SNS COLLEGE OF ALLIED HEALTH SCIENCES

SNS Kalvi Nagar, Coimbatore - 35

Affiliated to Dr MGR Medical University, Chennai

DEPARTMENT OF CARDIO PULMONARY PERFUSION CARE TECHNOLOGY

COURSE NAME : Pharmacology Pathology and Clinical Microbiology

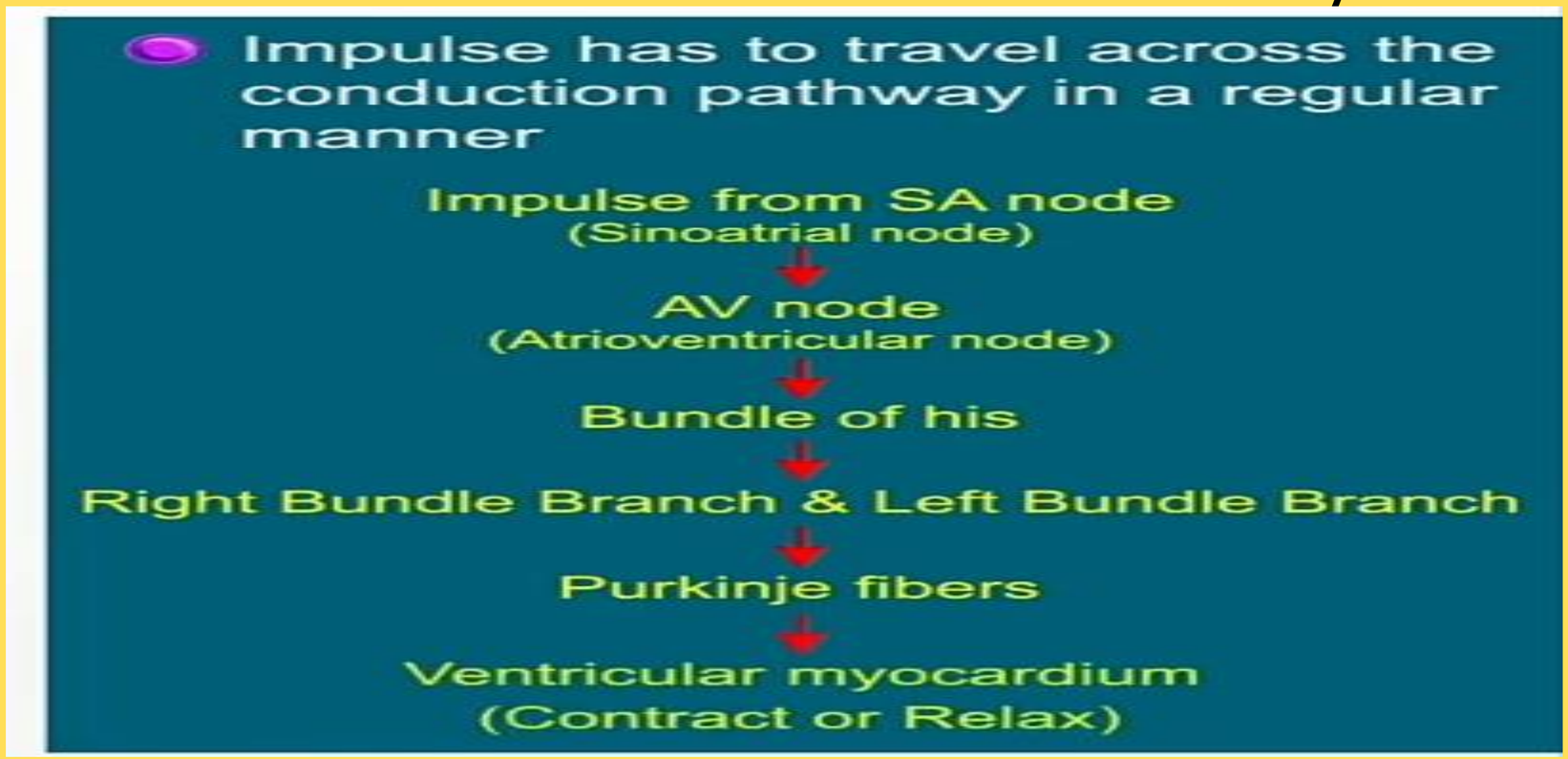
II nd YEAR

