The Practitioner®

CPD study pack

October 2020;264(1841)

The study pack contains this month's CPD exercise plus all relevant articles:

- Diagnosis and management of abdominal aortic aneurysm
- Suspected cardiac syncope requires urgent investigation
- Prompt diagnosis can improve outcomes in multiple sclerosis

Fillable PDF templates*

- CPD exercise is a fillable PDF

CPD prompt and framework templates

- Journal article
- Case review
- Audit

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CME - FILLABLE PDF FORM

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Practitioner CPD exercise

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Show impact
- Collection of data
- Practice audit to show improved care
- Case studies
- Implement a protocol
- Prescribing review
- Educational meetings
- Significant event audit
- Practice meeting
- Implement a new service
- Take on new role
- Significant event audits
- Change with feedback from patients and/or colleagues

Further options for sessional GPs
- Self audit of own practice:
  - Record-keeping
  - Referrals for investigations
  - Prospective condition based reviews
  - Random case analysis with colleagues
  - Review of telephone triage outcomes
- Update drugs in emergency bag

CPD Framework

Online all articles are associated with CPD prompts/frameworks to written reflection:

Adobe fillable PDFs
- Article review framework
- Case review framework
- Audit framework

Word documents
- Reflection on a journal article
- Stages of reflection on a situation
- Team reflection

ABDOMINAL AORTIC ANEURYSM

Which of the statements are true?

A The condition is normally asymptomatic
True ☐ **False** ☐

B The mainstay of imaging is duplex ultrasound
True ☐ **False** ☐

C Abdominal X-rays are generally helpful in sizing an aneurysm
True ☐ **False** ☐

D After successful surgery patients have 90% of the life expectancy of those who have not had an aneurysm
True ☐ **False** ☐

E Surgery aims to improve quality of life
True ☐ **False** ☐

2 Complete the statements:

The mainstay of management is

modification to improve

health for potential surgery and reduce the

of the aneurysm.

Two seminal studies found that intervention for abdominal aortic aneurysms of less than

cm in otherwise

patients had no benefit over

3 Answer the following:

A List three common risk factors for abdominal aortic aneurysm.

B Which other patients are also at increased risk?

4 List any changes to your clinical practice that you may make having read this article.

CARDIAC SYNCOPE

5 Which of the statements are true?

A The incidence of cardiac syncope rises significantly with age
True ☐ **False** ☐

B Carotid sinus massage should be performed routinely in patients aged ≥ 40 with syncope of unknown origin
True ☐ **False** ☐

C Prolonged ECG monitoring should be employed when there is a high pretest probability of capturing an arrhythmia
True ☐ **False** ☐

D Syncope may be multifactorial
True ☐ **False** ☐

6 Complete the statement:

Exercise testing should be performed under close supervision in patients presenting with

or

This stress test may unmask

or

However,

syncope may also be observed which is most commonly

»

CME

Time credits =

Impact credits =

7 Which of the following are high-risk features of syncope?

A Unexplained systolic BP < 90 mmHg

B Persistent bradycardia < 40 bpm

C Long history of similar syncope

D Syncope preceded by palpitation

E Features suggestive of vasovagal syncope

8 List any changes to your clinical practice that you may make having read this article.

MULTIPLE SCLEROSIS (MS)

9 Which of the statements are true?

A Clinical history and MRI findings may be sufficient to make a diagnosis of MS
True ☐ **False** ☐

B In the early phase of MS, patients generally recover from relapses fully, without treatment, within days or weeks
True ☐ **False** ☐

C Steps 4.0 to 7.5 on the Expanded Disability Status Scale indicate progressive reduction in walking ability
True ☐ **False** ☐

D Steroid treatment does not affect the overall outcome of relapses and/or long-term disease progression, but shortens time to recovery
True ☐ **False** ☐

E Pharmacological therapies are generally more effective than psychological therapies for fatigue in MS patients
True ☐ **False** ☐

10 Patients with MS have high rates of comorbidity. List four common comorbidities.

11 Complete the statement:
Disease modifying treatments can reduce the risk of new

symptoms, severe

impairment, and

in people with

MS.

