Cardiac Dysrhythmias

Two types of cardiac tissues.

Myocardial Muscle.

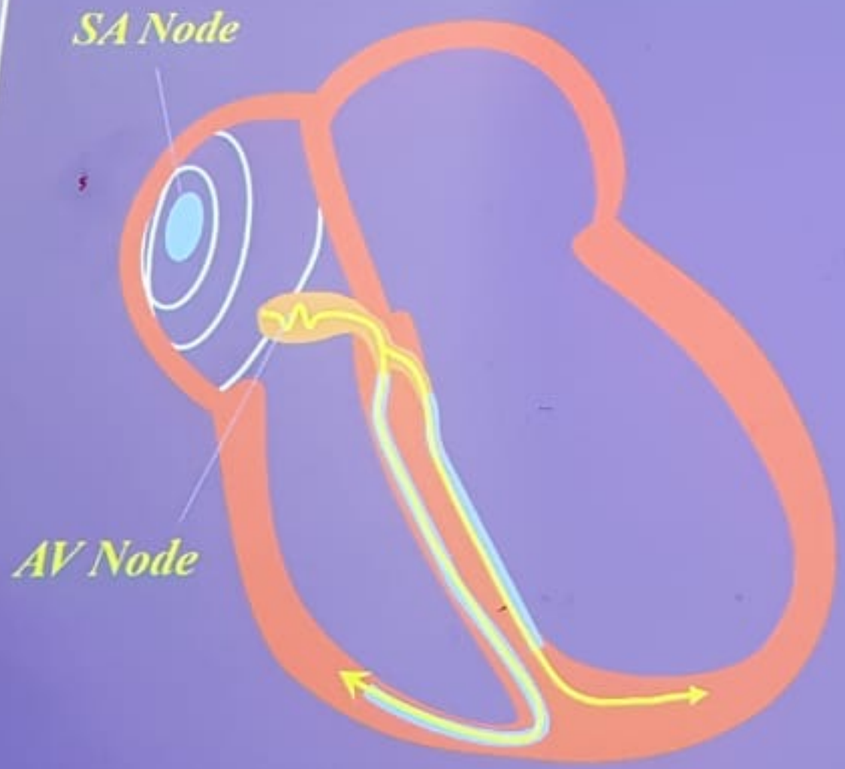
(atrial & ventricular) _____ responsible for pumping action of heart.

Specialized Conducting Tissue.

1-IMPULSE INITIATION
2-IMPULSE CONDUCTION

SA node (sinoatrial node),
AV node (atrioventricular), &
His – Purkinje System

Normal Conduction



- The impulse is initiated at the SA node and spreads from right to left atrium
- Slowing of conduction occurs at the AV node
- The right and left ventricle are simultaneously activated via the His Purkinje system

SA Node.

Impulse spontaneously formed----- Automatiaty.

Highest frequency of spontaneous discharge, 70 times / minute _____ so control the heart .

It is a pacemaker.

