Cardiac Arrhythmia

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Pharmacology

Heart

- The heart’s primary function is to pump blood throughout the body. This is done by an electrical connection that originates from the sinoatrial node (SA node).
- The electrical impulse begins at the SA node travels throughout the heart. The electrical impulse travels along a pathway through the heart to create the heart’s movement.
- The movement or pumping is what allows the blood to flow in and out of the heart in the appropriate direction.
- A disturbance in that electrical pathway can impact the heart’s ability to pump blood or heart rate.
- Changes to the heart’s electrical impulses result in irregular heart rhythm or cardiac arrhythmias.

What Is an Arrhythmia?

- An arrhythmia (also called dysrhythmia) is an irregular or abnormal heartbeat.
- **What are the types of arrhythmias?**
- **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).
- **Bradyarrhythmias:** Slow heart rhythms that may be caused by disease in the heart's conduction system, such as the sinoatrial (SA) node, atrioventricular (AV) node or HIS-Purkinje network.

What Are the Types of Arrhythmias?

Arrhythmias are divided up by where they happen. If they start in the ventricles, or lower chambers of your heart, they're called ventricular. When they begin in the atria, or upper chambers, they're called supraventricular.

Doctors also group them by how they affect your resting heart rate. Bradycardia is a heart rate of fewer than 60 beats per minute. Tachycardia is more than 100 beats per minute.

❑ Supraventricular arrhythmias include:

- ❖ Premature atrial contractions. These are early extra beats. They're harmless and generally don't need treatment.
- ❖ Atrial fibrillation (AFib). The upper chambers of your heart contract in an unusual way. Your heart might beat more than 400 times a minute.
- ❖ Atrial flutter. This is usually more organized and regular than atrial fibrillation. It happens most often in people who have heart disease and in the first week after heart surgery. It often changes to atrial fibrillation.
- ❖ Paroxysmal supraventricular tachycardia (PSVT). This is a rapid heart rate, usually with a regular rhythm. It begins and ends suddenly.
- ❖ Accessory pathway tachycardias. You can have a rapid heart rate because of an extra pathway between your heart's upper and lower chambers. Think of it as an extra road on your way home as well as your usual route. When that happens in your heart, it can cause a fast rhythm.
- ❖ AV nodal reentrant tachycardia (AVNRT). This is caused by an extra pathway through a part of your heart called the AV node. It can cause heart palpitations, fainting, or heart failure.

What Are the Types of Arrhythmias? (Cont)

- Ventricular arrhythmias include:
  - Premature ventricular contractions (PVCs). These are among the most common arrhythmias. They're the "skipped heartbeat" that many of us feel sometimes.
  - Ventricular tachycardia (V-tach). This is a rapid heart rhythm starting from your heart's lower chambers. Because your heart is beating too fast, it can't fill with enough blood. This can be a serious arrhythmia, especially in people who have heart disease, and it may be linked to other symptoms.
  - Ventricular fibrillation (V-fib). This happens when your heart's lower chambers quiver and can't contract or pump blood to the rest of your body. It’s a medical emergency that must be treated with CPR and defibrillation as soon as possible.
  - Long QT syndrome. Your heart’s lower chambers take too long to contract and release. This may cause dangerous rhythm problems and death.

What Are the Types of Arrhythmias?(cont)

- Another type of arrhythmia, bradyarrhythmia,

is a slow rhythm because of disease in your heart's electrical system or because of medication. It may make you pass out or feel like you will. Types of bradyarrhythmia include:

- Sinus node dysfunction. This is caused by a problem with your heart's sinus node, its natural pacemaker.
- Heart block. There’s a delay or a block of the electrical impulse as it travels from your heart's sinus node to its lower chambers.

If you have symptoms, they may include:

- Palpitations (a feeling of skipped heartbeats, fluttering, or "flip-flops")
- Pounding in your chest
- Dizziness or feeling lightheaded
- Fainting
- Shortness of breath
- Chest pain or tightness
- Weakness or fatigue (feeling very tired)
- Anxiety
- Blurry vision
- Sweating

What Causes Arrhythmia?

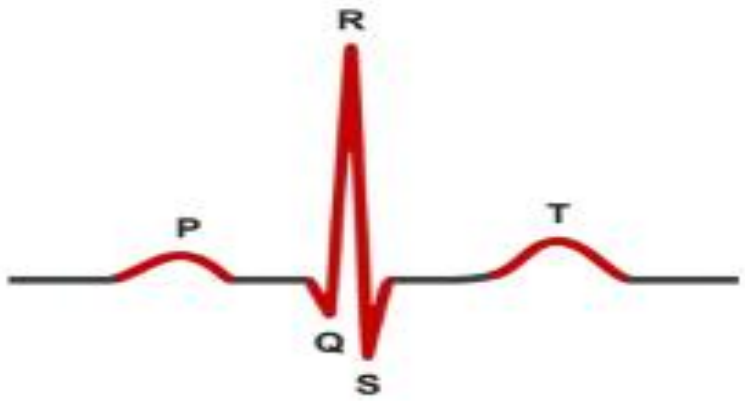
- You could have an arrhythmia even if your heart is healthy. Or it could happen because of:
- Heart disease
- The wrong balance of electrolytes (such as sodium or potassium) in your blood
- Heart injury or changes such as reduced blood flow or stiff heart tissue
- Healing process after heart surgery
- Infection or fever
- Certain medications
- Problems with the electrical signals in your heart
- Strong emotions, stress, or surprise
- Things in your daily life like alcohol, tobacco, caffeine, or exercise

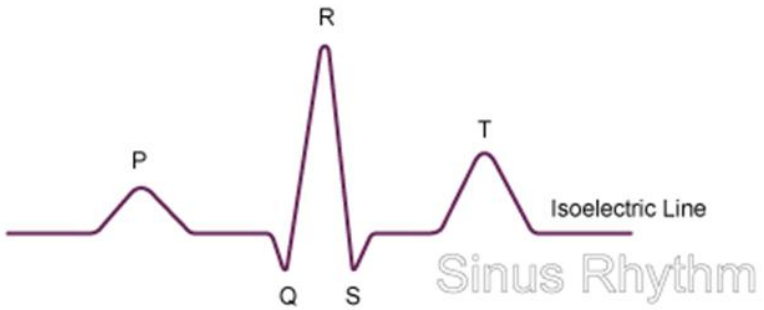
What Are Some Arrhythmia Risk Factors?

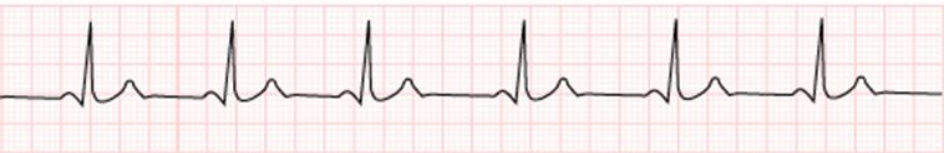
Things that may make you more likely to have an arrhythmia include your:

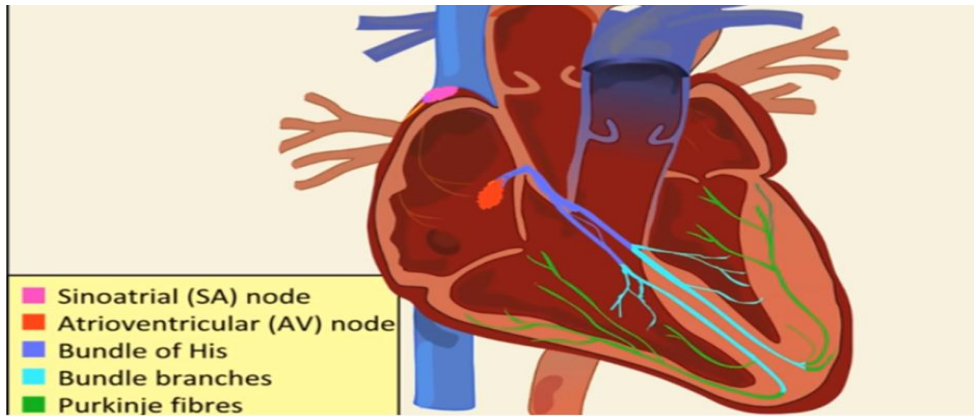
- Age. The chances go up as you get older.
- Genes. Your odds might be higher if a close relative has had an arrhythmia. Some types of heart disease can also run in families.
- Lifestyle. Alcohol, tobacco, and recreational drugs can raise your risk.
- Medical conditions. High blood pressure, diabetes, low blood sugar, obesity, sleep apnea, and autoimmune disorders are among the conditions that may cause heart rhythm problems.
- Environment. Things in the world around you, like air pollution, can make an arrhythmia more likely.

