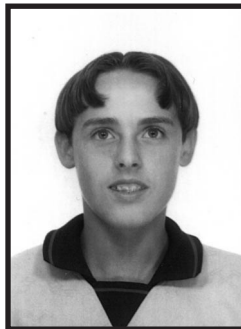


A child, young person, or adult under 65 may be at risk from sudden cardiac death due to an underlying heart condition. He or she will appear healthy and, in many cases, you will have absolutely no idea that something might be wrong. With knowledge of the signs, symptoms and genetic implications, these heart conditions can be diagnosed and treated appropriately. In patients with some heart conditions, 30% to 50% have symptoms before death – often a blackout – and prompt action to exclude a heart condition is essential.^{1,2}



Ashley Stephen Jolly, 1982-1998

This booklet is dedicated to Ashley Stephen Jolly, who continues to inspire the work of SADS UK. In his loving memory.

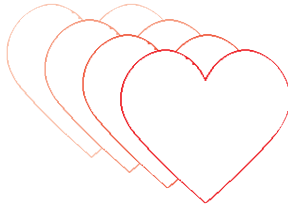
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Acknowledgements

SADS UK would like to thank Dr Andrew Grace, Consultant Cardiologist, for his help in producing this booklet.

Note: The main purpose of this booklet is for general guidance. Specialist advice on the conditions described in this booklet should be sought for individual cases.



Introduction

It is estimated that, each year in the UK, 3,500 apparently fit and healthy people under the age of 65 die suddenly and unexpectedly. Some of these are children and teenagers. These people have no previously documented heart disease.

Potentially dangerous cardiac conditions can affect all age groups. These conditions include:

- Hypertrophic Cardiomyopathy (HCM)
- Arrhythmogenic Right Ventricular Dysplasia (ARVD)
- Long QT Syndrome (LQTS)
- Wolff-Parkinson-White Syndrome (WPW)
- Brugada Syndrome, and
- Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT).

All of the above conditions can cause arrhythmia (an abnormal heart beat) and can be treated, and lives can be saved.

Many cardiac conditions have a hereditary (genetic) origin. If a cardiac condition is detected or suspected, or if there has been a premature sudden death of a healthy person, other family members should be referred to a cardiologist and genetic counsellor to find out whether they may have inherited the same condition.

Epilepsy is sometimes wrongly diagnosed instead of a cardiac condition. This is because a blackout caused by an arrhythmia can look just like a blackout caused by generalised epilepsy, with abrupt loss of consciousness, twitching arms and legs and incontinence. A significant number of patients who have suffered a sudden cardiac arrest have been diagnosed first with epilepsy, and given epilepsy treatment. Long QT Syndrome and other genetic conditions have later been diagnosed,

sometimes after death. In young people diagnosed with epilepsy, sudden cardiac death is 24 times more common than in other young people.³

Also, some people mistakenly think that a heart attack is the same as a **cardiac arrest**. We explain the difference between them on page 12.

Hypertrophic Cardiomyopathy (HCM)

HCM is a thickening of the heart muscle usually seen in the left ventricular septum. People with HCM often experience ventricular tachycardia or atrial fibrillation arrhythmias. This condition can cause arrhythmias which occasionally lead to sudden death.

Arrhythmogenic Right Ventricle Dysplasia (ARVD)

In people with ARVD, the right ventricle (the lower right pumping chamber of the heart) has an abnormal structure. (Dysplasia means abnormal development or structure.) The ventricle muscle tissue is progressively replaced by a fatty and fibrosis structure. This weakens the muscle and causes an abnormal heart rhythm.

Long QT Syndrome (LQTS)

Different triggers can cause people with Long QT Syndrome to experience symptoms of syncope (fainting or loss of consciousness) or irregular heart rhythm. These triggers include swimming, exercise, startle, sleep, and certain medications. Sudden death may occur, either with or without previous symptoms.

Wolff-Parkinson-White Syndrome (WPW)

An electrical short circuit within the heart may cause an arrhythmia. This may degenerate into ventricular fibrillation, which in some cases can lead to sudden death. Other symptoms of WPW include light-headedness, dizziness, palpitations, difficulty breathing, angina, shortness of breath and possibly chest discomfort.

Brugada Syndrome

Brugada Syndrome is more prevalent in people of South-East Asian origin. Symptoms include dizziness, chest pain, sweating, and rigidity and shaking of the limbs. In some cases it can cause sudden cardiac death. This is most likely to occur during sleep.

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

With CPVT, syncope is usually provoked by exercise or other forms of stress. The incidence of sudden death is rare in people with CPVT.

Genetic testing for these conditions

Genetic testing can be used to identify all of the above conditions except WPW, and is particularly useful when a genetic mutation has been identified in one member of the family.

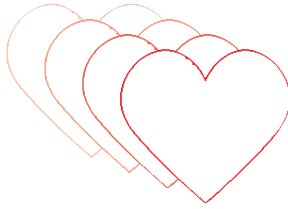
Defibrillation

In all of the above conditions, the syncope episode is due to an arrhythmia that has caused ventricular tachycardia (VT) (rapid heart beat). If the VT is not corrected, it could develop into ventricular fibrillation (VF) which is dangerous and may cause cardiac arrest. At this point, defibrillation is essential as it is the only way to restore the heart rhythm and prevent death. (Defibrillation means giving an electric shock to the heart to stop the abnormal rhythm and get the rhythm back to normal.) CPR (cardiopulmonary resuscitation) and defibrillation must be administered speedily as the chances of survival diminish with every minute that elapses:⁴

- After 2 minutes, there is a 75% chance of survival.
- After 4 minutes, there is a 55% chance of survival.
- After 6 minutes, there is a 36% chance of survival.
- After 8 minutes, there is a 16% chance of survival.
- After 10 minutes, the chances of survival are remote.

Automated External Defibrillators (AEDs) are available in some public places. Using an AED before the emergency services arrive greatly increases the chance of survival.

Patients with a previously diagnosed condition may have an Implantable Cardioverter Defibrillator (ICD) fitted inside their chest. This device will automatically provide a shock to return the heart to a normal rhythm. (For more on ICDs, see page 31.)



SADS – an umbrella term

Sudden Arrhythmic Death Syndrome (SADS) is an umbrella term which covers cardiac conditions that may cause sudden and unexpected death if not treated. SADS is sometimes reported as Sudden *Adult* Death Syndrome, but this term is misleading, as these types of death also occur in children and young people.

Conditions affecting the heart beat (cardiac arrhythmia) where there is no disease of the heart muscle structure are known as conditions of the ‘electrics’ (or conduction system) of the heart. This booklet is concerned with the conditions of the electrics of the heart that may be life-threatening if not treated. The main conditions are:

- Long QT Syndrome (LQTS)
- Wolff-Parkinson-White (WPW) Syndrome
- Brugada Syndrome, and
- Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT).

