ARRHYTHMIA

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CARDIAC ARRHYTHMIA

- Cardiac arrhythmia/Cardiac dysrhythmia/Irregular heart beat is a group of condition in which the heart beat is irregular, too fast or too slow.

- Bradycardia: Heart beat is too slow i.e. <60 beats/min
- Tachycardia: Heart beat is too fast i.e. >100 beats/min

Etiology:

- Emotional stress
- Myocardial ischaemia or infarction
- Mechanical injury
- Chronic obstructive pulmonary disease(COPD)
- Electrolyte and pH imbalance
- Neutrogenic and drug influences

Pathophysiology:

Cardiac arrhythmias are deviations from the normal pattern of cardiac rhythm.

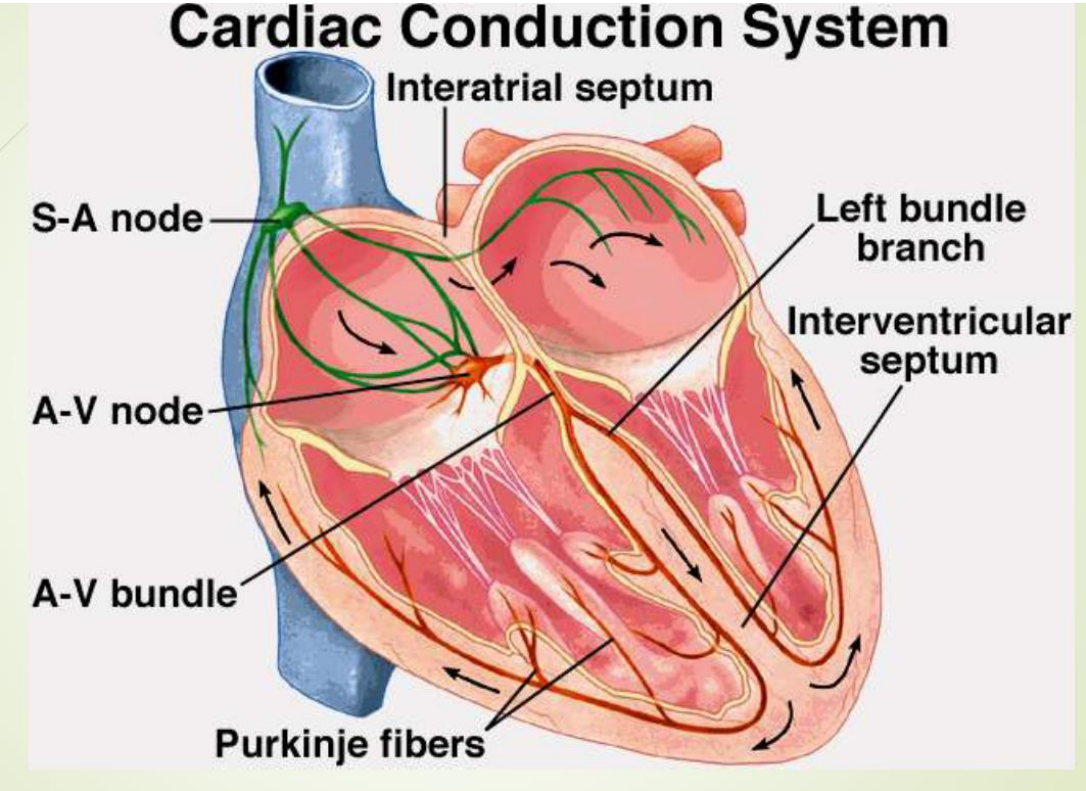
Theses includes

- **Abnormalities in Impulse formation**(such as heart rate, its rhythm or site of impulse).
- **Disturbances in impulse conduction** (which disrupt the normal sequence of atrial and ventricular depolarization).

Pathophysiology:

Impulse formation & conduction

- SA node----Internodal tracts-----AV node-----Bundle of His-----Purkinje fibres----Ventricles



Pathophysiology:

Myocardial Action potential:

For cardiac contractions to occur, cardiac cells must depolarise and then repolarise through alterations in their ionic permeabilities (mainly Na^+, K^+, Ca^{2+}) across the cell membrane.

The action potential can be divided into phases:

Phase:0 Rapid depolarisation

Phase:1 Early/Partial repolarisation

Phase:2 Plateau

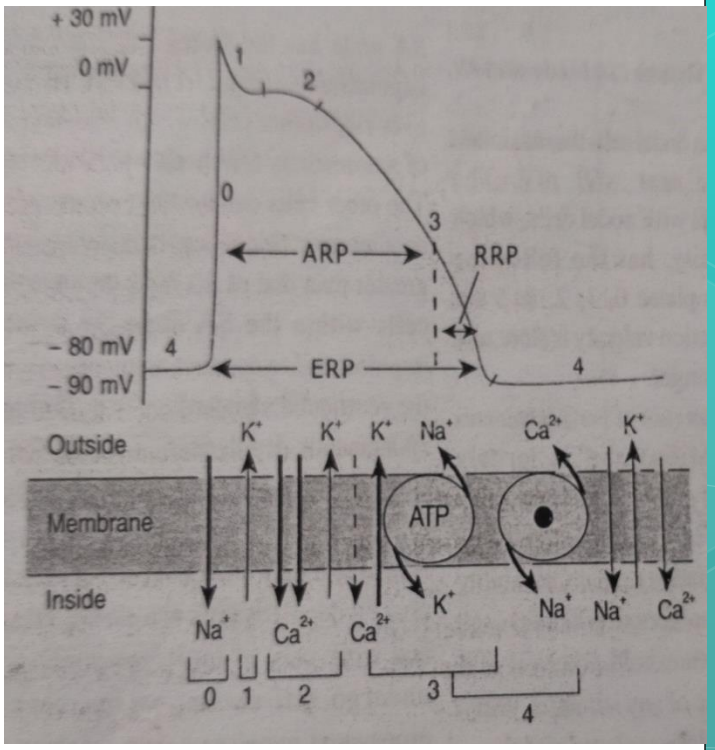
Phase:3 Rapid repolarisation

Phase:4 Diastolic depolarisation

Pathophysiology:

Phase:0 Rapid depolarization

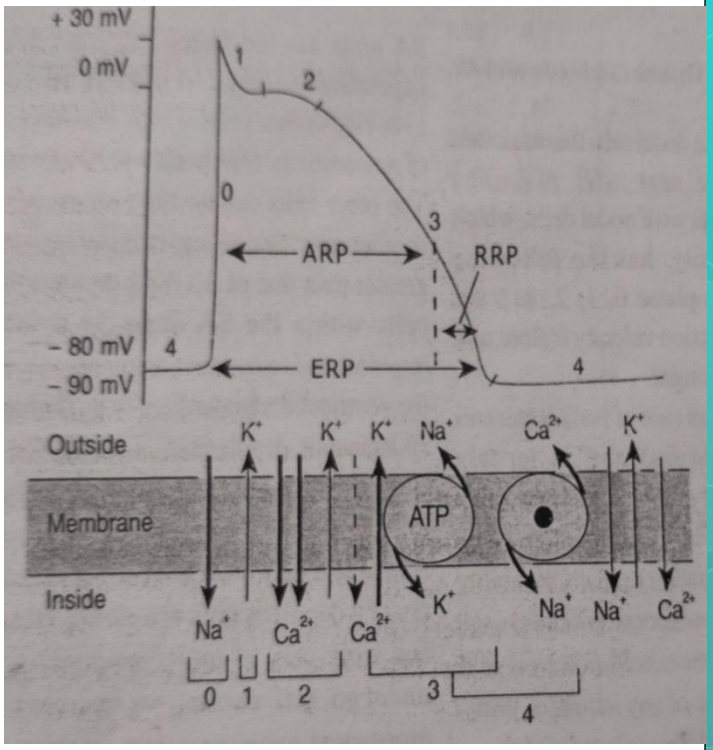
- This results when Na^+ ions enter the cell through fast inward Na^+ channels. The cell membrane's electrical charge changes from negative (-90mV) to less negative (-80mV) and finally to positive(+30 mV).
- The upstroke depolarisation ends as Na^+ inflow ceases. At this stage, the Na^+ channels become inactivated, i.e., they cannot be recruited to participate in generating a subsequent AP for a specified interval.



