On the Lighter Side…

https://youtu.be/KK-ZtH3jlhU

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Ventricular Arrhythmias Part 1

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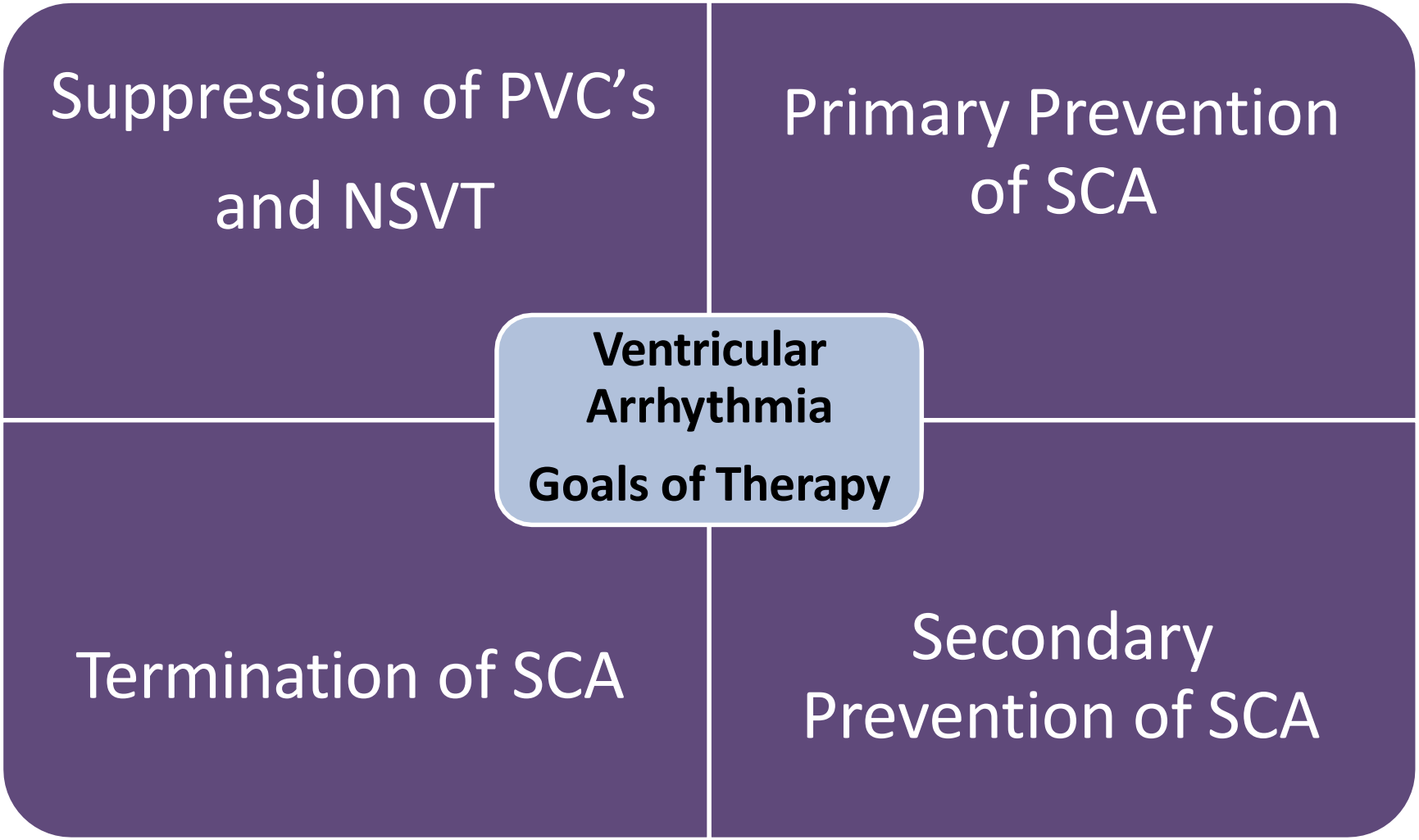
April 2021

Objectives (Part 1)

- Understand common correctable causes of PEA and asystolic arrest
- Demonstrate knowledge of appropriate cardiopulmonary resuscitation (CPR)
- Formulate a treatment plan for patients experiencing cardiac arrest arrhythmias (VF, pVT, PEA, asystole)
  - Pharmacologic therapies
  - Non-pharmacologic therapies
- Identify common classes of medications that prolong the QTc interval and formulate a plan to monitor these medication therapies



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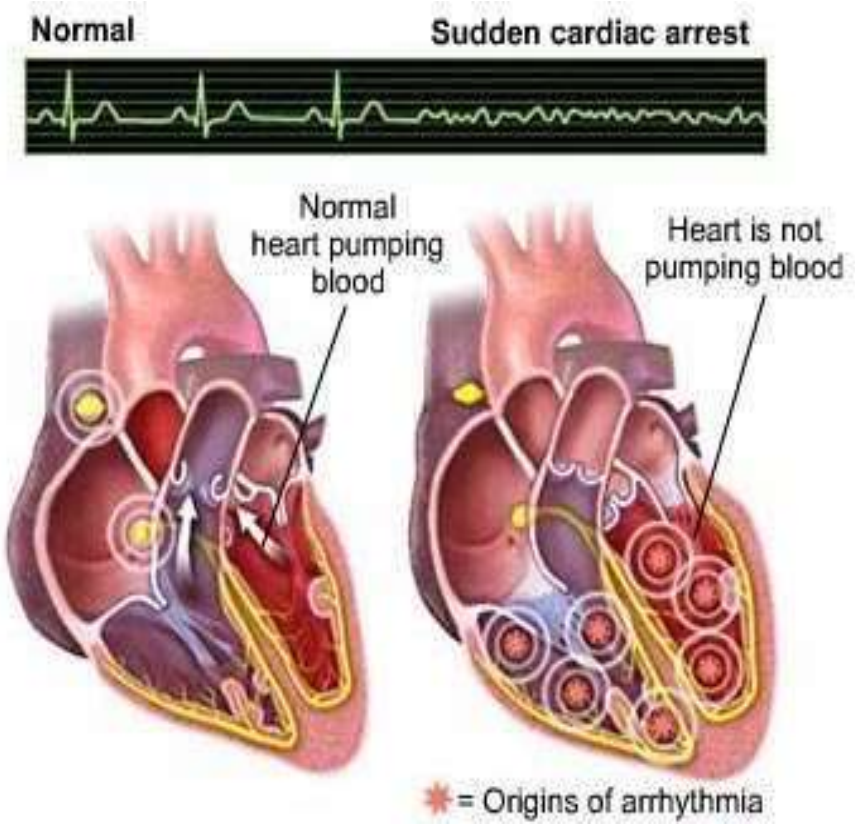
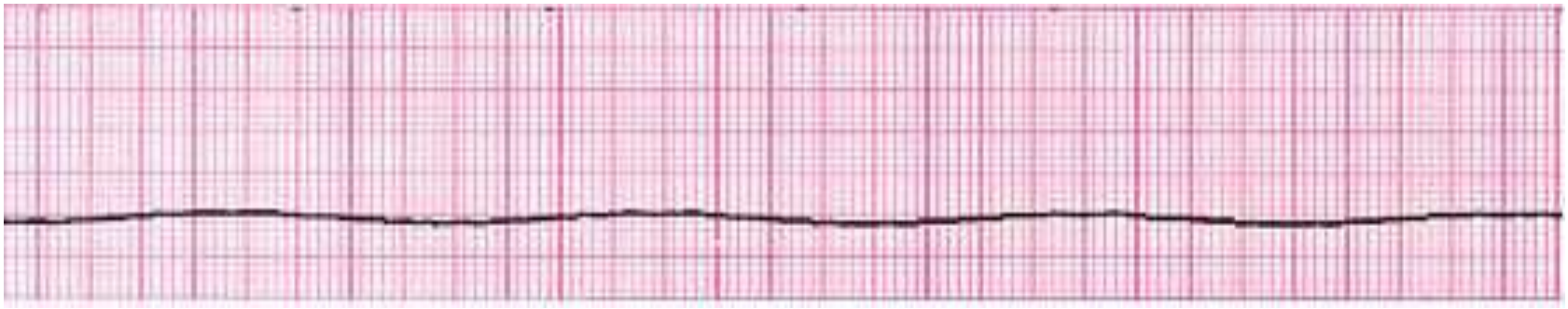
Sudden Cardiac Arrest (SCA)