Treatments such as beta-blockers, radio-frequency ablation or the implantation of an ICD (Implantable Cardioverter Defibrillator) or pacemaker may be necessary to correct the arrhythmia. We explain more about these treatments on page 31.

Common symptoms

Common symptoms of conditions that may lead to SADS include:

- syncope (fainting, loss of consciousness, blackout or collapse)
- palpitation
- light-headedness
- dizziness, and
- shortness of breath.

These symptoms are likely to occur at times of stress, excitement or startle, or with exercise.

Fainting

Most people faint at some stage during their life, so there is a readiness to assume that fainting is not a serious problem. Most people would therefore not contact their GP unless they have regular fainting episodes.

Normally, the causes of a fainting episode are of little consequence and no further investigation is needed. On the other hand, in a person who would normally be considered to be fit and healthy, a fainting episode could be the first sign of a potentially serious condition. People who have a fainting episode in any of the following situations should seek medical advice about whether they may have a heart condition:

- fainting that occurs during physical exertion
- fainting with emotional stress or extreme anger
- fainting with sudden noise or arousal from rest or sleep, or
- fainting or the appearance of seizing during sleep.

The medical term for fainting or loss of consciousness is **syncope**. The person loses consciousness, generally following symptoms of dizziness, light-headedness, alterations in or loss of vision, and sometimes extreme ringing in the ears or loss of hearing. Loss of muscle control will cause the person to fall to the ground, or slump if seated. There may be other symptoms, such as an irregular or rapid heart rhythm (arrhythmia), sweating and nausea. Jerks and spasms may occur. These movements may look similar to an epileptic seizure, but the *causes* of the blackout in syncope and epilepsy are different. In syncope, the blackout is due to a lack of blood flow to the brain. This is caused by an irregular, slow or rapid heart rhythm (arrhythmia). This reduces the ability of the heart to pump blood, which means that not enough oxygen is getting through to the brain. In epilepsy, the blackout is caused by deranged behaviour of brain cells, but the flow of blood to the brain is not interrupted. However, the symptoms may look very similar to an onlooker, and many patients will be referred to see a neurologist rather than a cardiologist.

Fainting caused by an arrhythmia is usually sudden and without warning. It may occur during or shortly after exercise and is accompanied by gasping or absence of breath. Loss of consciousness can last from one to several minutes, and in some cases resuscitation may be required.

Epilepsy

In some cases where the person has a cardiac condition, epilepsy may be suspected. However, studies have suggested that in up to 30% of people diagnosed with epilepsy, the diagnosis is incorrect and the symptoms are in fact due to a cardiac condition.^{5,6}

Medication

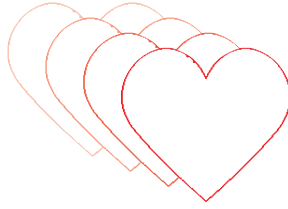
Some medications should be avoided by people living with the cardiac conditions listed on page 4, so careful prescribing is crucial. It is important to identify the cardiac condition that the patient has and to check any medications prescribed with those listed on the website: www.azcert.org. This website also gives details of medications that may induce an arrhythmia in a person who has no previous history of any heart condition.

Implications for other members of the person's family

In many cases, cardiac conditions are hereditary. If a genetic disorder is suspected, or if a condition is detected, the patient and his or her family members can be referred to a regional genetics centre to compile a family tree. The centre can provide genetic counselling and may offer genetic screening. For details of your regional genetics centre, see www.bshg.org.uk/genetic_centres/uk_genetic_centres.htm

If there is a sudden cardiac death in the family

If a fit and healthy person dies prematurely, suddenly and unexpectedly, there is a probability that he or she died from a cardiac condition. If the sudden death occurred at the time of an accident – such as an inexplicable car accident, or a drowning where there is no obvious reason – the possibility that a cardiac condition may have initiated the accident should be considered. If no abnormality of the heart muscle structure can be detected at *post mortem*, it may be suspected that the person died from a sudden arrhythmic death (SAD).



Department of Health Guidelines on Arrhythmias and Sudden Cardiac Death

SADS UK played a significant role in a campaign to include a new chapter in the Department of Health's *National Service Framework for Coronary Heart Disease*. Published in 2005, *Chapter 8 Arrhythmias and Sudden Cardiac Death*, includes the following recommendations for good practice for initial and ongoing treatment. Service improvements recommended in the document also included the development of local rapid access multidisciplinary arrhythmia and/or blackout clinics with a high level of expertise.

Initial treatment

- Patients should receive a hard copy of their ECG which shows their arrhythmia.
- Patients surviving cardiac arrest or having presented with pre-excited atrial fibrillation should be assessed by a heart rhythm specialist.
- The following patients should be **urgently assessed by a heart rhythm specialist**. Patients with:
 - syncope or other symptoms suggesting an arrhythmia, and a personal history of structural heart disease or family history of early sudden death
 - recurrent syncope associated with palpitations
 - syncope and pre-excitation
 - third degree AV block
 - recurrent syncope in whom a life-threatening cause has not been excluded, or
 - ventricular tachycardia.
- The following people should be **referred to a heart rhythm specialist**. People:
 - with suspected ventricular tachycardia
 - with Wolff-Parkinson-White (WPW) Syndrome

- with recurrent supraventricular tachycardia not controlled by medication
- with recurrent atrial flutter
- with symptomatic atrial fibrillation not controlled by medication
- who are first degree relatives of victims of sudden cardiac death who died below the age of 40 years, or
- with recurrent unexplained falls.

Any child with recurrent loss of consciousness, collapse associated with exertion, atypical seizures with a normal EEG (electroencephalogram), or with any documented arrhythmia, should be referred to a paediatric cardiologist.

Ongoing treatment

The recommendations for ongoing treatment are as follows.

- Patients with sustained or compromising arrhythmias receive timely referral for appropriate treatment.
- Patients identified as being at high risk or with life-threatening ventricular arrhythmias should be considered a candidate for an Implantable Cardioverter Defibrillator (ICD).
- For patients with sustained supraventricular tachycardia (SVT), catheter ablation should be considered.
- An outpatient care plan is devised between the patient, GP and arrhythmia care team, when further hospital treatment is not recommended.