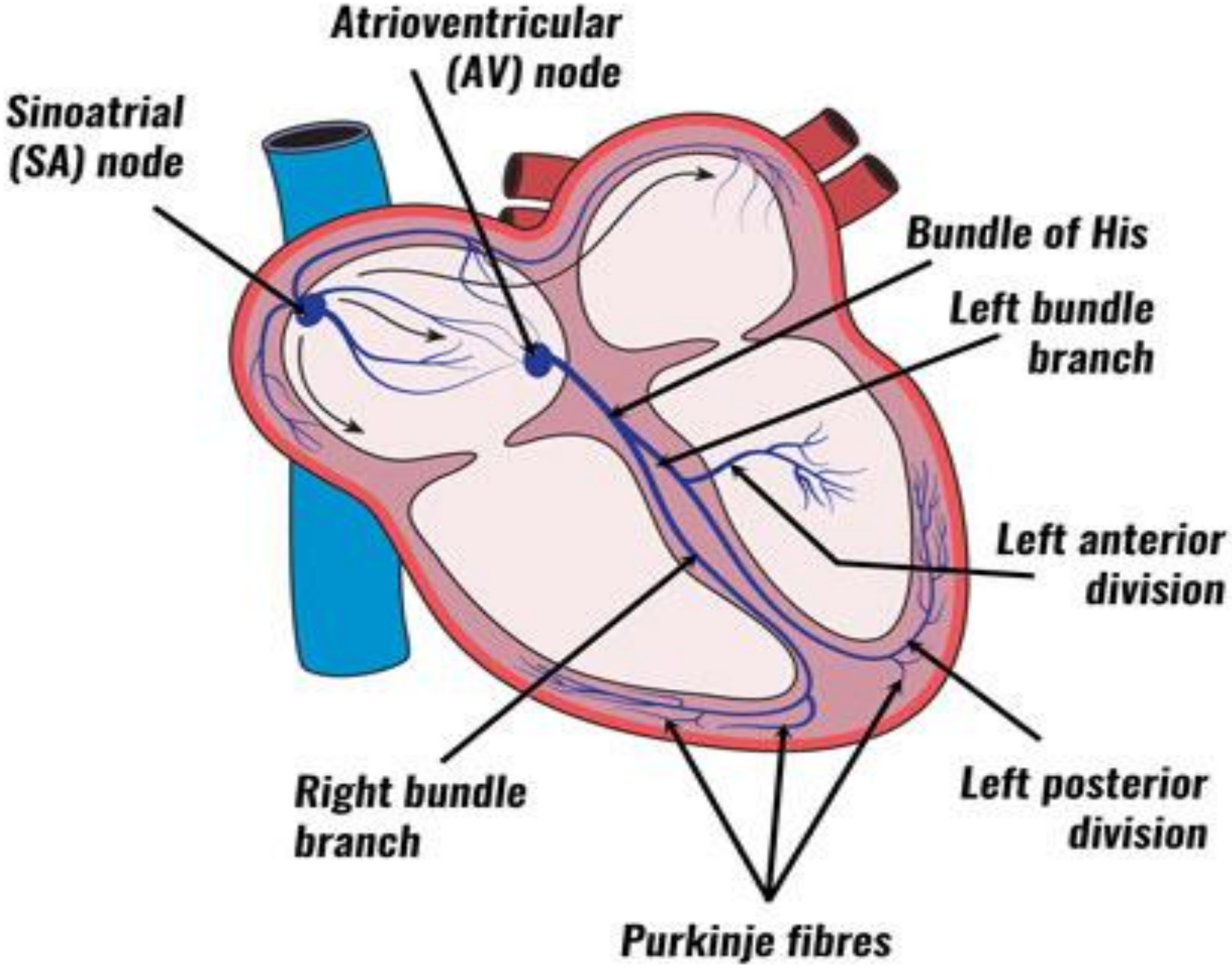
TOPIC : ANTI ARRYTHMIC

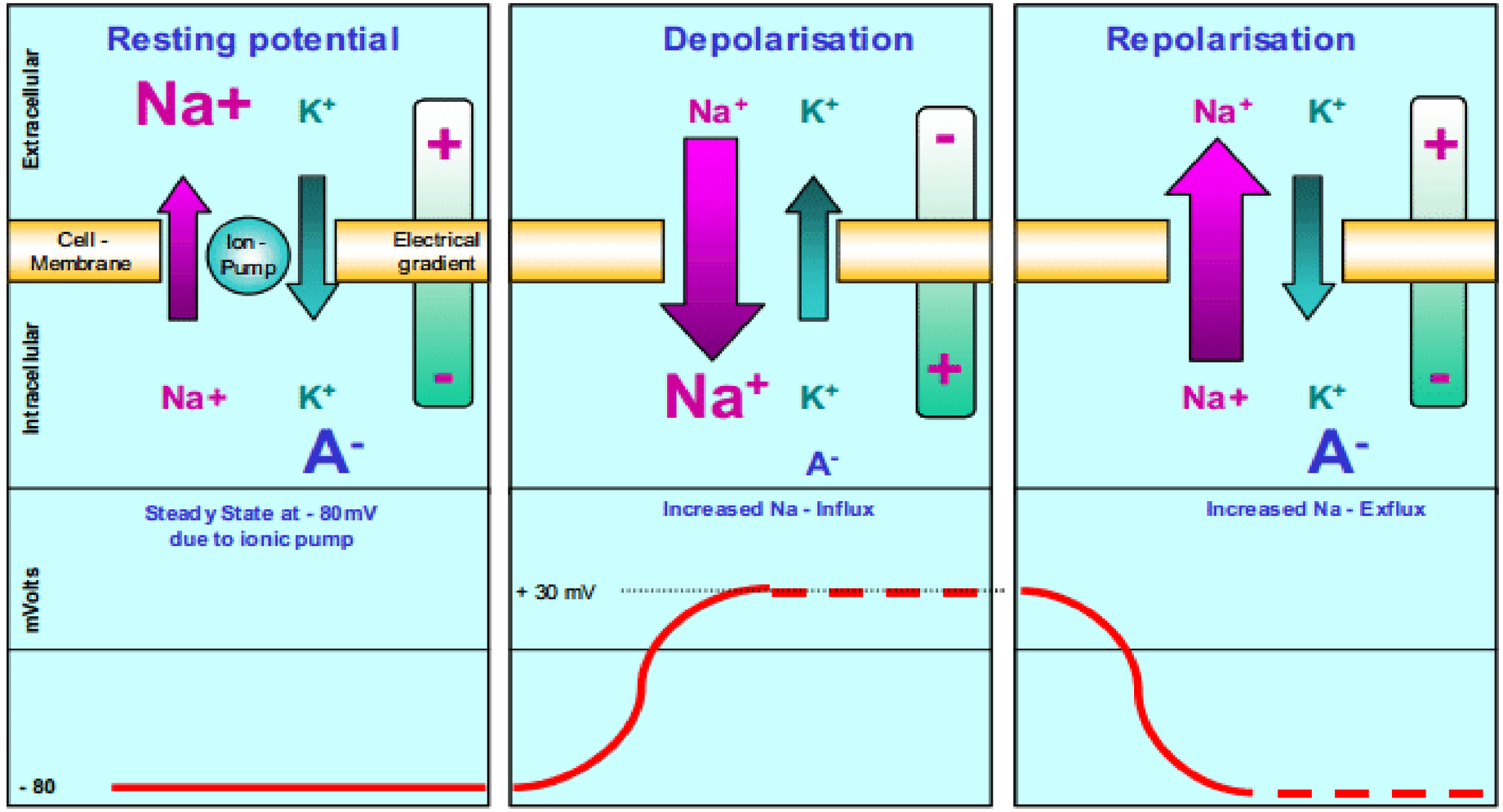
ANTI ARRYTHMIC

Cardiac Arrythmias

- Deviation from normal pattern of cardiac rhythm.
- 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
Depolarisation
Repolarisation
Extracellular
Intracellular
Na+
K+
A-
Cell - Membrane
Ion - Pump
