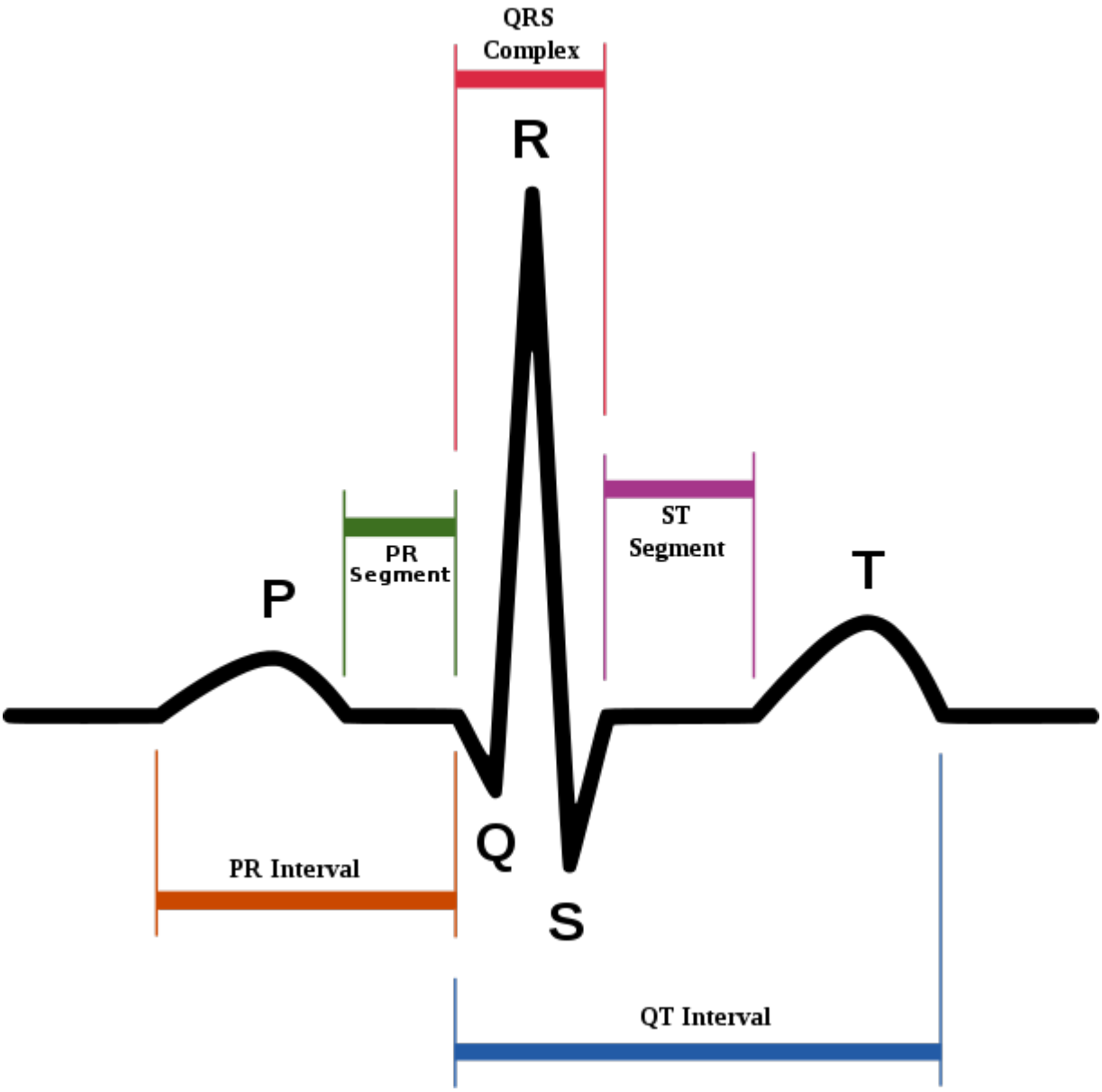
Special Conditions

Long QT Syndrome

The **long QT syndrome** (LQTS) is a rare inborn heart condition in which delayed repolarization of the heart following a heartbeat increases the risk of episodes of torsade de pointes (TDP, a form of irregular heartbeat that originates from the ventricles). These episodes may lead to palpitations, fainting and sudden death due to ventricular fibrillation. Episodes may be provoked by various stimuli, depending on the subtype of the condition.

