ANTIARRHYTHMIC DRUGS

Drugs that modify the rhythm and conduction of the heart are used to treat cardiac arrhythmias. Antiarrhythmic drugs may aggravate or produce arrhythmias (proarrhythmia) and they may also depress ventricular contractility and must therefore be used with caution. They are classified according to their effect on the action potential (Vaughan Williams' classification).

Vaughan Williams' classification of antiarrhythmic drugs:

Class I

Membrane-stabilising agents (sodium channel blockers):

Class Ia: Block Na^+ channel and prolong action potential, e.g. quinidine, procainamide, and disopyramide.

Class Ib: Block Na^+ channel and shorten action potential, e.g. mexiletine, phenytoin, and lidocaine.

Class Ic: Block Na^+ channel with no effect on action potential, e.g. Flecainide, propafenone.

Class II

β-Adrenoceptor blocking drugs, e.g. propranolol, timolol, and metoprolol.

Class III

Prolong action potential, e.g. sotalol, amiodarone, dronedarone, ibutilide, dofetilide and bretylium.

Class IV

Calcium-channel blockers, e.g. verapamil and diltiazem.

> ***Note//*** Some drugs (e.g. digoxin and adenosine) have no place in this classification, while others have properties in more than one class, e.g. amiodarone, which has actions in all four classes.

ATRIAL TACHYARRHYTHMIAS

Atrial tachyarrhythmias including atrial fibrillation, atrial flutter, atrial tachycardia and atrial ectopic beats all arise from the atrial myocardium. They share common aetiologies, which includes:

Cardiac causes:

(1) Hypertension **(2)** Congestive heart failure **(3)** Coronary artery disease and myocardial infarction **(4)** Valvular heart disease **(5)** Cardiomyopathy: dilated, hypertrophic Myocarditis and pericarditis **(6)** Wolff–Parkinson–White syndrome **(7)** Sick sinus syndrome **(8)** Cardiac tumours **(9)** Cardiac surgery **(10)** Familial tachyarrhythmia (e.g. lone AF) & Genetic predisposition.

Non-cardiac causes:

(1) Thyrotoxicosis **(2)** Phaeochromocytoma **(3)** Acute and chronic pulmonary disease (pneumonia, chronic obstructive pulmonary disease) **(4)** Pulmonary vascular disease (pulmonary embolism) **(5)** Electrolyte disturbances (hypokalaemia) **(6)** Increased sympathetic tone (exercise) **(7)** Increased parasympathetic tone (vagally induced and postprandial arrhythmia) **(8)** Alcohol abuse ('holiday heart' and long-term use) **(9)** Caffeine, smoking, recreational drug use, e.g. cannabis **(10)** Myotonic dystrophy type 1.

ATRIAL FIBRILLATION

This is a common arrhythmia, occurring in 5–10% of patients over 65 years of age. It also occurs, particularly in a paroxysmal form, in younger patients. Any condition resulting in raised atrial pressure, increased atrial muscle mass, atrial fibrosis, or inflammation and infiltration of the atrium, may cause atrial fibrillation.

During episodes of AF, the atria beat rapidly due to foci located predominantly within the pulmonary veins. The ventricles are activated irregularly at a rate determined by conduction through the AV node. This produces the characteristic 'irregularly irregular' pulse. The ECG shows normal but irregular QRS complexes; there are no P waves but the baseline may show irregular fibrillation waves.

AF Classification

The **clinical** classification of atrial fibrillation includes *paroxysmal*, *persistent*, *Long-standing persistent* and *permanent AF*.

Term	Definition
Paroxysmal AF	•AF that terminates spontaneously or with intervention within 7 d of onset.•Episodes may recur with variable frequency.
Persistent AF	•Continuous AF that is sustained >7 d.
Long-standing persistent AF	•Continuous AF >12 mo in duration.
Permanent AF	•The term “permanent AF” is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm

Other classification of AF according to the **etiology** includes *valvular* and *nonvalvular AF.*

Nonvalvular AF	•AF in the absence of moderate to sever rheumatic mitral stenosis or mechanical prosthetic heart valve

AF also can classify according to **duration** of AF and these include *acute AF* (onset within 48 hours) and *chronic AF*.