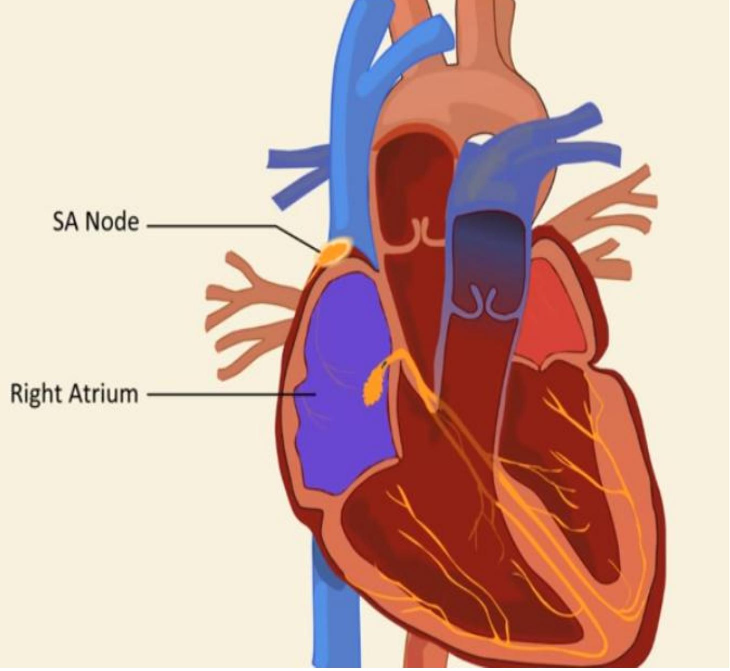
Normal and Abnormal Heart Rate

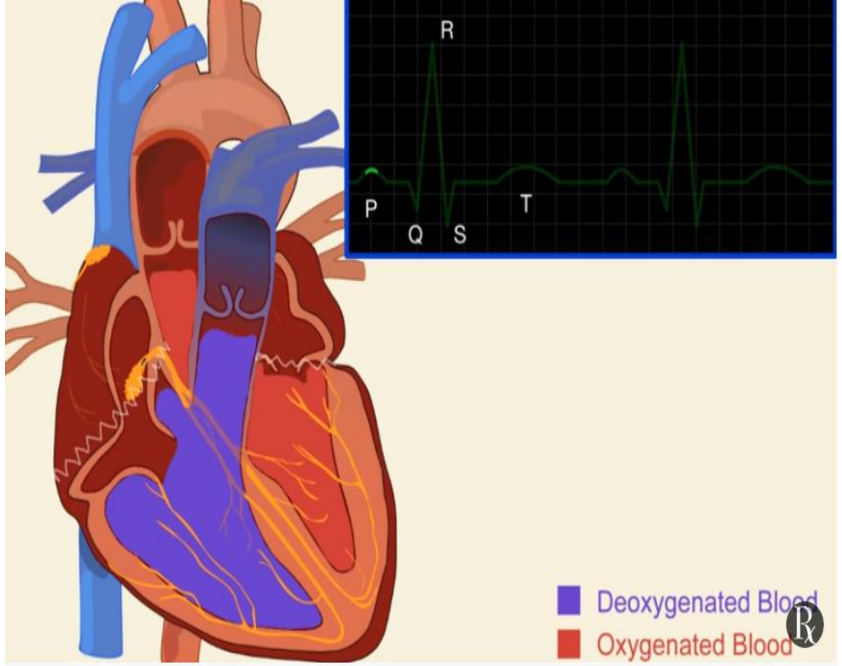









SA Node
Right Atrium


R
P
Q
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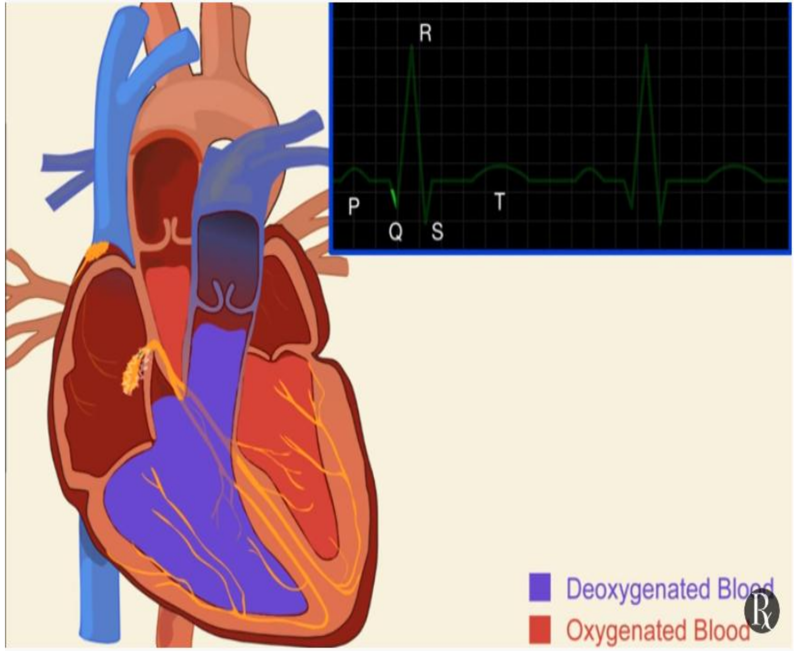
T
Deoxygenated
Oxygenated Blood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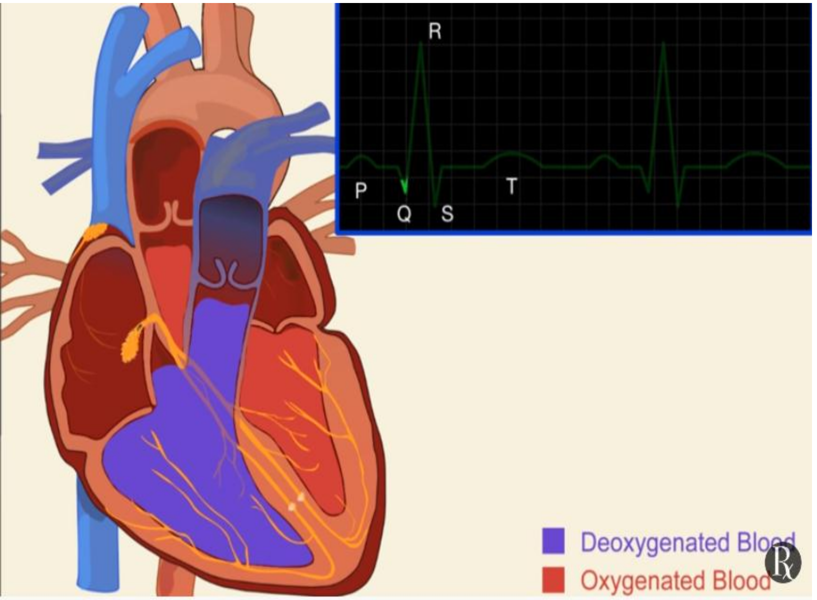
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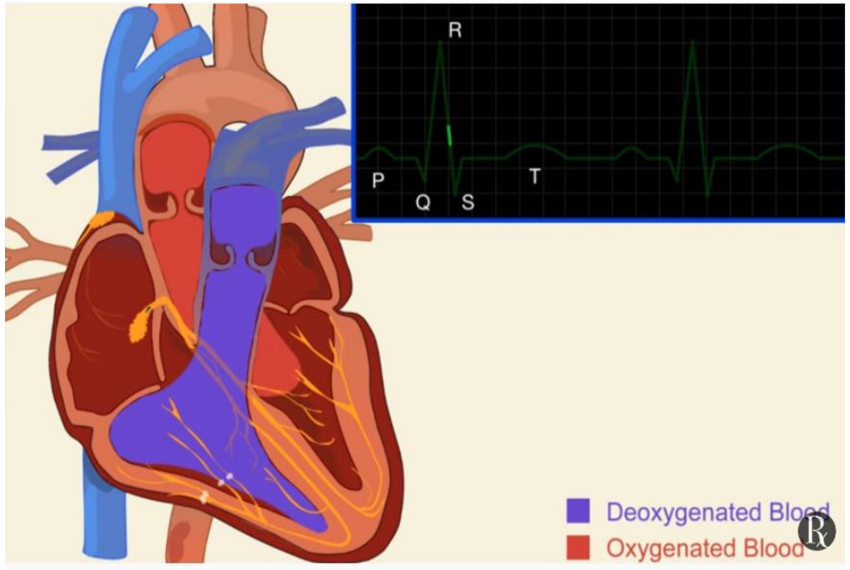
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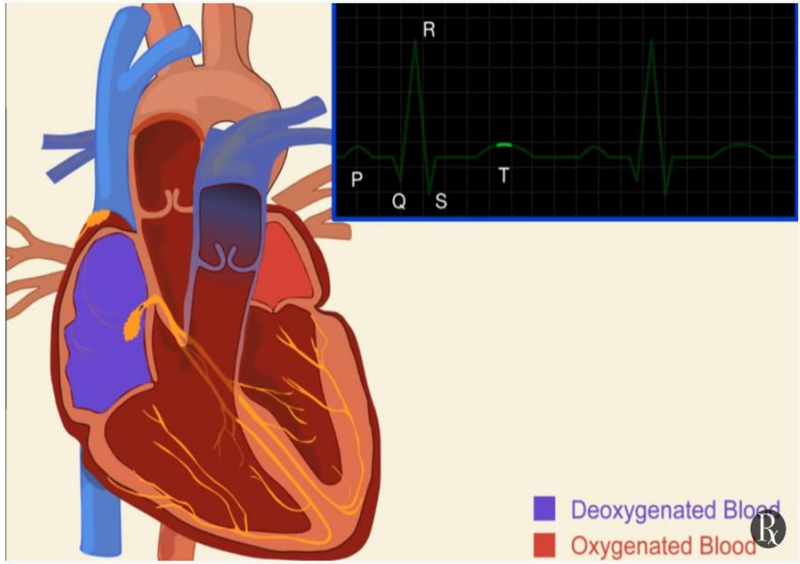
R
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Q
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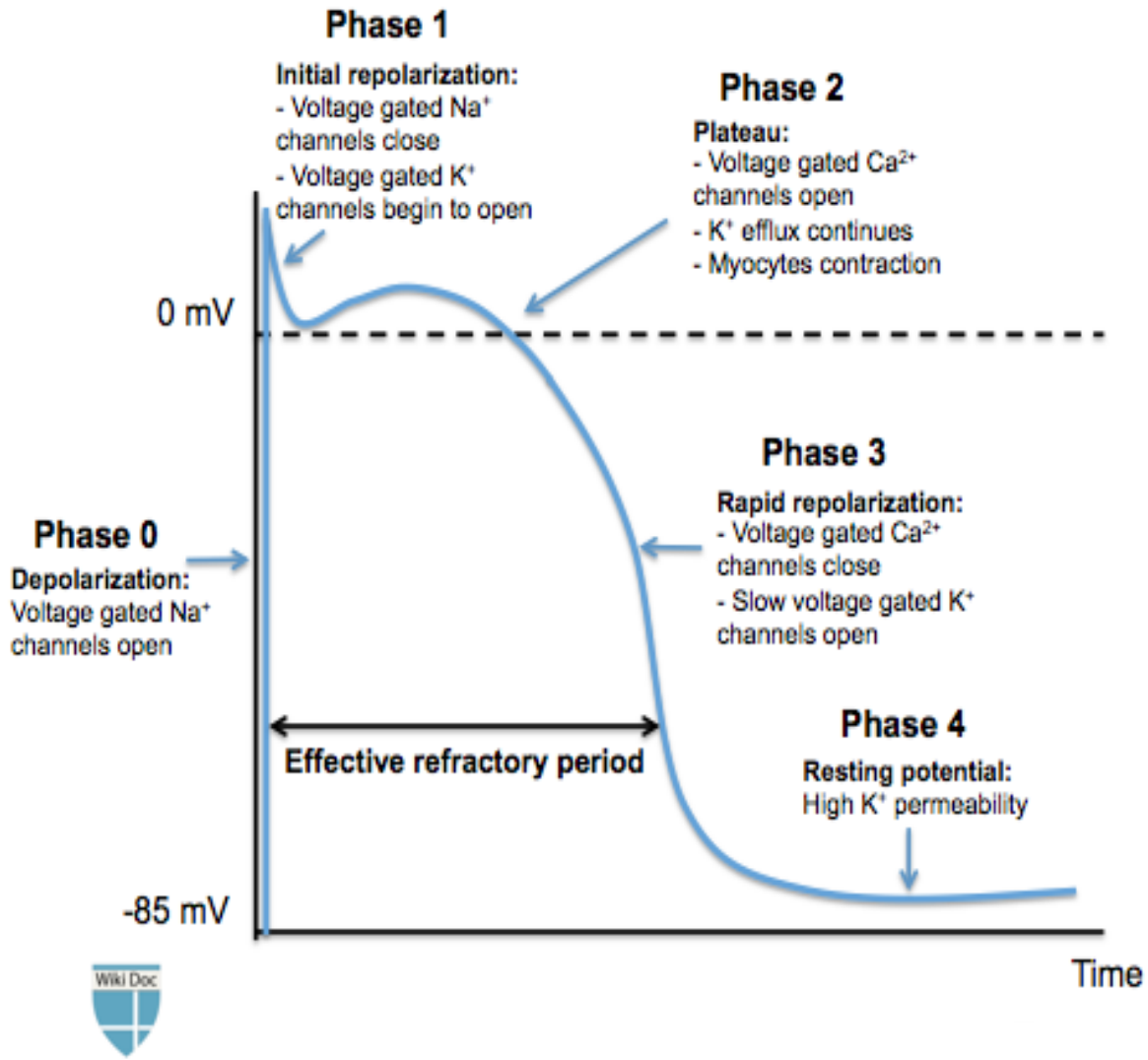
T
Deoxygenated
Oxygenated Blood

