Antiarrhythmic or Proarrhythmic?  
What You Should Know About Antiarrhythmic Drugs

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Conduction System

- Sinus node: 60-100 bpm
- AV node: 40-60 bpm
- Bundle of His
- Right bundle branch
- Left bundle branch
- Purkinje fibers. Purkinje cells can depolarize 20-40 bpm

These pacemaker cells represent normal automaticity.
Phase 0: depolarization of cell membrane as Na⁺ enters cell; corresponds to QRS. Ca²⁺ channels open at about -50mV and Ca²⁺ enters cell.

Phase 1: early rapid repolarization as Na⁺ channels close, K⁺ opens

Phase 2: plateau maintained mostly by Ca²⁺ ions; corresponds to ST segment

Phase 3: repolarization of cell membrane as K⁺ channels open and K⁺ leaves cell; corresponds to T wave

Phase 4: resting state maintained partly by Na⁺-K⁺ pump; isoelectric line
Normal Pacemaker Activity

- Determinants of spontaneous pacemaker discharge
  - Phase 4 slope
  - Threshold potential (TP)
  - Transmembrane resting potential (TRP): -60mV in SA and AV nodes; -90mV in Purkinje cells
  - Action potential duration

Normal pacemaker activity in sinus node and AV junction is due to calcium channels
**Refractory period**: period of time after a cell has depolarized during which it cannot depolarize again: similar to flushing a toilet!

- **Absolute refractory period**: cell cannot respond regardless of stimulus strength
- **Relative refractory period**: cell can respond to stronger than normal stimulus but response is abnormal
- **Each part of heart has its own refractory period – AV node is longest**

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**Refractory Period**

![Image of refractory period graph]

- **Absolute Refractory Period**
- **Relative Refractory Period**
- **Supernormal period**

Repolarization is due to potassium channels
Mechanisms of Arrhythmias

- Abnormal Impulse Initiation
  - Enhanced normal automaticity
  - Abnormal automaticity
  - Afterdepolarizations (early and delayed)
- Abnormal Impulse Conduction
  - Reentry
- Abnormal Repolarization

Abnormal Impulse Initiation

- Normal Automaticity
  - SA node cells, AV junction cells, and Purkinje cells automaticity can be enhanced by sympathetic stimulation, ischemia, hypokalemia, drugs, stretch and can result in arrhythmias.
    - Examples: sinus or junctional tachycardia
  - Impulse initiation can shift to a subsidiary pacemaker if rate of SA node slows due to vagal stimulation, drugs, ischemia, etc.
    - Examples: junctional or ventricular escape beats or rhythms due to bradycardia or AV block
Abnormal Automaticity

- Automaticity that develops in atrial or ventricular myocardial cells don’t normally have it
- Enhanced automaticity of Purkinje cells – especially during acute myocardia ischemia

Depolarization in atrial, ventricular, and Purkinje cells is due to sodium channels

- Abnormal Automaticity
  - Decreased TRP: cell is partially depolarized at rest by ischemia, hypoxia, hyperkalemia, digitalis toxicity, chamber enlargement, and diseased atrial and ventricular muscle tissue
  - Atrial and ventricular cells that do not normally have automaticity can develop it when their TRP is reduced (becomes less negative)
Early Afterdepolarizations

- Arise during phase 2 or 3 of AP – due to slow Ca++ channels
- If EAD is big enough a second upstroke occurs on phase 2 or 3 of AP and causes a “triggered” beat (i.e. a PVC)
  - Triggered beats are dependent on and arise as a result of the preceding AP – not automaticity
- If the triggered beat has its own afterdepolarization that reaches threshold, another beat occurs
  - Trains of triggered activity cause tachycardia

- Development of EADs is potentiated by bradycardia, hypokalemia, hypomagnesemia, and many drugs (including antiarrhythmics).
- They are often associated with prolonged repolarization (long QT interval)
  - Longer repolarization time allows more time for EADs to develop during Phase 2 or 3 of the AP
- Both acquired and congenital Torsades are thought to be due to EADs