12 List any changes to your clinical practice that you may make having read this article.

Answers

ABDOMINAL AORTIC ANEURYSM
1 **A** True **B** True **C** False **D** False (80%) **E** False (extend life)
2 Risk; factor; cardiovascular; growth
5.5; reasonably; fit; ultrasound surveillance
3 **A** Smoking; increasing age; family history **B** Those with connective tissue disorders such as Marfan's syndrome, Ehlers-Danlos syndrome and Loeys-Dietz syndrome

CARDIAC SYNCOPE
5 **A** True **B** True **C** True **D** True
6 Exertional; presyncope; syncope; arrhythmias; ischaemia; postexertional; reflex-mediated
7 A,B,D

MULTIPLE SCLEROSIS (MS)
9 **A** True **B** True **C** True **D** True **E** False
10 Depression; anxiety; cardiovascular disease; epilepsy; metabolic diseases; autoimmune diseases
11 Neurological; ambulatory; death; relapsing-remitting

The Practitioner®

Diagnosis and management of abdominal aortic aneurysm

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Diagnosis and management of abdominal aortic aneurysm

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FIGURE 1
3D reconstruction of a CT angiogram of an abdominal aortic aneurysm for treatment planning. The aneurysm diameter will be larger than seen in this image as the reconstruction is of the lumen only

How is abdominal aortic aneurysm diagnosed?

Where should patients be referred?

What are the management options?

AN ABDOMINAL AORTIC ANEURYSM IS A DILATION OF THE ABDOMINAL AORTA TO 150% OF THE NORMAL diameter (3 cm). Usually these aneurysms take the form of a relatively uniform tapering (fusiform) bulge, see figure 1, above.

Men over the age of 65 are most commonly affected, with an abdominal aortic aneurysm present in approximately 1%.[1,2] Thus a GP list size of 9,000 would expect to have approximately 50-75 patients with aneurysms of varying sizes.

Degradation of the layers of the arterial wall leads to a loss of strength and aneurysm formation. This is a process that occurs over years and decades. Once they have formed, aneurysms increase slowly in diameter by about 2-3 mm per year.[3] As the size of the aneurysm increases, the rate of growth and the risk of rupture increases.[4]

Just over 3,700 elective infrarenal repairs were performed in 2018 in the UK, with an additional 800 complex repairs (above the renal arteries) and 800 repairs of ruptured abdominal aortic aneurysms.[5] The rate of aneurysm treatment is decreasing as is the incidence found in the screening programme.[1,2] This is thought to be due to improved best medical therapy and reduced rates of smoking.

‘As the size of the aneurysm increases, the rate of growth and the risk of rupture increases’

DIAGNOSIS

Diagnosis is confirmed by duplex ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI). The mainstay of imaging is duplex ultrasound, ideally performed by vascular scientists in the vascular »

laboratory for accurate sizing.

Examination is routinely erroneous especially in patients who are obese or those who are thin. Up to 50% of threshold aneurysms (5.5 cm) are not palpable clinically.

Abdominal or spinal X-rays are often inaccurate in sizing an aneurysm due to projection.

As the condition is normally asymptomatic, most patients have their aneurysms discovered through the screening programme or incidentally via other imaging investigations. All men are invited to the national screening programme at the age of 65 in the UK. The vast majority of these abdominal aortic aneurysms are termed 'small' aneurysms. The seminal British UKSAT and American ADAM studies found that intervention for aneurysms < 5.5 cm in otherwise reasonably fit patients had no benefit over ultrasound surveillance.[6,7] This is because there is up to a 5% in-hospital mortality rate for elective repair, whereas the rate of rupture for aneurysms at 5.5 cm on ultrasound is 0.4% per year.[1]

'Intervention for aneurysms < 5.5 cm in reasonably fit patients had no benefit over ultrasound surveillance'

RISK FACTORS

Risk factors for abdominal aortic aneurysm formation include:

Smoking: Compared with never smoker, current smoker odds ratio (OR) 7,[8] former smoker OR 5[8]

Increasing age: 75-84 years OR 3.3; the OR increases by 1.7 every 7 years[4]

Family history: OR 1.9[4]

There appears to be a lower risk in patients with diabetes mellitus (OR 0.5)[9] and women (OR 0.2).[4] It is unclear why patients with diabetes appear to be at lower risk, though it may be due to changes in the aortic wall.[9] Research is ongoing. Previously rates of smoking were higher in men, leading to an increased incidence compared with women. Female smokers are 15 times more likely to have an abdominal aortic aneurysm than female non-smokers.[8]

Patients with connective tissue disorders such as Marfan's syndrome, Ehlers-Danlos syndrome, and Loeys-Dietz syndrome are all prone to aneurysm formation, which tends to be complex. The management of these patients is outside the scope of this article.

