Traditionally, the goal of atrial fibrillation (AF) management has been to restore sinus rhythm (SR). This strategy, known as rhythm control or cardioversion, can be achieved either electrically or pharmacologically. It is also important to control the ventricular rate (rate control) to minimise haemodynamic instability, which can be a consequence of AF. Moreover, preventing thromboembolism — thereby reducing the risk of stroke or other systemic emboli — for patients with AF is as important as managing the arrhythmia itself.

Following careful assessment of a patient with AF, management can include a combination of one or more of these goals. The strategy chosen will depend primarily on the severity of symptoms and the characteristics of the AF. In addition, it is essential to address any underlying causative factors (for example, high blood pressure, heart failure or hyperthyroidism).

Acute or recent-onset AF
Patients who present with recent-onset AF, defined as onset in the past 48 hours, and associated haemodynamic compromise (such as symptomatic hypotension, acute heart failure, unstable angina, loss of consciousness or shock) require urgent intervention.

For these patients, the usual aim is to revert them to SR using electrical direct current (DC) cardioversion. DC cardioversion involves the application of a controlled electric shock across the chest wall to override the disordered conduction and allow the sinus node to regain control of heart rate. Patients undergoing urgent DC cardioversion should be treated with heparin before the procedure and be fully anticoagulated after it.

For patients who are haemodynamically stable, pharmacological cardioversion can be attempted with drugs such as flecainide, amiodarone or propafenone. Recently published guidance from the European Society of Cardiology summarises the options for acute management of atrial fibrillation (see Figure 1, p359).

According to the ESC, drug choice for pharmacological cardioversion depends on the presence or absence of structural heart disease. Structural heart disease can include left-ventricular hypertrophy, bundle branch block, cardiomyopathy or ischaemia. If structural heart disease is present, intravenous amiodarone is the medicine of choice; if it is absent, flecainide is preferred. However, National Institute for Health and Clinical Excellence guidance published in 2006 recommends that intravenous amiodarone be used for patients with or without structural heart disease.

If early electrical or pharmacological cardioversion is being considered it is essential to exclude the presence of
atrial thrombus before cardioversion by confirming that the AF started within the past 48 hours.

**Persistent and permanent AF**

Patients with recurrent or ongoing AF should be assessed and an appropriate strategy of rhythm or rate control determined.1

Restoration and maintenance of SR improves exercise tolerance and cardiac output, protects against the development of cardiomyopathy and relieves symptoms. Attaining SR offers the theoretical advantages of reducing the risk of thromboembolism and relieves symptoms. Attaining SR offers the theoretical advantages of reducing the risk of thromboembolism and relieves symptoms.

Rhythm control Rhythm-control strategies aim to restore and maintain SR. NICE guidance recommends rhythm control for patients with persistent AF who:2

- Are symptomatic
- Are under 65 years of age
- Present with AF for the first time (ie, lone AF)
- Present with AF secondary to a precipitating factor (that has been treated or corrected)
- Have congestive heart failure

For patients with persistent AF, this is usually achieved by elective DC cardioversion. At first attempt, DC cardioversion is successful in up to 80% of patients, but relapse rates are high: 60–75% of patients relapse, often within the first month.3

Patients undergoing elective cardioversion must be anticoagulated for at least four weeks before, and following, the procedure to reduce the risk of systemic thromboembolism.3

If DC cardioversion fails, an antiarrhythmic medicine (such as amiodarone or sotalol) administered for four weeks before the procedure is repeated can improve efficacy. If patients relapse, long-term antiarrhythmic therapy may be required to maintain SR following DC cardioversion. In these circumstances, a beta-blocker is used first line — to slow conduction and prevent tachycardias that can precipitate reversion to AF.

If a beta-blocker is ineffective, contraindicated or not tolerated, second-line options are:2

- Amiodarone — in the presence of structural heart disease
- Flecaïnide or sotalol — in the absence of structural heart disease

Patients starting amiodarone therapy (in particular) should receive thorough advice on side effects — information in the British National Formulary can be used to guide counselling.

