The Long and Short of It

2014 Virginia EMS Conference

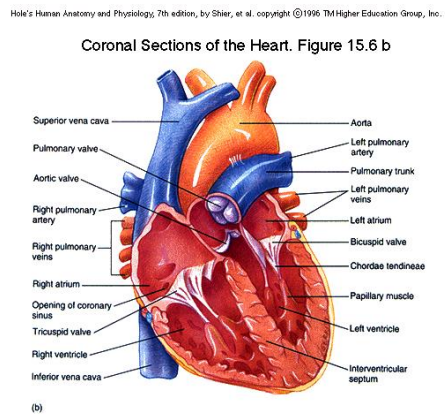
Objectives

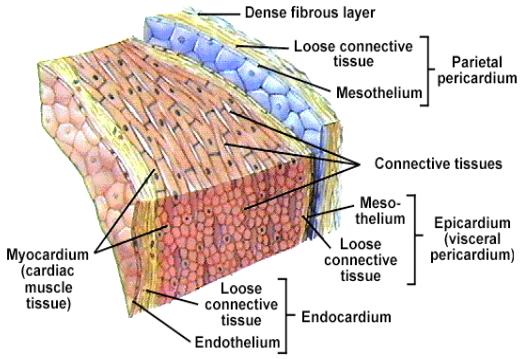
At the end of this session, the audience member shall be able to:

- Discuss heart anatomy and electrical conduction pathways.
- Explain what the QT interval is anatomically and on the ECG.
- Verbalize the genetic and acquired components of LQTS.
- Have an awareness of the medications that can cause LQTS.

Objectives

- Apply proper treatment to a patient with consequences of LQTS.
- Define what is meant by short QT syndrome.
- Describe the rhythm consequences of short QT syndrome.
- Discuss what type of therapy a patient with short QT syndrome may be undergoing.





The Conduction System

- ***Automaticity***- The heart's ability to initiate an impulse without stimulation from the CNS or hormones
- ***Nodal Cells***- "Pacemakers"
- ***Conducting Cells***- Allow the stimulus to spread throughout the myocardium

Nodal Cells

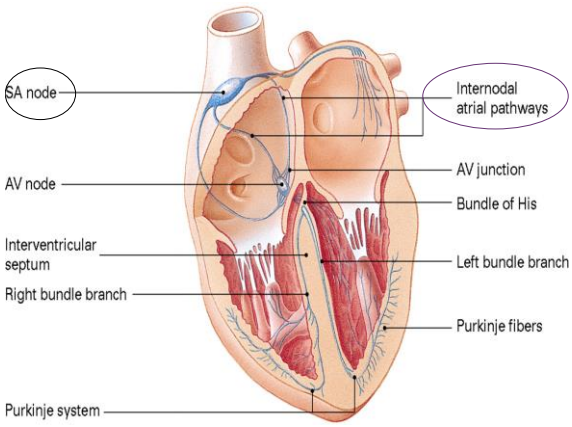
- Generate action potentials at regular intervals
  - Sino-atrial (SA), Atrio-ventricular (AV) and Purkinje Fibers
- Conducting cells are connected to normal cardiac muscle cells
- An action potential can reach all the heart's cells in less than **0.25 seconds**

S.A. (sino-atrial) Node

- Located in the R atrium near the entrance of the SVC
- Generates impulses at **60-100/minute**
- Depolarizes the right and left atria almost simultaneously

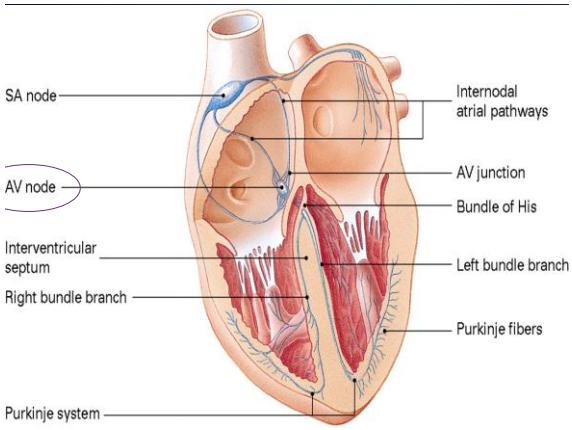
INTERNODAL ATRIAL PATHWAYS

- 3 tracts that run from the SA node through the wall of the right atrium to left atrium and down to the AV node
- Provide depolarization in syncytium so it allows the right and left atrium to contract at the same time



