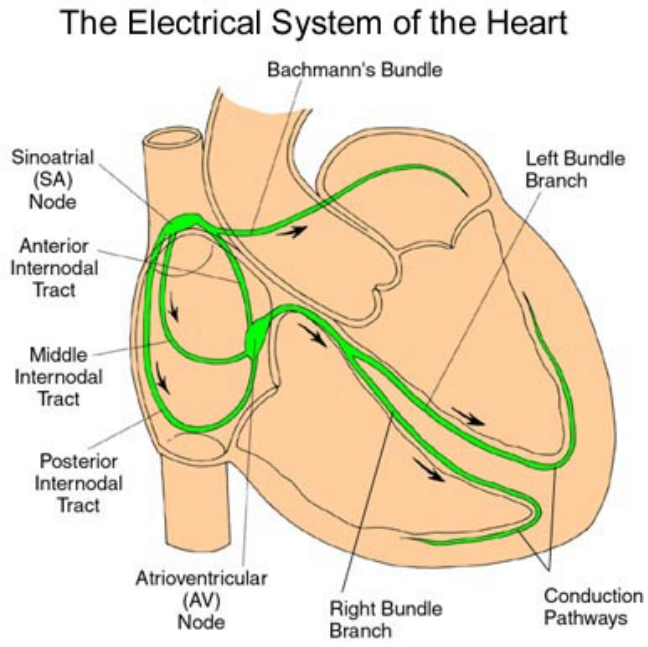
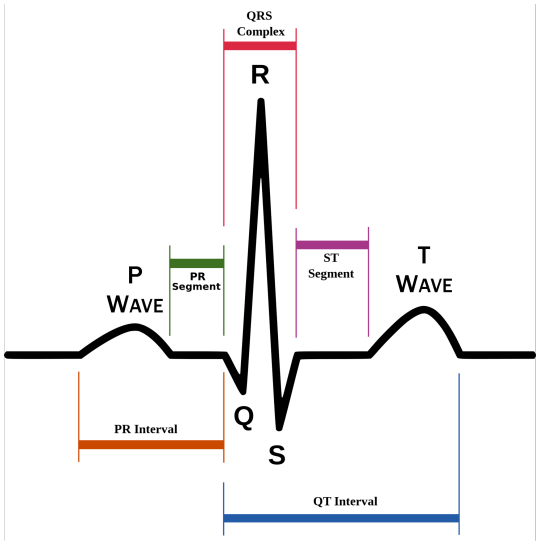
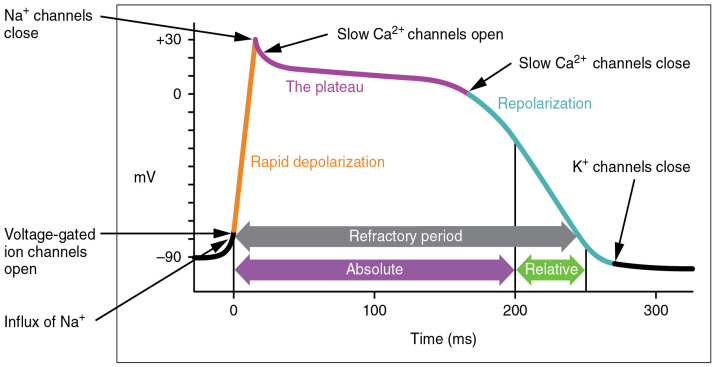
Antiarrhythmic agent

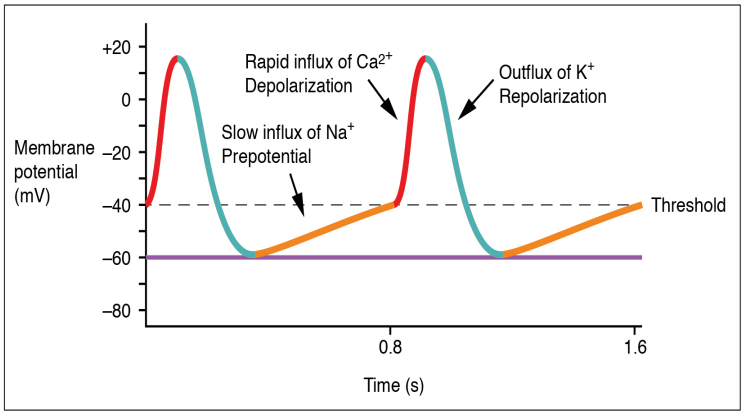




Action Potential in Cardiac Contractile Cells



Action Potential of Nodal Cell (SA Node)