'Patients with a new diagnosis of an abdominal aortic aneurysm should be referred to their local vascular service'

MANAGEMENT

Patients with a new diagnosis of an abdominal aortic aneurysm should be referred to their local vascular service, which will be centralised. Patients will then either be entered into surveillance, evaluated for surgery or managed conservatively by the vascular service.

Evidence-based guidelines have been produced most recently by NICE in 2020,[10] and also by the Society for Vascular Surgery (SVS),[11] and the European Society for Vascular Surgery (ESVS).[12] All three guidelines have slightly different approaches, but overall their recommendations are similar. The mainstay of management is risk factor modification to improve cardiovascular health for potential surgery and reduce the growth of the aneurysm.[13,14]

Intervention should be considered in those patients with a reasonable life expectancy. The intervention is prophylactic and therefore is aimed at extending life rather than improving quality of life. Patients with significant comorbidities should be counselled that the intervention itself may shorten their life. This should be done by a vascular surgeon.

The NICE guidance recommends that open surgical repair should be the mainstay of treatment, with endovascular repair reserved for special circumstances because of the risk of the need for reintervention.[10] The ESVS guidance recommends no operative treatment for patients with a life expectancy of 2-3 years, endovascular repair for those with a life expectancy of 4-9 years and open surgical repair where life expectancy is $\geq$10 years.[12] The SVS guidelines suggest that those patients with a limited life expectancy should not undergo repair.[11]

Potential complications

The most serious potential complication is death caused by rupture of the aneurysm. However, most patients die from other conditions such as cardiac disease, respiratory conditions or cancer.[15]

Rupture remains a catastrophic event which without treatment is almost always rapidly fatal, although the timeline of death can be prolonged due to containment by the retroperitoneum.

Despite all the advances in surgery and postoperative care, the 30-day mortality rate of patients with an aneurysm rupture remains 35-40%,[16] showing little, if any, improvement from the respective figure of 40% in 1991.[17]

Aneurysms can become symptomatic (deemed to be impending ruptures) and painful with abdominal and back pain but no frank rupture on imaging. This is rare but is treated urgently with admission to hospital and surgery on the next available operating list.

Embolic episodes can also occur due to dislodgement of a piece of the thrombus build-up in the aneurysm, although this is relatively rare. These aneurysms would also be treated urgently.

Because of the risk of rupture, patients in the UK should inform the DVLA when their aneurysm is 6 cm and should not drive when it reaches 6.5 cm.

'Patients with aneurysmal disease are at high risk of ischaemic heart disease and other vasculopathies. Atherosclerotic disease is often coexistent'

Reducing cardiovascular risk

There is no specific drug treatment that alters the growth rate of aneurysms or prevents rupture. Management involves good multidisciplinary care. Patients with aneurysmal disease are at high risk of ischaemic heart disease and other vasculopathies. Atherosclerotic disease, while a separate entity, is often coexistent because of the prevalence of smoking in these patients. Following successful surgery, patients have 80% of the life expectancy of individuals who have not had an aneurysm. The majority of deaths after intervention are from cardiovascular disease.[15] Therefore, patients' cardiovascular risk factors

should be aggressively managed.[18]

All aneurysm patients should receive the following:

Medical treatment

- High-dose statin therapy (target of atorvastatin 80 mg once a day) irrespective of cholesterol levels. This has a complex and stabilising interaction with the aneurysm, and reduces cardiovascular mortality
- An antiplatelet agent, NICE recommends first-line treatment with clopidogrel[10]
- Antihypertensive medication

Lifestyle measures

- Smoking cessation: poor lung function is a significant determinant of poor outcome
- Exercise to improve fitness for surgery and to reduce sarcopenia which has been shown to improve outcomes[19,20]

Surgery

The surgical treatment options are as follows:

Open surgical repair: see figure 2, right

There are two main techniques, transperitoneal and retroperitoneal. The former involves either a midline or transverse laparotomy incision. The latter involves a left-sided flank incision. All involve dissection to the retroperitoneal aneurysm sac, clamping of the aorta and iliac vessels and stitching in a polyester (Dacron) graft to exclude the aneurysmal segment. Some procedures are performed laparoscopically.

