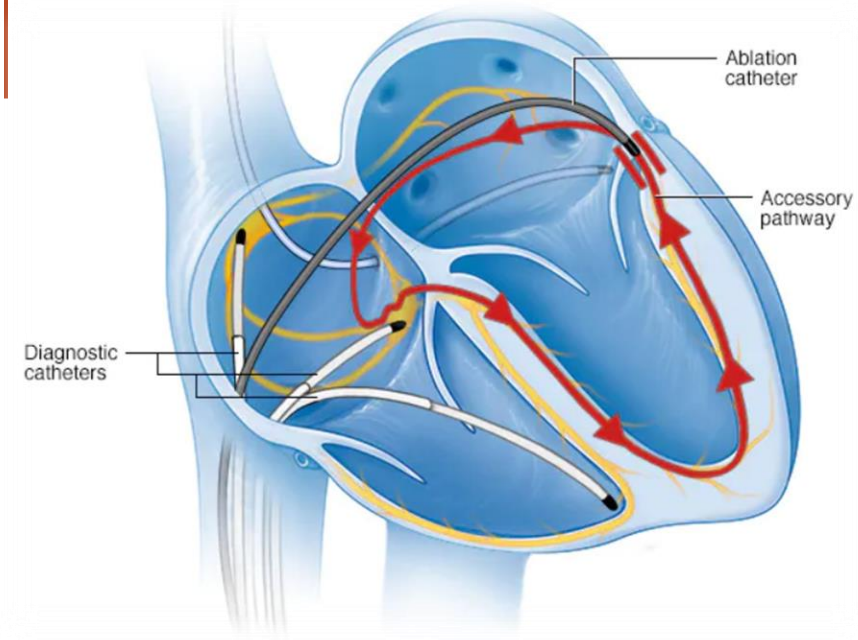
Block CVS-206



Antiarrhythmic Drugs

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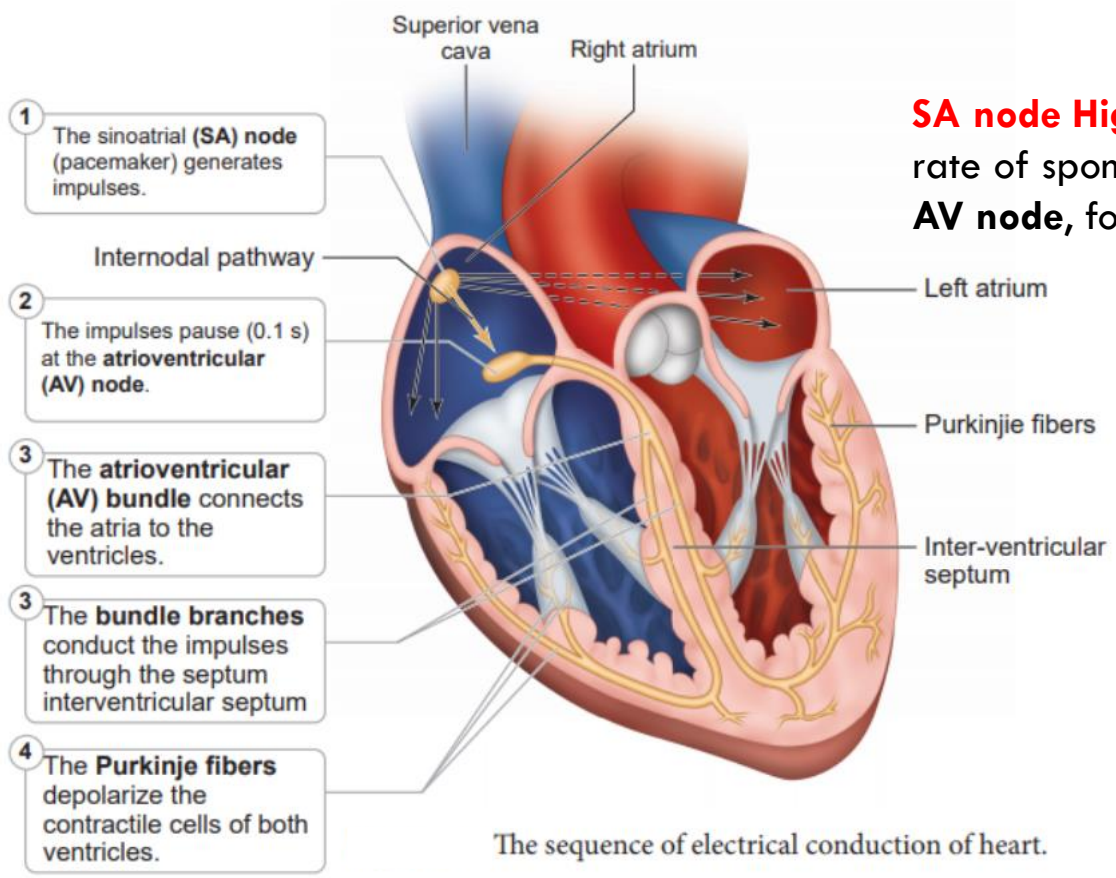
Faculty of medicine



The sequence of electrical conduction of heart.