- SCA= Heart suddenly stops beating, confirmed by an absence of signs of circulation
- Sustained VT, VF are primary causes
  - Other causes: PEA, asystole
- Leading cause of death in US
  - 350,000 cases/year in US
  - 80% of these patients have CHD



Asystole



- Absence of cardiac (electrical) activity
- Also know as “flat line”
- Ventricular arrhythmias will deteriorate to asystole if not treated
- **VERY poor prognosis**

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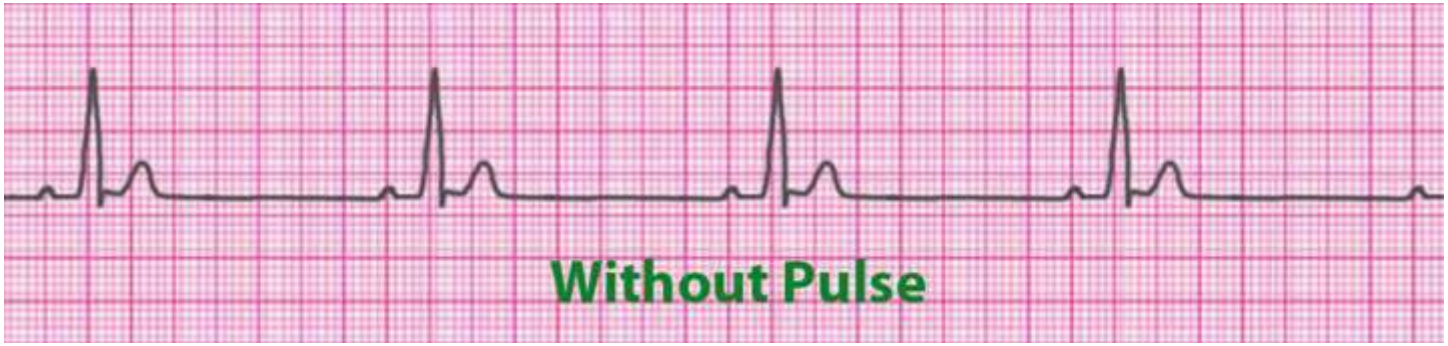
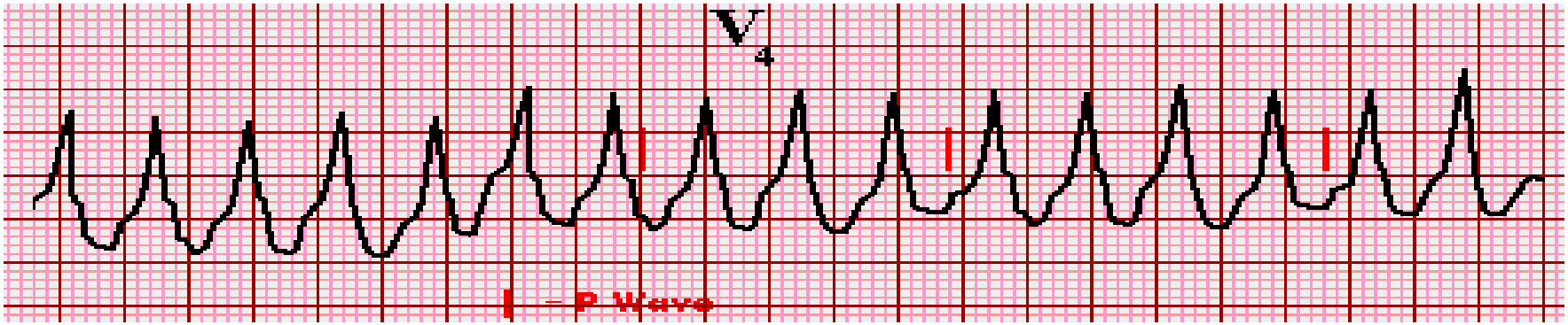
http://atlantaacls.com/2011/06/08/asystole/

Pulseless Electrical Activity (PEA)



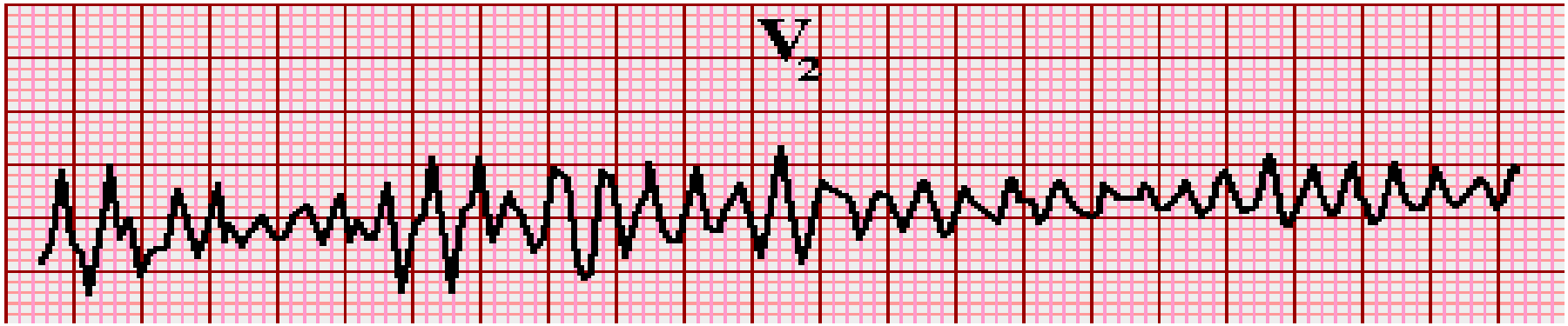
- Unresponsive with lack of a palpable pulse
- Organized cardiac electrical activity on EKG
  - Tachycardic or bradycardic

Pulseless Ventricular Tachycardia (pVT)

