

Table 1. Classification of tachyarrhythmias

Atrial tachycardias
Sinus tachycardia • Physiological sinus tachycardia • Inappropriate sinus tachycardia • Sinus nodal re-entrant tachycardia Focal AT Multifocal AT MRAT • Cavotricuspid isthmus-dependent MRAT - Typical atrial flutter, counter-clockwise (common) or clockwise (reverse) - Other cavotricuspid isthmus-dependent MRAT • Non-cavotricuspid isthmus-dependent MRAT - Right atrial MRAT - Left atrial MRAT AF
AV junctional tachycardias
Atrioventricular junctional reentrant tachycardia • Typical • Atypical Non-re-entrant junctional tachycardia • Automatic junctional tachycardia • Other non-re-entrant variants
Atrioventricular tachycardias
• Orthodromic (including PJRT) • Antidromic (with retrograde conduction through the AV node or, rarely, over another pathway)

AF = atrial fibrillation; AT = atrial tachycardia; AV = atrioventricular; AVRT = atrioventricular re-entrant tachycardia; AVNRT = atrioventricular nodal re-entrant tachycardia; MRAT = macro-re-entrant atrial tachycardia; PJRT = permanent junctional reciprocating tachycardia.

Ventricular tachycardias

Monomorphic ventricular tachycardia
Accelerated idioventricular rhythm
Polymorphic ventricular tachycardia
Pleomorphic ventricular tachycardia
Bidirectional ventricular tachycardia
Torsade de pointes
Ventricular flutter
Ventricular fibrillation

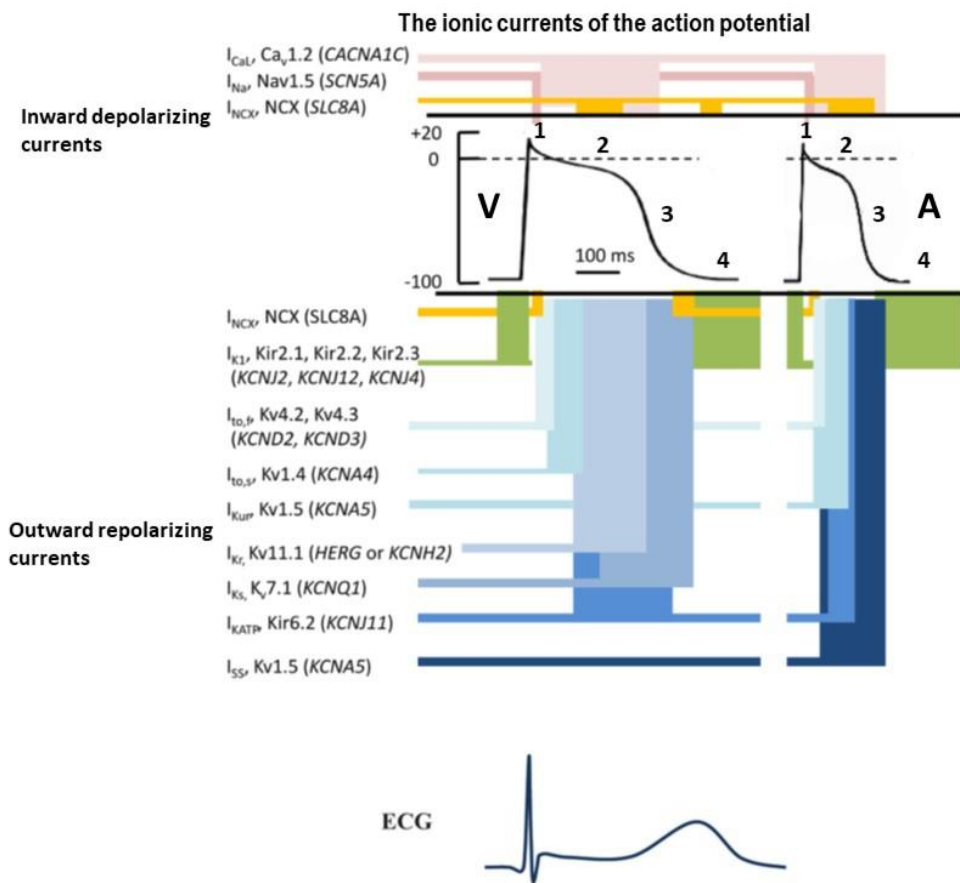


Figure 1. The ionic currents of the action potential (AP). Activation and inactivation of ion channels, currents, underlying proteins, and encoding genes and their contributions to inward depolarizing and outward repolarizing currents.

