Anti-arrhythmic Drugs

Definition: Cardiac arrhythmia is a disorder of rate, rhythm, origin or conduction of impulses with heart.

Types of Cardiac arrhythmias

1. Extra systoles(ES)
2. Paroxysmal supraventricular tachycardia (PSVT)
3. Aterial flutter
4. Aterial fibrillation
5. Ventricular tachycardia
6. Torsades de pointes (Twisting points)
7. Ventricular fibrillation
8. Atrio-ventricular block (A-V block)

Mechanism of cardiac arrhythmia

1. Defects in Impulse Formation (SA Node)

i) ***Altered Automaticity:*** In pathologic conditions, automaticity can be altered when latent pacemaker cells take over the SA node's role as the pacemaker of the heart.

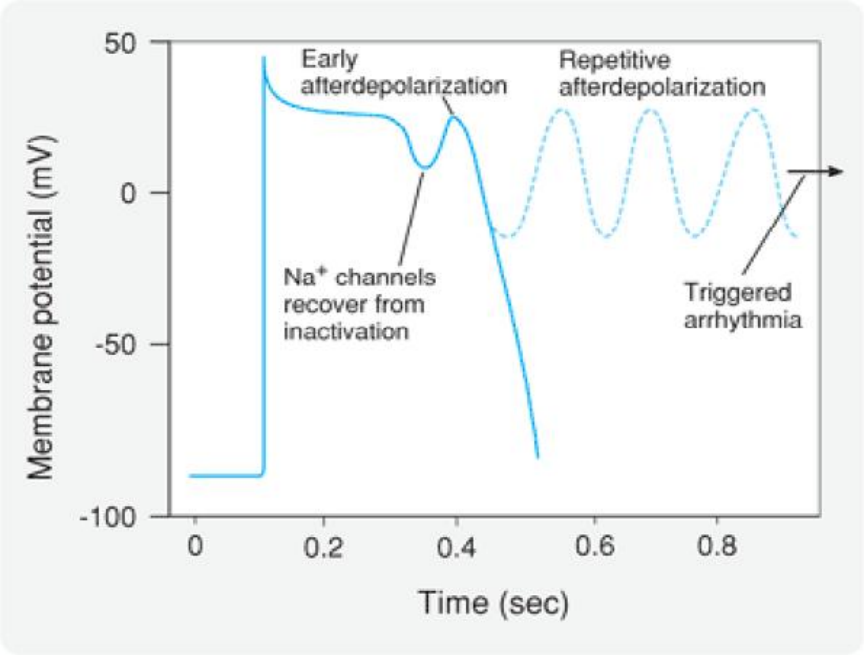
ii) **An escape beat** may occur as a latent pacemaker initiates an impulse. A series of escape beats, known as an escape rhythm, may result from prolonged SA nodal dysfunction.

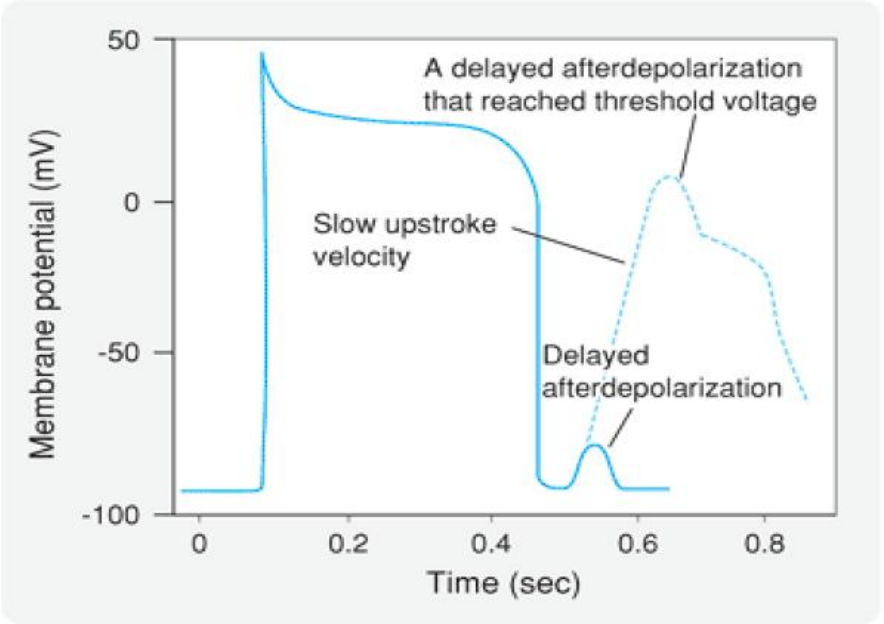
iii) On the other hand, **an ectopic beat** occurs when latent pacemaker cells develop an intrinsic rate of firing that is faster than the SA nodal rate.

