King Saud University
College of Medicine
1st Year, 4th block

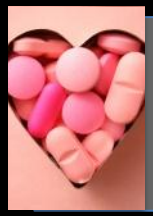
ANTIARRHYTHMIC DRUGS 3+4

Cardiovascular Block

OBJECTIVES

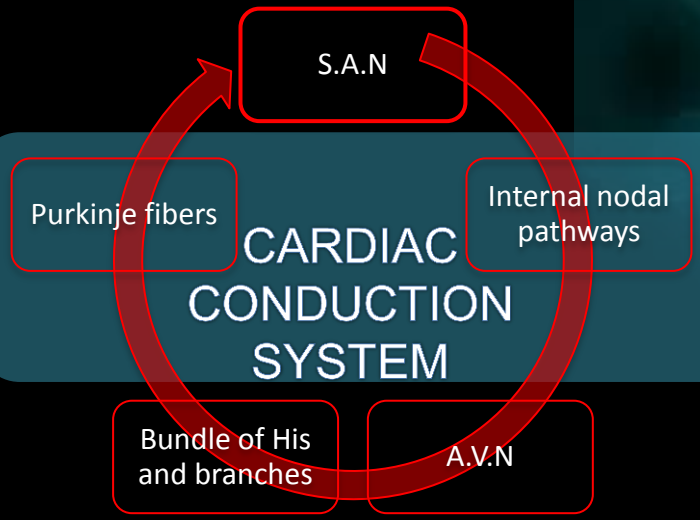
Classification of anti-arrhythmic drugs

Characters of each class



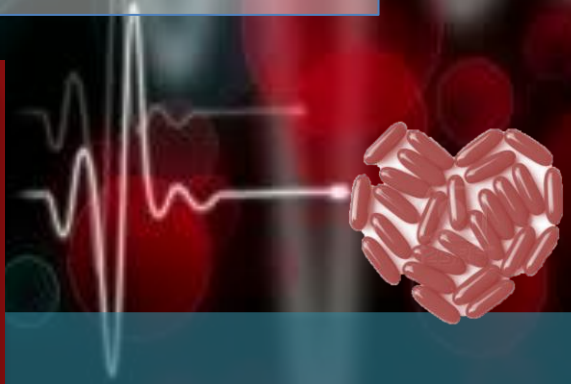
Examples of drugs in each class

Pharmacological effects , therapeutic uses , side effects of individual drugs



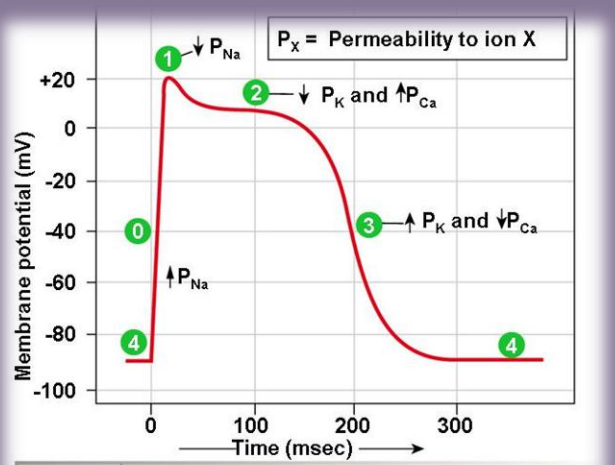
CARDIAC ACTION POTENTIAL

- Depolarization
- Repolarization
- Resting membrane potential
- Inward current
- Outward current

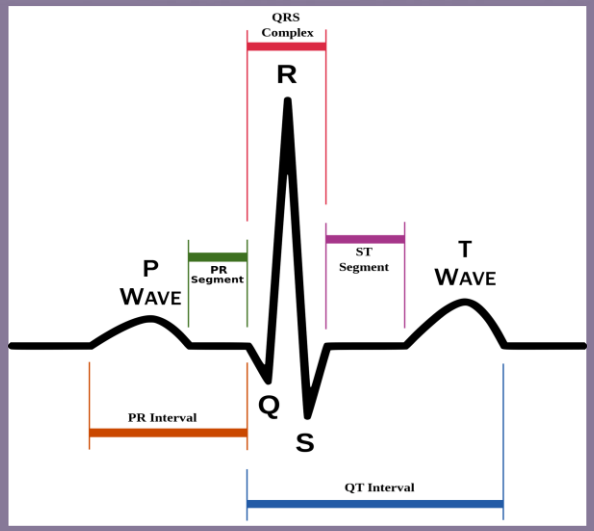


Remember

Remember



Phase	Membrane channels
0	Na^+ channels open
1	Na^+ channels close
2	Ca^{2+} channels open; fast K^+ channels close
3	Ca^{2+} channels close; slow K^+ channels open
4	Resting potential