QT = 800 ms
Delayed Afterdepolarizations

- Occur after repolarization of cell
- High amplitude DADs cause triggered beats and trains of triggered activity
- DAD amplitude increases with faster HR and short cycles (premature beats)
  - DAD triggered arrhythmias occur with faster heart rates
- DADs occur with increased intracellular Ca\(^{++}\) levels (digitalis toxicity, ischemia, heart failure, SNS stimulation)

Abnormal Impulse Conduction

- Reentry
  - Responsible for most clinically significant arrhythmias
  - Reentry means that an impulse travels through an area of myocardium, depolarizes it, and then reenters that same area to depolarize it again
  - In order for reentry to occur, there must be an area of slowed conduction and an area of unidirectional block
    - Unidirectional block means that an impulse can conduct in one direction through a tissue but not in the opposite direction
Macro-reentry Circuits

- Large tracts of tissue creating an anatomic circuit
  - Atrial Flutter
  - AV Nodal Reentry Tachycardia (AVNRT)
  - AV Reentry Tachycardia (AVRT) involving accessory pathway in WPW syndrome
  - Bundle Branch Reentry VT

Micro-reentry Circuits

- Small circuits within atrial or ventricular myocardium

Normal Conduction through Purkinje Fibers and Ventricle
Setup for Reentrant Arrhythmias

Abnormal Repolarization

- This is not a “primary” mechanism of arrhythmias but creates situations in which afterdepolarizations (abnormal impulse initiation) or reentry (abnormal conduction) can occur.
- Abnormal repolarization is reflected in a prolonged QT interval:
  - Causes longer Phase 2 and Phase 3 in action potential which potentiates EADs → Torsades

Normal action potential duration

Prolonged repolarization causes longer Phase 2 and 3 of AP and increases time for EADs to develop
Antiarrhythmic Drug Sites of Action

Class I: Na⁺ Channel Blockers
- Quinidine
- Procainamide (Pronestyl)
- Disopyramide (Norpace)

Class II: β Blockers ("olols")
- Lidoceaine
- Mexiletine
- Propranolol (Inderal)
- Metoprolol (Lopressor)

Class III: K⁺ Channel Blockers
- Diltiazem
- Verapamil
- Sotalol
- Betaxolol
- Nadolol
- %

Class IV: Ca²⁺ Blockers
- Dofetilide
- Procainamide
- Lidocaine
- Mexiletine

Classification of Antiarrhythmic Drugs

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Actions</th>
<th>ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Quinidine</td>
<td>Sodium channel blockade</td>
<td>↑QRS</td>
</tr>
<tr>
<td></td>
<td>Procainamide (Pronestyl)</td>
<td>Slow conduction velocity</td>
<td>↑QT</td>
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<tr>
<td></td>
<td>Disopyramide (Norpace)</td>
<td>Prolong repolarization time</td>
<td>↓HR</td>
</tr>
<tr>
<td>IB</td>
<td>Lidocaine</td>
<td>Sodium channel blockade</td>
<td>↓QT</td>
</tr>
<tr>
<td></td>
<td>Mexiletine</td>
<td>Works on ischemic tissue</td>
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<tr>
<td></td>
<td></td>
<td>Accelerates repolarization slightly</td>
<td></td>
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<tr>
<td>IC</td>
<td>Propafenone (Rythmol)</td>
<td>Sodium channel blockade</td>
<td>↑↑QRS</td>
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<tr>
<td></td>
<td>Flecainide (Tambocor)</td>
<td>Marked slowing of conduction</td>
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<td></td>
<td></td>
<td>Little effect on repolarization</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Beta blockers (&quot;olols&quot;)</td>
<td>Beta blockade (↑ effects of SNS)</td>
<td>↓HR ↑PR</td>
</tr>
<tr>
<td>III</td>
<td>Amiodarone, Dronedarone (Multaq)</td>
<td>Potassium channel blockade</td>
<td>↑↑QT</td>
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<tr>
<td></td>
<td>Ibutilide (Corvert)</td>
<td>Prolong repolarization time</td>
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<td>Dofetilide (Tycoxin)</td>
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<td>Sotalol (Betapace)</td>
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<tr>
<td>IV</td>
<td>Calcium channel blockers (verapamil, diltiazem)</td>
<td>Calcium channel blockade</td>
<td>↓HR ↑PR</td>
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<tr>
<td></td>
<td></td>
<td>↓automaticity in SA and AV nodes</td>
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<td></td>
<td></td>
<td>↓AV conduction</td>
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</table>
• **Class IA**: quinidine, procainamide, disopyramide
  ◦ Slow phase 0 conduction, prolong phase 3 repolarization
• **Class IB**: lidocaine, mexiletine
  ◦ Shortens repolarization slightly, works on ischemic tissue
• **Class IC**: flecainide, propafenone
  ◦ “Super slowers” of conduction (phase 0), slightly prolong phase 3 repolarization
• **Class III**: amiodarone, ibutilide, dofetilide, dronedarone, sotalol
  ◦ Prolong phase 3 repolarization

