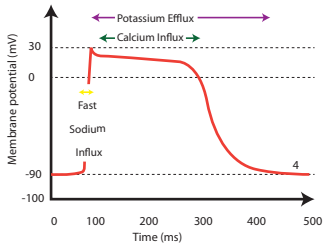
ANTI-ARRHYTHMIC DRUGS 1



Classification Schemes The most common classification scheme used is the Vaughan Williams Classification. This describes the various antiarrythmic medications in terms of their mechanism of action with regard to the cardiac action potential. This is useful when conceptualising in terms of the slow and fast cardiac action potential, but several of the antiarrythmics are not easily categorised such as amiodarone which may be included in several categories and some are ignored and lumped into the other category including digoxin, adenosine, and magnesium. It also is of little clinical benefit it terms of treatment modalities for various arrythmias. It also makes no allowance for the fact that some medications work differently in diseased and non diseased hearts.

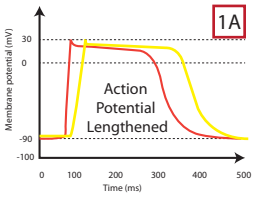
Vaughan Williams Classification

Class	Action	Effect	Drugs	Therapeutic Indications
I	Blocks Sodium Channels			
Ia		Prolongs refractory period of action potential	Procainamide	Atrial and ventricular arrhythmias especially post MI
Ib		Shortens refractory period of action potential	Lignocaine, Phenytoin	Ventricular arrhythmias post MI, digoxin induced arrhythmias
Ic		No effect on period of action potential	Flecainide	Refractory arrhythmias
II	Beta Adrenergic Blockers	Reduced SA firing	Propanolol* / Sotalol^	Rate control in AF, AT, Flutter and VT
III	Potassium Channel Blockers	Prolong refractory period of the action potential	Amiodarone#, ilbutalide	AF / Flutter termination
IV	Calcium Channel Blockers	↓AV conduction, PR prolonged, decreased contractility	Verapamil, Diltiazem	SVT and AF or Flutter
OTHER	Blocks $Na^+/K^+_{ATPASE,}$ leads to ↑Ca^{2+}, ↓K^+, ↑Ach	Increased contractility and ↓AV conduction	Digoxin	AF rate control and heart failure
	Opens K^+ channels via adenosine receptors	Hyperpolarises myocardium , ↓AV conduct, ↓SA firing	Adenosine	Terminate SVT or reveal underlying rhythm in tachycardias
	Stimulates Na^+/K^+_{ATPASE}	Membrane stabilisation	Magnesium	VF / Torsades de Pointes

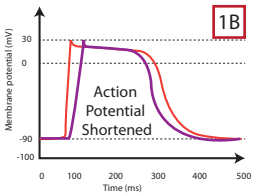
Notes
* Propanolol also has sodium channel blocking activity
^ Sotalol has two isomers, and is presented as a racemic mixture. One is an effective beta blocker and both have class III action potential prolongation activity
# Amiodarone is a special case. It blocks sodium, calcium, and potassium channels and exhibits beta blockade, although is usually categorised into Class III

Sodium Channel Blockers

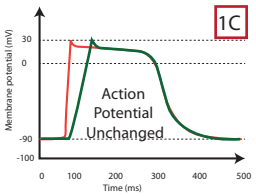
Procainamide is a Class 1A prototype. Other drugs with group 1A actions include quinidine and disopyramide. Amiodarone , often classified in group 3, also has typical group 1A actions. These drugs affect both atrial and ventricular arrhythmias. They block I_{Na}, and therefore slow conduction velocity in the atria, Purkinje fibers, and ventricular cells. At high doses they also slow AV conduction. The reduction in ventricular conduction results in increased QRS duration in the ECG. In addition, the 1A drugs block I_K and slow repolarization. Therefore, they increase AP duration and the effective refractory period (ERP) in addition to slowing conduction velocity and ectopic pacemakers. The increase in AP duration generates an increase in QT interval. Amiodarone has similar effects on sodium current (I_{Na} block) and has the greatest AP-prolonging effect (I_K block).