For more information

National Service Framework for Coronary Heart Disease. Chapter 8 Arrhythmias and Sudden Cardiac Death

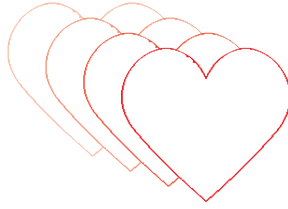
Department of Health, 2005.

www.dh.gov.uk/assetRoot/04/10/52/80/04105280.pdf

National Service Framework for Coronary Heart Disease. Chapter 8 Arrhythmias and Sudden Cardiac Death. Implementation Documents

Department of Health, 2007.

www.dh.gov.uk/en/Policyandguidance/Healthandsocialcaretopics/Coronaryheartdisease/DH_4117048



The heart: its electrical system, and problems that can occur

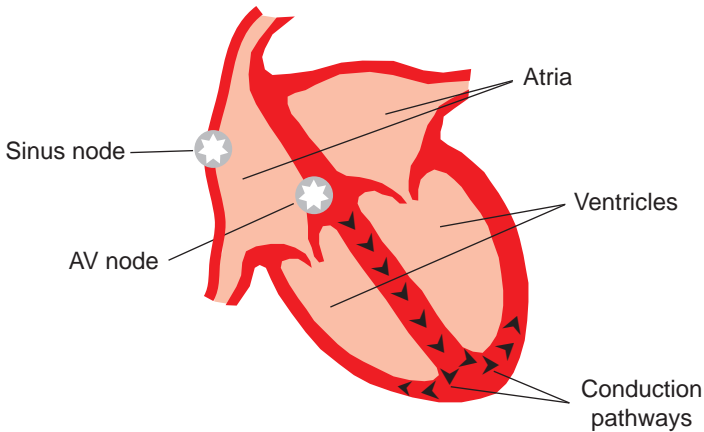
This section has been included for those patients or their relatives who may need an explanation of how the heart works, and what can go wrong.

The heart is a strong muscle that pumps blood around the body each time its chambers contract. The heart is divided into four chambers. The upper chambers are called the atria, and the lower chambers are the ventricles. The atria fill the ventricles with blood. The ventricles then contract, pumping the blood around the body. The right side of the heart pumps blood to the lungs to enrich the blood with oxygen. The blood then returns to the left side and the left side pumps the oxygen-rich blood to the brain and the rest of the body. The blood then returns to the right side of the heart and the process is repeated.

The electrical system of the heart

The heart has its own electrical system that controls each heart beat (contraction). When the heart is pumping normally, the beat (depolarisation) starts from the sinus node, which is in the right atrium, and passes through the atria, along the His bundle (conduction pathway) and its branches, to activate the ventricles. The atria and the ventricles are electrically insulated from each other except at a single point, called the AV (atrioventricular) node. The His bundle passes through the AV node and conducts the electrical signal from the atria to the ventricles. As the electrical impulse travels through the bundle branches and over the ventricles, the muscle contracts, forcing the ventricles to pump blood around the body.

The sinus node is sometimes called the heart's natural pacemaker, as it controls the heart rate.



Problems that can occur

Heart attack

(also called **myocardial infarction** or **coronary thrombosis**)

A heart attack occurs when blood flow to the heart muscle is blocked. To keep your heart healthy, the heart muscle needs to get a constant supply of oxygen-containing blood from the coronary arteries. If one of the coronary arteries becomes blocked – for example, by a blood clot – part of your heart muscle may be starved of oxygen and may become permanently damaged. A patient can survive more than one heart attack if the heart attack destroys only a small part of the muscle. The heart can continue to pump with a small loss of muscle function, but the output of blood flow will be reduced. The dead cells will gradually be replaced by scar tissue. A heart attack is different from cardiac arrest – see below.

Cardiac arrest

Cardiac arrest is when a sudden and severe disturbance of the heart rhythm (arrhythmia) stops the heart beating or causes it to beat so slowly or so fast that it cannot pump enough blood to sustain life. Ventricular fibrillation is the most dangerous arrhythmia as it is fast and irregular and often occurs without warning. It is the most common cause of cardiac arrest.

Heart block

Heart block is a restriction of the normal electrical pulse through the bundle of His conduction fibres to the ventricles. This can cause a slow

contraction rate of the ventricles. The ventricles may contract only once for every two or three contractions of the atria.

Arrhythmias

An arrhythmia is an abnormal heart rhythm (beat) outside the normally acceptable range for adults of 60 to 100 beats per minute (bpm). The heart may beat too slowly, too quickly or chaotically. Bradycardia is a rhythm below 60bpm. Tachycardia is a rhythm above 100bpm. A child's heart rate may be faster and the acceptable range varies according to their age.

What are the symptoms of an arrhythmia?

The symptoms of an arrhythmia are palpitation (unpleasant sensations of irregular and/or forceful beating of the heart), light-headedness, chest pain, or sudden fainting (syncope) during or shortly after exercise or emotional excitement.

Primary and secondary arrhythmias

Arrhythmias are divided into:

- primary arrhythmia syndromes – where the arrhythmia is caused by a disorder of the heart's electrical system, in people with a structurally normal heart, and
- secondary arrhythmia – where the arrhythmia is caused by structural damage to the heart muscle.

The main electrical disorders that cause primary arrhythmias are Long QT Syndrome, Wolff-Parkinson-White Syndrome, Brugada Syndrome, and exercise-induced Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT).

The most prevalent dangerous condition that causes secondary arrhythmia is hypertrophic cardiomyopathy, where the heart wall (septum) thickens.

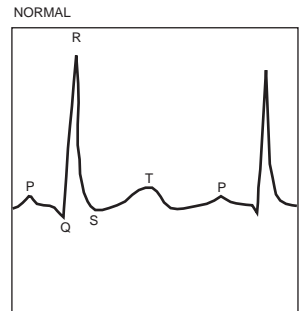
Arrhythmia may also be brought on by some medications that affect the heart's electrical system.

The electrocardiogram (ECG)

ECGs are commonly used to record the electrical activity of the heart and to detect the causes of arrhythmia. A standard ECG trace is shown overleaf. When interpreting an ECG trace:

- The P wave starts with depolarisation (the spontaneous change from a positive to a negative charge of the pacemaker cell) at the sinus node.

- The PR segment is the time required for atrial depolarisation.
- The QRS complex is the spread of electrical activity (depolarisation) over the ventricles.
- The QT interval is the total time for depolarisation and repolarisation (the change from a negative to a positive charge) of the ventricles. For more on the QT interval, see page 18.
- The ST segment represents the period between ventricular depolarisation and ventricular repolarisation.
- The T wave is the repolarisation of the ventricles.



For more information

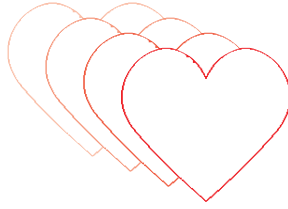
For best practice when taking an ECG recording, see:

Clinical Guidelines by Consensus – Recording a Standard 12-lead Electrocardiogram. An Approved Methodology.