SA node Highest automaticity (highest intrinsic rate of spontaneous automaticity), followed by **AV node,** followed by **purkinje fibers**)

Conducting System

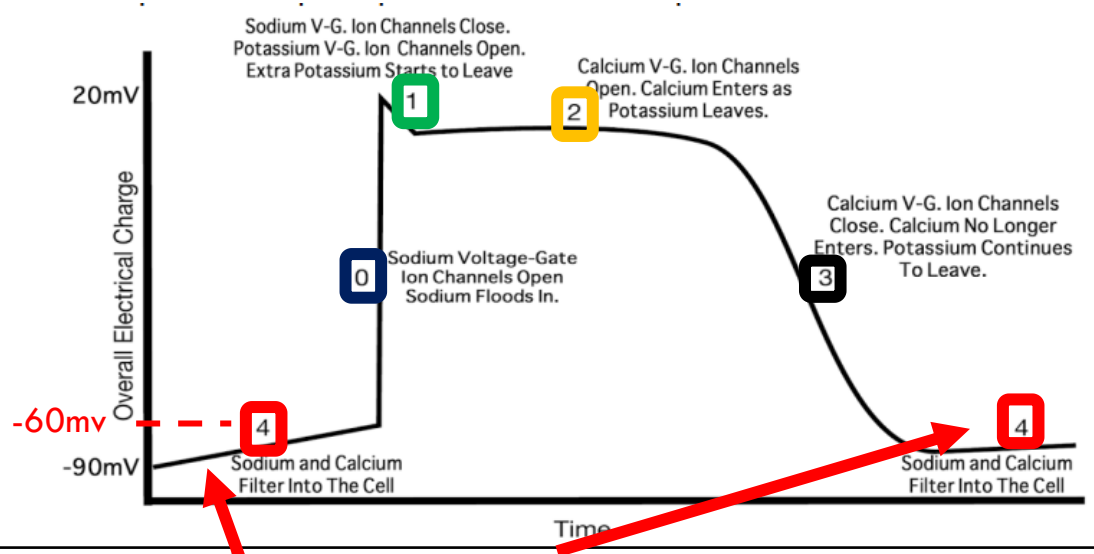
a) **Conducting tissues** (SA node, AV node and Purkinje fibers): they can initiate impulse which excites the rest of the heart and SA node is the pace maker **(automatic).**

b) **Contractile tissue** (atrial and ventricular muscles): can't initiate an impulse **(non automatic)** but can respond to an impulse giving excitation in the form of contraction. **Not allowed to has automaticity.**

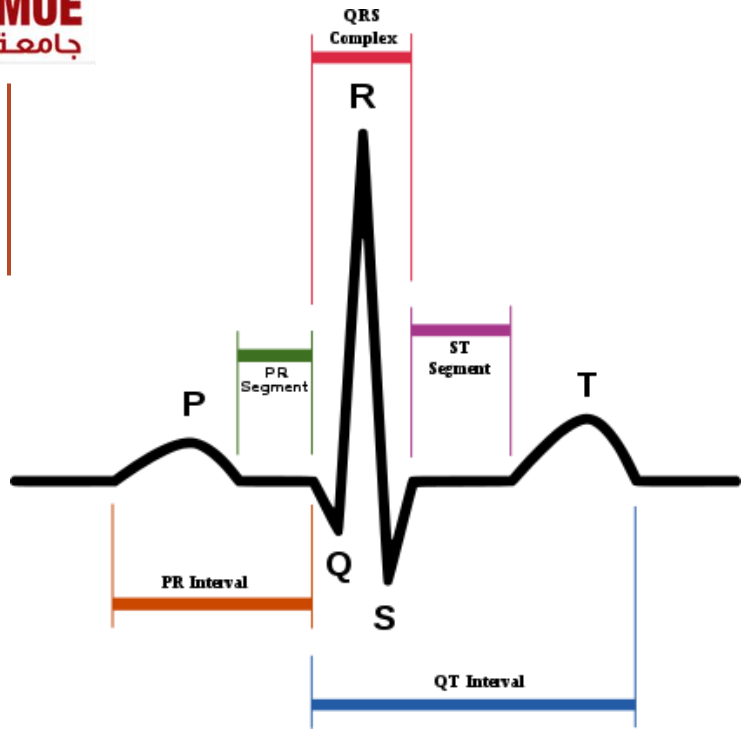
Cardiac action potential

- In the resting state, K^+ ions is found mainly intracellular, while Na^+ and Ca^{2+} are mainly extracellular making the interior of the cell electrically *negative*.
- Contraction and relaxation occur when rapid redistribution of ions across the cell membrane occurs during 4 phases known as **"action potential".**

Cardiac Action Potential Phases



Phase 4 *Spontaneous Depolarization*	• **Electrolytes rebalance,** thus Na+ gained during phase 0 is extruded out of the cell and K+ lost during phase 3 enter into the cell again under the influence of Na+/K+ ATPase enzyme **(Resting State)**. • It occurs in cells of **S-A node, A-V node and His Purkinje fibers** with **spontaneous depolarization to the threshold potential (-60) due to influx of Na+ and Ca++.**
***Phase 0** *Rapid Depolarization*	• **Rapid depolarization from (-60) to (+20) due to massive influx of Na+ through fast Na+ channels (Myocardial Contraction),** then inactivation of Na+ channel occurs.
Phase 1 *Initial rapid transient repolarization*	• Rapid closure of fast Na+ channels, Na+ levels equalize & **transient efflux of K+ (to discard positive charges)**
Phase 2 *Plateau phase*	• **Slow influx of Ca++ through the slow L-channels of Ca++ (retard K exit leading to plateau)**
Phase 3 *rapid repolarization*	• A second phase of rapid repolarization due to **rapid outflux of K+ (to get rid rapidly of positive charges to save the hear)**

