CVS- Pharmacology 2

Antiarrhythmics 1

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Arrhythmias

- The normal heart beats is regular.
- Arrhythmias and conduction disorders are caused by **abnormalities in the generation or conduction of the heart electrical impulses or both.**
- Causes:

1. **Heart disorders:**

- Including congenital abnormalities of structure e.g., accessory atrioventricular connection
- Function (e.g., hereditary ion channelopathies)

2. **Systemic factors:**

- Electrolyte abnormalities (particularly low potassium or magnesium), hypoxia
- Hormonal imbalances (e.g., hypothyroidism, hyperthyroidism)
- Drugs and toxins (e.g., alcohol, caffeine).

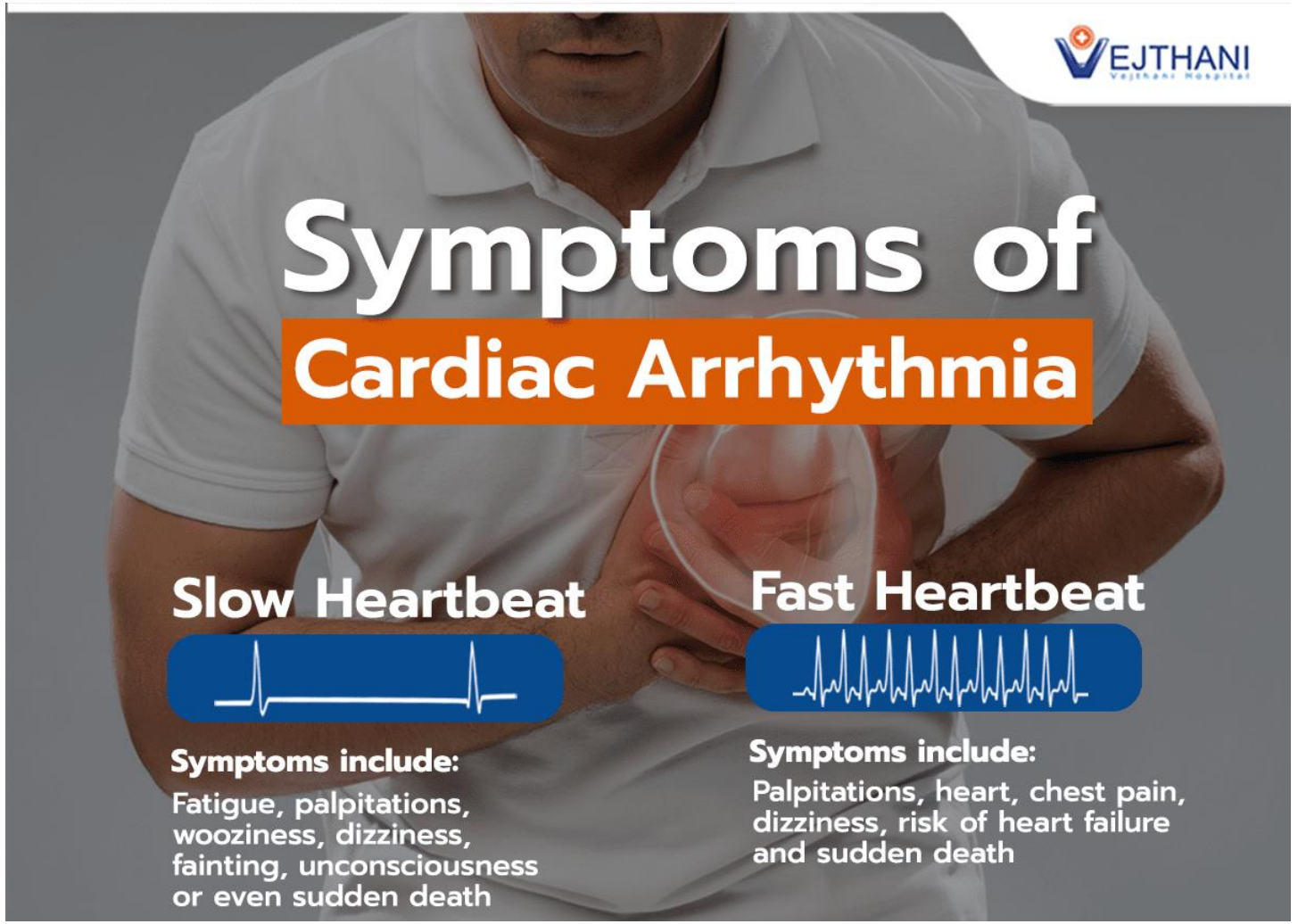
Cardiac Arrhythmias, Animation.en.srt

Arrhythmias

NB: This video is for you to understand arrhythmias and it is not required for the exam.