Symptoms and signs

AF can cause palpitation, breathlessness and fatigue. In patients with poor ventricular function or valve disease it may precipitate or aggravate cardiac failure because of loss of atrial function and heart rate control. A fall in blood pressure may cause lightheadedness, and chest pain may occur with underlying coronary disease. However, AF is often completely asymptomatic, in which case it is usually discovered as the result of a routine examination or ECG.

Management

Assessment of patients with newly diagnosed AF includes a full history, physical examination, 12-lead ECG, echocardiogram and thyroid function tests. Additional investigations such as exercise testing may be needed to determine the nature and extent of any underlying heart disease. When AF complicates an acute illness (e.g. chest infection, pulmonary embolism), effective treatment of the primary disorder will usually restore sinus rhythm.

Paroxysmal atrial fibrillation

Occasional attacks that are well tolerated do not necessarily require treatment, but β-blockers are the drug of choice if symptoms are troublesome. Beta-blockers are particularly useful for treating patients with AF associated with ischaemic heart disease, hypertension and cardiac failure. Class Ic drugs such as propafenone or flecainide are also effective at preventing episodes but should be avoided in patients with coronary disease or left ventricular dysfunction. Amiodarone is the most effective agent for preventing AF but its side-effects restrict its use to patients in whom other measures fail. Digoxin and verapamil are not effective drugs for preventing paroxysms of AF, but it can limit the heart rate when AF occurs by blocking the AV node. Radiofrequency ablation has emerged as a promising treatment for paroxysmal AF in patients who do not have structural heart disease.

Persistent and permanent atrial fibrillation

Two strategies are available for the long-term management of atrial fibrillation:

1) ***'Rate control'*** (AV nodal slowing agents).

2) ***'Rhythm control'*** (antiarrhythmic drugs plus DC cardioversion).

Rhythm control

An attempt to restore sinus rhythm is particularly appropriate if the arrhythmia has precipitated symptoms and there is a treatable underlying cause. Electrical cardioversion is initially successful in around 80% of patients but relapse is frequent. Attempts to restore and maintain sinus rhythm are most successful if AF has been present for < 3 months, the patient is young, and there is no important structural heart disease.

Immediate DC cardioversion, after the administration of intravenous heparin, is appropriate if AF has been present for less than 48 hours. If AF present for more than 48 hours DC cardioversion should be deferred until the patient has been established on warfarin, with an international normalised ratio (INR) of between 2 and 3, for a minimum of 3 weeks, and should be maintained for at least 1 month following successful cardioversion. Pharmacological Cardioversion can be restore sinus rhythm by using Flecainide, dofetilide, propafenone, intravenous ibutilide and amiodarone.

Rate control

If sinus rhythm cannot be restored, treatment should be directed towards maintaining an appropriate heart rate. Digoxin, β-blockers or rate-limiting calcium antagonists such as verapamil or diltiazem will reduce the ventricular rate by increasing the degree of AV block. Beta-blockers and rate-limiting calcium antagonists are often more effective than digoxin at controlling the heart rate during exercise and may have additional benefits in patients with hypertension and/or structural heart disease.

Prevention of thromboembolism

Loss of atrial contraction and left atrial dilatation cause stasis of blood in the left atrium, and may lead to thrombus formation in the left atrial appendage. This predisposes patients to stroke and other forms of systemic embolism.

Treatment with adjusted-dose warfarin (target INR 2-3) reduces the risk of stroke by about two-thirds. Warfarin is thus indicated for patients with AF who have specific risk factors for stroke according to CHA2DS2-VASc score (Congestive heart failure, Hypertension, Age ≥75 years [doubled], Diabetes mellitus, Prior Stroke or TIA or thromboembolism [doubled], Vascular disease, Age 65 to 74 years, female Sex).

ATRIAL FLUTTER

Atrial flutter is characterised by a large (macro) re-entry circuit within the right atrium, usually encircling the tricuspid annulus. The atrial rate is approximately 300/min. It is usually associated with 2:1, 3:1, or 4:1 AV block (with corresponding heart rates of 150, 100, 75). The ECG shows

saw-toothed flutter waves.

Management and prevention of thromboembolism are same like in atrial fibrillation. Catheter ablation offers a 90% chance of complete cure and is the treatment of choice for patients with persistent and troublesome symptoms.