A.V. (atrio-ventricular) node

- Located on the inferior portion of the intra-atrial septum- above the tricuspid valve
- Primary function is to relay electrical impulse from atria to the ventricles
- Allows for a short delay - atrial kick
- Intrinsic firing rate of **40-60/minute**

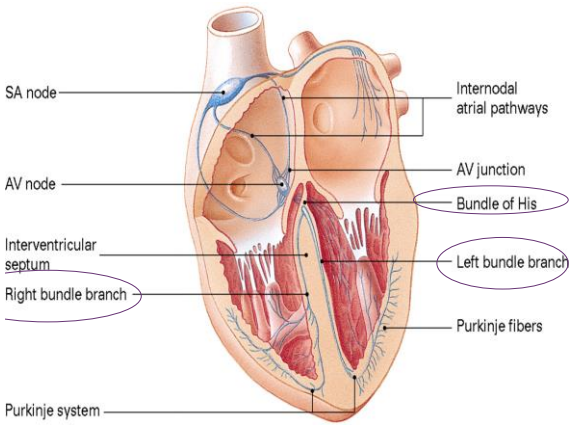


Bundle of His

- Located at the top of the intraventricular septum
- Divides into two branches
- Right bundle branch runs along intraventricular septum to R. ventricle branching into Purkinje fibers

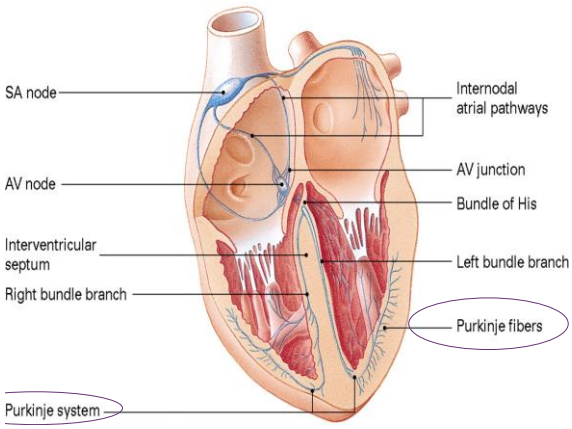
Bundle of His

- Left bundle branch divides into a Left anterior fascicle and a Left posterior fascicle
- Provide innervation to left ventricle to stimulate the large muscle mass to produce systole
- Branch off into the Purkinje fibers



Purkinje Fibers

- The last defense against cardiac arrest
- Fire at a rate of **20-40/minute**
- Produce just enough C.O. to sustain minimal oxygenation to brain and heart for a very short period of time



What is the QT Interval?

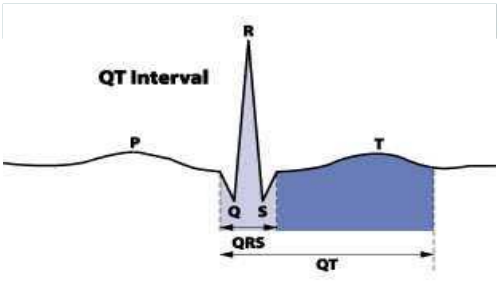
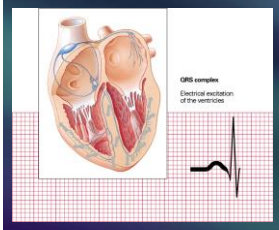


Figure 1. A typical ECG signal consists of the P wave, QRS complex, and T wave. The duration and strength (amplitude) of these pulses directly correspond to the condition of the conduction pathways within the heart.

QT Intervals

- The normal QTc interval varies from approximately 350-480 milliseconds
- About 90% of people have a value between 380 and 440 ms, which is the generally the "normal" range

QRS Complex

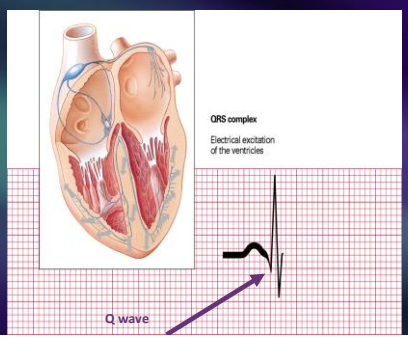


- Indicates electrical stimulation of the ventricular muscle
- Marks the beginning of mechanical systole

Q Wave

- First negative deflection seen after the P-wave
- Represents electrical conduction through the intraventricular septum