Ventricular (V) and atrial (A) APs comprise rapid depolarizing (phase 0), early repolarizing (phase 1), brief (atrial) or prolonged (ventricular) phase 2 plateaus (phase 2), phase 3 repolarization, and phase 4 electric diastole. In these, inward Na^+ or Ca^{2+} currents drive phase 0 depolarization and Ca^{2+} current maintains the phase 2 plateau, and a range of outward K^+ currents drive phase 1 and phase 3 repolarization. Phase 4 resting potential restoration is accompanied by a refractory period required for Na^+ channel recovery.

Adapted from Huang CL. Murine Electrophysiological Models of Cardiac Arrhythmogenesis. *Physiol Rev.* 2017;97:283-409, and Lei M, et al. Modernized Classification of Cardiac Antiarrhythmic Drugs. *Circulation.* 2018

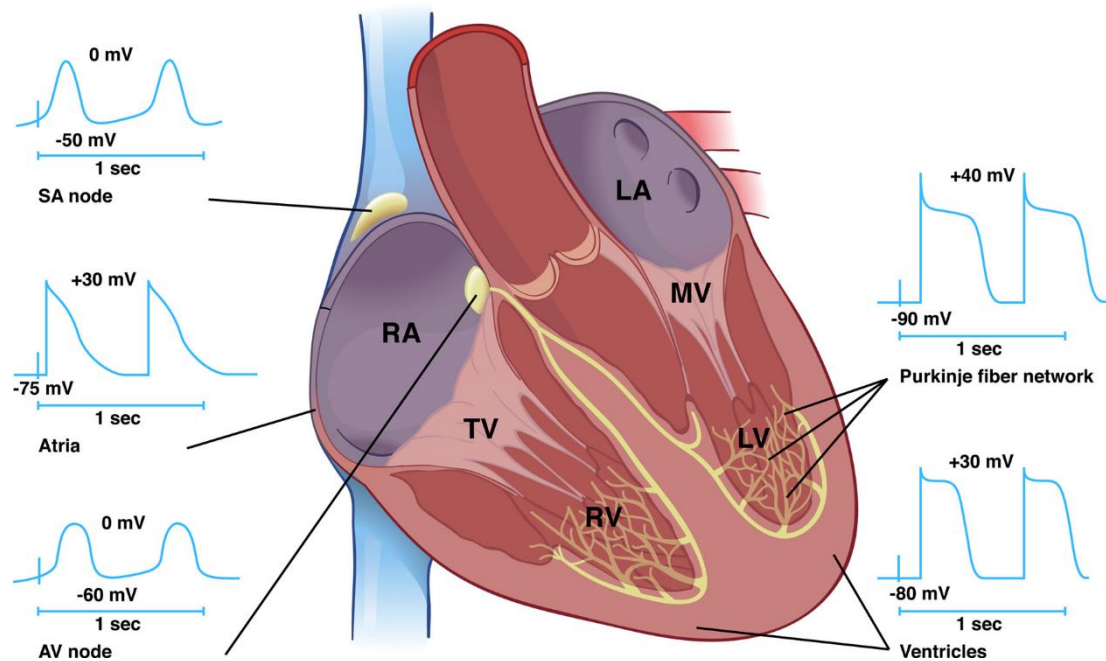


Figure 2. Functional anatomy of the cardiac conduction system.