ATRIAL TACHYCARDIA

Atrial tachycardia may be a manifestation of increased atrial automaticity, sinoatrial disease or digoxin toxicity. It produces a narrow complex tachycardia with abnormal P-wave morphology, sometimes associated with atrioventricular block if the atrial rate is rapid. Treatment of underlying cause like hypoxia due to COPD can eliminate this arrhythmia, it may respond to β-blockers, which reduce automaticity, or class I or III antiarrhythmic drugs. Catheter ablation therapy can be offered to patients with recurrent or drug-resistant atrial tachycardia.

SUPRAVENTRICULAR TACHYARRHYTHMIAS

The term 'supraventricular tachycardia' (SVT) is commonly used to describe a range of regular tachycardias that have a similar appearance on an ECG. These tachycardias are usually associated with a narrow QRS complex and are characterised by a re-entry circuit or automatic focus involving the atria.

AV NODAL RE-ENTRY TACHYCARDIA (AVNRT)

This is due to re-entry in the right atrium and AV node and produces a regular tachycardia with a rate of 140-220/min. It tends to occur in hearts that are otherwise normal, and episodes may last from a few seconds to many hours. The patient is usually aware of a fast heart beat and may feel faint or breathless. Polyuria, mainly due to the release of atrial natriuretic peptide, is sometimes a feature, and cardiac pain or heart failure may occur if there is coexisting structural heart disease.

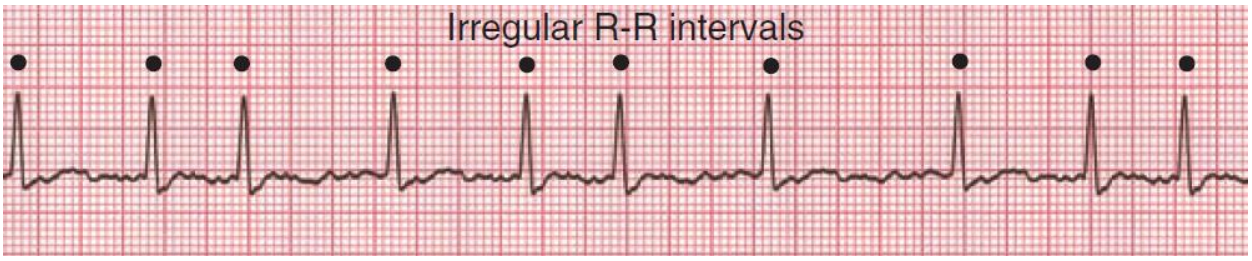
Management

The attack may be terminated by carotid sinus pressure or other measures that increase vagal tone (e.g. Valsalva manoeuvre). Intravenous adenosine or verapamil will restore sinus rhythm in most cases. Suitable alternative drugs include β-blockers, flecainide and digoxin. In an emergency when there is severe haemodynamic compromise, the tachycardia should be terminated by DC cardioversion. Catheter ablation offers a very high chance of complete cure and is usually preferable to long-term drug treatment.

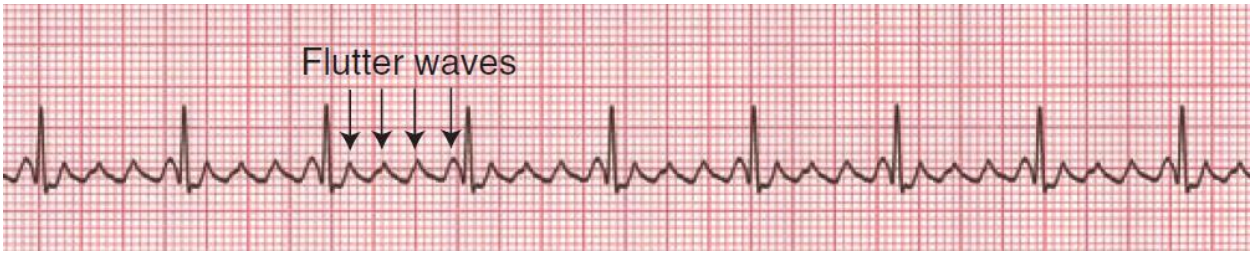
ATRIOVENTRICULAR RE-ENTRANT TACHYCARDIA (AVRT) AND WOLFF-PARKINSON-WHITE SYNDROME (WPW)

In these conditions there is an abnormal band of conducting tissue which connects the atria and ventricles, and is known as an accessory pathway. In around half of cases this pathway only conducts in the retrograde direction (from ventricles to atria) and thus does not alter the appearance of the ECG in sinus rhythm. This is known as a *concealed accessory pathway*. In the remainder of cases, conduction takes place partly through the AV node and partly through the rapidly conducting accessory pathway during sinus rhythm. Premature activation of ventricular tissue via the pathway produces a short PR interval and a 'slurring' of the QRS complex, called a delta wave. This is known as a *manifest accessory pathway*, when this is associated with symptoms, the condition is known as Wolff-Parkinson-White syndrome. If atrial fibrillation occurs, it may produce a dangerously rapid ventricular rate because the accessory pathway lacks the rate-limiting properties of the AV node. This is known as pre-excited atrial fibrillation and may cause collapse, syncope and even death. It should be treated as an emergency, usually with DC cardioversion.

