Arrhythmias

- Simple-dysfunction cause abnormalities in impulse formation and conduction in the myocardium.

- However, in clinic it present as a complex family of disorders that show variety of symptoms, for example, cardiac arrhythmias may cause the heart to:

  1. beat too slowly (sinus bradycardia).

  2. beat too rapidly (sinus or ventricular tachycardia, atrial or ventricular premature depolarization, atrial flutter).

  3. respond to impulses originating from sites other than the SA node.

Causes of Arrhythmias

- Abnormal automaticity, The SA node sets the pace of contraction for the myocardium, and underlying pacemakers are depolarized by impulses coming from the SA node.

  However, if other cardiac sites show enhanced automaticity, they may generate competing stimuli, and arrhythmia may occur.

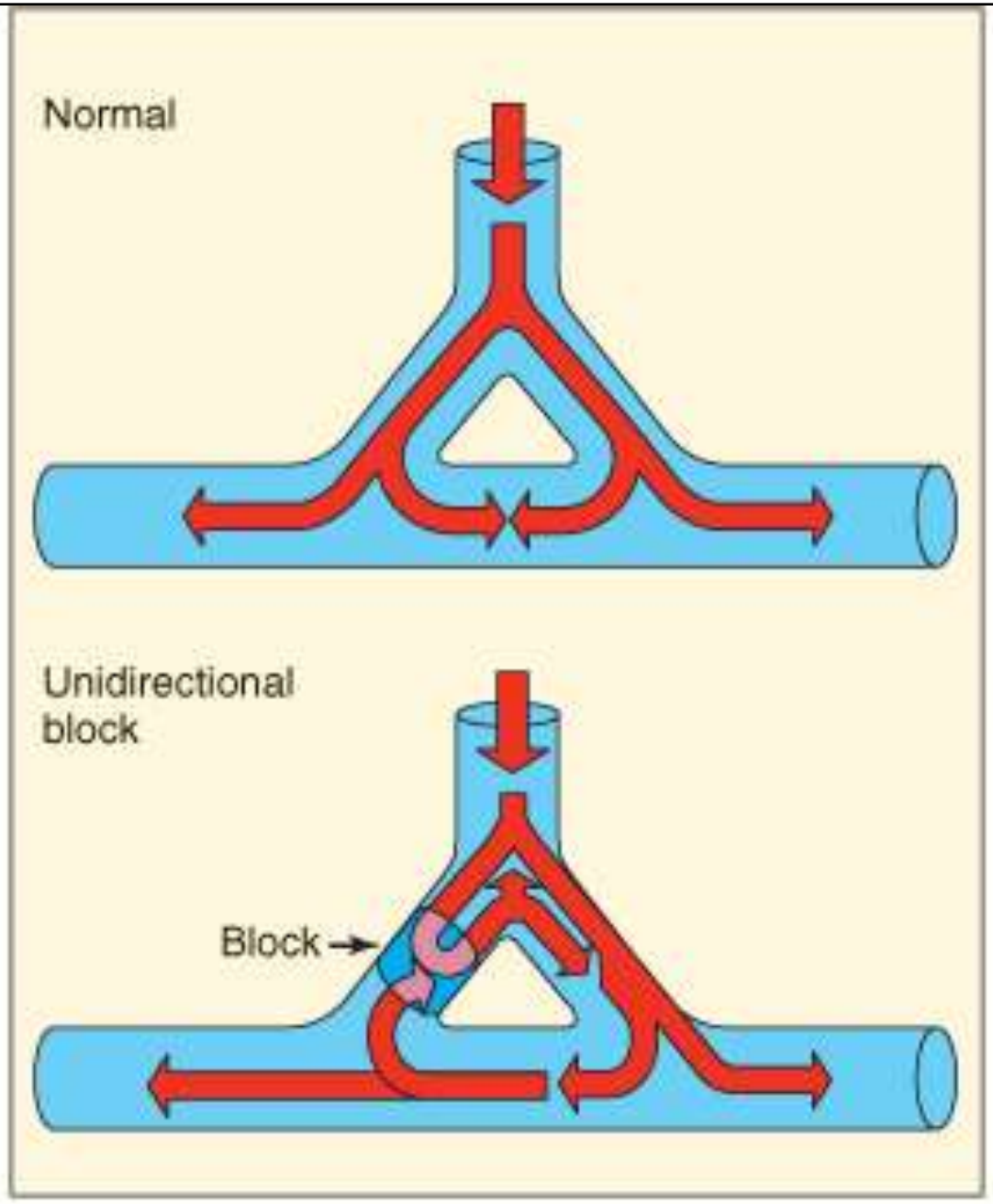
  Abnormal automaticity may also occur if myocardial cells are damaged, in which the damaged cells may stay depolarized during diastolic (the relaxation period) and reach firing threshold earlier than normal cells.