Arrhythmias happen due to ionic movement → change in action potential

- S.A.N don't have **plateau (phase2) and resting potential (phase4)**

A.V.N. & S.A.N depend on ca^{2+} influx

- **ECG**

PR interval → time of conduction between atrial & ventricles

QT interval → duration of ventricular action potential

Abbreviation	
AF	Atrial fibrillation
AF	Atrial Flutter
A.V.N	Atrioventricular node
S.A.N	senatorial node

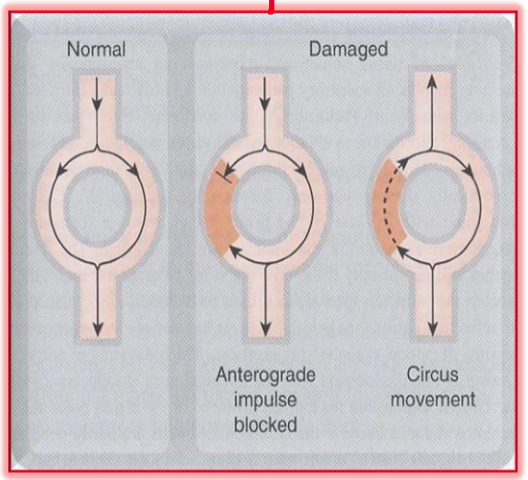
ARRHYTHMIA

Genesis

- ALTERED AUTOMATICITY
- ALTERED CONDUCTION

It is Abnormality in the ;

- **Heart rate**
  - high= tachycardia
  - low = bradycardia
- **Regularity**
  - Extrasystoles (dropped beat)
- **Site of origin**
  - ectopic pacemakers
- **Disturbance in conduction**