The condition is so named because of the appearances of the electrocardiogram (ECG/EKG), on which there is a prolongation of the QT interval. In some individuals, the QT prolongation only occurs after the administration of certain medications.



LQTS can arise from mutation of one of several genes.These mutations tend to prolong the duration of the ventricular action potential (APD), thus lengthening the QT interval.

LQTS can be inherited in an autosomal dominant or an autosomal recessive fashion.

The autosomal recessive forms of LQTS tend to have a more severe phenotype, with some variants having associated syndactyly (two or more digits are fused together) (LQT8) or congenital neural deafness (LQT1).

A number of specific gene loci have been identified that are associated with LQTS.

Genetic testing for LQTS is clinically available and may help to direct appropriate therapies.

The most common causes of LQTS are mutations in the genes KCNQ1 (LQT1), KCNH2 (LQT2), and SCN5A (LQT3)

Jervell and Lange-Nielsen syndrome

The Jervell and Lange-Nielsen syndrome (JLNS) is an autosomal recessive form of LQTS with associated congenital deafness. It is caused specifically by mutation of the KCNE1 and KCNQ1 genes

In untreated individuals with JLNS, about 50 percent die by the age of 15 years due to ventricular arrhythmias.

Romano-Ward syndrome

Romano-Ward syndrome is an autosomal dominant form of LQTS that is not associated with deafness.

Pathophysiology

All forms of the long QT syndrome involve an abnormal repolarization of the heart. The abnormal repolarization causes differences in the refractory period of the myocytes. After-depolarizations (which occur more commonly in LQTS) can be propagated to neighbouring cells due to the differences in the refractory periods, leading to re-entrant ventricular arrhythmias.

It is believed that the so-called early after-depolarizations (EADs) that are seen in LQTS are due to re-opening of L-type calcium channels during the plateau phase of the cardiac action potential. Since adrenergic stimulation can increase the activity of these channels, this is an explanation for why the risk of sudden death in individuals with LQTS is increased during increased adrenergic states (i.e. exercise, excitement) -- especially since repolarization is impaired. Normally during adrenergic states, repolarizing currents will also be enhanced to shorten the action potential. In the absence of this shortening and the presence of increased L-type calcium current, EADs may arise.

The so-called delayed after-depolarizations (DADs) are thought to be due to an increased Ca2+ filling of the sarcoplasmic reticulum. This overload may cause spontaneous Ca2+ release during repolarization, causing the released Ca2+ to exit the cell through the 3Na+/Ca2+-exchanger which results in a net depolarizing current.

Diagnosis

The diagnosis of LQTS is not easy since 2.5% of the healthy population have prolonged QT interval, and 10-15% of LQTS patients have a normal QT interval.

The QT interval on the ECG, measured from the beginning of the QRS complex to the end of the T wave, represents the duration of activation and recovery of the ventricular myocardium. QT intervals corrected for heart rate (QTc) longer than 0.44 seconds are generally considered abnormal, though a normal QTc can be more prolonged in females (up to 0.46 sec).

The ***Bazett formula*** is the formula most commonly used to calculate the QTc, as follows: QTc = QT/square root of the R-R interval (in seconds).

Arrhythmia prevention

Arrhythmia suppression involves the use of medications or surgical procedures that attack the underlying cause of the arrhythmias associated with LQTS. Since the cause of arrhythmias in LQTS is after depolarizations, and these after depolarizations are increased in states of adrenergic stimulation, steps can be taken to blunt adrenergic stimulation in these individuals. These include:

Administration of beta receptor blocking agents: which decreases the risk of stress-induced arrhythmias. Beta blockers are the first choice for treating Long QT syndrome.