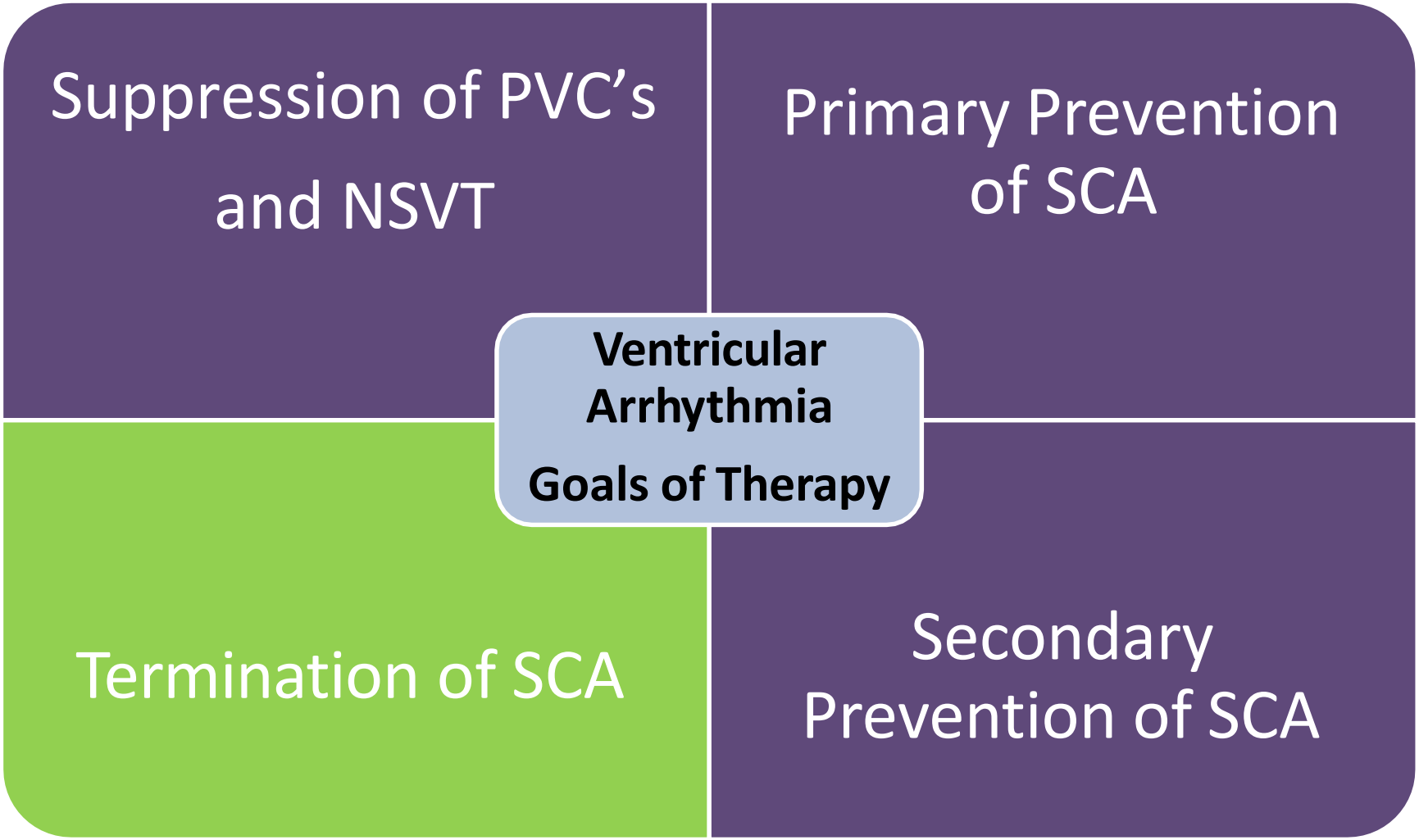


- Consists of >/= 3 consecutive complexes in a row that originates in the ventricles
- Ventricular rate > 100 bpm
- QRS complexes may appear similar (monomorphic) or multiform (polymorphic) organized, no visible P or T waves
- **No pulse is present, patient is unresponsive**

Ventricular Fibrillation (VF)



- Absence of organized electrical activity in the heart
- Ventricular rate >300 bpm
- Lack of recognizable P waves, QRS Complexes, and T waves
- **Complete loss of cardiac output**


Suppression of PVC's and NSVT
Primary Prevention of SCA
Ventricular Arrhythmia
Goals of Therapy
Termination of SCA
Secondary Prevention of SCA

Sudden Cardiac Arrest
"Chain of Survival"

GOAL = Return of Spontaneous Circulation (ROSC)

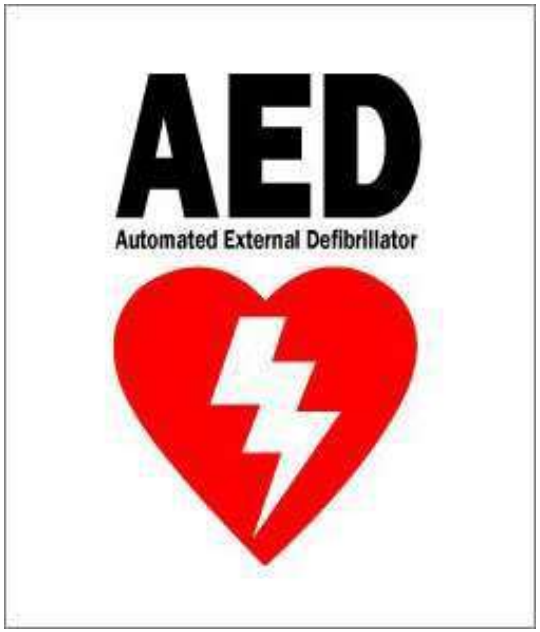
1. Initiate emergency response
2. Bystander CPR – BLS or Hands-only
3. Early Defibrillation
4. Transport to hospital
5. Early ACLS

5 Critical Components of CPR

1. **Minimize interruptions in chest compressions**
   - Chest compression fraction >80% of cardiac arrest time
   - Limit interruptions to <10 seconds
2. **Compression rate 100-120 cpm**
   - <100 cpm, ROSC decreases by 30%
   - >120 cpm, decreased coronary blood flow due to decreased percentage of compressions at adequate depth
3. **Compression depth >2 inches for adults**
   - <1.5 inches, decreases survival by 30% with out of hospital cardiac arrest
4. **Allow chest recoil**
5. **Avoid excessive ventilation**
   - <12 ventilations per minute to avoid the impact of positive pressure ventilation on blood flow

Circulation 2013;128:417-435

Automated External Defibrillator (AED)



Which of the four rhythms associated with SCA are 'shockable'?

Treatment of SCA

Adult Cardiac Arrest Algorithm (VF/pVT/Asystole/PEA)

1. **Start CPR**
   - Give oxygen
   - Attach monitor/defibrillator

Rhythm shockable?

Yes

2. **VF/pVT**
3. **Shock**
4. **CPR 2 min**
   - IV/IO access

Rhythm shockable?

Yes

5. **Shock**
6. **CPR 2 min**
   - **Epinephrine** every 3-5 min
   - Consider advanced airway, capnography

Rhythm shockable?

Yes

7. **Shock**
8. **CPR 2 min**
   - **Amiodarone** or **lidocaine**
   - Treat reversible causes

No

9. **Asystole/PEA**
10. **Epinephrine ASAP**

CPR 2 min
- IV/IO access
- **Epinephrine** every 3-5 min
- Consider advanced airway, capnography

Rhythm shockable?

Yes

No

11. **CPR 2 min**
    - Treat reversible causes

Rhythm shockable?

No

Yes

12.
- If no signs of return of spontaneous circulation (ROSC), go to **10** or **11**
- If ROSC, go to Post–Cardiac Arrest Care
- Consider appropriateness of continued resuscitation

Go to 5 or 7

CPR Quality

- Push hard (at least 2 inches [5 cm]) and fast (100-120/min) and allow complete chest recoil.
- Minimize interruptions in compressions.
- Avoid excessive ventilation.
- Change compressor every 2 minutes, or sooner if fatigued.
- If no advanced airway, 30:2 compression-ventilation ratio.
- Quantitative waveform capnography
  - If $PETCO_2$ is low or decreasing, reassess CPR quality.

Shock Energy for Defibrillation

- **Biphasic**: Manufacturer recommendation (eg, initial dose of 120-200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered.

Drug Therapy

- **Epinephrine IV/IO dose:** 1 mg every 3-5 minutes
- **Amiodarone IV/IO dose:** First dose: 300 mg bolus. Second dose: 150 mg.
  or
  Lidocaine IV/IO dose: First dose: 1-1.5 mg/kg. Second dose: 0.5-0.75 mg/kg.