Open surgical repair is a bigger operation, with a higher in-hospital mortality rate. It is more cost effective than endovascular repair.[10]

Endovascular repair: see figure 3, right

This involves the placement of expanding stent grafts made of polyester fabric stitched to metal (steel or nitinol) stents under X-ray guidance via the femoral arteries. The stent grafts are placed compressed and then released to spring to their correct size. The stent graft is held in place by a combination of small hooks and the expansile radial force from the stent. It is a smaller operation, but with a higher reintervention rate.

There is no long-term difference in mortality (beyond 5 years) found in randomised clinical trials.[21-25]

Surgical treatment has two facets; elective and emergency care. Emergency care provides an easy decision tree for patients and doctors as a ruptured aneurysm is a deadly condition. Therefore, the risk of attempted repair (35% mortality) is balanced against palliation with a relatively swift resolution.

However, elective care provides a nuanced decision for patients and clinicians as not all aneurysms will »

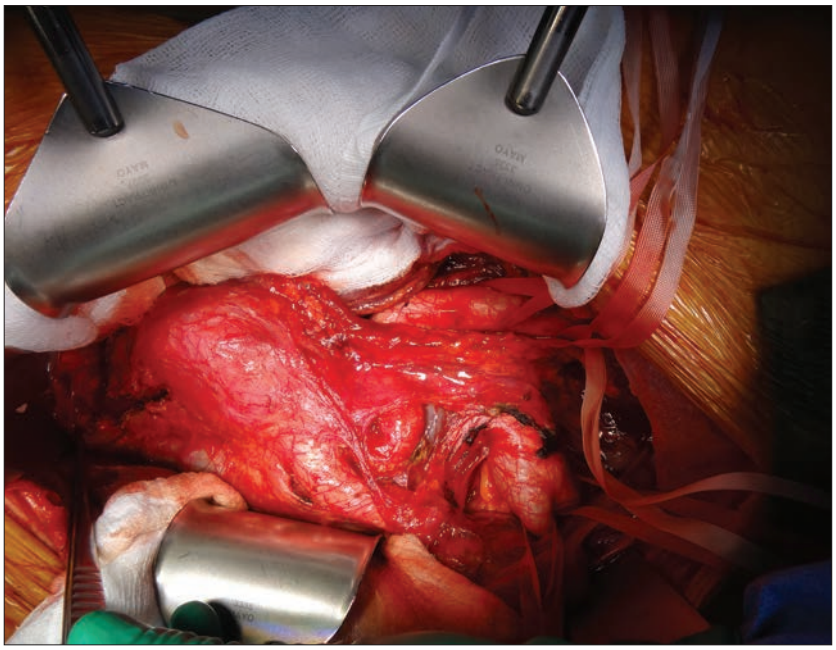


FIGURE 2
Open surgical repair of an infra-renal abdominal aortic aneurysm via a transperitoneal midline laparotomy approach



FIGURE 3
Angiographic image of an endovascular repair of an infra-renal abdominal aortic aneurysm — a proximal contrast fluoroscopy run showing proximal placement of the aortic stent and patency of the renal arteries

key points

SELECTED BY

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An abdominal aortic aneurysm is a dilation of the abdominal aorta to 150% of the normal diameter (3 cm). Men over the age of 65 are most commonly affected, with an abdominal aortic aneurysm present in approximately 1%. The mainstay of imaging is duplex ultrasound. Examination is routinely erroneous especially in patients who are obese or those who are thin. Up to 50% of threshold aneurysms (5.5 cm) are not palpable clinically.

As the condition is normally asymptomatic, most patients have their aneurysms discovered through the screening programme or incidentally via other imaging investigations. All men are invited to the national screening programme at the age of 65 in the UK. The vast majority of these abdominal aortic aneurysms are termed 'small' aneurysms. The seminal British UKSAT and American ADAM studies found that intervention for aneurysms < 5.5 cm in otherwise reasonably fit patients had no benefit over ultrasound surveillance.

Risk factors for abdominal aortic aneurysm formation include: smoking (compared with never smoker, current smoker OR 7, former smoker OR 5); increasing age (75-84 years OR 3.3; the OR increases by 1.7 every 7 years); family history OR 1.9. Patients with connective tissue disorders such as Marfan's syndrome, Ehlers-Danlos syndrome, and Loeys-Dietz syndrome are all prone to aneurysm formation, which tends to be complex.

