CVS- Pharmacology 3

Antiarrhythmics 2

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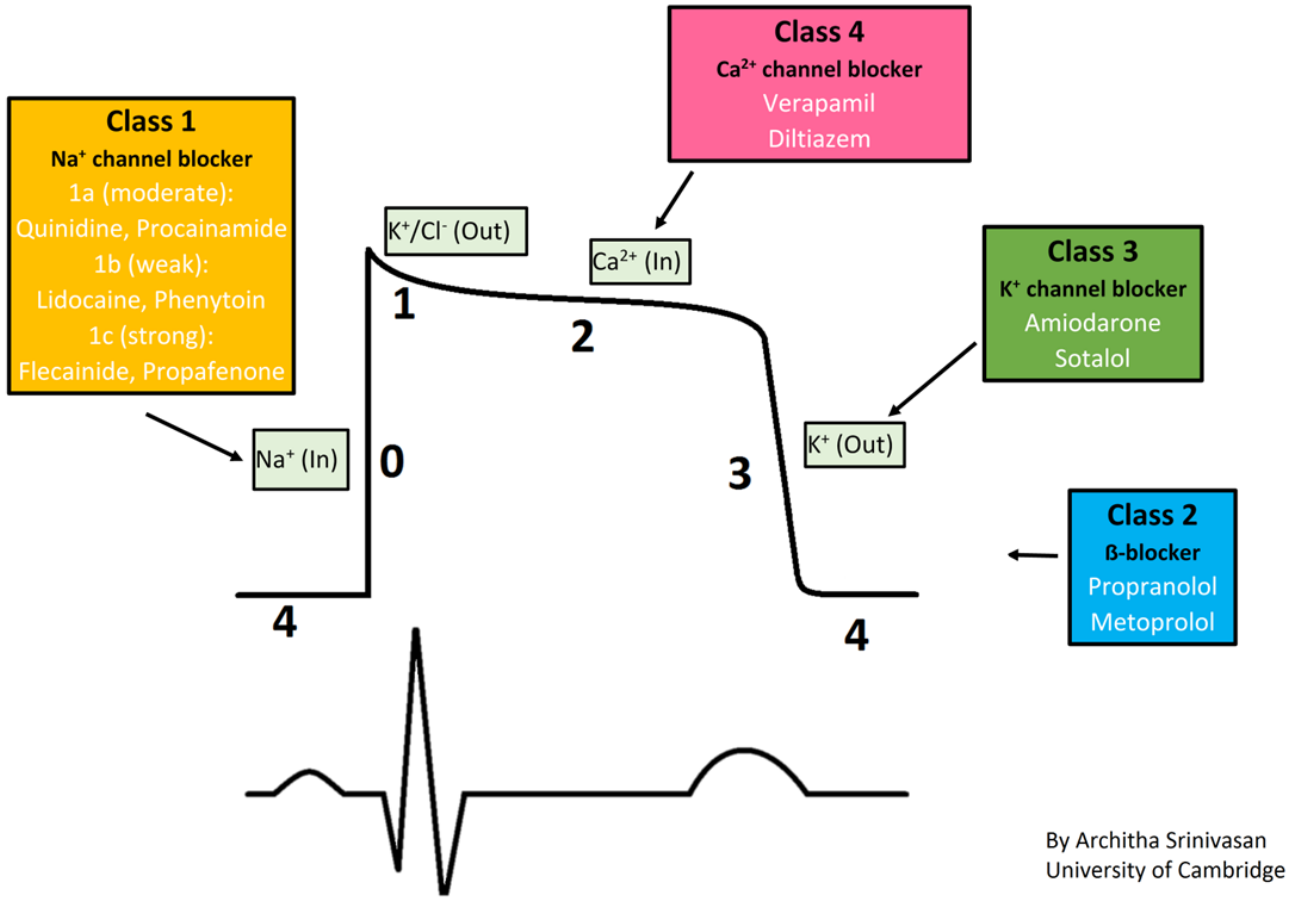
Antiarrhythmic drugs



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Class II

Beta blockers? Lol

Propanolol

Atenolol

Metoprolol

Class II Antiarrhythmic Drugs

β-adrenergic antagonists, or β -blockers.

Mechanism of action:

Diminish phase 4 depolarization and, thus, depress automaticity, prolong AV conduction, and decrease **heart rate and contractility**.