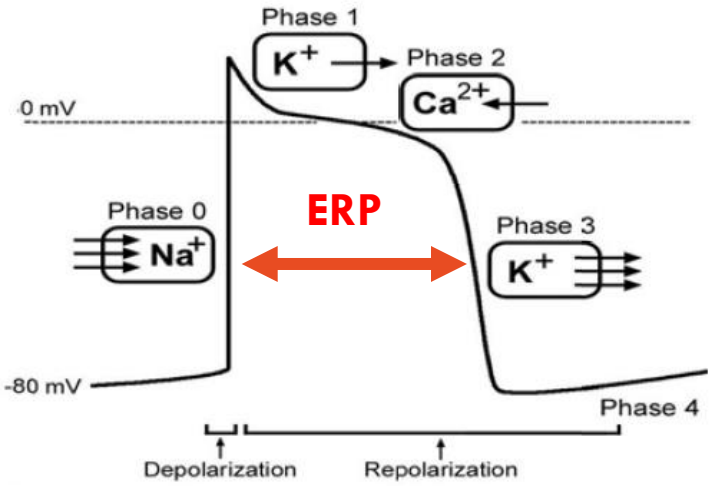


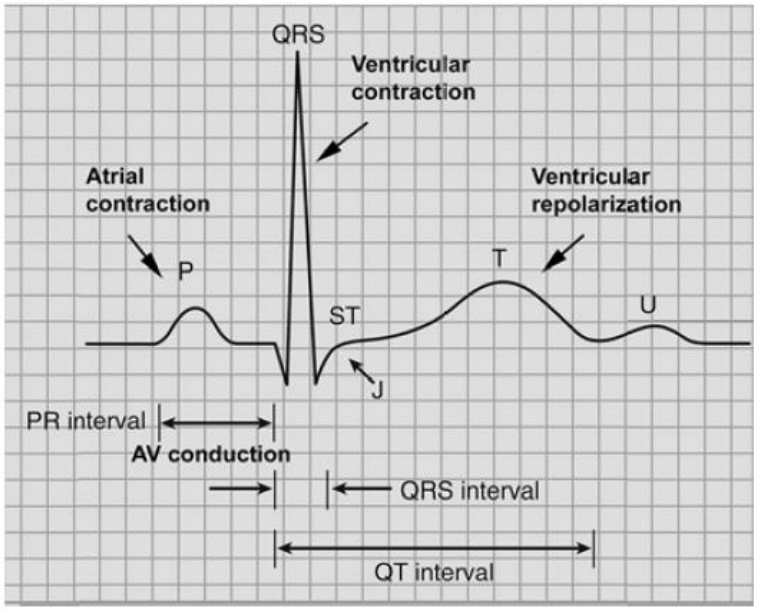
Interval	What it measures
PR interval	Time for the electrical impulse to travel from the atria to the ventricles
QRS complex	Ventricular depolarization (contraction)
QT interval	Time for the ventricles to depolarize and repolarize
RR interval	One complete cardiac cycle; used to calculate heart rate

There are three main components to an ECG:

- the P wave, which represents the depolarization of the atria;
- the QRS complex, which represents the depolarization of the ventricles; and
- the T wave, which represents the repolarization of the ventricles.

N.B. The drug that prolong action potential duration (prolong QT interval) and can induce Torsade de pointe (polymorphic ventricular tachycardia).





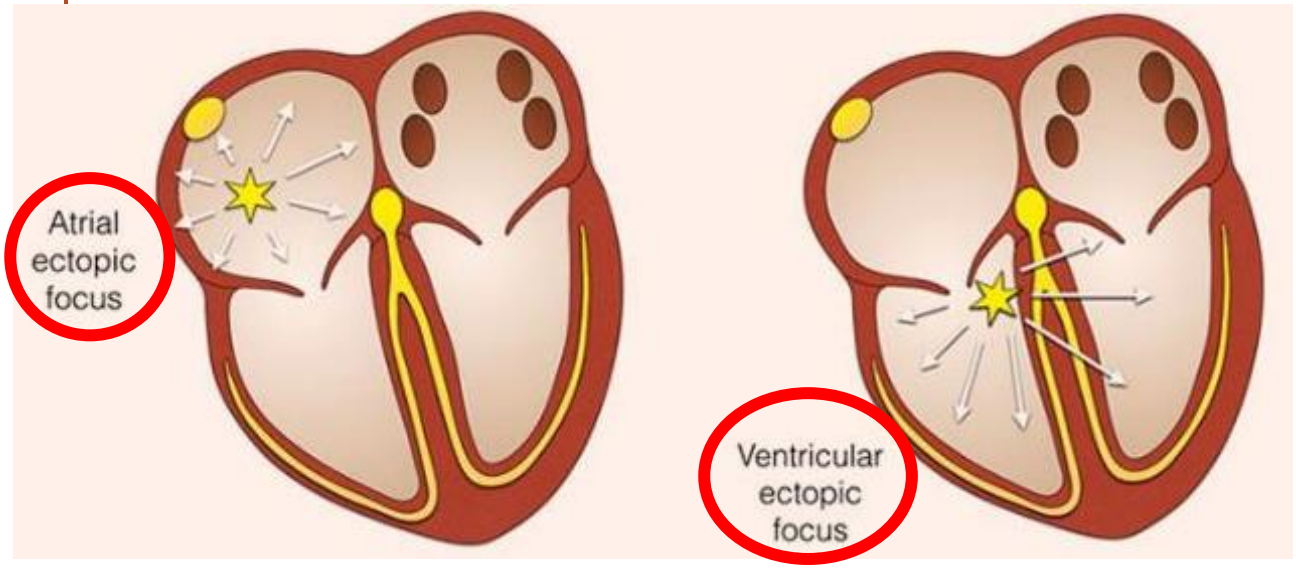
Effective Refractory Period……. Phases **0, 1, 2, 3**