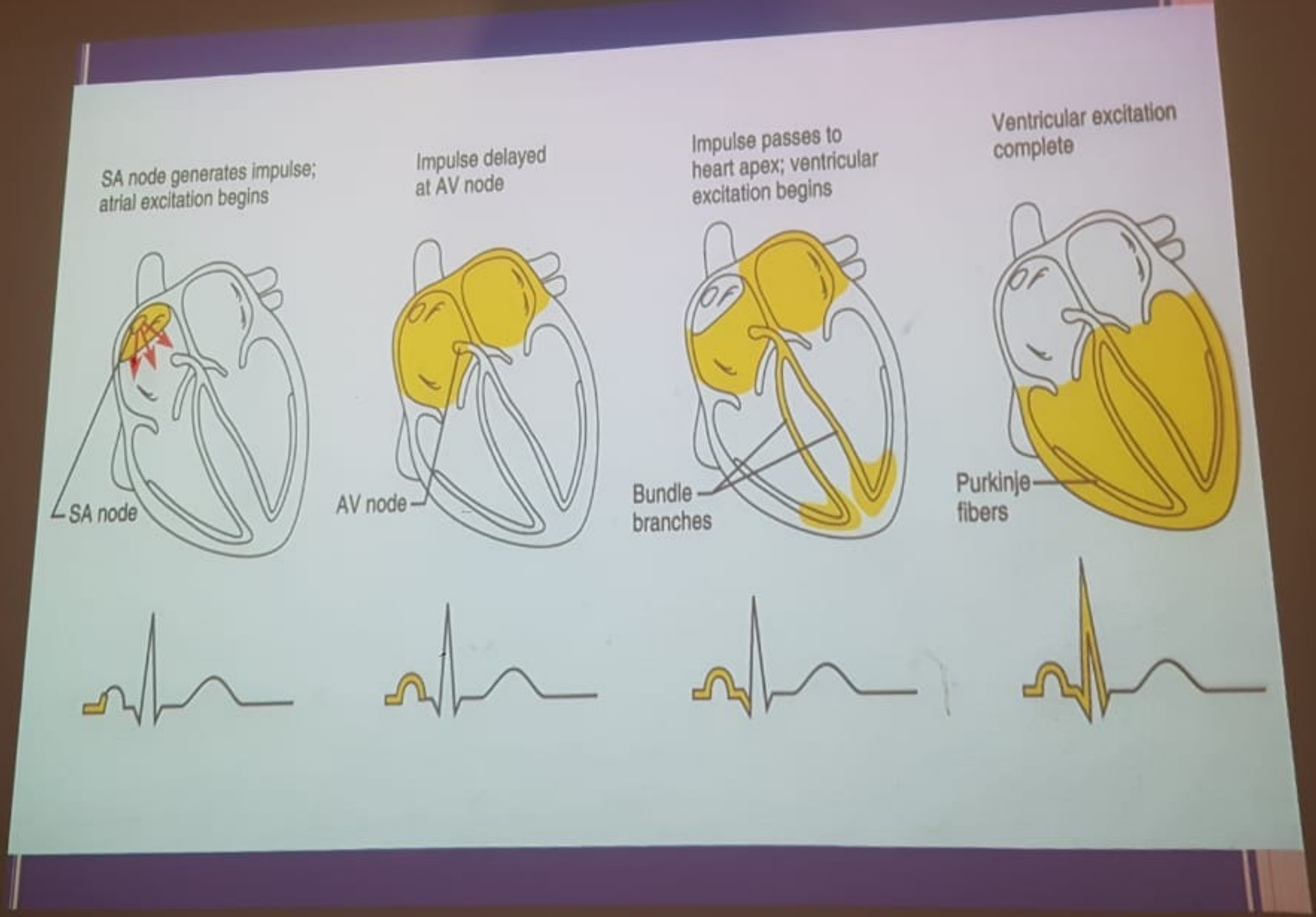
AV Node.

If SA node fails to function, next part that takes over the function is AV node _____ 45 discharges / minute.

A Site in His – Purkinje System.

Frequency 25 discharge / min.

Recording of Impulse generation & Conduction


SA node generates impulse; atrial excitation begins
SA node
Impulse delayed at AV node
AV node
Impulse passes to heart apex; ventricular excitation begins
Bundle branches
Ventricular excitation complete
Purkinje fibers

Arrhythmias or Dysrhythmias

(Defect of Heart Rate & Rhythm)

Altered **rate** of automatic discharge

or

Abnormality of the **mechanism** by which **Impulse is generated**

or

Abnormality in Conduction of impulses .

or

Both

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Both

Cardiac Dys or Arrhythmias.

Two types

1. Atrial arrhythmias
2. Ventricular arrhythmias

Atrial Arrhythmias

1. Arrhythmias of SA node Origin.
2. Atrial Pre mature or Extrasystole
3. Atrial Tacycardia
4. Atrial Flutter
5. Atrial Fibrilation

1. Arrhythmias of SA node Origin.

a)Sinus Bradycardia. b)Sinus tachycardia

c) sinus Arrhythmias

A) Sinus Bradycardia

Heart rate below 60 / min, may be as low as 35, but usually between 45 – 50 / min

1) Normally common in athletes & physically trained people.