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**Abolishing Reentry**

• Turn unidirectional block into bidirectional block by **slowing conduction velocity**
• Class IA, IB, and IC drugs that slow conduction by blocking Na\(^+\) channels
Abolishing Reentry

• **Speed conduction** through ischemic tissue to abolish unidirectional block
• Class IB drugs (lidocaine) that work on ischemic tissue may do this

[Diagram of speed conduction through ischemic tissue]

Abolishing Reentry

• **Increase refractory period** of tissue (make toilet run longer!)
• Class III drugs that prolong repolarization by blocking K⁺ channels

[Diagram of increased refractory period]
How are these drugs “anti”arrhythmic?

- **Depress phase 4 depolarization** (block Na⁺ and/or Ca⁺⁺ channels)
  - ↓ automaticity of abnormal pacemaker cells
  - Slow heart rate to suppress DADs
- **Slow conduction velocity** (block Na⁺ channels)
  - Increase block in reentry pathways
- **Increase refractory period** (block K⁺ channels)
  - Make tissues unresponsive to premature stimulation or reentry
- **Decrease effects of SNS stimulation and catecholamines** (beta blockers)
  - Decrease phase 4 depolarization rate

Types of Proarrhythmia

- **Worsening of preexisting arrhythmia**
  - Increased frequency of PVCs, VT or atrial fib
  - Conversion from nonsustained to sustained VT or from atrial fib to flutter
  - Incessant VT that can’t be terminated
- **Development of new arrhythmias**
  - Sustained monomorphic VT
  - Polymorphic VT
  - Torsade de pointes, VF
  - Atrial flutter with 1:1 conduction
  - SVT
- **Development of bradyarrhythmias**
  - Sinus node dysfunction (bradycardia, sick sinus syndrome)
  - AV block
How are these drugs “pro”arrhythmic?

- **Depress phase 4 depolarization**
  - Cause bradycardia
  - Slow HR increases risk of torsade due to **afterdepolarizations**

- **Slow conduction velocity**
  - Create block which can induce **reentry** arrhythmias
  - Cause AV block and bundle branch blocks

- **Increase refractory period and repolarization time**
  - Prolong QT interval - increase phase 2 and 3 repolarization time which increases chance of **afterdepolarizations** (torsades)

- **Create heterogeneous electrical properties in adjacent tissues**
  - Create differences in conduction time and repolarization time in adjacent areas of ventricle which is a setup for **reentry**

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<th>Proarrhythmic</th>
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<td>• Increase block in reentry pathways to abolish reentrant arrhythmias</td>
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<td>• Cause AV block and bundle branch blocks</td>
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Risk for Proarrhythmic Effects