- https://youtu.be/6LrptveKYus

Arrhythmias



Antiarrhythmic drugs

Three Primary Indications for Treatment of Cardiac Arrhythmias

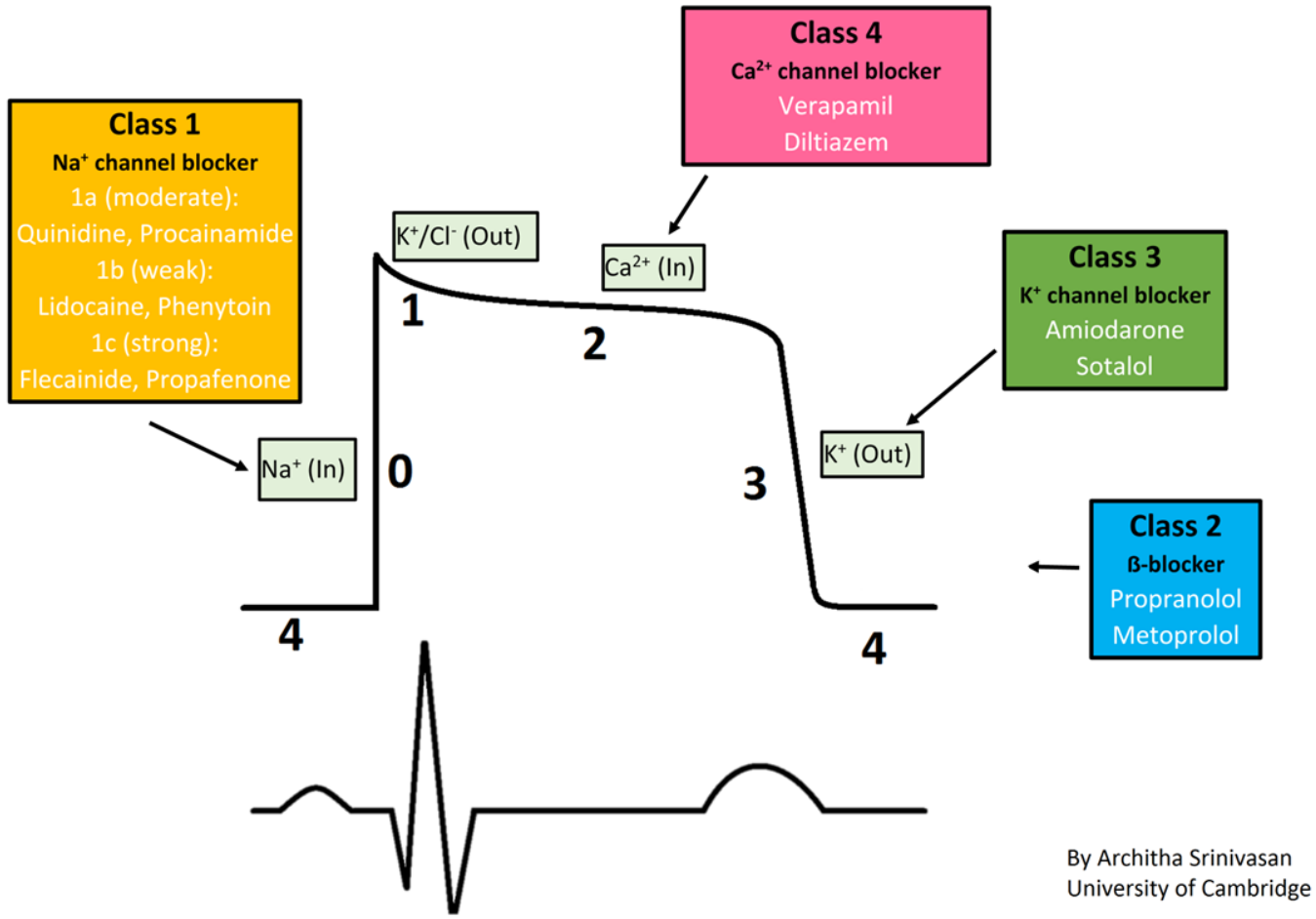
1. Arrhythmias that **decrease cardiac output** (e.g., severe bradycardia, ventricular tachycardia or fibrillation)
2. Arrhythmias that are likely to **precipitate more serious arrhythmias** (e.g., atrial flutter may lead to sustained ventricular tachycardia)
3. Arrhythmias that are likely to **precipitate an embolism** due to creation of vascular stasis (e.g., chronic atrial fibrillation)

