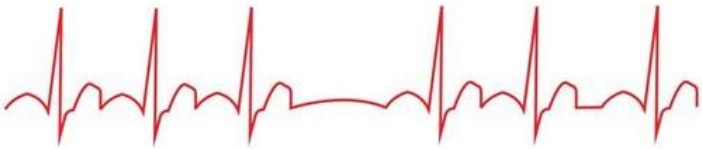
DEFINITION

- Arrhythmia is defined as loss of cardiac rhythm, especially irregularity of heartbeat.
- A group of conditions caused by an abnormality in the rate, regularity, or sequence of cardiac activation.

Normal Heatbeat

Irregular Heartbeat



What are the types of *arrhythmias?*

- *Tachycardia: A fast heart rhythm with* a rate of more than 100 beats per minute.
- Bradycardia: A slow heart rhythm with a rate below 60 beats per minute.
- Supraventricular arrhythmias: Arrhythmias that begin in the atria (the heart's upper chambers). "Supra" means above; "ventricular" refers to the lower chambers of the heart, or ventricles.
- Ventricular arrhythmias: Arrhythmias that begin in the ventricles (the heart's lower chambers).

Classification of Antiarrhythmic Drugs

Class I: Sodium channel blockers (membrane-stabilizing agents)

1 a: Block Na^+ channel and prolong action potential
1 b: Block Na^+ channel and shorten action potential
1 c: Block Na + channel with no effect on action potential

Class II: β- blockers

Class III: Potassium channel blockers (main effect is to prolong the action potential)

Class IV: Slow (L-type) calcium channel blockers

CLASS IA: QUINIDINE

- Depress pacemaker rate
- Depress conduction & excitability
- Slows repolarization & lengthens AP duration

  → due to K+ channel blockade with reduction of repolarizing outward current → reduce maximum reentry frequency → slows tachycardia
- (+) alpha adrenergic blocking properties → vasodilatation & reflex ↑ SA node rate

CLASS IA: QUINIDINE

- *Pharmacokinetics:*
  - Oral → rapid GI absorption
  - 80% plasma protein binding
  - 20% excreted unchanged in the urine → enhanced by acidity
  - $t_{1/2}$ = 6 hours
  - Parenteral → hypotension

- *Dosage:* 0.2 to 0.6 gm 2-4X a day

CLASS IA: QUINIDINE

- *Therapeutic Uses:*
  - Atrial flutter & fibrillation
  - Ventricular tachycardia
  - IV treatment of malaria

- *Drug Interaction:*
  - Increases digoxin plasma levels

CLASS IA: QUINIDINE

- *Toxicity:*
  - Antimuscarinic actions → inh. vagal effects
  - Quinidine syncope (lightheadedness, fainting)
  - Ppt. arrhythmia or asystole
  - Depress contractility & ↓ BP
  - Widening QRS duration
  - Diarrhea, nausea, vomiting
  - Cinchonism (HA, dizziness, tinnitus)
  - Rare: rashes, fever, hepatitis, thrombocytopenia,etc

CLASS IA: PROCAINAMIDE

- Less effective in suppressing abnormal ectopic pacemaker activity
- More effective Na+ channel blockers in depolarized cells
- Less prominent antimuscarinic action
- (+) ganglionic blocking properties → ↓PVR → hypotension (severe if rapid IV or with severe LV dysfunction)

CLASS IA: PROCAINAMIDE

PHARMACOKINETICS:

- Oral, IV, IM
- N-acetylprocainamide (NAPA) → major metabolite
- Metabolism: hepatic
- Elimination: renal
- $t_{1/2}$ = 3 to 4 hrs.