Therapeutic uses:

1. Treating tachyarrhythmias caused by increased sympathetic activity.
2. Atrial flutter and fibrillation and for AV nodal reentrant tachycardia.
3. **Prevent life-threatening ventricular arrhythmias following a myocardial infarction.**

Class II Antiarrhythmic Drugs

Class II

Beta blockers? Lol

Propanolol

Atenolol

Metoprolol

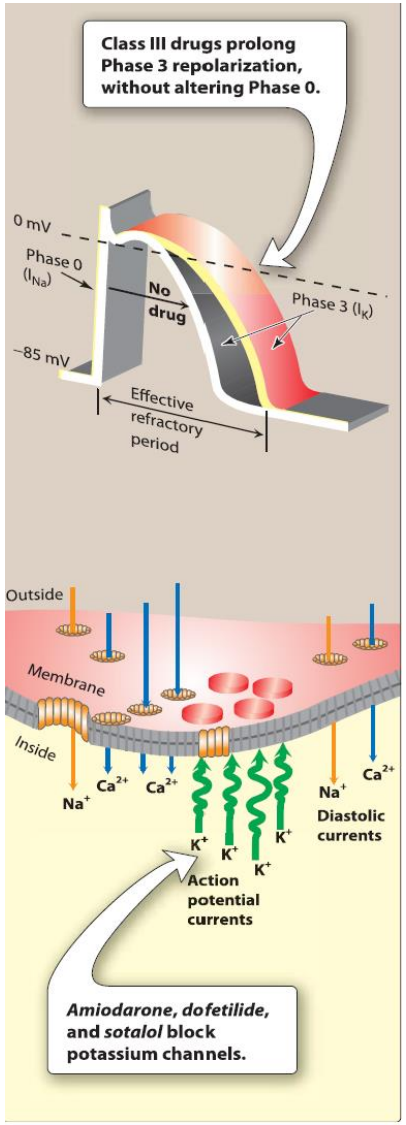
- **Metoprolol** is the most widely used β -blocker for the treatment of cardiac arrhythmias. Compared to nonselective β -blockers, such as propranolol it reduces the risk of bronchospasm.
- **Esmolol** is a very short and fast-acting β -blocker used for intravenous administration in acute arrhythmias that occur during surgery or emergency situations.
- **Common adverse effects** with β-blockers include bradycardia, hypotension, and fatigue.

Class III Antiarrhythmic Drugs

Class III

This is SAD
Sotalol
Amiodarone
Dofelitide

- Block K+ channels leading to diminish the outward K+ current during repolarization of cardiac cells.
- They **prolong the duration of the action potential** without altering phase 0 of depolarization or the resting membrane potential.
- They prolong the effective refractory period, increasing refractoriness.
- All class III drugs have the potential to induce arrhythmias.



Class III

This is SAD

Sotalol

Amiodarone

Dofelitide

Class III Antiarrhythmic Drugs

A)Amiodarone

- Mechanism of action:

It has complex effects, showing class I, II, lll, and IV actions, as well as α-blocking activity.

Its dominant effect is **prolongation of the action potential duration and the refractory period by blocking K+ channels.**

Therapeutic uses:

- *Amiodarone* is effective in the treatment of severe refractory supraventricular and ventricular tachyarrhythmias.
- ***Amiodarone* has been a mainstay of therapy for the rhythm management of atrial fibrillation or flutter.**

Class III

This is SAD

Sotalol

Amiodarone

Dofelitide

Class III Antiarrhythmic Drugs

- **A)Amiodarone**
- **Adverse effects**:
- pulmonary fibrosis, neuropathy, hepatotoxicity, corneal deposits, optic neuritis, blue-gray skin discoloration, and hypo- or hyperthyroidism.
- *Amiodarone* is the least proarrhythmic of the class I and Ill antiarrhythmic drugs.

Class III

This is SAD

Sotalol

Amiodarone

Dofelitide

Class III Antiarrhythmic Drugs

- **B) Sotalol**
- A class Ill antiarrhythmic agent with a nonselective β -blocker activity.
- Blocks a **rapid outward K+ current (delayed rectifier current**). Used for maintenance of sinus rhythm in patients with atrial fibrillation, atrial flutter, or refractory paroxysmal supraventricular tachycardia and in the treatment of ventricular arrhythmias.
- For his β -blocking properties, it is commonly used in patients with left ventricular hypertrophy or atherosclerotic heart disease.
- **To reduce the risk of proarrhythmic effects, *sotalol* should be initiated in the hospital to monitor QT interval.**