The cardiac impulse is initiated in the sinoatrial node and propagates through the atria. The electric impulse is then delayed in the AVN before rapid conduction through the right and left bundle branches before terminating in the Purkinje fiber network, which directly interfaces with ventricular cardiomyocytes. Distinct time-voltage relationships are noted in the sinoatrial node, atria, AVN, Purkinje fibers, and ventricles.

RA indicates right atrium; LA, left atrium; TV, tricuspid valve; MV, mitral valve; RV, right ventricle; LV, left ventricle.

Munshi NV. Gene regulatory networks in cardiac conduction system development. *Circ Res* 2012; 110:1525–1537

Table 2. Human atrial and ventricular ionic currents

Current/Symbol	Protein	Gene	Ventricle	Atrium
Voltage-gated inward currents				
Fast Na ⁺ current, I_{Na}	Nav1.5	<i>SCN5A</i>	+++	+++
L-type Ca ²⁺ current, I_{CaL} (dihydropyridine receptor: DHPR)	Ca _v 1.2	<i>CACNA1C</i>	+++	++
Voltage-gated outward currents				
Fast transient outward K ⁺ current, $I_{to,f}$	Kv4.2	<i>KCND2</i>	++	+++
	Kv4.3	<i>KCND3</i>		
Slow transient outward K ⁺ current, $I_{to,s}$	Kv1.4	<i>KCNA4</i>	++	+++
Delayed rectifier K ⁺ current, I_{Kr}	Kv11.1	<i>KCNH2 (HERG)</i>	+++	+
Delayed rectifier K ⁺ current, I_{Ks}	Kv7.1	<i>KCNQ1</i>	+++	+
4-Aminopyridine-sensitive, rapidly activating, slowly inactivating K ⁺ current, I_{Kslow1}	Kv1.5	<i>KCNA5</i>	–	–
4-Aminopyridine-insensitive, rapidly activating, slowly inactivating K ⁺ current, I_{Kslow2}	Kv2.1	<i>KCNB1</i>	–	–
Sustained 4-aminopyridine-sensitive delayed rectifier K ⁺ current, I_{ss}	Kv1.5	<i>KCNA5</i>	–	–
Atrial-specific 4-aminopyridine-sensitive ultrarapid delayed rectifier K ⁺ current, I_{Kur}	Kv1.5	<i>KCNA5</i>	–	++
Inward rectifiers				
Inwardly rectifying current, I_{K1}	Kir2.1	<i>KCNJ2</i>	+++	++
	Kir2.2	<i>KCNJ12</i>		
	Kir2.3	<i>KCNJ4</i>		
Acetylcholine-activated, K ⁺ current, I_{KACh}	Kir3.1	<i>KCNJ3</i>	–	+++
ATP-sensitive potassium channel, I_{KATP}	Kir3.4,	<i>KCNJ5</i>		
	Kir6.2	<i>KCNJ11</i>	++	++
Leak currents				
Two-pore domain K ⁺ leak current, I_{K2p}	K2p3.1	<i>KCNK3</i>	+++	++
Ca ²⁺ -activated K ⁺ currents, I_{KCa}	K _{Ca} 2.x-	<i>KCNNx</i>	–	+++
Exchange currents				
Transient, inward, Na ⁺ -Ca ²⁺ exchange current, I_{ti}	NCX	<i>SLC8A1</i>	++	++

Huang CL. Murine Electrophysiological Models of Cardiac Arrhythmogenesis. *Physiol Rev.* 2017;97:283-409.