Patients with a new diagnosis of an abdominal aortic aneurysm should be referred to their local vascular service, which will be centralised. Patients will then either be entered into surveillance, evaluated for surgery or managed conservatively by the vascular service. The NICE guidance recommends that open surgical repair should be the mainstay of treatment, with endovascular repair reserved for special circumstances because of the risk of the need for reintervention.

All aneurysm patients should receive the following: high-dose statin therapy (target of atorvastatin 80 mg once a day) irrespective of cholesterol levels. This has a complex and stabilising interaction with the aneurysm, and reduces cardiovascular mortality; an antiplatelet agent, NICE recommends first-line treatment with clopidogrel; antihypertensive medication. Lifestyle measures include: smoking cessation (poor lung function is a significant determinant of poor outcome); exercise to improve fitness for surgery and to reduce sarcopenia which has been shown to improve outcomes.

We welcome your feedback

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rupture. Although the threshold for intervention is currently 5.5 cm, more than 50% of ruptured aneurysms treated in the UK between 2013 and 2018 were ≥ 7.5 cm.[26,5] Therefore the patient's wishes, fitness for surgery and life expectancy are key factors as are the technical complexities of the surgery. Having a thorough dialogue with the patient and providing detailed information will enable robust patient-centred decision making.

MONITORING AND FOLLOW-UP

Conservative management may be with continued monitoring and a modified higher aneurysm size intervention threshold agreed with the patient, or the patient may be discharged from vascular surgery review as intervention is not suitable or not wanted. It is key that patients who do not want, or are not suitable for, elective repair have put in place documentation of their wishes, in the event of a rupture, which may be for an emergency attempt or for palliation.

After endovascular repair routine surveillance is required to assess the need for reintervention, this is not uncommon. As the stents are not sutured in place, stent graft migration, dislocation and vessel expansion leading to leakage around the ends of the graft are known long-term complications. Surveillance is normally a combination of duplex ultrasound and CT.

After open repair, ESVS guidelines recommend assessment of the area above the repair (supra-renal aorta) five years postoperatively with a CT scan. Incisional hernias, in line with all laparotomies, are common.[12]

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Useful information

Circulation Foundation
www.circulationfoundation.org.uk

NICE NG156
www.nice.org.uk/guidance/ng156

Vascular Society
www.vascularsociety.org.uk/

ESVS Virtual Vascular textbook
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Suspected cardiac syncope requires urgent investigation

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Suspected cardiac syncope requires urgent investigation

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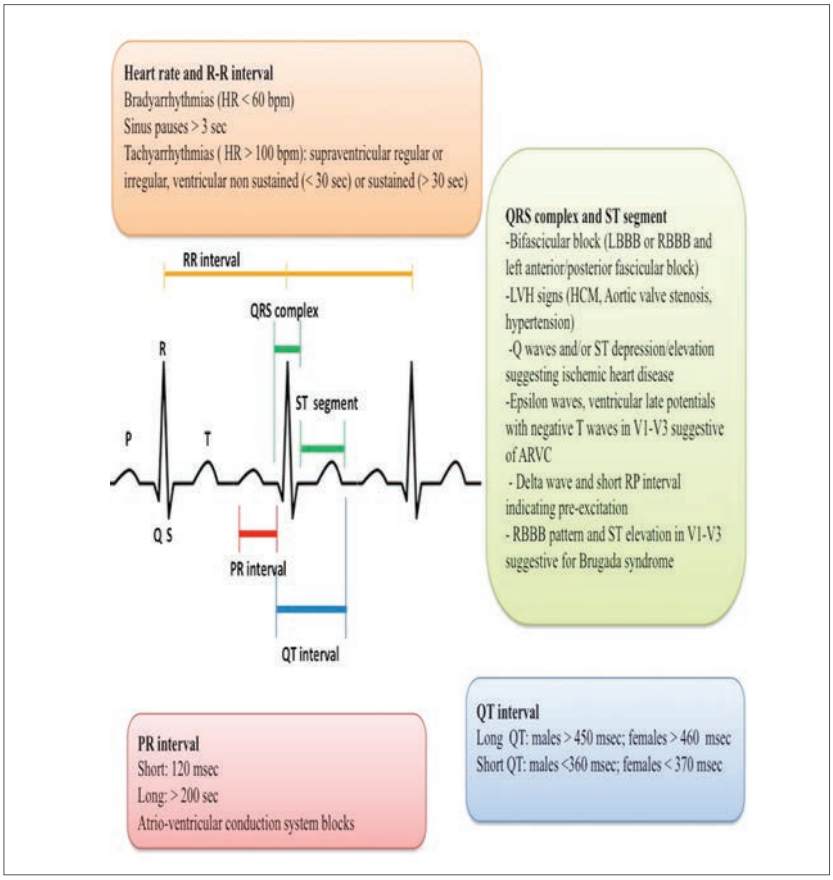


