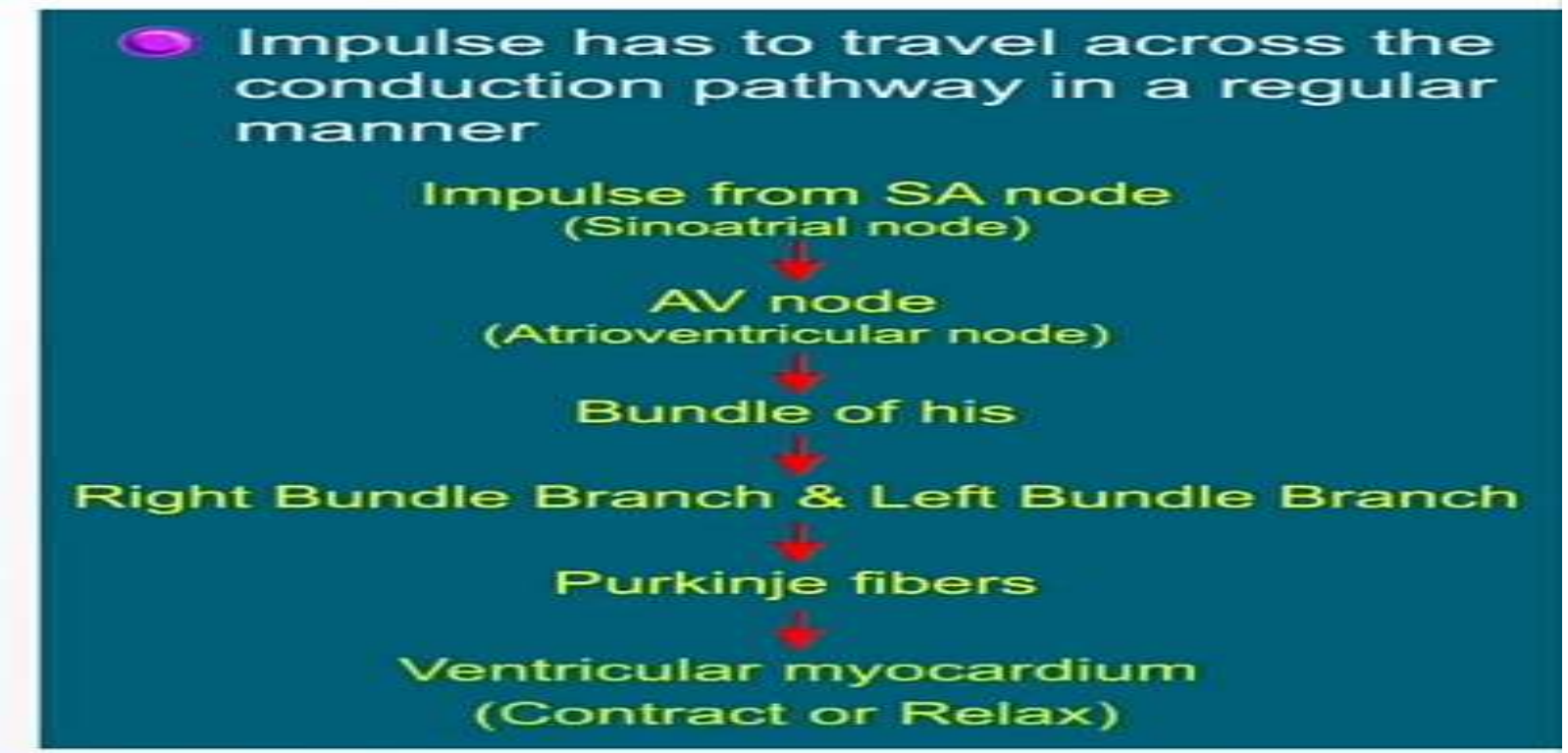