Arrhythmias in pregnancy

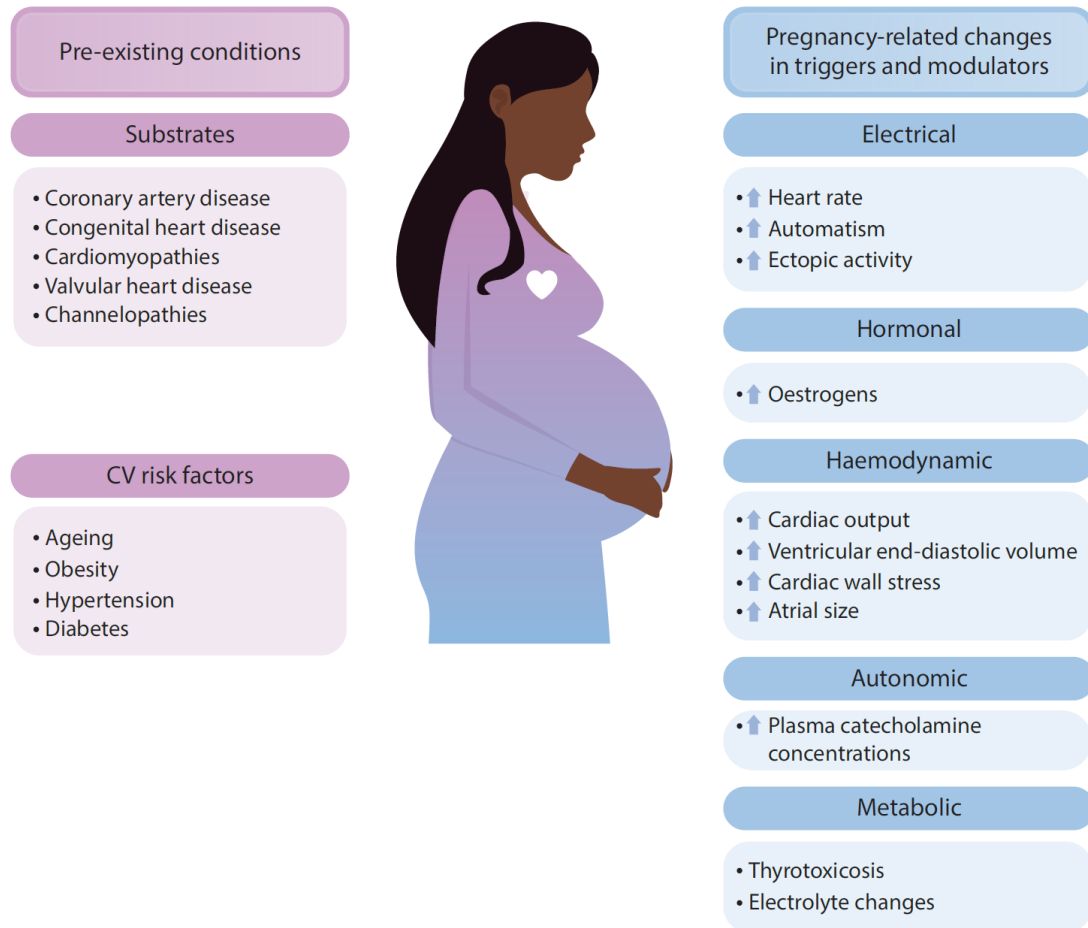


Figure 3. ESC 2025 GL on Pregnancy. Arrhythmogenesis in pregnant women.

Table 3. Vaughan Williams Classification

Class I	Fast Na⁺ channel blockers (slowing of conduction)
	IA (quinidine, procainamide)
	IB (lidocaine)
	IC (propafenone, flecainide)
Class II	Beta-blockers
Class III	Repolarization K⁺ channel blockers (prolongation of repolarization) (amiodarone, * ibutilide, dofetilide, vernakalant, sotalol)
Class IV	Calcium channel blockers (non-dihydropyridine: verapamil, diltiazem)

*Amiodarone exhibits effects of all classes.