Rate control Generally, a patient’s heart rate is considered controlled when the ventricular response to AF ranges from 60 to 80 beats/min at rest and between 90 and 115 beats/min during moderate exercise, although this varies depending on patient age.1

Rate-control strategies are recommended by NICE for patients with persistent AF who:2

- Are over 65 years of age
- Have coronary artery disease
- Have contraindications to antiarrhythmic medicines
- Are unsuitable for cardioversion

Rate control is also recommended for patients with permanent AF with a rapid ventricular response.2

Standard beta-blockers (such as atenolol or bisoprolol) or rate-controlling calcium channel blockers (such as verapamil or diltiazem) are the agents of choice for controlling heart rate.1,2

Digoxin is only recommended for patients who are mainly sedentary since it does not offer adequate rate control during exercise.2

Furthermore, medicine choice for rate control will be influenced by any comorbidities (see Box 1, p360).

**Paroxysmal AF**

In paroxysmal AF the episodes of arrhythmia, known as paroxysms, are self-limiting. The objective of therapy is to reduce the frequency, or to prevent the occurrence, of paroxysms and to control the ventricular rate during episodes to minimise the likelihood of haemodynamic compromise.

Some patients have infrequent paroxysms that are associated with minimal symptoms and resolve spontaneously; these patients may not require drug treatment for their arrhythmia (although they might need antithrombotic therapy for stroke prevention).

---

### Table: European Society of Cardiology guidance for the acute management of AF

<table>
<thead>
<tr>
<th>Recent-onset atrial fibrillation (&lt;48 hours)</th>
<th>Haemodynamic instability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

**Electrical cardioversion**

- Yes
  - Amiodarone IV
  - Propafenone IV
  - Ibutilide IV

- No
  - Flecaïnide IV

*This is not available in the UK.*
A "pill-in-the-pocket" strategy can be appropriate for certain patients with infrequent but symptomatic paroxysms. This approach involves the patient using medicines such as flecainide or propafenone on an "as required" basis to restore SR rapidly when a paroxysm occurs. These patients should be assessed fully to exclude left-ventricular dysfunction or valve disease before implementing such a strategy.

For patients with more frequent episodes, or more severe symptoms, ongoing drug treatment to suppress AF episodes should be started. First-line treatment for all patients is a standard beta-blocker. Flecainide, propafenone or sotalol should be considered second line in the absence of structural heart disease. For patients with structural heart disease, amiodarone is recommended for second-line treatment of paroxysmal AF.

Patients with paroxysmal AF should be advised to avoid any known precipitants such as alcohol, caffeine or stress.

**Non-pharmacological strategies**

Specialist, non-pharmacological strategies are available to manage AF for patients who have failed pharmacological treatment strategies, or those who are suspected to have underlying electrophysiological disorders. Examples of such specialist interventions are:

- Implantable atrial defibrillators or atrioverters: these are devices that function like pacemakers, delivering electrical impulses with the aim of maintaining SR. Because the shock they deliver can be strong and somewhat painful, they are best suited to those with recurrent rather than a permanent AF.
- Pulmonary vein isolation: this is the ablation of cardiac tissue around the pulmonary veins to treat patients with paroxysmal AF. These areas are often the origin of ectopic beats that precipitate some attacks of paroxysmal AF.
- Atrioventricular (AV) nodal ablation: this involves the destruction of AV nodal tissue to prevent the conduction of AF waves to the ventricles and is a highly effective method of controlling ventricular rate. Following the procedure, patients require implantation of a permanent pacemaker to maintain ventricular rate thereafter.
- The maze procedure: a surgical procedure whereby a number of small cuts are made in the atrial wall. These prevent the rapid and unco-ordinated depolarisation of atrial cells and therefore interrupt the signals responsible for initiating and perpetuating episodes of AF.

**New medicines**

**Vernakalant** Vernakalant is a sodium and potassium channel blocker with atrial-selective, anti-arrhythmic effects. Placebo-controlled studies have demonstrated that vernakalant can chemically cardiovert patients.

The AVRO study demonstrated that vernakalant could cardiovert patients to SR significantly faster than intravenous amiodarone — 51% of patients reverted to SR at 90 minutes with vernakalant compared with 5.2% with amiodarone (P=0.0001).

In September 2010, vernakalant was granted marketing approval in the EU for the rapid conversion of recent-onset AF to SR in adults. Vernakalant is likely to be launched in the UK in the coming months.

The exact place of vernakalant in therapy has not been determined, but it is possible that it could rival first-line therapies in the management of recent-onset AF. However, cost may limit its use in clinical practice. At the time of writing, vernakalant was not scheduled for review by NICE.

**Dronedarone** Dronedarone, a new oral antiarrhythmic, was launched in the UK in 2010. It has a similar mechanism of action to amiodarone but, in line with other antiarrhythmics, is less effective at attaining and maintaining SR.