Advanced Airway

- Endotracheal intubation or supraglottic advanced airway
- Waveform capnography or capnometry to confirm and monitor ET tube placement
- Once advanced airway in place, give 1 breath every 6 seconds (10 breaths/min) with continuous chest compressions

Return of Spontaneous Circulation (ROSC)

- Pulse and blood pressure
- Abrupt sustained increase in $PETCO_2$ (typically ≥40 mm Hg)
- Spontaneous arterial pressure waves with intra-arterial monitoring

Reversible Causes

- **H**ypovolemia
- **H**ypoxia
- **H**ydrogen ion (acidosis)
- **H**ypo-/hyperkalemia
- **H**ypothermia
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary

SCA Drugs

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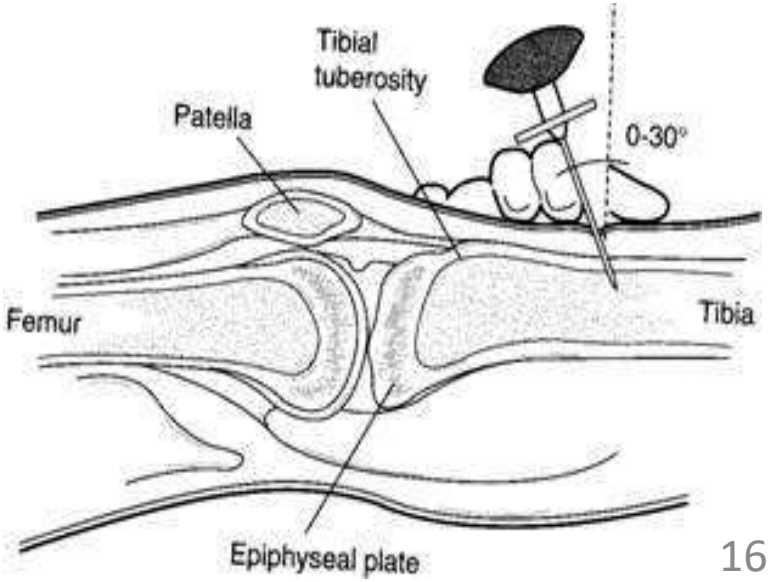
- **T**ension pneumothorax
- **T**amponade, cardiac
- **T**oxins
- **T**hrombosis, pulmonary
- **T**hrombosis, coronary

Intraosseous Infusion

- Drug delivery similar to central venous access possible
- Average access time <2 minutes
- Any drug given IV can be given IO at same dose



Epinephrine in SCA

- Adrenergic agonist:
  - Alpha 1: vasoconstriction, increases coronary and cerebral blood flow
  - Beta 1: increase HR, conduction velocity, and contractility
    - Makes ventricles more responsive to direct-current shock

- pVT/VF dosing: 1mg every 3-5 min given immediately after <u>second</u> unsuccessful defibrillation attempt
- PEA/Asystole dosing: 1mg every 3-5 min

Amiodarone Dosing for pVT/VF Arrest

- Initial Bolus
  - 300mg IV/IO undiluted after 3rd shock
  - Flush with 10-20 mL NS

- Refractory Bolus
  - 150mg IV/IO undiluted every 3-5 minutes

Lidocaine Dosing for pVT/VF Arrest

- Initial: 1-1.5 mg/kg IV/IO bolus
- Refractory: give 0.5-0.75 mg/kg IV/IO bolus every 5-10 minutes
- Proven to be less effective compared to amiodarone

Cardiac Arrest Patient Case

SC is a 54 yo female who chokes on a bite of brat-wurst while tailgating at a Brewers game. No one she is with knows the Heimlich maneuver so call 911 for help.

During the wait for EMS to arrive, the patient loses consciousness. When EMS arrives, she is found to be in VF arrest.

Cardiac Arrest Patient Case

Which treatment options give this patient the best chance of survival?

a) Amiodarone + defibrillation
b) Amiodarone + epinephrine
c) CPR + defibrillation
d) CPR + epinephrine
e) Epinephrine + lidocaine

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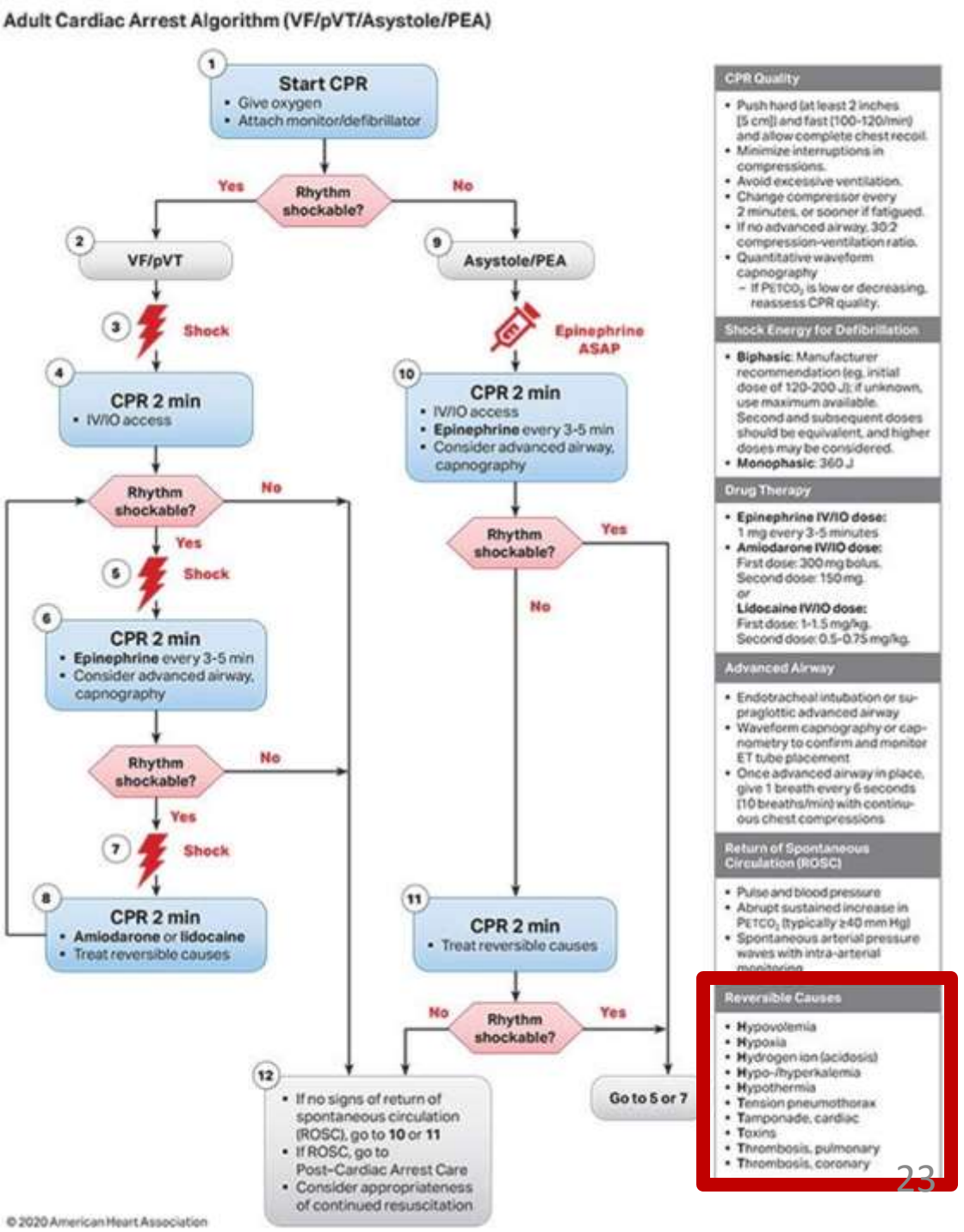
Reversible Causes of SCA



Reversible Causes of Sudden Cardiac Arrest

5 H's

- Hypovolemia
- Hypoxia
- Hydrogen ion (acidosis)
- Hyper-/hypokalemia
- Hypothermia

5 T's

- Toxins
- Tamponade
- Tension pneumothorax
- Thrombosis (coronary)
- Thrombosis (pulmonary)