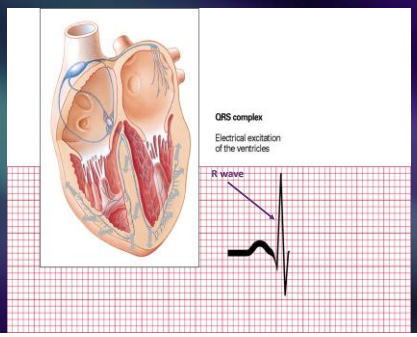
Q Wave



R Wave

- First positive deflection seen after the P-wave
- Represents electrical conduction moving toward the left ventricle

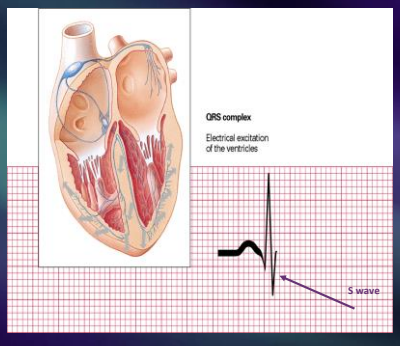
R Wave



S Wave

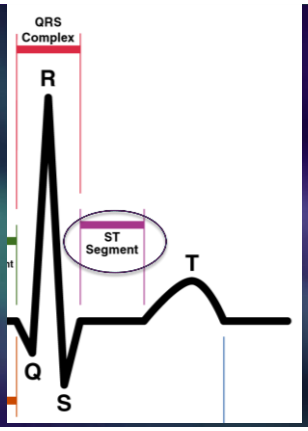
- First negative deflection seen after the R-wave
- Represents electrical conduction through both ventricular walls

S Wave

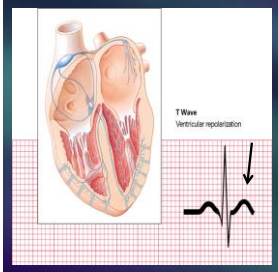


S-T Segment

- Distance between the S-wave of the QRS complex and the beginning of the T-wave
- Represents the beginning of ventricular repolarization



T Wave



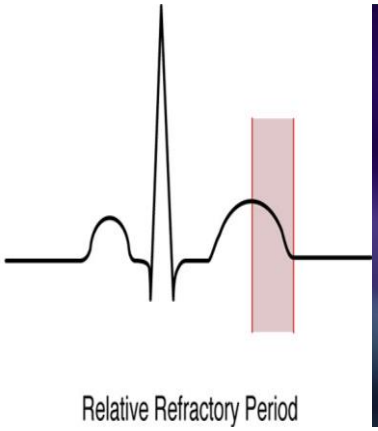
- Rounded wave following the QRS complex
- Indicates repolarization of the ventricles

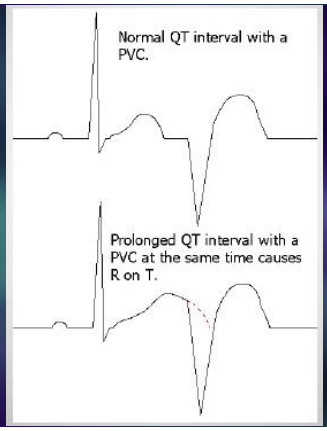
Absolute Refractory Period

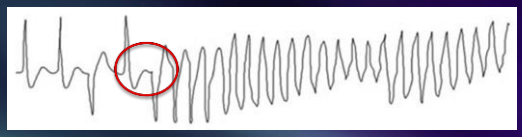
- Time when the cardiac cells have been depolarized and cannot be depolarized a second time until the process of repolarization has occurred
- Occurs from the beginning of the QRS to the apex (middle) of the T-wave

Relative Refractory Period

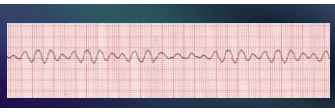
- Extends from the middle of the T-wave to the end of the T-wave
- Time when stimulation may cause premature depolarization of the ventricles
  - 'R on T' phenomenon
- Can cause a ventricular malfunction
  - VT/VF, Torsades, SVT







=



Sudden Cardiac Death (SCD)

- Affects 350,000 - 400,000 each year in the U.S. alone
- Only 5% of victims survive
- Causes of SCD may include structural heart disease or a genetic channelopathy

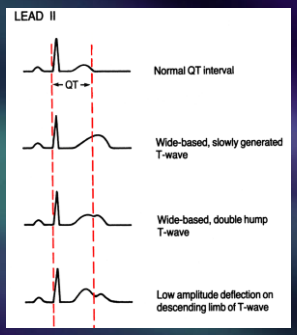
Features common to the cardiac channelopathies

- Subjects are outwardly normal, otherwise healthy
- 50% of family members are gene carriers
- Sudden death may be the first symptom
- Misdiagnosis as epilepsy/sudden syncopal episode is common

