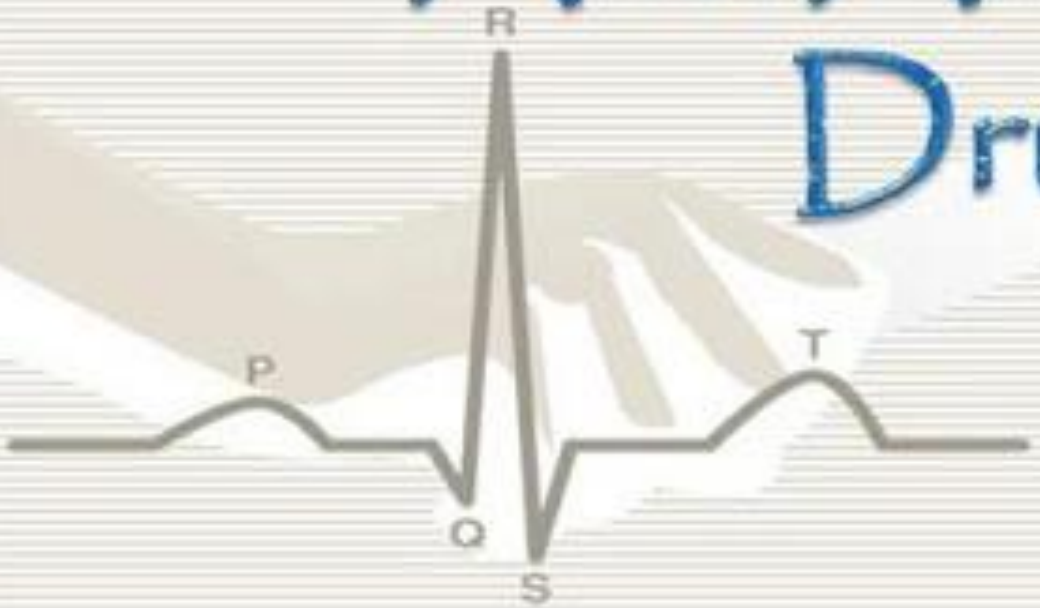
Anti Arrhythmic Drugs



Dr.Mohammad Jadaan

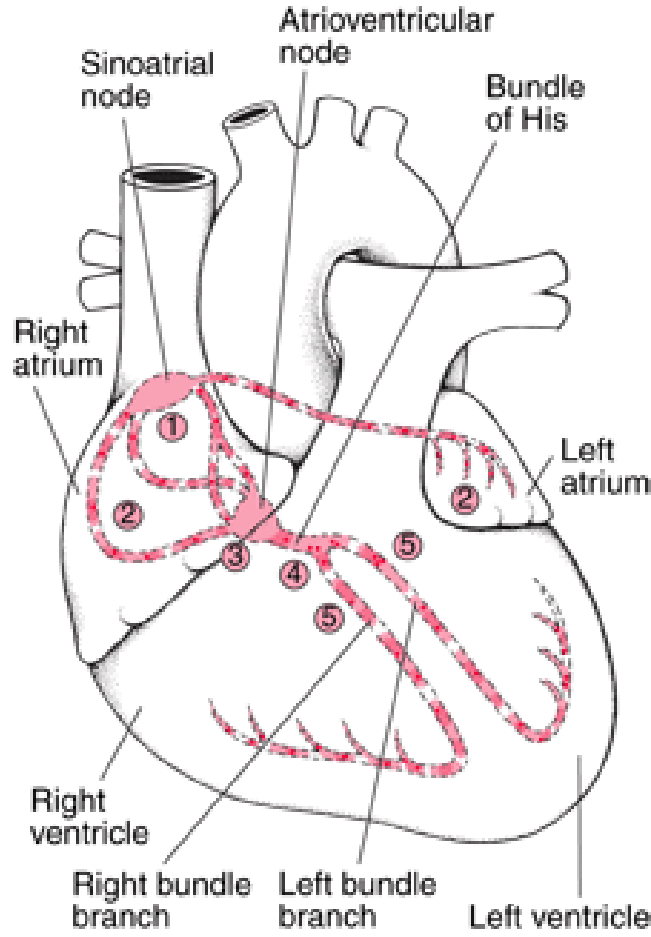
A-RHYTHM–IA

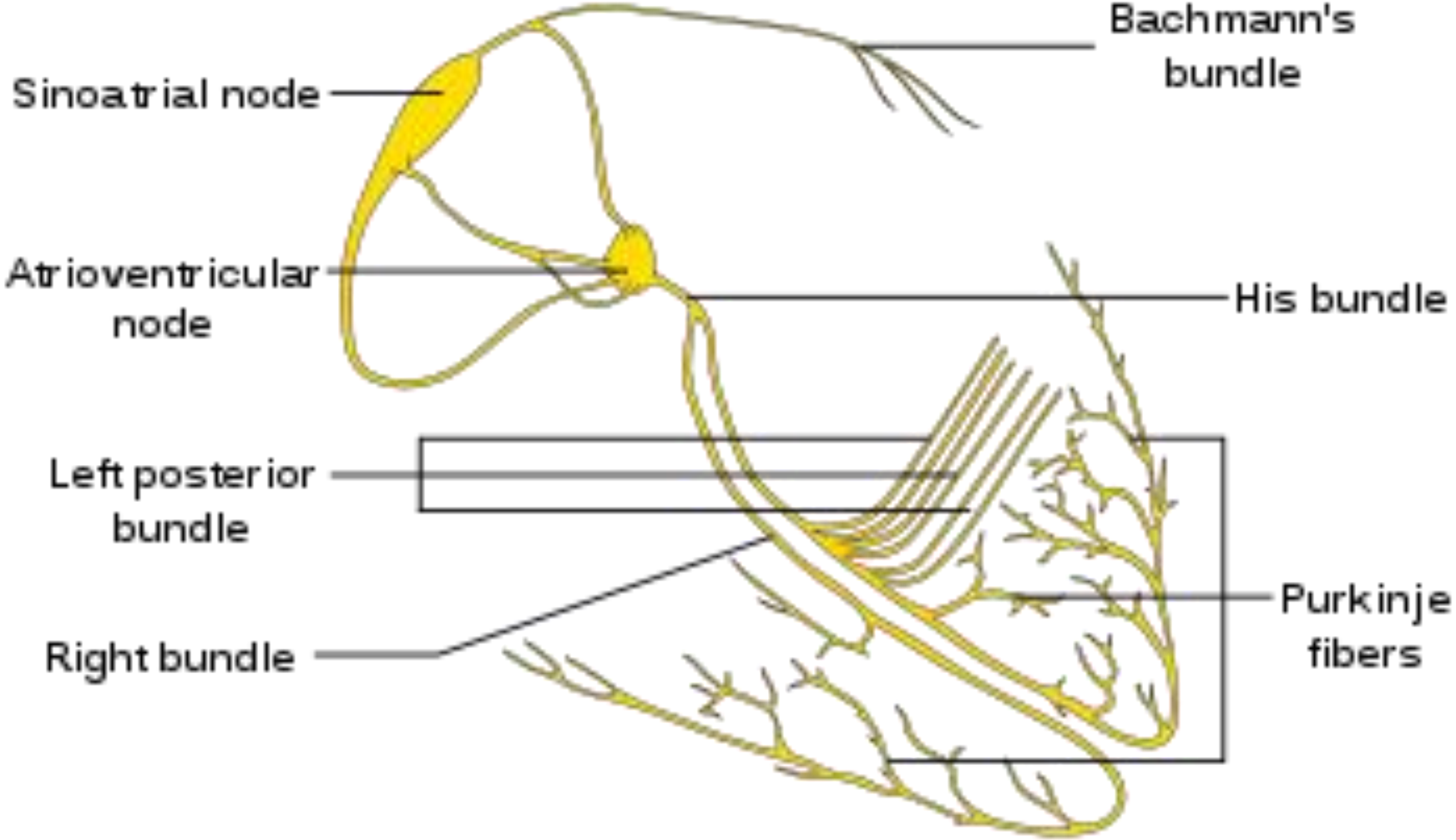
- Arrhythmia is deviation of heart from normal RHYTHM.
- *RHYTHM*

1) HR- 60-100

2) Should origin from SAN

3) Cardiac impulse should propagate through normal conduction pathway with normal velocity.



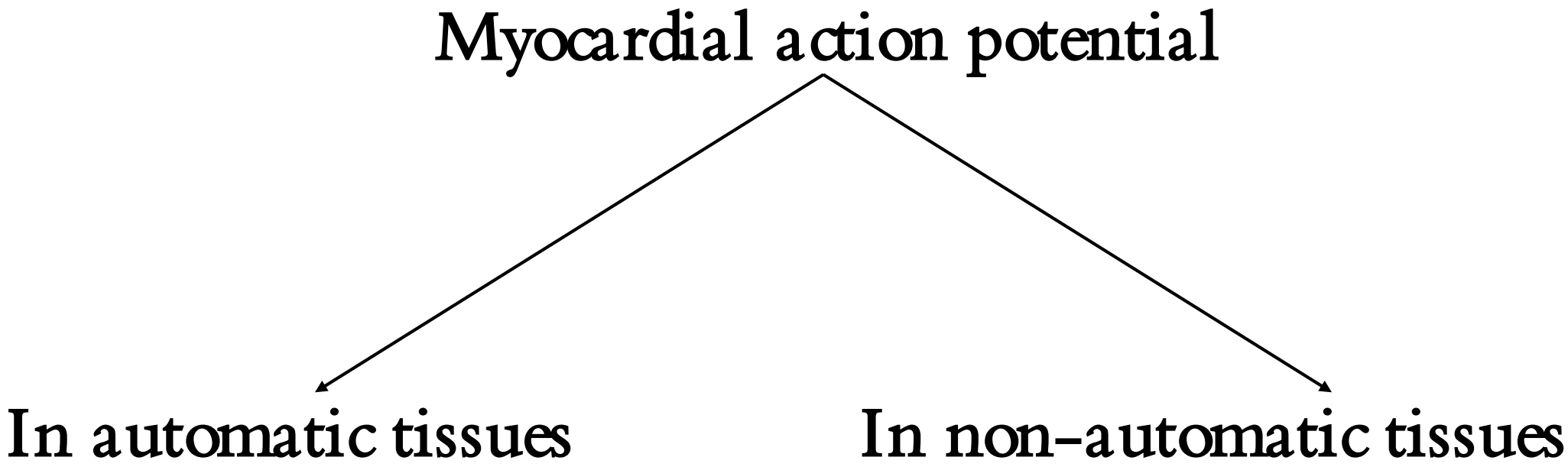

Bachmann's bundle
Sinoatrial node
Atrioventricular node
His bundle
Left posterior bundle
Purkinje fibers
Right bundle