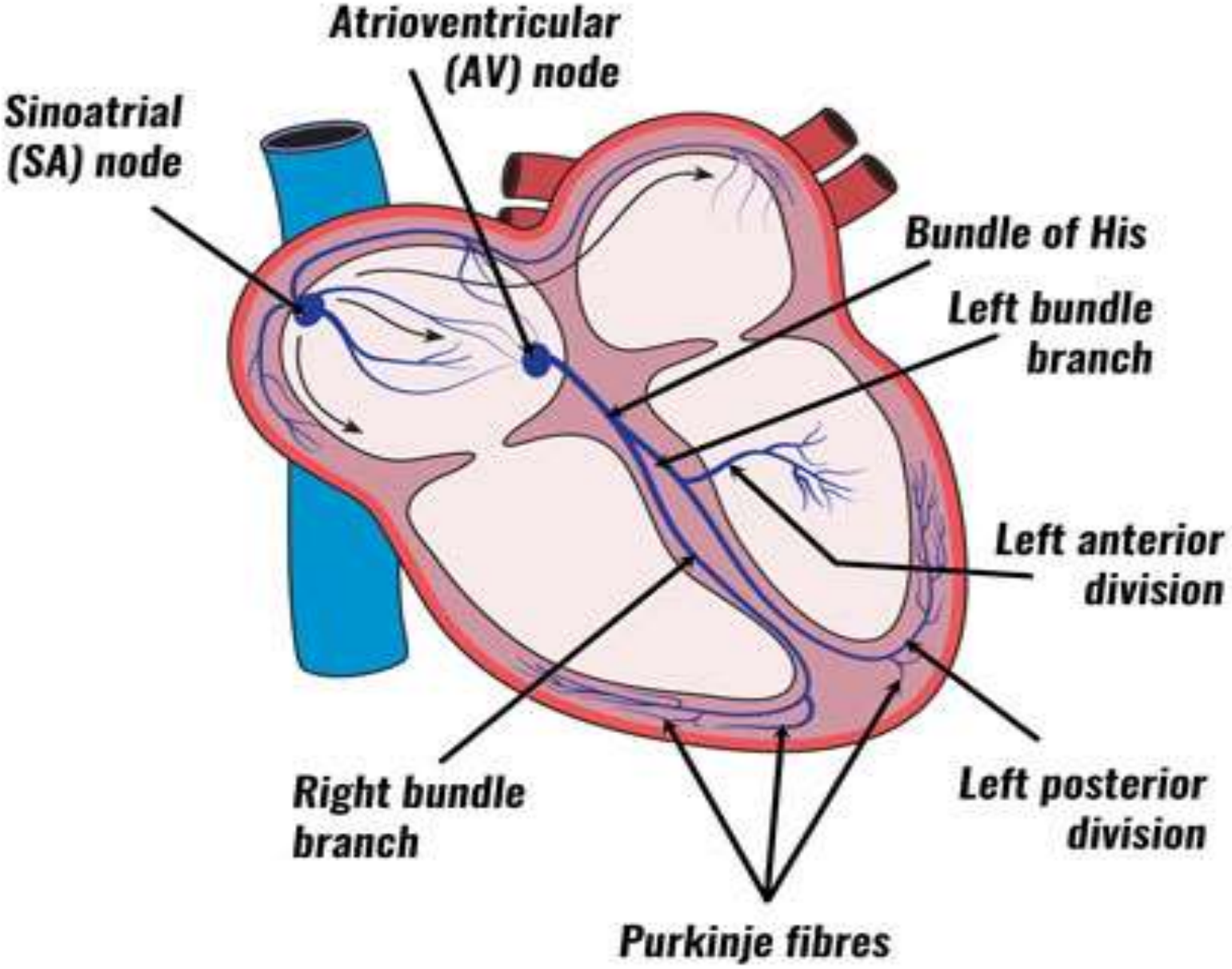
