

# Torsade de pointes

## Beware of drugs that induce this condition

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Torsade de pointes is a low frequency event but a potentially life-threatening condition. It's an arrhythmia with ventricular tachycardia and long QT interval. The name "twisting of points" was given by F. Dessertenne in 1966 to refer to the undulating pattern of QRS complexes along the isoelectric line of the electrocardiogram (ECG). The condition is either congenital or acquired mainly as an iatrogenic disease. In the presence of secondary risk factors, certain drugs inhibit the potassium rapidly activating rectifier outward current ( $I_{Kr}$ ) in the cardiac action potential, prolonging the QT interval. The incidence appears to be 3-15% for a wide range of products. To prevent unnecessary exposure to risk, doctors need to be aware of these interactions and of the typical features of torsade, its diagnosis and management. Choosing the lowest effective dosage and close clinical and electrocardiographic monitoring of the QT interval would be prudent during treatment.

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### Etiology of QT prolongation

- based on clinical findings and response to therapy
  - congenital, or idiopathic
    - adrenergic-dependent
  - acquired
    - pause-dependent
    - most frequently induced by drug effects/interactions or electrolyte disturbances
- more than 2 agents that prolong QT behave synergistically on repolarization
  - interaction of torsadogenic drug with agent that inhibits cytochrome P-450 metabolism, especially CYP3A4

### Predisposing factors

#### Susceptible hearts

- organic heart disease
- bradycardia
- myocardial ischemia
- low left ventricular ejection fraction
- abnormal baseline ECG, prominent U wave
- prolonged QT interval
- presence of atrial arrhythmias, fibrillation/flutter
- sick sinus syndrome
- pacemaker or prosthetic valve dysfunction

#### Central nervous system disorders

- tumours
- subarachnoid hemorrhage
- encephalitis/meningitis

#### Endocrine and electrolyte disturbances

- hypothyroidism
- hypokalemia
- hypomagnesemia
- hypocalcemia

#### Environment and gender

- co-administration of several QT-prolonging drugs
- cytochrome P-450 metabolism interactions
- hypothermia
- female

### Symptoms

- may be asymptomatic
- otherwise, low cardiac output leading to syncope, palpitations, dizziness, exertional dyspnea, fatigue, angina, signs and symptoms of congestive heart failure
- if attack was prolonged or in rapid succession, seizures, syncope, death

### ECG

#### The following features distinguish torsade de pointes from other ventricular tachycardias

- heart rate — 200-240 beats/min, range 160-280 beats/min
- rhythm — irregular
- R-R interval — variable, with a long/short cycle often seen before torsade begins
- QRS complex — wide (> 0.12 secs) and bizarre in appearance with varying amplitude and axis
- torsade — clusters over runs of 5-20 beats
- AV-dissociation — if the P waves are visible
- QT interval — delay in repolarization — long QT and often the appearance of a U wave. This should be measured in several leads and the longest QT (QT-max) should be used. Prolonged QT interval is at least 500 msec or QTc 440 msec.
- T wave — distorted or broad
- end of torsade — arrhythmia is non-sustained — either terminates spontaneously or degenerates to ventricular fibrillation and sudden death

### Dangerous drugs

#### Some agents with risk for torsade de pointes

- class 1A antiarrhythmics — quinidine, disopyramide, procainamide
- class 1C — encainide
- class III — potassium channel blockers — sotalol, amiodarone, N-acetyl procainamide, dofetilide, ibutilide
- class IV — calcium channel blockers, e.g. bepridil
- class V — adenosine
- psychotropic drugs — phenothiazines (thioridazine, chlorpromazine), haloperidol, tricyclic and tetracyclic antidepressants
- antimicrobials — macrolides (e.g. erythromycin, tacrolimus), quinolones (e.g. chloroquine), amantadine, trimethoprim-sulfamethoxazole
- histamine receptor H1 antagonists — astemizole, terfenadine
- lipid-lowering agents — probucol
- prokinetic medications — cisapride
- toxins — zinc, organophosphates
- tamoxifen, arsenic trioxide, methadone, domperidone

### Congenital long QT

- dynamic long QT or QTU segments during  $\beta_1$  adrenergic stimulation — e.g. exercise, pain/emotion and provocation with beta-adrenergic agents
- Romano-Ward syndrome
- Jervell and Lange-Nielsen syndrome
- six mutations identified so far — LQT1 to LQT6 — in genes encoding ion channels
- reduced potassium outflow current prolongs action potential and QT interval
- mutations may correlate with specific therapies

### Emergency therapy

- do not confuse with other ventricular tachycardias — class IA antidysrhythmic drugs can be disastrous
- if degenerates to ventricular fibrillation — current cardioversion (DC shock) for termination
- urgent measures to prevent immediate recurrence
  - removal of any potentially torsadogenic agents
  - magnesium infusion
  - supplemental potassium to increase serum levels to 4.5 mmol/L — this will accelerate repolarization
  - transvenous cardiac pacing to 100-140 beats/min — may be life-saving; the inverse relationship between basic heart rate and repolarization time means faster pacing will result in shorter QT interval.