CLASSIFICATION OF ARRHYTHMIAS

HR (Beats/Min)	Case
500	Atrial fibrillation
350	350
200	Paroxysmal TA
150	Simple tachyarrhythmia
60-100	Normal range
40	Mild bradyarrhythmia's
20	moderate BA

Types of cardiac tissue (on the basis of impulse generation)

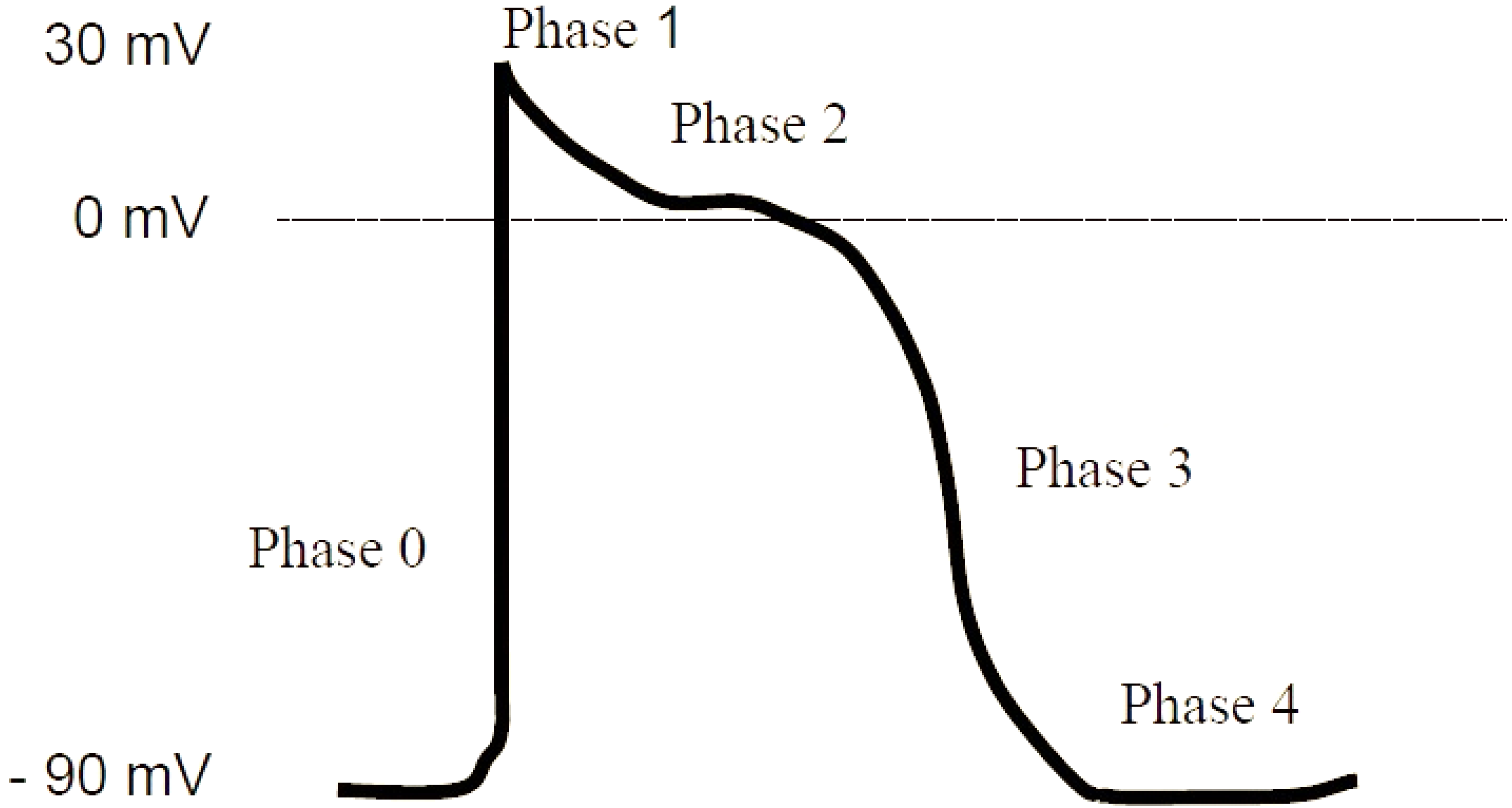
- **AUTOMATIC/ PACEMAKER/ CONDUCTING FIBRES**
  - (Ca++ driven tissues)
  - Includes SA node, AV node, bundle of His, Purkinje fibres
- **NON-AUTOMATIC MYOCARDIAL CONTRACTILE FIBRES**
  - (Na+ driven tissues)
  - Cannot generate own impulse
  - Includes atria and ventricles

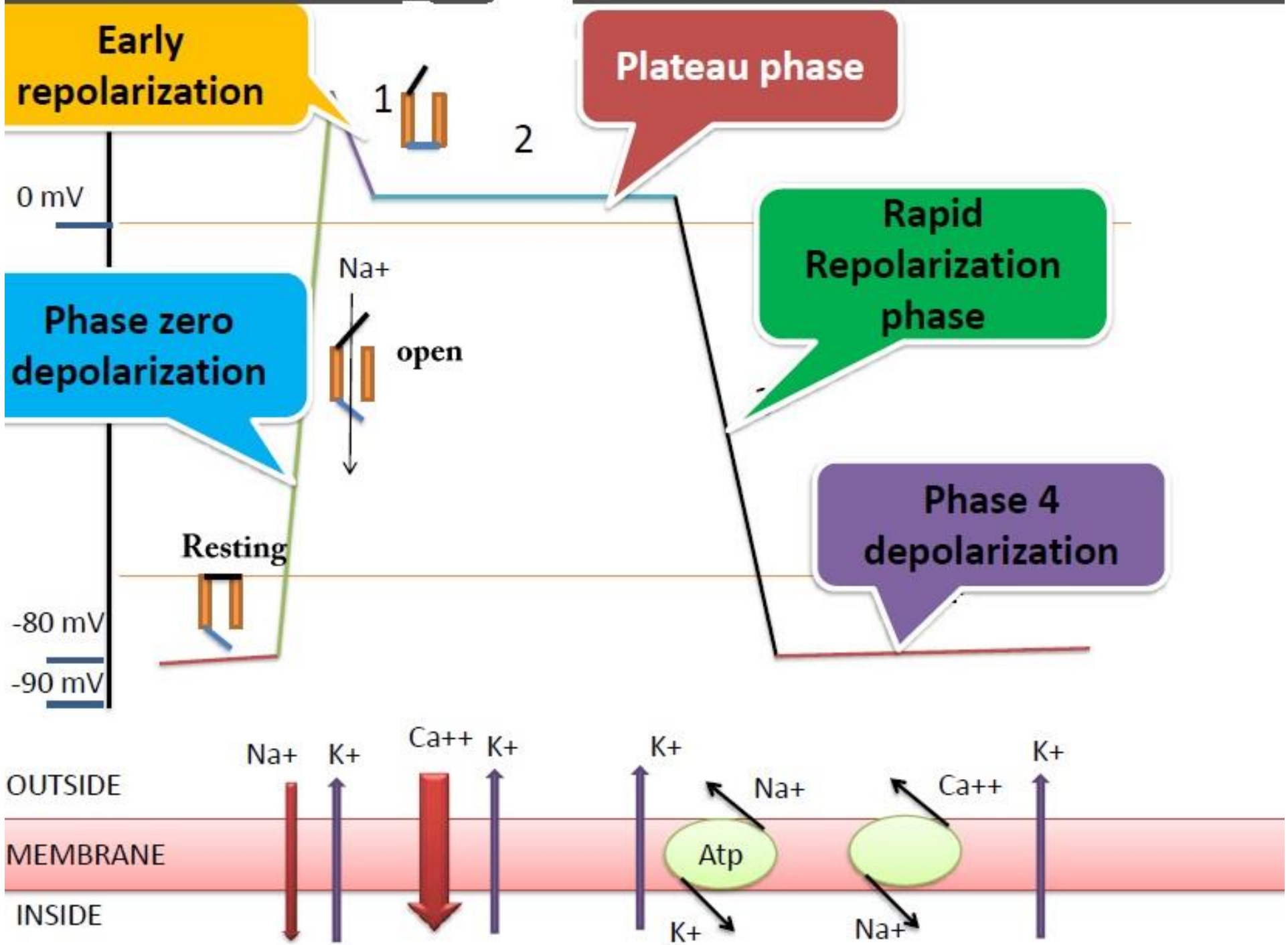

Myocardial action potential
In automatic tissues
In non-automatic tissues

CARDIAC ACTION POTENTIAL
(In non-automatic tissues)

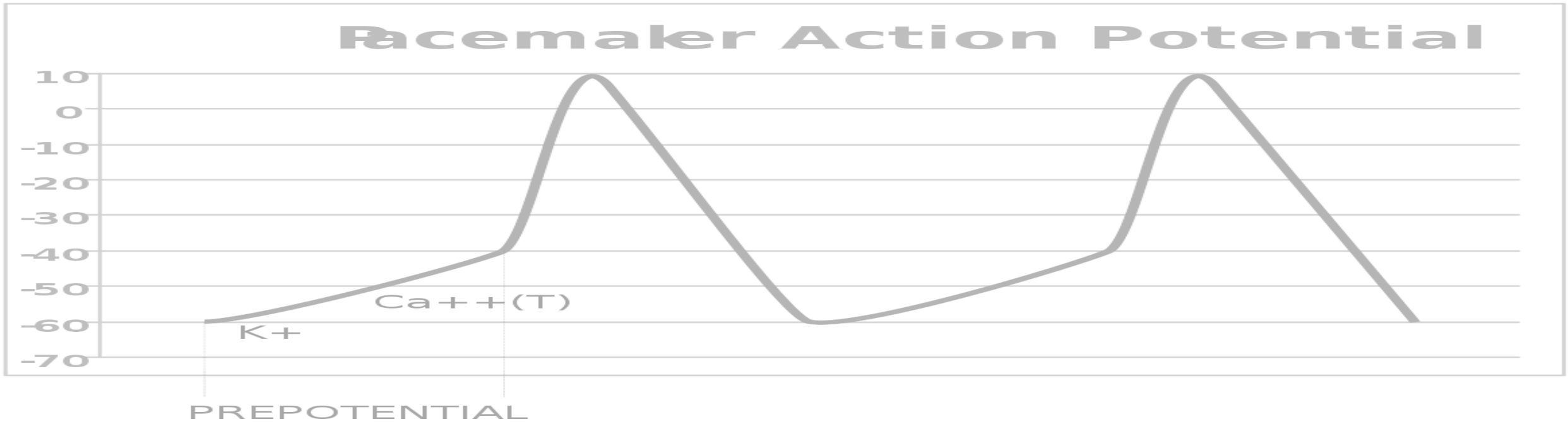
Divided into five phases (0,1,2,3,4)

I. **Phase 0:** Depolarization; Rapid Sodium Influx; Resting voltage has become positive.
II. **Phase 1:** Early Repolarization; brief K+ & Cl- eflux
III. **Phase 2:** Plateu phase; Ca++ influx
IV. **Phase 3:** Rapid repolarization; K+ & Cl- eflux
V. **Phase 4 (automaticity):** Ratio of Na+/K+ permeability; cellular electrolyte balance is slowly restored.