Published by the Society for Cardiological Science and Technology, 2006.

Go to www.scst.org.uk and select the link to *Reference documents and guidelines*.

A library of ECG traces can be found on the Medelect website www.ecglibrary.com



Long QT Syndrome

What it is

The heart is made up of millions of cells that form the muscle of the heart. Each of these cells has pores in the cell membrane, called ion channels. The movement of sodium, potassium and calcium through these pores produces an electrical signal that stimulates the cells, causing the heart to beat and thereby pump blood. Long QT Syndrome – or LQTS – is caused by a disorder of those pores, which affects the production of the electrical signal. This delays the recovery of the signal before the next beat can start, and extends the QT interval shown on a typical ECG trace. (We explain what the QT interval is on page 18.) This extended QT interval can be associated with the onset of rapid, chaotic heart rhythms that cause improper pumping of the blood, which may result in abrupt fainting (syncope) episodes without forewarning. It can also cause sudden unexpected death. These fainting episodes may occur at any age, but are most likely to occur between the ages of 10 and 25 years.

The QT period can also be prolonged by some medications. See www.azcert.org

Who is affected?

The exact number of people affected is unknown, although it is estimated that around 1 in 5,000 people have LQTS.⁷ Conditions of the electrics of the heart cannot be detected by a standard *post mortem*, so some deaths caused by LQTS may be recorded as unascertained. It is therefore difficult to know exactly how many people are affected.⁸

Clinical studies show that more females than males have LQTS.⁹ Men with LQTS risk having a first cardiac event in childhood, and the risk diminishes after the age of 15 years. (By a ‘cardiac event’ we mean an arrhythmia which has been serious enough to have caused at least a syncope or possibly cardiac arrest.) In females, the possibility of the first

cardiac event continues throughout life. Women are at risk of experiencing their first cardiac event immediately after childbirth, probably due to altered levels of female hormones.

Symptoms

Most patients with LQTS do not experience symptoms, but when symptoms do occur they include syncope (fainting or loss of consciousness), or irregular heart rhythm. Sudden death may occur either with or without previous symptoms.

The symptoms of LQTS differ depending on the gene inherited. The three most common genotypes are:

- Genotype LQT1 – Gene mutated *KCNQ1* (=KvLQT1). Cardiac events are triggered by exercise and stress. Diving and swimming are typical triggers of LQT1.
- Genotype LQT2 – Gene mutated *KCNH2* (=HERG). Cardiac events are triggered by both exercise and rest. Events provoked by noise such as an alarm clock are almost exclusive to LQT2.
- Genotype LQT3 – Gene mutated *SCN5A*. Cardiac events are triggered by rest and sleep. This is because the LQTS interval is excessively prolonged at slow heart rates when the body is at rest. Patients with LQT3 are at high risk of slow heart rates.

LQT4, LQT5 and LQT6 are much less common. Most LQT Syndrome genes carry the information responsible for the assembly of the potassium channels. The exception is LQT3 which is responsible for the sodium channels. New LQT genes continue to be discovered.

LQT1 and LQT2 are the most common variants connected with syncope, and the usual clinical sign of this is seizure-like activity. Approximately 85% of events are related to physical activity or emotional stress.¹ Female LQT2 patients have a high incidence of syncope occurring during menstruation and in the *post partum* period after childbirth.¹

The number of non-fatal cardiac events that occur before the age of 40 is significantly higher in patients with LQT1 and LQT2 than in patients with LQT3.⁷ The likelihood of sudden death during a cardiac event is much higher in patients with LQT3.⁷

As the LQTS genes are identified, they are now classified by number as described above (LQT 1-6). However, the following two earlier classifications are still used:

- The Romano-Ward Syndrome (autosomal dominant disorder without deafness) describes all forms of LQTS without deafness.
- The Jervell and Lange-Nielsen Syndrome (autosomal recessive disease with congenital deafness) is characterised by the presence of LQTS and deafness. This is much less common and mainly affects young children.

The classification of LQT Syndrome therefore covers several different genetic diseases caused by mutations in cardiac ion channels. These all have the effect of prolonging ventricular repolarisation and thereby limiting the ability to initiate the next electrical signal to start the following heart beat.

In patients with LQT Syndrome, episodes of sudden loss of consciousness are almost always due to *torsade de pointes* arrhythmias. An important characteristic of *torsade de pointes* is its potential to self-terminate or to deteriorate into ventricular fibrillation. This explains why some affected patients may survive several attacks of syncope before succumbing to a fatal one. In patients who experience syncope only, the *torsade de pointes* rhythm has spontaneously returned to normal, usually within one minute, and the patient then regains consciousness with little disorientation or confusion. On the other hand, in a minority of patients the rhythm persists and then degenerates into ventricular fibrillation. This rarely reverts back to normal rhythm without medical intervention (defibrillation), and may cause sudden death.

Detection and diagnosis

Making a diagnosis of congenital LQT Syndrome is difficult even for the most experienced electrophysiologist. The standard ECG test may not identify which members of a patient's family have the syndrome. An exercise ECG may improve the accuracy of diagnosis, as the heart rate is monitored during both the exercise and the recovery period.

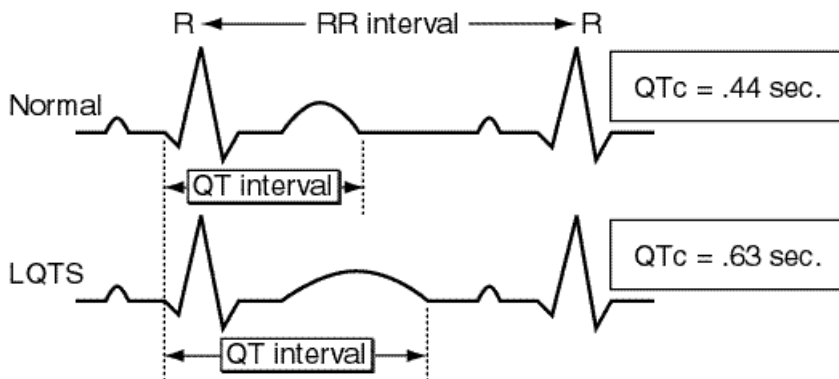
What is the QT interval?

The QT is a time interval on an ECG. It represents the time from the electrical stimulation (depolarisation) of the heart's pumping chambers (ventricles), to the end of the recharging of the electrical system (repolarisation). It is measured in seconds or milliseconds and is approximately the time from the beginning of the contraction of the ventricles until the end of relaxation.

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

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

The normal QTc interval varies from 0.35 to 0.45 seconds (350 to 450 milliseconds). About 95% of people have a value of between 0.38 and 0.44 seconds, which is the range doctors generally consider as the 'normal' range. The diagram below shows two examples of a QTc. The first shows a normal QTc interval and the second shows a prolonged QTc interval. The RR interval determines the heart rate.