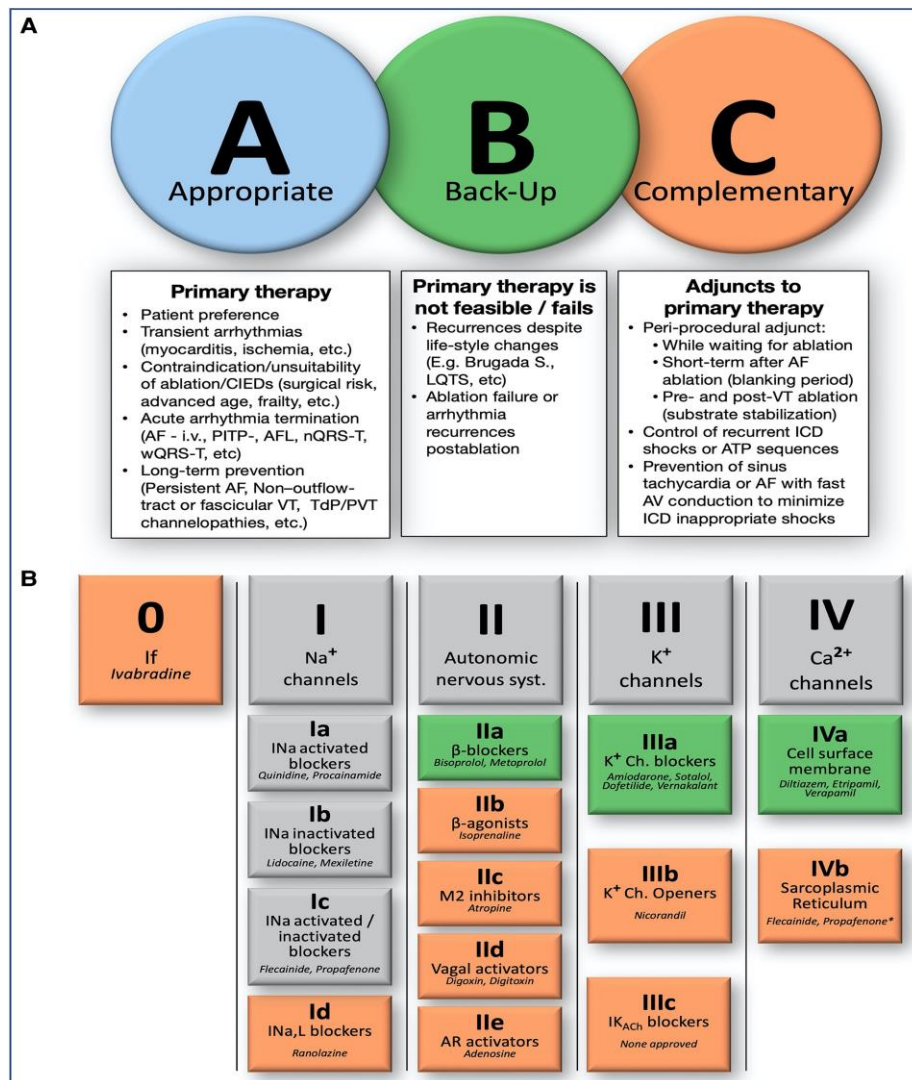


Figure 4. EHRA Practical Compendium of Antiarrhythmic Drugs

Panel A: Framework for the Clinical Use of Antiarrhythmic Drugs (AADs). The ‘ABC’ model from the EHRA Practical Compendium classifies antiarrhythmic drug use as A—Appropriate primary therapy, B—Back-up when primary therapy is not feasible or fails, and C—Complementary as an adjunct to procedures or devices.

Examples of typical clinical scenarios for each category are provided within the panel. Panel B: Simplified update of the Vaughan–Williams classification of antiarrhythmic drugs (AADs). Classes 0–IV are shown with representative drug examples. Each class and subclass is highlighted in bold, accompanied by its principal ion-channel/receptor/body system target and sample agents presented in boxes. Boxes are colour-coded as follows: grey—no significant change from the previous classification; green—relabelled compared with the classical VW scheme; light red—newly introduced classes. *Flecainide and propafenone are Class Ic AADs but also exhibit a secondary intra-cellular sarcoplasmic reticulum RyR2-Ca²⁺ + channel-blocking effect (Class IVb), which is particularly relevant in specific arrhythmias such as catecholaminergic PVT. AF, atrial fibrillation; ACh, acetylcholine; AR, adenosine receptor; ATP, antitachycardia pacing; Ca²⁺, calcium; Ch, channel; CIED, cardiac implantable electronic device; ICD, implantable cardioverter-defibrillator; If, funny current; INa and IK, sodium and potassium currents; INa,L, late INa; K⁺, potassium; LQTS, long QT syndrome; M2, type-2 muscarinic receptor; Na⁺, sodium; nQRS-T, narrow QRS complex tachycardia; PITP, pill-in-the-pocket; PVT, polymorphic ventricular tachycardia; S, syndrome; Syst., system; TdP, torsades de pointes; VT, ventricular tachycardia; wQRS-T, wide QRS complex tachycardia.