Cardiac Arrythmia

- Simply dysregulation causes abnormalities in impulse formation and conduction in the myocardium
- cardiac arrhythmias may cause the heart to beat
  - ✓ too slowly or too rapidly, and
  - ✓ irregularly
- Arrhythmias are heart-rhythm problems - they occur when the electrical impulses to the heart that coordinate heartbeats are not working properly, making the heart beat too fast/slow or inconsistently.
- An electrocardiogram (ECG) provides a record of the electrical activity of the heart. Careful interpretation of the ECG along with a thorough physical assessment is necessary to determine the cause and type of arrhythmia.

Antiarrythmic drug

- Antiarrythmic drug act by blocking myocardial Na^+, K^+ or Ca^{++} channels.
- the antiarrhythmic drugs can modify impulse generation and conduction.

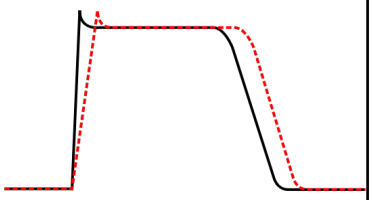
Vaugham-Williams classification

Class I – Na+ Channel Blockers
Class II – Beta-adrenergic Blockers
Class III – Potassium channel blockers
Class IV – Calcium Channel Blocker

CLASS I-Na^+ Channel blocker

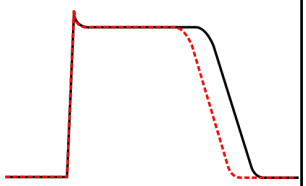
- These agents work by selectively blocking the fast sodium channels and depressing phase 0 of the action potential.
- The decrease in phase 0 depolarization results in decreased conduction velocity
- Class I agents can be further subdivided based on their effects on the refractory period and the rate of repolarization.
  - ✓ Ia lengthens the action potential (right shift)
  - ✓ Ib shortens the action potential (left shift)
  - ✓ Ic does not significantly affect the action potential (no shift)

Class IA



- Moderate sodium channel blocker
- Lengthen action potential
- Slow rate of rise of phase 0
- Prolong repolarization
- Increased duration of action potential
- Includes
  - ✓ Quinidine: 1st antiarrhythmic used, treat both atrial and ventricular arrhythmias, increases refractory period
  - ✓ Procainamide
  - ✓ Disopyramide

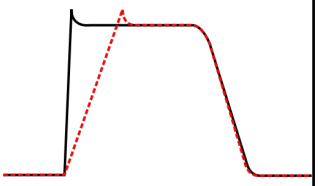
CLASS IB



- Mild sodium channel blocker
- Shortened action potential, repolarization
- Limited effect on rate of rise of phase 0
- Includes
  - – Lidocane (also acts as local anesthetic) – blocks Na+ channels mostly in ventricular cells
  - – Mexiletine - oral lidocaine derivative, similar activity
  - – Phenytoin – anticonvulsant that also works as antiarrhythmic similar to lidocane

CLASS IC

- Marked sodium channel blocker
- Markedly reduces rate of rise of phase 0
- No effect of repolarization
- No effect on action potential duration
- Includes
  - ✓ Flecainide
  - ✓ Propafenone

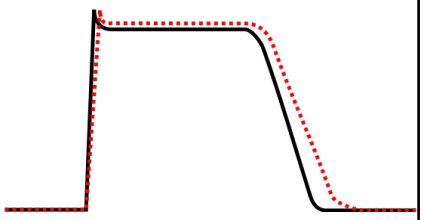


CLASS II- β–adrenergic blockers

- Decrease sympathetic activity of the heart
- Inhibits phase 4 depolarization in SA and AV nodes
- depress automaticity, prolonging AV conduction, and decreasing heart rate and contractility.
- Useful in the treatment of supraventricular tachycardias , Atrial fibrillation and atrial flutter.
- Includes
  - ✓ Propranolol
  - ✓ Metoprolol
  - ✓ Atenolol
  - ✓ esmolol