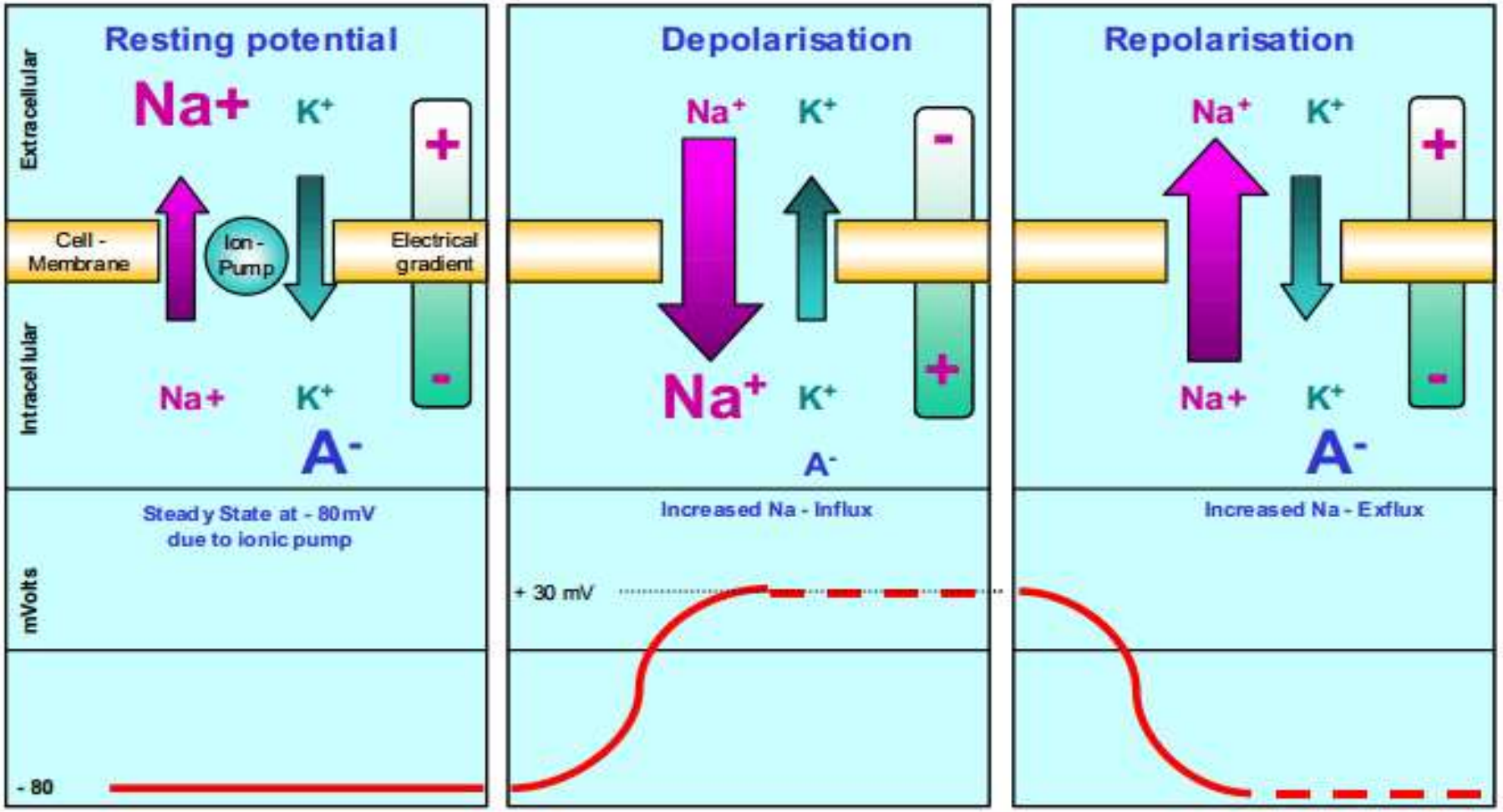
Anti arrythmic