Antiarrhythmic drugs

While drug therapy is still the most common method for treating arrhythmias, other non-pharmacological therapies are also in current use. Which includes:

1. DC cardioversion, implanting of a pacemaker, or defibrillator device (ICD)
2. Carotid sinus massage (↑ vagal tone)
3. Surgical or catheter-mediated ablation of an ectopic focus, coronary bypass surgery
4. Lifestyle modification (avoiding events that aggravate an arrhythmia - e.g., exertion, emotional stress, non-ideal diet)

Antiarrhythmic drugs



By Architha Srinivasan
University of Cambridge

Antiarrhythmic Drugs, Animation.en.srt

Antiarrhythmic drugs

https://youtu.be/OnLsLByuo0E

Antiarrhythmic Drugs

Class Ia

1 Double Quarter Pounder

Disopyramide

Quinidine

Procainamide

Class Ib

with Lettuce, Mayo

Lidocaine

Mexeletine

Class Ic

Fries Please!

Flecainide

Propefanone

Class II

Beta blockers? Lol

Propanolol

Atenolol

Metoprolol

Class III

This is SAD

Sotalol

Amiodarone

Dofelitide

Class IV

I and V in Class IV?

Diltiazem

Verapamil

Class I Antiarrhythmic Drugs

- Act by blocking **voltage-sensitive Na+ channels.**
- They **bind more rapidly to open or inactivated Na+ channels** than to channels that are fully repolarized.
- These drugs have **use dependence (or state dependence)** property as show a greater degree of blockade in tissues that are frequently depolarizing. Which enables these drugs **to block cells that are discharging at an abnormally high frequency, without interfering with the normal beating of the heart.**

Class I Antiarrhythmic Drugs

- They have proarrhythmic effects, particularly in patients with reduced **left ventricular function and atherosclerotic heart disease.**
- Class I drugs are further subdivided into three groups according to their effect on the duration of the cardiac action potential.

CLASSIFICATION OF DRUG	MECHANISM OF ACTION	COMMENT
IA	Na^+ channel blocker	Slows Phase 0 depolarization in ventricular muscle fibers
IB	Na^+ channel blocker	Shortens Phase 3 repolarization in ventricular muscle fibers
IC	Na^+ channel blocker	Markedly slows Phase 0 depolarization in ventricular muscle fibers

Class I Antiarrhythmic Drugs

Bind to and block the **fast Na channels in non-nodal tissue** (e.g., myocytes of the atria and ventricles, His-Purkinje system):

- **Blocking fast Na channels** :
  - ↓ Slope of phase 0 → ↓ in the amplitude of action potential
  - ↓ Velocity of action potential: **Transmission within the heart (↓ conduction velocity)**
    - **Important mechanism for suppressing tachycardias caused by abnormal conduction (e.g., reentry mechanisms)**
    - **Reentry mechanisms can be interrupted by ↓ abnormal conduction**