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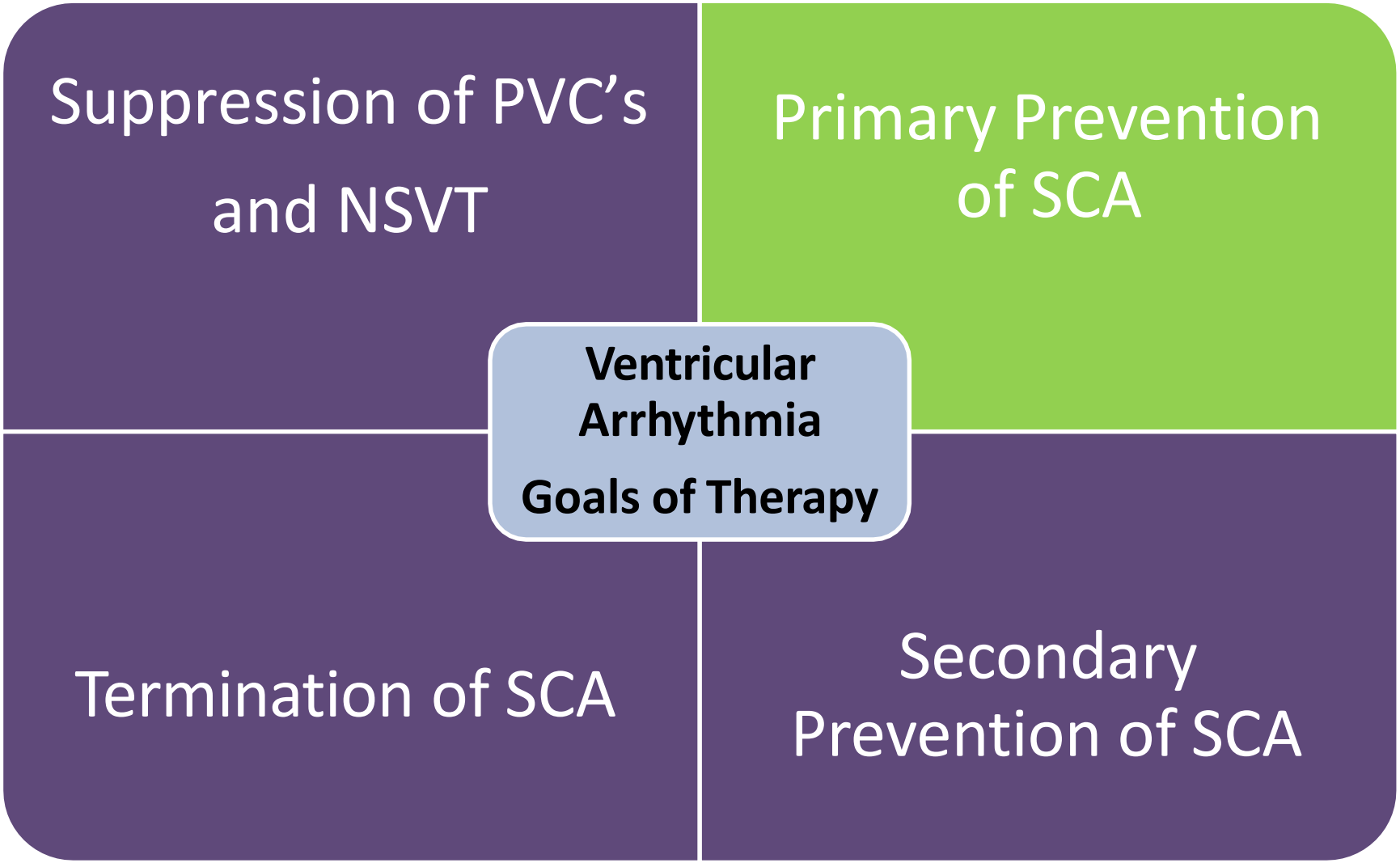

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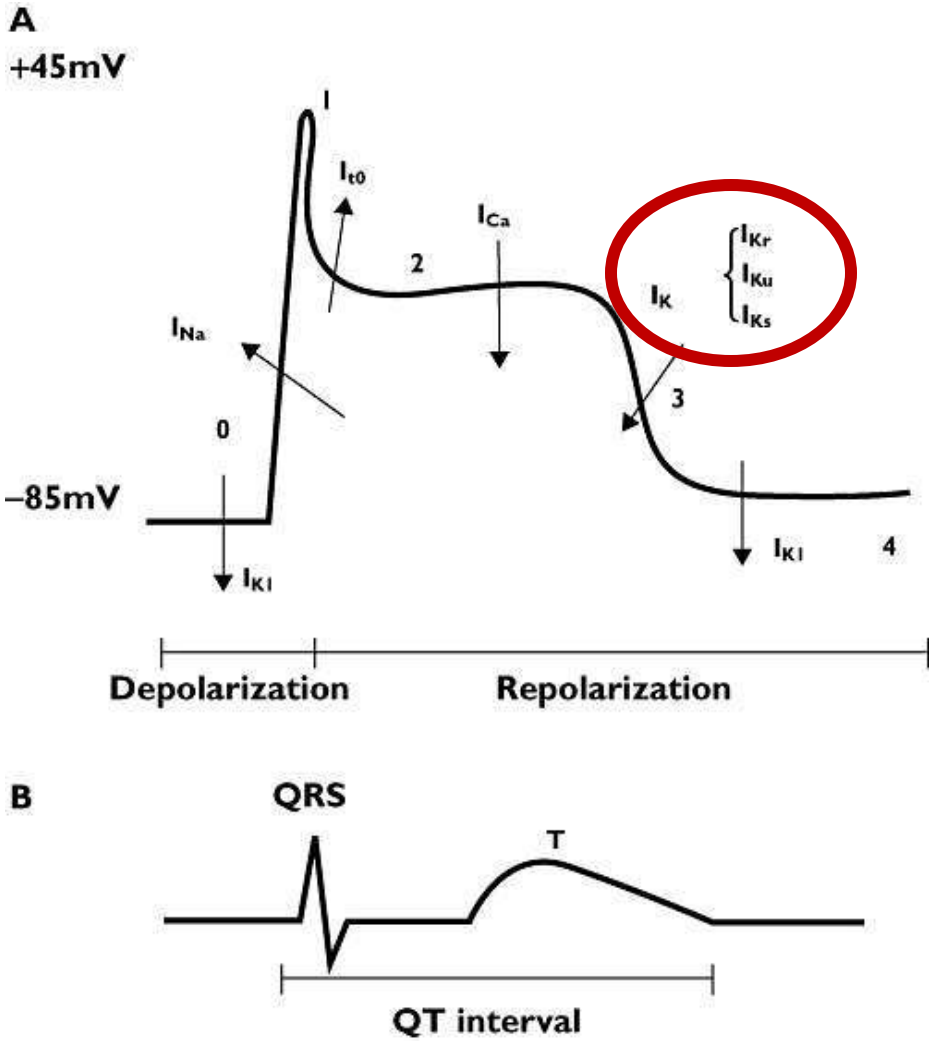
Drug-Induced Long QT Syndrome