2)Also manifests when ⬆ vagal tone e.g vomiting, fainting, vasovagal attack.

3)T/M with parasympathomimetics or sympatholytics (propranolol) hypothermia, Dec.pressure

b. Sinus Tachycardia.

Sinus initiated heart rate above 100 / min

_____ not exceed 160 / min in adults _____

With carotid massage.

⬇ slowly but gradually

May be seen in

1. Hereditary, during physical & mental stress.
2. Psychogenic
3. Hypotension, acute hemorrhage, chronic anemia, pulmonary embolism, & in fever.

4. Acute rheumatic fever & pericarditis
5. Organic heart disease ____ sinus tachycardia ____ early sign of heart failure.

c. Sinus Arrhythmias.

Common in children & youth.

Pulse rate slow & irregular rhythm.

2. **Atrial Premature Beats or Extrasystoles.**

The beats occur prematurely.

An **ectopic focus** develop in some portion of atria which discharge intermittently at variable intervals producing premature beats.

Re-entry mechanism may also responsible for this condition.

2. Atrial Tachycardia.

Atrial heart rate **above** 100 / min.

ECG shows **three or more** consecutive atrial premature beats.

3. Atrial Flutter.

Due to abnormal focus or group of foci atria beat very **rapidly** but **regular** rate.

ECG ____ Continuous regular activity that occur at a rate of **250 to 350** per minute .

The P wave ____ **identical** in spacing, size & contour, showing **saw teeth** appearance.

4. Atrial Fibrillation.

Due to **rapid irregular** heart action, **no coordination** between atrial muscle fibers, some muscle fibers contract while other relax.

The **contraction** is quite **incomplete** i.e. fibers only **fibrillate**.

Thus **atria** are only ineffective

e.g mitral stenosis, hyperthyroidism, ischemic heart disease, digitalis toxicity.

ECG ____ **absence** of " **P** "wave.

" F " waves occur usually at rates of 300 to 600 per minute and vary in amplitude and contour.

AV block results in the ventricles beating at a slower rate than atria.

Ventricular beats are weak , so they fail to produce pulse in the arteries.

Heart rate taken by feeling an artery will be less than that by listening over heart.

This is **called Pulse Deficit**.

In this resting state ____ interior of the cell is negative with respect to the exterior(+ ve) due to deposition of ions (Na+, K+, and Ca++) across its membrane i.e. it is polarized.

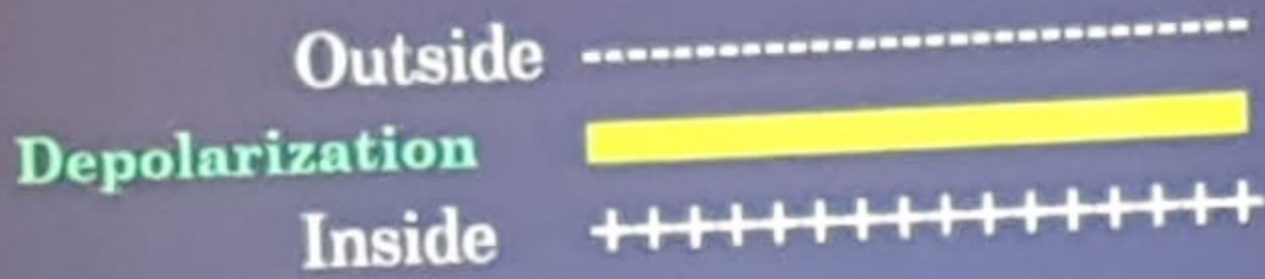
Physiological Aspect of Formation & propogation of Elec. Impulses (Ionic Movements Into & Out of Cardiac Cells)

All cells in the body show a **difference** in electrical voltage between their interior & exterior ____ membrane potential.

Phase "O" is a rapid depolarization of the cell membrane that is associated with a fast inflow of sodium ion through channels that are selectively permeable to these ions.