Class III Antiarrhythmic Drugs

Class III

This is SAD

Sotalol

Amiodarone

Dofelitide

C) Dofetilide

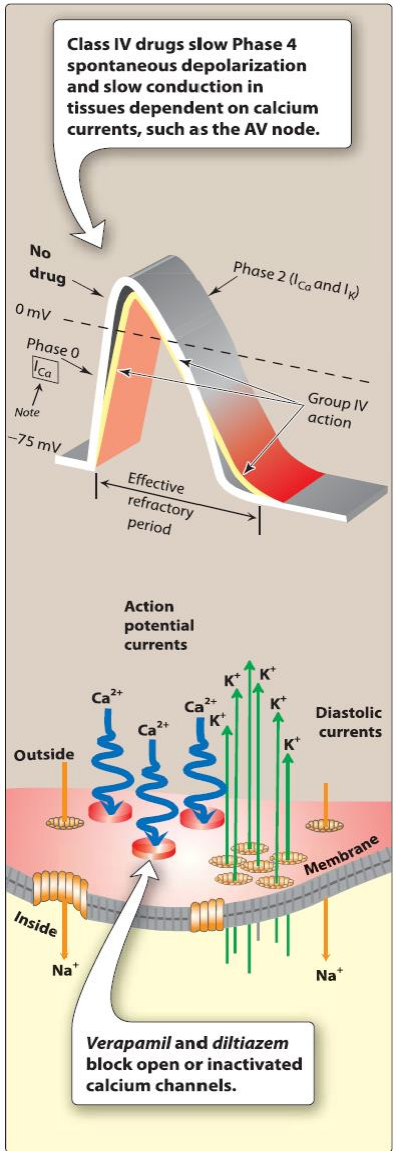
- Is a pure K+ channel blocker.
- Can be used as a first-line antiarrhythmic agent in patients with persistent atrial fibrillation and heart failure or in those with coronary artery disease.
- Because of the risk of proarrhythmia, dofetilide initiation is limited to the inpatient setting.

Class IV Antiarrhythmic Drugs

- Non-dihydropyridine Ca2+ channel blockers: verapamil and diltiazem
- Although voltage sensitive Ca2+ channels occur in many different tissues, the major effect of Ca2+ channel blockers is on vascular smooth muscle and the heart.

- In the heart, verapamil and diltiazem bind only to open depolarized voltage-sensitive channels, thus decreasing the inward current carried by Ca2+.

Class IV Antiarrhythmic Drugs



Class IV

I and V in Class IV?

Diltiazem

Verapamil

- These drugs are **use dependent** as they prevent repolarization until the drug dissociates from the channel, resulting in a decreased rate of phase 4 spontaneous depolarization.
- They also slow conduction in tissues that are dependent on Ca2 currents, such as the AV and SA node.

Class IV Antiarrhythmic Drugs

- **Therapeutic use:**

These agents are more effective against atrial than against ventricular arrhythmias

1. Treating reentrant supraventricular tachycardia
2. Reducing the ventricular rate in atrial flutter and fibrillation.

- **Adverse effects:**
- bradycardia, hypotension, and peripheral edema.

Other Antiarrhythmic Drugs

Digoxin

- Inhibits the Na+/K+-ATPase pump, shortening the refractory period in atrial and ventricular myocardial cells while prolonging the effective refractory period and diminishing conduction velocity in the AV node.
- Used to control ventricular response rate **in atrial fibrillation and flutter**; however, sympathetic stimulation easily overcomes the inhibitory effects of *digoxin.*
- At toxic concentrations, *digoxin* causes ectopic ventricular beats that may result in VT and fibrillation.

Other Antiarrhythmic Drugs

- **Adenosine**
- At high doses, the drug decreases conduction velocity, prolongs the refractory period, and decreases automaticity in **the AV node.**
- Intravenous *adenosine* is **the drug of choice for converting acute supraventricular tachycardias.**
- It has low toxicity but **causes flushing, chest pain, and hypotension**.