In the diagram above, the heart rate (RR) is the same for both examples but the QT interval is longer in the second example. The QTc value is therefore larger in the second example.

LQTS is diagnosed primarily on recognition of a prolonged QTc interval on the ECG. (See *What is the QT interval?* above.) A QTc of greater than 0.47 seconds in males and 0.48 in females appears to be diagnostic of LQTS, in the absence of QT prolongation medications or other forms of heart disease. A QTc of less than 0.40 in males and less than 0.41 in females makes the diagnosis unlikely. The computer-generated QTc may be incorrect. So, when a diagnosis of LQTS is considered, the electrophysiologist should verify (hand measure) the computer measurement. However, not all LQTS patients have a prolonged QTc on the initial ECG. About 12% have a normal QTc of 0.44 seconds or less, and about 30% have a QTc between 0.40 and 0.46 seconds – values which are found in many people who do not have LQTS. A QTc in the range 0.40 to 0.46 seconds is, therefore, inconclusive and must be clarified by additional testing.¹⁰

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 person to exercise for 10 minutes or more without reaching a heart rate in excess of 150 to 160 beats per minute. A Holter ECG may also help to clarify the diagnosis. The main abnormality to be identified during these tests is a prolonged QTc interval. Certain T wave abnormalities occurring during the test also support the diagnosis of LQTS. Values indicative of the Long QT Syndrome are higher for the Holter test than for the exercise ECG and a QTc of 0.5 or higher on the Holter test is particularly valuable in order to refine a diagnosis of LQTS.

Influence of age and sex

The LQTS interval is shorter in men than in women, and QT prolongation can be diagnosed more readily in women than men.

Treatment

Beta-blockers are often effective in preventing ventricular arrhythmias for people with LQT1 and LQT2.

Where the use of beta-blockers and/or a pacemaker has not stopped the recurrent symptoms, an ICD and combined beta-blocker therapies may be recommended.

Competitive sport should be discouraged, but recreational sports that do not cause a significant increase in heart rate may be acceptable.

Patients should be given advice on what to do if there is excessive electrolyte loss – for example, during diarrhoea or excessive perspiring. The advice for such patients is to take drinks that contain potassium and to seek specialist medical advice.

For more information on beta-blockers, ICDs and pacemakers, see page 31.

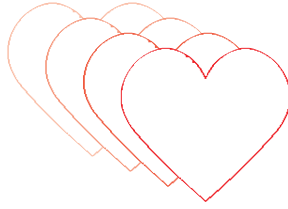
Implications for other family members

Long QT Syndrome is usually inherited by autosomal dominant transmission. This means that it affects boys and girls equally and that each child has a 50% chance of inheriting the gene. Once a family member is identified as having LQTS, it is extremely important that all family members are examined for evidence of the syndrome. It is especially important to know which parent and grandparent have evidence of the condition, since brothers, sisters, aunts, uncles, nephews, nieces and cousins on the affected side of the family are potentially at risk. It can be very helpful to construct a family tree and identify the causes of deaths within the family, looking for a history of sudden death. Causes of death such as epilepsy, pneumonia and asthma should be considered, as these may have been used to classify death in the past, before knowledge of the LQT Syndrome emerged. Cases of drowning and other unexplained accidents should also be considered. Regional genetics centres can provide additional information (see page 33).

Genetic analysis can identify about 65% of people with LQTS.¹¹

Short QT Syndrome

Short QT Syndrome has recently been recognised, but the number of patients who are affected is not yet clear. It has the same sort of genetic basis as the Long QT Syndrome, but to our knowledge no cases have yet been recognised in the UK.



Wolff-Parkinson-White Syndrome (WPW)

What it is

When the heart is beating normally, the beat (electrical impulse) starts from the sinus node which is in the right atrium (the upper chamber of the heart) and passes through the atria, along the His bundle and its branches to activate the ventricles. The atria and the ventricles are electrically insulated from each other except at a single point, the AV (atrioventricular) node.

When there is extra myocardial tissue in the electrically-insulated region (atrioventricular ring) between the atria and the ventricles, a short circuit may be caused. This extra tissue is called an accessory pathway. The presence of such tissue changes the electrical flow between the atria and the ventricles. The pathway may pass current in one direction only, or in both directions. A pathway can be concealed and, if it is, its effect on the electrical impulse signal cannot be picked up by an ECG machine. A concealed pathway only allows the impulse to travel from the ventricles to the atria, but in people with the WPW Syndrome, the accessory pathway allows the impulse to travel in both directions.

When there is an accessory pathway, the impulse from the sinus node activates the ventricles in the normal way via the His bundle and also more rapidly through the accessory pathway. The faster signal passing through the accessory pathway prematurely activates the ventricular muscle tissue, causing the ECG to show pre-excitation that is characteristic of WPW. Any tachycardia that is initiated by the presence of accessory pathway myocardial tissue breaching the insulating layer (atrioventricular ring) is called supraventricular tachycardia or SVT. 'Tachycardia' is a heart beat which, in an adult, is above 100 beats per minute. 'Supra' means 'above'. The atria are above the ventricles, so an arrhythmia starting in the atria is called supraventricular tachycardia.¹²

The type of SVT that a patient has is classified according to the way in which the electrical impulse travels from the atria. There are two main types:

- orthodromic atrioventricular re-entrant tachycardia, and
- antidromic atrioventricular re-entrant tachycardia.

Orthodromic atrioventricular re-entrant tachycardia

This is the most common type of supraventricular tachycardia in patients with WPW Syndrome. The re-entry circuit starts with the impulse from the sinus node, as it does in a normal heart. The impulse travels correctly towards the ventricles down the His bundle past the AV node and over the ventricles via the His bundle branches and Purkinje fibres. But, because there is an accessory pathway, the impulse is able to return (re-entrant) to the atrium via the accessory pathway.

With orthodromic atrioventricular re-entrant tachycardia, the impulse has started normally via the His bundle, so ventricular depolarisation (initiation of muscle contraction) is normal. The QRS complexes are thus narrow and a retrograde P wave follows shortly after the QRS complex. A delta wave is not seen.

Antidromic atrioventricular re-entrant tachycardia

This type of tachycardia occurs in a small number of patients with WPW Syndrome. The impulse travels from atrium to ventricle via the accessory pathway, instead of travelling down the His bundle. The impulse then re-enters the atrium, travelling the wrong way up the His bundle and through the atrioventricular node to the atrium. The QRS complexes are broad – an exaggeration of the delta wave. Antidromic atrioventricular re-entrant tachycardia is more common when there are multiple accessory pathways. This arrhythmia can mistakenly be thought to originate in the ventricles rather than in the atria.