30 mV
0 mV
- 90 mV
Phase 0
Phase 1
Phase 2
Phase 3
Phase 4


Early repolarization
1
2
Plateau phase
0 mV
Rapid Repolarization phase
Na+
open
Phase zero depolarization
Resting
Phase 4 depolarization
-80 mV
-90 mV
Na+
K+
Ca++
K+
K+
Na+
Ca++
K+
OUTSIDE
MEMBRANE
INSIDE
Atp
K+
Na+

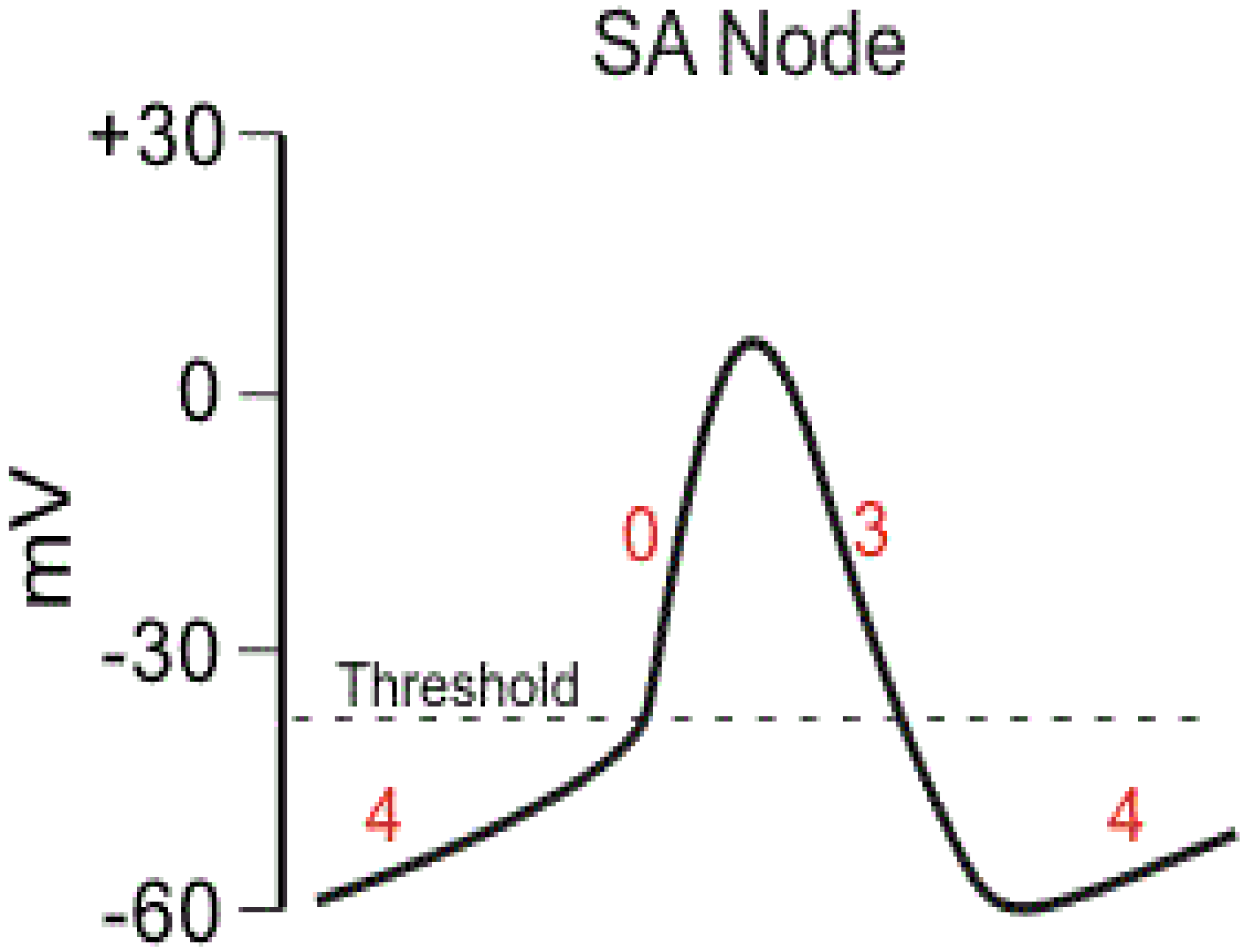
CARDIAC ACTION POTENTIAL
(In automatic tissues)