(the cardiac tissue can not respond to any stimuli either nodal or ectopic.

Arrhythmia means disturbance in the normal heart rhythm.

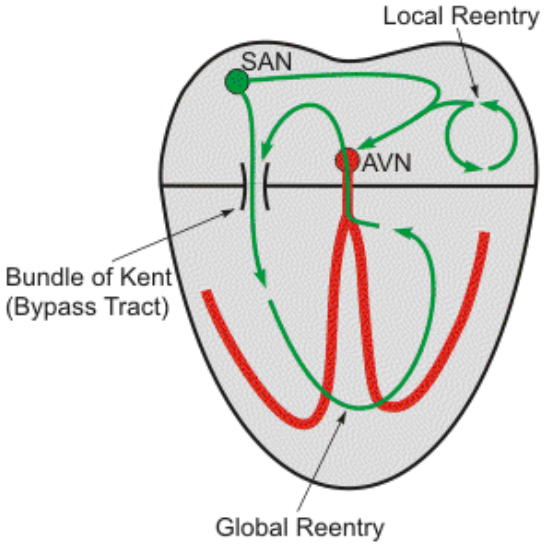
- Abnormal impulse generation;
- Abnormal impulse conduction;
- Both.

Pathogenesis



Abnormal generation

- **Nodal**
- **Ectopic**



Abnormality in conduction

- **Heart block**
  - 1st
  - 2nd
  - 3rd
- **Reentry**
  - AF
  - WPW

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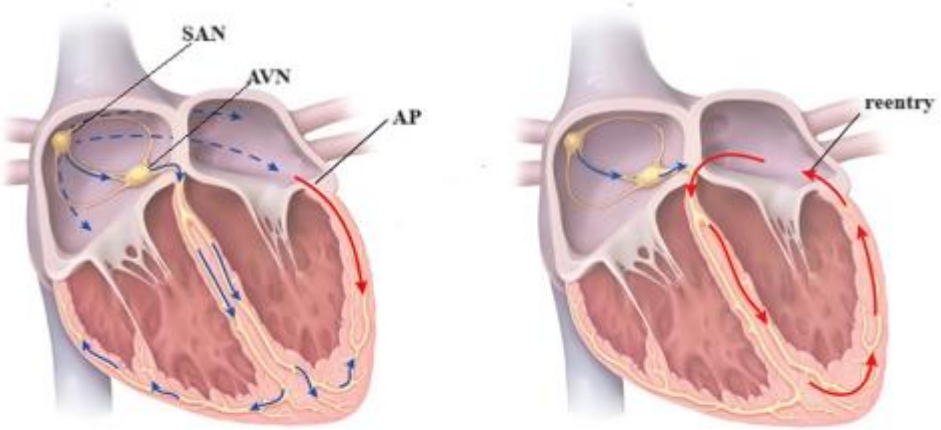
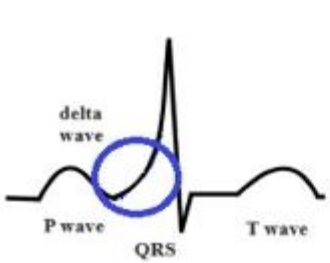
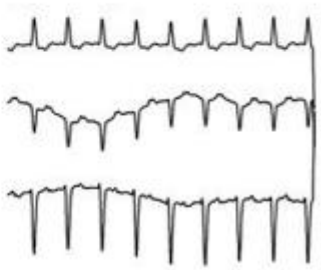


Wolf–Parkinson–White (WPW) Syndrome





– Wolff–Parkinson–White syndrome (WPW) is an example of anatomically defined re-entry. WPW syndrome is an atrioventricular re-entrant tachycardia, secondary to an accessory AV conducting pathway (see before).

Causes

a) **Electrolyte disturbance** hypokalemia and hypercalcemia that cause tachycardia and hyperkalemia that causes bradycardia,
b) **Myocardial ischemia** particularly MI,
c) **Autonomic disturbances** and
d) **Drug toxicity** (as digitalis and anti arrhythmics).

*Arrhythmia occurs in **25 % of patients with digitalis therapy** and in **70 % of the cases of acute myocardial infarction (MI)**.*

Types

A- Supraventricular arrhythmia:

1. Sinus tachycardia
2. Premature atrial contractions
3. Atrial flutter & Atrial fibrillation
5. Sinus bradycardia
6. Atrial tachycardia
7. A-V nodal tachycardia.