- **Cardiac arrythmias**
- Deviation from normal pattern of cardiac rythm.
- Normal heart beat is 60-100 beats/min.




Atrioventricular (AV) node
Sinoatrial (SA) node
Bundle of His
Left bundle branch
Left anterior division
Right bundle branch
Left posterior division
Purkinje fibres

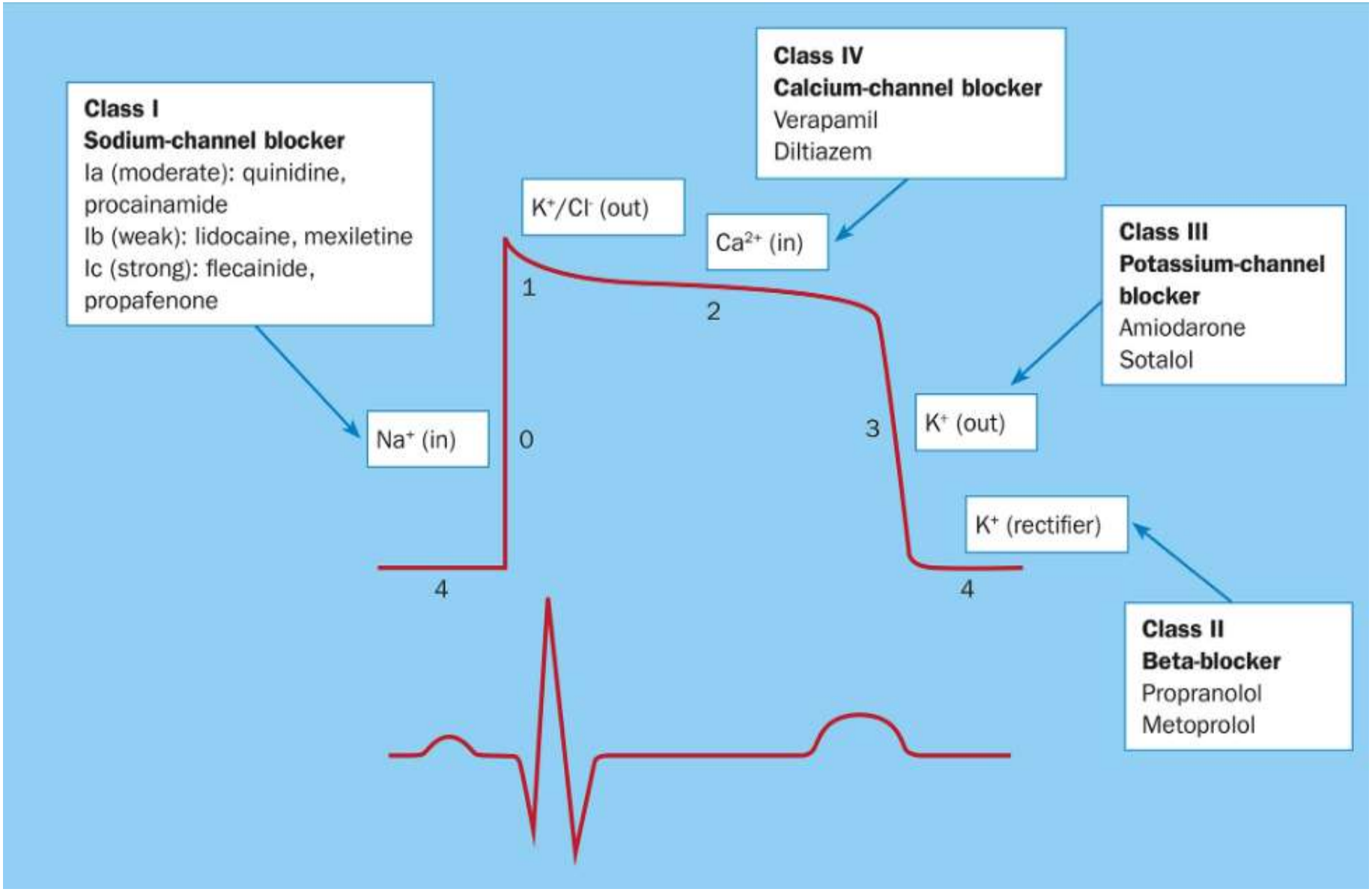

Resting potential
Extracellular
Na+
K+
Cell - Membrane
Ion - Pump
Electrical gradient
+
-
Intracellular
Na+
K+
A-
Steady State at - 80mV due to ionic pump
mVolts
- 80
Depolarisation
Na+
K+
-
+
Na+
K+
A-
Increased Na - Influx
+ 30 mV
Repolarisation
Na+
K+
+
-
Na+
K+
A-
Increased Na - Exflux

SNO	cardiac arrhythmias	condition
1	Extrasystoles (ES)	premature ectopic beats due to abnormal automaticity
2	Paroxysmal supraventricular tachycardia (PSVT)	150–200/min
3	Atrial flutter (AFI)	200– 350/min
4	Atrial fibrillation (AF)	350–550/min
5	Ventricular tachycardia (VT)	4 or more consecutive ventricular extrasystoles
6	Torsades de pointes	life-threatening form of polymorphic ventricular tachycardia (with long Q-T interval.)
7	Atrio-ventricular (A-V) block	depression of impulse conduction through the A-V node and bundle of His
8	Ventricular fibrillation (VF)	irregular, rapid and fractionated activation of ventricles resulting in incoordinated contraction of its fibres with loss of pumping function

- Antiarrhythmic drugs are used to treat abnormal cardiac rhythms such as atrial fibrillation, atrial flutter, ventricular tachycardia, ventricular fibrillation, etc.
- There are several different classes of antiarrhythmic medications and they act on different phases of cardiac myocyte and/or pacemaker cell **action potentials**.

THE VAUGHAN WILLIAMS CLASSIFICATION SYSTEM FOR ANTIARRHYTHMIC THERAPY

CLASS	TYPE	DRUGS
I	Sodium channel blockers	
	CLASS I A	Quinidine, Procainamide, Disopyramide
	CLASS I B	Lidocaine, Mexiletine
	CLASS I C	Propafenone, Flecainide
II	Beta blockers	Propranolol, Esmolol, Sotalol
III	Potassium channel blockers	Amiodarone, Dronedarone, Dofetilide, Ibutilide
IV	Calcium channel blockers	Verapamil, Diltiazem
V	Miscellaneous	Adenosine, Digoxin