Potassium supplementation:

- If the potassium content in the blood rises, the action potential shortens and due to this reason it is believed that increasing potassium concentration could minimize the occurrence of arrhythmias. It should work best in

LQT2 since the HERG channel is especially sensitive to potassium concentration, but the use is experimental and not evidence-based.

Mexiletine:

- A sodium channel blocker. In LQT3 the problem is that the sodium channel does not close properly. Mexiletine closes these channels and is believed to be usable when other therapies fail. It should be especially effective in LQT3 but there is no evidence-based documentation.

Amputation of the cervical sympathetic chain (left stellectomy):

- This may be used as an add-on therapy to beta blockers but modern therapy mostly favours ICD implantation if beta-blocker therapy fails.

Arrhythmia termination

Arrhythmia termination involves stopping a life-threatening arrhythmia once it has already occurred. One effective form of arrhythmia termination in individuals with LQTS is the placement of an implantable cardioverter-defibrillator (ICD). Alternatively, external defibrillation can be used to restore sinus rhythm. ICDs are commonly used in patients with syncopes despite beta-blocker therapy, and in patients who have experienced a cardiac arrest.

History

The first documented case of Long QT syndrome was described in Leipzig by Meissner in 1856, where a deaf girl died after her teacher yelled at her. When the parents were told about her death, they told that her older brother who also was deaf died after a terrible fright. This was several decades before the ECG was invented, but is likely the first described case of Jervell and Lange-Nielsen syndrome. In 1957, the first case documented by ECG was described by Anton Jervell and Fred Lange-Nielsen, working in Tønsberg, Norway. Italian pediatrician Cesarino Romano, in 1963, and Irish pediatrician Owen Conor Ward, in 1964, separately described the more common variant of Long QT syndrome with normal hearing, later called Romano-Ward syndrome. The establishment of the International Long-QT Syndrome Registry in 1979 allowed numerous pedigrees to be evaluated in a comprehensive manner. This helped in detecting many of the numerous genes involved

A drowning victim of Long QT Syndrome
Download the video file [0.0 MB]

Drugs to avoid in LQTS [view/annotate inline]
https://www.crediblemeds.org/index.php/?cID=328

Pre excitation Syndrome

Normally, the atria (chambers taking venous blood) and the ventricles (chambers pumping blood towards organs) are electrically isolated, and electrical contact between them exists only at the " atrioventricular node ". In all pre-excitation syndromes, at least one more conductive pathway is present. Physiologically, the normal electrical depolarization wave is delayed at the atrioventricular node to allow the atria to contract before the ventricles. However, there is no such delay in the abnormal pathway, so the electrical stimulus passes to the ventricle by this track faster than via normal atrioventricular/ bundle of His system, so the ventricles are depolarized (excited) before (pre-) normal conduction system.

Types

Several different types have been described.

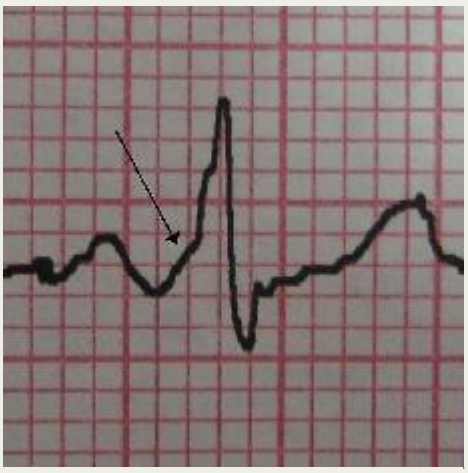
Type	Conduction pathway	PR interval	QRS interval	Delta wave?
Wolff-Parkinson-White syndrome	Bundle of Kent (atria to ventricles)	short	long	yes
Lown-Ganong-Levine syndrome	"James bundle" (atria to bundle of His)	short	normal	no
Mahaim-type	Mahaim fibers	normal	long	yes