Phases of a cardiac action potential

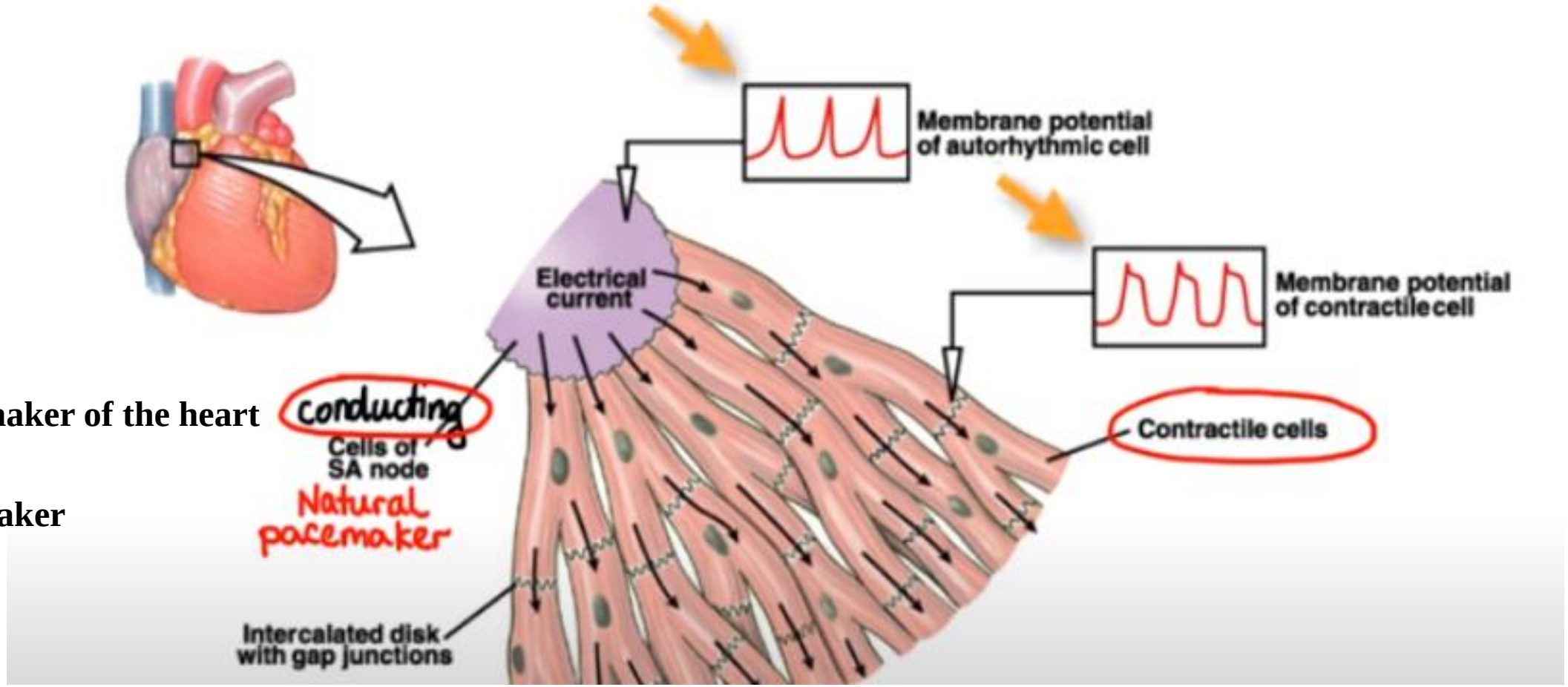
- Phase-0 - rapid depolarization
- Phase-1 – repolarization
- phase-2 - plateau phase
- Phase-3 - rapid repolarization
- Phase-4 – stable phase or resting membrane potential



Cardiac cells types

1.Natural pacemaker of the heart

2.latent pacemaker



Action potential

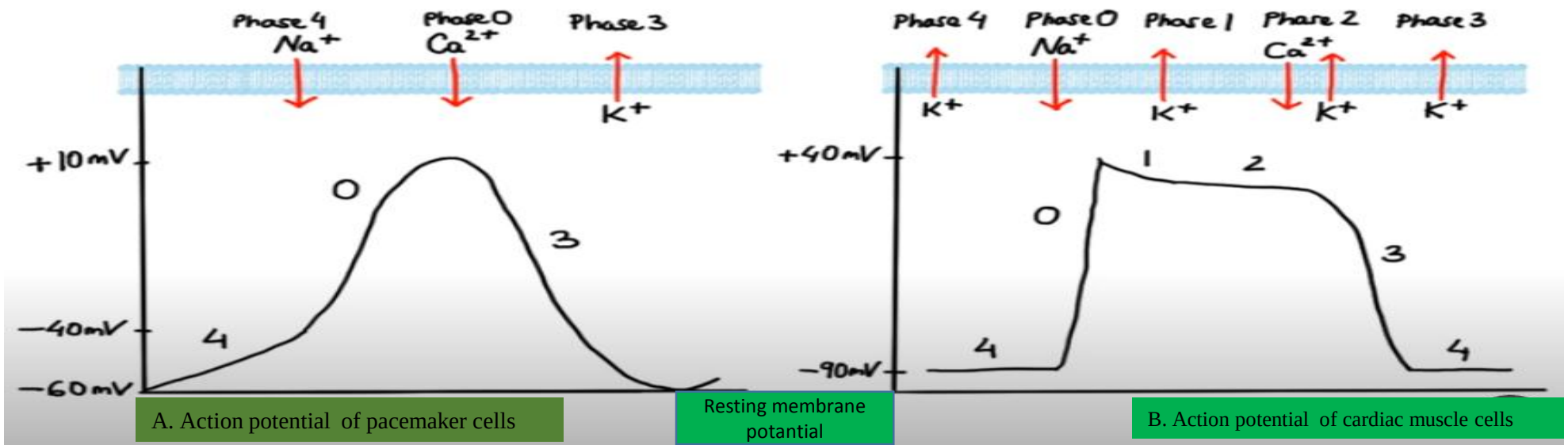
A. Action potential of pacemaker cells

B. Action potential of cardiac muscle cells

1. Cardiac cells contain and surrounded electrolyte fluids the main ions responsible for the electrical activity within the heart (sodium and calcium and potassium)

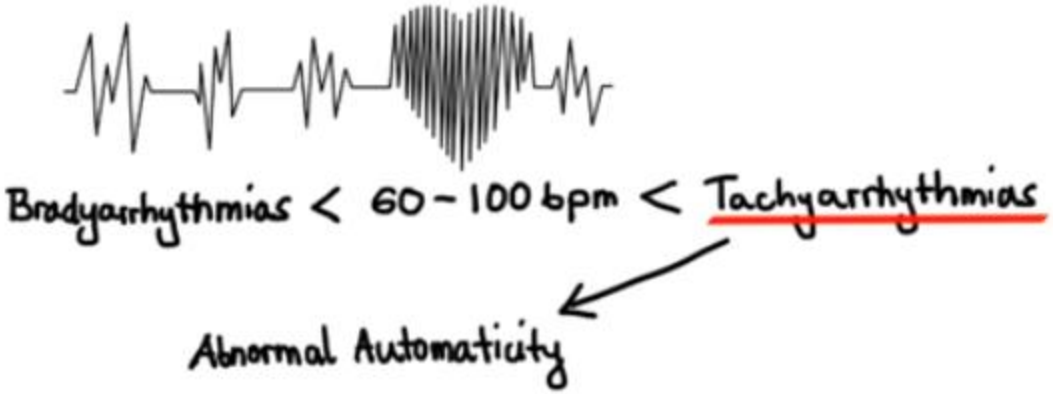
2. When cardiac cells are stimulated by an electrical impulse their membranes permeability change and the ions move across the membrane that generating an action potential

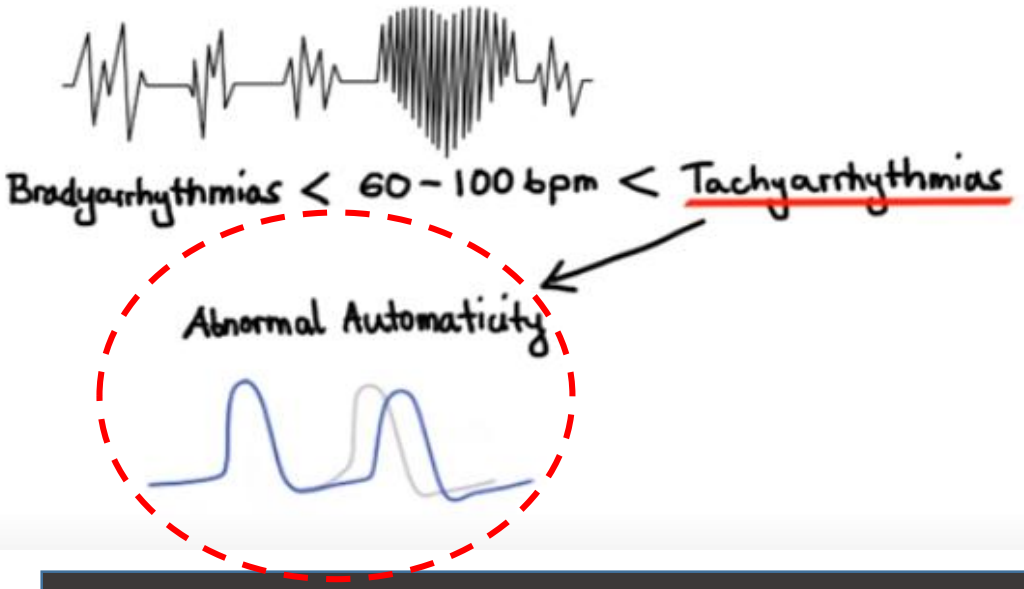
3. There is no phase 1 or phase 2 in the action potential of the pacemaker cells