Electrical gradient
+
-
Steady State at - 80 mV due to ionic pump
Increased Na - Influx
Increased Na - Exflux
mVolts
+ 30 mV
- 80

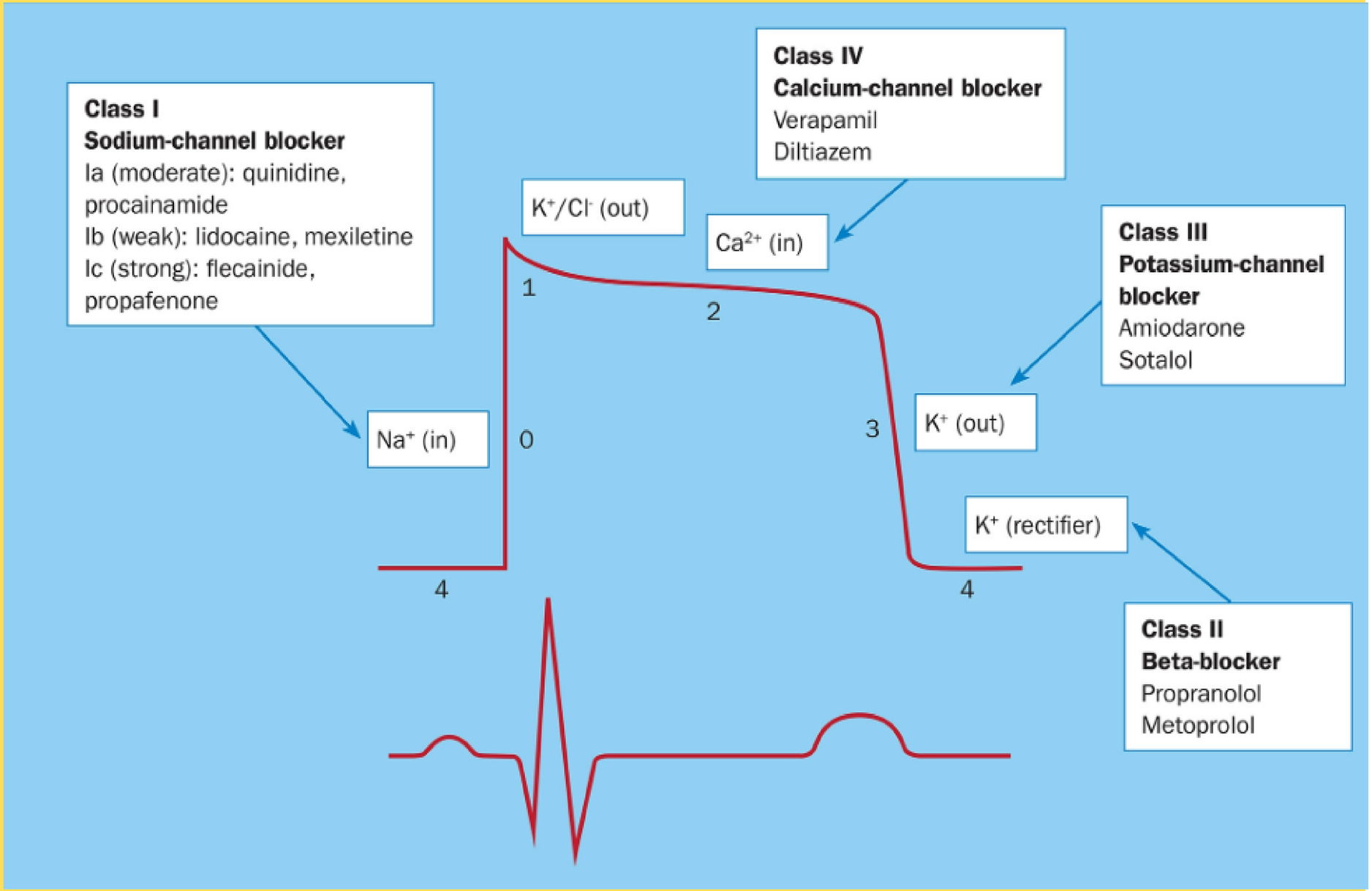
SNO	cardiac arrhythmias	condition
1	Extrasystoles (ES)	premature ectopic beats due to abnormal automaticity
2	Paroxysmal supraventricular tachycardia (PSVT)	150–200/min
3	Atrial flutter (AFI)	200– 350/min
4	Atrial fibrillation (AF)	350–550/min
5	Ventricular tachycardia (VT)	4 or more consecutive ventricular 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 in coordinated contraction of its fibers 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.