Phase 1 is a short initial period of rapid repolerization brought about mainly by an outflow of potassium ions.

When ionic changes occur ____ a rapid **redistribution of ions** ____ potential alters to positive inside (depolarization).



Then subsequent and flows of ions restore he resting potential (repolarization).

These ionic movements may be separated into **phases in cardiac AP**

Phase 2 is a period where there is a delay in repolarization caused by mainly a slow movement of Ca++ ions from the exterior into the cells through the channel that are selectively permeable to these ions.

Phase 3 is a second period of rapid repolarization during which K+ ions move out of the cell.

Phases of Myocardial Action Potential

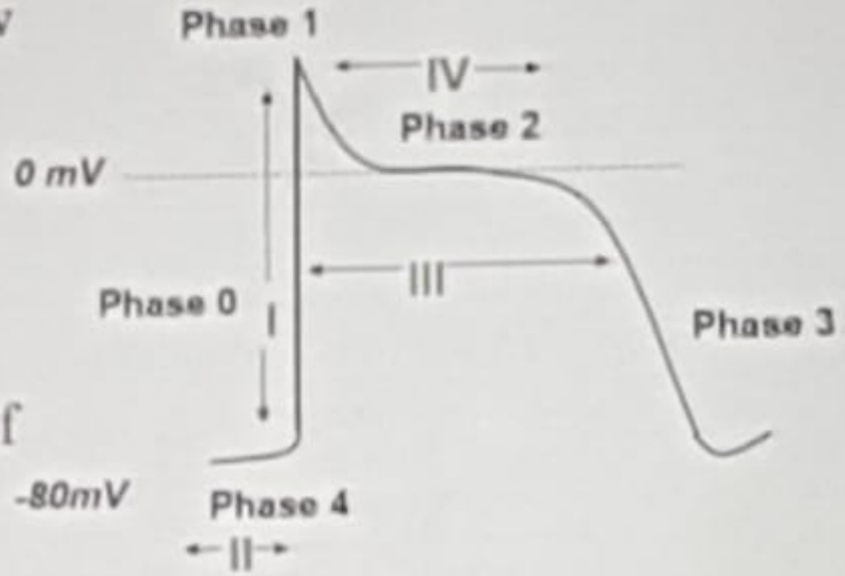
Phase 0
Depolarization;(Inflow Of Na+)

Phase 1
Early Repolarization;
(rapid outflow of K+)

Phase 2
Plateu phase;(Inflow of **Ca++)**

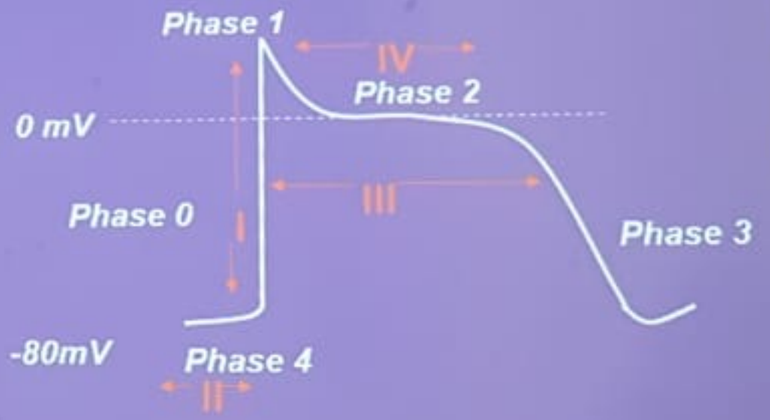
Phase 3
Rapid Repolarization;(K+ outflow)

Phase 4 (automaticity):
(Na+ outflow,K+ inflow,Ca++ outflow)



