Long QT Syndrome (LQTS)

Epidemiology:
Sudden cardiac death: 350K-400K/yr in US
~ 5% victims survive
LQTS: estimates 1:5000 – 1:10000 in US have LQTS
~ 3000 deaths/yr.

LQTS can be:
Acquired:
Metabolic disorders: low K, Mg, Ca; starvation; anorexia nervosa; liquid protein diets
Bradyarrhythmias: sinus node dysfunction; AVB
Drugs:
Antiarhythmics: quinidine, procainamide, sotalol, amiodarone, disopyramide, dofetilide, ibutilide, selamitide, beperdil,
Antihistamines: terfenadine, astemizole
Psychotropics: phenothiazines, butyrphenones, TCA’s, halperidol, SSRI, risperidone, thioridazine
Antibiotics: E/clarithro/azithromycin, TMP-SMX, ketoconazole, ampicillin, pentamidine, quinolones
 list is not exhaustive 😊

Congenital:
Jervell-Lange-Nielson: LQTS + congenital deafness; autosomal recessive
Romano-Ward: LQTS w/o deafness; autosomal dominant
Idiopathic
Other: MVP, intracranial disease, HIV

Natural History:
Torsade de pointes (TdP)
Up to 80% present with syncope or nonfatal sudden cardiac death
Female predominance
But sx usually presents at later age (16+/−13 yrs vs. 11+/−11 for boys)
Risk of cardiac event higher in males til puberty; higher for females in adulthood
Triggers: exercise, emotional stress, sleep/rest states.
QTC >440 ms (males); >450ms (females)
Up to 12% can have normal QT interval at rest
QTC strong/significant predictor of cardiac event rate (the longer the higher risk)
**Pathophysiology:**

- **Increased sympathetic activity:** usually in the inherited LQTS. Increased/unopposed activity of left sympathetic stellate ganglion; decreases refractory period → premature stimulation?
- **Derangements in ion flow:** increase AP duration, prolonging repolarization → early afterdepolarization (EAD) & triggered activity → reach threshold potential → depolarize cells → causes an AP, which if propagated can produce ventricular premature depolarizations → polymorphic VT (TdP).
  - EAD’s potentiated by many meds…notables:
    - Class IA antiarrhythmics block Na & K channels (low dose quinidine preferentially blocks Kout)
    - IIIA: blocks K channels; ex: sotalol; amiodarone, ibutilide (differs by increasing inward Na during plateau phase thus prolonging it)

**Genetics**

- **LQTS1:** chrom 11; gene KvLQT1 encodes alpha-subunit of the slowly acting component of the outward-rectifying K current (IKs)
  - Accounts for > 50% of all cases of LQTS
  - Homozygous mutations cause Jervell-Lange-Nielson (KvLQT1 needed for inner ear development)
- **LQTS2:** chrom 7; gene HERG (human ether-a-go-go-related gene) encodes for rapidly acting component of outward-rectifying K current (IKr)
- **LQTS3:** chrom 3; gene SCN5A encodes Na channel; mutation causes impaired inactivation of inward Na channel; mutation can be de novo (non-inherited)
- **LQTS4:** chrom 4; gene??
- **LQTS5:** mutation of mink gene (chrom21); this gene product required to combine with KvLQT1 to make IKs.
- **LQTS6:** mutation in mink related peptide 1 (MiRP1 or KCNE2) (chrom 21), which combines with HERG to alter its function affecting Ikr; mutants form outward K channels that open slowly & closes rapidly, decreasing the K current.

**Treatment**

- **Acquired LQTS:** stop the offending medications; correct metabolic abnormalities
  - For immediate Rx: IV Mg sulfate; pacing; IB antiarrhythmics (lidocaine, phenytoin); alkalinization w/ Na bicarb if TdP due to quinidine; K supplements.
- **Congenital:** B blockers (can still have recurrences); left cervicothoracic sympathectomy (resect left stellate ganglion…can cause Horner’s); pacemakers; ICD’s
  - Other modalities: spironolactone (increases K); K channel openers (nicorandil); mexiletine (IB: blocks Na channel to shorten plateau phase)

**Biblio:**

www.longqt.org
www.sads.org/lqts.html