Bundle of Kent

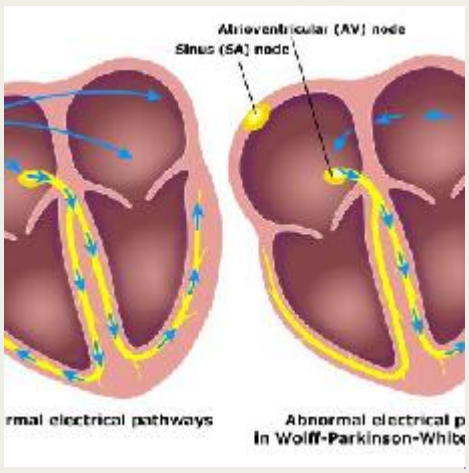
The **Bundle of Kent** is an extra or accessory conduction pathway between the atria and ventricles in the heart. It is an abnormal pathway that is present in a small percentage of

the general population. This pathway is a bundle of connecting tissue that may be either between the left atrium and the left ventricle , in which case it is termed a *type A pre-excitation* , or the right atrium and the right ventricle , in which case it is termed a *type B pre-excitation* . Problems arise when this pathway creates an electrical circuit that bypasses the AV node . The AV node has rate-slowing electrical (regulation) properties, whereas the pathway via the Bundle of Kent does not. When an aberrant electrical connection is made via this bundle, tachyarrhythmia occurs.

In order to treat persons with WPW, destruction of the Bundle of Kent is accomplished by radiofrequency catheter ablation . This procedure is performed almost exclusively by cardiac electrophysiologists .