Despite this, dronedarone has some substantial advantages over amiodarone including a simple dosing regimen, shorter half-life, far less onerous monitoring requirements and fewer toxic adverse effects.

Placebo-controlled studies have demonstrated that dronedarone can maintain SR better than placebo, but not better than amiodarone. Relapse rates with dronedarone remain high (around 60%).

NICE guidance recommends dronedarone be used for patients who have failed to respond to first-line therapy and:

- Have hypertension requiring at least two different classes of medicine
- Have diabetes mellitus
- Have a history of transient ischaemic attack, stroke or systemic embolism
- Have a left-atrial diameter of 50mm or greater or left-ventricular ejection fraction less than 40%
- Are 70 years of age or older
- Do not have unstable New York Heart Association class III or IV heart failure

---

**Box 1: Choice of medicine for rate control**

<table>
<thead>
<tr>
<th>CLASS OF DRUG</th>
<th>ISCHAEMIC HEART DISEASE</th>
<th>HYPERTENSION</th>
<th>HEART FAILURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>+</td>
<td>++</td>
<td>–</td>
</tr>
<tr>
<td>Digoxin</td>
<td>+/-</td>
<td>+/-</td>
<td>+</td>
</tr>
</tbody>
</table>

Key: ++ Strongly indicated; + May be of benefit; +/- Equivocal benefit; – Avoid
This position allows amiodarone to be reserved for patients who fail dronedarone therapy while minimising exposure of certain patients to the toxic side effects of amiodarone. It is expected that dronedarone use will be limited to secondary care specialists while clinical experience is gained. Shared care arrangements may be required to ensure adequate monitoring, particularly of renal function, following initiation.

**Editor** — for more information on dronedarone see **Clinical Pharmacist 2010;2:334.**

**Stroke prevention**

**Risk assessment** People with AF are five times more likely to have a stroke than people without AF. In addition, AF-related strokes are more severe and associated with more disability than non-AF strokes. Adequately controlled anticoagulation with warfarin reduces the risk of stroke for patients with AF by 68% and can prevent three out of four AF-related strokes.1

Risk-scoring systems are needed to balance the benefits of preventing stroke against the risk of bleeding with oral anticoagulants. Numerous systems to assess stroke risk have been developed, but the most commonly used in clinical practice is the CHADS2 score (see Box 2).

According to CHADS2, the bleeding risk outweighs the benefit of anticoagulation for patients with fewer risk factors, but for patients with multiple risk factors, or with prior stroke or transient ischaemic attack, the benefits of oral anticoagulation outweigh the bleeding risk. Data from clinical trials suggest an annual risk of bleeding of approximately 2% with warfarin.1,14 Accordingly, warfarin is recommended for all patients with a stroke risk greater than the bleeding risk, that is a CHADS2 score ≥2.

This year has seen the introduction of an extended risk factor scoring system to replace CHADS2, known as CHA2DS2-VASc, although this has yet to be incorporated into UK clinical practice.15

**Anticoagulation** For patients in AF, anticoagulation with warfarin is the standard of care, with the aim of maintaining the international normalised ratio between 2 and 3. However, the duration of anticoagulant therapy in patients converted to SR remains a subject of much debate.1

Emerging data suggest that newer agents may challenge the central role of warfarin in AF stroke prevention. The RE-LY study compared the direct thrombin inhibitor dabigatran with open-label warfarin for stroke prevention in patients with AF. The results indicate that dabigatran is at least as good as warfarin in preventing AF-related stroke.16 Low-dose dabigatran (110mg twice daily) was as effective as warfarin with a lower risk of bleeding, while higher-dose dabigatran (150mg twice daily) offered greater protection against stroke with equivalent bleeding risk. Despite this, the number needed to treat (NNT) to accrue the benefit is large: the NNT to prevent one haemorrhagic stroke with dabigatran 150mg twice daily compared with warfarin is 357.

The ROCKET AF trial — a randomised, double-blind study comparing the direct factor Xa inhibitor rivaroxaban with warfarin for stroke prevention in AF — is expected to be reported at the American Heart Association conference this year.

The advantages of these newer medicines are simpler dosing regimens and fewer ongoing monitoring requirements. Nonetheless, there are concerns about compliance with medicines that do not require the intensive monitoring of warfarin, something that cannot be tested in clinical trials.

In addition, the costs of the newer medicines are likely to be substantially higher than the current costs associated with warfarin, even taking into account the costs of INR monitoring.