Tachyarrhythmias Mechanism

First mechanism



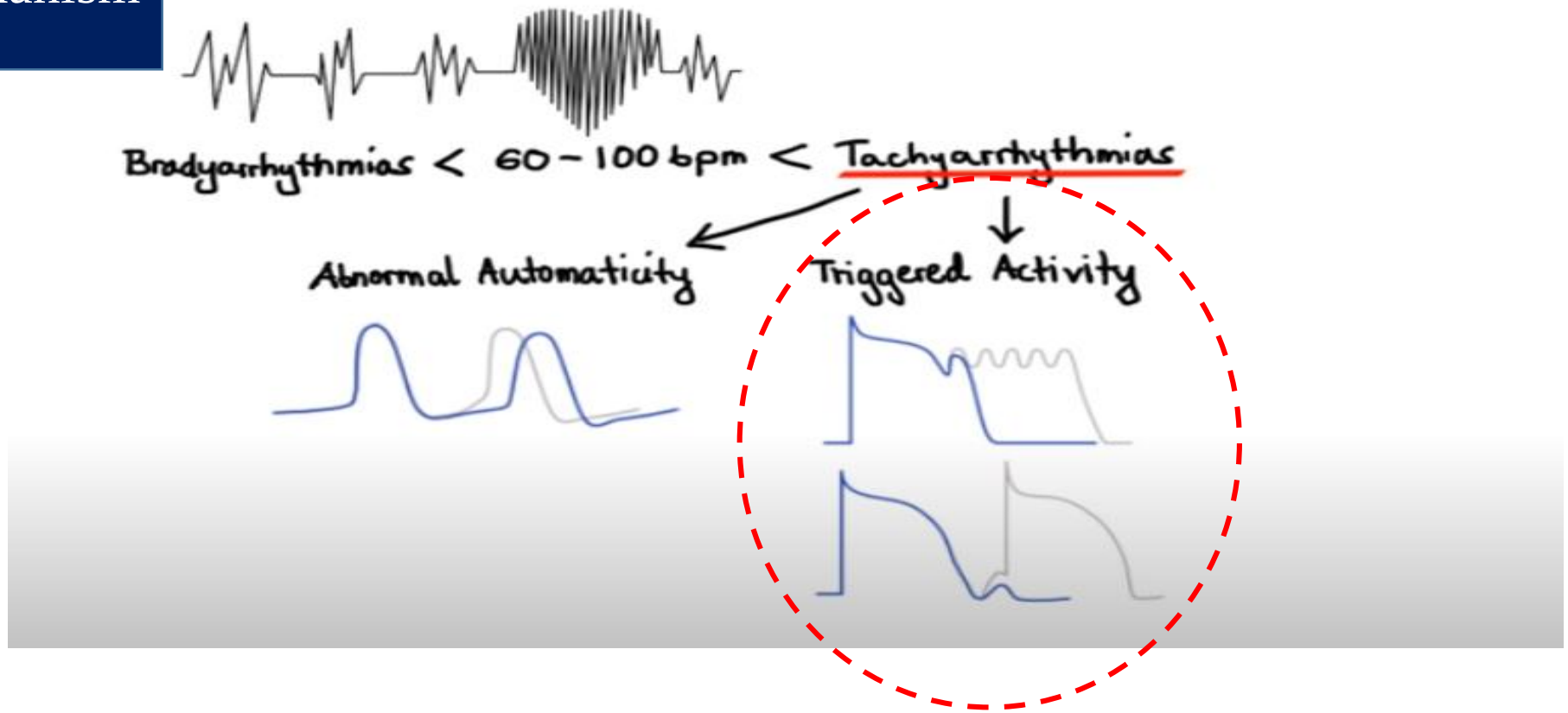


the cell membrane becomes abnormally permeable to sodium during phase 4 which results in increase in the slope of phase 4

Increase in the slope od depolarization and
That generate impulse faster in the SA node

Tachyarrhythmias Mechanism

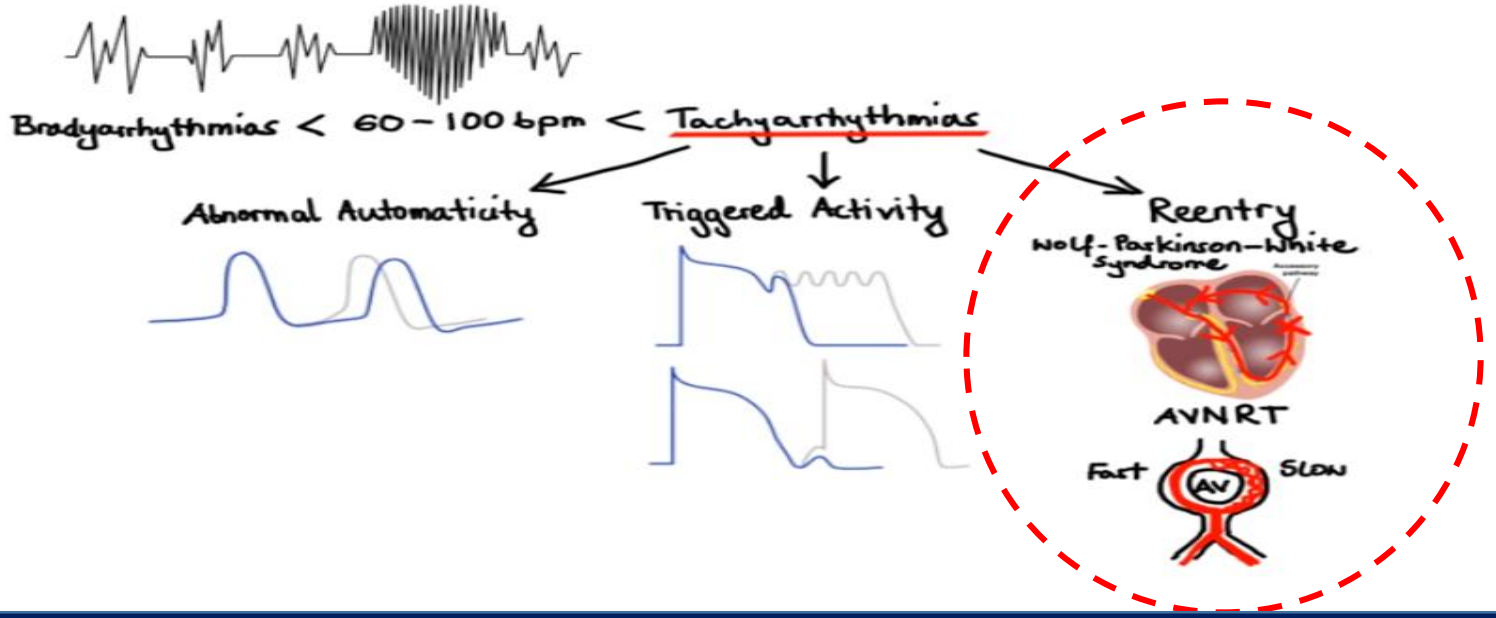
Second mechanism



- Trigger activity involve the abnormal leakage of positive ions into the cardiac cell leading to this bump on the action potential called after depolarization
- these after depolarization can occure during phase 2 , 3, or 4

Tachyarrhythmias Mechanism

Third mechanism



- Third types of mechanism is called reentry example of the wolff- Parkinson –white
- Syndrome in which an extra or so called accessory pathway exists between the upper and lower chambers of the heart
- So normally the electrical signal travels from the AV node to bundle branches and once it reaches the Purkinje fibers it stop and wait or another signal from the SA node.
- Now when the accessory pathway appears the signal travels through this pathway from ventricles back to atria causing them to contract before SA node fires again this creates this abnormal loop of electrical activation circulating through region of heart tissue causing tachyarrythemia
- another example of reentry is atrioventricular nodal reentry tachycardia AVNRT for short so typically there are two anatomic pathways for carrying signal through the AV node first pathway is called the fast pathway because it allows fast conduction however it has a long refractory period meaning it recovery slowly , on the other side this second pathway is called the slow pathway because it only allows slow conduction and because of that it has short refractory period meaning it recovers fast