- Drug combinations
  - Multiple antiarrhythmics used together
  - Antiarrhythmics used with other drugs that prolong QT interval
- Electrolyte imbalance
  - Hypo- or hyperkalemia
  - Hypomagnesemia
- Myocardial ischemia, cardiomyopathy
- LV dysfunction, heart failure (EF ≤ 35%)
- Changes in autonomic tone
  - Enhanced sympathetic stimulation – increased HR
  - Enhanced parasympathetic stimulation (vagal stimulation) – decreased HR

Class I
Antiarrhythmic Drugs
Na+ Channel Blockers

- IA: Quinidine, Procaainamide, Disopyramide
- IB: Lidocaine, Mexiltiline
- IC: Flecaainide, Propafenone
Quinidine (IA)

- Effects (Na⁺ channel block)
  - Slows conduction velocity
  - Prolongs refractory period (has K⁺ blocking effects)
  - Decreases myocardial excitability
  - Vagolytic effects (increases conduction through AV node)
- Indications
  - Conversion of atrial fibrillation and/or flutter
  - Maintain normal sinus rhythm after conversion
  - Suppression of serious recurrent ventricular arrhythmias
- Proarrhythmic Effects
  - Torsades de pointes (2-8%) - “quinidine syncope”
  - Increased ventricular rate in atrial flutter
  - Increases pacing & defib thresholds (ICDs)
- Other adverse effects
  - Diarrhea (hypokalemia)
  - Nausea, vomiting
  - Thrombocytopenia
  - Cinchonism: tinnitus, high-frequency hearing loss, deafness, vertigo, blurred vision, photophobia, headache, confusion, and delirium

- Quinidine induced increase in ventricular rate
  - Slows rate of atrial flutter which allows AV node to conduct 1:1
  - AV nodal blocking drug must be administered with quinidine
Proarrhythmic Effects
- Torsades de pointes (TdP)
- Increased ventricular rate in atrial flutter
- Marked slowing of conduction (widens QRS)

Other Effects
- Potentially fatal bone marrow depression
- Lupus-like syndrome (15-25% of patients on drug for >1 year)

Development of infra-His (Type II) block in patient receiving IV procainamide
- Note constant PR intervals and wide QRS indicating block below AV node
Disopyramide (Norpace) (IA)

- **Effects (Na⁺ channel block)**
  - Slows conduction
  - Prolongs refractory period
  - Decreases automaticity
  - Anticholinergic (vagolytic)
  - Peripheral vasoconstriction
  - Negative inotropic effects

- **Indications**
  - Maintain sinus rhythm after conversion of atrial flutter/fib
  - Prevent recurrence of VT or VF
  - Preexcited atrial fib

- **Proarrhythmic Effects**
  - Torsades de pointes
  - Increased ventricular rate in atrial flutter
  - Marked slowing of conduction (widens QRS)

- **Other Effects**
  - Anticholinergic effects: precipitates glaucoma, constipation, dry mouth, urinary retention
  - Heart failure (decreases contractility)

Useful in treating HOCM due to negative inotropic effects

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Lidocaine (only IV), Mexiletine (oral) - IB

- **Effects (Na⁺ channel block)**
  - Suppress automaticity in ventricle (no effect on atria)
  - Works on ischemic tissue and with faster HR
  - Slightly shortens AP duration (repolarization)
  - Increases ventricular stimulation threshold

- **Indications**
  - Treatment of VT, VF (especially ischemia induced)
  - Polymorphic VT with normal or prolonged QT interval
  - Treatment of dig toxic ventricular arrhythmias

- **Proarrhythmic Effects**
  - Lidocaine rarely causes bradycardia or asystole (usually with high doses)
  - Seizures with high dose
  - Decreased dose needed with liver failure, heart failure, heart block, bradycardia

- **Other Effects**
  - CNS: tremor, drowsiness, confusion

Mexiletine rarely causes TdP
Flecainide (Tambocor) (IC)