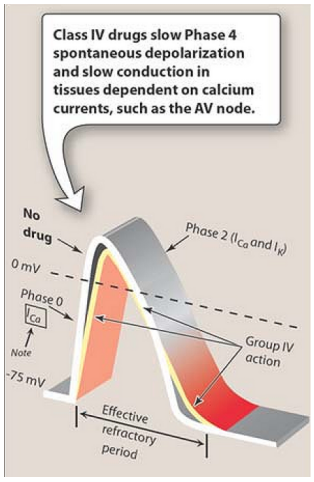
ClASS III-K^+ channel blockers

- Blocks K^+ channel therefore prolong repolarization (phase 3 of cardiac action potential) with out altering phase 0 of depolarization.
- Prolong the action potential duration (APD) and refractory period.
- Class III agents have the potential to prolong the QT interval of the EKG.
- Useful in the treatment of supraventricular tachycardias (SVT) and ventricular tachycardia (VTach)
- Includes
  - Amiodarone
  - Ibutilides
  - Bretylium



CLASS IV – Ca^{2+} channel blockers

- They decrease conduction through the AV node.
- Decrease slow inward current by calcium, resulting in a decreased rate of Phase 4 spontaneous depolarization
- reduces the force of contraction
- include verapamil and diltiazem.



Class	Basic Mechanism	Comments
I	sodium-channel blockade	Reduce phase 0 slope and peak of action potential.
IA	- moderate	Moderate reduction in phase 0 slope; increase APD; increase ERP.
IB	- weak	Small reduction in phase 0 slope; reduce APD; decrease ERP.
IC	- strong	Pronounced reduction in phase 0 slope; no effect on APD or ERP.
II	beta-blockade	Block sympathetic activity; reduce rate and conduction.
III	potassium-channel blockade	Delay repolarization (phase 3) and thereby increase action potential duration and effective refractory period.
IV	calcium-channel blockade	Block L-type calcium-channels; most effective at SA and AV nodes; reduce rate and conduction.

Abbreviations: APD, action potential duration; ERP, effective refractory period; SA, sinoatrial node; AV, atrioventricular node.

Miscellaneous

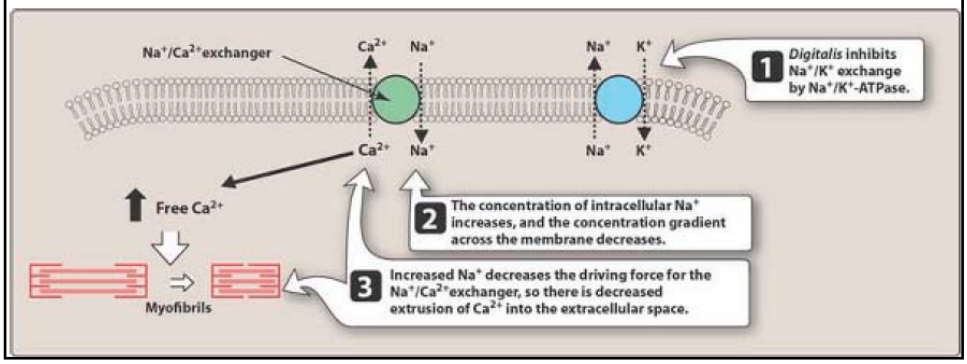
- adenosine - electrolyte supplement (magnesium and potassium salts) - digitalis compounds (cardiac glycosides) - atropine (muscarinic receptor antagonist)

Digoxin

- Cardiac glycosides obtained from the foxglove plant *Digitalis Lanata*

MOA: inhibit Na+/K+ ATPase

✓ Increases the force of contraction
✓ slowing of the heart rate;
✓ decreased conduction velocity through the AV node



A/E

- Narrow therapeutic index (0.8-2.0ng/mL).
- Most common: Hypokalemia
- loss of appetite, nausea, vomiting and diarrhea
- Visual disturbance (Blurred or yellow vision), confusion, drowsiness, dizziness
- Less: heart block

Reversal of Toxicity

Digoxin immune FAB (Digibind)

Contraindication

Hypokalemia, hypercalcemia, Ventricular tachycardia, Wolf-Parkinson-White syndrome

Nursing Consideration

- Monitor apical pulse for 1 min before administering; hold dose if pulse < 60 in adult or < 90 in infant; retake pulse in 1 hr. If adult pulse remains < 60 or infant < 90, hold drug and notify prescriber.
- Monitor ECG, rhythm or rate.
- Monitor carefully for adverse reactions.
- Report weight gain >1 kg/d.
- Maintain intake/ output for the few first days because it increases renal output.
- Monitor serum digoxin, potassium, magnesium and calcium level.