Long QT Syndrome

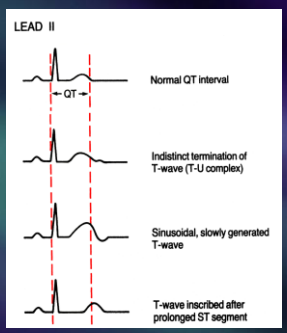
- Genetic disorder (1:5,000-10,000)
- ECG evidence: QTc interval prolonged
  - Upper limit women
    - 0.46
  - Upper limit men
    - 0.45
- Hallmark arrhythmia: Torsades de Pointes / VF

LQTS ECG Patterns



Circ 1992;85[Suppl I]:I140-I144

Additional LQTS ECG Patterns



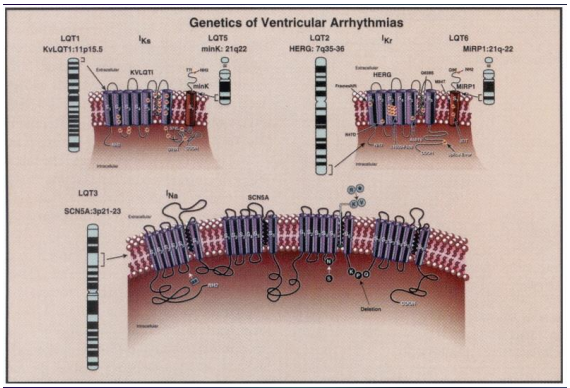
Circ 1992;85[Suppl I]:I140-I144

People at risk of long QT syndrome

- Children, teenagers and young adults or family members of them
  - unexplained fainting, unexplained near drowning or other accidents, unexplained seizures, or a history of cardiac arrest
- First-degree relatives of people with known long QT syndrome
- People taking medications known to cause prolonged Q-T intervals
- People with low potassium, magnesium or calcium blood levels
  - anorexia nervosa/bulimia

Congenital LQTS

- Congenital LQTS is caused by an abnormality in the gene code for the ion channels.
  - Slows the recovery phase of the heartbeat.
- Forms of inherited LQTS include:
  - Multiple ion channel abnormalities
    - The most common ones include LQT1, LQT2, LQT3, LQT4, LQT5
      - Classified by the type of channel which causes the LQTS
      - Those with LQT3 having the highest risk of life-threatening arrhythmias

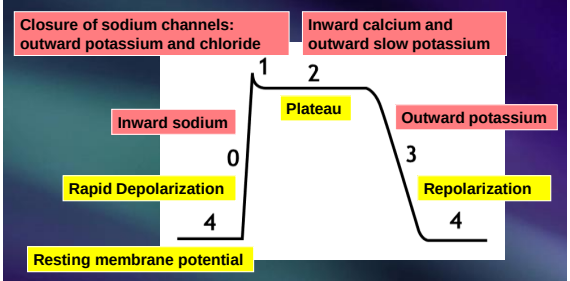


Towbin 2001

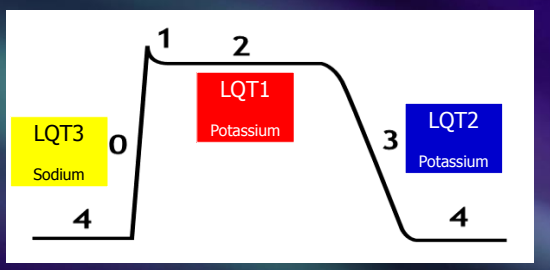
Congenital LQTS

- Other forms of inherited LQTS include:
  - Jervell, Lange-Nielsen Syndrome (autosomal recessive inheritance pattern)
    - Both parents are carriers of the abnormal gene (rare), but they may not manifest LQTS
    - This syndrome is associated with deafness at birth
  - Romano-Ward Syndrome (autosomal dominant inheritance pattern)
    - One parent has LQTS and the other parent usually does not.
    - Hearing is normal; however the likelihood that children in this family would have LQTS is greater

Ventricular Myocyte Action Potential



Genetics of LQT syndrome



Triggering Events for Syncope or SCD

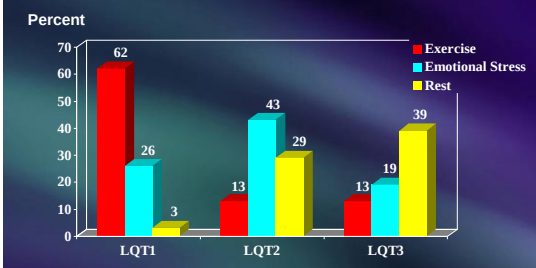
- 3 main factors contributing to syncope or SCD
  - Exercise (LQT1), especially swimming
  - Emotions or emotional stress (LQT2)
  - Events occurring during sleep or at rest,
    slow heart rate during sleep (LQT3)