Pathophysiology:

Phase:1 Early/Partial repolarisation

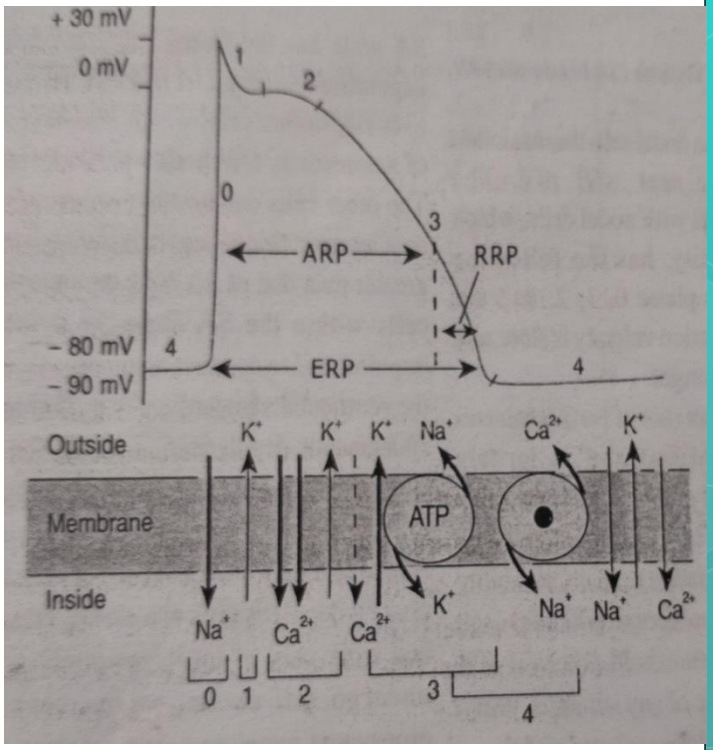
- ✓ At this stage, as voltage-gated Na^+ channels close, potassium channels rapidly open.
- ✓ The cell therefore rapidly repolarizes (membrane potential returns toward 0mV).
- ✓ This produces a spike and dome configuration of AP.



Pathophysiology:

Phase:2 Plateau

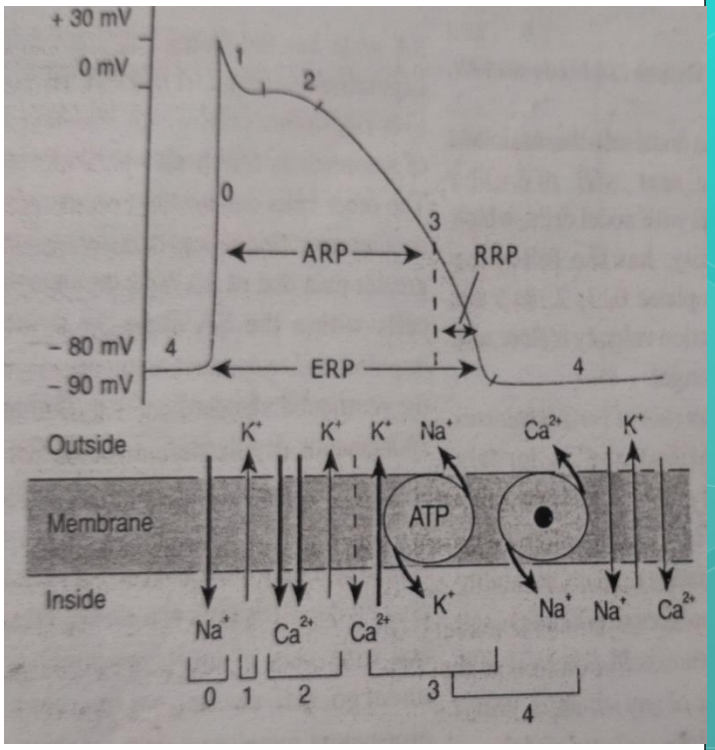
- ✓ In this phase, voltage-sensitive L-type Ca^{2+} channels open, causing slow inward current.
- ✓ This is then balanced by the slow outward K^{+} current, i.e., depolarization=repolarization($Ca^{2+} = K^{+}$).
- ✓ The cell membrane's electrical activity stabilises temporarily and the AP reaches a plateau.
- ✓ This is preceded by a notch at the beginning of the plateau phase.



Pathophysiology:

Phase:3 Rapid Repolarization

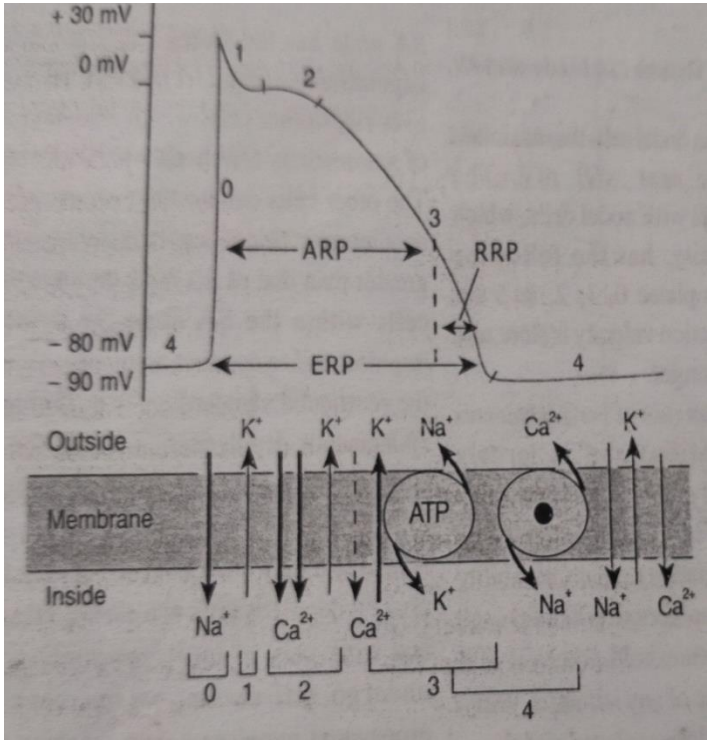
- At this phase Ca^{2+} channels close, and K^{+} channels open.
- K^{+} are pumped out of the cell as the cell rapidly repolarises and resumes its initial negativity (-80mV approximately).
- From phase 0 to phase 3 there has been a gain of Na^{+} and loss of K^{+}
- This imbalance is now corrected by Na^{+} K^{+} ATPase pump which restores the intracellular as well as extracellular positive ion concentrations to their pre-excitation levels.