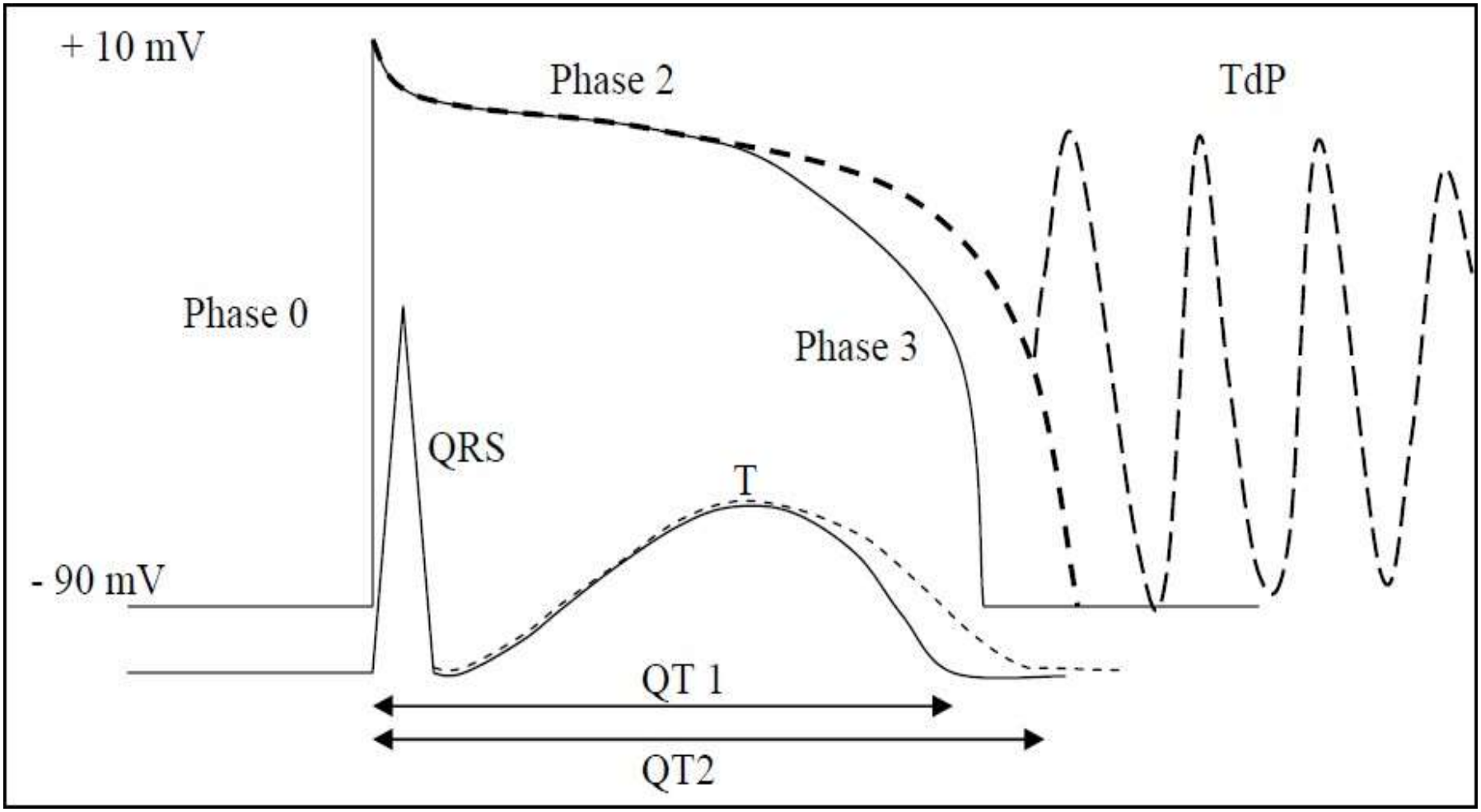
- Many medications increase ventricular repolarization (prolong QT interval)
  - Suppression of rapid component of delayed rectifier potassium current (Ikr)
- Antiarrhythmic medications cause proarrhythmias in 1-3% of patients
  - Exception is amiodarone <1%
- Non-antiarrhythmic medications <0.01-0.1%
- QT prolongation is concentration dependent
  - Renal dysfunction
  - Hepatic dysfunction
  - Drug-drug interactions

Ikr Blockage Delays Repolarization



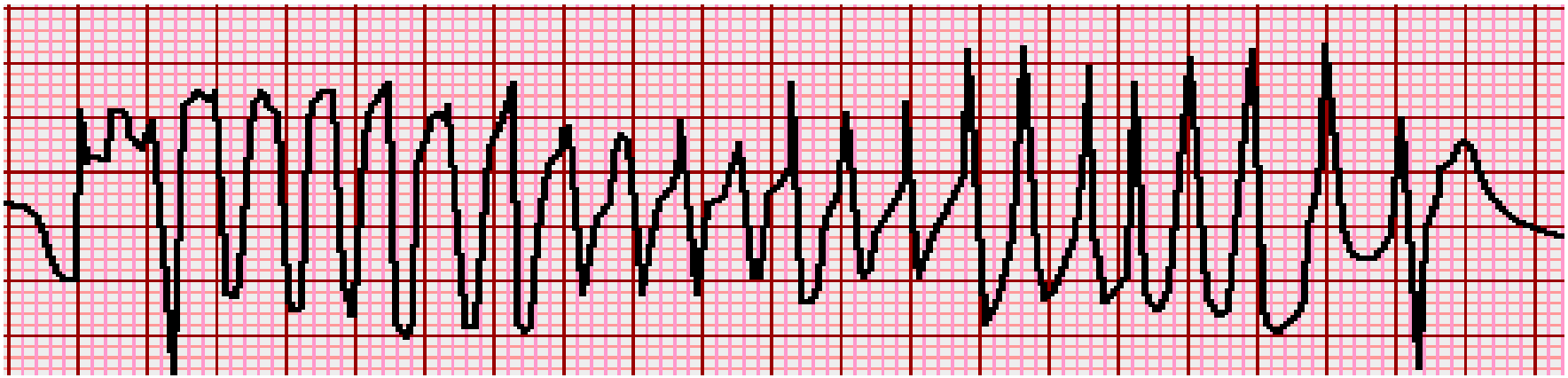
British Journal of Clinical Pharmacology 2010; 70:16-23

Mechanism of TdP



Circulation. 2010;121:1047-1060

Torsades de Pointes (TdP)



- A form of polymorphic VT
- “twisting of points”
- Associated with prolonged QT or QTc interval
- QTc prolongation is caused by delayed ventricular repolarization as a result of abnormal conduction through potassium channels (Ikr)
- Often self-limiting, but may deteriorate to VF

Risk Factors for Drug-Induced Long QT Syndrome

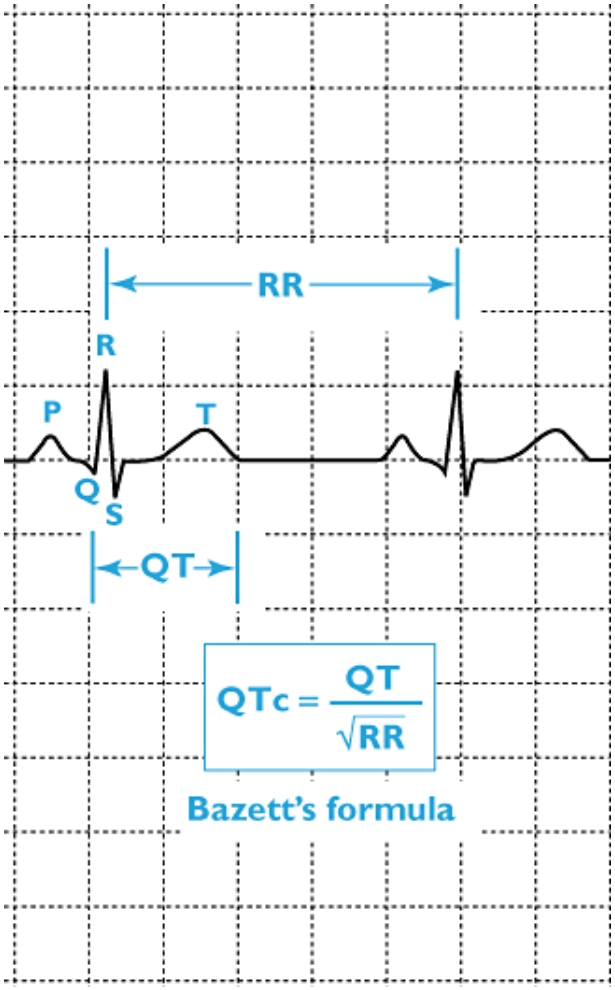
- Genetic predisposition (congenital long QT syndrome)
- Baseline prolonged QT interval
- Bradycardia (HR < 60 bpm) or rhythms with long pauses
- Advanced age
- Female sex
- Heart disease (heart failure and MI)
- Acute illness/hospitalization
- Electrolyte disorders (hypokalemia and hypomagnesemia)
- Treatment with more than 1 QT-prolonging drug
- Drug-drug interactions
- Renal or hepatic dysfunction

Circulation. 2010;121:1047-1060

QT vs. QTc (FYI)

QTc-interval corrects for fast HR (standardizes to HR = 60 bpm)

- Bazett's correction: $QTc = QT/RR^{0.5}$
  - Most often used formula
  - Produces long QTc values at high HR
- Fridericia's correction: $QTc = QT/RR^{0.33}$
  - Sometimes used for HR >85 bpm