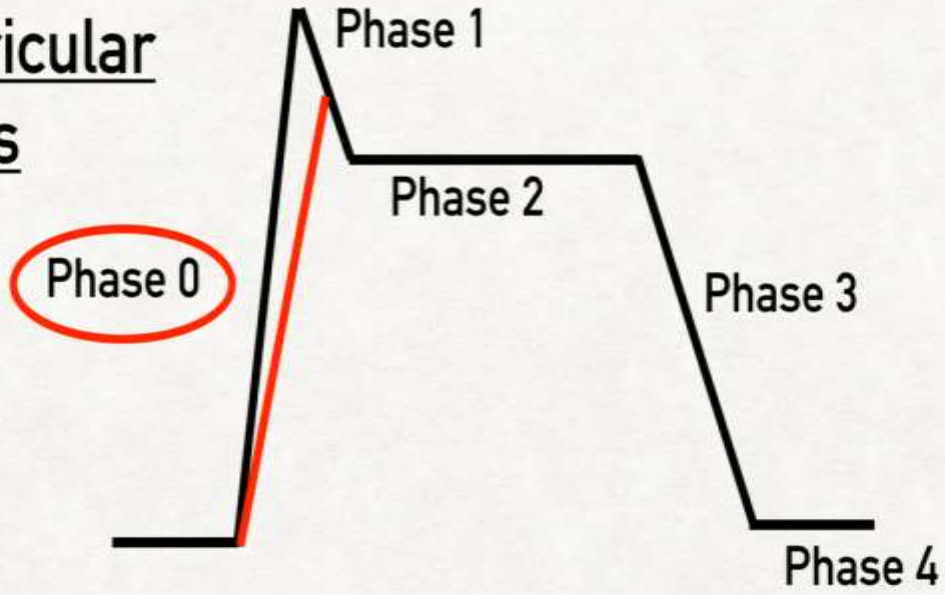

Class I
Sodium-channel blocker
Ia (moderate): quinidine, procainamide
Ib (weak): lidocaine, mexiletine
Ic (strong): flecainide, propafenone
Class IV
Calcium-channel blocker
Verapamil
Diltiazem
Class III
Potassium-channel blocker
Amiodarone
Sotalol
Class II
Beta-blocker
Propranolol
Metoprolol
K+/Cl- (out)
Ca2+ (in)
Na+ (in)
K+ (out)
K+ (rectifier)
0
1
2
3
4
4

Sodium channel blockers:

- **sodium channel blockers** decrease the slope of phase 0, and the depolarization rate and amplitude will be reduced.
- Cardiac myocyte conduction velocity and transmission will be decreased as a result.
- This will decrease atrial and ventricular myocyte excitability and serve to suppress abnormal conduction rhythms.
- Since pacemaker cells use calcium ions to depolarize, sodium channel blockers have little effect on the SA node and AV node (pacemaker cells).

Sodium Channel Blockers

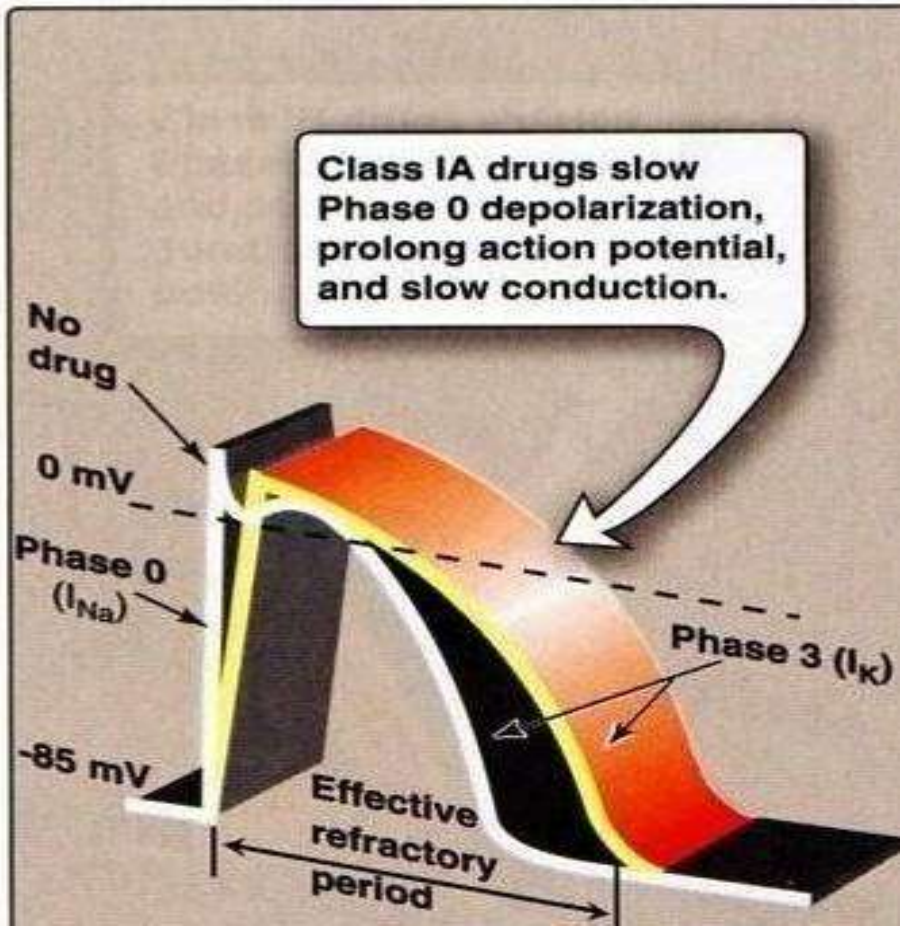
Atrial & Ventricular Myocytes



- Sodium channel blockers act on phase 0 of non-pacemaker cardiac myocyte action potentials by blocking the influx of sodium ions into the cell.
- This decreases depolarization rate and amplitude thereby decreasing myocyte conduction velocity and transmission.