FIGURE 1
ECG features suggesting cardiac syncope

What are the causes of cardiac syncope?

How should patients be investigated?

How should diagnosis be confirmed?

SYNCOPE IS DEFINED AS A TRANSIENT LOSS OF CONSCIOUSNESS (T-LOC) AND POSTURAL TONE DUE to global cerebral hypoperfusion with rapid onset, brief duration and prompt spontaneous recovery.[1,2]

It is a relatively common clinical entity with 40% of people experiencing a syncopal event during their lifetime and accounts for 1% of emergency department attendances and 6% of hospital admissions.[3,4] The incidence increases with age, with two peaks in the second and eighth decades.

Syncope is often a source of anxiety and may lead to injuries.[5] Up to 13% of patients have recurrent syncope with a reported detrimental impact on quality of life similar to chronic conditions such as low back pain.[6] Moreover, the prognosis varies greatly with the diagnosis: ranging from benign in reflex syncope to life-threatening in those with structural heart disease.[2]

The assessment of syncope is built around identification of the small minority in which it is a marker of an underlying pathology that has a risk of sudden cardiac death, while reassuring the vast majority who have a benign cause.

CLASSIFICATION OF SYNCOPE

Syncope can be classified into three primary groups: reflex (neurally mediated), orthostatic hypotension and cardiac syncope.

Identifying the underlying cause of syncope is often challenging, but it is important to differentiate it from other causes of T-LOC which can be neurological (epileptic seizures, subarachnoid haemorrhage and migraine), metabolic (hypoglycaemia, hypoxia and hyperventilation) or psychogenic.

Reflex syncope is the most common cause of syncope, accounting for 50% of all episodes of T-LOC. Its hallmark is a precipitating event or trigger which elicits a centrally mediated response through withdrawal of sympathetic tone resulting in vasodilatation and hypotension (vasodepressive reflex), an increase in vagal tone with bradycardia and asystole (cardioinhibitory reflex) or a combination of both (mixed).

The main types of reflex syncope are: vasovagal, situational and carotid sinus hypersensitivity.[7] Vasovagal syncope occurs typically in young patients and the trigger is either emotional (e.g. the sight of blood or stress) or physical (e.g. pain or prolonged standing) leading to an abrupt reduction in blood pressure (BP) with or without bradycardia. Syncope is usually preceded by nausea, sweating, visual changes (typically tunnel vision) and dizziness. However, in as many as a third of patients, particularly the elderly, reflex syncope occurs without a prodrome.

In carotid sinus hypersensitivity there is an augmented vagal response to »

stimulation of the carotid sinus. Typical triggers include head turning, neck extension, shaving and tight neckwear. It is a common finding in the asymptomatic elderly patient and up to 25% of patients following a fall. Thus, diagnosis must only be made if symptoms occur during carotid sinus massage.

Situational syncope is characterised by distension of mechanoreceptors in the bladder (micturition), rectum (defecation) or oesophagus (swallowing).[8]

In orthostatic hypotension, blood pooling in the lower extremities upon standing leads to a reduction in venous return and cardiac output. Defined as a drop of at least 20 mmHg in systolic BP or 10 mmHg in diastolic BP within 3 minutes of standing, it typically occurs in elderly patients due to a combination of polypharmacy with vasoactive/diuretic drugs, reduced baroreceptor sensitivity, renal sodium wasting and impaired thirst.