Causes of Arrhythmias

- Abnormalities in impulse conduction, impulses from pacemaker centers normally conducted divide to activate the entire ventricular surface.

  If unidirectional block happened, which may caused by myocardial injury or a prolonged refractory period results in an abnormal conduction pathway, this phenomena called reentry.

  Reentry is the most common cause of arrhythmia and can occur at any level of the cardiac conduction system.



Drugs and arrhythmias

- **Effect of drugs on automaticity**

  Most of the arrhythmic agents suppress automaticity by blocking either sodium or calcium channels to reduce the ratio of these ions to potassium,

  thus result in a reduction in the depolarization and raises the threshold of discharge to a less negative voltage.

- **Effect of drugs on conduction abnormalities**

  Prevent reentry by slowing conduction and/or increasing the refractory period,

IA

- **lengthen AP duration**

  Intermediate interaction with Na+ channels

  Quinidine, Procainamide, Disopyramide

Quinidine

- Bind to sodium channels and prevent sodium influx, and so slower the rapid depolarization.
- **Slows repolarization & lengthens AP duration**

  → due to K+ channel blockade with reduction of repolarizing outward current → reduce maximum reentry frequency → slows tachycardia

- Inhibit arrhythmias, which caused by increased automoticity, and also prevent reentry arrhythmias by producing bidirectional block.

Quinidine

- ***Therapeutic Uses:***
  - **Atrial flutter & fibrillation**
  - **Ventricular tachycardia**
- ***Toxicity:***
  - **Antimuscarinic actions → inh. vagal effects**
  - **Quinidine syncope (lightheadedness, fainting)**
  - **Depress contractility & ↓ BP**
  - **Diarrhea, nausea, vomiting**
  - **Cinchonism (Headache, dizziness, tinnitus)**

IB

- **shorten AP duration**

  rapid interaction with Na+ channels

  Lidocaine, Mexiletene, Tocainide, Phenytoin

Lidocaine and Mexiletine

- Lidocaine is a local anesthetic that decrease the duration of action potential, unlike quinidine, it suppresses arrhythmia caused by abnormal automaticity (quinidine used to treat arrhythmia caused by increased automoticity).

- Useful in the treatment of ventricular arrhythmia arising during myocardial ischemia (experience during myocardial infarction), has little effect on the atrial arrhythmias.

- Adverse effects: cardiac arrhythmia may occur but its main side effects are on the CNS, including confusion and convulsions.

- Mexiletine, oral drug, has similar action to Lidocaine and is used for chronic treatments of ventricular arrhythmias with previous myocardial infarction

Class II
Reduce or block sympathetic nervous system stimulation

- β-adrenergic blocking agents

Depress automaticity and decrease heart rate and contractibility, Propranolol being the most widely used.

Useful in treating tachyarrhythmias caused by increased sympathetic activity.