VAUGHAN WILLIAMS CLASSIFICATION OF ANTI-ARRHYTHMIC DRUGS

- **Class I**: block sodium channels
  - Ia (quinidine,) ↑AP
  - Ib (lignocaine) ↓AP
  - Ic (flecainide) ↔AP
- **Class II** ß-adrenoceptor antagonists (atenolol, sotalol)
- **Class III**: prolong action potential and prolong refractory period (suppress re-entrant rhythms) (amiodarone, sotalol)
- **Class IV**: Calcium channel antagonists. Impair impulse propagation in nodal and damaged areas (verapamil)

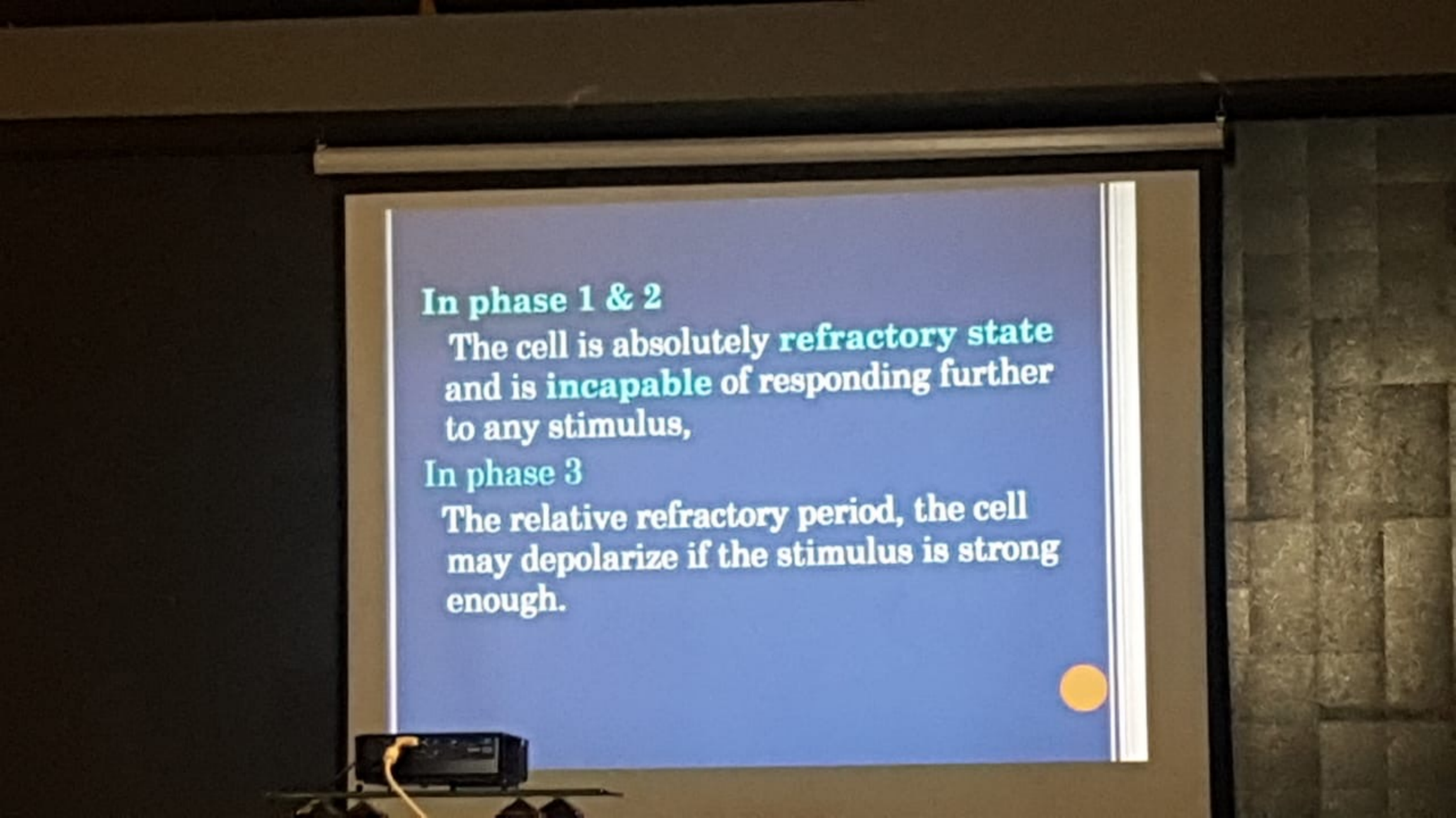


Classification of Drugs & Mode of Action

Therapeutically useful channel blocking drugs have a **high affinity for activated channels** (i.e. during phase 0) or inactivated channels i.e. during phase 2, but low affinity for rested channels.