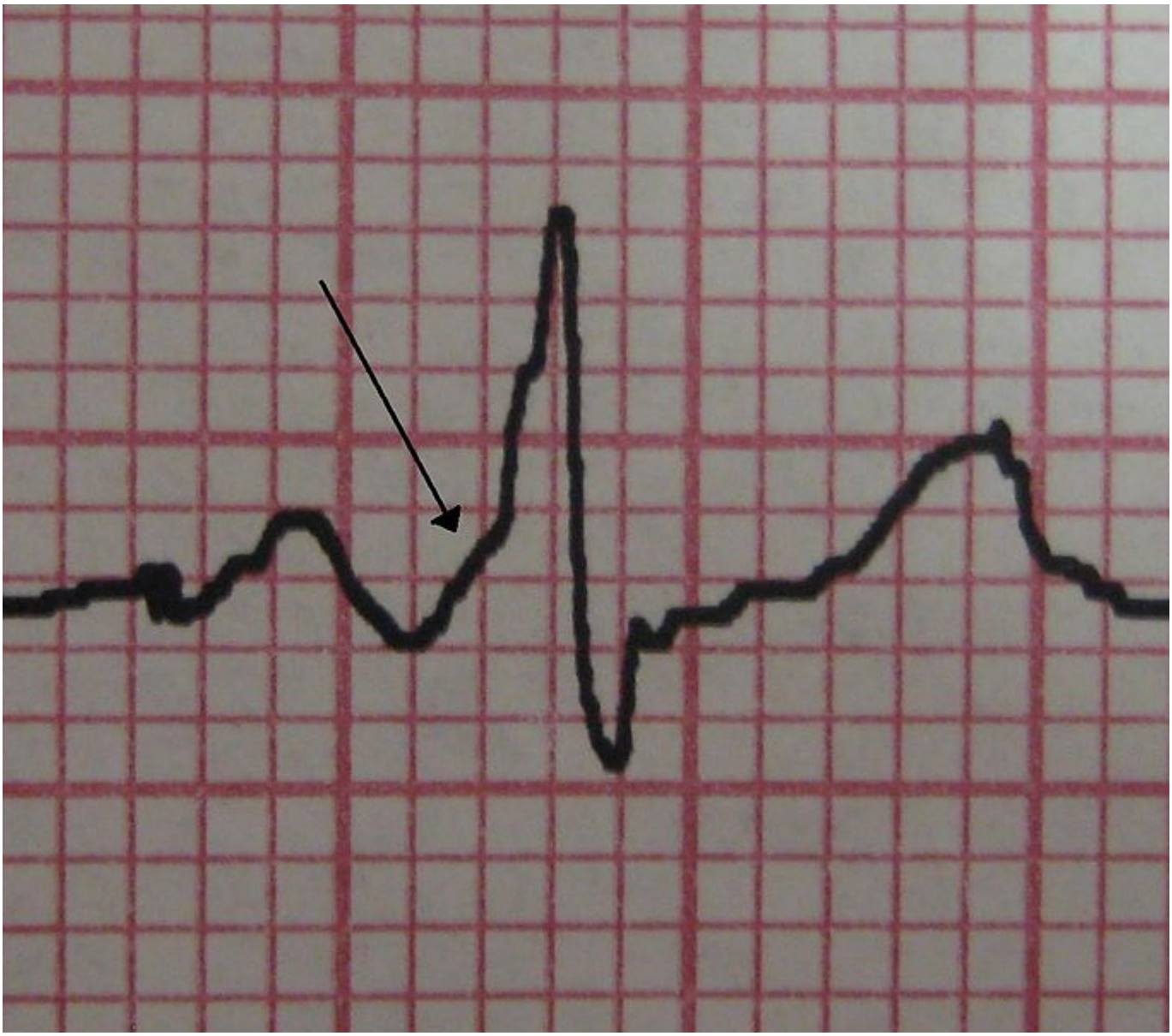


Delta Wave

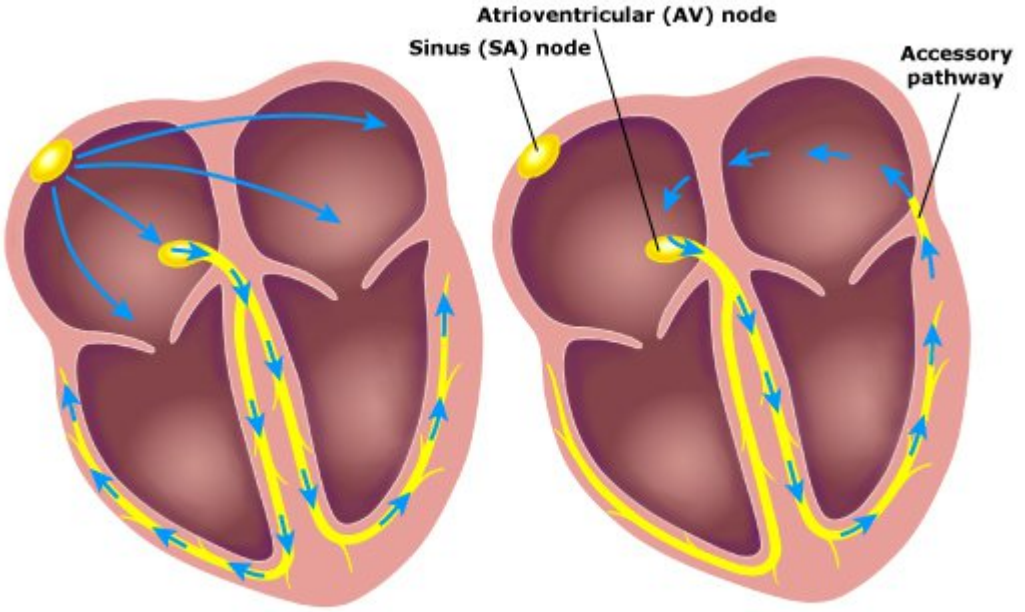


WPW

Author: James Heilman, MD
Source: http://en.wikipedia.org/wiki/File:DeltaWave09.JPG



Author: Tom Lück
Source: http://en.wikipedia.org/wiki/File:WPW.jpeg



Normal electrical pathways

Abnormal electrical pathway in Wolff-Parkinson-White syndrome