Circ 2001;103:89-95
Mayo Clin Proc. 1999;74:1088-1094

Triggers

LQT1	LQT2	LQT3

Triggers of cardiac events v. genotype



Circ 2001;103:89-95

LQTS: Identification of Risk

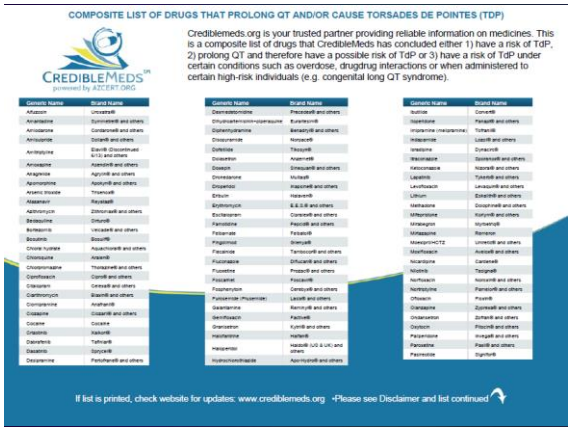
- Most common presenting symptom: unexplained syncope
- Syncope on exertion in pediatric patients should be considered malignant until proven otherwise
- History & ECG:
  - Onset and offset of syncopal episode
  - Siblings, or family members with unexplained syncope or sudden death
  - Family history of "seizures" or congenital deafness
  - Prolonged QTc on ECG

Acquired LQTS

- More than 50 common **medications** can lengthen the Q-T interval in otherwise healthy people
  - Causes a form of acquired long QT syndrome known as *drug-induced long QT syndrome*

Acquired LQTS

- People who develop drug-induced long QT syndrome may also have some subtle genetic defects in their hearts
  - More susceptible to disruptions in heart rhythm from taking drugs that cause prolonged Q-T intervals



COMPOSITE LIST OF DRUGS THAT PROLONG QT AND/OR CAUSE TORSADES DE POINTES (TDP)

CREDIBLEMEDS powered by AZCERT.ORG

Crediblemeds.org is your trusted partner providing reliable information on medicines. This is a composite list of drugs that CredibleMeds has concluded either 1) have a risk of TdP, 2) prolong QT and therefore have a possible risk of TdP or 3) have a risk of TdP under certain conditions such as overdose, drugdrug interactions or when administered to certain high-risk individuals (e.g. congenital long QT syndrome).

Generic Name	Brand Name
Albuterol	Ventolin®
Amantadine	Symmetrel® and others
Amiodarone	Cordarone® and others
Amisulpride	Solian® and others
Amitriptyline	Elavil® (Discontinued 6/10) and others
Amoxapine	Asendin® and others
Aripiprazole	Abilify® and others
Apomorphine	Apokyn® and others
Arsenic trioxide	Trisenox®
Astemizole	Hismanal®
Azithromycin	Zithromax® and others
Bedaquiline	Sirturo®
Bortezomib	Velcade® and others
Bosutinib	Bosulif®
Chloral hydrate	Aquachloral® and others
Chloroquine	Aralen®
Chlorpromazine	Thorazine® and others
Ciprofloxacin	Cipro® and others
Citalopram	Celexa® and others
Clarithromycin	Biaxin® and others
Clomipramine	Anafranil®
Clozapine	Clozaril® and others
Cocaine	Cocaine
Crizotinib	Xalkori®
Dabrafenib	Tafinlar®
Dasatinib	Sprycel®
Desipramine	Pertofrane® and others

Generic Name	Brand Name
Dexmedetomidine	Precedex® and others
Dihydroartemisinin+piperaquine	Eurartesim®
Diphenhydramine	Benadryl® and others
Dofetilide	Tikosyn®
Dolasetron	Anzemet®
Doxepin	Sinequan® and others
Droperidol	Inapsine® and others
Erythromycin	E.E.S.® and others
Escitalopram	Cipralex® and others
Felodipine	Plendil® and others
Felbamate	Felbatol®
Fingolimod	Gilenya®
Flecainide	Tambocor® and others
Fluconazole	Diflucan® and others
Fluoxetine	Prozac® and others
Fluvoxamine	Fluvoxa®
Foscarnet	Foscavir® and others
Furosemide (Frusemide)	Lasix® and others
Gatifloxacin	Zeymar® and others
Gemifloxacin	Factive®
Granisetron	Kytril® and others
Haloperidol	Haldol®
Halofantrine	Halofan® (US & UK) and others
Hydrochlorothiazide	Apo-Hydro® and others