Class Ia

1 Double Quarter Pounder

Disopyramide

Quinidine

Procainamide

Class IA Antiarrhythmic Drugs

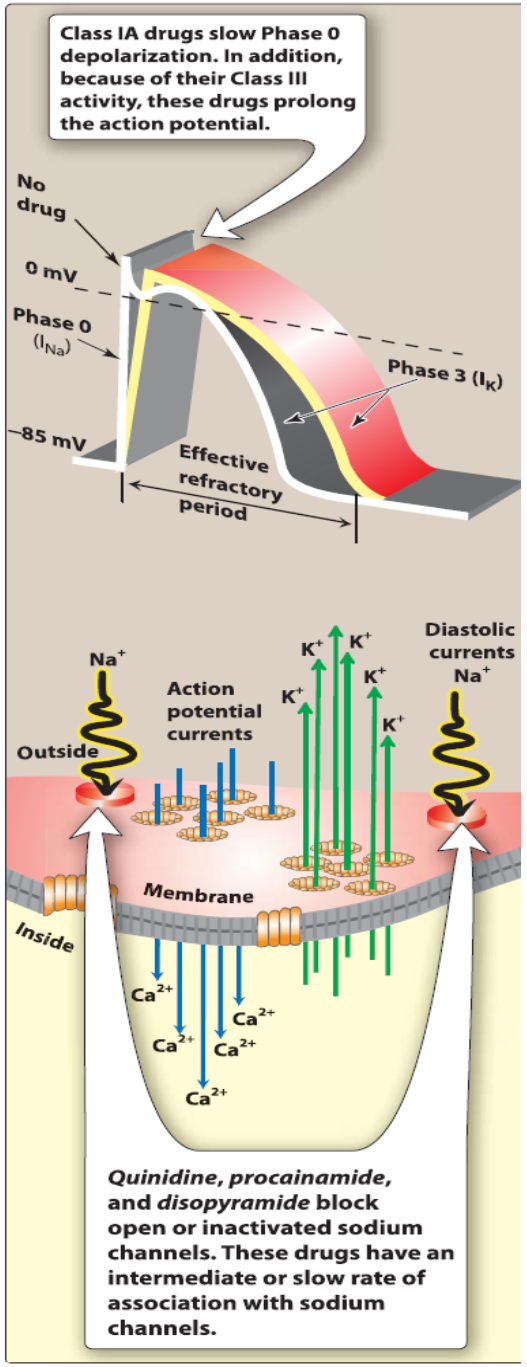
1. **Quinidine is the prototype class lA drug.**
2. **Procainamide**
3. **Disopyramide**

- They have concomitant **class lll activity** (K channel blockers).
- They can cause **arrhythmias that can progress to ventricular fibrillation.**

Class IA Antiarrhythmic Drugs

Mechanism of action:

- Na channel effects:
  - Intermediate speed of binding and dissociation from voltage-gated Na channels
  - Slows the upstroke of action potential and conduction
- K channel effects:
  - Blocks K channels → ↓ K efflux → slows repolarization
  - Leads to ↑ ERP and action potential duration → QT prolongation
- Other effects:
  - Anticholinergic activity → can ↑ sinoatrial rate and atrioventricular conduction ↓ Myocardial contractility



Class Ia

1 Double Quarter Pounder

Disopyramide

Quinidine

Procainamide

Class IA Antiarrhythmic Drugs

- **Quinidine** has mild α-adrenergic blocking and anticholinergic actions.
- **Procainamide** has no α -adrenergic blocking and less anticholinergic activity than quinidine
- **Disopyramide** has no α -adrenergic blocking and more anticholinergic activity than quinidine. It produces a greater negative inotropic effect, and unlike the other drugs, it causes peripheral vasoconstriction.

Class Ia

1 Double Quarter Pounder

Disopyramide

Quinidine

Procainamide

Class IA Antiarrhythmic Drugs

- **Therapeutic uses:**

1. **Quinidine:** atrial, **AV junctional, and ventricular tachyarrhythmias**.
2. **Procainamide**: to **treat acute atrial and ventricular arrhythmias** but it is not often use as it is **replaced by** electrical cardioversion or defibrillation and amiodarone
3. **Disopyramide : Ventricular tachyarrhythmias and atrial fibrillation and flutter** (not first choice)

- **Contraindications:** patients with atherosclerotic heart disease or systolic heart failure.
- **Sides effects**: Large doses of **quinidine** may induce the symptoms of cinchonism (blurred vision, tinnitus ,headache , disorientation, and psychosis).