Pathophysiology:

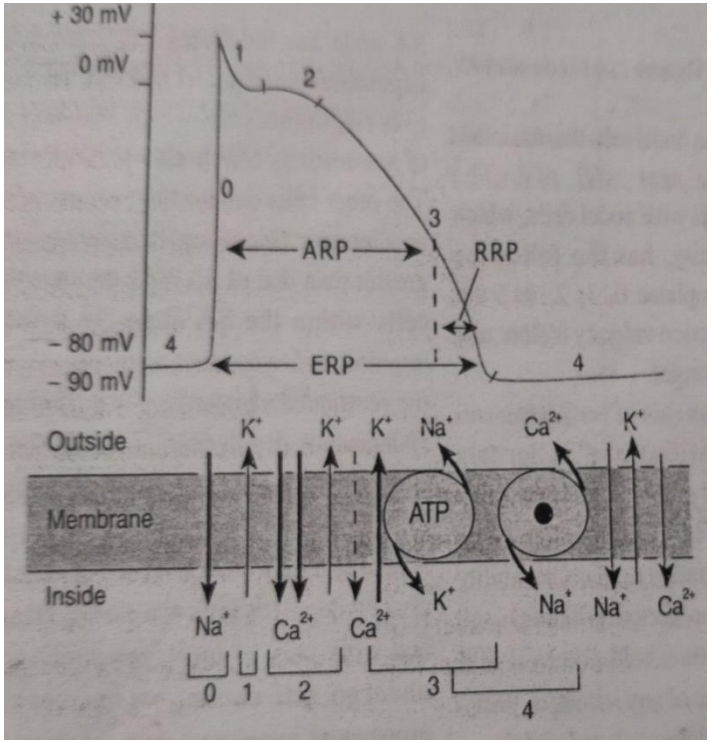
Phase:4 Diastolic depolarization

- In phase 4, the ion balance is returned to normal by Na^+ K^+ ATPase pump, outward K^+ , Na^+ Ca^{2+} exchanger which removes the remaining Ca^{2+} from the cell.
- The resting membrane potential of ventricular myocyte becomes stable and is held at -90mV.
- It is during phase 4 that the Na^+ channels involved in atrial and ventricular myocyte depolarization recover completely from inactivation and become available for action again.



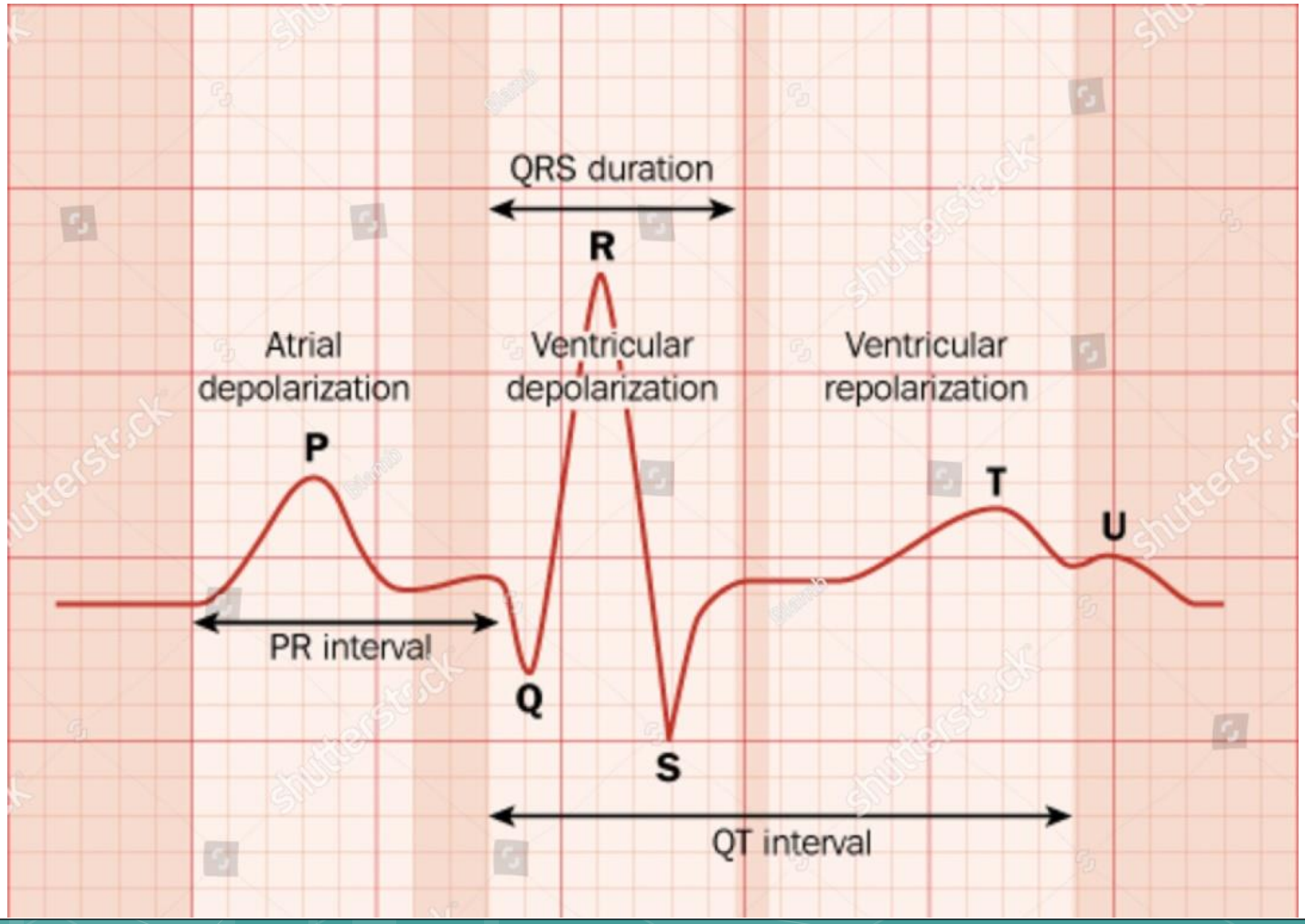
Pathophysiology:

- From phase 0 to mid phase 3, the cell does not respond to any stimulus. This period is called an **Absolute Refractory Period(ARP).**
- The cell's ability to respond to stimulus increases as repolarization continues. Hence from midphase 3 to the end of phase 3, the cell can respond to strong stimulus. This is called **Relative Refractory Period(RRP).**

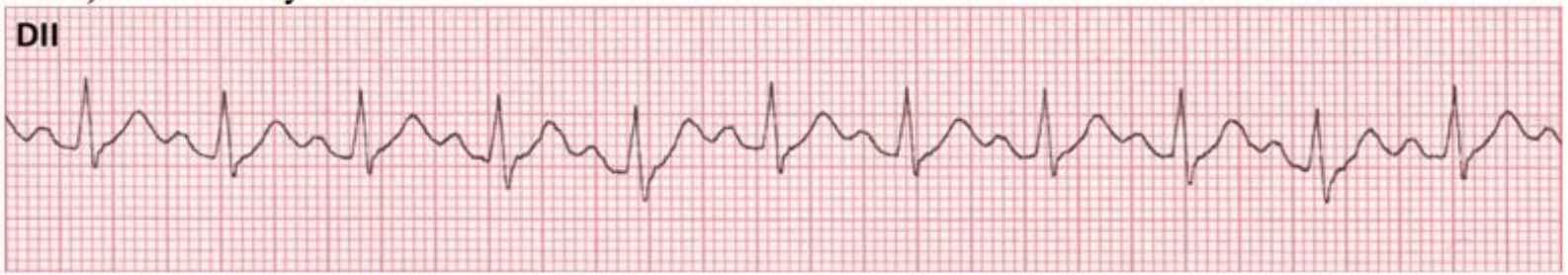


ARP + RRP = **ERP(Effective Refractory Period)**

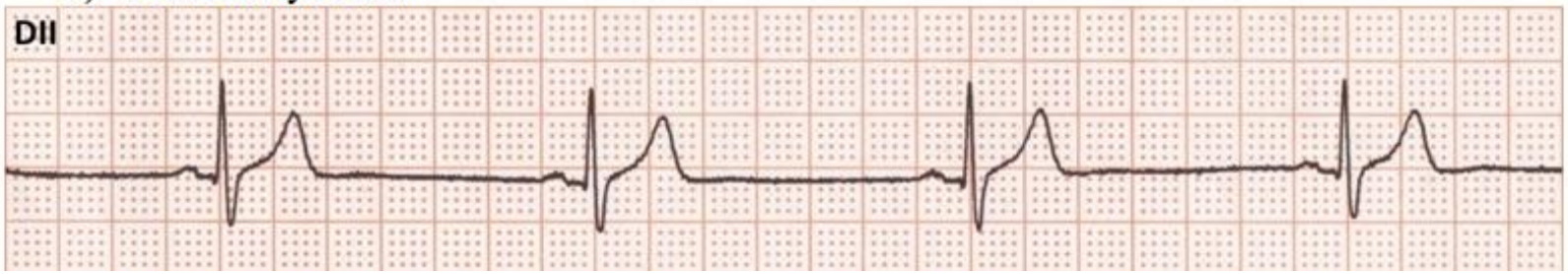
Depolarisation & Repolarisation waves in ECG