B- Ventricular arrhythmia:

i. Premature ventricular contractions (PVCs)
ii. Ventricular fibrillation.
iii. Torsade de pointes
iv- Ventricular tachycardia.
v- Bundle branch block

N.B. Ventricular arrhythmias are life-threatening.

Management

Goals of treatment of arrhythmias:

a) To terminate already present arrhythmias
b) To prevent recurrence of arrhythmias in susceptible patients.
c) To protect ventricles against arrhythmias during atrial arrhythmias.
d) To control rate and regularity of cardiac arrhythmias and convert them to normal sinus rhythms.

Management Approaches:

a) ***Non-pharmacological approach:*** by using a) pacemaker or catheter ablation in cases of SVT as AF, or b) implantable cardioverter / defibrillator (ICD) in cases of VT and VF.
b) ***Pharmacological approach:*** using antiarrhythmic drug therapy.

ANTIARRHYTHMIC DRUGS

Blocking Na+ and Ca++ influx, K+ efflux, cardiac β- receptors and decreasing A-V conductivity either directly or indirectly may terminate arrhythmias through affecting:

- Automaticity
- Conduction velocity
- Refractory period
- Membrane responsiveness

N.B. Most of antiarrhythmic drugs have limited efficacy and may be prorrhythmics & increase the mortality rate in some patients.

ANTIARRHYTHMIC DRUGS

Classification of antidysrhythmic drugs

Class I (Na^+ channel blockers):

1. ***IA*:** quinidine, procainamide and disopyramide.
2. ***IB*:** Lidocaine, phenytoin, tocainide and mexiletine.
3. ***IC***: propafenone, moricizine and flecainide.

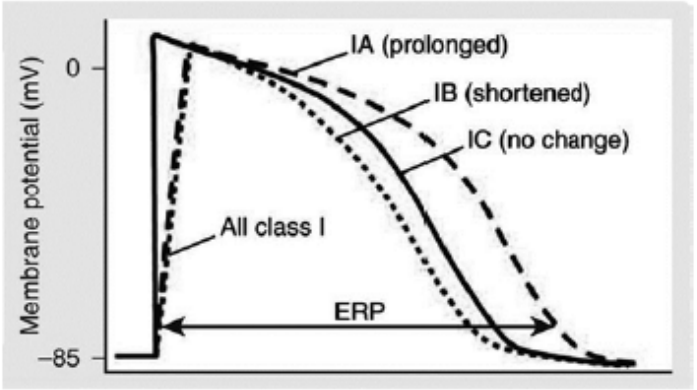
Class II (B-adrenergic blockers): e.g., propranolol, esmolol and metoprolol.

Class III (K^+ channel blockers): e.g., amiodarone, dronedarone, sotalol and dofetilide.

Class IV (Ca^{++}- channel blockers): e.g., verapamil and diltiazem

Miscellaneous drugs: e.g., digoxin, adenosine and magnesium.

Class I: **Na⁺ channel blockers:**



- **Class IA: e.g. quinidine, procainamide, disopyramide**: moderately block **Na⁺** channels and ↑ ERP (effective refractory period) and APD (action potential duration)
- **Class IB: e.g. lidocaine, mexiletine:** weakly block **Na⁺** channels and ↓ ERP and APD.
- **Class IC: e.g. flecainide, propafenone:** strongly block **Na⁺** with no effect on ERP or APD.

Class II: **Beta-blockers: e.g. propranolol, bisoprolol, metoprolol**

They ↓ AV conduction and inhibit phase 4 depolarization.

Class III: **K⁺ channel blockers: e.g. amiodarone, dronedarone, ibutilide, sotalol**

They inhibit mainly **K⁺** channels and ↑ ERP.

Class IV: **Ca⁺ channel blockers: e.g. verapamil and diltiazem**

They inhibit mainly **Ca^{2+}** channels and ↑ ERP.

Other unclassified drugs: **digoxin, adenosine, Mg sulphate**

Class	Potency	Effect on repolarization	Effect on K-channels	Effect on ERP
I A I B I C	High The lowest The most potent	Prolonged Shortened Little effect	Blocked Opened No effect	Prolonged Shortened Not affected

Class I
(Na Channel Blockers)

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Class I
(Na Channel Blockers)

Class 1A	Quinidine, Procainamide, Disopyramide
Class 1B	Lidocaine, Mexiletine
Class 1C	Flecainide, Propafenone

Class 1A

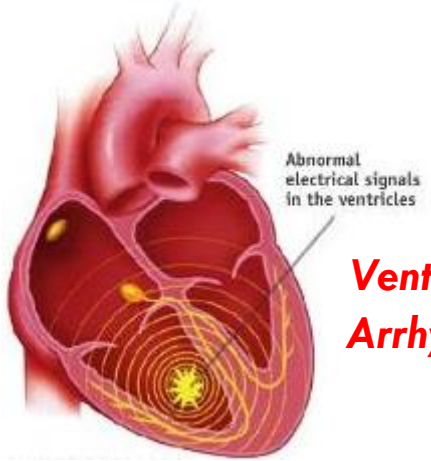
1-QUINIDINE

Mechanism of Action:

Dual actions on the heart **(direct & indirect)**:

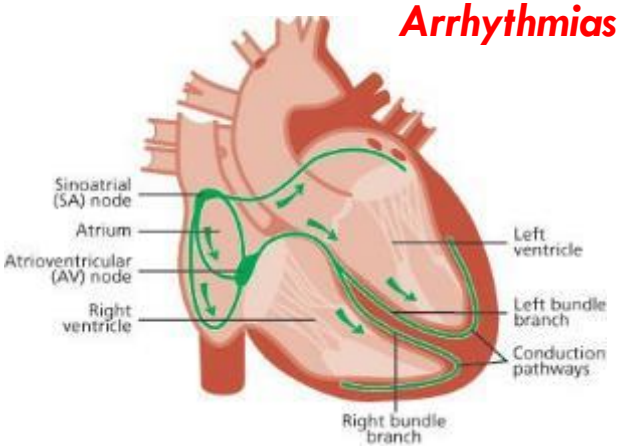
a) **Direct blocking activated Na+ channels leading to decreased phase 0 depolarization, decrease excitability and increase APD and ERP.**

b) **Indirect cardiac actions:**
   - ***atropine-like action (vagolytic)***: increases SA node firing & AV node conductivity leading to paradoxical tachycardia and
   - **α- *adrenergic blocking activity*** producing vasodilation that may causes postural hypotension.



Ventricular Arrhythmias

Supraventricular Arrhythmias



Quinidine was used for many years to treat **supraventricular** and **ventricular** arrhythmias, and to **maintain** sinus rhythm after conversion from atrial flutter and fibrillation; however, it is **rarely** used today because of availability of more effective and less toxic drugs.

Adverse effects

- **Cinchonism:** tinnitus (i.e. hearing of ringing or hiss), headache, blurred vision, vomiting, and diarrhea.
- **Hypotension:** after rapid i.v. infusion due to α-receptors blockade.
- **Paradoxical tachycardia:** quinidine has atropine-like action and, it may ↑ AV conduction and cause "*paradoxical tachycardia*". Digitalis or verapamil should be given before quinidine to offer rate control by ↓ AV conduction.
- **Quinidine syncope:** quinidine ↑ QT interval and may predispose the patient to a serious type of arrhythmia *(torsade de pointes)*. Quinidine therefore should not be given to patients with long QT syndrome or with other drugs that ↑ QT interval.

2-PROCAINAMIDE

- This drug is equivalent to quinidine as an antiarrhythmic agent and has similar cardiac and toxic effects. Like quinidine, its use now is very **limited.**
- **Additional adverse effect:** procainamide is metabolized by hepatic acetylation; 30% of patients (slow acetylators) develop drug-induced systemic lupus erythematosus (SLE) after long term therapy.

Class 1B

1-LIDOCAINE

- Lidocaine (lignocaine) is exclusively **Na^+ channel blocker**; it is highly selective for damaged tissues.
- It undergoes extensive first-pass metabolism so, it is **not given orally**.
- It is given only **i.v.** for acute suppression of ventricular arrhythmia associated with **acute MI** (not for long-term treatment). The usual dose is 50-100 mg i.v. half of this dose may be repeated after 5-10 min if necessary.
- It has **no effect** on AV conduction, so it is **not used** for supraventricular arrhythmia.
- Most adverse effects are **neurologic**.

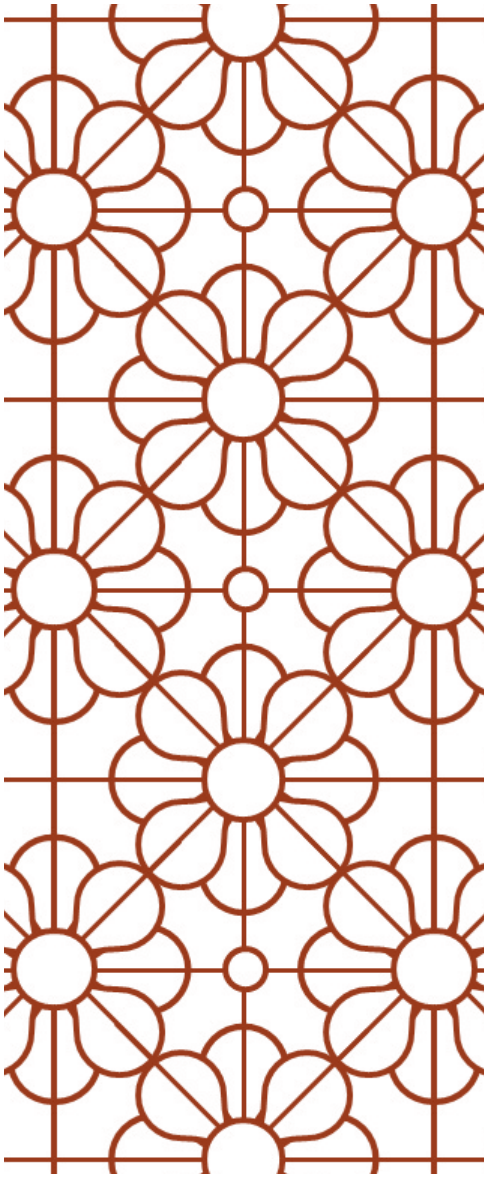
2- MEXILETINE 3- PHENYTOIN

- **Mexiletine** is very similar to lidocaine but can be given **orally**. It is used primarily for long-term treatment of ventricular arrhythmias associated with **previous MI**.
- **Phenytoin** is antiepileptic drug with class 1B activity. It is used primarily in the treatment of **digitalis-induced tachyarrhythmia**. It has a limited role in the treatment of other ventricular arrhythmias. The IV loading dose is 250 mg given over 10 minutes.