Generic Name	Brand Name
Isoniazid	Convera®
Isopelletierine	Panapelle® and others
Imipramine (Imipramine)	Tofranil®
Indapamide	Lozol® and others
Ketoconazole	Nizoral® and others
Lapatinib	Tykerb® and others
Levofloxacin	Levaquin® and others
Lithium	Eskalith® and others
Methadone	Dolophine® and others
Mifepristone	Korlym® and others
Mirtazapine	Remeron
Moxifloxacin	Avelox® and others
Nicardipine	Cardene®
Nilotinib	Tasigna®
Norfloxacin	Noroxin® and others
Nortriptyline	Pamelor® and others
Ofloxacin	Floxin®
Olanzapine	Zyprexa® and others
Ondansetron	Zofran® and others
Oxytocin	Pitocin® and others
Paliperidone	Invega® and others
Paroxetine	Paxil® and others
Pazopanib	Votrient®

If list is printed, check website for updates: www.crediblemeds.org •Please see Disclaimer and list continued

COMPOSITE LIST OF DRUGS THAT PROLONG QT AND/OR CAUSE TORSADES DE POINTES (TDP)

CREDIBLEMEDS™ powered by AZCERT.ORG

Crediblemeds.org is your trusted partner providing reliable information on medicines. This is a composite list of drugs that CredibleMeds has concluded either 1) have a risk of TdP, 2) prolong QT and therefore have a possible risk of TdP or 3) have a risk of TdP under certain conditions such as overdose, drugdrug interactions or when administered to certain high-risk individuals (e.g. congenital long QT syndrome).

Generic Name	Brand Name
Pazopanib	Votrient®
Pentamidine	NebuPent® and others
Perflutren lipid microspheres	Definity®
Pimozide	Orap®
Posaconazole	Noxafil® and others
Procainamide (Oral-off US mkt)	Procanbid® and others
Promethazine	Phenergan®
Protriptyline	Vivactil®
Quetiapine	Seroquel®
Quinidine	Quinaglute® and others
Quinine sulfate	Qualaquin®
Ranolazine	Ranexa® and others
Ripondone	Eskarnil® and others
Risperidone	Risperdal®
Ritonavir	Norvir®
Saquinavir	Invirase®(combo)
Sertindole	Zilredi® and others
Sevoflurane	Ultane® and others
Sotalol-racemic	Sotalol® and others
Sotalol-D	Sotalol®
Sotalol-D	Betapace® and others
Sotalol	Betapace® and others

Generic Name	Brand Name
Sunitinib	Sutent®
Tacrolimus	Prograf® and others
Tamoxifen	Nolvadex®(discontinued 6/13) and others
Telaprevir	Incivek® and others
Telavancin	Vibativ®
Telithromycin	Ketek®
Telithromycin (Orphan drug in US)	Nolvamycin and others
Thioridazine	Mellaril® and others
Tiapridine	Zaroxolyn® and others
Tolterodine	Detrol® and others
Toremifene	Fareston®
Trazodone	Desyrel® (discontinued 6/13) and others
Trimethoprim-Sulfa	Septra® and others
Trifluoperazine	Eskarnil® and others
Vandetanib	Caprelsa®
Vardenafil	Levitra®
Vemurafenib	Zelboraf®
Venlafaxine	Effexor® and others
Voriconazole	Vfend®
Vorinostat	Zolinza®
Zuclopenthixol	Clopixol® and others

Note: Medicines on this list are reviewed on an ongoing basis to assure that the available evidence supports their continued placement on this list. The list changes regularly and we recommend checkingthe website at crediblemeds.org for the most up-todate information. There may be many additional brand names that are not listed on this form.

Disclaimer and Waiver: The information presented is intended solely for the purpose of providing general information about health-related matters. It is not intended for any other purpose, including but not limited to medical advice and/or treatment, nor is it intended to substitute for the users relationships with their own health care providers. To that extent, by use of this website and the information it contains, the user affirms the understanding of the purpose and releases AZCERT, Inc. from any claims arising out of his/her use of the website and its lists. The absence of drugs from these lists should not be considered an indication that they are free of risk of QT prolongation or TdP. Many medicines have not been tested for this risk in patients, especially those with congenital long QT syndrome.