Class 1 Na+ Channel Blockade.

These drugs **restrict the rapid inflow** of sodium during phase " **0** " .


In phase 1 & 2
The cell is absolutely refractory state and is incapable of responding further to any stimulus,
In phase 3
The relative refractory period, the cell may depolarize if the stimulus is strong enough.

Aims of the therapy of arrhythmias

- To reduce [illegible]
- [illegible]

The major mechanisms to accomplish these goals are

1. **Sodium Channel Blockers**
2. **Blockade of Sympathetic Autonomic Effects in the Heart**
3. **Prolongation of Effective Refractory Period**

Phase 4 is fully repolarized state during which K+ ions move back into and Na+ & Ca++ move out of the cell.

During this phase, the interior of the cells become gradually less negative until a potential is reached which allows the rapid repolarization (Phase 0) to occur and the cycle is repeated.

Characteristics of Antiarrhythmic Drugs

1. Antiarrhythmic drugs decrease the automaticities of ectopic pace maker more than that of the SA node.
2. They also reduce conduction and excitability.
3. They increase the refractory period to a greater extent in depolarized tissue than in normal polarized tissue.

USES Effective only in ventricular dys-rhythmias.

Class 1 C.

e.g. Flecainide, Propafenone,

- They act by **blocking the Na+ channel**
- They have negligible effect or no effect on action potential and refractoriness & dissociate from the channel with slow kinetics

USES -Effective for supra ventricular and ventricular dysrhythmias

Class ll.

e.g Sympatholytic especially, β-blockers,

Drugs include those that **reduce adrenergic activity in the heart,**

& thus slow the maximum rate of depolarization.

Another term for this property is **membrane stabilizing activity ”,** because they have local anesthetic effect as well.

. Class 1(Na+ Channel Blockers) ARE

Sub divided Class 1A,1B & 1C

Due to the reasons-----they differ from kinetic properties although the basic mechanism is the same(Na+ channel blocked)

SO

Sub classification reflects on APD(action potential Duration) & kinetics of Na+ channel

Class 1 A.

e.g Quinidine, procainamide, disopyramide

- They block the Na+ channel.
- These drugs **lengthen action potential** duration(APD), refractoriness & dissociate from the channel with intermediate kinetics

USES.. Effective for supra ventricular & ventricular dysrhythmias.

Class 1 B.

e.g. lignocaine, mexiletine, phenytoin etc.

- They block the Na+ channel.
- The drugs **shorten action potential** duration and refractoriness & dissociate from the channel with rapid kinetics-

How Antiarrhythmic Effect is produced(As APD dec.)

- Though APD decreased but this increases diastole & Extends the time for recovery

i.e. they **reduce** the **sympathetic tone** in the heart, reduce automatic discharge (phase 4) and protect against adrenergically stimulated ectopic pacemaker.

Class III.

- e.g. Amiodarone, Bretylium

- Drugs that **prolong effective refractory period** by prolonging action potential (no effect on sodium inflow in phase 0).

Prolongation of cellular refractoriness (phase 1, 2, & 3) **beyond a critical** point may prevent a reentry circuit being completed.

Class V (Miscellaneous):

Adenosine
Magnesium sulphate
Digoxin
Ranolazine
Atropine

2. Catheter Ablation:

3. Implantable Cardioversion Defibrillator (ICD):

as it has antimuscarinic action which will **enhance AV conduction** and heart rate may increase.

Toxicity.

Cardiac.

a. Due to antimuscarinic effect in heart, vagal effects are inhibited ____ **sinus rate** and atrioventricular conduction.