Class IB Antiarrhythmic Drugs

- **Lidocaine and Mexiletine**
- **Mechanism of action :**

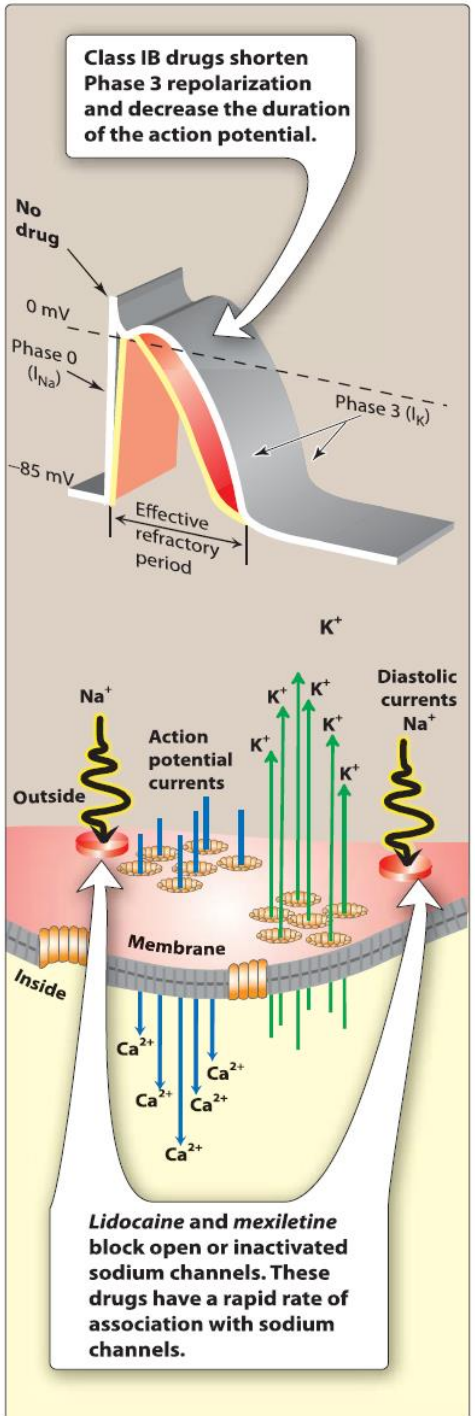
1. Na+ channel blockade:bind primarily to channels in the inactivated state.

Very useful for arrhythmias in **ischemic myocardium:** because ischemia leads to slow cellular depolarization that inactivates sodium channels, and therefore enhanced binding of IB drugs.

2. ↓ Velocity of action potential: **Transmission within the heart (↓ conduction velocity)**

Shorten phase 3 repolarization and decrease the duration of the action potential

- Neither drug contributes to negative inotropy.



Class IB Antiarrhythmic Drugs

Class Ib
with Lettuce, Mayo
Lidocaine
Mexeletine

- Therapeutic uses:
- **Lidocaine:**

1. As an alternative to amiodarone ventricular fibrillation or ventricular tachycardia (VT).
2. May also be used in combination with amiodarone for VT storm.

- **Mexiletine:**

Is used for chronic treatment of ventricular arrhythmias, often in combination with amiodarone.

Class IB Antiarrhythmic Drugs

Class Ib

with Lettuce, Mayo

Lidocaine

Mexeletine

- Adverse effects:
- **Lidocaine:** Central nervous system (CNS) effects include nystagmus (early indicator of toxicity), drowsiness, slurred speech, paresthesia, agitation, confusion, and convulsions.

- **Mexiletine**: Nausea, vomiting, and dyspepsia.

Class IC Antiarrhythmic Drugs

- **Flecainide and propafenone**
- Mechanism of action:
- Suppresses phase 0 upstroke in Purkinje and myocardial fibers (slowing of conduction in all cardiac tissue)
- Automaticity is reduced by an increase in the threshold potential

Class IC Antiarrhythmic Drugs

- Therapeutic uses:
- **Flecainide**

1. Maintenance of sinus rhythm in atrial flutter or fibrillation
2. Treating refractory ventricular arrhythmias.

- **Propafenone**: Restricted mostly to **atrial arrhythmias**

1. Rhythm control of atrial fibrillation or flutter and paroxysmal supraventricular tachycardia
2. Prophylaxis in patients with AV reentrant tachycardias.

Class IC Antiarrhythmic Drugs

Flecainide and propafenone

- Due to their negative inotropic and proarrhythmic effects, use of these agents **is avoided in patients with structural heart disease (left ventricular hypertrophy, heart failure, atherosclerotic heart disease).**

Class IC Antiarrhythmic Drugs

Adverse effects:

- **Flecainide :**blurred vision, dizziness, and nausea

- **Propafenone:** blurred vision, dizziness, nausea and may cause **bronchospasm and should be avoided in patients with asthma.**