Diagnosis

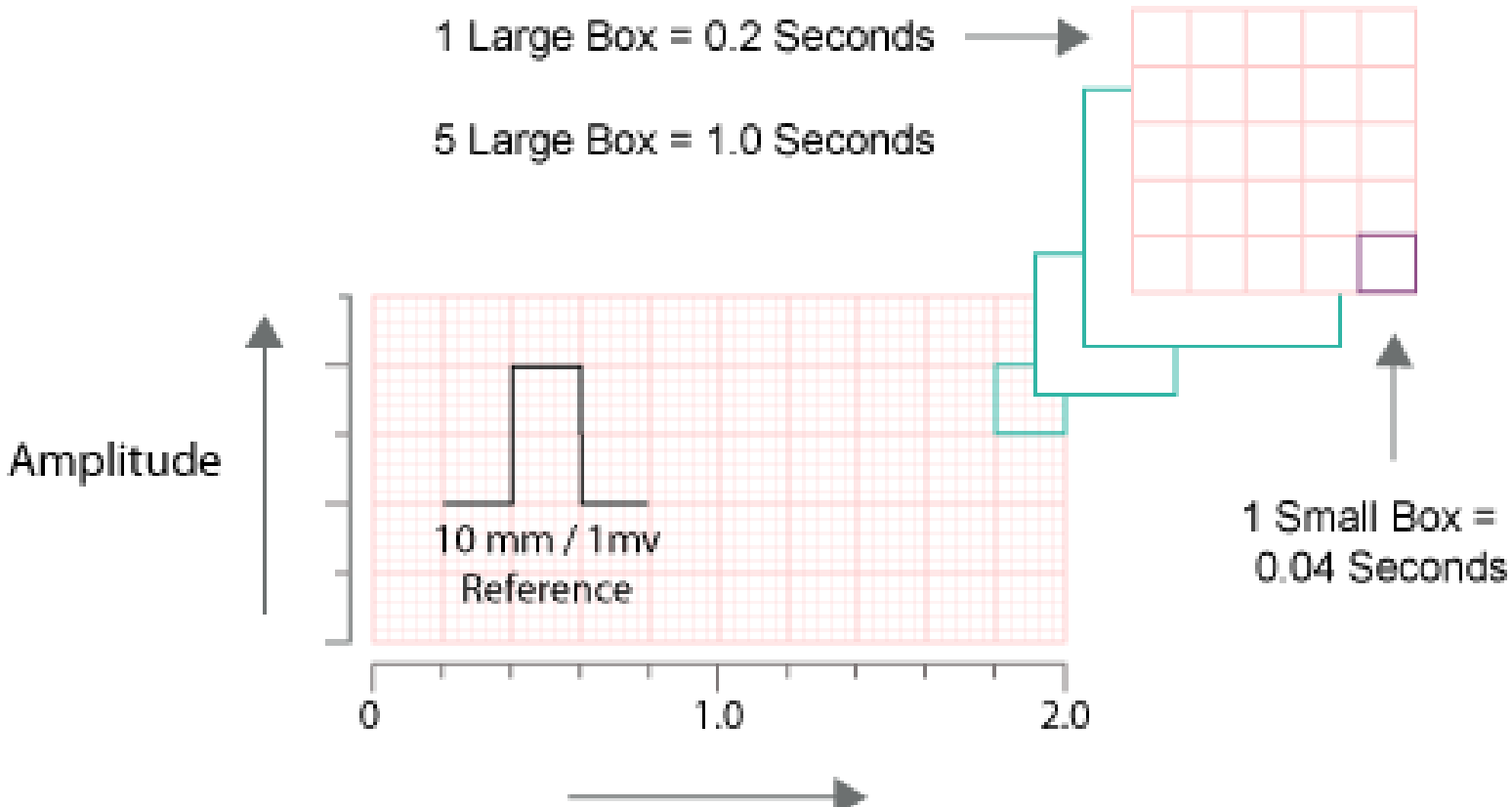
- To diagnose a heart arrhythmia, the doctor will usually do a physical exam and ask questions about your medical history and symptoms. Tests may be done to confirm an irregular heartbeat and look for conditions that can cause arrhythmias, such as heart disease or thyroid disease.

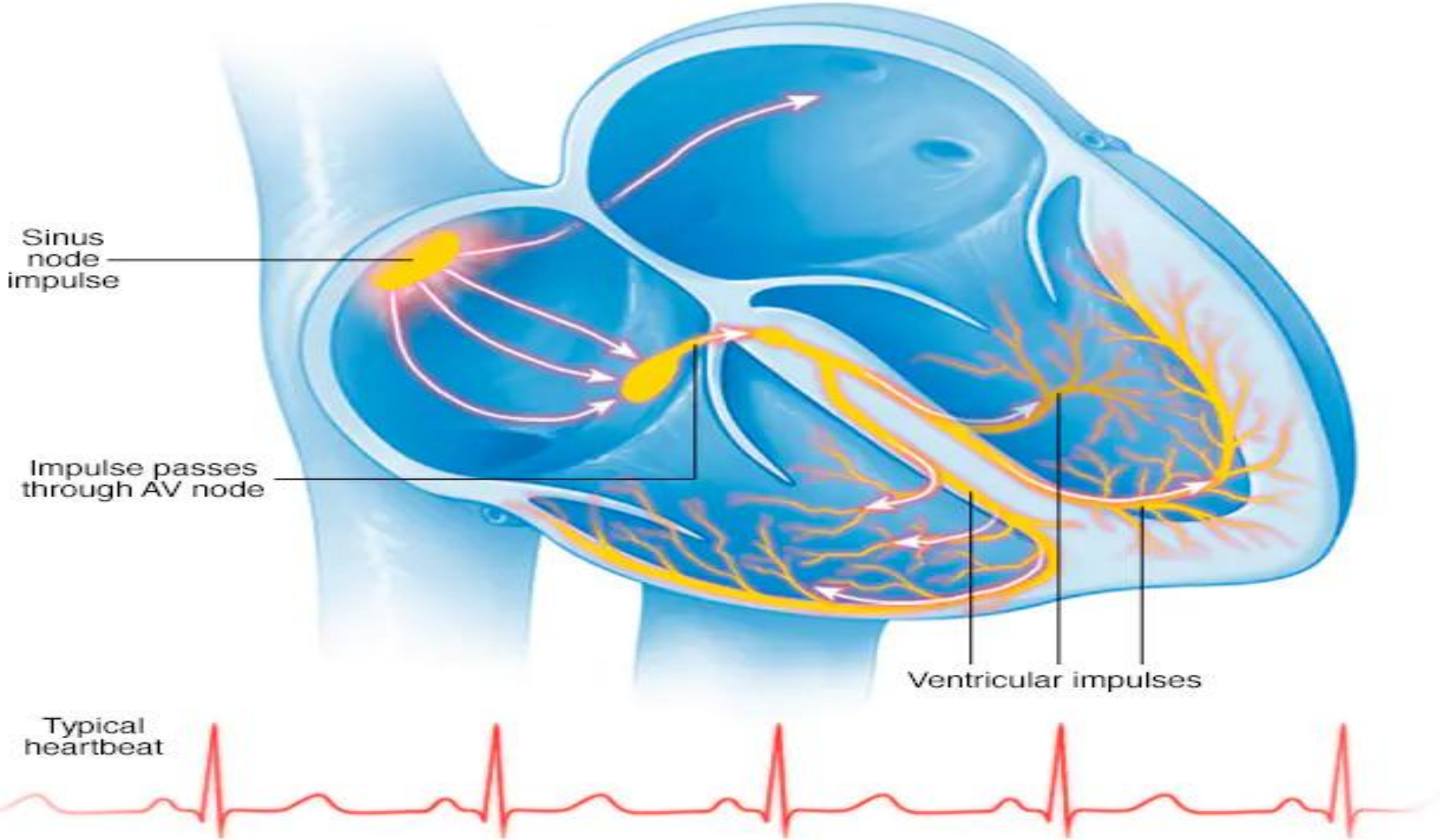
- Tests to diagnose heart arrhythmias may include:

- Electrocardiogram (ECG or EKG). During an ECG, sensors (electrodes) that can detect the electrical activity of the heart are attached to the chest and sometimes to the arms or legs. An ECG measures the timing and duration of each electrical phase in the heartbeat.

Role of the ECG Machine

The ECG machine is designed to recognise and record any electrical activity within the heart. It prints out this information on ECG paper made up of small squares 1mm squared.




Sinus node impulse
Impulse passes through AV node
Ventricular impulses
Typical heartbeat

What medications treat arrhythmias?

A variety of drugs are available to treat arrhythmias.

Because everyone is different, it may take trials of several medications and doses to find the one that works best for patient . Several types of drugs are used:

- Anti-arrhythmic drugs are drugs used to convert the arrhythmia to sinus rhythm (normal rhythm) or to prevent an arrhythmia.
- Heart-rate control drugs are drugs used to control the heart rate.
- Anticoagulant or antiplatelet therapy are drugs, such as warfarin (a blood thinner) or aspirin, that reduce the risk of clots forming or having strokes.
- Medications used to treat related conditions that may be causing an abnormal heart rhythm.

How Are Arrhythmias Treated?

Treatment will depend on what type of arrhythmia.

❑Medications : Medicines that treat uneven heart rhythms include:

- Adenosine (Adenocard)
- Atropine (Atropen)
- Beta-blockers
- Calcium channel blockers
- Digoxin (Digitek, Digox, Lanoxin)
- Potassium channel blockers
- Sodium channel blockers

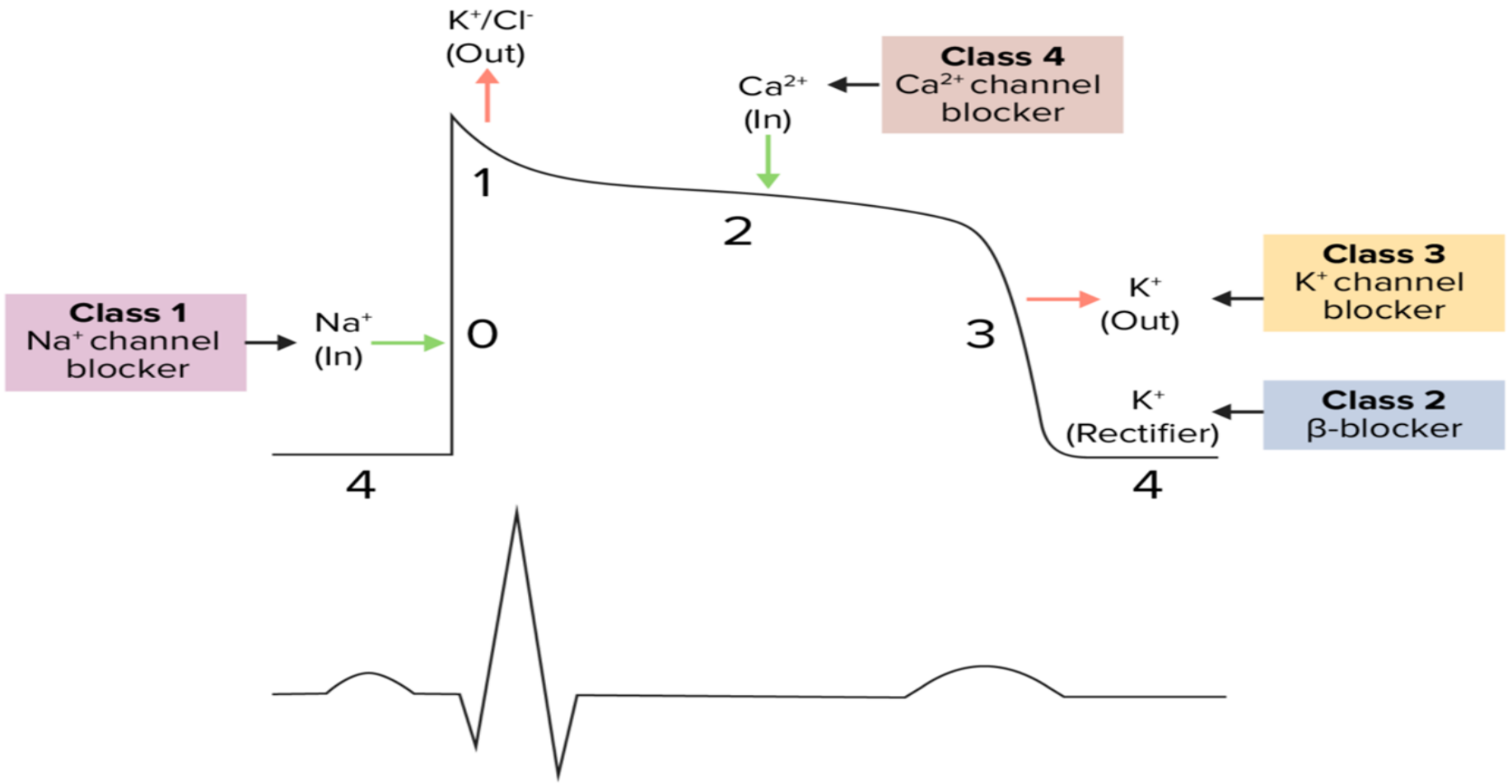
Antiarrhythmic Drugs

- The effects of cardiac antiarrhythmic drugs on the action potential and effective refractory period of the cardiac action potential determine the clinical effect of these drugs.
- Drugs that primarily **block inward sodium ion flow** will slow conduction and **result in suppression of the maximum upstroke velocity (Vmax) of the cardiac action potential.**
- **Potassium channel blocking drugs prolong repolarization by increasing the duration of the cardiac action potential** and the effective refractory period **resulting in prolongation of the QTc interval on the electrocardiogram (ECG).**
- **Calcium channels are present in myocardial cells, and the α subunit of L and T calcium ion channels is the site of action of some cardiac antiarrhythmic drugs.**