- **Effects** (Na⁺ channel block)
  - Markedly slows conduction in atria and ventricles
  - Shortens repolarization in Purkinje fibers but slightly prolongs it in atrial and ventricular cells (widens QRS)

- **Indications**
  - Conversion of paroxysmal A Fib (not for chronic AF)
  - Maintain NSR after conversion
  - WPW arrhythmias
  - Life threatening ventricular arrhythmias
  - Used only in patients with no structural heart disease

- **Proarrhythmic Effects**
  - Exacerbates and provokes lethal VT
  - Can cause incessant VT
  - 1:1 conduction of atrial flutter
  - Increased mortality in CAST study
  - Heart block

- **Other Effects**
  - Prolongs PR, QRS, QT intervals
  - Blurred vision
  - Alters pacing and defib thresholds

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Propafenone (Rythmol) (IC)

- **Effects** (Na⁺ channel block)
  - Slows conduction in all cardiac tissues
  - Prolongs effective refractory period in ventricle
  - Beta blocking effects

- **Indications**
  - Conversion of atrial fib
  - Maintenance of NSR
  - WPW arrhythmias
  - Life threatening ventricular arrhythmias
  - Only used in patients with no structural heart disease

- **Proarrhythmic Effects**
  - Increased ventricular rate in atrial flutter
  - Increased frequency or severity ventricular tachycardia

- **Other effects**
  - Exacerbation of heart failure (negative inotrope)
  - Sinus bradycardia and bronchospasm (beta blocker)
CAST
(Cardiac Arrhythmia Suppression Trial) - 1989

- Evaluated the effect of antiarrhythmic therapy (encainide, flecainide, or moricizine) in patients with asymptomatic or mildly symptomatic ventricular arrhythmia (six or more PVCs per hour) after MI.
- Patients randomly assigned to receive one of study drugs or placebo.
- Mortality rate 2-3 times higher in patients treated with active drug than with placebo even though drug was effective in suppressing PVCs.

CAST

- Encainide and flecainide accounted for most of deaths from arrhythmia and nonfatal cardiac arrests.
- Conclusion: neither encainide nor flecainide should be used in the treatment of patients with asymptomatic or minimally symptomatic ventricular arrhythmias after MI.
- Encainide no longer made
- Recommendation is generalized to all Class IC antiarrhythmics.
Class III Antiarrhythmic Drugs

- **K⁺ Channel Blockers**
  - Amiodarone
  - Dronedarone (Multaq)
  - Ibutilide (Corvert)
  - Dofetilide (Tikosyn)
  - Sotalol (Betapace)

Amiodarone

- **Actions**
  - Class III antiarrhythmic (K⁺ channel blocker)
    - Prolongs repolarization and refractory period in all cardiac tissues
  - Also has class I, II, IV effects
    - Blocks Na⁺, Ca²⁺ and K⁺ channels and beta blocking effects
  - Decreases AV conduction and sinus node function
  - Vasodilating effects (α blockade)
  - Less negative inotropic effects than other antiarrhythmics (safer in HF)
• **Indications (FDA approved)**
  - Management of life-threatening VF or recurrent hemodynamically **unstable VT** refractory to other antiarrhythmic agents

• **Off label uses**
  - Stable monomorphic VT
  - Polymorphic VT (normal QT)
  - Atrial fib
    - Pharmacological conversion to NSR
    - Maintenance of NSR after conversion (**most effective drug**)
    - Rate control
    - Prevention of post-op AF in cardiothoracic surgery
  - Wide QRS tachycardia of uncertain type
  - SVT – AV nodal reentry and accessory pathways (not first choice drug)
  - Adjunct to ICD to reduce rate and incidence of VT and reduce number of shocks

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**Amiodarone Side Effects**

• **Proarrhythmic Effects**
  - QT prolongation but rarely causes TdP
  - Bradycardia
  - AV block

  Prolongs repolarization uniformly throughout the heart so does not create electrical gradients from one area to another.

