Long QT Syndrome - Information for Families

Background
Long QT syndrome (LQTS) is an uncommon hereditary disorder characterised by abnormal electrical activity in the heart. It affects mostly children and young adults with frequent faints or even sudden death. The most common form of LQTS is inherited in a dominant pattern, which means that each child of an affected parent has a 50% chance of inheriting the disorder. Once a diagnosis is made, treatment is available. However, an accurate diagnosis can be difficult, because not all people affected by LQTS become ill and display symptoms.

Usually, LQTS can be seen on an electrocardiogram (ECG). Every heart beat is triggered by an electrical signal that tells the heart’s muscle cells to contract. After contracting, these cells must recover – or relax – before the next heart beat is initiated. The amount of time needed by these cells to recover can be measured on an ECG and this is called the QT interval. During the last part of this interval, the heart is vulnerable and electrically unstable. People with LQTS have an abnormally long QT interval. If the next electrical signal arrives before the muscle cells have completed their recovery period a dangerously fast heart rate can occur leading to a fall in blood pressure and loss of consciousness.

Schematic diagram of the electrical activity of one heart beat recorded by an ECG. The electrical discharge (depolarization) of the ventricle is represented by the QRS complex, with the T wave reflecting electrical recovery (repolarization). The QT interval, corrected for heart rate at the time, is the time interval from the beginning of the QRS complex to the end of the T wave, and is generally less than 0.46 seconds in males and 0.47 in females.

In subjects with the long-QT syndrome, the QT is usually longer than these values. There is considerable overlap between those with and those without long QT syndrome, and they change with time so repeated ECGs may be needed.
LONG QT SYNDROME

People with LQTS are sometimes identified after an unexplained fainting episode. These episodes are usually associated with surges of adrenaline, such as with sudden loud noises, intense emotional reactions, awakening from sleep or during intense physical activity, especially swimming. Events may result in seizures which are commonly misdiagnosed as epilepsy, especially when they occur at night. Currently, the primary treatment for LQTS is a beta blocker medication, which inhibits the effects of adrenaline on the heart. Some patients (not the majority) may benefit from pacemakers or implantable defibrillators or surgical resection of a group of nerves connecting the brain and the heart. Everyone with LQTS should avoid medications which are known to prolong the QT interval. A constantly updated list is available on http://www.azcert.org/medical-pros/drug-lists/drug-lists.cfm.

Research
Scientific breakthroughs – including the discovery of ten groups of genes that cause LQTS – may soon lead to better therapies and ultimately a cure. It seems likely that different forms of LQTS, caused by the different genes, may benefit from “gene-specific” therapies yet to be developed. We already know that some types of LQTS respond better to beta blocker medication than others. Much of the current research into LQTS aims to improve the reliability of the tests we use to make the diagnosis – some people who carry the abnormal genes can have a normal QT interval on the routine ECG. Exercise tests and 24 hour ECG monitoring show considerable promise and are already useful clinically. It is likely your physician may request either or both of these during evaluation of your family. Other research is at a molecular level – identifying the gene defects and the effects these have on the heart muscle cells. Only about 70% of affected families will have a gene defect which has thus far been identified.

Screening family members
Since the gene runs in families, screening of family members is very important, yet this is complex and time consuming. Not only are the tests difficult to interpret, but the family members may be spread across New Zealand and the rest of the world. Centralised registries – such CIDG (Cardiac Inherited Disease Group, www.cidg.org) in New Zealand – are vital. These help achieve successful family screening programmes, and allow dissemination of new information to affected family members and their clinicians. They also permit useful research studies into this uncommon yet widespread disease.

Other sources of information
There are a number of physicians in New Zealand who have a special interest in the management of families with long QT syndrome and some of these are listed below. There are many web sites to visit, of varying quality. A good start is www.SADS.org and www.cidg.org.

National Long QT Registry in New Zealand:
A registry is based in Auckland co-ordinated by Jackie Crawford (Senior Cardiac Technician) and Dr Jon Skinner as part of the inherited cardiac disease service. A molecular diagnostic service is available via labplus Auckland, with all tests being referred via CIDG. A research programme is based at Auckland University (Associate Professor Andrew Shelling).
LONG QT SYNDROME

Genetic diagnosis:
Your supervising physician, after obtaining formal informed consent from yourself, often with the assistance of a genetic counsellor, will send your blood for genetic testing to the place that seems most appropriate for your case at that time.