Table 4. Examples of Common Proarrhythmic Actions of Antiarrhythmic Pharmacological Drugs

Class	Arrhythmia	Likely Mechanisms
0	Hyperpolarization-activated cyclic nucleotide-gated channel blockers ¹⁵	
Ivabradine	Sinus bradycardia	Depressing sinus node automaticity by block of I_f
I	Voltage-gated Na^+ channel blockers ^{16,28,29}	
Quinidine	Torsades de pointes with prolonged QT interval; vagolytic effect with increase in ventricular rate in atrial flutter	EAD-related triggered activity Conduction slowing in the atrium with enhanced or unaltered atrioventricular conduction
Disopyramide	Torsades de pointes with prolonged QT interval	EAD-related triggered activity
Procainamide	Torsades de pointes with prolonged QT interval Ventricular tachycardia in the presence of ischemic heart disease	EAD-related triggered activity Conduction slowing in the ventricle
Flecainide	Increase in ventricular rate in atrial flutter Ventricular tachycardia in the presence of ischemic heart disease or old myocardial infarction	Conduction slowing in the atrium with enhanced or unaltered atrioventricular conduction Conduction slowing in the ventricle or myocardial scar areas
Propafenone	Increase in ventricular rate in atrial flutter Ventricular tachycardia in the presence of ischemic heart disease or old myocardial infarction Slowed sinus rate	Conduction slowing in the atrium with enhanced or unaltered atrioventricular conduction Conduction slowing in the ventricle or myocardial scar areas Depressing sinus node automaticity by block of I_f
II	Autonomic inhibitors and activators ^{5,16,24-27,29,34}	
β -Adrenergic receptor inhibitors	Sinus bradycardia; atrioventricular block Sinus tachycardia or other type of tachycardia	β -Blockade Upregulation of β -receptors with long-term therapy; β -blocker withdrawal
β -Adrenergic receptor activators	Sinus tachycardia, increased triggering activity	β -Receptor activation
M_2 receptor activators: carbachol, digoxin	Sinus bradycardia; atrioventricular block; ventricular tachycardia	Depression of SAN automaticity and atrioventricular node conduction Increase in vagal tone Increased delayed afterdepolarization-related triggered activity
M_2 receptor inhibitors: atropine	Exacerbated ventricular bradycardia and exacerbated effects of low atrioventricular block	Increased SAN automaticity and atrioventricular conduction despite persistent degenerative atrioventricular block at or below His bundle level
A_1 receptor activators: adenosine	Sinus bradycardia, sinus arrest, or atrioventricular block associated with adenosine terminating paroxysmal supraventricular tachycardia Frequent atrial or premature ventricular beats; atrial fibrillation	Depressing sinoatrial node automaticity and atrioventricular node conduction Unknown mechanism
III	K^+ channel blockers and openers ^{16,24,27,29}	
Dofetilide, ibutilide, D/L -sotalol	Torsades de pointes with prolonged QT interval	EAD-related triggered activity
IV	Ca^{2+} handling modulators ^{5,16,24,26,27,29}	
Ca^{2+} channel blockers eg, verapamil	Sinus bradycardia; atrioventricular block Increase in ventricular rate in patients with atrial fibrillation with Wolff-Parkinson-White syndrome	Depressing SAN automaticity and atrioventricular node conduction by block of Ca^{2+} channel; decreased accessory pathway

Lei M, et al. Modernized Classification of Cardiac Antiarrhythmic Drugs. *Circulation*. 2018.