A) Sinus tachycardia



B) Sinus bradycardia



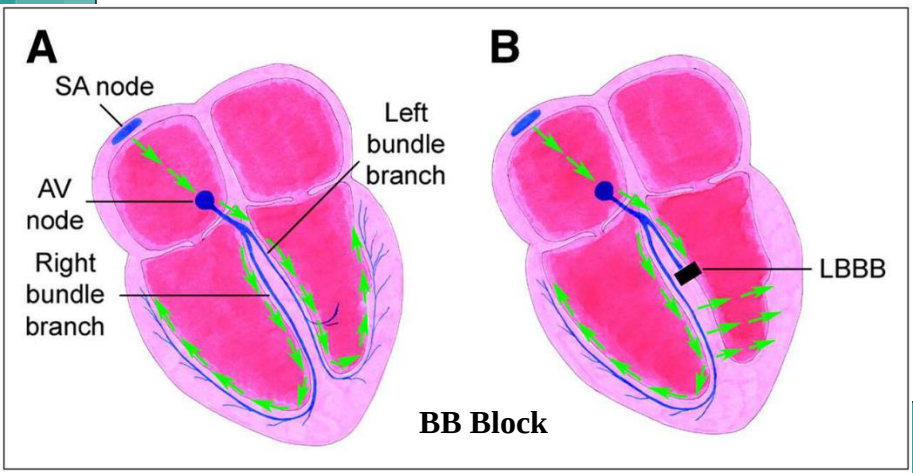
Brady-arrhythmia/Bradycardia

1.) Sinus bradycardia:

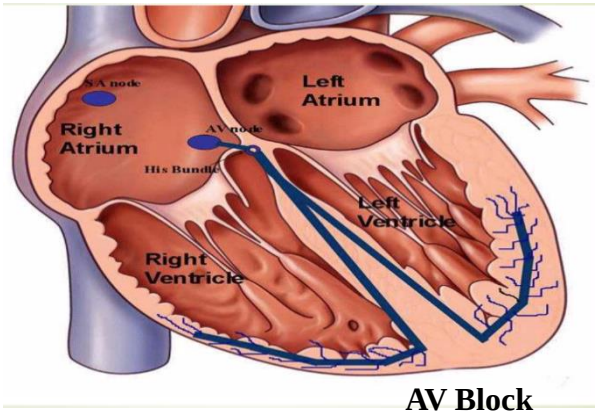
- ✓ It is due to increased parasympathetic and decreased sympathetic stimulation.
- ✓ If SA node rate ↓ enough, AV node & purkinje fibres initiate impulses called **escape beats.**

2.) AV Block, Bundle of His(BB) Block:

Delayed propagation of impulse due to electrically unexcitable tissue(from ischaemia, fibrosis, inflammation, drugs)



BB Block



AV Block

Tachy-arrhythmia/Tachycardia

1.) Sinus tachycardia:

- ✓ It is due to increased sympathetic and decreased parasympathetic stimulation.

2.) AV tachycardia:

If AV node and purkinje fibres intrinsically depolarize faster than SA node produce **ectopic beats**.

3.) Atrial Flutter:

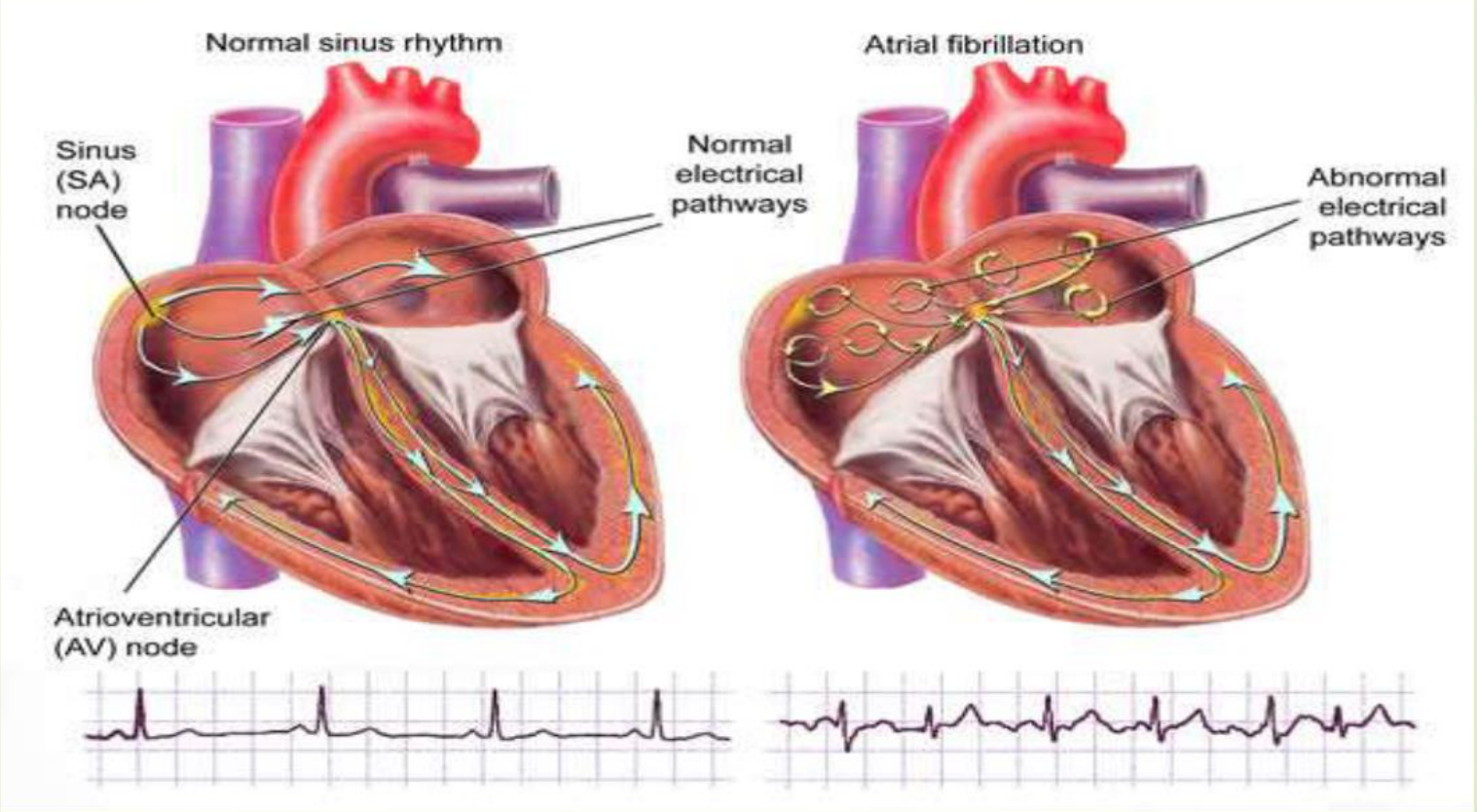
In this condition, Atria beat regularly, but faster than usual.