Class 1C

FLECAINIDE

- It blocks **Na channels** leading to decrease the rate of phase-0 depolarization and **slows AV conduction**. Due to its complex effects on cardiac tissue, the APD is **not altered**.
- It is used for atrial and ventricular arrhythmia and for maintenance sinus rhythm after conversion from atrial flutter and fibrillation.
- Flecainide increases the incidence of ventricular fibrillation and sudden death after MI (proarrhythmic effect), so it is **contraindicated** for patients with ischemic heart disease or structural heart disease (e.g. LV hypertrophy).



Class II
(Beta Blockers)

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Class II (Beta-Blockers)

- ***Propranolol, metoprolol, esmolol*** and ***sotalol*** are most commonly used beta blockers in arrhythmias.

Mechanism of action

They ↓ sympathetic stimulation, inhibit phase 4 depolarization, depress automaticity, prolong AV conduction , decrease heart rate & contractility

Therapeutic uses

- All arrhythmia induced by sympathetic overactivity.
- Arrhythmia due to thyrotoxicosis.
- Arrhythmia associated with HOCM.
- Supraventricular arrhythmia (AF).
- Arrhythmia due to mitral valve prolapse.

Class III
(Potassium Channel Blockers)

(Drugs that increase ERP)

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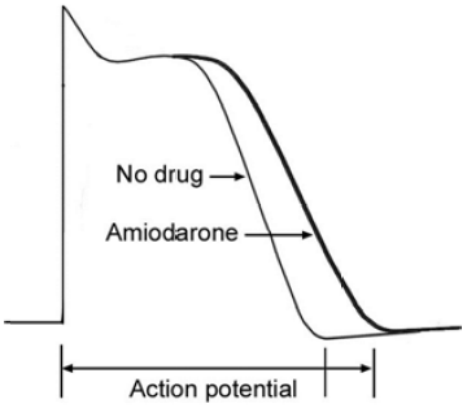
AMIODARONE

- It is structurally related to thyroxine. It contains ~ 40% iodine. **Dronedarone** is chemically similar to amiodarone but does not contain iodine.
- Amiodarone has **long t½** and **large Vd** so, it can accumulate in many tissues leading to wide range of adverse effects.

Mechanism of action

- Blocks mainly **K^+** channels → slowing of phase 3 → ↑ ERP.
- Blocks **Na^+** channels → ↓ excitability.
- Blocks **Ca^{2+}** channels → – ve inotropic and chronotropic effects.



Therapeutic uses: (most types of arrhythmia)

- Supraventricular and ventricular arrhythmia.
- WPW syndrome.
- Arrhythmia resistant to other drugs.

Adverse effects

- Dose-related **pulmonary toxicity** (fibrosis) is the most important adverse effect.
- **Hepatic** toxicity.
- **Thyroid dysfunction**: hypo- or hyperthyroidism because of its iodine content.
- **Corneal microdeposits:** reversible, does not affect vision.
- **Bradycardia** and heart block.
- **Photosensitivity** leading to gray-blue skin discoloration in sun-exposed areas.

Class IV
(Calcium Channel Blockers)

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Class IV
(Ca++ CHANNEL BLOCKERs)

Verapamil (Isoptin), Diltiazem (Dilzium)

Mechanism of action: They ↓ SAN activity and AV conduction

Therapeutic uses

- Non-dihydropyridines (verapamil and diltiazem) are primarily used to reduce HR in **supraventricular tachycardia** (SVT) and arrhythmia associated with HOCM.
- CCBs have **no role** in the chronic management of **ventricular tachycardia** (VT). IV verapamil should **never be used** in the acute management of VT, as it may cause hemodynamic collapse.

Other antiarrhythmic agents: Adenosine

- It is a purinergic **A1 receptor agonist**; this leads to opening of K^+ channels and inhibition of Ca^{2+} channels (i.e. hyperpolarization) in the AV conducting system and directly **inhibits AV nodal conduction**.
- It has very short half-life of 8-10 seconds.
- It is the drug of choice for immediate termination of paroxysmal supraventricular tachycardia (including WPW syndrome). It is given as a bolus dose of 6 mg i.v. followed, if necessary, by a dose of 12 mg.
- The drug is less effective in the presence of adenosine receptor blockers such as **theophylline** or caffeine.
- It is contraindicated in patients with **asthma** because it can cause **bronchospasm**.