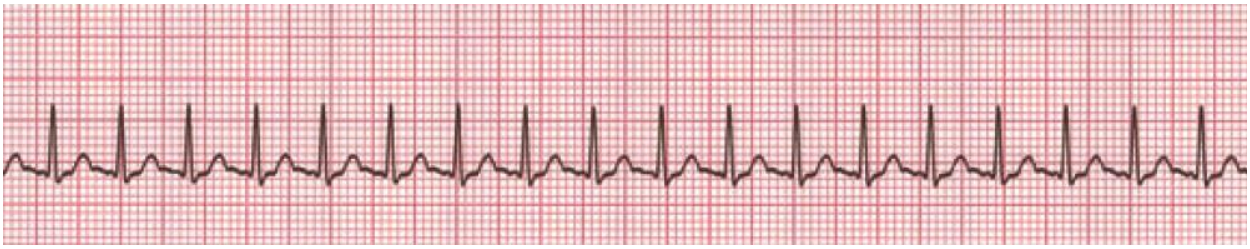
Prophylactic anti-arrhythmic drug therapy is only indicated in symptomatic patients and is aimed at slowing the conduction rate and prolonging the refractory period of the bypass tract, using agents such as flecainide, propafenone or amiodarone; digoxin and verapamil shorten the refractory period of the accessory pathway and should be avoided. Catheter ablation of the accessory pathway is the treatment of choice for symptomatic patients.



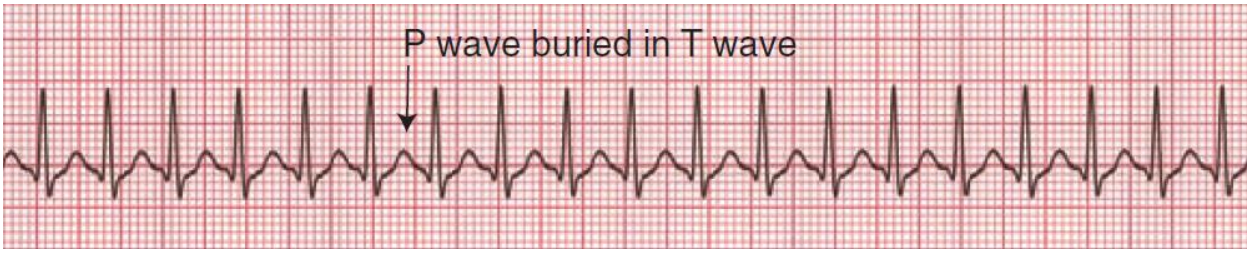
Atrial Fibrillation (AF)



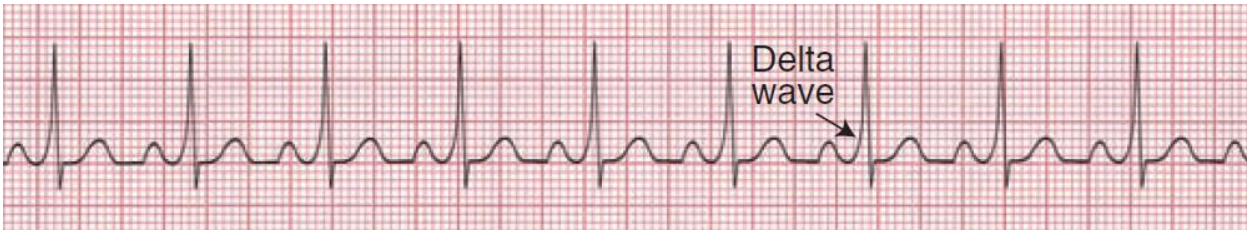
Atrial Flutter (A Flutter)



Atrial Tachycardia



Supraventricular Tachycardia (SVT)



Wolff-Parkinson-White (WPW) Syndrome