iv) A series of ectopic beats, termed an ectopic rhythm, can result from ischemia, electrolyte abnormalities, or heightened sympathetic tone.

v) Direct tissue damage (such as can occur after a myocardial infarction) also results in altered automaticity.

ii) Triggered Activity: After depolarizations occur when a normal action potential triggers extra abnormal depolarizations.



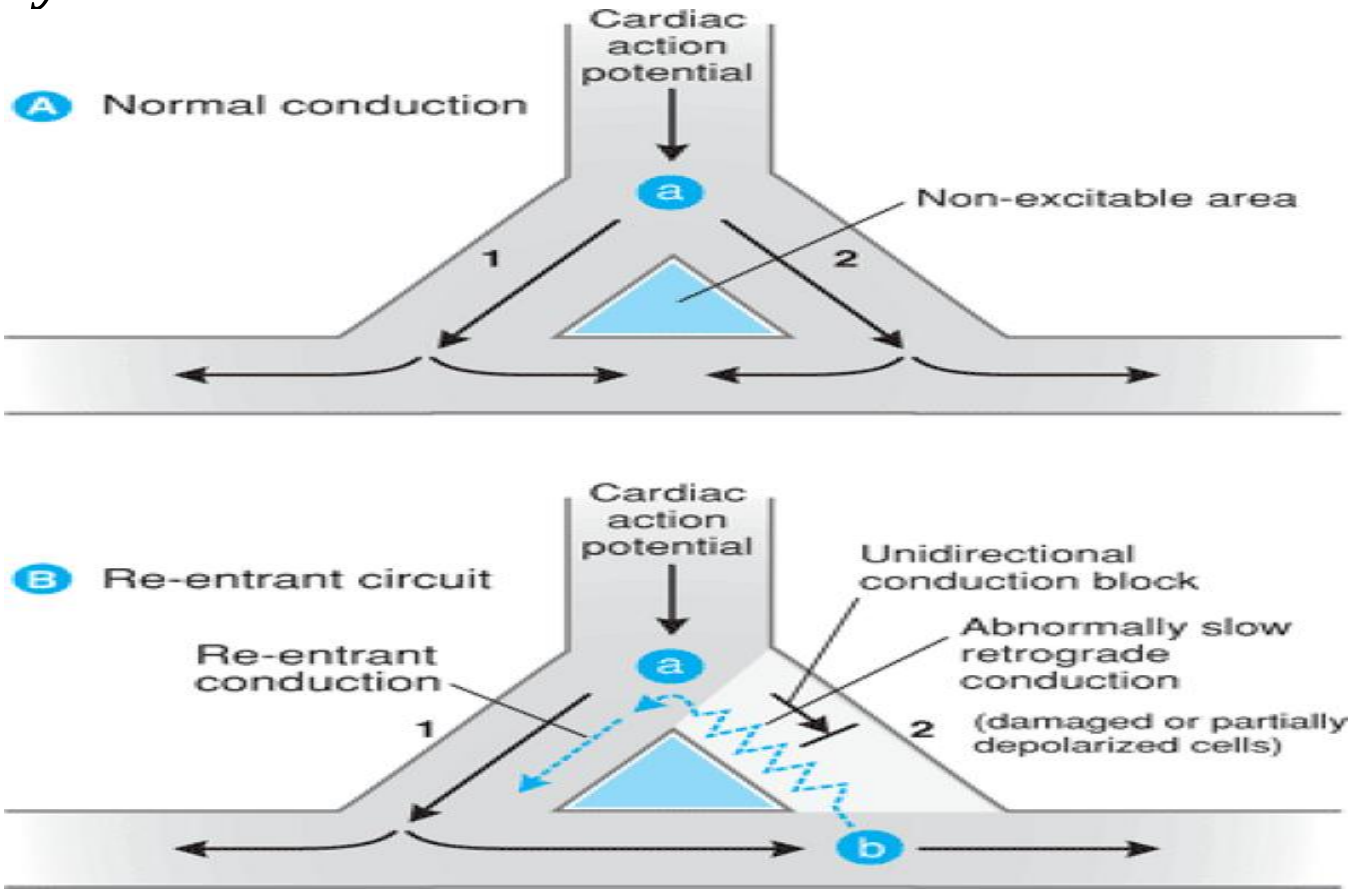


Early after depolarizations

Delayed after depolarizations

2. Defects in Impulse Conduction

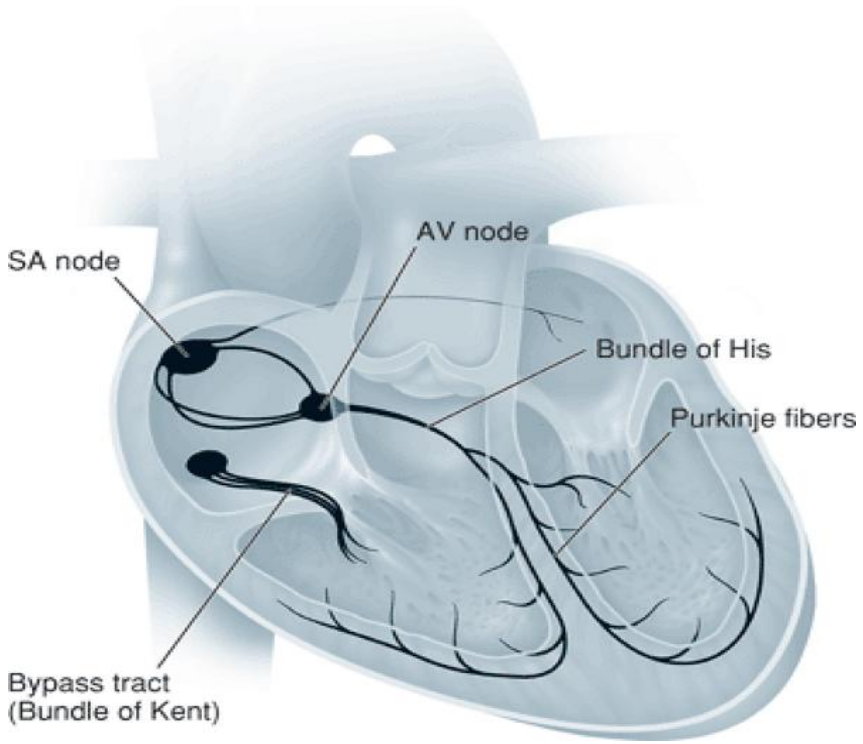
i) Re-entry



ii) Conduction Block

Conduction block occurs when an impulse fails to propagate because of the presence of an area of inexcitable cardiac tissue.

iii) Accessory Tract Pathways: Some individuals possess accessory electrical pathways that bypass the AV node.



Classification of Antiarrhythmic drugs

(Vaughan Williams classification)

Class	Example(s)	Mechanism
Ia	Disopyramide, Qunidine, Procainamide	Sodium channel block (intermediate dissociation)
Ib	Lidocaine, Mexiletine	Sodium channel block (fast dissociation)
Ic	Flecainide, Propafenone,	Sodium channel block (slow dissociation)
II	Propranolol, Esmolol, Sotalol	β-Adrenoceptor antagonism
III	Amiodarone, Bretylium Sotalol, Dofetilide, Ibutilide	Potassium channel blockers
IV	Verapamil, Diltiazem	Calcium channel block
Others	1. Adenosine, Digitalis 2.Sympathomimetics- Isoprenaline, etc. Anticholinergic-Atropine. 3.Digitalis	1.For PSVT 2.For A-V block 3. AF, AFI and PSVT

Class I drugs

Class I drugs block sodium channels. Because this inhibits action potential propagation in many excitable cells, it has been referred to as 'membrane-stabilising' activity

Class Ia: Procainamide is a group 1A prototype.