4.) Atrial Fibrillation:

In this condition, Atria beat irregularly.

……Arrhythmia

- Atrial Fibrillation

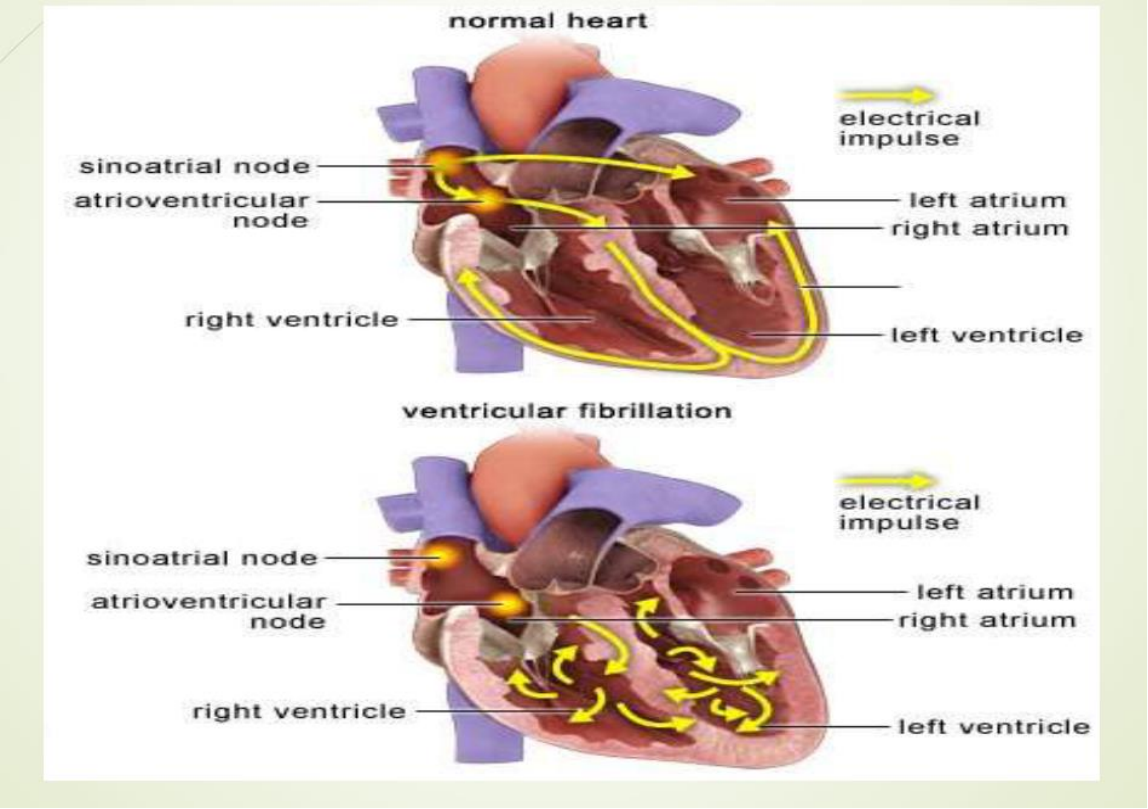


Tachy-arrhythmia/Tachycardia

5.) Ventricular Flutter: In this condition, ventricles beat regularly, but faster than usual.

6.) Ventricular Fibrillation:

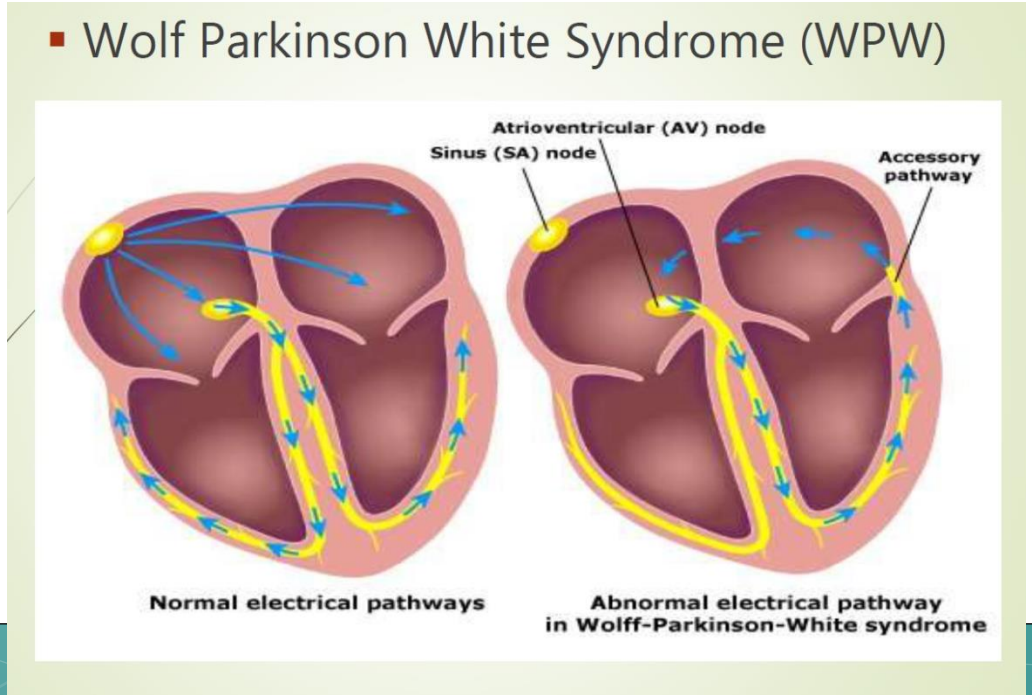
In this condition, ventricles beat irregularly.



Tachy-arrhythmia/Tachycardia

7.) WPW:

- ✓ It is caused by the presence of an abnormal accessory electrical conduction pathway between the atria and the ventricles.
- ✓ Electrical Signals through abnormal pathway stimulate the ventricles to contract prematurely
- ✓ A unique type of supraventricular tachycardia referred to as an ”atrioventricular reciprocating tachycardia”.



Symptoms:

- Dyspnea
- Hypotension
- Dizziness, syncope
- Chest pain
- Altered level of consciousness
- Reduced urinary output
- Skin pallor or cyanosis

Complications:

- Sudden cardiac death
- Myocardial infarction
- Heart failure
- Thromboembolism

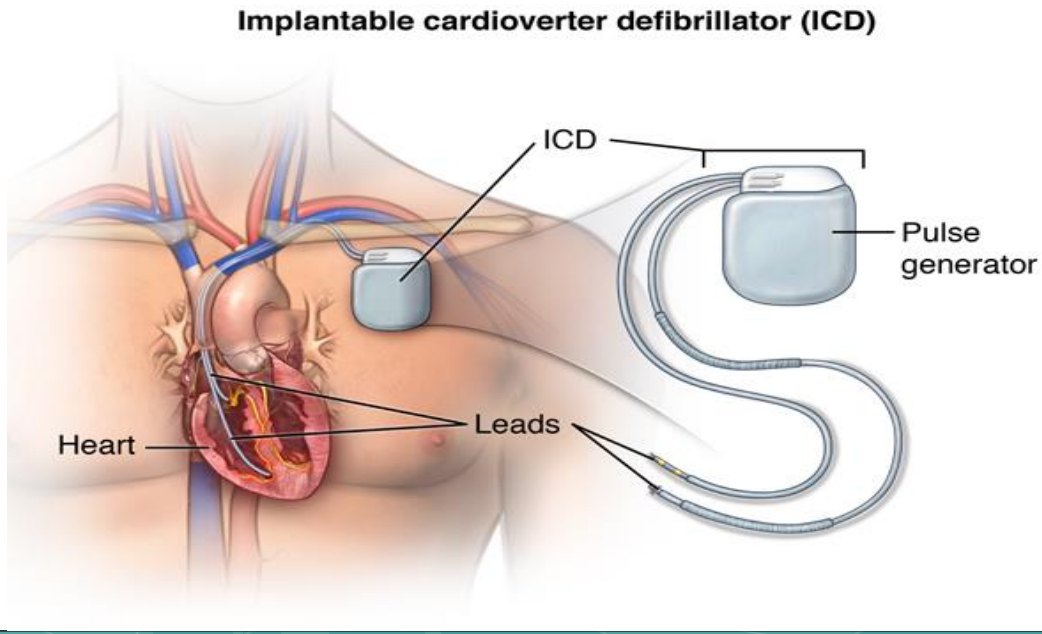
Diagnosis:

- Electrocardiography
- Laboratory testing may reveal electrolyte abnormalities, acid-base abnormalities, or drug toxicities that may cause arrhythmias.
- Holter monitoring detects arrhythmias and effectiveness of drug therapy during a patient's daily activities.

Treatment :

- **Non-Pharmacological Treatment:** Lifestyle changes
- **Pharmacological Treatment**: Anti-Arrhythmic drugs
- **Surgical Methods:**

An **implantable cardioverter defibrillator**(ICD) is a small device that's placed in the chest or abdomen. Doctors use the device to help treat irregular heartbeats called arrhythmias



Anti-Arrhythmic drugs

Anti-Arrhythmic drugs:

These drugs are used to restore normal sinus rhythm and conduction by

- ✓ Decrease conduction velocity
- ✓ Change the duration of the effective refractory period (ERP)
- ✓ Suppress abnormal automaticity

Classification of Anti-Arrhythmic drugs

Class-I Sodium channel blockers

- IA-------Quinidine, Procainamide, Disopyramide
- IB------ Lignocaine, Phenytoin, Mexiletine
- IC-----Flecainide, Propafenone

Class-II β blockers

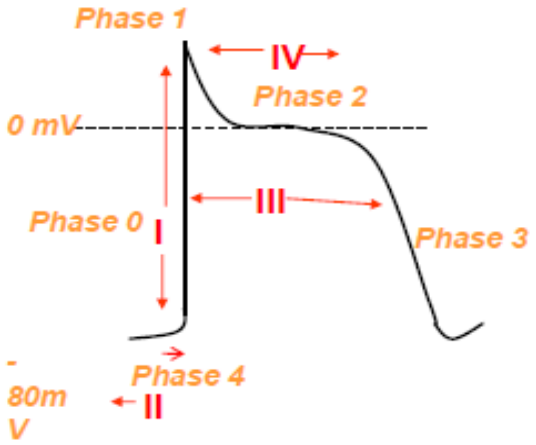
- Propranolol, Acebutolol, Esmolol

Class-III Potassium channel blockers

- Amiodarone, Bretylium, Sotalol

Class-IV Calcium channel blockers

- Verapamil, Diltiazem



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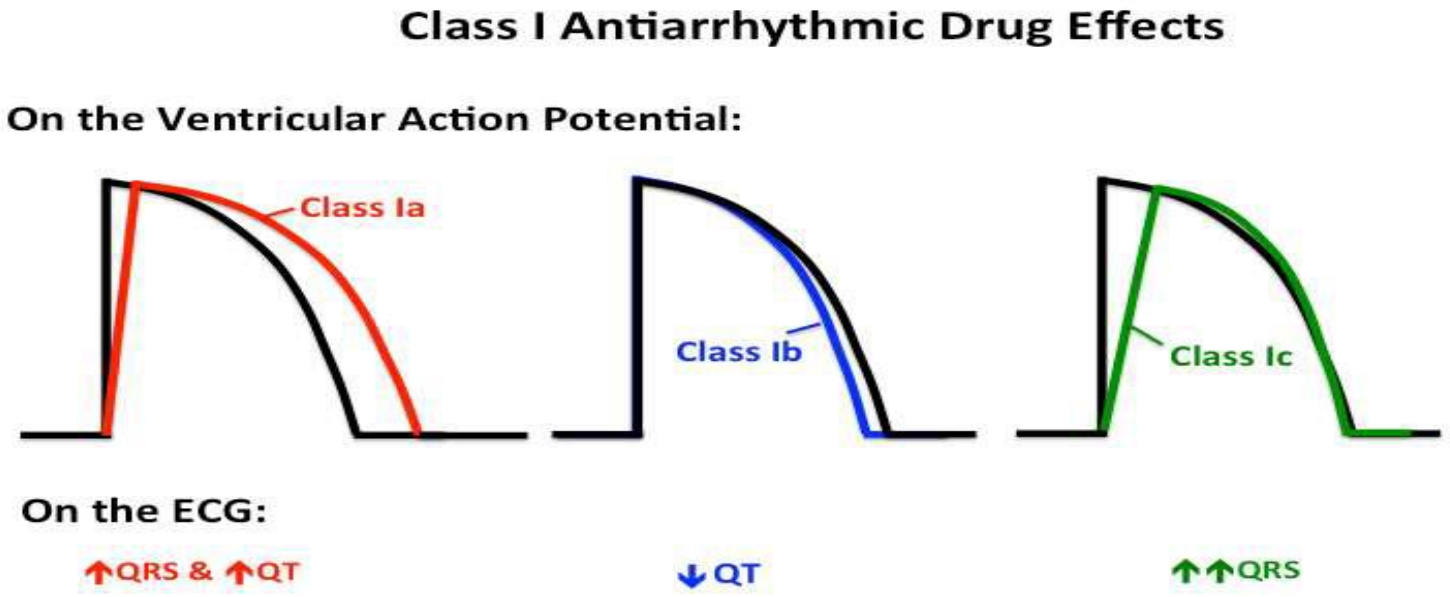


Mechanism of Action:

- Bind to and block Na+ channels
- Act on initial rapid depolarisation (slowing effect)
- Local Anaesthetic (higher concentration): block nerve conduction
- Do not alter resting membrane potential (Membrane Stabilisers)

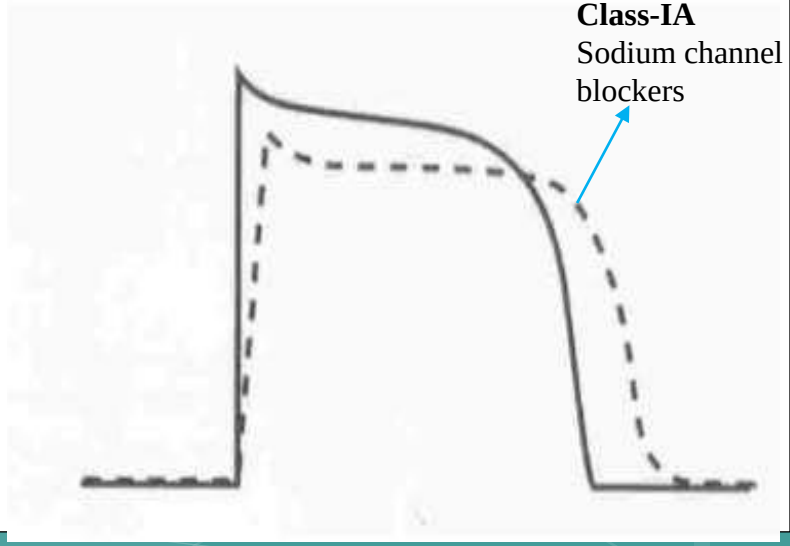
Class-I Sodium channel blockers

Ia	Ib	Ic
Moderate Na channel blockade	Mild Na channel blockade	Marked Na channel blockade
Slow rate of rise of Phase 0	Limited effect on Phase 0	Markedly reduces rate of rise of phase 0
Prolong refractoriness by blocking several types of K channels	Little effect on refractoriness as there is minimal effect on K channels	Prolong refractoriness by blocking delayed rectifier K channels
Lengthen APD & repolarization	Shorten APD & repolarization	No effect on APD & repolarization
Prolong PR, QRS	QT unaltered or slightly shortened	Markedly prolong PR & QRS