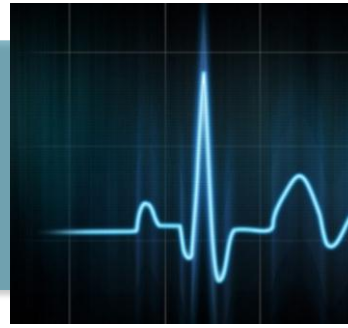


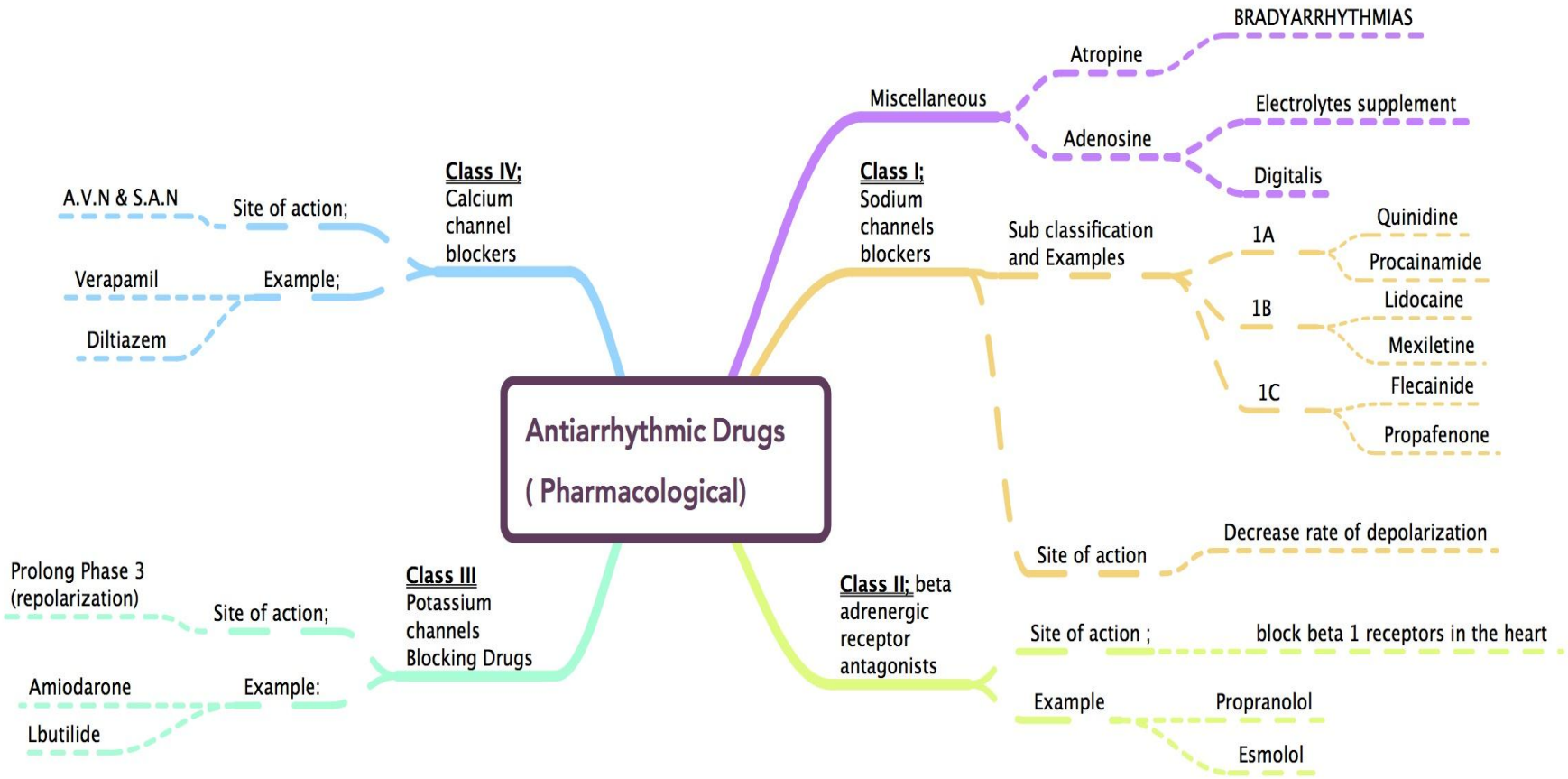
Therapeutic uses of anti-arrhythmic drugs

The ultimate goal of anti-arrhythmic drugs

to restore normal rhythm & conduction → Not possible → **prevent more serious & lethal arrhythmias**

CLASSIFICATION of ANTIARRHYTHMIC DRUGS According to Vaughan-Williams





CLASS I

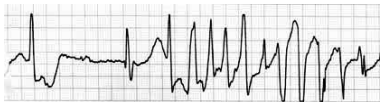
Mechanism of action	**Sodium channels blockers, this result in:**	• Decreased rate of depolarization (phase 0). • Suppression of action potential generation	
Characteristics	1. Act on non-nodal tissues (atria, ventricles, purkinje tissues) which are depending on sodium ion to start depolarization 2. have local anesthetic effect that slow conduction in atrial &ventricular tissues		
Sub classification	**Class (1A)**	**Class (1B)**	**Class (1C)**
Action	Potassium channel blocking effect: 〰 Prolong the action potential duration →Prolong Effective refractory period (ERP) → ECG change → Prolong QT interval. 〰 Anticholinergic actions (1) 〰 Negative inotropic effect	Shorten action potential duration and effective refractory period of Purkinje & ventricular cells → ↓ ERP	• Slow conduction in all cardiac tissues. • Depress cardiac contractility • No prominent effect on the duration of the action potential • negative inotropic effect
Clinical uses	• Atrial flutter or fibrillation (2) • Ventricular tachycardia or fibrillation. • At high concentration they have local anesthetic effect	• Ventricular arrhythmias • Ischemia of cardiac tissue	• Paroxysmal AF or AF. • Life –threatening ventricular arrhythmias • used in arrhythmias not responding to other therapy
Examples	• Quinidine • Procainamide	• Lidocaine • Mexiletine	• Flecainide • Propafenone

(1) increase AV conduction that can precipitate lethal ventricular arrhythmias in AF or AF
(2) These drugs should not be used alone for treatment of AF or AF because the ventricular rate may dramatically increase