Generated: January 28, 2014. List last revised: December 12, 2013

Meds of Note

- Amiodarone
- Zithromax
- Celexa/Effexor
- Benadryl
- Pepcid
- Prozac
- Diflucan
- Cerebyx
- Levitra
- Lasix
- Haldol
- Zofran
- Ritalin
- Cipro
- Elavil
- Inapsine
- Paxil
- Phenergan

DRUGS TO BE AVOIDED BY CONGENITAL LONG QT PATIENTS

CREDIBLEMEDS™ powered by AZCERT.ORG

Crediblemeds.org is your trusted partner providing reliable information on medicines. If at all possible, medications on this list should be avoided for use in patients with diagnosed or suspected Congenital Long QT Syndrome.

Generic Name	Brand Name
Albuterol (salbutamol)	Proventil® and others
Alfuzosin	Uroxatral®
Amantadine	Symmetrel® and others
Amiodarone	Cordarone® and others
Amisulpride	Solian® and others
Amitriptyline	Elavil® (Discontinued 6/13) and others
Amoxapine	Asendin® and others
Amphotericin	Abelcet®/AmB and others
Anagrelide	Agrylin® and others
Apomorphine	Apokyn® and others
Arformoterol	Brovana®
Arsenic trioxide	Trisenox®
Atazanavir	Reyataz®
Atomoxetine	Strattera®
Azithromycin	Zithromax® and others
Bedaquiline	Sirturo®
Bortezomib	Velcade® and others
Bosutinib	Bosulif®
Chloral hydrate	Aquachloral® and others
Chlorpromazine	Thorazine® and others
Cisapride	Propulsid® and others
Citalopram	Celexa® and others
Clarithromycin	Biaxin® and others
Clomipramine	Anafranil®
Clozapine	Clozaril® and others
Cocaine	Cocaine
Droperidol	Inapsine®
Dofetilide	Tikosyn®
Doxepin	Sinequan® and others
Dronedarone	Multaq®

Generic Name	Brand Name
Erythromycin	Ery-Tab® and others
Escitalopram	Lexapro®
Flecainide	Tambocor® and others
Fluconazole	Diflucan® and others
Fluoxetine	Prozac® and others
Formoterol	Foradil® and others
Fosaprepitant	Emend®
Foscarnet	Foscavir®
Fosphenytoin	Cerebyx® and others
Furosemide (Furosemide)	Lasix® and others
Gatifloxacin	Tequin® and others
Gemifloxacin	Factive®
Granisetron	Kytril® and others
Haloperidol	Haldol® (US & UK) and others
Ibutilide	Corvert®
Iloperidone	Fanapt® and others
Imipramine (Imipramine)	Tofranil®
Indapamide	Lozol® and others
Isoproterenol	Isuprel® and others
Ketoconazole	Nizoral® and others
Lapatinib	Tykerb® and others
Levofloxacin	Levaquin® and others
Levomethadyl	Orlaam®
Lithium	Eskalith® and others
Mesoridazine	Serentil® and others
Methadone	Dolophine® and others
Methylphenidate	Ritalin® and others
Moxifloxacin	Avelox® and others
Nicardipine	Cardene®
Nilotinib	Tasigna®
Nortriptyline	Pamelor® and others
Ofloxacin	Floxin®
Ondansetron	Zofran® and others
Oxybutin	Ditropan® and others

If list is printed, check website for updates: www.crediblemeds.org +Please see Disclaimer and list continued

DRUGS TO BE AVOIDED BY CONGENITAL LONG QT PATIENTS

CREDIBLEMEDS™ powered by AZCERT.ORG

Crediblemeds.org is your trusted partner providing reliable information on medicines. If at all possible, medications on this list should be avoided for use in patients with diagnosed or suspected Congenital Long QT Syndrome.

Generic Name	Brand Name
Pentamidine	NebuPent® and others
Perflutren lipid microspheres	Definity®
Phenothiazine	Adapes PR and others
Phenylpropanolamine	Acutrim® and others
Pimozide	Orap®
Posaconazole	Noxafil® and others
Procainamide (Oral-off US mkt)	Procanbid® and others
Promethazine	Phenergan®
Protriptyline	Vivactil®
Pseudoephedrine	PseudoCed® and others
Quetiapine	Seroquel®
Quinidine	Quinaglute® and others
Quinine sulfate	Qualaquin®
Ranolazine	Ranexa® and others
Ripondone	Eskarnil® and others
Risperidone	Risperdal®
Ritonavir	Norvir®
Saquinavir	Invirase®(combo)
Sertindole	Zilredi® and others
Sevoflurane	Ultane® and others