Classification

- Cardiac arrhythmic drugs are most commonly classified into four groups based primarily on the ability of the drug to control arrhythmias by blocking specific ion channels and currents during the cardiac action potential
- **Few cardiac antiarrhythmic drugs demonstrate completely specific effects on cardiac ion channels.**
- **Other characteristics including the impact of the drug on autonomic nervous system activity and myocardial contractility may be more important clinically.** Antiarrhythmic drugs also differ in their pharmacokinetics and efficacy in treating specific types of arrhythmias

Phase and place of action



Vaughan-Williams classification

- Most commonly used classification for antiarrhythmic drugs
- 5 classes based on the general effect (mechanism of action) of the drug class:
  - Class 1: Na channel blockers (divided into 3 subgroups):
    - 1A: prolong the action potential
    - 1B: shorten the action potential
    - 1C: minimal effect on action potential duration
  - Class 2: beta blockers
  - Class 3: K channel blockers
  - Class 4: Ca channel blockers
  - Class 5: agents that cannot be categorized into the above groups

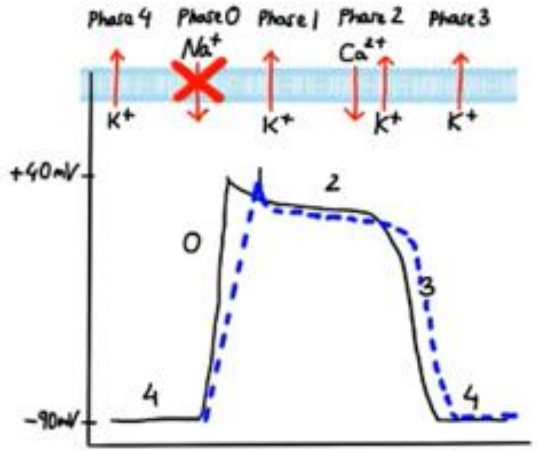
- **All anti-arrhythmic drugs act by altering the movement of electrolytes within the electrical conduction pathways of the myocardium.**
- The Vaughan Williams classification system groups drugs according to their ability to block the movement of one or more of these ions across the myocardial cell membrane.

Antiarrhythmic Drugs

Vaughn-Williams Classification of Antiarrhythmic Drugs

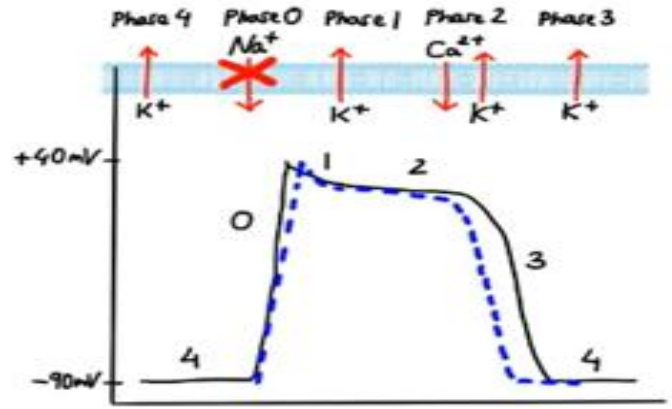
Class	Mechanism of action	Main effects	Drug examples
IA	Moderate block of sodium (Na) channels	Moderate decrease in Phase 0 depolarization; QRS and QT intervals prolonged	Quinidine, procainamide, disopyramide
IB	Mild block of sodium (Na) channels	Mild decrease in Phase 0 depolarization, decrease in ventricular automaticity	Lidocaine, mexiletine
IC	Marked block of sodium (Na) channels	Marked decrease in Phase 0 depolarization, prolongation of QRS interval	Flecainide, propafenone
II	Blockade of adrenergic beta-1 receptors	Decrease in heart rate, AV conduction, and ventricular automaticity; increased PR interval	Propranolol, acebutolol, esmolol
III	Blockade of potassium (K) channels	Prolongation of ventricular repolarization (Phases 1–3), prolongation of QT interval	Amiodarone, dofetilide, ibutilide, sotalol
IV	Blockade of calcium (Ca) channels in SA and AV nodes	Decrease in heart rate and AV conduction, increase in PR interval	Diltiazem, verapamil

Vaughan–Williams CLASS I A



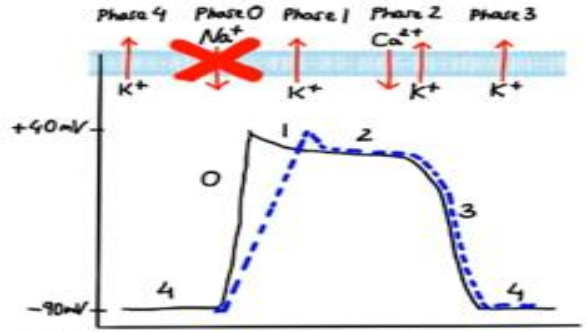
Procainamide Quinidine Disopyramide

Vaughan–Williams CLASS I B



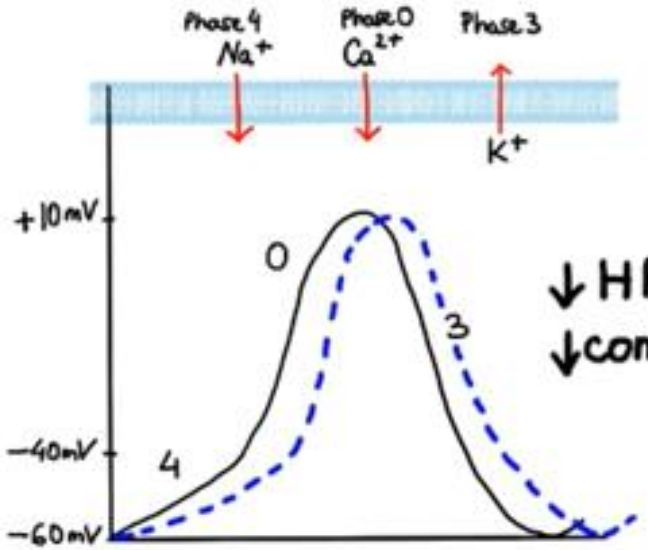
Lidocaine Mexiletine

Vaughan–Williams CLASS I C



Flecainide Propafenone

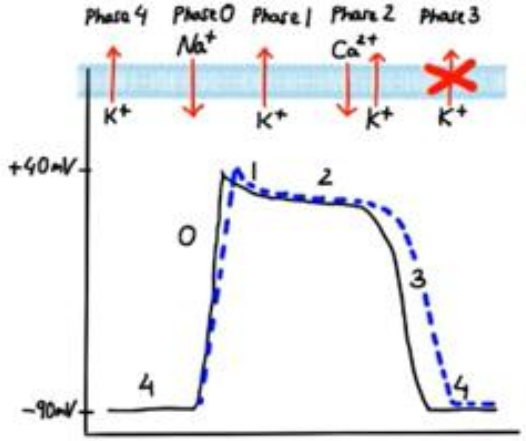
Vaughan–Williams CLASS II



↓HR
↓contractility

Propranolol Metoprolol Atenolol Esmolol

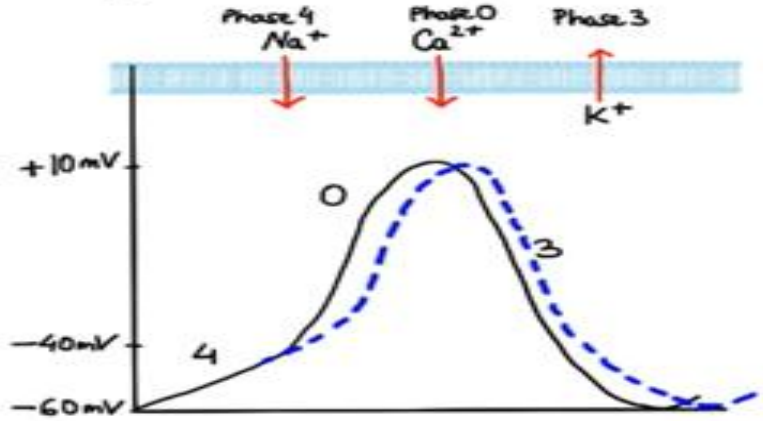
Vaughan–Williams CLASS III



Amiodarone Dronedarone Sotalol Dofetilide Ibutilide

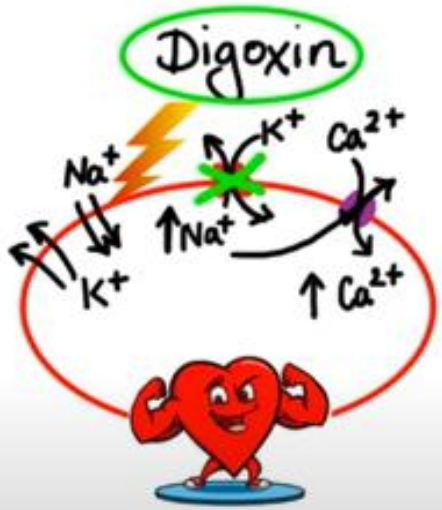
(β)

Vaughan–Williams CLASS IV

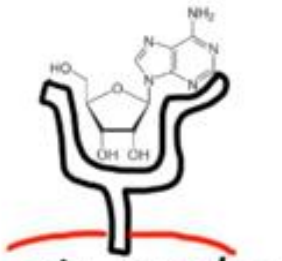


Verapamil Diltiazem

NONDIHYDROPYRIDINE CALCIUM CHANNEL BLOCKERS

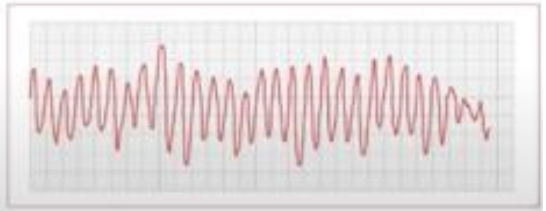


Adenosine



A1-Receptor

Magnesium Sulfate



Sinus tachycardia	Class II, IV	Other underlying causes may need treatment
Atrial fibrillation/flutter	Class IA, IC, II, III, IV digitalis	Ventricular rate control is important goal; anticoagulation is required
Paroxysmal supraventricular tachycardia	Class IA, IC, II, III, IV adenosine	
AV block	atropine	Acute reversal
Ventricular tachycardia	Class I, II, III	
Premature ventricular complexes	Class II, IV magnesium sulfate	PVCs are often benign and do not require treatment
Digitalis toxicity	Class IB magnesium sulfate	

Arrhythmia Prevention

- You can’t always prevent arrhythmias. Regular checkups with your doctor can help keep you from having more heart rhythm problems. Be sure they know all of the medications you’re taking. Some cold and cough medicines can trigger an arrhythmia, so talk to your doctor before using them.