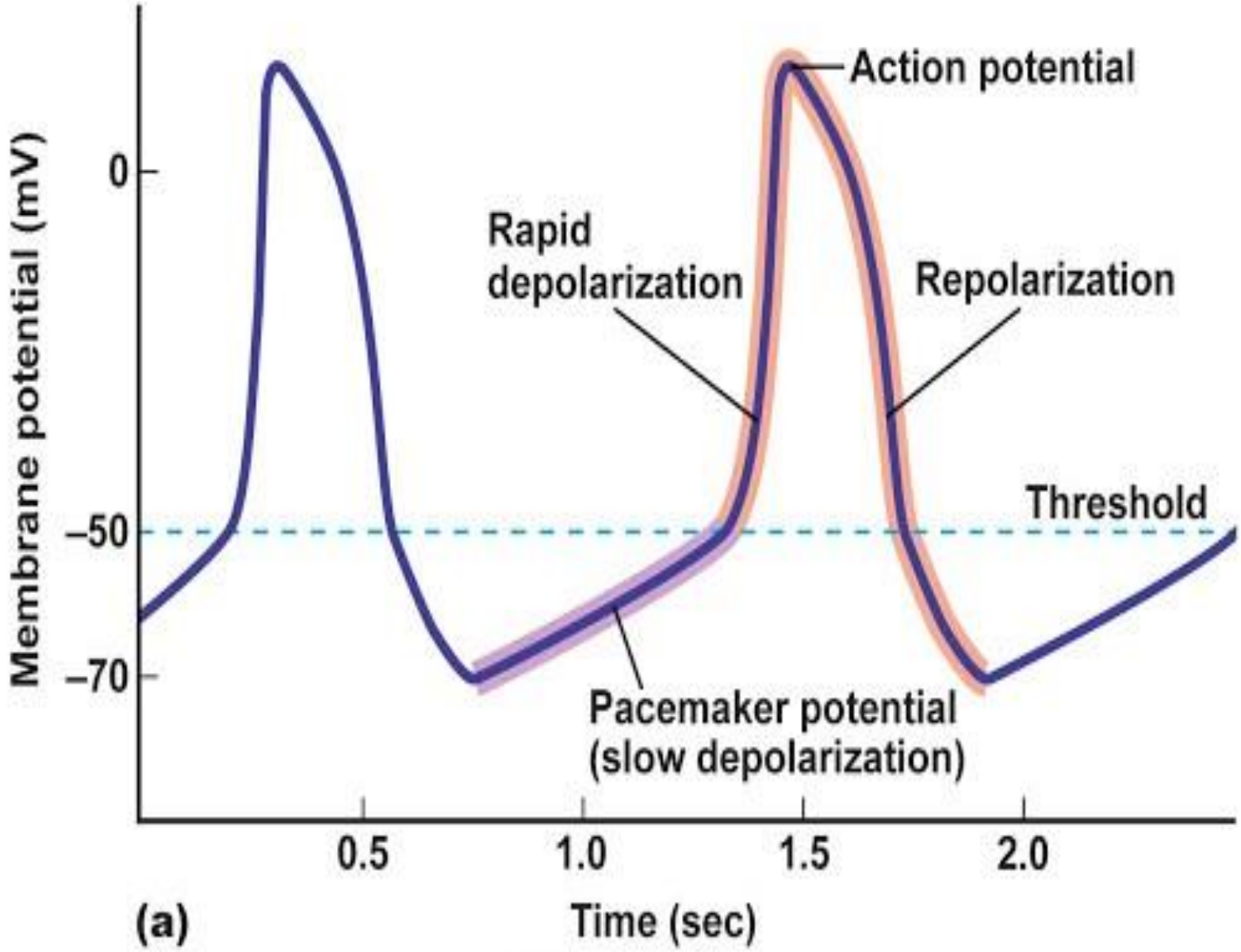


Phase 4 (automaticity): Ratio of Na+/K+

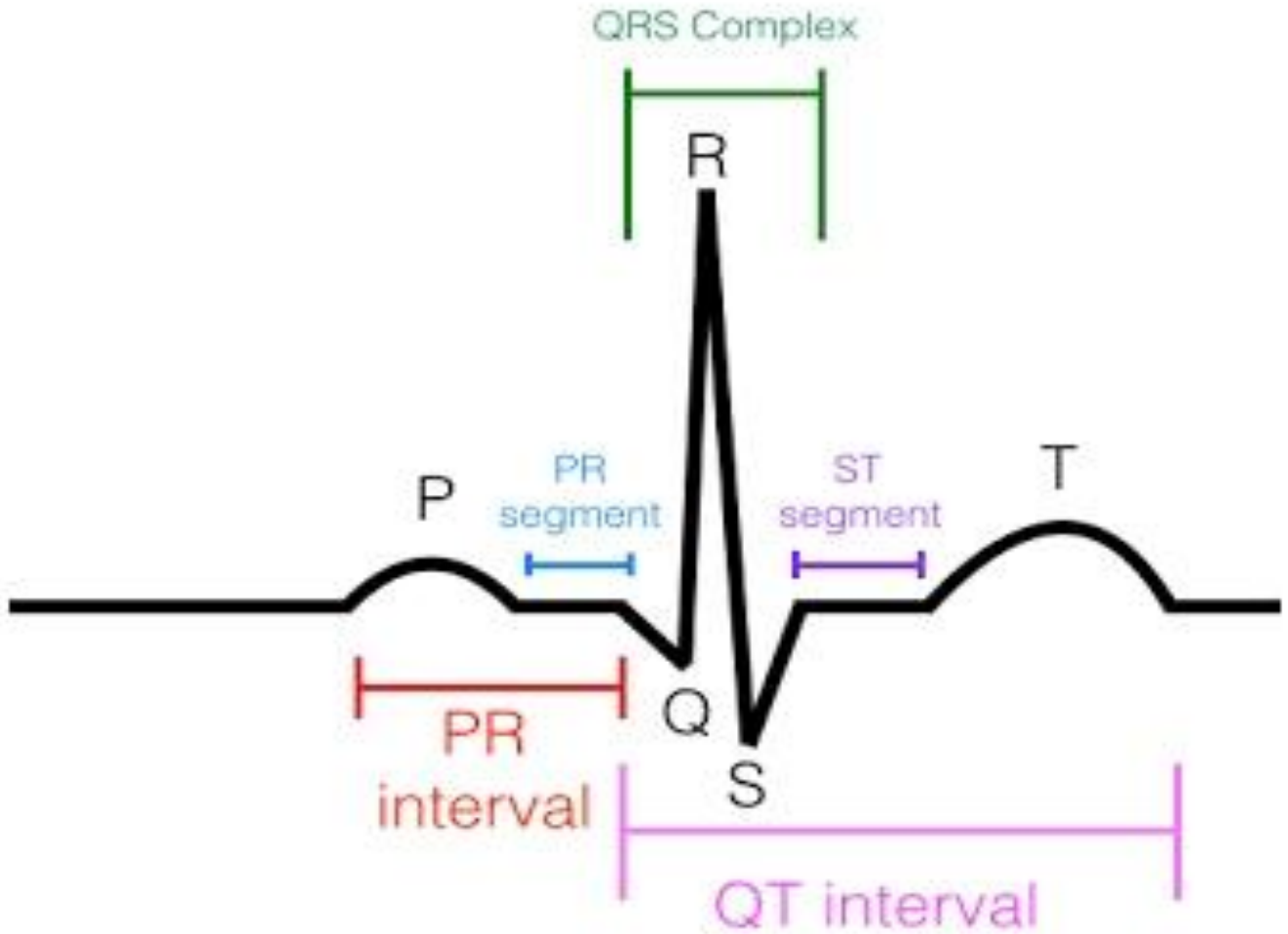
Phase 0: Depolarization; Rapid Sodium Influx

Phase 3: Rapid repolarization; K+ & Cl- eflux

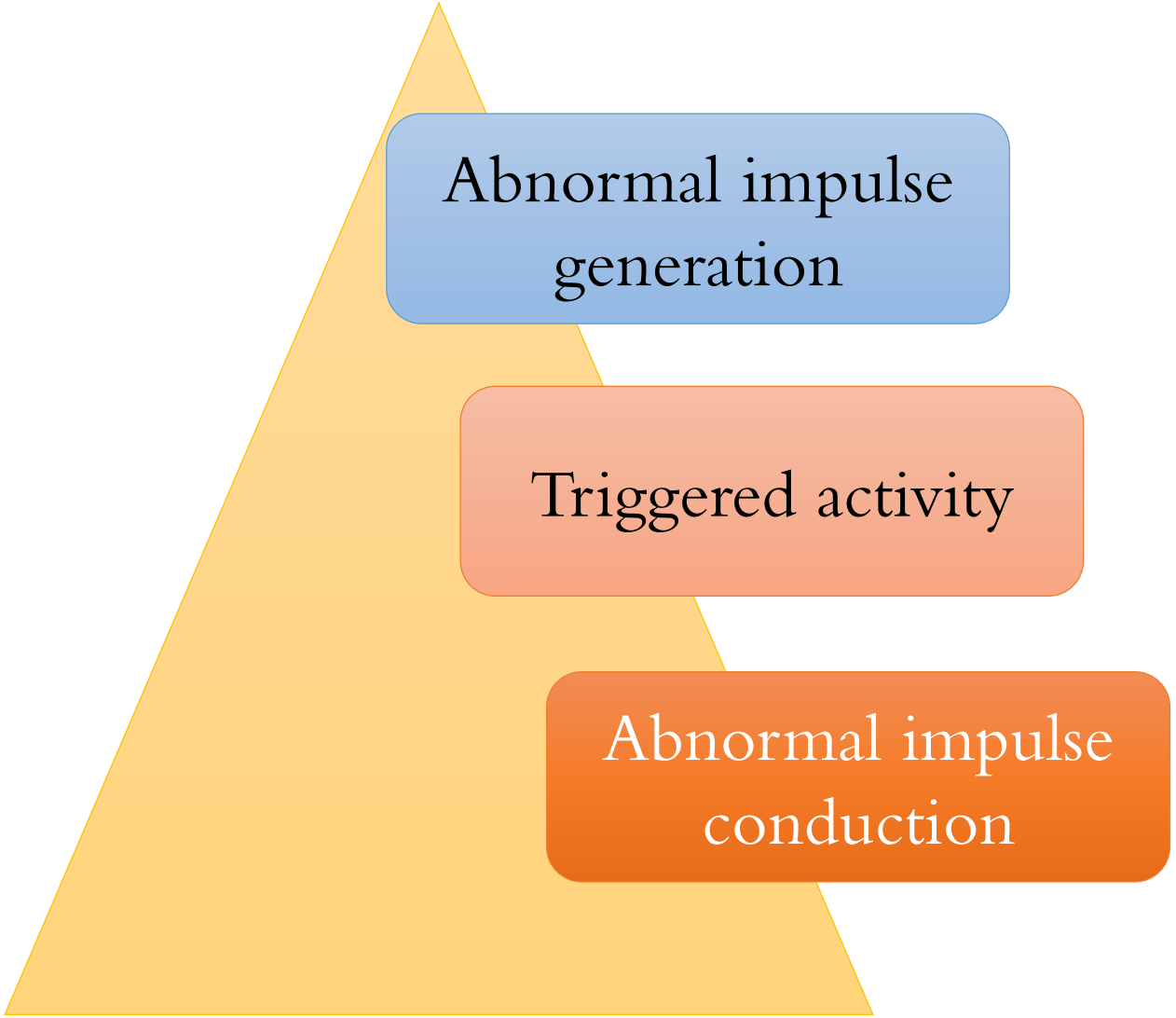



Membrane potential (mV)
0
–50
–70
Action potential
Rapid depolarization
Repolarization
Threshold
Pacemaker potential (slow depolarization)
0.5
1.0
1.5
2.0
(a)
Time (sec)

Segments and Intervals



Mechanism of Arrhythmias



Mechanisms of cardiac arrythmia

1-Abnormal impulse generation:

- Depressed automaticity
- Enhanced automaticity

2-Triggered activity (after depolarization):

- Delayed after depolarization
- Early after depolarization

3-Abnormal impulse conduction:

- Conduction block
- Re-entry phenomenon
- Accessory tract pathways

Abnormal impulse generation

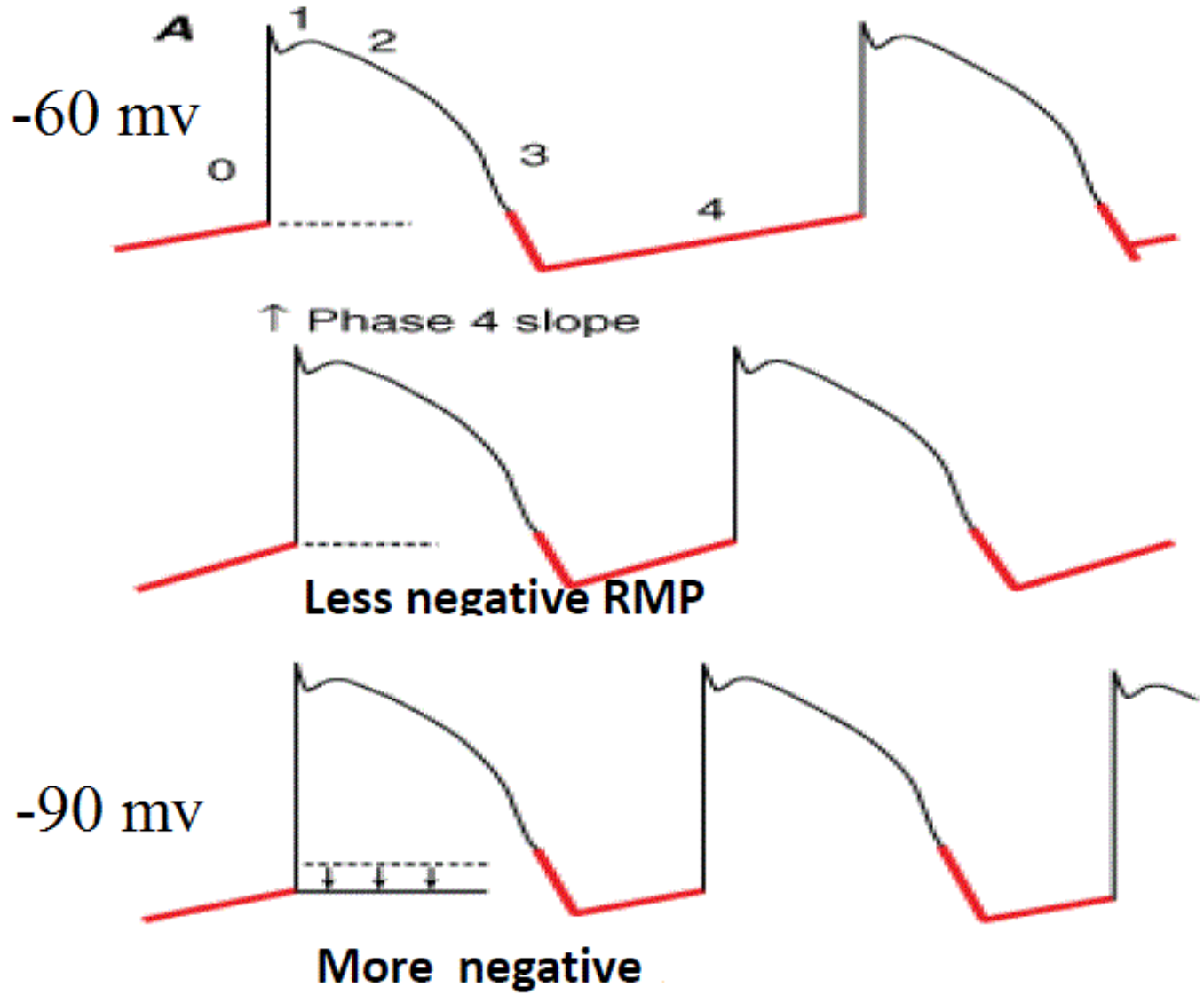
1-Depressed automaticity of SA node

2-Enhanced automaticity of SA node

❖Caused by Ischaemia/digitalis/catecholamines/acidosis/ hypokalemia ➡ Nonpacemaker nodal tissues comes to -60mv ➡ Increased slope of phase 4 depolarization

Become ➡ **ECTOPIC PACEMAKERS**.