Class IA (Quinidine, Procainamide, Disopyramide)

- These drugs blocks myocardial Na+ channels in the open state—reduces automaticity and maximal rate of 0 phase depolarization in a frequency dependent manner.
- Prolongation of APD is due to K+ channel block, while lengthening of ERP is caused by its moderate effect on recovery of Na+ and K+ channels.
- At high concentrations it also inhibits L type Ca2+ channels. Quinidine decreases the availability of Na+ channels as well as delays their reactivation


Class IA drugs slow
Phase 0 depolarization,
prolong action potential,
and slow conduction.
No
drug
0 mV
Phase 0
(I_{Na})
Phase 3 (I_K)
-85 mV
Effective
refractory
period

Quinidine

Side effects:

- hypotension,
- GI problems (diarrhea and vomiting), and
- cinchonism (tinnitus, blurred vision, and headaches).

Drug interaction:

- Marked fall in BP in patients receiving vasodilators.
- Risk of *torsades de pointes is increased by hypokalaemia* caused by diuretics.
- Synergistic cardiac depression with β-blockers, verapamil, K+ salts.

Use:

Atrial and ventricular arrhythmias

Dose:

QUINIDINE SULPHATE 200 mg tab; QUININGA 300 mg tab, 600 mg/2 ml inj; NATCARDINE 100 mg tab.

Procainamide:

It is orally active amide derivative of the local anaesthetic procaine, with cardiac electrophysiological actions almost identical to those of quinidine, *viz. slowing of 0 phase depolarization* and impulse conduction, prolongation of APD, ERP, QRS complex and Q-T interval.

Adverse effects:

- nausea and
- vomiting do occur.
- weakness,
- mental confusion and hallucinations are noted at higher doses.
- Flushing
- *torsades de pointes*
- Long-term high dose procainamide therapy can cause systemic lupus erythematosus (SLE

Use :

monomorphic VT and some supraventricular arrhythmias

Dose:

PRONESTYL 250 mg tab., 1 g/10 ml inj.

Disopyramide:

It is a quinidine like Class IA drug that has prominent cardiac depressant and anticholinergic Actions

Adverse effects :

- dry mouth,
- constipation,
- urinary retention (especially in elderly males) and blurred vision

Use:

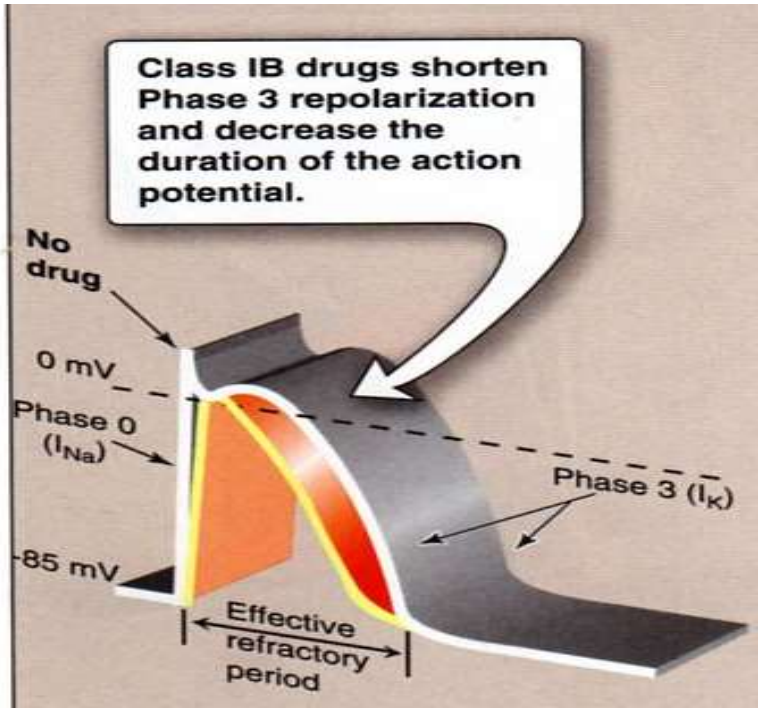
- ventricular arrhythmia

Dose: *100–150 mg 6–8 hourly oral.*

NORPACE 100, 150 mg cap, REGUBEAT 100 mg tab.