❑They may also recommend some lifestyle changes:

- Eat a healthy diet. Get plenty of fruits and vegetables, fish, and plant-based proteins. Avoid saturated and trans fats.
- Keep cholesterol and blood pressure under control.
- Don’t smoke.
- Keep a healthy weight.
- Exercise regularly.
- Manage stress.
- Limit alcohol and caffeine.

Antiarrhythmic Drug Pharmacology

Quinidine

- Quinidine is a class IA drug that is effective in the treatment of acute and chronic supraventricular arrhythmias.

- Due to its side effect profile and low therapeutic index and the availability of newer agents, quinidine is rarely used.

- It can prevent recurrence of supraventricular tachyarrhythmias or suppress premature ventricular contractions and can slow the ventricular rate in the presence of atrial fibrillation, and about 25% of patients with new-onset atrial fibrillation will convert to normal sinus rhythm when treated with quinidine.

- **Supraventricular tachyarrhythmias associated with Wolff-Parkinson-White syndrome are effectively suppressed by quinidine.**

Quinidine

- Quinidine is most often administered orally in a dose of 200 to 400 mg four times daily.
- Oral absorption of quinidine is rapid, with peak concentrations in the plasma attained in 60 to 90 minutes and an elimination half-time of 5 to 12 hours.
- The therapeutic blood level of quinidine is 1.2 to 4.0 µg/mL.
- Intravenous (IV) quinidine is rarely used due to vasodilation and myocardial depression.

Metabolism and Excretion

- Quinidine is hydroxylated in the liver to inactive metabolites, which are excreted in the urine.
- About 20% of quinidine is excreted unchanged in the urine.
- Enzyme induction significantly shortens the duration of action of quinidine.
- **The concurrent administration of phenytoin, phenobarbital, or rifampin may lower blood levels of quinidine by enhancing liver clearance. Because of its dependence on renal excretion and hepatic metabolism for clearance from the body,**
- accumulation of quinidine or its metabolites may occur in the presence of impaired function of these organs. About 80% to 90% of quinidine in plasma is bound to albumin.
- Quinidine accumulates rapidly in most tissues except the brain.

Side Effects

- Quinidine has a low therapeutic ratio, with heart block, hypotension, and proarrhythmia being potential adverse side effects. As the plasma concentration increases to more than 2 µg/mL, the P-R interval, QRS complex, and QTc interval on the ECG are prolonged. **Patients with preexisting prolongation of the QTc interval or evidence of atrioventricular heart block on the ECG should not be treated with quinidine**.

- Allergic reactions may include drug rash or a drug fever that is occasionally associated with leukocytosis. **Thrombocytopenia is a rare occurrence that is caused by drug–platelet complexes that evoke production of antibodies.** Discontinuation of quinidine results in return of the platelet count to normal in 2 to 7 days. Nausea, vomiting, and diarrhea occur in about one-third of treated patients.

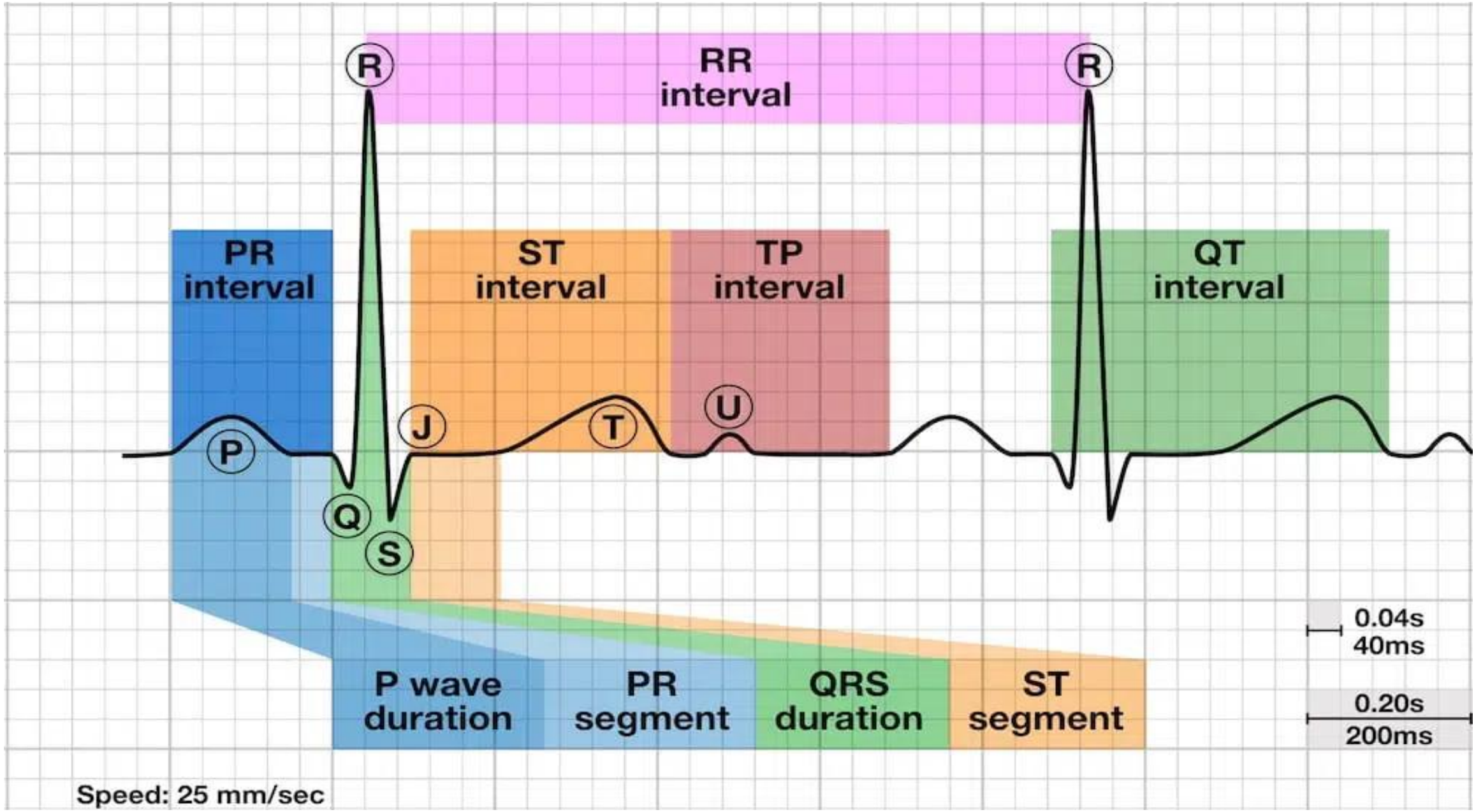
- Because quinidine is an α-adrenergic blocking drug, it can interact in an additive manner with drugs that cause vasodilation. Quinidine also interferes with normal neuromuscular transmission and may accentuate the effect of neuromuscular blockings drugs. Recurrence of skeletal muscle paralysis in the immediate postoperative period has been observed in association with the administration of quinidine.

Procainamide

- Procainamide is as effective as quinidine for the treatment of ventricular tachyarrhythmias, but less effective in abolishing atrial tachyarrhythmias
- Premature ventricular contractions and paroxysmal ventricular tachycardia are suppressed in most patients within a few minutes after IV administration, which is better tolerated than IV quinidine but may still cause hypotension.
- Procainamide can be administered IV at a rate not exceeding 100 mg every 5 minutes until the rhythm is controlled (maximum 15 mg/kg).
- When the cardiac arrhythmia is controlled, a constant rate of infusion (2 to 6 mg per minute) is used to maintain a therapeutic concentration of procainamide.
- The systemic blood pressure and ECG (QRS complex) are monitored continuously during infusion of this drug.
- The therapeutic blood level of procainamide is 4 to 8 µg/mL.

Mechanism of Action

- Procainamide is an analogue of the local anesthetic procaine.
- Procainamide possesses an electrophysiologic action similar to that of quinidine but produces less prolongation of the QTc interval on the ECG.
- As a result, paradoxical ventricular tachycardia is a rare feature of procainamide therapy.
- Procainamide has no vagolytic effect and can be used in patients with atrial fibrillation to suppress ventricular irritability without increasing the ventricular rate.
- Like quinidine, procainamide may prolong the QRS complex and cause ST-T wave changes on the ECG.


R
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R
PR
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ST
interval
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interval
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P
J
T
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P wave
duration
PR
segment
QRS
duration
ST
segment
0.04s
40ms
0.20s
200ms
Speed: 25 mm/sec

Metabolism and Excretion / Procainamide

- Procainamide is eliminated by renal excretion and hepatic metabolism.
- In humans, 40% to 60% of procainamide is excreted unchanged by the kidneys.
- The dose of procainamide must be decreased when renal function is abnormal.
- In the liver, procainamide that has not been excreted unchanged by the kidneys is acetylated to N-acetyl procainamide (NAPA), which is also eliminated by the kidneys.
- This metabolite is cardioactive and probably contributes to the antiarrhythmic effects of procainamide. In the presence of renal failure, plasma concentrations of NAPA may reach dangerous levels. Eventually, 90% of an administered dose of procainamide is recovered as unchanged drug or its metabolites.
- The activity of the N-acetyltransferase enzyme response for the acetylation of procainamide is genetically determined.
- In patients who are rapid acetylators, the elimination half-time of procainamide is 2.5 hours compared with 5 hours in slow acetylators.
- The blood level of NAPA exceeds that of procainamide in rapid but not slow acetylators. Unlike its analogue, procaine, procainamide is highly resistant to hydrolysis by plasma cholinesterase. Evidence of this resistance is the fact that only 2% to 10% of an administered dose of procainamide is recovered unchanged in the urine as paraaminobenzoic acid.

