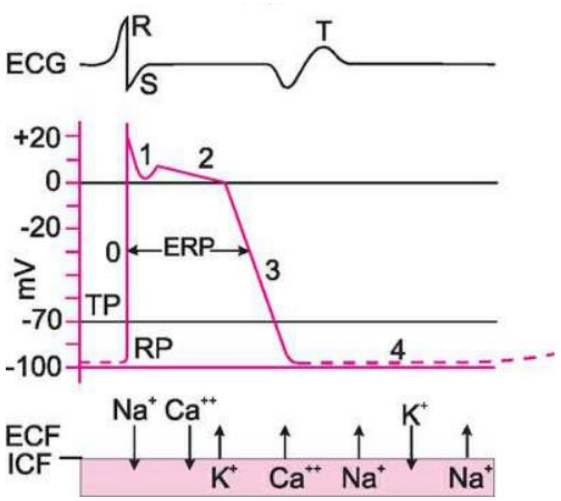
ANTIDYSRHYTHMIC AGENTS

Cardiac arrhythmia is defined as disturbance of initiation or conduction of cardiac impulse i.e., deviation from the normal pattern of cardiac rhythm is known as arrhythmia. Understanding of electrophysiology of heart muscle is essential for better understanding the pharmacology of anti-arrhythmic drugs.

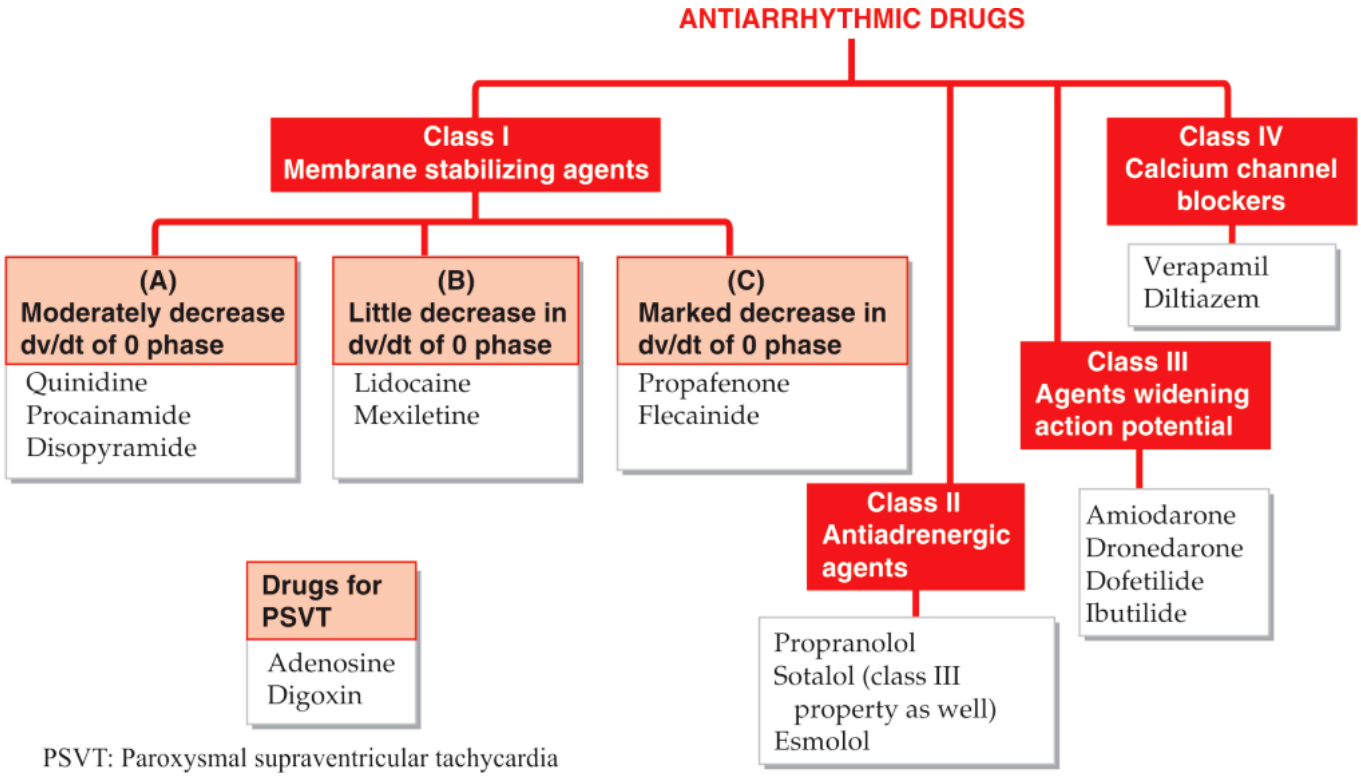
Relation of Various Phases of Cardiac Action Potential with ECG

Phase 0 and 1	QRS complex (depolarization)
Phase 2	ST segment (plateau phase)
Phase 3	T wave (repolarization)



Anti-arrhythmic drugs are the drugs used to prevent or correct cardiac arrhythmias. A classification of antidysrhythmic drugs based on their electrophysiological effects was proposed by Vaughan Williams in 1970. There are four classes:

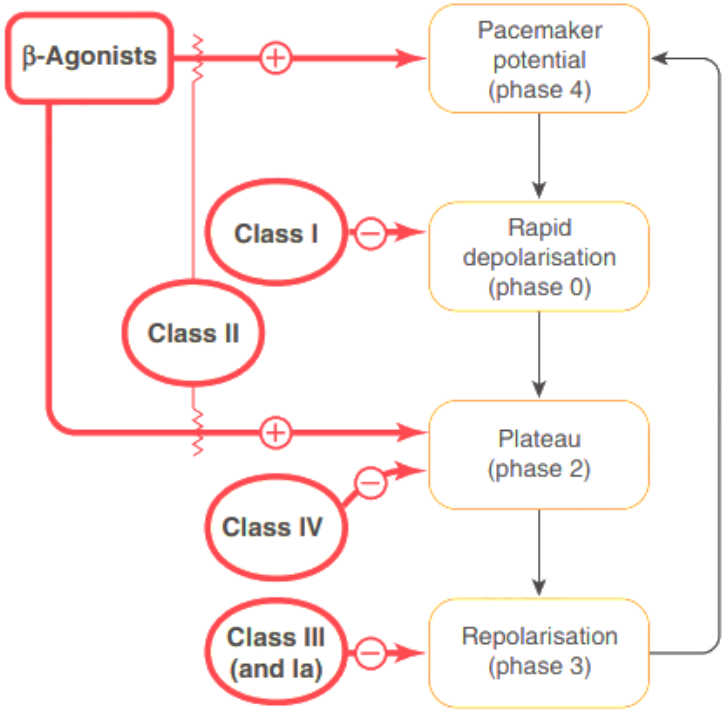
- Class I: drugs that predominately block voltage-sensitive Na^+ channels. They are subdivided: Ia, Ib and Ic.
- Class II: β-adrenoceptor antagonists.
- Class III: drugs that substantially prolong the cardiac action potential.
- Class IV: calcium antagonists



PSVT: Paroxysmal supraventricular tachycardia

Source: KDT; JP Bro.

Effects of antidysrhythmic drugs on the different phases



Class I Agents

These agents interfere with the activity of Na^+ channels. Thus, all of these drugs can decrease the slope of phase '0'. More frequently the overactive sodium channels use to be blocked by these drugs. These are further classified according to action of these drugs on K^+ channels.

CLASS Ia AGENTS

Apart from its action on sodium channels (block Na^+ channel in open state), these drugs also block cardiac K^+ channels (thus delaying repolarization resulting in prolonged action potential duration). Agents in this class also cause decreased conductivity and increased refractoriness. These drugs dissociate from the sodium channels with intermediate kinetics. Quinidine, Procainamide, and Disopyramide are the important members of Class Ia.

CLASS Ib AGENTS

Agents of this class includes Lignocaine, Mexiletine, Tocainide and Phenytoin; are sodium channel blockers that possess K^+ channel opening property. Class Ib agents have fast onset and offset kinetics (means that they have little or no effect at slower heart rates, and more effects at faster heart rates). These agents shorten the APD and reduce refractoriness (because of the opening of K^+ channels). *These drugs are used only for ventricular arrhythmia.*

CLASS IC AGENTS

These agents have the most potent sodium channel blocking effects with negligible effect on K^+ channels (therefore no effect on APD). Drugs in this group include Encainide, Moricizine, Flecainide and Propafenone. These drugs have maximum proarrhythmic property, therefore indicated only for the resistant and life-threatening ventricular tachycardia or ventricular fibrillation and for the treatment of refractory supraventricular tachycardia. *Flecainide can be used for acute treatment of Wolff Parkinson White* (WPW) syndrome.

Class II Agents

Class II agents are conventional beta blockers. They act by blocking the effects of adrenaline and nor-adrenaline at the β_1 receptors, thereby decreasing the sympathetic activity on the heart. These agents

are particularly useful in the treatment of supraventricular tachycardia. These drugs decrease the slope of phase 4 (responsible for automaticity) and conduction through the AV node. Important β blockers used as antiarrhythmic agents are Esmolol, Propranolol, and Metoprolol. *Esmolol is the shortest acting beta blocker*. It can be used i.v. for the emergency control of ventricular rate in atrial fibrillation or flutter.

Class III Agents

Class III agents predominantly block the K^+ channels, thereby prolonging repolarization (prolongation of APD). These drugs exhibit reverse use dependent prolongation of the action potential duration (means that the refractoriness increases at lower heart rates, therefore these are more efficacious at preventing a tachyarrhythmia than treating it). Because of this property class III antiarrhythmic agents may paradoxically be more arrhythmogenic at low heart rates. Drugs in this group are Amiodarone, Bretylium, Sotalol, Ibutilide and Dofetilide

Class IV Agents

Class IV agents are the blockers of L-type voltage gated Ca^{++} channels. They decrease the rate of phase 4 depolarization in SA and AV nodes. This results in decreased automaticity of SA node and decreased conduction through the AV node. Verapamil and Diltiazem are mainly indicated for PSVT and for control of ventricular rate in atrial fibrillation and flutter. Verapamil is drug of choice for the treatment of supraventricular tachycardia (SVT) and for the prophylaxis of PSVT

Class V Agents

Class V agents include digoxin, adenosine, magnesium, atropine and potassium.