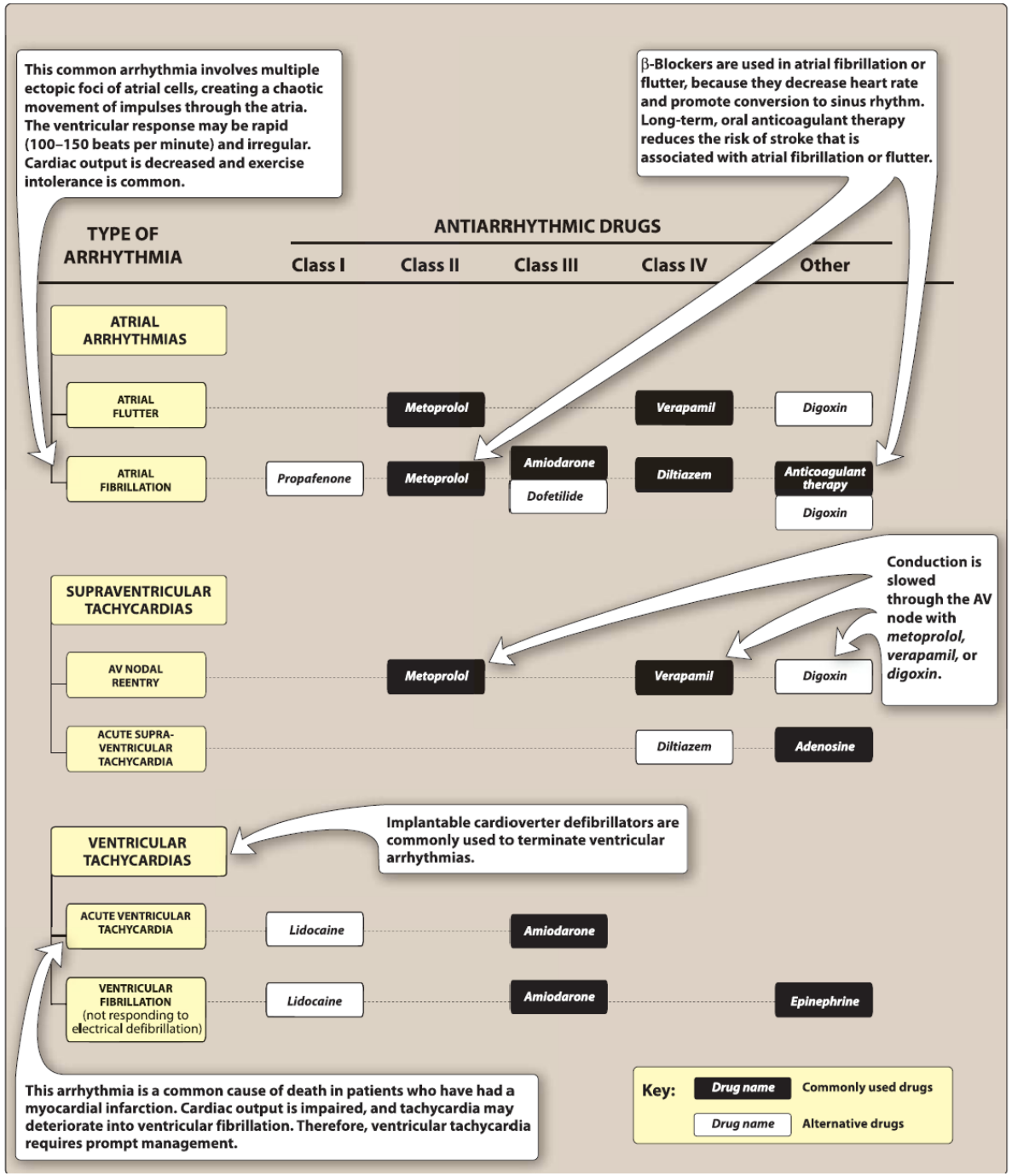
Other Antiarrhythmic Drugs

- **Magnesium sulfate**
- *Magnesium* is necessary for the transport of Na+, Ca2+, and K+ across cell membranes.
- It slows the rate of SA node impulse formation and prolongs conduction time along the myocardial tissue.
- **Therapeutic use:**
- To treat torsades de pointes and digoxin-induced arrhythmias.

Antiarrhythmic Drugs

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
II	β-Adrenoreceptor blocker	Inhibits Phase 4 depolarization in SA and AV nodes
III	K^+ channel blocker	Prolongs Phase 3 repolarization in ventricular muscle fibers
IV	Ca^{2+} channel blocker	Inhibits action potential in SA and AV nodes

Therapeutic indications for some commonly encountered arrhythmias.



Study Questions

1-A 60-year-old woman had a myocardial infarction. Which agent should be used to prevent life-threatening arrhythmias that can occur post myocardial infarction in this patient?

A. Digoxin

B. Flecainide

C. Metoprolol

D. Procainamide

2- A 57-year-old man is being treated for an atrial arrhythmia. He complains of dry mouth, blurred vision, and urinary hesitancy. Which antiarrhythmic drug is he mostly like taking?

A. Metoprolol

B. Disopyramide

C. Verapamil

D. Sotalol

3- Which arrhythmia can be treated with lidocaine?

A. Paroxysmal supraventricular tachycardia

B. Atrial fibrillation

C. Atrial flutter

D. Ventricular tachycardia

4-A clinician would like to initiate a drug for rhythm control of atrial fibrillation. Which of the following coexisting conditions would allow for initiation of flecainide?

A. Hypertension

B. Left ventricular hypertrophy

C. Coronary artery disease

D. Heart failure

5- Which one of the following drugs binds bile acids in the intestine, thus preventing their return to the liver via the enterohepatic circulation?

A. Niacin.

B. Fenofibrate.

C. Cholestyramine.

D. Fluvastatin.

E. Lovastatin.

6-Which one of the following drugs is most likely to block K+ channels in the heart responsible for cardiac repolarization, and also blocks calcium channels in the AV node?

A. Amiodarone

B. Quinidine

C. Lidocaine

D. Sotalol

E. Verapamil

7- The treatment of hyperlipidemic patients with nicotinic acid (niacin) results in

A. increases in VLDL

B. decreases in both plasma cholesterol and TGs

C. inhibition of HMG-CoA reductase

D. decreases in HDL

E. no change in total cholesterol in the plasma