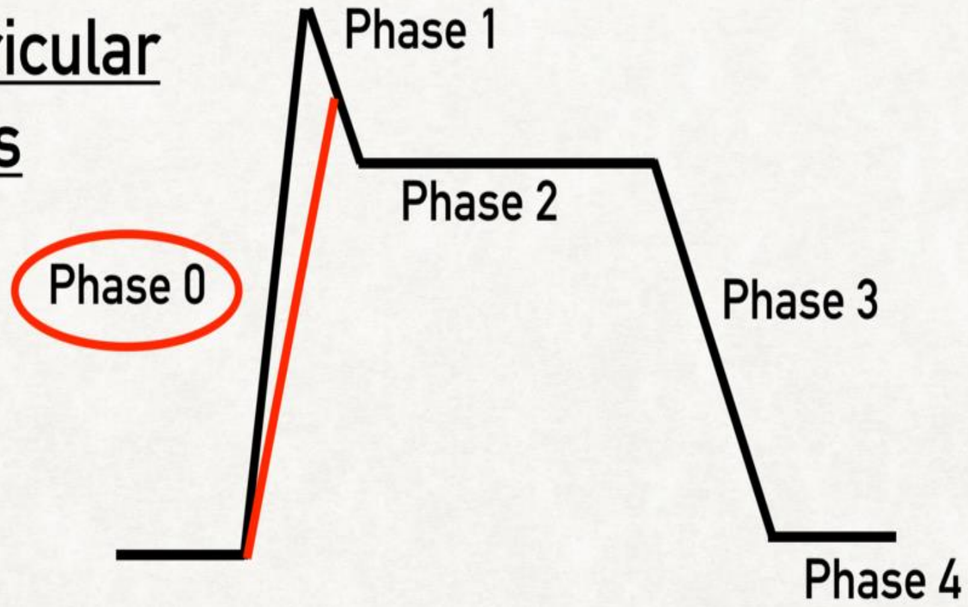
➢Cardiac myocyte conduction velocity and transmission will be decreased as a result.