'Cardiac syncope accounts for 10% of presentations. The incidence rises significantly with age'

Cardiac syncope accounts for 10% of presentations. The incidence rises significantly with age. A drop in cardiac output and subsequent cerebral hypoperfusion results from either an arrhythmia (tachycardia or bradycardia) or from an anatomical obstruction to cardiac output (aortic stenosis, pulmonary embolism, hypertrophic cardiomyopathy), see table 1, below. Syncope may occur at rest or supine with arrhythmia or on exertion with obstructive causes.

Table 1

Causes of cardiac syncope

Anatomic
- Aortic stenosis
- Atrial myxoma
- Cardiac tamponade
- Hypertrophic cardiomyopathy
- Myocardial ischaemia
- Pulmonary embolism

Arrhythmias
Bradyarrhythmia: Sinus node dysfunction, atrioventricular block
Tachyarrhythmia: Ventricular and supraventricular tachycardias

INITIAL EVALUATION

Establishing a definitive cause can be challenging as syncopal episodes are infrequent, unpredictable, brief and often unwitnessed. Physicians can rarely examine patients or capture the underlying rhythm during a syncopal event unless there are reproducible triggers.

Assessment should therefore be systematic: a thorough history, physical examination including lying and standing BP measurements and 12-lead electrocardiogram (ECG).

The European Society of Cardiology (ESC) 2018 syncope guidelines propose a framework on how to evaluate patients following an episode of T-LOC.[2]
- Establish if the episode of T-LOC was due to syncopal or non-syncopal causes
- Identify the underlying cause through accurate history of events before, during and after the episode of T-LOC (see table 2, below)
- Risk stratify patients into low- and high-risk groups to inform decisions regarding admission to hospital and further investigations (see table 3, p17).

The medical history and physical examination are key components which, when used in combination, can distinguish a syncopal event from other causes of T-LOC in 60% of cases and identify the probable cause of syncope in a quarter of cases.[9,10]

Every effort should be made to obtain a history from a witness if available.

In addition to a comprehensive history of the events surrounding the syncope, the medical history should focus on:
- Identifying and characterising any prior presyncopal or syncopal episodes
- Personal or family history of cardiac disease and sudden cardiac death.

Conditions with a higher risk profile include ischaemic heart disease, conduction disorders, hypertrophic cardiomyopathy, and inherited cardiac conditions such as Brugada syndrome and long QT syndrome.

Table 2

Key features in the medical history when assessing patients with episodes of T-LOC (Adapted from Saklani et al)[5]

Circumstances
Vasovagal: Classical triggers include pain, medical interventions, prolonged standing in warm environments, post-exertion
Situational: Cough, sneeze, micturition and defecation
Carotid sinus syncope: Head rotation, extension, shaving
Orthostatic: Shortly after standing, worse in the morning and after meals, recent introduction of new medications, prolonged standing in warm environments
Cardiac: Rest, supine or on exertion. Known history of structural heart disease or family history of sudden cardiac death. Provocation by sudden noise suggests long QT

Prodrome
Vasovagal: Long prodrome (> 5 sec), consistent in the same individual. Typically, nausea, diaphoresis, light-headedness and blurred vision. May be absent in the elderly
Cardiac: Shorter prodrome (< 5 sec) or absent. Palpitations or chest pain may be present but non-specific
Seizures: Sudden onset or brief aura (olfactory, gustatory or déjà vu)

Observations during T-LOC
Syncope is characterised by brief episodes of T-LOC generally < 5 minutes and usually < 30 seconds. Incontinence and brief clonic movements may occur
Vasovagal: Pallor, diaphoresis, dilated pupils, low blood pressure
Cardiac: Cyanosis but not pallor
Seizures: Prolonged syncope (> 5 minutes), cyanosis, tongue biting, horizontal ocular deviation, incontinence more likely, frothing at the mouth, tachycardia and high blood pressure, tonic-clonic movements
Psychogenic: Atypical features with bizarre movements and resisting attempts to open eyes

Recovery
Vasovagal: Quick recovery but prolonged fatigue is common (often hours)
Cardiac: Quick recovery without any residual symptoms in tachyarrhythmias and bradyarrhythmias
Seizure: Post-ictal confusion and transient neurological deficit

- Identifying medication that may cause or exacerbate symptoms

A general examination may provide clues to the aetiology and uncover complications such as laceration, fractures and injuries. A complete cardiovascular examination is recommended to identify any features suggestive of structural heart disease, particularly abnormal rates or rhythms and heart murmurs. Neurological assessment for focal deficits should also be undertaken.