Side Effects

- Similar to quinidine, use of procainamide has dramatically decreased due to its side effect profile and availability of newer agents.
- Hypotension that results from procainamide is more likely to be caused by direct myocardial depression than peripheral vasodilation.
- Indeed, rapid IV injection of procainamide is associated with hypotension, whereas higher plasma concentrations slow conduction of cardiac impulses through the atrioventricular node and intraventricular conduction system.
- Ventricular asystole or fibrillation may occur when procainamide is administered in the presence of heart block, as associated with digitalis toxicity.
- Direct myocardial depression that occurs at high plasma concentrations of procainamide is exaggerated by hyperkalemia. As with quinidine, ventricular arrhythmias may accompany excessive plasma concentrations of procainamide.
- Chronic administration of procainamide may be associated with a syndrome that resembles systemic lupus erythematosus.
- As with many drugs, procainamide may cause drug fever or an allergic rash. Although agranulocytosis is rare, leukopenia and thrombocytopenia may be seen after chronic use of procainamide, often in association with the lupus-like syndrome. The most common early, noncardiac complications of procainamide are gastrointestinal disturbances, including nausea and vomiting.

Lidocaine

- Lidocaine is used principally for suppression of ventricular arrhythmias, having minimal if any effect on supraventricular tachyarrhythmias .
- This drug is particularly effective in suppressing reentry cardiac arrhythmias, such as premature ventricular contractions and ventricular tachycardia.
- The efficacy of prophylactic lidocaine therapy for preventing early ventricular fibrillation after acute myocardial infarction has not been documented and is no longer recommended .
- In adult patients with a normal cardiac output, hepatic function, and hepatic blood flow, an initial administration of lidocaine, 2 mg/kg IV, followed by a continuous infusion of 1 to 4 mg per minute should provide therapeutic plasma lidocaine concentrations of 1 to 5 µg/mL.

Lidocaine

- Decreased cardiac output and/or hepatic blood flow, as produced by anesthesia, acute myocardial infarction, or congestive heart failure, may decrease by 50% or more of the initial dose and the rate of lidocaine infusion necessary to maintain therapeutic plasma levels.
- **Concomitant administration of drugs such as propranolol and cimetidine can result in decreased hepatic clearance of lidocaine.**
- Advantages of lidocaine over quinidine or procainamide are the more rapid onset and prompt disappearance of effects when the continuous infusion is terminated, greater therapeutic index, and a much reduced side effect profile.
- Lidocaine for IV administration differs from that used for local anesthesia because it does not contain a preservative.
- Lidocaine is also well absorbed after oral administration but is subject to extensive hepatic first-pass metabolism.As a result, only about one-third of an oral dose of lidocaine reaches the circulation.
- Intramuscular (IM) absorption of lidocaine is nearly complete. In an emergency situation, lidocaine, 4 to 5 mg/kg IM, will produce a therapeutic plasma concentration in about 15 minutes. This level is maintained for about 90 minutes.

Mechanism of Action

- Lidocaine delays the rate of spontaneous phase 4 depolarization by preventing or diminishing the gradual decrease in potassium ion permeability that normally occurs during this phase.
- The effectiveness of lidocaine in suppressing premature ventricular contractions reflects its ability to decrease the rate of spontaneous phase 4 depolarization. The ineffectiveness of lidocaine against supraventricular tachyarrhythmias presumably reflects its inability to alter the rate of spontaneous phase 4 depolarization in atrial cardiac cells.
- In usual therapeutic doses, lidocaine has no significant effect on either the QRS or QTc interval on the ECG or on atrioventricular conduction. In high doses, however, lidocaine can decrease conduction in the atrioventricular node as well as in the His–Purkinje system.

- **Metabolism and Excretion**
- Lidocaine is metabolized in the liver, and resulting metabolites may possess cardiac antiarrhythmic activity.

Side Effects

- Lidocaine is essentially devoid of effects on the ECG or cardiovascular system when the plasma concentration remains less than 5 µg/mL.
- In contrast to quinidine and procainamide, lidocaine does not alter the duration of the QRS complex on the ECG, and activity of the sympathetic nervous system is not changed.
- Lidocaine depresses cardiac contractility less than any other antiarrhythmic drug used to suppress ventricular arrhythmias.
- Toxic plasma concentrations of lidocaine (>5 to 10 µg/mL) produce peripheral vasodilation and direct myocardial depression, resulting in hypotension.
- In addition, slowing of conduction of cardiac impulses may manifest as bradycardia, a prolonged P-R interval, and widened QRS complex on the ECG.
- Stimulation of the central nervous system (CNS) occurs in a dose-related manner, with symptoms appearing when plasma concentrations of lidocaine are greater than 5 µg/mL.
- Seizures are possible at plasma concentrations of 5 to 10 µg/mL.
- CNS depression, apnea, and cardiac arrest are possible when plasma lidocaine concentrations are greater than 10 µg/mL.
- The convulsive threshold for lidocaine is decreased during arterial hypoxemia, hyperkalemia, or acidosis, emphasizing the importance of monitoring these parameters during continuous infusion of lidocaine to patients for suppression of ventricular arrhythmias.

Digoxin

- **What is digoxin?**
- Digoxin is derived from the leaves of a digitalis plant. Digoxin helps make the heart beat stronger and with a more regular rhythm.
- It is a cardiac glycoside used in the treatment of mild to moderate heart failure and for ventricular response rate control in chronic atrial fibrillation.
- is used to treat heart failure and abnormal heart rhythms (arrhythmias).
- It helps the heart work better and it helps control your heart rate.
- Digoxin is one of the oldest cardiovascular medications used today. It is a common agent used to manage atrial fibrillation and the symptoms of heart failure. Digoxin is classified as a cardiac glycoside and was initially approved by the FDA in 1954
- This drug originates from the foxglove plant, also known as the Digitalis plant

Digoxin

- Digoxin is a positive inotropic and negative chronotropic drug
- meaning that it increases the force of the heartbeat and decreases the heart rate.
- **The decrease in heart rate is particularly useful in cases of atrial fibrillation, a condition characterized by a fast and irregular heartbeat**

- Absorption: Digoxin is approximately 70-80% absorbed in the first part of the small bowel.
- The bioavailability of an oral dose varies from 50-90%, however, oral gelatinized capsules of digoxin are reported to have a bioavailability of 100%.
- Warnings : You should not use digoxin if you have ventricular fibrillation (a heart rhythm disorder of the ventricles, or lower chambers of the heart that allow blood to flow out of the heart).

Mechanism of action

❑Digoxin exerts hemodynamic, electrophysiologic, and neurohormonal effects on the cardiovascular system.

❑ It reversibly inhibits the Na-K ATPase enzyme, leading to various beneficial effects. The Na-K ATPase enzyme functions to maintain the intracellular environment by regulating the entry and exit of sodium, potassium, and calcium (indirectly). Na-K ATPase is also known as the sodium pump.

- The inhibition of the sodium pump by digoxin increases intracellular sodium and increases the calcium level in the myocardial cells, causing an increased contractile force of the heart.
- This improves the left ventricular ejection fraction (EF), an important measure of cardiac function.

❑Digoxin also stimulates the parasympathetic nervous system via the vagus nerve·

- leading to sinoatrial (SA) and atrioventricular (AV) node effects, decreasing the heart rate.
- Part of the pathophysiology of heart failure includes neurohormonal activation, leading to an increase in norepinephrine.
- Digoxin helps to decrease norepinephrine levels through activation of the parasympathetic nervous system.

Propranolol

- **Propranolol**-Brand names: Bedranol, Beta-prograne, Half Beta-prograne, Hemangeol, Inderal LA, Inderal XL, InnoPran XL, Inderal, Propranolol Hydrochloride ER

❖. About propranolol

- Propranolol belongs to a group of medicines called beta blockers. It's used to treat heart problems, help with anxiety and prevent migraines.
- Propranolol is used to treat tremors, angina (chest pain), hypertension (high blood pressure), heart rhythm disorders, and other heart or circulatory conditions. It is also used to treat or prevent heart attack, and to reduce the severity and frequency of migraine headaches.

❖If you have a heart problem, you can take propranolol to:

- treat high blood pressure
- treat conditions that cause an irregular heartbeat (arrhythmia), like atrial fibrillation
- help prevent future heart disease, heart attacks and strokes
- help prevent chest pain caused by angina
- Propranolol can help reduce your symptoms if you have too much thyroid hormone in your body (thyrotoxicosis). You'll usually take it together with medicines to treat an overactive thyroid.
- This medicine is only available on prescription. It comes as tablets, slow release capsules, or as a liquid that you swallow.

Propranolol

- The usual doses for adults and children over the age of 12 are:
- **high blood pressure** – the starting dose is usually 80mg, taken twice a day. If this dose is not working well enough to reduce your blood pressure, your doctor may increase it to a maximum of 160mg twice a day
- **migraine or angina (chest pain)** – 40mg, taken 2 or 3 times a day. This can be increased to 120mg to 240mg a day. Your doctor or pharmacist will explain how to split the dose over the day
- **irregular heartbeat (arrhythmia)** – 10mg to 40mg, taken 3 or 4 times a day
- **anxiety** – 40mg taken once a day which can be increased to 40mg taken 3 times a day
- **too much thyroid hormone (thyrotoxicosis)** – 10mg to 40mg, taken 3 or 4 times a day

Electrophysiologic and Electrocardiographic Effects of Cardiac Antiarrhythmic Drugs

	Class IA	Class IB	Class IC	Class II	Class III	Class IV
Depolarization rate (phase 0)	Decreased	No effect	Greatly decreased	No effect	No effect	No effect
Conduction velocity	Decreased	No effect	Greatly decreased	Decreased	Decreased	No effect
Effective refractory period	Greatly increased	Decreased	Increased	Decreased	Greatly increased	No effect
Action potential duration	Increased	Decreased	Increased	Increased	Greatly increased	Decreased
Automaticity	Decreased	Decreased	Decreased	Decreased	Decreased	No effect
P-R duration	No effect	No effect	Increased	No effect or increased	Increased	No effect or increased
QRS duration	Increased	No effect	Greatly increased	No effect	Increased	No effect
QTc duration	Greatly increased	No effect or decreased	Increased	Decreased	Greatly increased	No effect


THANK
YOU