➢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

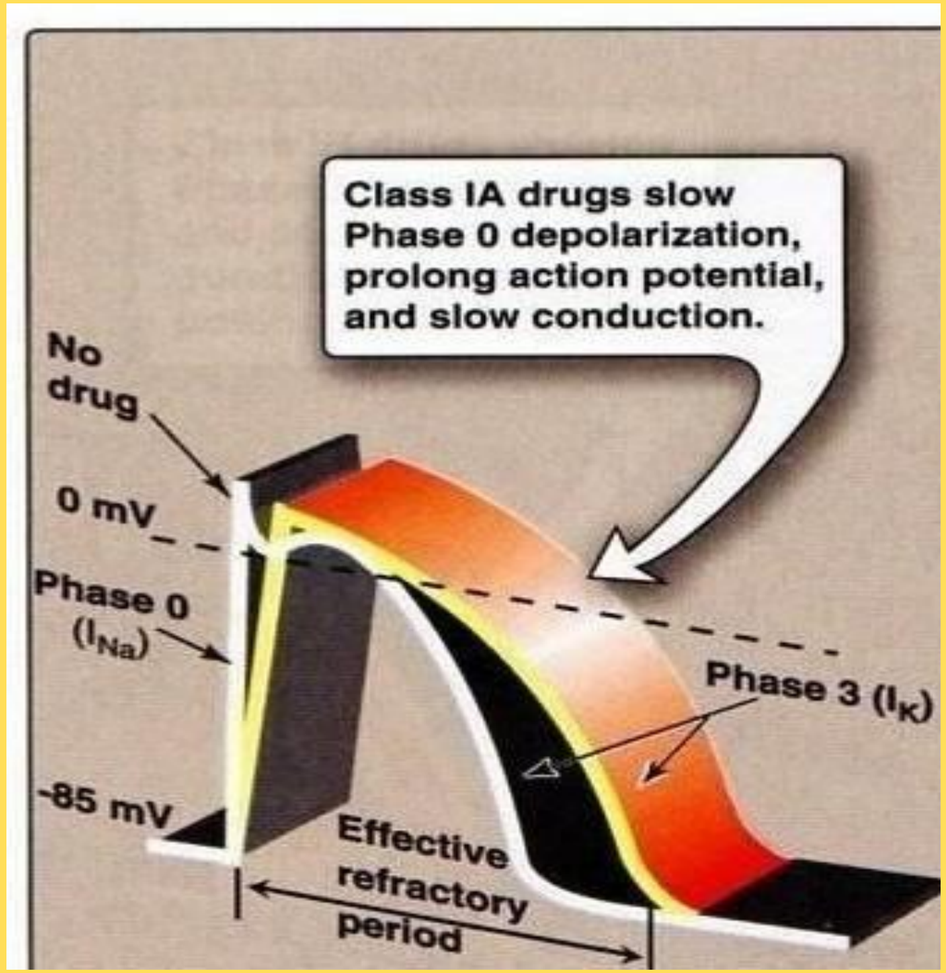


➢Sodium channel blockers act on phase 0 of non-pacemaker cardiac myocyte action potentials by blocking the influx of sodium ions into the cell.

➢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.

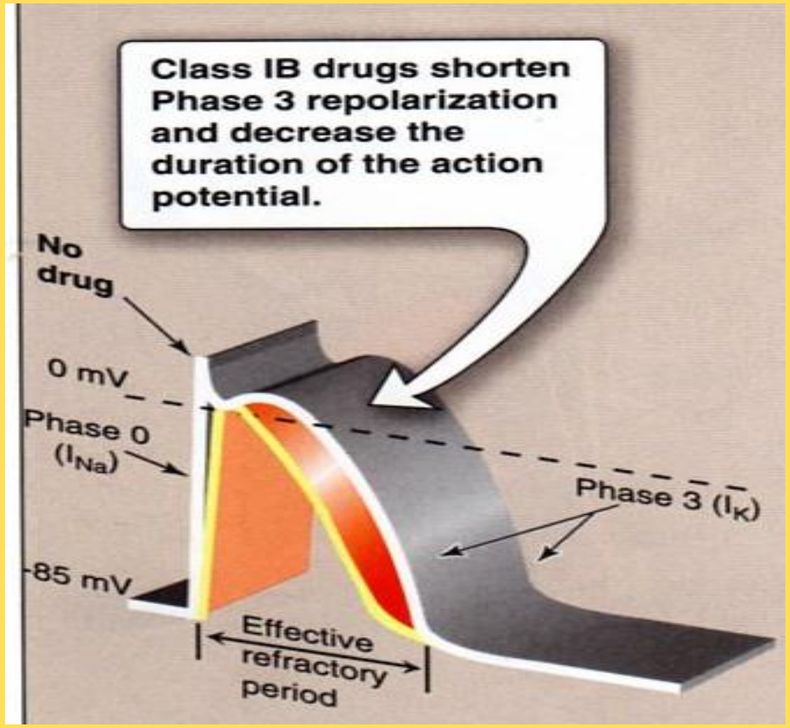
➢They shorten Phase 3 repolarization

➢↓ 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

➢No effect on conduction velocity



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:

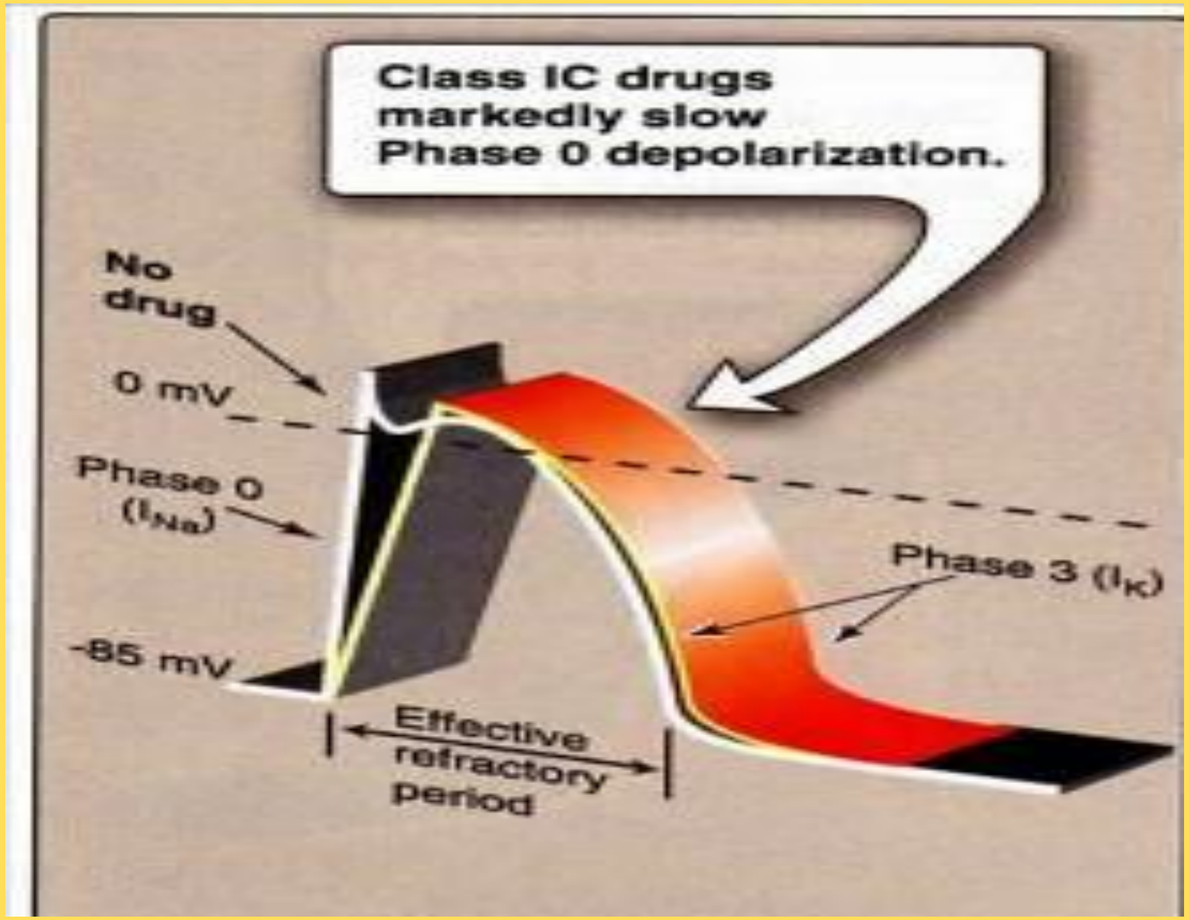
- ventricular arrhythmias

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.

THANK YOU