Class-IA Sodium channel blockers

IA-------Quinidine, Procainamide, Disopyramide

- Slowing the rate of rise in phase 0
- They prolong action potential & ERP
- ↓ the slope of Phase 4 spontaneous depolarization
- ↑ QRS & QT interval



Quinidine

Mechanism of action:

- Quinidine binds to open and inactivated sodium channels and prevents sodium influx, slowing the rapid upstroke during phase o.

- It also decreases the slope of phase 4 spontaneous depolarization and inhibits potassium channels.

Quinidine

Adverse effects:

- Diarrhoea
- “Cinchonism” – tinnitus
- Vertigo
- Headache
- Nausea
- Blurred vision

Contraindication:

AV block, QT prolongation- Torsades de pointes, Digoxin, enzyme Inducer, Myasthenia gravis

Quinidine

Drug interactions:

- Quinidine can interact the plasma concentration of digoxin, which may in turn lead to signs and symptoms of digitalis toxicity.
- Cimetidine increases hepatic metabolism of quinidine

Uses:

- Ventricular tachyarrhythmias.

Procainamide

- Procaine derivative, quinidine like action

Mechanism of action:

- Procainamide binds to open and inactivated Na+ channels and prevents sodium influx, slowing the rapid upstroke during phase 0

Adverse effects:

- Hypotension
- Hypersensitivity reaction

Procainamide

Drug interactions:

- Cimetidine inhibits the metabolism of procainamide

Contraindication:

- Hypersensitivity
- Bronchial asthma

Uses:

- Premature atrial contractions
- Paroxysmal atrial tachycardia

Disopyramide

Mechanism of action:

- Disopyramide produces a negative inotropic effects that is greater than weak effect exerted by quinidine and procainamide, and unlike the latter drugs, disopyramide causes peripheral vasoconstriction.

Adverse effects:

- Myocardial depression
- Urinary retention
- Constipation

Disopyramide

Contraindication:

- CHF

Drug interactions:

- In the presence of phenytoin, the metabolism of disopyramide is increased and the accumulation of its metabolite is also increased, there by increasing the probability of anticholinergic properties.

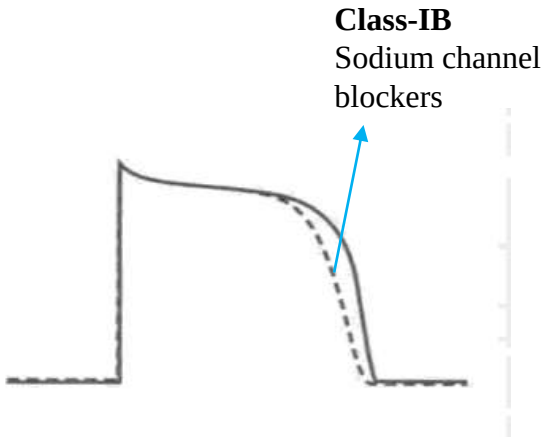
Uses:

- Ventricular tachycardia
- AF & AFI

Class-IB Sodium channel blockers

IB-------Lignocaine, Phenytoin, Mexiletine

- Block sodium channels also shorten repolarization
- They shorten Phase 3 repolarization
- ↓ the duration of the cardiac action potential
- Prolong phase 4



Lignocaine/Lidocaine

Mechanism of action:

It shorten phase 3 repolarization and decreases the duration of action potential

Adverse effects:

- Drowsiness
- Slurred speech
- Confusion and convulsions

Lignocaine/Lidocaine

Contraindication:

- Lidocaine is contraindicated in the presence of second and third degree heart block, since it may increase the degree of block and can abolish the idioventricular Pacemaker responsible for maintaining the cardiac rhythm.

Drug interactions:

- Propranolol increases its toxicity.
- The myocardial depressant effect of lidocaine is enhanced by phenytoin administration.

Uses:

- Ventricular arrhythmia

Phenytoin

Mechanism of action:

- Phenytoin was originally introduced for the control of convulsive disorders but now also been shown to be effective in the treatment of cardiac arrythmias.

Adverse effects:

- Respiratory arrest
- Hypotension

Contraindication:

- Severe bradycardia
- Severe heart failure
- AF & AFI

Phenytoin

Drug interactions:

- Plasma phenytoin concentrations are increased in the presence of chloramphenicol, disulfiram, and isoniazid, since the later drugs inhibit the hepatic metabolism of phenytoin.

Uses:

- Digitalis induced ventricular arrhythmia in children

Mexiletine

Mechanism of action:

- It is a local anaesthetic and an active antiarrhythmic by the oral route; chemically and pharmacologically similar to lidocaine.

Adverse effects:

- Tremor
- Hypotension
- Bradycardia

Contraindication:

- Cardiogenic shock
- Second or third-degree heart block

Mexiletine

Drug interactions:

- When mexiletine is administered with phenytoin or rifampin, since these drugs stimulate the hepatic metabolism of mexiletine, reducing its plasma concentration.

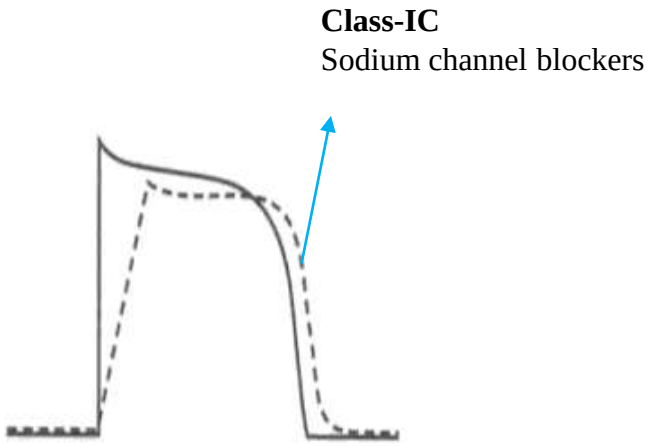
Uses:

- VA
- Congenital long QT syndrome

Class-IC Sodium channel blockers

IC-------Flecainide, Propafenone

- ***markedly slow Phase 0*** depolarization
- **minor effects on the duration of action potential and ERP**



Flecainide

Adverse effects:

- Torsades de point
- Visual disturbances & headache
- Digoxin toxicity

Contraindication:

- Cardiogenic shock

Uses:

- Ventricular arrhythmia

Propafenone

- Structural similarities with propranolol

Contraindication:

- Heart failure

Adverse effects:

- Metallic taste & constipation

Uses:

- VT & supra ventricular arrhythmias.

Class-II β blockers

Propranolol, Acebutolol, Esmolol

- **β**-receptor stimulation:
  - ↑ automaticity,
  - ↑ AV conduction velocity,
  - ↓ refractory period
- **β**-adrenergic blockers competitively block catecholamine induced stimulation of cardiac receptors

Class-II β blockers

- 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

Propranolol

Mechanism of action:

- Propranolol decreases the slope of phase 4 depolarization and other ectopic foci.
- Prolong the ERP of A-V node.