Ectopic pacemaker activity encouraged by



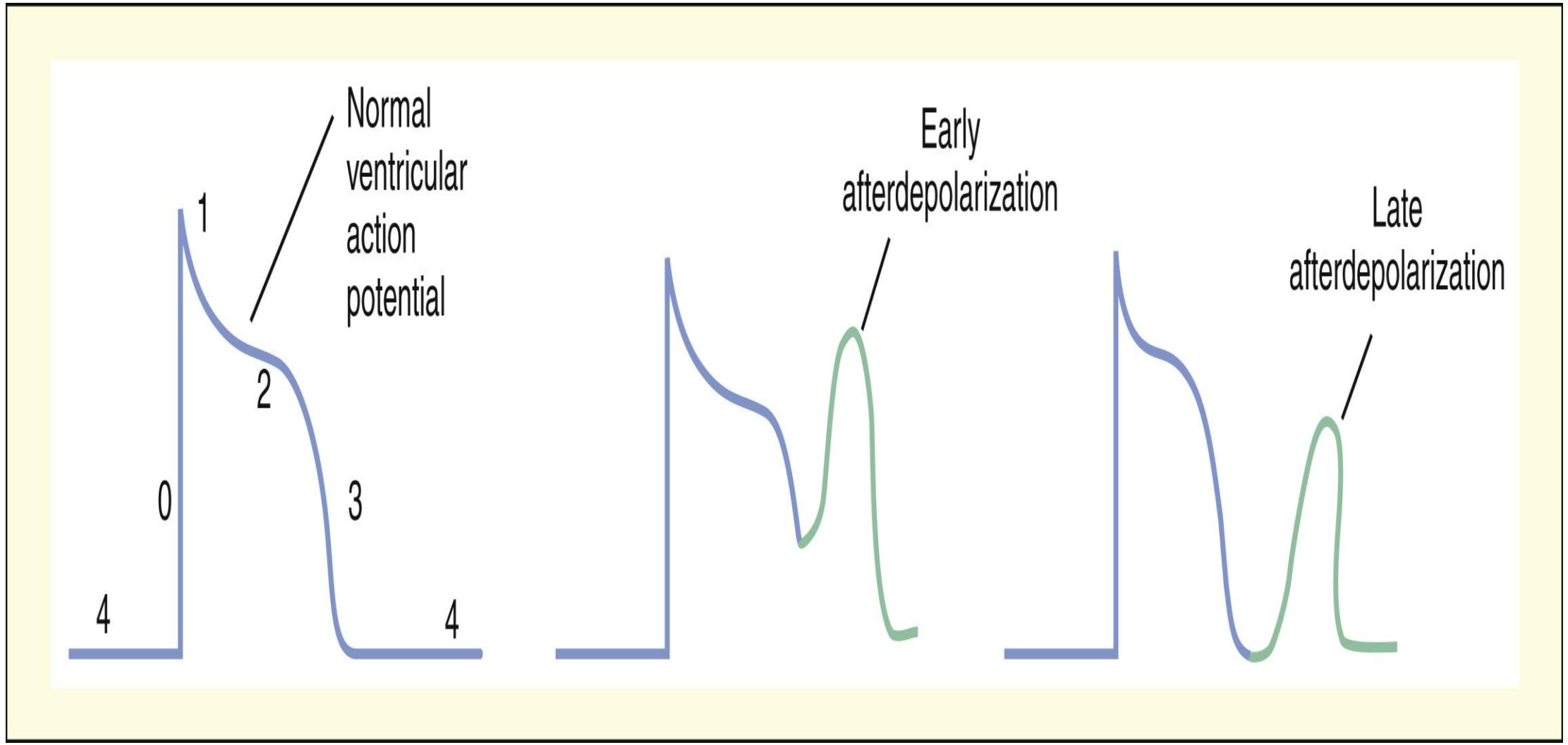
Triggered activity

❖Extra abnormal depolarisation

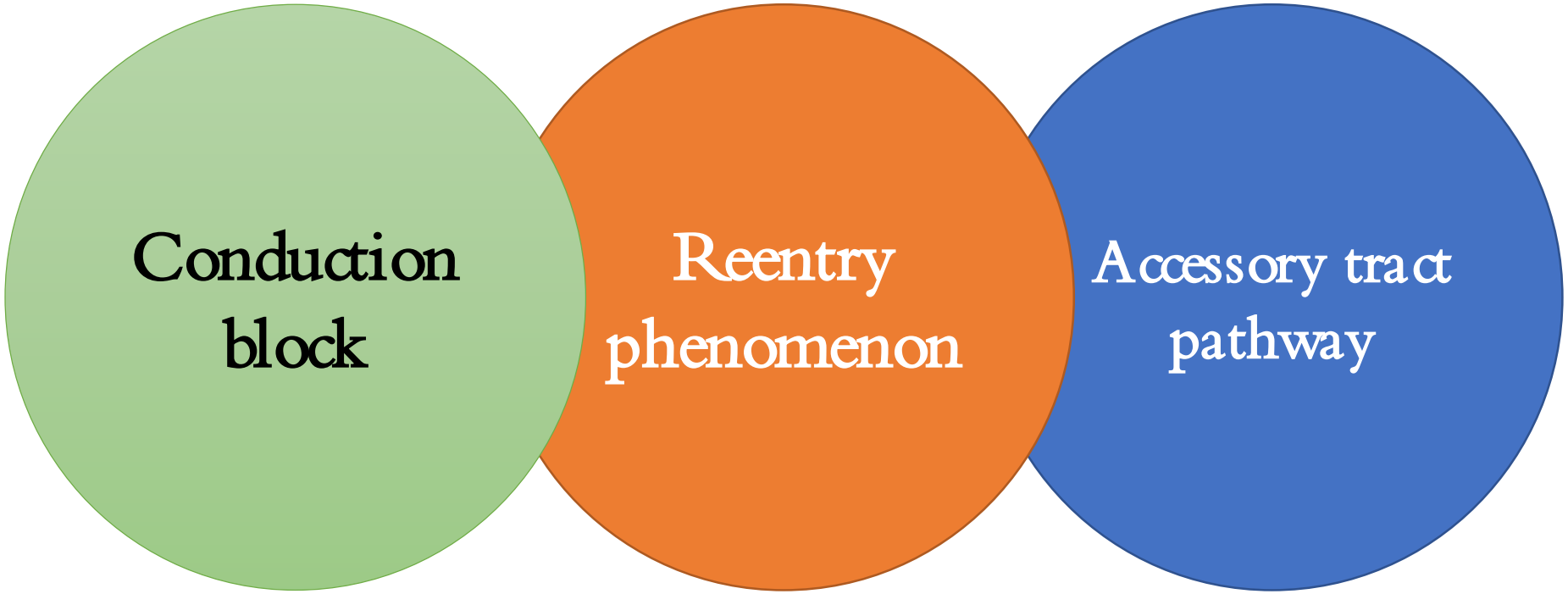
- Due to abnormal intracellular Ca2+ regulation
- During or immediately after phase 3

❖After depolarisation may be categorized in to

- Early after depolarisation
- Delay after depolarisation


Normal
ventricular
action
potential
1
2
0
3
4
4
Early
afterdepolarization
Late
afterdepolarization

Abnormal impulse conduction



Conduction block

Due to depression of impulse conduction at AV node & bundle of His, due to vagal influence or ischemia.

Types:

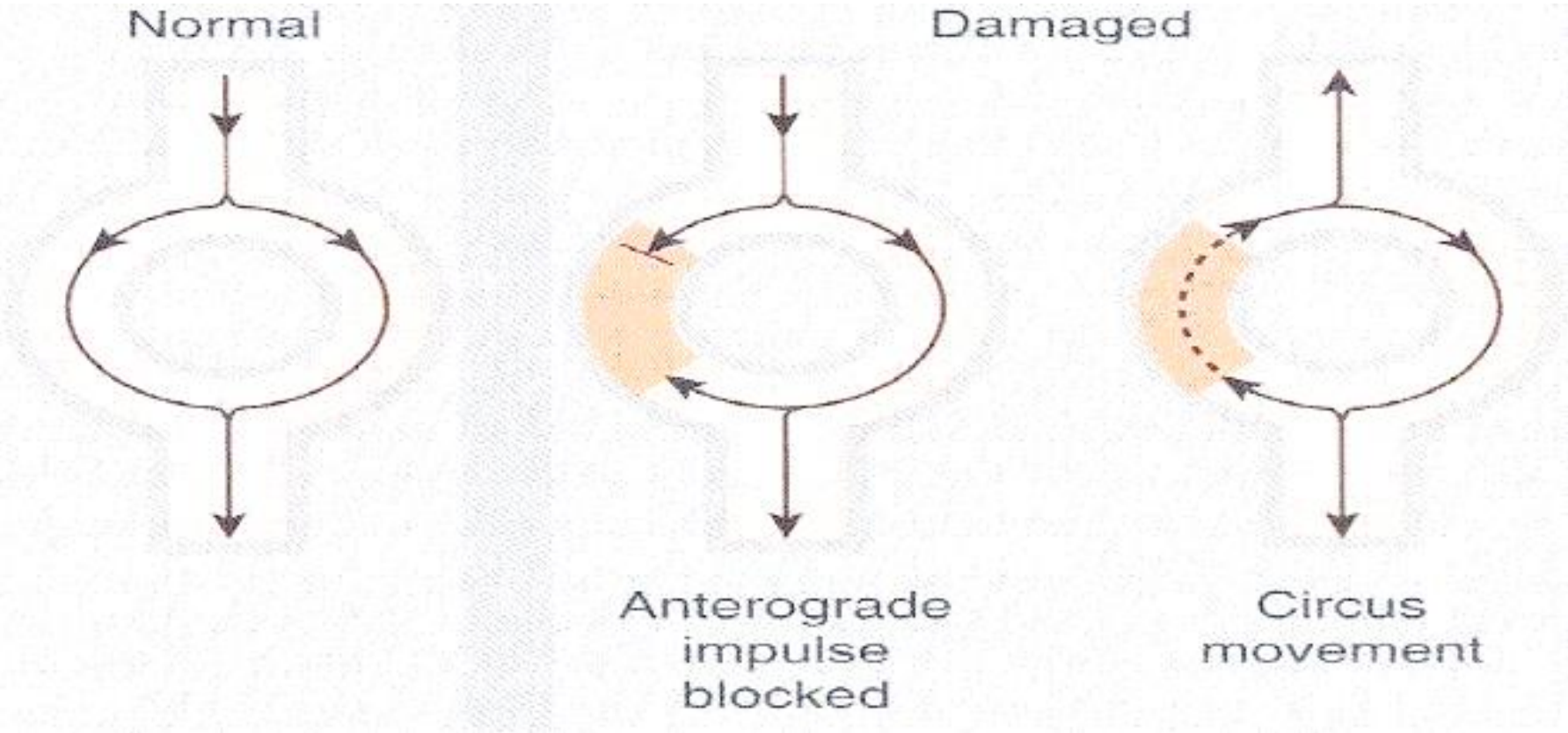
1st degree heart block – slowed conduction

