

Australian Genetic Heart Disease Registry Information Sheet

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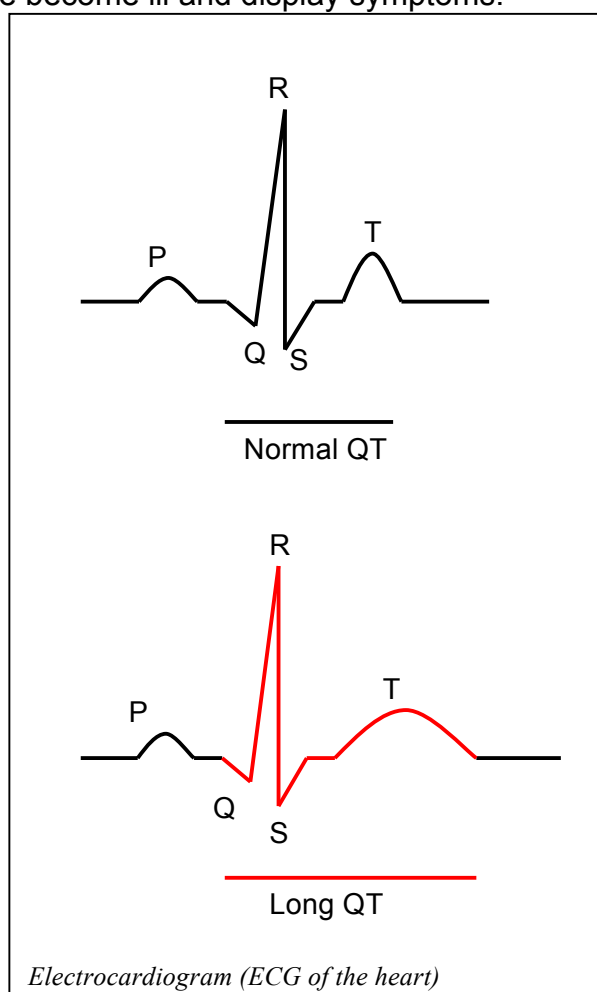
Long QT Syndrome (LQTS)

What is long QT syndrome?

Long QT syndrome is characterised by abnormal electrical activity in the heart. It affects mostly children and young adults causing frequent faints or collapse sometimes resulting in sudden death. Once a diagnosis is made, treatment is available. However, an accurate diagnosis can be difficult, because not all people affected by long QT syndrome become ill and display symptoms.

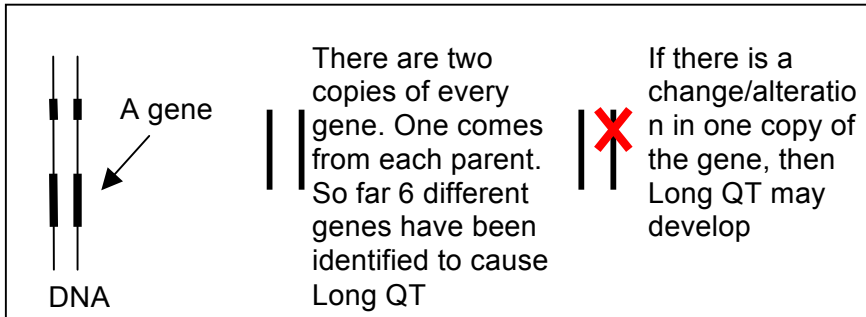
Usually, long QT syndrome can be seen on an electrocardiogram (ECG). Every heartbeat is triggered by an electrical signal that tells the heart's muscle cells to contract. This electrical signal is divided up into 5 parts (labelled P - T). After contracting, the heart muscle cells must recover – or relax – before the next heartbeat is initiated. The amount of time these cells need 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 long QT syndrome 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.

People with long QT syndrome 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. As some medications can further prolong the QT interval or increase the risk of an abnormal fast heart rhythm, patients with long QT syndrome must avoid certain medications. All patients with suspected or confirmed long QT syndrome should be familiar with the full list of drugs that must be avoided. This list is available at: <http://www.qtdrugs.org>



What causes Long QT syndrome?