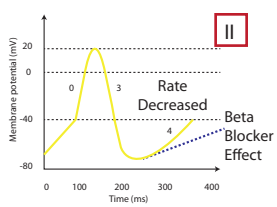
Class IB Lignocaine is the prototype 1B drug and is used exclusively by the IV or IM routes. Lignocaine selectively affects ischemic or depolarized Purkinje and ventricular tissue and has little effect on atrial tissue; the drug reduces AP duration in some cells, but because it slows recovery of sodium channels from inactivation it does not shorten (and may even prolong) the effective refractory period. Because these agents have little effect on normal cardiac cells, they have little effect on the ECG. Phenytoin , an anticonvulsant and not a true local anesthetic, is sometimes classified with the group 1B antiarrhythmic agents because it can be used to reverse digitalis-induced arrhythmias. It resembles lignocaine in lacking significant effects on the normal ECG.



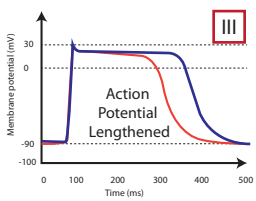
Class IC Flecainide is the prototype drug with group 1C actions. These drugs have no effect on ventricular AP duration or the QT interval. They are powerful depressants of sodium current, however, and can markedly slow conduction velocity in atrial and ventricular cells. They increase the QRS duration of the ECG.



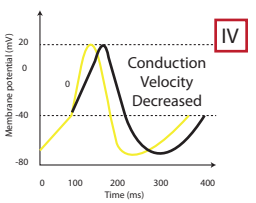
Beta adrenergic blockers Propranolol and esmolol are prototypic antiarrhythmic blockers. The antidysrhythmic effects of beta-adrenergic antagonists most likely reflect a blockade of the responses to beta-receptors in the heart to sympathetic nervous system stimulation (decreasing G-protien S responses and reducing intracellular cAMP), as well as the effects of circulating catecholamines. As a result, the rate of spontaneous phase 4 depolarization is decreased and the rate of sinoatrial node discharge is decreased. The AV node is particularly sensitive to blockers and the PR interval is usually prolonged by group 2 drugs. Sotalol and amiodarone, generally classified as group 3 drugs, also have group 2 -blocking effects.



Potassium Channel Blockers The hallmark of group 3 drugs is prolongation of the AP duration. This AP prolongation is caused by blockade of I_K potassium channels that are responsible for the repolarization of the AP. AP prolongation results in an increase in effective refractory period and reduces the ability of the heart to respond to rapid tachycardias. Sotalol, ibutilide, dofetilide, and amiodarone (and group 1A drugs; see above) produce this effect on most cardiac cells; the action of these drugs is, therefore, apparent in the ECG as an increase in QT interval. Antiarrhythmic agents that prolong the duration of the action potential may be of value in the management of patients with supraventricular tachyarrhythmias, or in arrhythmias associated with anomalous conduction pathways. Nevertheless, all drugs that prolong the ventricular action potential may induce torsade de pointes (prolongation of the Q-T interval followed by episodes of polymorphic tachycardia).



Calcium Channel Blockers Verapamil is the prototype. Diltiazem is also an effective antiarrhythmic drug. Nifedipine and the other dihydropyridines are not useful as antiarrhythmics, probably because they decrease arterial pressure enough to evoke a compensatory sympathetic discharge to the heart. Pacemaker cells in the SA and the AV node are almost entirely dependent on inward Ca^{2+} currents for depolarization. Verapamil and Diltiazem cause a state- and use-dependent selective depression of calcium current in tissues that require the participation of L-type calcium channels. AV conduction velocity is decreased and effective refractory period increased by these drugs. PR interval is consistently increased. Drugs that block Ca^{2+} channels are particularly effective in preventing reentrant arrhythmias in the AV node and including nodal tachycardia.



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