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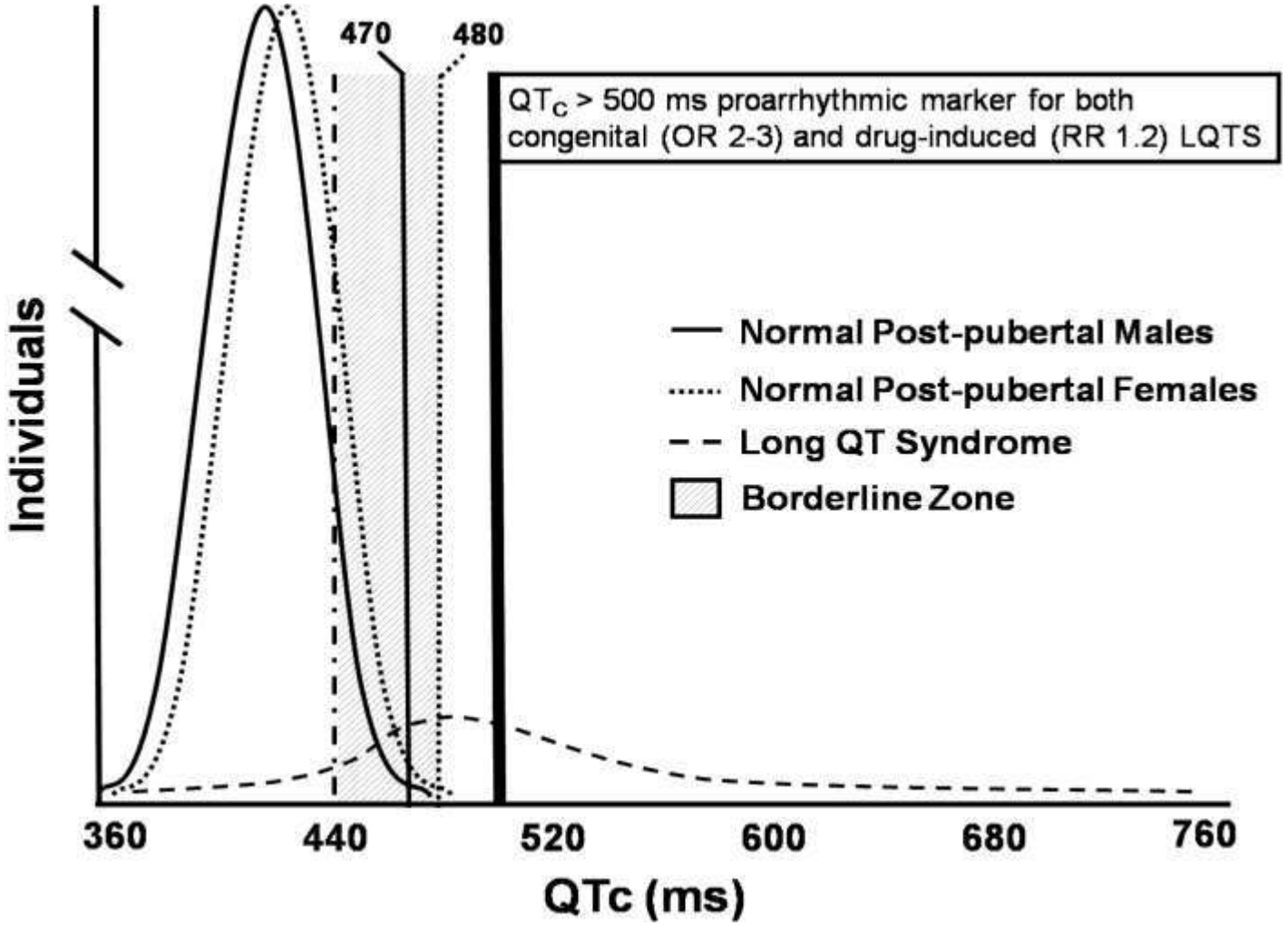
QTc Interval Distribution



Circulation. 2010;121:1047-1060

QTc Prolongation

- Expert consensus: QTc over the 99th percentile should be considered abnormally prolonged
  - **Males = 470 msec**
  - **Females = 480 msec**
  - **> 500 msec is considered highly abnormal**
- Baseline EKG and follow-up EKG on regular basis for high-risk patients

Circulation. 2010;121:1047-1060

Credible Meds.org

Classification of QT Prolonging Meds

- **<u>Known risk of TdP</u>** - These drugs prolong the QT interval <u>AND</u> are associated with a known risk of TdP, even when taken as recommended
  - Examples: antiarrhythmic drugs, macrolides, fluoroquinolones

- **<u>Possible risk of TdP</u> -** These drugs can cause QT prolongation, but lack evidence for a risk of TdP when taken as recommended
  - Examples: some atypical antipsychotics, some TCA

Classification of QT Prolonging Meds Continued

- **<u>Conditional risk of TdP</u>** - These drugs are associated with TdP <u>BUT</u> only under certain circumstances:
  - excessive dose
  - used in patients with conditions such as hypokalemia
  - when taken with interacting drugs

  <u>OR</u> by creating conditions that facilitate or induce TdP by:
  - inhibiting metabolism of a QT-prolonging drug
  - causing an electrolyte disturbance that induces TdP

  Examples: most azoles, some SSRIs

- **<u>Drugs to avoid in congenital long QT</u> -** These drugs pose a special risk of TdP for patients with CLQTS
  - Example: TMP/Sulfa

Class III Antiarrhythmic Medications

	TdP Classification	Notes
Amiodarone	Known risk of TdP	30-60 msec **Lowest risk of TdP (<0.5%)**
Dofetilide	Known risk of TdP	25-50 msec
Dronedarone	Known risk of TdP	10 msec Increased mortality in HF
Ibutilide	Known risk of TdP	60-100 msec 5% rate of TdP Substrate for P-glycoprotein Magnesium sulfate 2 grams prior to administration decreases QT prolongation
Sotalol	Known risk of TdP	25-50 msec

Class I Antiarrhythmic Medications

	TdP Classification	Notes
Disopyramide	Known risk of TdP	More pronounced QT prolongation at lower doses
Flecainide	Known risk of TdP	Increased arrhythmic death after AMI
Procainamide	Known risk of TdP	Active metabolite NAPA blocks Ikr NAPA is renally eliminated
Quinidine	Known risk of TdP	First anti-arrhythmic drug associated with QT prolongation

Antibacterial Medications

	TdP Classification	Notes
Fluoroquinolones		
Ciprofloxacin	Known risk of TdP	Drug-drug interactions
Levofloxacin	Known risk of TdP	
Moxifloxacin	Known risk of TdP	
Macrolides		
Azithromycin	Known risk of TdP	New “box warning”
Clarithromycin	Known risk of TdP	CYP 3A4 inhibitor
Erythromycin	Known risk of TdP	CYP 3A4 inhibitor
Miscellaneous		
Pentamidine	Known risk of TdP	
TMP/sulfa	Avoid in congenital long QT	

Antifungal Medications

	TdP Classification	Notes
Fluconazole	Known risk of TdP	CYP 2C9 inhibitor, prolongs QT interval at doses ≥800 mg/day
Itraconazole	Conditional risk of TdP	CYP 3A4 inhibitor
Ketoconazole	Conditional risk of TdP	CYP 3A4 inhibitor
Posaconazole	Conditional risk of TdP	
Voriconazole	Conditional risk of TdP	CYP 3A4 inhibitor

Antipsychotic Medications

	TdP Classification	Notes
First Generation		
Chlorpromazine	Known risk of TdP	15-30 msec
Haloperidol	Known risk of TdP	15-30 msec IV > PO Substrate for CYP 2D6
Thioridazine	Known risk of TdP	CYP 2D6 substrate
Atypical Antipsychotics		
Aripiprazole	Possible risk of TdP	
Clozapine	Possible risk of TdP	Low risk
Olanzapine	Conditional risk of TdP	Low risk
Quetiapine	Conditional risk of TdP	15-20 msec Substrate for CYP 3A4
Risperidone	Possible risk of TdP	10 msec Substrate for CYP 2D6
Ziprasidone	Conditional risk of TdP	20 msec