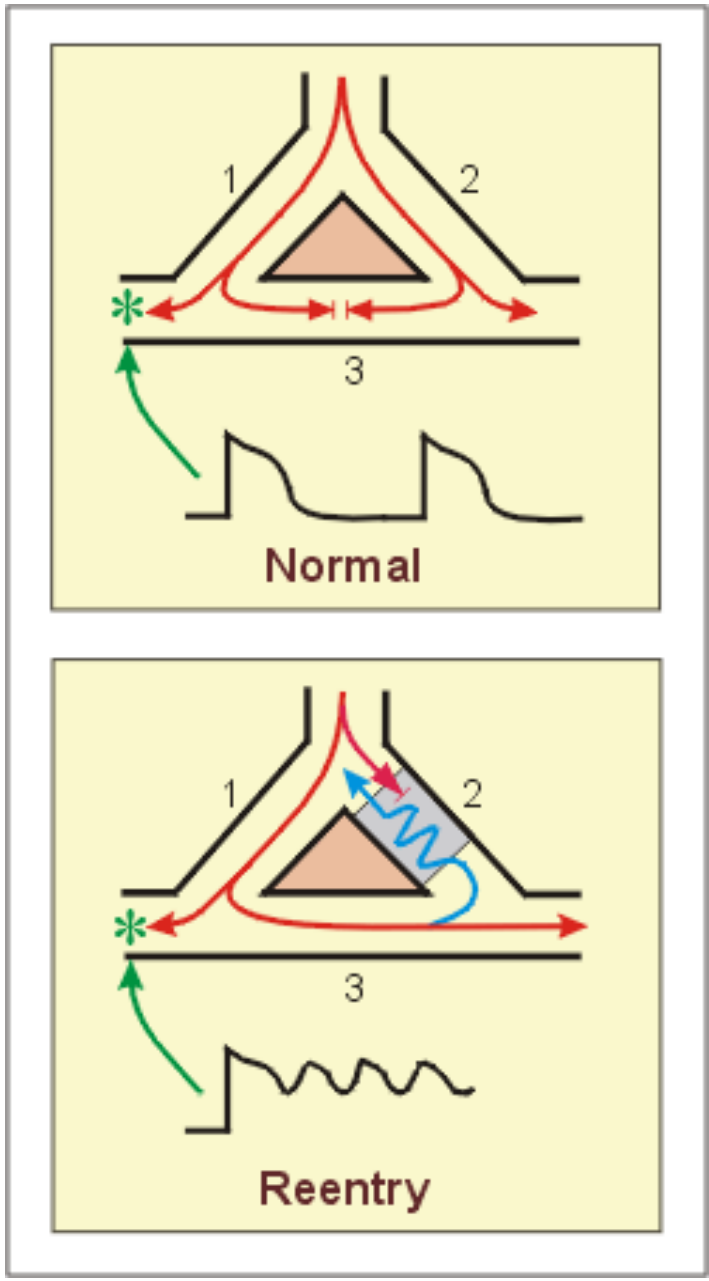
2nd degree block – some supraventricular complex not conducted

3rd degree block – no supraventricular complex are conducted

Reentry phenomenon

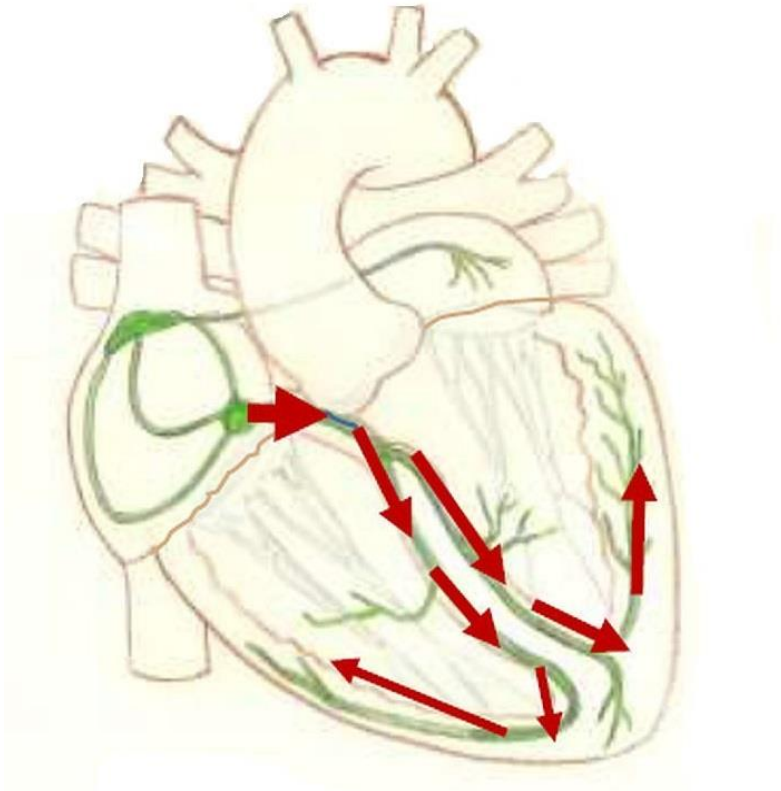
Due to abnormality of conduction , an impulse may recirculate in the heart and causes repetitive activation without the need for any new impulse to be generated. These are called reentrant arrythmias.

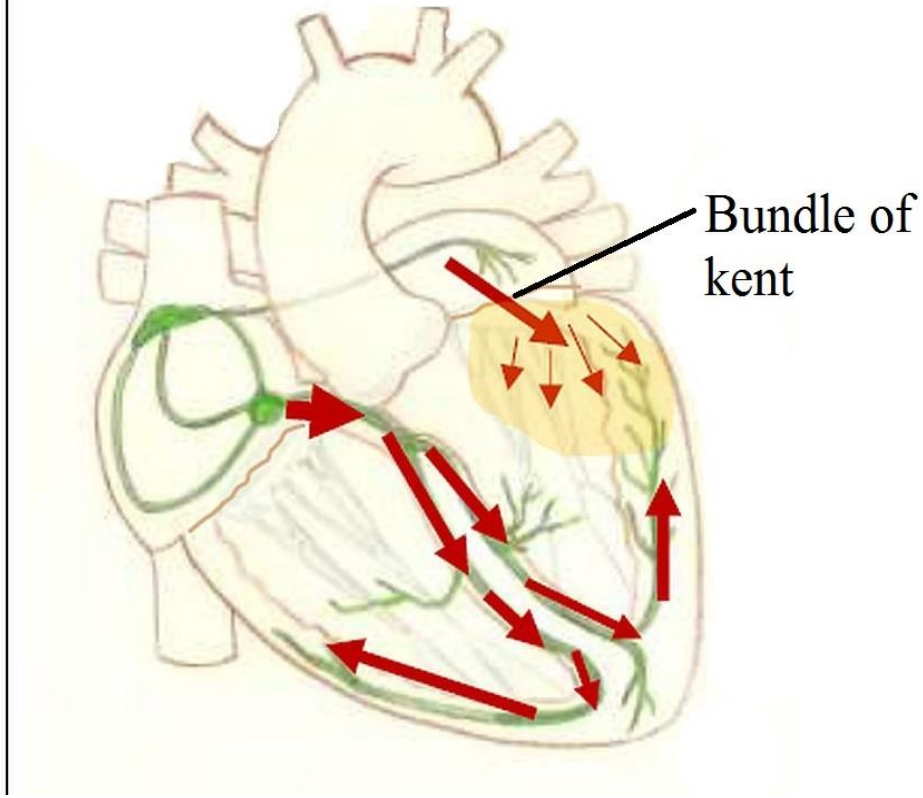

Normal
Damaged
Anterograde impulse blocked
Circus movement


1
2
3
Normal
1
2
3
Reentry

Accessory tract pathway

Wolff- Parkinson-White syndrome (WPW)





Classification of Anti-Arrhythmic Drugs

1-Class I: Na+ channels block

- Ia (quinidine, procainamide, disopyramide) (1-10s)
- Ib (lignocaine) (<1s)
- Ic (flecainide) (>10s)

2-Class II: ß-adrenoceptor antagonists (Propranolol, **Esmolol**)

3-Class III: prolong action potential and prolong refractory period (amiodarone, dofetilide, sotalol)

4-Class IV: Ca2+ channel antagonists (verapamil, diltiazem)

Classification based on clinical use

- ❖Drugs used for supraventricular arrhythmia`s
  - ➢Adenosine, verapamil, diltiazem
- ❖Drugs used for ventricular arrhythmias
  - ➢Lignocaine, mexelitine, bretylium
- ❖Drugs used for supraventricular as well as ventricular arrhythmias
  - ➢Amiodarone, - blockers, disopyramide, procainamide

Class IA Na+ channels block

1-Quinidine

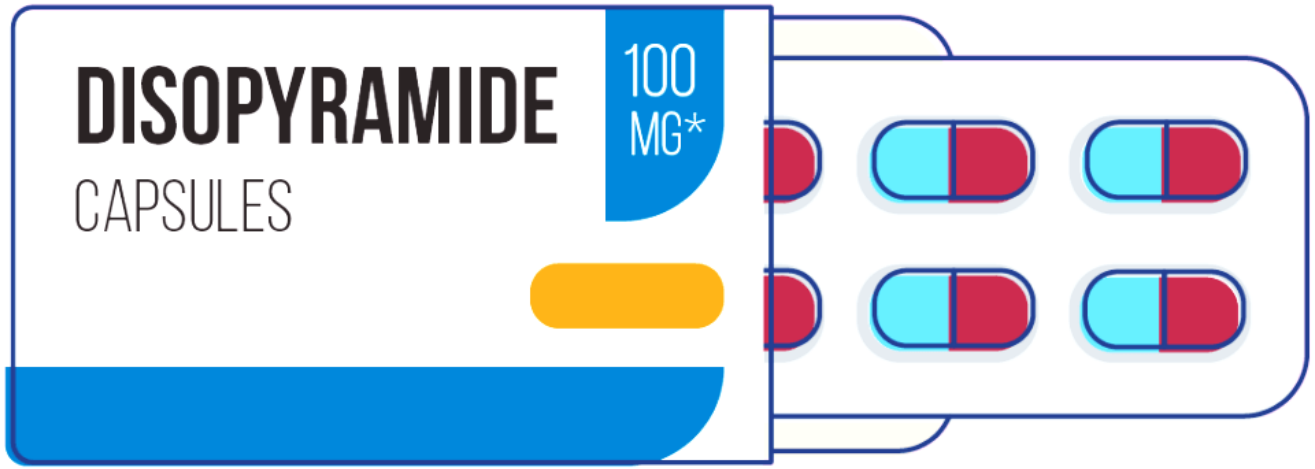
- Historically first antiarrhythmic drug used.
- 3-hydroxyquinidine, is nearly as potent as quinidine in blocking cardiac Na+ channels and prolonging cardiac action potentials.
- *Uses*
  - to maintain sinus rhythm in patients with atrial flutter or atrial fibrillation
  - to prevent recurrence of ventricular tachycardia or VF

2-Disopyramide

- Exerts electrophysiologic effects very similar to those of quinidine.
- Better tolerated than quinidine
- exert prominent anticholinergic actions
- Negative ionotropic action.