The importance of the genetic test is two-fold. A genetic diagnosis can be found in about 70%
1). It defines the sub-type of Long QT syndrome, so treatment and advice can be adjusted appropriately
2). It enables screen of family members to see who may be at risk, and if they could pass it on to their children.

There are three common types
Type 1 and 2 respond well to betablocker treatment, because the triggers for type 1 (60%) is exercise; swimming is especially dangerous. For type 2 (30%) the commonest triggers are sudden and loud noise (especially at night), and emotional excitement; women tend to be at higher risk. In type 3 (10%) events usually occur at night, men tend to be at higher risk, and defibrillator pacemakers are most commonly needed in this group in whom beta blocker treatment is of doubtful benefit.
LONG QT SYNDROME

Medications to be avoided, or requiring special caution, in people with Long QT syndrome.

This list includes medications which prolong the QT interval and is meant as a guide for people with Long QT syndrome, or acquired long QT interval from heart muscle disease, and their parents or guardians. It should not be seen as all inclusive. Those prescribing any medication to someone with Long QT syndrome should always check the drug specifications and contra-indications. The list has been compiled by review of publications and/or drug advice sheets provided with medications. Check also www.SADS.org and www.azcert.org/medical-pros/drug-lists/drug-lists.cfm.

Antibiotics
Erythromycin, Clarithromycin, Gatifloxacin, levofloxacin, Moxifloxacin
Sulfamethoxazole-trimethoprim (Septrin/Bactrim), Spiramycin, Pentamidine

Antihistamines
Terfenadine, Astemizole, Diphenhydramine,
(These are particularly to be avoided (even in normal subjects) in combination with Erythromycin or grapefruit juice or the antifungals ketoconazole, miconazole, fluconazole or itraconazole)
[Antihistamines that may be used safely are loratidine, cetirizine and fexofenadine, and phenergan]

Appetite suppressants
Fenfluramine, phentermine, Sibutramine

Asthma treatments
The Beta-2 agonists (eg. Terbutaline, Salbutamol, Salmeterol) both work against the B-Blockers given to subjects with long QT and lower blood potassium levels and therefore should be given only in hospital with careful monitoring. Inhaled steroids (eg. Becotide/Flixotide) and Ipatropium (Atrovent) are safer.

Decongestants
Ephedrine, phenylephrine, phenylpropanolamine, pseudoephedrine

Psychotropics/ Antidepressants/ Anticonvulsants
• Antipsychotics (including Thoridazine, Haloperidol Mesoridazine, chlorpromazine)
• Antidepressants (including Maptiline, Amitriptyline, imipramine, fluoxetine, desipramine, paroxetine)
• Anticonvulsants (Felbamate and Fosphenytoin are to be avoided).

Vasodilators
(used to dilate blood vessels in treatment of heart failure angina or high blood pressure)
Prenylamine Lidoflazine, Fenoxedil, Bepridil

Antiarrhythmics
(Pure Beta Blockers are safe! (eg Nadolol, Propranolol, Atenolol))
The others are not safe eg.
• Type IA Quinidine (particularly dangerous), Procainamide, Disopyramide
• Type IC Encainide, Flecainide
• Type III Ibutilide, Amiodarone, Sotalol, Sematilide
Long QT Syndrome

Liquorice
This lowers potassium level even in small doses, and is dangerous in big doses (more than one liquorice twist) or over long periods. Is present as Glycyrrhizinic acid (GZA), found in many sweets including; Stimorol and Ben Bits Coolmint chewing gum, Fisherman’s Friend, turkish Pepper and herbal medicines for gastric ulcer treatments. Drinks include Belgian beers, Pastis, Raki, Ouzo and Pernod.

Miscellaneous
Adrenaline (epinephrine)
Amantadine (antiviral and Parkinson’s disease agent)
Chloral hydrate (sedative)
Corticosteroids
Diuretics (via electrolyte disturbance-low potassium, magnesium, calcium: Frusemide and other loop diuretics particularly dangerous)
Chloroquine (antimalarial)
Cocaine
Dopamine
Dobutamine (used in intensive care)
Dolasetron (anti-emetic)
Droperidol (sedative)
Foscarnet (antiviral)
Halofantrine (antimalarial)
Isoproterenol (adrenaline like substance)
Levomethadyl (narcotic dependance)
Midodrine (to treat low blood pressure)
Suxamethonium and Atropine (anaesthetic agents)
Ritodrine
Vasopressin
Cisapride (for oesophageal reflux- indigestion)
Tacrolimus (to suppress immune responses)
Liquid protein diets.

Your dentist should use local anaesthetic WITHOUT ADRENALIN.