Our body is made up of millions of cells. There are many different types of cells, including brain cells, liver cells and heart cells to name a few. Each cell contains 46 chromosomes, which hold the genetic material that decides features such as the colour of our eyes and whether we are tall or short. These 46 chromosomes are grouped into 23 pairs, one of each pair coming from mum and the other from dad. One of these pairs is known as the sex chromosomes, and these decide whether we are male or female.



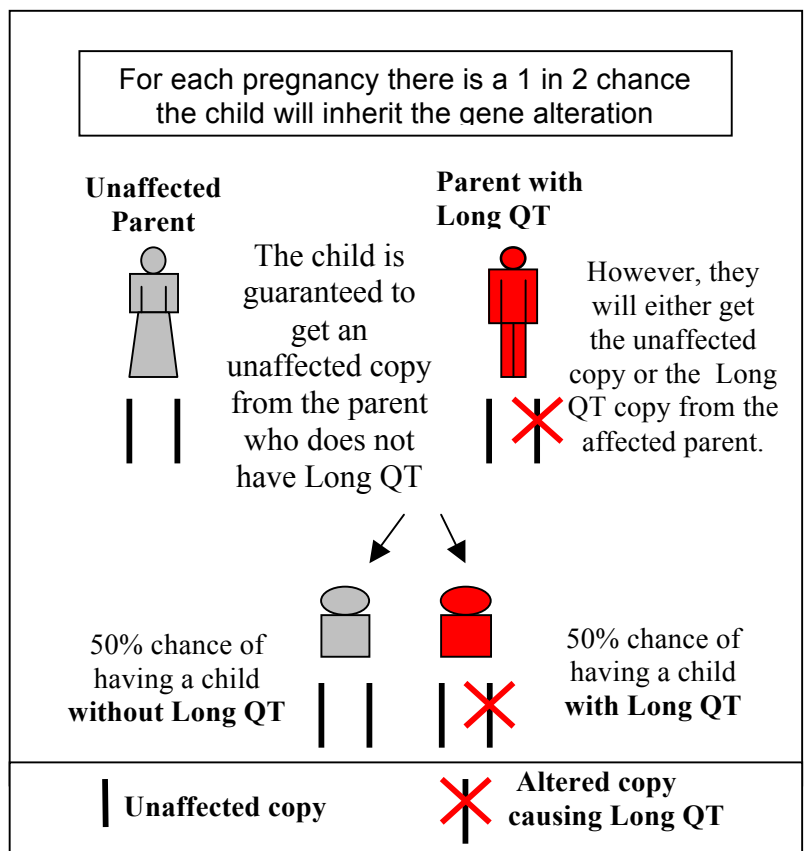
If you imagine a chromosome as being like a ball of wool, you could stretch it out into one long strand, which is known as the DNA. Along the length of DNA there are regions called genes. As there are two copies of every chromosome, there are also two copies of every gene (as

mentioned, one from each parent). Genes act as recipes to make certain things in the body, and each recipe is unique based on the order of units it is made up of. If there is a mistake in one of these genes (a mix-up in the order of these units) it may lead to the development of disease. This mistake is known as a gene alteration.

In the case of long QT we know of alterations in at least 6 genes that can cause the condition. If there is an alteration in one of these genes long QT syndrome may result. The genes involved in Long QT syndrome are all different types of ion channels that transport ions in and out of cells to help the cell contract. A gene alteration can alter the channel so it is not as efficient or too efficient at its job.

How is long QT inherited?

Long QT is known as an autosomal dominant condition, whereby the gene with the alteration “dominates” over the unaffected gene, causing the condition. This means that an affected person has inherited one altered long QT copy of the gene from one parent, and one unaffected copy from the other parent. Likewise, if a person who carries this long QT copy of the gene has a child, then **the chance that the child will be affected is 50%, or 1 in 2**. This is because they are guaranteed to get an unaffected copy of the gene from the unaffected parent, and they can either get an altered (long QT) copy or an unaffected copy from the parent with the condition. This is illustrated in the diagram.



Is it possible to have an LQTS gene that's not inherited?

On rare occasions, a person may have a gene alteration that has not been inherited from their parents. Instead, the alteration has arisen some time after conception. This means that their brothers and sisters are not likely to develop the condition, however the gene alteration can still be passed down to any children of the affected person.