A tachycardia (an abnormally fast heart beat) can degenerate into ventricular fibrillation, leading to cardiac arrest.

Who is affected?

WPW is most common in children with congenital heart disease, although the syndrome may occur in an otherwise normal heart. Symptoms can

develop at any age, but they occur more frequently among adults between the ages of 30 and 40. Between 1 and 3 people per 1,000 are thought to have Wolff-Parkinson-White Syndrome.^{13,14}

Symptoms

Symptoms of supraventricular tachycardia can include light-headedness, dizziness, palpitation, difficulty with breathing, angina, and possibly chest discomfort. If the patient has symptoms, he or she needs an electrophysiological study to find out if there are any accessory pathways and, if so, how many.

The symptoms can be so subtle that the patient may be unaware of them and may not seek treatment. Syncope (fainting or loss of consciousness) is not normally associated with WPW Syndrome.

Implications for other family members

WPW Syndrome can be inherited. It is believed that the gene for some patients with WPW is located on chromosome 7. Unfortunately there is no genetic test for WPW.

Detection and diagnosis

If the patient has SVT while connected to an ECG machine, a distinctive change to the trace will be seen. Where the symptoms occur randomly over the day, a 24-hour Holter test may be used to record the heart trace. Where the occurrence is infrequent, a loop recorder should be used.

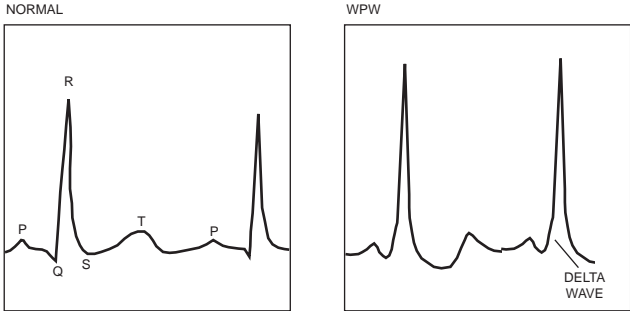
Treatment

The preferred treatment for WPW Syndrome is ablation, which destroys the accessory pathway tissue with a short pulse of radio-frequency energy. (For more information on ablation, see page 32.)

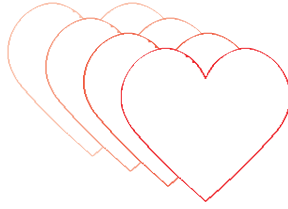
Calcium channel-blockers or digitalis should not be used as the only method of treatment. Beta-blockers have little or no effect, and antiarrhythmic drugs can be a possible risk.

Atrial fibrillation and atrial flutter are commonly seen in patients with WPW Syndrome. In these patients, ventricular rates may rise to around 300bpm or above. This can be serious, due to the nature of the conducting accessory pathways. Care must be taken to stop the atrial fibrillation and flutter that are causing the ventricles to fibrillate, as this can have

life-threatening consequences. Atrial flutter is a very small re-entry circuit inside the right atrium at the base near the AV node. Ablation is again the preferred treatment as antiarrhythmic drugs have little effect. Atrial fibrillation originates from a very small re-entry wave of energy circulating in the great venous structures. The use of ablation to cure fibrillation is difficult and success rates vary.



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Brugada Syndrome

What it is

Brugada Syndrome is an inherited cardiac electrical disorder occurring in the absence of obvious structural heart disease. The electrical activity around the ventricles may go into disarray and cause the heart muscle to beat in an uncoordinated way, causing ventricular tachycardia. If the tachycardia develops into ventricular fibrillation, the condition can be life-threatening.

Several genes are thought possibly to cause Brugada Syndrome, but the only one that has been positively identified is the *SCN5A* gene on chromosome 3, where the sodium channels of the cells that make up the heart muscle are affected. Sodium channel deficiency leads to polymorphic ventricular tachycardia and is probably a direct result of slow conduction through the heart. Mutations in the sodium channel genes that cause Brugada Syndrome can also cause LQTS3 (see page 16) and progressive conduction disturbances. Brugada Syndrome has autosomal dominant inheritance in most patients. This means that it affects boys and girls equally and that each child has a 50% chance of inheriting the gene.

Who is affected?

Brugada Syndrome can affect both male and female members of the family. It may affect as many as 3 in 1,000 people in the West. It is most prevalent in South-East Asia, where it affects more males than females – with a ratio of approximately 8:1.¹⁵ It can affect people of all ages, from babies to elderly people, but it is more common in 35-45 year olds.¹⁵

Symptoms

Brugada Syndrome is characterised by episodes of rapid polymorphic ventricular tachycardia. These episodes may self-terminate with the patient suffering a syncope episode. Or, the tachycardia may continue to degenerate into ventricular fibrillation, resulting in cardiac arrest. Most

patients with Brugada Syndrome have a history of these syncope episodes or cardiac arrests.

Some of the symptoms associated with Brugada Syndrome – such as episodes of dizziness and loss of consciousness, sometimes associated with chest pain, sweating, and rigidity and shaking of the limbs – can sometimes be mistaken for idiopathic epilepsy.

High temperature during fever can cause a typical Brugada ECG pattern. The high temperature affects the ionic mechanism. This results in premature closing of the sodium channels, dramatically reducing the electrical charge carried by the sodium channel.

Unfortunately, many people with Brugada Syndrome have no symptoms and occasionally the victim is found having died in their sleep. This may be referred to as Sudden Unexplained Nocturnal Death Syndrome – or SUNDS. In the Philippines it is called ‘bangungut’, in Thailand it is called ‘lai-tai’, and in Japan ‘pok-kuri’. Brugada Syndrome episodes normally start when the heart rate is slow, which is probably why so many people are affected in their sleep, particularly in the early hours of the morning.

There is substantial evidence that patients with Brugada Syndrome have an above-average occurrence of supraventricular tachycardia including atrial and atrioventricular re-entrant tachycardia. Monomorphic ventricular tachycardia is not usually present; polymorphic tachycardia is most often detected.

Detection and diagnosis

Where structural abnormalities of the heart have been ruled out, the Brugada ECG patterns will show abnormalities of repolarisation and depolarisation with ST-segment elevation. The three distinctive ECG patterns, which look not dissimilar to incomplete or complete right bundle branch block and ST segment elevation in the precordial leads V1 to V3 with a coved or saddleback morphology, are:

- Type 1: Prominent coved ST-segment elevation in the right precordial leads, followed by a negative T wave.
- Type 2: High ST-segment take-off and elevation, followed by a positive T wave with saddleback configuration.
- Type 3: ST-segment elevation in the right precordial leads. It may display saddleback or coved form and has the possibility of displaying both forms.