CLASS I

Sub classification	Class (1A)	
Example	**Quinidine**	**Procainamide**
Characteristics	1. Has α adrenergic blocking effect 2. At toxic concentration will cause asystole (cardiac arrest). 3. Drug interaction with digoxin.	1. less toxic on the heart. 2. More effective in ventricular than in atrial arrhythmias 3. less depressant on cardiac contractility 4. Weak anticholinergic or α-blocking actions
Given	Orally (rarely given I.V. because of cardiac toxicity)	can be given I.V. (common route)
Clinical uses	1. Atrial flutter or fibrillation. 2. Ventricular tachycardia or fibrillation.	For treatment of ventricular tachycardia after acute myocardial infarction (AS Second drug of choice after lidocaine)
Side effects	1. GIT: diarrhea 2. CARDIAC: Torsades de pointes(1) (quinidine syncope) 3. Hypotension 4. Anticholinergic adverse effects 5. (dry mouth , dry skin ,constipation) 6. Cinchonism: (ringing in the ears , diarrhea)	1. lupus erythematosus-like syndrome 2. Hypotension 3. Torsades de pointes 4. Hallucination & psychosis

(1) A condition of the heart , it's a polymorphic ventricular tachycardia



CLASS I

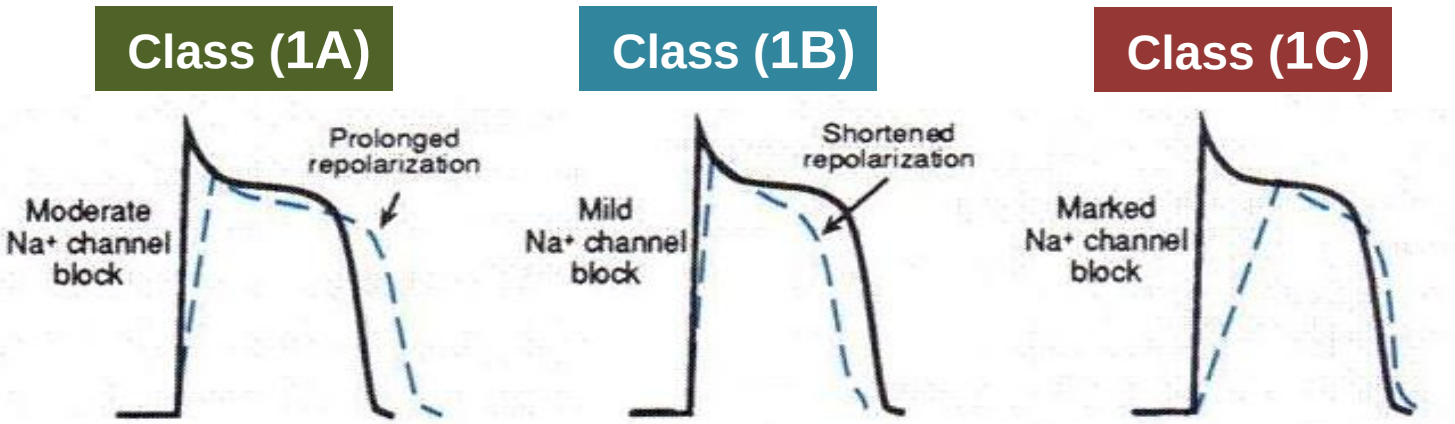
Sub classification	Class (1B)	
Example	**Lidocaine**	**Mexiletine**
Rout of administration	Given I.V. bolus or slow infusion	Given Orally
Pharmacokinetics	• Not given orally because of its extensive first –pass hepatic metabolism • only 3% of orally administered lidocaine appears in plasma. • T1/2 2 hours	• t1/2 long (10 hr)
Clinical uses	1. Very effective for suppressing arrhythmias due to ischemia, digitalis toxicity 2. **First drug of choice for emergency** treatment of ventricular arrhythmias following cardiac surgery or acute myocardial infarction 3. NOT effective in atrial arrhythmias	1. treatment of ventricular arrhythmia. 2. digitalis-induced arrhythmias. 3. chronic pain e.g. diabetic neuropathy and nerve injury.
Side effects	1.Neurological such as: Convulsions , tremors	1. Gastric upset 2. Neurological manifestation