What is genetic testing?

Genetic testing involves looking for the alteration in the genes known to cause long QT syndrome. It is a long and difficult task that has been likened to looking for a single spelling mistake in an encyclopaedia set. This is because most families have their own unique gene alteration that may exist in one of the genes we have already identified, or even in a gene not yet discovered to be involved in this condition. A genetic result may take more than 6 months. In an individual with long QT syndrome, when they look for the gene alteration in the 6 most common long QT genes, they find the gene alteration that causes this condition in about 75% of families.

If genetic testing does not reveal a gene alteration then we call it an inconclusive test result. This means that a gene alteration most likely exists, but either our current technology is not yet good enough to detect the alteration, or the alteration is in a gene which has not yet been identified.

Once the gene alteration is identified in the affected person we can then offer a gene test to other family members. This test takes 4-6 weeks for a result, and will quickly determine if the individual has inherited the long QT copy or the unaffected copy of the gene. This is called preclinical genetic testing, and allows a person to know if they are likely to develop the condition even before symptoms are present. If they do not carry the gene alteration then we can say that they will not develop long QT, and future ECG's are not necessary. If they are shown to have the long QT gene alteration then there is a good chance they will develop the condition, and close follow-up would be recommended.

Genetic testing of the known long QT genes is a commercial test. This means that there is a cost involved for the patient and testing needs to be organised on their behalf by a doctor. If you would like to know more about centres offering commercial genetic testing, please look at our Information Sheet on Cardiac Genetic Services, contact the Registry Coordinator on registry@centenary.org.au or (02) 9565 6185 or speak to your regular cardiologist or doctor.

Genetic testing can affect applications for life insurance. If you would like to more please visit the Financial Services Council website at www.fsc.org.au for current guidelines (go to the Search bar and type in "Genetic") or call (02) 9299 3022.

Will a diagnosis of long QT change my lifestyle?

There are key recommendations that we advise people about when they are diagnosed with this condition. These guidelines help to reduce the risk of the most devastating outcome – sudden cardiac death.

- **Avoid competitive and strenuous sports:** Competitive sports include those that require significant exertion, for example: Touch football, Basketball, Netball, Squash, running and even social games that you may not think are too strenuous. We recommend people avoid competitive sports because it has been observed that a large proportion of the young people who die suddenly due to long QT, die during or just after exercise.
- **Avoid drugs that might prolong the QT interval** and therefore worsen disease. This list of drugs to avoid can be found at: <http://www.qtdrugs.org>
- **Regular light exercise:** Although there is a lot of emphasis on avoiding sport, it is still important to maintain a healthy lifestyle. Regular light exercise such as walking is not only good for your heart, but also good for your general health.
- **Regular check-ups with your cardiologist:** It is important to monitor the progression of the disease, and you should also report any new symptoms. This is because we use many different factors to determine whether you are at an increased risk of sudden death. Your risk of sudden death determines what mode of treatment will most benefit you.
- **Surgical procedures:** You should inform the attending doctor of your condition before any surgical/dental procedures.
- **Consult with your GP or cardiologist before taking any new medications:** It is important to talk to your doctor before taking any new medications, including over-the-counter (OTC) medications, complementary medicines, natural products and herbal remedies. Some drugs can prolong your QT interval and these should be avoided. A list is available at www.qtdrugs.org
- **Encourage relatives to be screened:** As mentioned, siblings and children of an affected person have a 1 in 2 (50%) chance of being affected. Screening of relatives involves them seeing a cardiologist where they will have a physical examination and an ECG. The relative needs to inform the doctor that there is a family history of long QT syndrome to ensure no signs are missed. Find a specialist cardiac genetic service, like the Genetic Heart Disease Clinics held at the Sydney Heart Centre at RPAH (tel 02 9517 2011). To find your local Cardiac Genetic Service please see our Information Sheet on Cardiac Genetic Services or speak to your regular cardiologist about organising screening for family members.

Contacts:

If you have any further questions, please contact:

Your local GP or cardiologist

Your local Genetic Cardiac Service (see our Information Sheet on Genetic Cardiac Services)

Australian Genetic Heart Disease Registry

www.heartregistry.org.au

Tel: 02 9565 6185 or registry@centenary.org.au