So it should not be given alone.

Give a drug which **slows atrioventricular conduction** e.g. a Ca++ blocker or β- blocker or digitalis then give quinidine.

Quinidine Syncope ___ 1-5 % characterized recurrent light headedness and episodes of fainting.

These symptoms are a result of torsade de pointes i.e. **serious ventricular dysrhythmias** associated with electrocardiographic QT prolongation.

Extra Cardiac Effects.

1. *GIT* ___ diarrhea, nausea, vomiting ____ *1/3 or half of the patients.*
2. *Cinchonism* ____ headache, dizziness, *tinnitis*

3. Rarely rashes, angioneurotic edema, fever, hepatitis & thrombocytopenia.

4. Can ⬆ digoxin plasma levels and precipitate digitalis toxicity in patients taking digoxin.

Pharmacokinetics.

Given orally, rapidly absorbs from GIT.

80 % bound to plasma proteins.

Metabolized in liver ____ 20 % excreted unchanged in urine.

Half life is 6 hours.

Procainamide

Half life ____ 3 hrs.

Cardiac Effects.

Similar to quinidine.

Somewhat less effective in suppressing abnormal ectopic pacemaker activty, but more effective in blocking NA+ channel in depolarized cells.

Extra Cardiac Effects.

Ganglion blocking properties ____ ⬇

peripheral vascular resistance ____

hypotension, especially with I/V use.

Toxicity.

Cardiac.

Same as quinidine ____ hypotension, cardiac failure (-ve inotrpic effect occur and dysrhythmias may be included e.g. torsade de pointes)

Extra Cardiac.

1. In long term use (in 80% patients) ____ develop abnormal **antinuclear (ANA) factor titers** in the blood 30 % proceed to systemic lupus erythematous like syndrome ____ consisting of arthralgia

and arthritis.

These symptoms are **dose related** and is more common in **slow accetylators**and usually regress when drug is withdrawn.

2. Some patients ____ pleuritis, pericarditis, parenchymal pulmonary disease.

Other effects include nausea, diarrhea, rash, hepatitis, &agranulocytosis (approximately 0.2 %)

SLE less common in these patients.

Procainamide is eliminated by hepatic metabolism to NAPA and by renal elimination.

Dose.

If a rapid procainamide effect ____ I/V loading dose up to 12 mg/kg at a rate of 0.3 mg/kg/min ____ followed by maintenance dose ___ 2.5 mg/min.

Uses.

1. Used in atrial and ventricular arrhythmias.

Pharmacokinetics.

Safely can be given I / V or I / M.

Well absorbed **orally**.

Major metabolite is **N-acetylprocainamide** (NAPA).

⬆ accumulation ____ torsade de pointes during therapy, especially in patients with renal failure.

Some patients **rapidly acetylate** procainamide and develop high levels of NAPA.

2. It is a drug of **second choice** after lidocaine for the treatment of sustained ventricular arrhythmias associated with acute myocardial infarction.

Disopyramide

Effects similar to those of quinidine but **antimuscarinic actions** are more than quinidine.

About **50 %** of the dose is **eliminated in the urine** by glomerular filtration and the remainder is metabolized.

Toxicity.

Cardiac.

- Same as quinidine.
- In addition, disopyramide possesses negative inotropic effects, more dangerous in patients with left ventricular failure.
- So **should not be** used in patients with congestive cardiac failure.

Extra Cardiac.

Antimuscarinic, effects (atropine-like)

Toxicity.

Cardiac.

- Same as quinidine.
- In addition, disopyramide possesses negative inotropic effects, more dangerous in patients with left ventricular failure.
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Extra Cardiac.

Antimuscarinic, effects (atropine-like)

Toxicity.

Cardiac.

Least cardiotoxic.

Some times can **exacerbate ventricular arrhythmias** in less than 10 % of patients.

In 1 % of patents with acute myocardial infarction, lidocaine patients should stand still.

In large doses ___ patients with congestive cardiac failure ___ hypotension.