CLASS I

Sub classification	Class (1C)	
Example	**Flecainide**	**Propafenone**
Characteristics	1.Slow conduction in all cardiac tissues. 2.Depress cardiac contractility 3.negative inotropic effect 4.No prominent effect on the duration of the action potential	
Clinical uses	1. supraventricular arrhythmias in patients with normal hearts 2. Are used in arrhythmias not responding to other therapy 3. Wolff-Parkinson-White syndrome*	
Side effects	• Significant risk of • Heart failure. • Proarrhythmias	
Note	These drugs are not used anymore because they may increase mortality when administered to patients surviving myocardial infarction	

***Pre-excitation of the ventricles due to an accessory pathway known as the Bundle of Kent.**

This accessory pathway is an abnormal electrical communication from the atria to the ventricles



CLASS II

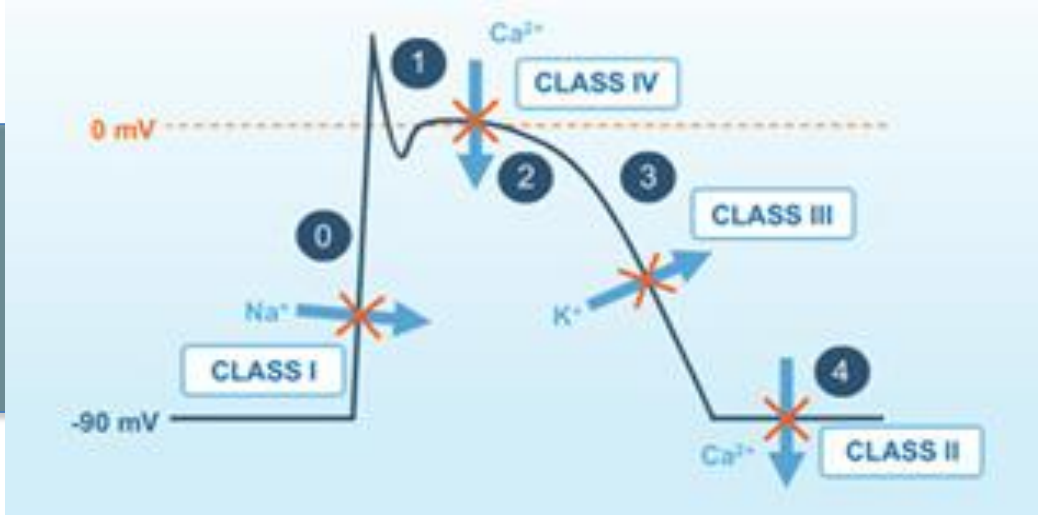
Mechanism	β- Adrenergic receptor Antagonists	
Action	**blocking β_1- receptors in the heart → reduce the sympathetic effect on the heart causing :**	~ **decrease automaticity of S.A. node and ectopic pacemakers** ~ **slow conduction of the A.V node** ~ **Heart rate.** ~ **Contractility.**
Clinical uses	1. Atrial arrhythmias associated with emotion, exercise 2. Digitalis-induced arrhythmias 3. Drugs of choice to reduce the incidence of ventricular fibrillation following acute myocardial infarction.	
Examples	• Propranolol • Esmolol	

CLASS III

Mechanism	**Potassium channels blocking drugs**	
Action	**Prolong the action potential duration & effective refractory period . (Prolong phase3)**	
Examples	**Amiodarone**	**Ibutilide**
Characteristics	• Main effect is to prolong action potential duration and refractory period • Has an additional actions of classes : I, II & IV • Has an α and β-adrenoceptor blocking effects .	
Clinical uses	1. Treatment of recurrent ventricular tachycardia – Fibrillation 2. It is restricted for life-threatening arrhythmias. 3. maintenance of sinus rhythm after D.C. cardioversion of atrial flutter and fibrillation.	for acute (rapid) conversion of atrial flutter or atrial fibrillation to normal sinus rhythm.
Adverse effects	1. Bradycardia & heart block, heart failure 2. pulmonary fibrosis ,interstitial pneumonitis 3. hyper- or hypothyroidism 4. Skin deposits causes photodermatitis , gray-blue skin rash. 5. Peripheral neuropathy 6. Constipation 7. corneal opacities 8. Hypotension	QT interval prolongation (precipitates torsades de pointes).
Pharmacokinetics	extremely long $t_{1/2}$ = 13 - 103 DAYS	Given by a rapid I.V. infusion
Drug Interactions	reduce renal clearance of several drugs (quinidine, procaiamide, flecainide)	

CLASS IV

Mechanism	Inhibits calcium entry through L-type **calcium** in the myocardium and depress AV nodal transmission.
Action	Site of action is A.V.N & S.A.N (slow conduction & prolong effective refractory period).
Clinical uses	1. Atrial flutter – fibrillation 2. Av nodal reentry NOT effective in ventricular arrhythmias
Examples	• Verapamil, • Diltiazem
Side effects	Sinus arrest or complete AV nodal blockade in the presence of β-adrenergic receptor blockers



MISCELLANEOUS GROUP

Adenosine

Naturally occurring nucleoside
half-life= less than 10 sec.

