental illness
Sotalol (Betapace®)	Antiarrhythmic
Tamoxifen (Nolvadex®)	Breast cancer treatment
Terfenadine (Seldane®)	Antihistamine (allergy)
Thioridazine (Mellaril®)	Mental illness
Thiothixene (Navane®)	Mental illness
Tocainide (Tonocard®)	Antiarrhythmic
Trifluoperazine (Stelazine®)	Mental illness
Trimethoprim Sulfamethoxazole (Bactrim®, Septra®)	Antibiotic



The Australian SADS Foundation is pleased to provide information about the long QT syndrome.

For further information about the long QT syndrome, please access our website at

[www.sads.org.au](http://www.sads.org.au)

or Email: [sadsau@optushome.com.au](mailto:sadsau@optushome.com.au)

**Australian Sudden Arrhythmia Death  
Syndromes Foundation (SADS)**

P.O. BOX 19  
NOBLE PARK, VIC. 3174

# The Long QT Syndrome

An information pamphlet for  
Patients, families and physicians



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