Adverse effects:

- Hypoglycemia (infants)
- Asthma
- Bronchospasm

Contraindication:

- Asthma
- Bradycardia
- Severe CHF

Uses:

- AF
- Digitalis-induced arrhythmias

Acebutolol

- Acebutolol is a cardioselective β1-adrenoreceptor blocking agent that also has some minor membrane stabilizing effect on the action potential.

Mechanism of action

- Acebutolol reduces blood pressure in patients with essential hypotension primarily through its negative inotropic and chronotropic effects.

Adverse effects:

- Bradycardia
- GI upset

Contraindication:

- Cardiogenic shock
- Severe bradycardia

Uses:

- VA
- Angina pectoris

Esmolol

- Esmolol is a short-acting β1-selective adrenoreceptor blocking agent.
- It doesn't posses membrane-stabilizing activity.

Adverse effects:

- Hypotension
- Nausea
- Headache
- Dyspnea

Contraindication:

- Asthma
- Sinus bradycardia
- A-V block
- Severe CHF

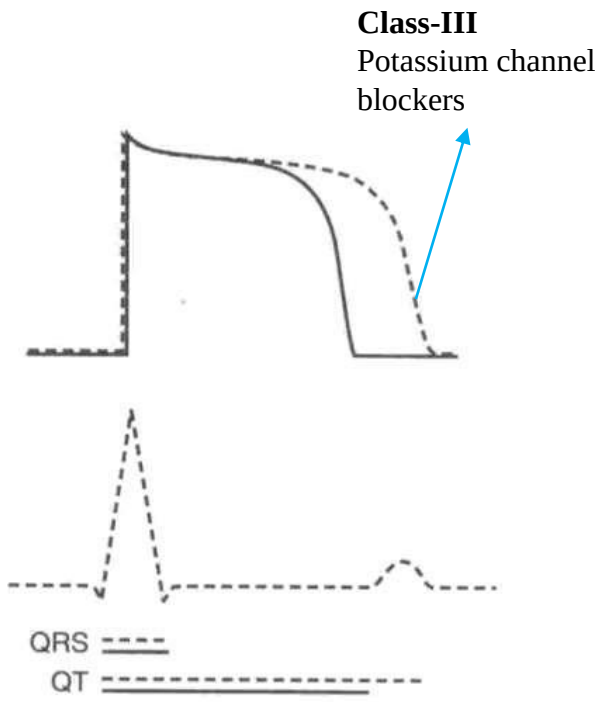
Uses:

Supraventricular tachyarrhythmias

Class-III Potassium channel blockers

Amiodarone, Bretylium, Sotalol

- Prolong AP / ERP without affecting phase 0 / 4
- Prolong QT & PR



Amiodarone

- Long acting and highly lipophillic and Iodine containing compound

Mechanism of action: (Multiple actions)

- Prolongs APD by blocking K+ channels
- blocks inactivated sodium channels
- β blocking action , Blocks Ca^{2+} channels
- ↓ Conduction, ↓ectopic automaticity

Adverse effects:

- Cardiac: heart block , QT prolongation, bradycardia, cardiac failure, hypotension
- Pulmonary: pneumonitis leading to pulmonary fibrosis
- Bluish discoloration of skin, corneal microdeposits
- GIT disturbances, hepatotoxicity
- Blocks peripheral conversion of T4 to T3 can cause hypothyroidism or hyperthyroidism

Uses:

- VF, VT & AF

Newer class III

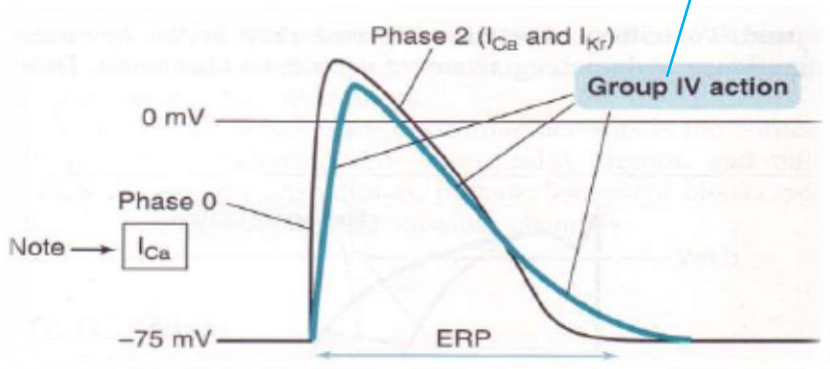
- Dronedarone
- Vernakalant
- Azimilide
- Tedisamil

Class-IV Calcium channel blockers

Non-Dihydropyridine derivatives-----**Verapamil, diltiazem**

Mechanism of action:

- Block L-type calcium channels.
- Rate of phase 4 in SA / AV node
- Slow conduction – prolong ERP
- Phase 0 upstroke



Adverse effects:

- Ankle oedema, constipation

Contraindication:

- AV block, Hypotention & WPW

Dihydropyridine derivatives of calcium channel blockers are not used for the treatment of Arrhythmia.

Because, they may worsen arrhythmias.

SUMMARY

ARRHYTHMIA

- Cardiac arrhythmia/Cardiac dysrhythmia/Irregular heart beat is a group of condition in which the heart beat is irregular, too fast or too slow.
- Bradycardia: Heart beat is too slow i.e. <60 beats/min
- Tachycardia: Heart beat is too fast i.e. >100 beats/min

- ✓ Tachy-arrhythmia/Tachycardia-Sinus tachycardia, AV tachycardia, Atrial Flutter, Atrial Fibrillation, Ventricular flutter, ventricular fibrillation and WPW.
- ✓ Brady-arrhythmia/Bradyycardia-Sinus bradycardia, AV block, BB block

SUMMARY

Classification of Anti-Arrhythmic drugs

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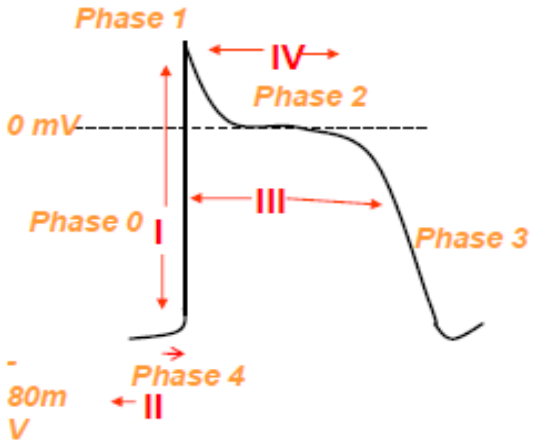

MCQs

1.) Bretylium is an example for ----------

a. Potassium channel blockers
b. Sodium channel blockers
c. Calcium channel blockers
d. β channel blockers

MCQs

2.) Lignocaine is an example for ----------

a. IC Sodium channel blockers
b. IA Sodium channel blockers
c. IB Sodium channel blockers
d. β blockers

MCQs

3.) Verapamil is an example for ----------

a. Sodium channel blockers
b. Calcium channel blockers
c. Potassium channel blockers
d. β blockers

MCQs

4.) Which of the following drug is an example for calcium channel blockers?

a. Amiodarone
b. Diltiazem
c. Bretylium
d. Phenytoin

MCQs

5.) Which of the following drug is an example for Potassium channel blockers?

a. Bretylium
b. Diltiazem
c. Lignocaine
d. Phenytoin

MCQs

6.) Which of the following drug is an iodine containing compound and blocks sodium, calcium, beta-adrenergic and potassium channels?

a. Bretylium
b. Diltiazem
c. Amiodarone
d. Phenytoin

Thank you