Esmolol **- short acting hence used primarily for intra-operative & other acute arrhythmias**

Sotalol **Used in supraventricular & ventricular arrhythmias in pediatric age group**

Class III
Prolong repolarization in phase 3

- **Amiodarone**

Approved only in serious ventricular arrhythmias

Broad spectrum of action on the

Very effective Na+ channel blocker

Markedly lengthens AP by blocking also K+ channels

Weak Ca++ channel blocker

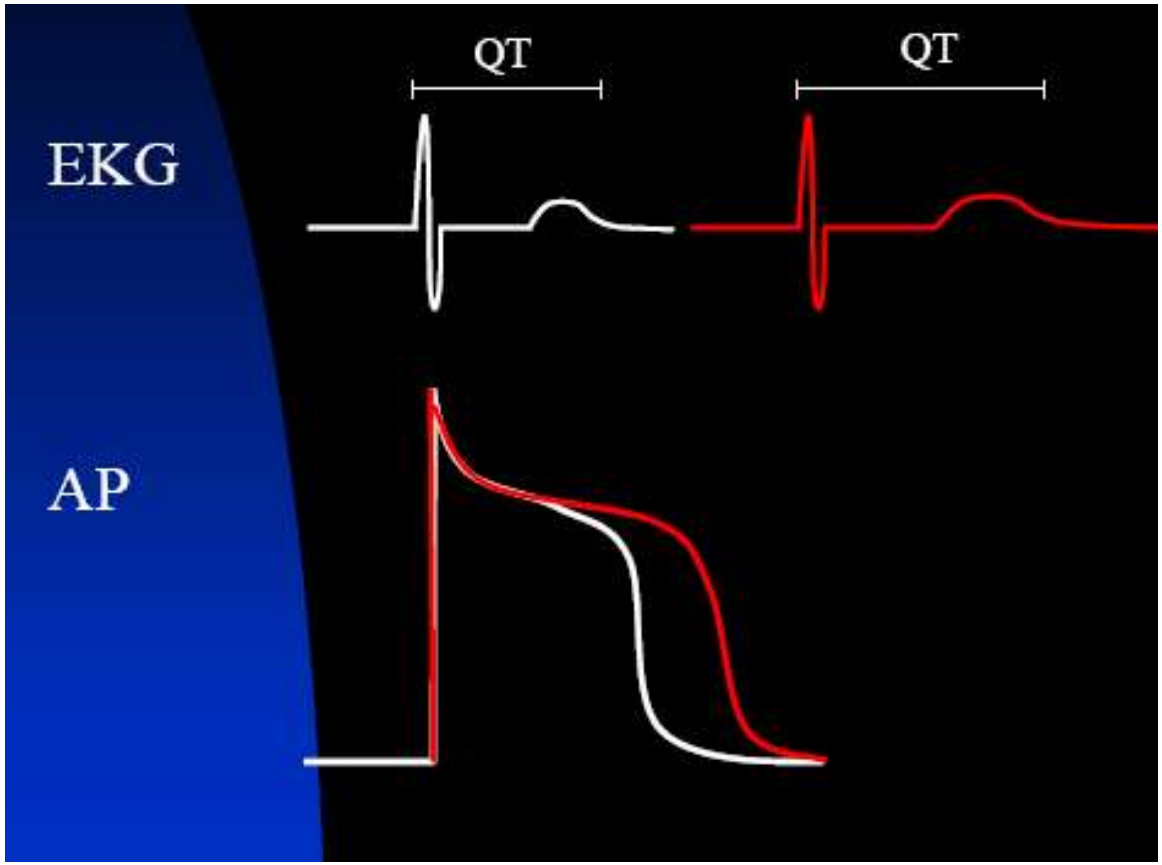
Noncompetetive inhibitor of beta adrenoceptors

Powerful inhibitor of abnormal automaticity.

Therapeutic Use: **Supraventricular & Ventricular arrhythmias**

Adverse effect: fatal pulmonary fibrosis

Effects of K+channel block



Adenosine

Intravenous Adenosine is the drug of choice for stopping acute superventricular.

Class IV

- **Calcium channel blockers**

Varapamil and dialtiazem They slow conduction and prolong the refractory periods.