Class I B

- These drugs block Na+ channels more in the inactivated than in the open state, but do not delay channel recovery (channel recovery time < 1S).
- They do not depress A-V conduction or prolong (may even shorten) APD, ERP and Q-T.
- They shorten Phase 3 repolarization
- ↓ the duration of the cardiac action potential
- They suppress arrhythmias caused by abnormal automaticity
- They show ***rapid association & dissociation*** (weak effect) with Na^+ channels with appreciable degree of use-dependence
- <u>No effect on conduction velocity</u>



Pharmacokinetics :

Lidocaine is inactive orally due to high first pass metabolism in liver.

Dose:

- XYLOCARD, GESICARD 20 mg/ml inj. (5, 50 ml vials)

Adverse effects :

- Drowsiness,
- nausea,
- paresthesias,
- blurred vision,
- disorientation,
- nystagmus,
- twitchings and fits.

USES:

- Ventricular tachycardia
- Ventricular fibrillation

Mexiletine:

It is a local anaesthetic and an orally active antiarrhythmic;

Side effects:

- Tremor
- Nausea
- Vomitting

Uses:

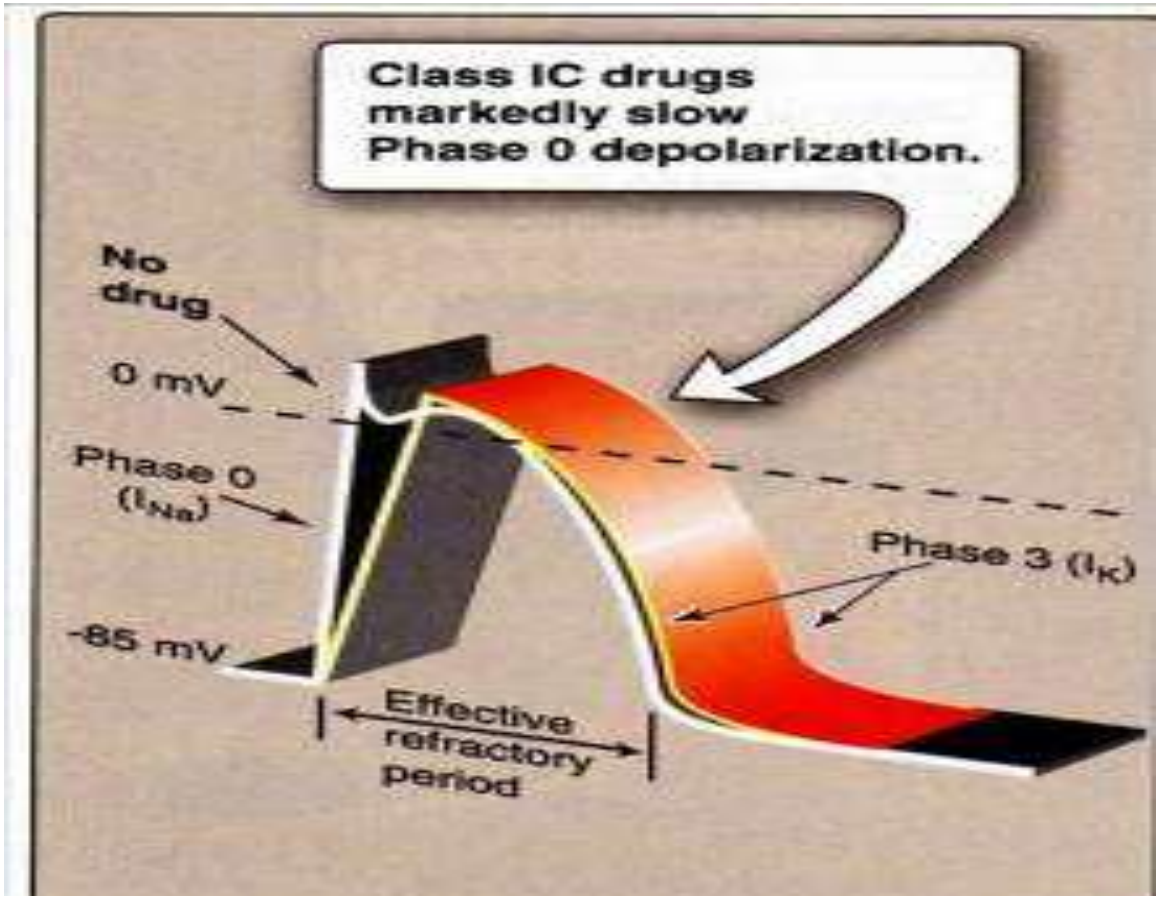
- ventricular arrhythmias

Dose:

MEXITIL 50, 150 mg caps, 250 mg/10 ml. inj.