Antidepressant Medications

	TdP Classification	Notes
Selective Serotonin Reuptake Inhibitors		
Citalopram	Known risk of TdP **Dose - QTc prolongation** 20 mg – 8.5 msec 40 mg – 12.6 msec 60 mg – 18.5 msec	Do not exceed 40 mg daily Do not exceed 20 mg daily if - Age >60 - Hepatic impairment - CYP 2C19 poor metabolizer or drug-drug interactions
Escitalopram	Known risk of TdP	Do not exceed 20 mg daily - 10 mg dose = 4.5 msec - 30 mg dose = 10.7 msec
Fluoxetine	Conditional risk of TdP	Case reports demonstrate a rare risk of QTc prolongation
Paroxetine	Conditional risk of TdP	Lowest risk of SSRI's
Sertraline	Conditional risk of TdP	Case reports demonstrate a rare risk of QTc prolongation

Pharmacotherapy 2014;34(4):358-372; Ann Pharmacother. 2013;47(10):1330-1341

Antidepressant Medications

	TdP Classification	Notes
Tricyclic Antidepressants		
Amitriptyline	Conditional risk of TdP	Risk of TdP with over dosage
Clomipramine	Possible risk of TdP	
Desipramine	Possible risk of TdP	
Doxepin	Conditional risk of TdP	
Imipramine	Possible risk of TdP	Risk of TdP with over dosage
Nortriptyline	Possible risk of TdP	Risk of TdP with over dosage

Electrolytes

- QT prolongation correlates with intracellular potassium and magnesium levels

- Potassium <4 mEq/L and magnesium <2 mEq/L intensifies Ikr blocking

Use of QT-Prolonging Medications

- Retrospective trial with almost 5 M patients
- Evaluated use of QT-prolonging medications and medications that inhibit metabolic clearance of QT-prolonging medications

Number of QT-prolonging medications	Number of Patients
≥1	22.8%
≥2	9.4%
≥3	0.7%

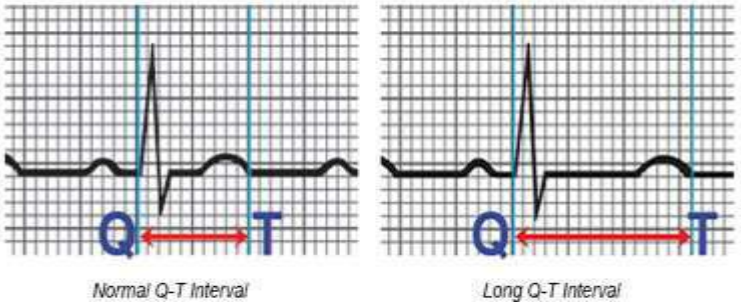
Am J Med. 2003;114:135-141

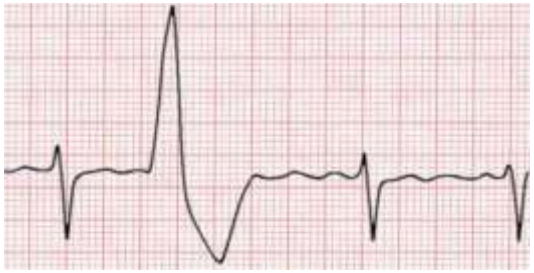
Whose QTc should be monitored?

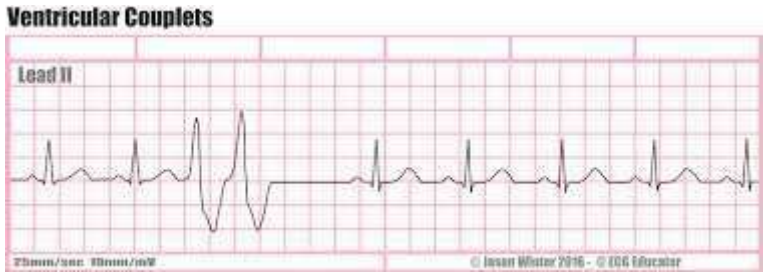
- In general:
  - Initiation of a drug known to cause TdP
  - Overdose from potentially proarrhythmic agents
  - New-onset bradyarrhythmias
  - Severe hypokalemia or hypomagnesemia

Monitoring QTc

- After initiation of a drug associated with TdP, ECG signs indicative of risk for arrhythmia:
  - An increase in QTc from pre-drug baseline of 60 msec
  - Marked QTc interval prolongation ≥ 500 ms
  - New-onset ventricular ectopy
  - Couplets
  - Non-sustained polymorphic ventricular tachycardia initiated in the beat after a pause

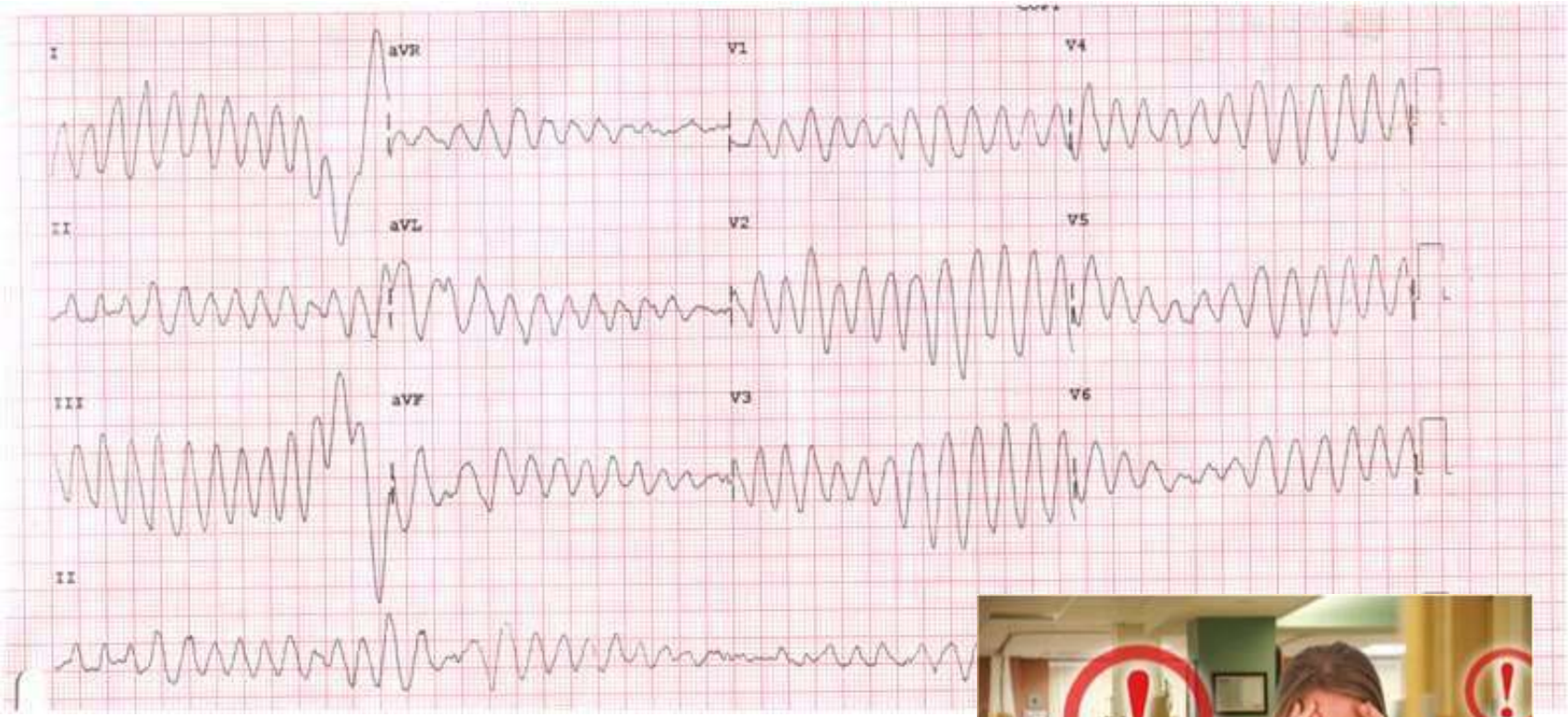






Circulation. 2010;121:1047-1060

Best Treatment of TdP is Prevention!



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End of Part 1

Thank you!