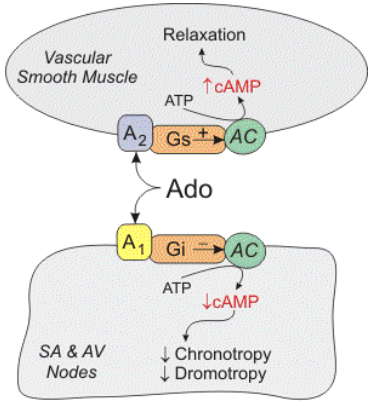
MECHANISM

In cardiac tissues → Binds to type 1 (A1) receptors which are coupled to Gi-proteins → activation → Opening of potassium channels (hyperpolarization)

Decrease cAMP which inhibits L-type calcium channels (↓ calcium influx) → decrease AV nodal conduction → Adenosine increases the vagal tone of the AV node → decrease conduction velocity in Av node

CLINICAL USES

Drug of first choice for terminating an Episode of paroxysmal supraventricular tachycardia



ADVERSE EFFECTS

Flushing & headache

Dyspnea and chest pain

brief AV block (contraindicated in heart block)

Hypotension

BRADYARRHYTHMIAS

Atropine

Used

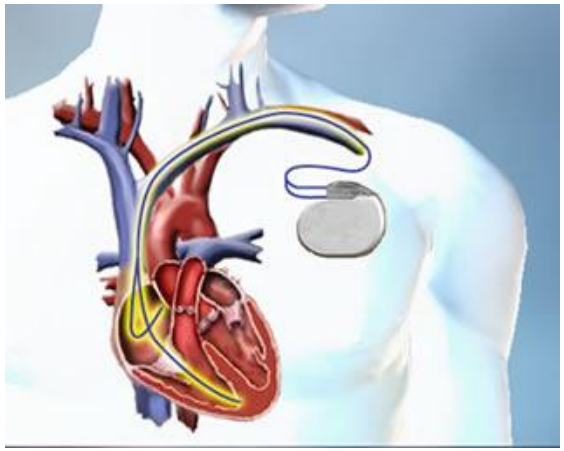
- sinus bradycardia after myocardial infarction and in heart block
- severe heart block isoprenaline may be combined with atropine

NONPHARMACOLOGIC THERAPY OF ARRHYTHMIAS

Implantable Cardiac Defibrillator (ICD)

can automatically detect and treat fatal arrhythmias

such as ventricular fibrillation



SUMMARY

Classification	Sub-Classification	Clinical uses	Example of drugs
CLASS I Sodium channels blockers	Class (1A)	1- Atrial flutter or fibrillation 2-Ventricular tachycardia or fibrillation 3-[Procainamide] Second drug of choice (after lidocaine) for treatment of ventricular tachycardia after acute myocardial infarction	1- Quinidine Has α adrenergic blocking effect 2-Procainamide
	Class (1B)	1- Very effective for suppressing arrhythmias due to ischemia, digitalis toxicity 2-First drug of choice for emergency treatment of ventricular tachycardia following cardiac surgery or acute myocardial infarction	Lidocaine
		Chronic treatment of ventricular arrhythmia digitalis-induced arrhythmias	Mexiletine
	Class (1C)	1-Paroxysmal atrial flutter or fibrillation 2-life-threatening ventricular arrhythmias 3- (Are used in arrhythmias not responding to other therapy)	Flecainide Propafenone
CLASS II	β- Adrenergic receptor Antagonists	1- Atrial arrhythmias associated with emotion, exercise 2- Digitalis-induced arrhythmias 3- Drugs of choice to reduce the incidence of ventricular fibrillation following acute myocardial infarction.	Propranolol Esmolol