CLASS I C

- They **markedly slow Phase 0** fast depolarization
- They markedly slow conduction in the myocardial tissue
- They possess **slow rate of association and dissociation (strong effect)** with sodium channels
- They only have **minor effects on the duration of action potential and refractoriness**
- They reduce automaticity by increasing the threshold potential rather than decreasing the slope of Phase 4 spontaneous depolarization.


Class IC drugs
markedly slow
Phase 0 depolarization.
No
drug
0 mV
Phase 0
(I_{Na})
Phase 3 (I_K)
-85 mV
Effective
refractory
period

Propafenone:

Side effects :

- Nausea,
- Vomiting,
- Bitter taste,
- Constipation and
- Blurred vision.

uses:

- for prophylaxis and treatment of ventricular arrhythmias and
- tachycardia

Dose: *150 mg BD–300 mg TDS;*

RHYTHMONORM 150 mg tab.

- Class Ia agents act at intermediate speed and include quinidine and procainamide.
- Class Ib agents are the fastest acting and include lidocaine and mexiletine.
- Finally, class Ic agents such as flecainide work by slow sodium channel association and dissociation.

CLASS II (Beta blockers)

Mechanism of action:

- Negative inotropic and chronotropic action.
- Prolong AV conduction (delay)
- Diminish phase 4 depolarization → suppressing automaticity(of ectopic focus)

Clinical indications:

- Beta-blockers are useful in the management of tachyarrhythmias not only as treatment and prevention, but also offering rate control in AF and atrial flutter.
- chronic heart failure (HF),
- glaucoma
- MI.
- Certain non-cardioselective agents (*eg carvedilol and propranolol) are useful in* anxiety and tremor.

Contraindications:

- The main contraindication to beta-blockade is obstructive lung disease (*ie asthma)*, due to the risk of bronchoconstriction.

Adverse effects:

- Fatigue and
- sleep disturbance.

Dose:

MINIBLOCK 100 mg/10 ml, 250 mg/10 ml inj.;

CLASS III (Potassium channel blockers)

Mechanism of action:

- Potassium channels are responsible for cardiomyocyte repolarisation through potassium efflux, allowing electrical conduction of an action potential through the heart.
- Blockage of these channels to prevent potassium release slows repolarisation by increasing action potential and refractory period duration and slowing conduction, translating as a prolonged QT interval on the ECG.
- The most commonly used class III agents are amiodarone, sotalol and dronedarone, although all have crossover actions: amiodarone having some class I, II and IV activity, sotalol non-selective class II activity, and dronedarone class I, II, III and IV activity.

Uses:

- Atrial and ventricular tachyarrhythmias.

Side effects:

- Chest pain,
- Breathlessness and
- Palpitations.

Class IV agents – calcium-channel blockers

- Calcium channel blockers decrease inward Ca^{2+} currents resulting in a decrease of phase 4 spontaneous depolarization (SA node)
- They slow conductance in Ca^{2+} current-dependent tissues like AV node.
- Examples: verapamil & diltiazem
- Because they act on the heart only and not on blood vessels.
- Dihydropyridine family are not used because they only act on blood vessels

Mechanism of action:

The non-dihydropyridine calcium-channel blockers (diltiazem and verapamil) prevent influx of calcium into cardiomyocytes, thereby decreasing conduction through the AV node and overall cardiac contractility.

Uses:

- Non-dihydropyridines are predominantly used in the prevention and treatment of supraventricular tachycardia (SVT).

Contraindications:

- As class IV agents reduce cardiac contractility, they are contraindicated in HF

Adverse effects :

- bradycardia,
- AV block,
- dizziness,
- flushing and
- headaches.
- Verapamil may additionally cause constipation, rash and nausea.

ADENOSINE

- It activates ACh sensitive K+ channels and causes membrane hyperpolarization through interaction with A1 type of adenosine GPCRs on SA node (pacemaker depression → bradycardia), A-V node (prolongation of ERP → slowing of conduction) and atrium (shortening of AP, reduced excita-bility).
- It indirectly reduces Ca2+ current in A-V node. Depression of the reentrant circuit through A-V node is responsible for termination of majority of PSVTs.

Uses :

Paroxysmal supra ventricular tachycardia

Adverse effects:

transient dyspnoea, chest pain, fall in BP and flushing in 30–60% patients;

Dose:

ADENOJECT, ADENOCOR 3 mg adenosine (base) per ml in 2 ml and 10 ml amp.