CLASS IA: PROCAINAMIDE

- *Dosage:*

  Loading IV – 12 mg/kg at 0.3 mg/kg/min or less rapidly

  Maintenance – 2 to 5 mg/min

- *Therapeutic Use:*

  2nd DOC in most CCU for the treatment of sustained ventricular arrhythmias asstd. with MI

CLASS IA: PROCAINAMIDE

- *Toxicity:*

  - ppt. new arrhythmias
  - LE-like syndrome
  - pleuritis, pericarditis, parenchymal pulmonary disease
  - ↑ ANA
  - nausea, DHA, rash, fever, hepatitis, agranulocytosis

CLASS IB: LIDOCAINE

- Intravenous route only
- Arrhythmias asstd with MI
- Potent abnormal cardiac activity suppressor
- Rapidly act exclusively on Na+ channels
- Shorten AP, prolonged diastole → extends time available for recovery
- Suppresses electrical activity of DEPOLARIZED, ARRHYTHMOGENIC tissues only

CLASS IB: LIDOCAINE

- Pharmacokinetics:
  - Extensive first-pass hepatic metabolism
  - $t_{1/2}$ = 1 to 2 hrs
- Dosages: loading- 150 to 200 mg
  maintenance- 2-4 mg
- Drug Interaction:
  propranolol, cimetidine – reduce clearance
- Therapeutic Use:
  DOC for suppression of recurrences of ventricular tachycardia & fibrillation in the first few days after AMI.

CLASS IB: PHENYTOIN

- Anti-convulsant with anti-arrhythmic properties
- Suppresses ectopic pacemaker activity
- Useful in digitalis-induced arrhythmia
- Extensive, saturable first-pass hepatic metabolism
- Highly protein bound
- Toxicity: ataxia, nystagmus, mental confusion, serious dermatological & BM reactions, hypotension, gingival hyperplasia
- D/I: Quinidine, Mexiletene, Digitoxin, Estrogen, Theophyllin, Vitamin D

CLASS II : BETA ADRENERGIC BLOCKERS

- ↑ AV nodal conduction time (↑ PR interval)
- Prolong AV nodal refractoriness
  - Useful in terminating reentrant arrhythmias that involve the AV node & in controlling ventricular response in AF & A.fib.
- Depresses phase 4 → slows recovery of cells, slows conduction & decrease automaticity
- Reduces HR, decrease IC Ca^{2+} overload & inhibit after depolarization automaticity
- Prevent recurrent infarction & sudden death in patients recovering from AMI

CLASS II: BETA ADRENERGIC BLOCKERS

- "membrane stabilizing effect"
  - Exert Na+ channel blocking effect at high doses
  - Acebutolol, metoprolol, propranolol, labetalol, pindolol
- "intrinsic sympathetic activity"
  - Less antiarrhythmic effect
  - Acebutolol, celiprolol, carteolol, labetalol, pindolol
- Therapeutic indications:
  - Supraventricular & ventricular arrhythmias
  - hypertension

CLASS III: POTASSIUM CHANNEL BLOCKERS

- Drugs that prolong effective refractory period by prolonging action potential
- Prolong AP by blocking K+ channels in cardiac muscle (↑ inward current through Na+ & Ca++ channels)
- *Quinidine & Amiodarone* → prolong AP duration
- *Bretylium & Sotalol* → prolong AP duration & refractory period
- *Ibutilide & Dofetilide* → "pure" class III agents
- Reverse use-dependence

CLASS IV: CALCIUM CHANNEL BLOCKERS

VERAPAMIL

- Blocks both activated & inactivated calcium channels
- Prolongs AV nodal conduction & effective refractory period
- Suppress both early & delayed afterdepolarizations
- May antagonize slow responses in severely depolarized tissues
- Peripheral vasodilatation → HPN & vasospastic disorders

- Oral administration → 20% bioavailability
- $t_{1/2}$ = 7 hrs
- Liver metabolism
- Dosage:

  IV: 5-10 mg every 4-6 hrs or infusion of 0.4 ug/kg/min

  Oral: 120-640 mg daily, divided in 3-4 doses
- Tptic use: SVT, AF, atrial fib, ventricular arrhythmias
- Toxicity: AV block, can ppt. sinus arrest

  constipation, lassitude, nervousness, peripheral edema