SUMMARY

	Class 3 Amiodaron (Broad anti-Arrhythmic spectrum)	**Class 4** Verapamil, Diltiazem	**Miscellaneous group** Adenosine
Mechanism	Block the K+ channels (prevent K+ ions discharge)	Ca2+ channels blockers **in Nodal tissues**: Atria, Supraventricular) except: ventricles	It works on cardiac tissue and opens **the K+ channels** by: 1) binding to **A1 receptors (directly)** that are coupled With **Gi-proteins** >> Dec. cAMP >> hyper-reploarization. (dec. Ca2+ influx) 2) **(Indirectly)** Vagal tone stimulation
Effecacy	-It **prolongs** the Action potential duration & Effective Refractory period (Phase 3). -**It has the longest T1/2= 13-103days**. -It reduces the renal clearance during **drugs interaction**.	-Decreases the depolarization (phase 0) in Ca2+ dependent tissue. -Reduces the conduction pathway/transmission (Sa node+AV node). -Decreases the cardiac work & output.	-Dec. AV node conduction + velocity + automaticity. -Rapid onset of action
Clinical uses	-Recurrent **Ventricular Fibrillation** and **Tachycardia**. -Life-threatening arrhythmias. -Maintain sinus rhythm.	-Atrial flutter or fibrillation. -AV node Re-entery.	Drug of choice in proxysemal Supraventricular Tachycardia >> given by I.V (6mg) followed by 12 mg if necessary

MCQS

1. The mechanism of class 2 antiarrhythmic drugs (B adrenergic receptor blockers) is to : **A. reduce the parasympathetic effect** **B. reduce the sympathetic effect** **C. increase the sodium flow**	**5.The site of action of class 4 antiarrhythmic drugs is :** **A.non-nodal tissue** **B. A.V & S.A nodes** **C. non of the above**
2. a patient has a history of myocardial infarction what is the best drug to reduce the incidence of ventricular fibrillation : **A.varapamil** **B. adenosine** **C.esmolol**	**6. the mechanism of adenosine is to :** **A.inhibit the sympathetic effect** **B.increase the vagal tone** **C.decrease the impulses**
3. A patient taking antiarrhythmic drug. On a follow-up appointment the doctor found that he developed an interstitial pneumonitis. What is the drug he was taking : A. **amiodarone** B. **Ibutilide** C. **adenosine**	**7. a patient has an episode of paroxysmal supravenrticular tachycardia, what is the best drug to prescribe :** A.adenosine B.varapamil C.diltiazm
4. The best rout of administration for Ibutilide is : **A. I.V** **B. oral** **C. S.C**	**8. which class of antiarrhythmic drugs can be used in case of atrial arrhythmia associated with emotion or exercise :** **A. class 1** **B. class 2** **C. Miscellaneous**

Ans. 1.B 2.C 3.A 4.A 5.B 6.B 7.A 8.B

MCQS

1. one of the action of class A1 is potassium channel block and this lead to :

A. Prolong the action potential duration and decrease the effective refractory period .
B. Prolong the action potential duration and increase the effective refractory period
C. prolong the QT interval
D. both B & C .

2. MEXILETINE use for treatment of emergency ventricular tachycardia following cardiac surgery or acute myocardial infarction

A. T
B. F

3. class 1 act on nodal tissue :

A. T
B. F

4. A patient brought to the emergency department unconscious. His relatives said the he have complained recently of hypotension, nausea and vomiting
ECG is immediately performed and it shows torsades de pointes. What is the most likely drug to cause those symptoms?

A. Flecainide
B. Propafenone
C. Qunidine
D. Lidocaine

5. which one of this drugs have no effect on AP duration :

A. Flecainide
B. Propafenone
C. Qunidine
D. Both a & b

6. a patient had ventricular tachycardia after acute myocardial infarction , what is the second drug of choice in this case :

A. Flecainide
B. Propafenone
C. Qunidine
D. PROCAINAMIDE

Ans. 1.D , 2.B , 3.B, 4.C, 5.D, 6.D

We hope we made this lecture easier for you
Contact us for any questions or comments
Good Luck !

Nada Dammas

Ahmed Aldakhil

Sara Alkharashi

Budoor alsalman

Jumana Albeeybe

Rawan Alotaibi

Areej Alwahaib

Ziyad Alajlan

Pharma_433@yahoo.com

@pharma_433