Other drugs with group 1A actions include **quinidine and disopyramide.**These drugs affect both atrial and ventricular arrhythmias. Therefore slow conduction velocity in the atria, Purkinje fibers, and ventricular cells. At high doses they also slow AV conduction. The reduction in ventricular conduction results in increased QRS duration in the ECG.

Class Ib: Lidocaine is the prototype 1B drug and is used exclusively by the IV or IM routes. Lidocaine selectively affects ischemic or depolarized Purkinje and ventricular tissue and has little effect on atrial tissue; the drug reduces AP duration in some cells, but because it slows recovery of sodium channels from inactivation it does not shorten (and may even prolong) the effective refractory period. **Mexiletine** is an orally active 1B agent.

Class Ic: Flecainide is the prototype drug with group 1C actions. These drugs have no effect on ventricular AP duration or the QT interval. They are powerful depressants of sodium current, however, and can markedly slow conduction velocity in atrial and ventricular cells. They increase the QRS duration of the ECG.

Class II (β- Blokers)

Propranolol and **esmolol** are prototypic antiarrhythmic β-blockers. Their mechanism in arrhythmias is primarily cardiac β-adrenoceptor blockade and reduction in cAMP, which results in the reduction of both sodium and calcium currents and the suppression of abnormal pacemakers. The AV node is particularly sensitive to β- blockers and the PR interval is usually prolonged by class II drugs.

Class III (Potassium channel blockers)

1. Dofetilide and ibutilide are typical group III drugs.

2. Sotalol is a chiral compound (ie, it has 2 optical isomers). One isomer is an effective β-blocker, and both isomers contribute to the antiarrhythmic action. The clinical preparation contains both isomers.

3. Amiodarone is usually classified as a class 3 drug because it blocks the same K channels and markedly prolongs AP duration as well as blocking sodium channels.

4. Dronedarone is a new drug, similar to amiodarone but less efficacious and less toxic.

Class IV (Calcium channel blockers)

1. Verapamil is the prototype. Diltiazem is also an effective antiarrhythmic drug.
2. Nifedipine and the other dihydropyridines are *not* useful as antiarrhythmics

Mechanism and Effects

1. Verapamil and diltiazem are effective in arrhythmias that must traverse calcium-dependent cardiac tissue (eg, the AV node)
2. These agents cause a state- and use-dependent selective depression of calcium current in tissues that require the participation of **L-type calcium channels**.
3. AV conduction velocity is decreased and effective refractory period increased by these drugs. PR interval is consistently increased.

Miscellaneous Antiarrhythmic Drugs

Adenosine

1. Adenosine is a normal component of the body, but when it is given in high doses **(6–12 mg)** as an intravenous bolus, the drug markedly slows or completely blocks conduction in the atrioventricular node, probably by **hyperpolarizing** this tissue and by reducing calcium current.
2. Adenosine is extremely effective in abolishing AV nodal arrhythmias, and because of its very low toxicity it has become the drug of choice for this arrhythmia. Adenosine has an extremely short duration of action **(about 15 s).**
3. Toxicity includes flushing and hypotension, but because of their short duration these effects do not limit the use of the drug. Transient chest pain and dyspnea (probably due to bronchoconstriction) may also occur.

Potassium Ion

1. Potassium depresses ectopic pacemakers, including those caused by digitalis toxicity.
2. Hypokalemia is associated with an increased incidence of arrhythmias, especially in patients receiving digitalis.
3. Conversely, excessive potassium levels depress conduction and can cause reentry arrhythmias.
4. Therefore, when treating arrhythmias, serum potassium should be measured and normalized if abnormal.

Magnesium Ion

1. Magnesium appears to have similar depressant effects as potassium on digitalis-induced arrhythmias.
2. Magnesium also appears to be effective in some cases of torsade de pointes arrhythmia.