It is expected that dabigatran and rivaroxaban will gain licences for the prevention of stroke in patients with AF.

---

**Box 2: Risk of stroke in AF using CHADS2**

The CHADS2 score is a tool used to calculate the risk of a patient with atrial fibrillation having a stroke, based on their medical history and comorbidities.

A patient’s CHADS2 score is calculated by assigning points as described below:

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic heart failure (current or history of)</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension (current or history of)</td>
<td>1</td>
</tr>
<tr>
<td>Age greater than 75 years</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke or transient ischaemic attack (current or history of)</td>
<td>2</td>
</tr>
</tbody>
</table>

A patient’s resulting CHADS2 score corresponds to the stroke risk for that patient (see below):

<table>
<thead>
<tr>
<th>CHADS2 SCORE</th>
<th>STROKE RISK PER 100 PATIENT YEARS</th>
<th>CHADS2 RISK LEVEL</th>
<th>ANTITHROMBOTIC RECOMMENDED</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>Low</td>
<td>Aspirin or no treatment</td>
</tr>
<tr>
<td>1</td>
<td>2.8</td>
<td>Low</td>
<td>Aspirin or warfarin</td>
</tr>
<tr>
<td>2</td>
<td>4.0</td>
<td>Moderate</td>
<td>Warfarin</td>
</tr>
<tr>
<td>3</td>
<td>5.9</td>
<td>Moderate</td>
<td>Warfarin</td>
</tr>
<tr>
<td>4</td>
<td>8.5</td>
<td>High</td>
<td>Warfarin</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>High</td>
<td>Warfarin</td>
</tr>
<tr>
<td>6</td>
<td>18.2</td>
<td>High</td>
<td>Warfarin</td>
</tr>
</tbody>
</table>

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within the next 12 months, and NICE health technology appraisals are expected shortly after licensing. Many more oral anticoagulants are in development and are expected to be licensed in the coming years.

You will discuss the most appropriate treatment strategy for James, a 63-year-old man admitted to your A&E department with suspected paroxysmal atrial fibrillation. The questions will invite you to consider the side effects associated with antiarrhythmic drugs and explore the challenges of initiating and monitoring patients on amiodarone.

For more information about taking part in a learning@lunch flex session or setting up your own learning community, turn to the contact details on p358.

References

Try our Lifelong Learning modules at www.clinicalpharmacist.com

Atrial fibrillation

Lifelong Learning questions are available to complete in an online module on the Clinical Pharmacist section of PJ Online — accessible via www.clinicalpharmacist.com.

To complete the module, you will need to log in to the site. If you are a new visitor, it is simple to register as a user (registration is free to all Royal Pharmaceutical Society members).

Questions
This month’s Lifelong Learning questions are based on the CLINICAL FOCUS articles on atrial fibrillation, commissioned from independent authors. The information in the Box (below) is there to help you identify knowledge gaps and undertake continuing professional development. This online module will close on 1 February 2011.

Answers
When you have completed the online module, your answers will be submitted for marking and Clinical Pharmacist will send you a certificate and your results by email within two weeks of the module closing. Please do not hesitate to contact us if you have technical problems with the module. E: clinicalpharmacist@pharmj.co.uk

How to undertake CPD

Our CLINICAL FOCUS articles and the online Lifelong Learning modules can help you plan your CPD and record the benefits of the activity at www.uptodate.org.uk.

Reflect on your gaps in knowledge

● Why does atrial fibrillation (AF) occur and how are the various types of AF classified?
● What are the different treatment strategies for AF and which medicines are used?
● How can strokes be prevented in patients with AF?

Act to enhance your practice

● Read the CLINICAL FOCUS articles in this issue (pp355–62)
● Consider making this activity one of your nine CPD entries this year

Answers from September’s module

Atopic eczema

1 (a) T, (b) F, (c) T, (d) T, (e) F
2 (a) T, (b) T, (c) T, (d) T, (e) F
3 (a) T, (b) T, (c) F, (d) T, (e) F
4 (a) T, (b) F, (c) T, (d) T, (e) T
5 (a) T, (b) T, (c) F, (d) T, (e) F
6 (a) T, (b) F, (c) T, (d) T, (e) T
7 (a) F, (b) F, (c) T, (d) F, (e) F
8 (a) T, (b) F, (c) T, (d) F, (e) F
9 (a) T, (b) F, (c) T, (d) F, (e) T
10 (a) F, (b) F, (c) T, (d) F, (e) T