Care must be taken when connecting the patient to the ECG machine precordial leads because, for the Brugada ECG pattern to be correctly identified, the leads need to be placed very precisely.

ECG patterns recorded shortly after resuscitation or immediately after a DC (direct current) shock should not be considered when identifying Brugada Syndrome.

It can be difficult to differentiate between Brugada Syndrome and Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), because ARVC can sometimes mimic Brugada Syndrome. The structural changes of the heart muscle caused by ARVC may not be identified until post mortem. Before making a final diagnosis of Brugada Syndrome, LQT 3 should be excluded. Also, if the patient has been given class 1A or class 1C antiarrhythmic drugs, these may influence the ECG trace.

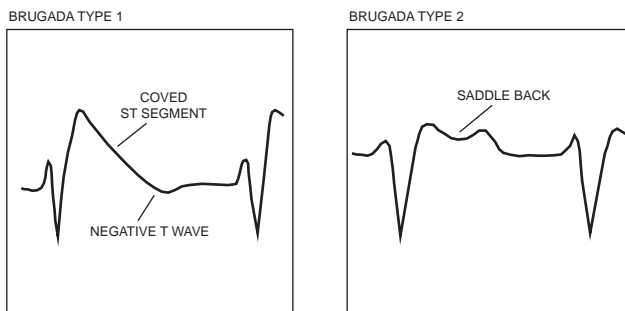
Treatment

Those patients with Brugada Syndrome who are at high risk – having a history of syncope and a spontaneously abnormal ECG (not provoked with sodium channel-blocking drugs) – should be considered for an ICD (Implantable Cardioverter Defibrillator – see page 31.) Patients who have only spontaneous ST segment elevation without a history of syncope may be considered as at low risk.

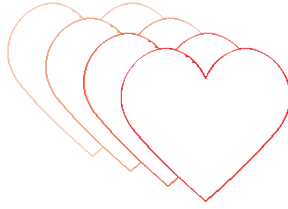
Implications for other family members

A history of sudden death at a young age in the family should be considered seriously and other family members should be referred to an electrophysiologist.

Genetic analysis can identify 10% to 20% of patients with Brugada Syndrome.¹¹



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Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

What it is

CPVT is an inherited condition that causes cardiac arrhythmias due to an electrical instability in the heart's pacing system. There is no apparent physical problem with the heart muscle.

The origin of the CPVT arrhythmia is thought to be in the right ventricle, where QRS morphology (ECG pattern) shows a left bundle branch block pattern, and in the left ventricle when a right bundle branch block pattern is present. The electrical signal that causes the onset of CPVT is mostly single or double origin, and usually originates from the right ventricular outflow tract instead of at the sinus node. The following beat tends to originate from within the left ventricle.

CPVT is usually characterised by bidirectional polymorphic ventricular tachycardia that can be induced during exercise or catecholamine infusion and other events provoking sympathetic nervous system activation.

Symptoms

Symptoms of CPVT are palpitation, dizziness and syncope occurring during physical activity or stress.

Without treatment, a patient with CPVT is prone to ventricular tachycardia (VT). This may self-terminate or degenerate to ventricular fibrillation, which can in some cases cause sudden death. However, the incidence of sudden death is rare.

Who is affected?

CPVT is thought to affect approximately 1 in 10,000 people. However, the number affected may be higher than this.¹⁶

The majority of people affected by CPVT may experience episodes of ventricular tachycardia in childhood and adolescence. Sixty per cent of

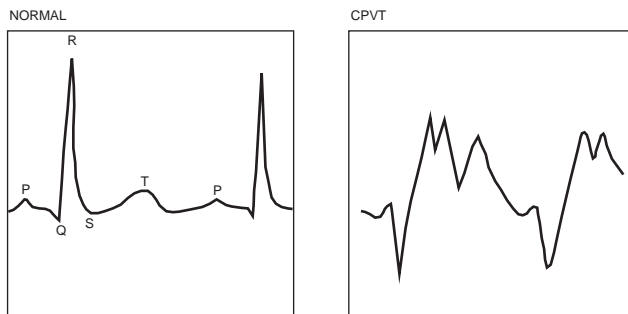
patients with CPVT have their first episode of syncope before the age of 20 years.¹⁶ The first syncope event will generally occur in males much earlier than in females. Childhood and adolescence are normally when individuals are most active, and when sporting and other strenuous activities are more likely to induce the CPVT arrhythmias.

In 30% of families affected by CPVT there is likely to be a history of sudden death.⁵ In 60% to 70% of the individuals affected by CPVT there will be a history of syncope.¹⁶

Detection and diagnosis

It is not practical to make a diagnosis of CPVT with a standard 12-lead ECG recording taken at rest. The patient needs to have an ECG test where he or she undertakes exercise or is under some other stress. The exercise is gradually increased in severity to see if ventricular tachycardia (VT) can be induced. As the severity of the exercise continues to be increased, the VT may become sustained.

Adrenaline infusion through a peripheral intravenous line with ECG monitoring may also be used to help induce ventricular arrhythmia and to help make a diagnosis. The use of adrenaline may cause polymorphic ventricular ectopy, non-sustained ventricular tachycardia, or frequent ventricular ectopy. Studies suggest that adrenaline can be more effective at revealing evidence of CPVT in patients than using exercise testing.¹⁷ The number of patients who have positive adrenaline tests may be higher than has been thought, and this is an area of active research.



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An alternating 180 degree change of the QRS axis (see diagram of the ECG trace above) on a beat-to-beat basis – so called bi-directional VT – is the usual ECG manifestation. The changes in QRS waveform will be

abrupt, which is very different to the *torsade de pointes* noted in LQT Syndrome. The QRS waveform will be regular, not chaotic.

Treatment

Beta-blocker therapy is an effective treatment for approximately 60% of patients with CPVT.^{5, 18} The correct dosage is guided by exercise testing. In some cases, taking beta-blockers alone may not be effective enough, as it may still be possible to provoke the arrhythmias at high heart rates. In these cases, the patient should be considered for an ICD (Implantable Cardioverter Defibrillator).

The beta-blocker used should block both beta 1 and beta 2 receptors in the heart and so either propranolol or nadolol are typically used. Some so-called selective beta-blockers may be hazardous for people with this condition.

High-risk patients are those with recurrent syncope or those who have survived a cardiac arrest, or both. High-risk patients would benefit from having an ICD fitted, along with the beta-blocker treatment.

Antiarrhythmic drugs such as amiodarone, sodium channel-blockers and calcium antagonists appear ineffective in providing arrhythmia suppression for CPVT.

For more information on beta-blockers and ICDs, see page 31.