• **Other Effects**
  - Hypotension (IV form)
  - Pulmonary fibrosis
  - Thyroid dysfunction (hypo & hyper)
  - Liver dysfunction (elevated enzymes, hepatitis, cirrhosis)
  - Corneal microdeposits
  - Photosensitivity
  - Blue skin tone
  - Peripheral neuropathy
  - Tremor, ataxia
  - GI upset
• Unusual Features
  ▫ Very lipid soluble – accumulates in adipose tissue and must saturate them before it achieves adequate blood and cardiac concentrations
    • Slow onset of action – oral may take weeks, IV faster but still prolonged
    • Steady state drug effect can take several months
    • Very slow elimination
  ▫ Half life = 26 - 107 days (average = 40-55 days)
    • Duration of action can continue for up to 50 days after drug discontinued

• Recommended baseline tests
  ▫ Chest X-ray
  ▫ Renal, liver, thyroid, pulmonary function tests

• Drug interactions
  ▫ Increases protime with Coumadin
  ▫ Increases dig levels - ↑ risk of dig toxicity
  ▫ Additive effects with class IA drugs, beta blockers, Ca^{2+} blockers
  ▫ Additive proarrhythmic effects with many drugs = ↑ risk of torsades
Dronedarone (Multiq) (Class III)

- **Effects** (K⁺ channel block)
  - Noniodinated derivative of amiodarone
  - Also blocks Na⁺ and Ca⁡⁺⁺ channels and has beta blocking effects
  - Prolongs repolarization and refractory period
- **Indications**
  - Maintenance of NSR in patients with history of paroxysmal or persistent atrial fib (not for permanent atrial fib)
- **Proarrhythmic Effects**
  - Prolongs QT but rarely causes TdP
  - Discontinue if QTc 500ms or longer
- **Other Effects**
  - Increased risk of death, stroke, and HF in patients with decompensated HF or permanent A fib
  - Potential liver and pulmonary toxicity (less than amiodarone)

Sotalol (class III and beta blocker)

- **Effects**
  - Prolongs repolarization in atria, ventricles, and accessory pathways
  - Slows heart rate
  - Slows AV conduction
  - Increases AV nodal refractoriness
- **Indications**
  - Life threatening ventricular arrhythmias
  - Prevention of atrial fib (not effective for conversion)
- **Proarrhythmic Effects**
  - Prolongs QT and can cause TdP (1.5% - 2%)
  - Beta blocker effects: bradycardia, AV block
- **Sotalol and amiodarone are the most effective drugs for long-term treatment of ventricular arrhythmias but are not as effective as an ICD for preventing SCD.**
Ibutilide (Corvert) (Class III)

- **Effects** (pure K⁺ channel blocker)
  - Prolongs refractory period and repolarization
  - Effects more prominent at slow heart rates
- **Proarrhythmic Effects**
  - Increased PVCs (5%)
  - Torsades (1.7%)
  - Polymorphic VT with normal QT
  - AV block
  - Bradycardia

- **Indications**
  - IV for rapid conversion of atrial fib or flutter
  - Works better for flutter than fib
  - Works better if arrhythmia present ≤ 7 days
  - Conversion of A fib with WPW

Check K⁺ level prior to use. Should be in high normal range.

Ibutilide induced torsades

![ECG Image of torsades de pointes](image_url)
Dofetilide (Tikosyn) (Class III)

- **Effects** (K⁺ channel blocker, ↑ slow inward Na⁺ current)
  - Prolongs refractory period and repolarization time
- **Indications**
  - Conversion of atrial fibrillation and flutter
  - Maintain NSR in patients converted from A fib/flutter
- **Proarrhythmic Effects**
  - Torsades (most occur within first 3 days of therapy)
- **Administration restrictions**
  - Initiate therapy in hospital for minimum of 3 days with continuous ECG monitoring
  - Available only to hospitals and prescribers who have received education on initiation and dosing
  - Dose adjusted based on creatinine clearance and QTc