❖A/E-

- precipitation of glaucoma,
- constipation, dry mouth,
- urinary retention

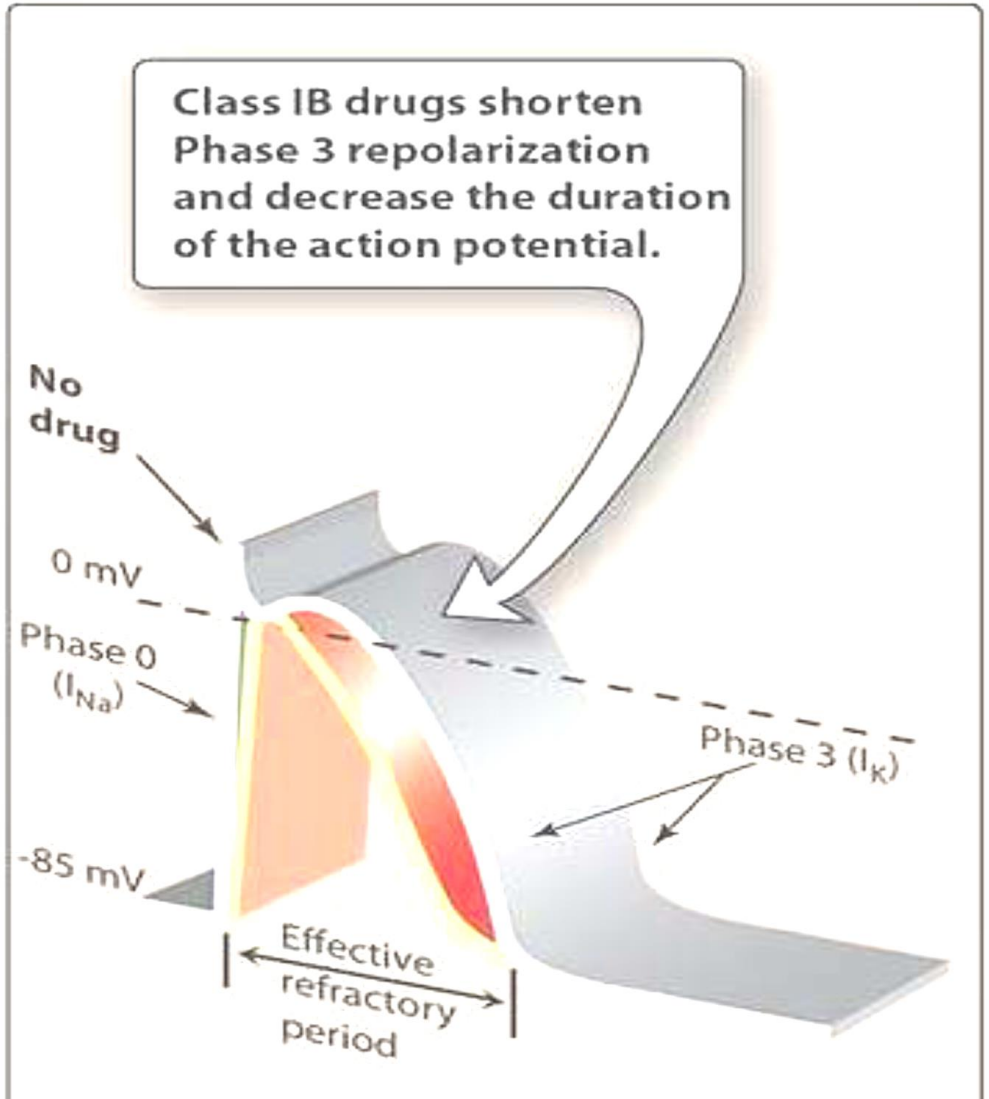


3-Procainamide

- Lesser vagolytic action , depression of contractility & fall in BP
- Can cause **Systemic lupus erythematosus** (**SLE**) not recommended > 6 months
- Use: Monomorphic VT, WPW Syndrome

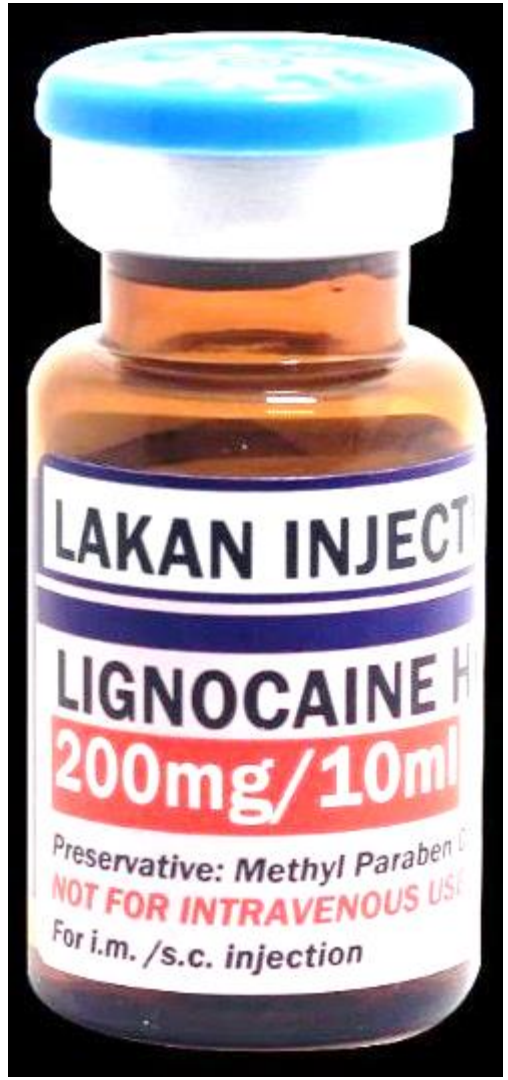
Class IB drugs

- Lignocaine, phenytoin, mexiletine
- Block sodium channels also shorten repolarization



Lignocaine

- Blocks inactivated sodium channels more than open state
- Relatively selective for partially depolarized cells
- Selectively acts on diseased myocardium
- Rapid onset & shorter duration of action
- Useful only in ventricular arrhythmias , Digitalis induced ventricular arrnhythmias



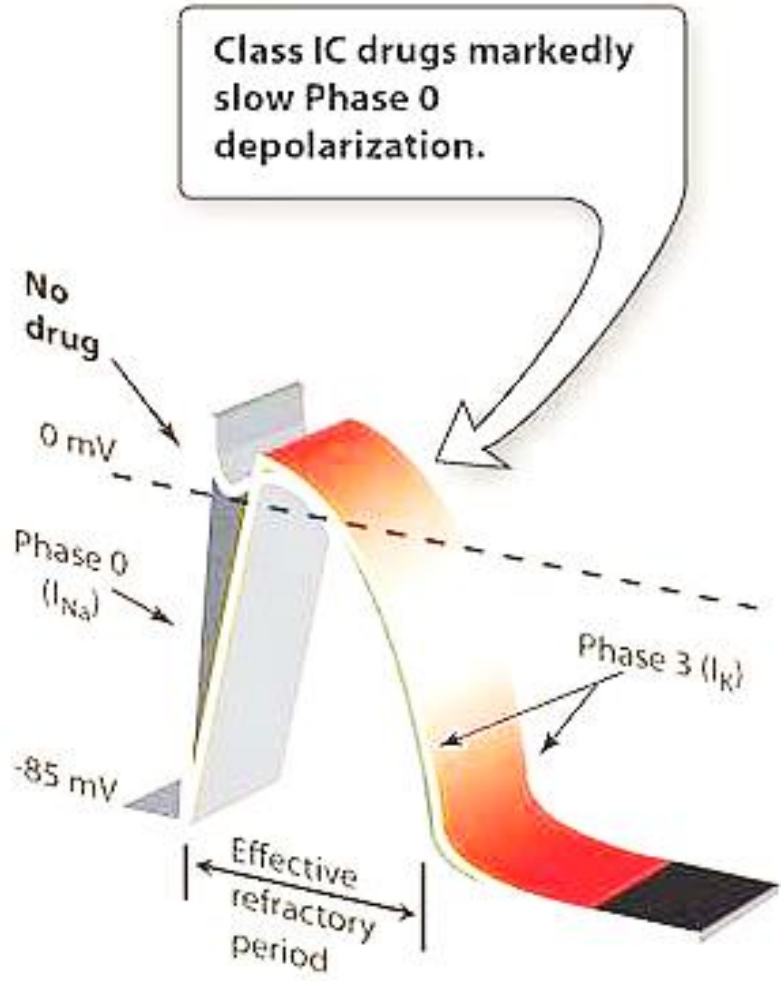
Mexiletine

- Oral analogue of lignocaine
- No first pass metabolism in liver
- **Use:**
  - chronic treatment of ventricular arrhythmias
  - associated with previous MI
  - Unlabelled use in diabetic neuropathy
  - Tremor is early sign of mexiletine toxicity
  - Hypotension, bradycardia, widened QRS ,
  - dizziness, nystagmus may occur

Class I C drugs
Encainide, Flecainide, Propafenone

- Have minimal effect on repolarization
- Are most potent sodium channel blockers

- Risk of cardiac arrest , sudden death so not used commonly
- May be used in severe ventricular arrhythmias