Generic Name	Brand Name
Sotalol-racemic	Sotalol® and others
Sotalol-D	Sotalol®
Sotalol-D	Betapace® and others
Sotalol	Betapace® and others
Tacrolimus	Prograf® and others
Tamoxifen	Nolvadex®(discontinued 6/13) and others
Telaprevir	Incivek® and others
Telavancin	Vibativ®
Telithromycin	Ketek®
Terfenadine	Seldane® and others
Telithromycin (Orphan drug in US)	Nolvamycin and others
Thioridazine	Mellaril® and others
Tiapridine	Zaroxolyn® and others
Tolterodine	Detrol® and others
Toremifene	Fareston®
Trazodone	Desyrel® (discontinued 6/13) and others
Trimethoprim-Sulfa	Septra® and others
Vandetanib	Caprelsa®
Vardenafil	Levitra®
Vemurafenib	Zelboraf®
Venlafaxine	Effexor® and others
Voriconazole	Vfend®
Vorinostat	Zolinza®
Zuclopenthixol	Clopixol® and others
Zuclopenthixol	Clopixol® and others
Zuclopenthixol	Clopixol® and others

Treatment Therapy for LQTS Patients

- Beta-adrenergic blocking agents are the drugs of choice to treat long QT syndrome
  - Propranolol
  - Nadolol
  - Metoprolol
  - Atenolol

Treatment Therapy for LQTS Patients

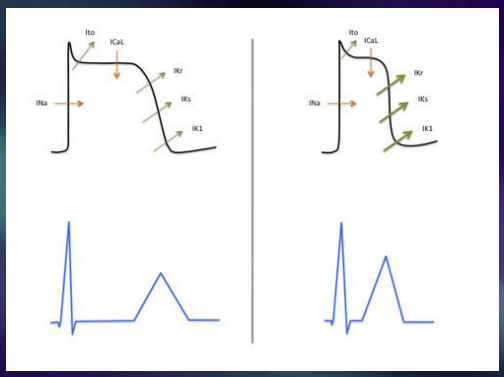
- Mexiletine
  - LQT3 patients
    - Taking this anti-arrhythmic drug in combination with propranolol may help shorten the Q-T interval
- Potassium supplements

Treatment Therapy for LQTS Patients

- Surgical intervention
  - Implantation of cardioverter-defibrillator
  - Placement of a pacemaker
- Patients with long QT syndrome should avoid participation in competitive sports, strenuous exercise, and stress-related emotions

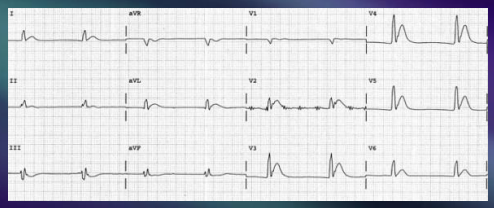
Short QT Syndrome

- Rare
- Related to several mutations affecting the function of ion channels responsible for the currents that generate the cardiac action potential
  - hyperfunction of the potassium current or
  - hypofunction of the calcium current



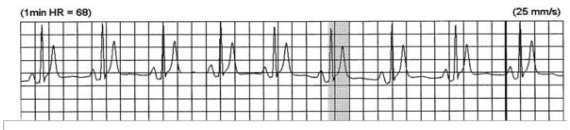
Other Short QT causes

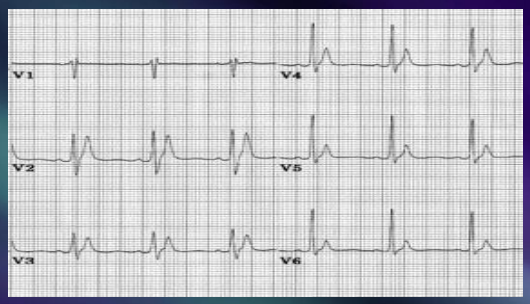
- Hypercalcemia
- Digoxin



Short QT ECG Characteristics

- QT < 300msec
- Re-entrant arrhythmias
- No significant QT change with HR changes
- Short ST segment with tall, narrow peaked T-waves in V1-V6





SQTS Characteristics

- Age of presentation ranges from a few months to 60's
- No specific triggers for episodes that took place at rest, during exercise, or after loud noises
- Excluded in patients without structural heart disease presenting with SCD

SQTS Characteristics

- Symptoms often documented are syncope and palpitations
  - Self-terminating VF episodes were considered the most likely mechanism
  - Atrial fibrillation constitutes one of the main findings of SQTS
    - Taken it into account in the management of young patients with lone atrial fibrillation

Short QT

- Management
  - Pharmacological (small studies)
    - Only quinidine effective in increasing the QTI
  - ICD experience (limited)
    - T wave oversensing/inappropriate shocks