Beta Blockers (Class II)

- **Effects**
  - Decrease automaticity (phase 4 depolarization) of normal and abnormal pacemaker sites
  - Slow HR and AV conduction
  - ↓ contractility
- **Proarrhythmic Effects**
  - Sinus bradycardia
  - AV block
- **Other Effects/Uses**
  - ↓ mortality in acute MI
  - ↓ mortality in HF
  - Hypertension
  - Treatment of HOCM
- **Indications for arrhythmias**
  - Rate control in atrial fibrillation and other SVTs
  - Termination of AV nodal active SVTs (AVNRT, WPW tachycardias)
  - May ↓ incidence of atrial fibrillation in HF
  - ↓ incidence of ventricular arrhythmias – especially ischemia or exercise induced VT
  - Treatment of congenital LQTS
Verapamil, Diltiazem
(Class IV - Ca++ channel blockers)

• Effects
  ▫ Slow HR
  ▫ Slow conduction in AV node
  ▫ Increase refractory period in AV node
  ▫ Decrease refractory period in accessory pathway (WPW)
  ▫ Little effect in ventricle (one type of verapamil sensitive VT)
  ▫ Prevent coronary artery spasm – Printzmetal’s angina

• Indications for Arrhythmias
  ▫ Rate control in atrial fib/flutter and other SVTs
  ▫ Termination of AV nodal active SVTs (AVNRT, WPW tachycardias)

• Proarrhythmic Effects
  ▫ Sinus bradycardia
  ▫ AV block
  ▫ Increased ventricular rate in preexcited A Fib (WPW) – contraindicated

Unclassified Antiarrhythmics

• Digitalis
• Adenosine
• Atropine
Digoxin

• **Effects**
  - Inhibits Na-K-ATPase pump on cardiac cell membrane → ↑ intracellular Na⁺ concentration → stimulates Na⁺/Ca²⁺ exchange → ↑ intracellular Ca²⁺ → ↑ contractility
  - Slows AV node conduction and ↑ AV node refractory period
  - Increases automaticity in atrial & ventricular cells
  - Enhances delayed afterdepolarizations

• **Indications**
  - Rate control in A fib/flutter (not drug of choice)
  - + inotrope in HF

• **Proarrhythmic Effects**
  - AV block – any degree, including atrial fibrillation with 3rd degree block

• **Dig toxic arrhythmias**
  - Sinus exit block, sinus bradycardia
  - Atrial tachycardia with block
  - Accelerated junctional rhythm
  - Bidirectional VT
  - Polymorphic VT (normal QT)
  - Fascicular VT

• Dig toxic arrhythmias

Atrial rate = 187
Adenosine

• Effects
  ▫ Increases K⁺ conductance through K⁺ channels
  ▫ Decreases Ca²⁺ currents
  ▫ Decreases sinus node automaticity
  ▫ Increases AV nodal refractoriness, slows AV conduction
  ▫ Inhibits DADs

• Indications
  ▫ Termination of AV nodal active SVTs (AVNRT, AVRT)

• Proarrhythmic Effects
  ▫ Acute AV nodal block resulting in transient asystole
  ▫ Polymorphic VT during periods of asystole

• Other Effects
  ▫ Flushing, dyspnea, chest pressure
  ▫ Exacerbation of asthma

Would you give Adenosine?

Would you give Adenosine?
Would you give Adenosine?

Atropine

**Effects**
- Vagolytic (blocks effects of vagal stimulation)
- Increases sinus node rate
- Speeds conduction through AV node

**Indications**
- Symptomatic bradycardia (sinus brady, junctional brady)
- AV block at AV node level (Wenckebach - Type I second degree AV block)

**Proarrhythmic Effects**
- Tachycardia
- Paradoxical slowing of rate at doses < 0.5 mg
- May slow ventricular rate in Type II AV block
- Rarely causes VT or VF

**Other Effects**
- May increase ischemia in ACS
Make it Stop!!