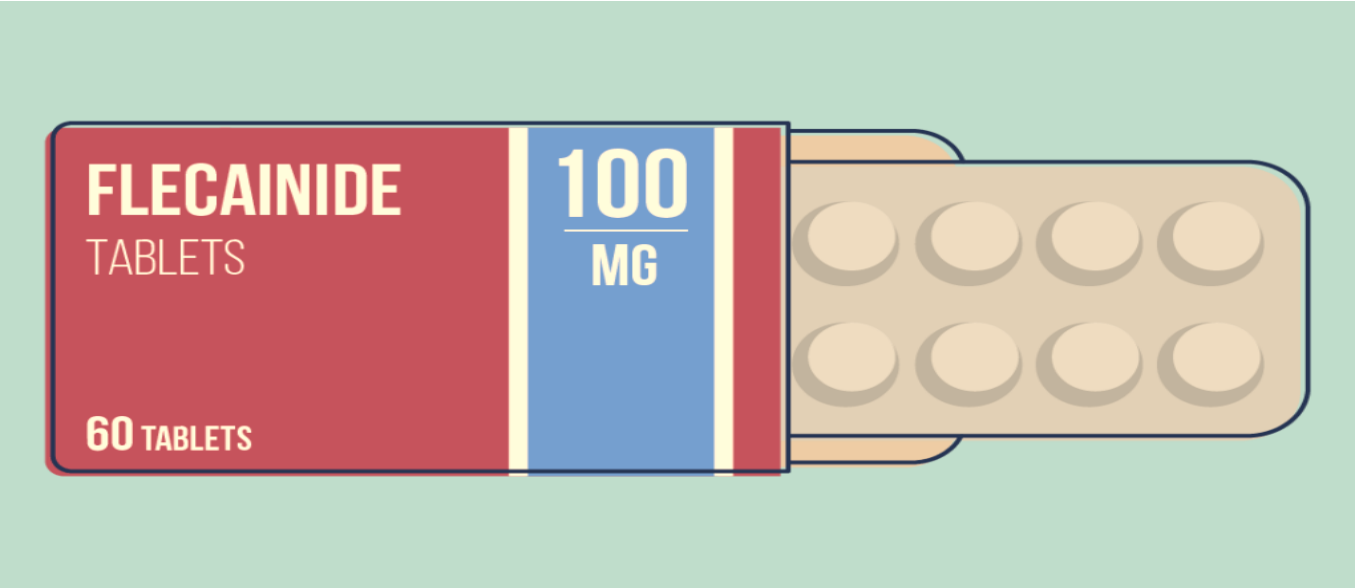


Propafenone

- Structural similarity with propranolol & has - blocking action
- Undergoes variable first pass metabolism
- Reserve drug for ventricular arrhythmias, reentrant tachycardia involving accessory pathway
- Adverse effects: metallic taste, constipation and is proarrhythmic

Flecainde

- Potent blocker of Na & K channels
- Blocks K channels but does not prolong APD & QT interval
- Maintain sinus rhythm in supraventricular arrhythmias



Class II: Beta blockers

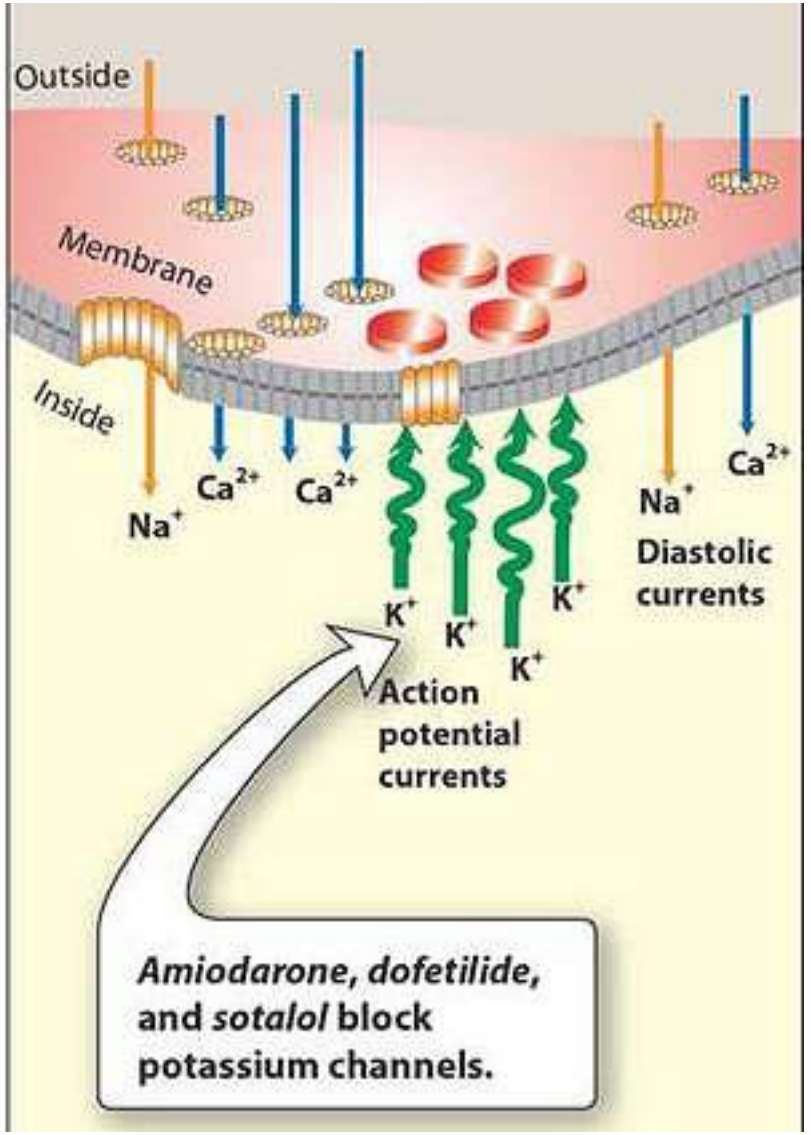
- β -receptor stimulation:
- ↑ automaticity,
- ↑ AV conduction velocity,
- ↓ refractory period
- β-adrenergic blockers competitively block
- catecholamine induced stimulation of cardiac β- receptors
- Depress phase 4 depolarization of pacemaker cells
- Slow sinus as well as AV nodal conduction : ↓ HR, ↑ PR
- ↑ ERP, prolong AP Duration by ↓ AV conduction
- Reduce myocardial oxygen demand

Esmolol

- β1 selective agent
- Very short elimination t1/2 :9 mins
- Metabolized by RBC esterases
- Rate control of rapidly conducted AF
- Use:
  - Arrythmia associated with anaesthesia
  - Supraventricular tachycardia

Class III Antiarrythmia (prolong action potential and prolong refractory period)

- ↑APD & ↑RP by blocking the K+ channels



1-Amiodarone

- Iodine containing long acting drug
- Mechanism of action: (Multiple actions)
  - Prolongs APD by blocking K+ channels
  - blocks inactivated sodium channels
  - β blocking action , Blocks Ca2+ channels
  - ↓ Conduction, ↓ectopic automaticity
- Can be used for both supraventricular and ventricular tachycardia

2-Bretylium:

- Adrenergic neuron blocker used in resistant ventricular arrhythmias

3-Sotalol:

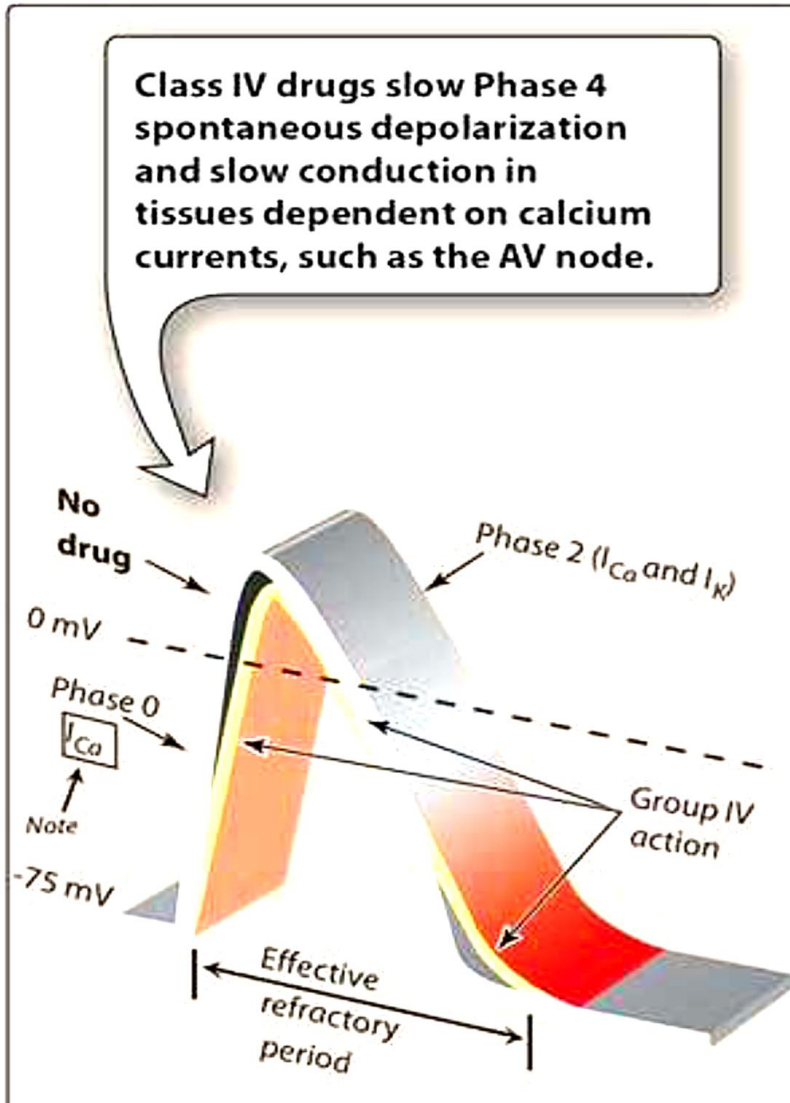
- Beta blocker

4-Dofetilide, Ibutilide :

- Selective K+ channel blocker, less adverse events
- use in AF to convert or maintain sinus rhythm
- May cause QT prolongation

Calcium channel blockers (Class IV)

- Inhibit the inward movement of calcium ↓ contractility, automaticity , and AV conduction.
- Verapamil & diltiazem



Verapamil

- Uses:
  - Terminate PSVT
  - control ventricular rate in atrial flutter or fibrillation
- Drug interactions:
  - Displaces digoxin from binding sites
  - ↓ renal clearance of digoxin

Other antiarrhythmics

Adenosine :

- Purine nucleoside having short and rapid action
- IV suppresses automaticity, AV conduction and dilates coronaries
- Drug of choice for PSVT
- Adverse events: Nausea, dyspnoea, flushing, headache

شعراء