NON-PHARMACOLOGICAL MEASURES

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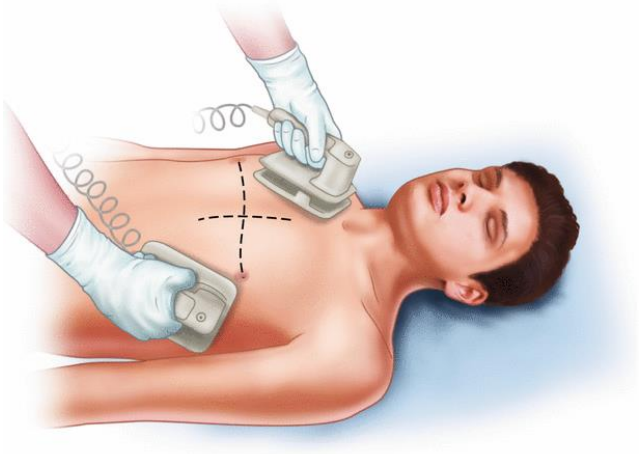
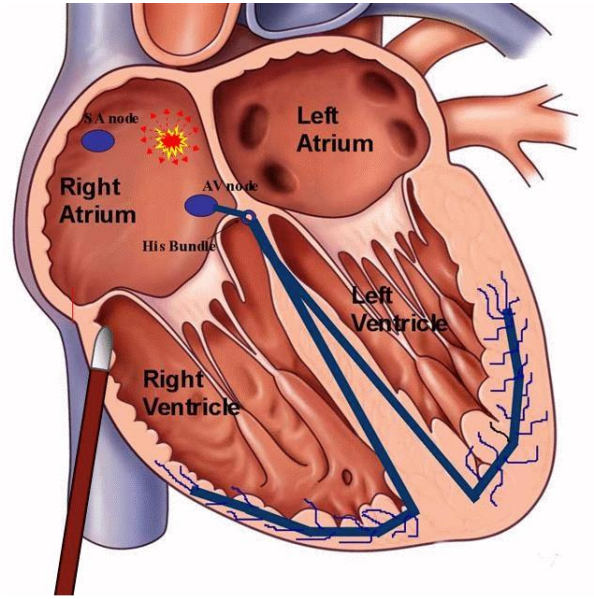
2025-2026

DC cardioversion

- It is application of direct current (electric shock) to the chest wall for **emergency** control of any type of arrhythmia especially **rapid AF** in an unstable patient (i.e. hypotensive).
- The patient should be **heparinized** before the procedure.
- Following electrical cardioversion, patients should be anticoagulated for at least 4 weeks.



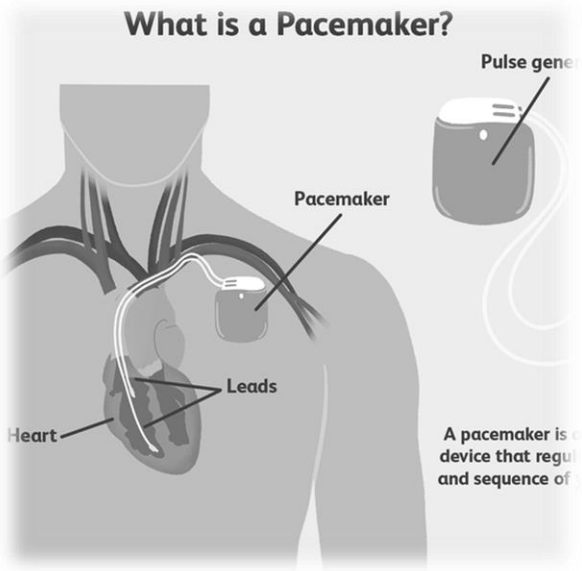


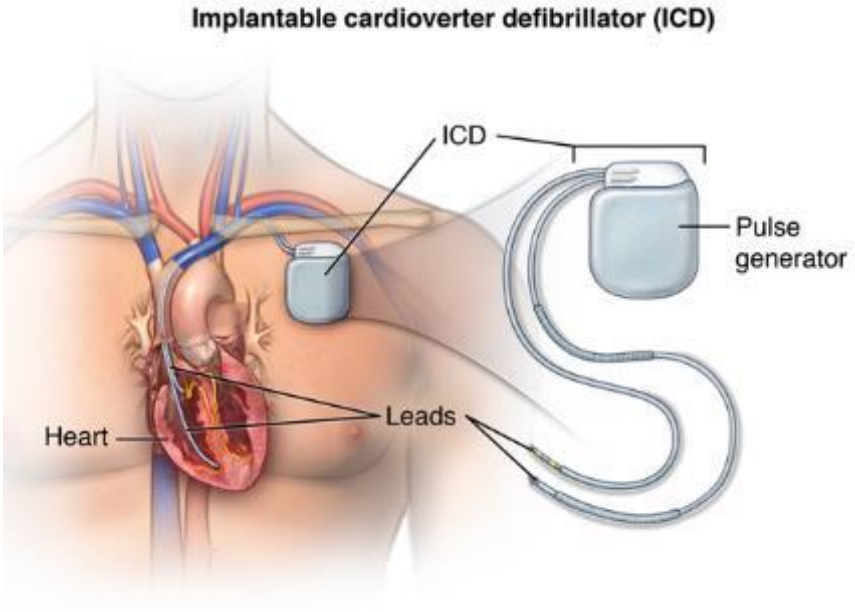
Laser ablation

- It is used for many types of arrhythmias.
- A catheter is inserted into a specific area of the heart. A special machine directs energy through the catheter to small areas of the heart muscle that causes the abnormal heart rhythm. This energy "disconnects" the pathway of the abnormal rhythm.
- Laser radiofrequency ablation is the definite treatment of **WPW syndrome**.

Artificial pacemakers and implantable cardioverter defibrillators

- They are battery-powered electronic devices that are implanted under the skin or in the chest cavity to monitor and pace the heart.





Thank You

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