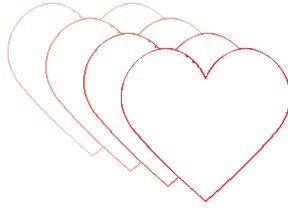
Implications for other family members

Familial CPVT is a genetic disorder with autosomal dominant inheritance. This means that it affects boys and girls equally and that each child has a 50% chance of inheriting the gene. The genes associated with CPVT are *RyR2* and *CASQ2*. The ryanodine receptor gene *RyR2* mutates in an autosomal dominant form of familial CPVT. This may increase sensitivity to calcium ions. The *CASQ2* inheritance is often an autosomal recessive form and encodes calsequestrin, a calcium-buffering protein of the sarcoplasmic reticulum. Males with the *RyR2* mutation are at significantly higher risk of experiencing a cardiac event than females.

Genetic analysis can identify about 60% of patients with CPVT.¹¹

All first degree relatives of a patient with CPVT should be tested to see if they have symptoms of CPVT. In selected cases, check-ups every 6 to 12 months with an exercise test at the maximum heart rate for the individual's age are recommended.

Families with phenotype testing results suggesting that they could be affected by CPVT should be considered for beta-blocker therapy.



Treatments for conditions of the electric of the heart

Beta-blockers

Beta-blockers work by reducing the signals between the nerves and muscles caused by the chemical noradrenaline. This helps to stabilise the heart beat, and lowers blood pressure and heart rate, stopping arrhythmias.

Some patients may get side effects, including tiredness, possibly nightmares, and cold hands and feet.

For information on beta-blockers used in the UK, see www.bnf.org/bnf/

ICDs and pacemakers

An ICD (Implantable Cardioverter Defibrillator) is a small device containing a microprocessor and battery. The device has thin leads connecting it to the heart. The ICD constantly monitors the heart and can detect tachycardia (fast heart rhythms). Some ICDs may also detect bradycardia (slow heart rhythms). The ICD may also treat ventricular tachycardia – an unstable, irregular heart beat. When an abnormal rhythm is detected, the ICD delivers small electrical signals, via the thin leads, to the heart muscle to restore the normal heart rhythm. If these small signals do not correct the heart rhythm and the heart goes into ventricular fibrillation, the ICD will deliver a strong signal (defibrillation shocks) to restart the heart beat.

Normally the signals from the ICD are not noticeable, although the patient may notice some of the symptoms from the onset of the abnormal heart beat such as dizziness. If the ICD needs to restart the heart, the patient will feel what has been described as a kick in the chest.

The ICD provides treatment for the heart rhythm disorder (arrhythmia), but it does not provide a cure for cardiac arrhythmias.

Modern ICDs store information about the treatment they have given. A specialist can interrogate this information while leaving the ICD in position and undisturbed.

A **pacemaker** is very similar to the ICD but it only treats bradycardia, a slow heart beat. The pacemaker monitors the heart and delivers an electrical signal via the thin lead, to speed up the heart rate. The improved circulation increases the oxygen supply to the body, generally providing the patient with more energy and alleviating shortness of breath.

For more information about implantable devices, see: **www.medtronic.com** or **www.guidant.com** or **www.sjm.com** or the British Heart Foundation booklet *Implantable Cardioverter Defibrillators*, which is available at **www.bhf.org.uk/publications.aspx**

Ablation

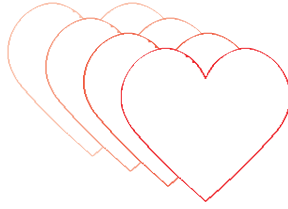
Ablation is used as a treatment for Wolff-Parkinson-White Syndrome.¹⁹ It destroys small amounts of heart muscle tissue by using a short pulse of radio-frequency energy. A probe (catheter) is inserted usually into the femoral vein near the groin, or alternatively into a vein near the collarbone, and is carefully steered to the atrium. The tip of the probe is guided to the extra pathway tissue, which is then quickly burned away. The techniques currently used were pioneered in the early 1980s and are now widely used in the UK.

For more information

For more information on ablation see:

<https://www.medtronic.com/mdtConnectPortal/registration/index.jsp>

<http://www.my.americanheart.org/portal/professional/patientinfo>



Genetic testing

Families with a particular genetic condition can be referred to an NHS Regional Genetics Centre where they can be screened for single gene disorders.

The information obtained from genetic testing helps doctors to confirm a diagnosis if a person has a specific condition. The information also helps them decide on the most appropriate treatment for patients. This applies both to those who already have symptoms and to other family members who are screened and found to have the condition. Many diseases can be treated effectively once identified.

Genetic testing is now being used more widely and is generally capable of identifying about 65% of patients with LQTS, 50% to 60% of patients with CPVT, and 10% to 20% of patients with Brugada Syndrome.¹¹ Unfortunately there is no genetic test for Wolff-Parkinson-White Syndrome. The yield for genetic screening of the secondary arrhythmia hypertrophic cardiomyopathy (HCM) is 70%.¹¹ Other structural diseases have lower yields.

The high yield rates for LQTS, CPVT and HCM are particularly useful as the type of treatment and prognosis are partially dependent on the genotype identified.

For more information

To find out where your nearest genetics centre is, see the Directory of UK Genetics Centres at:

www.bshg.org.uk/genetic_centres/uk_genetic_centres.htm

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Technical terms

autosomal dominant	Affects males and females equally with only a single copy of the gene needed to cause the condition.
catecholamines	Chemical compounds including adrenaline, noradrenaline and dopamine. They increase the heart rate, blood pressure and breathing rate.
depolarisation	When there is a spontaneous change from a positive to a negative charge of the pacemaker cells in the sinus node, triggering a heart beat.
genotype	The internally coded inheritable (genetic) information.
heart block	Restriction of the normal electrical pulse through the bundle of HIS. This can cause a slow ventricular contraction rate. The ventricles may only contract once for every two or three contractions of the atria.
monomorphic morphology	Having only one form (structure).
phenotype	Form and structure.
polymorphic precordial	The outward physical manifestation of a genetic change.
repolarisation	Having more than one form (structure).
supraventricular tachycardia	Relating to the precordium – the region over the heart and stomach.
tachycardia	The change of polarity of each cell back to a positive charge as the ventricles and atria expand ready for the next heart beat.
ventricular ectopy	A fast heart rhythm, above 100 beats per minute, originating from the atria.
ventricular fibrillation	A fast heart rhythm above 100 beats per minute
	A heart beat originating in the ventricle and not from the sinus node.
	Very rapid beats (nearly 300 bpm) of the ventricles causing loss of pumping of the blood. It is fatal if not treated quickly with a DC shock to reset the natural pacing rhythm.