During examination it is essential that supine BP is measured, followed by standing BP every minute for at least 3 minutes to uncover orthostatic hypotension. Several studies report a high prevalence of delayed orthostatic hypotension and, if history suggests symptoms occurred only after several minutes, standing measurements should continue for at least 10 minutes to unmask a delayed drop in BP.[11,12]

Although an ECG has a low diagnostic yield, it can identify several abnormalities such as conduction disturbances, arrhythmias, ischaemic changes, pre-excitation and prolonged QT interval (see figure 1, p15) and must be performed routinely.[7] In contrast, a 'normal' ECG has a very high negative predictive value (> 99%) for a serious underlying cardiac cause and provides reassurance.

A broad panel of blood tests is commonly requested but there is often little added diagnostic value or data to support their use. Instead, they should be targeted either to exclude or confirm a diagnosis, for example, if the patient is hypoxic and has chest pain there is value in adding a D-dimer. A routine transthoracic echocardiogram is also not recommended unless initial assessment suggests structural heart disease or there is a known cardiac disorder.

Finally, carotid sinus massage should be performed routinely in patients 40 years or older with syncope of unknown origin. The left and right sides are sequentially assessed in supine and sitting positions by a firm massage for 5-10 seconds with continuous ECG and BP monitoring. A positive response (>3 second pause and/or a > 50 mmHg drop in systolic BP) and reproducible syncope is diagnostic of carotid sinus syncope.[1,2] Contraindications include the presence of a carotid bruit, TIA or stroke within the past 3 months and a > 70% carotid stenosis on ultrasound.[13] If carotid examination is normal the chance of carotid sinus massage causing a transient ischaemic attack (TIA) or stroke is very low (0.14-0.28%).[13,14]

Table 3

Diagnostic criteria with initial evaluation (Adapted from the ESC syncope guidelines)[2]

Dagnosis	Typical features
Classical vasovagal syncope	Typical precipitating events (fear, severe pain, emotional distress, or prolonged standing) associated with typical prodromal symptoms
Situational syncope	Syncope during or immediately after urination, defecation, coughing or swallowing
Orthostatic hypotension	Syncope or presyncope with: ● ≥ 20 mmHg drop in systolic BP or systolic BP < 90 mmHg
Cardiac ischaemia-related syncope	ECG demonstrates ongoing ischaemia or previous myocardial infarction
Arrhythmia-related syncope	ECG demonstrates the following: ● Bradyarrhythmias: sinus pause > 3 seconds, persistent bradycardia < 40 bpm, 2nd degree Mobitz type II or 3rd degree AV block ● Alternating bundle branch block ● Tachyarrhythmias: Ventricular tachycardia or rapid SVT

CONFIRMING DIAGNOSIS

Following initial evaluation, the diagnosis may be graded as likely/confirmed, probable, or remain uncertain. The ESC guidelines have set out criteria to aid diagnosis, see table 3, below.[2]

It is not uncommon for the cause of syncope to remain unknown despite several investigations. In 36% of patients with syncope in the Framingham Heart substudy the aetiology remained unexplained following investigations.[7] With greater access to specialised syncope units the number of unexplained syncopal episodes has dropped significantly and can be as low as 10%; many studies report concomitant reduction in hospital admissions and overall investigations.[15] The frequency, severity and presence of high-risk features will dictate further diagnostic and treatment strategies.

RISK STRATIFICATION

Ten percent of patients presenting with syncope to the emergency department will have a serious event within the next 30 days and the mortality at one year is 1%.[2] Thus, if a diagnosis remains elusive despite a comprehensive initial evaluation, risk stratification is warranted.

Several risk scores have been put forward to help inform decision making and identify those at greater risk for adverse outcomes by mainly combining ancillary and biochemical tests with vital signs and medical history.[16-18] The ESC guidelines propose a simplified risk stratification tool based on medical history, syncope characteristics, physical examination and ECG (see table 4, p18).[2]

Low-risk features are most commonly present in reflex syncope; the prognosis is benign and patients can be reassured and discharged.[1,2,7] Indeed, unnecessary admission is harmful and a burden to the healthcare system.[15,19]

Conversely, high-risk features are more likely to be due to an underlying cardiac condition. One year mortality following cardiac syncope may be up to 30% and therefore requires rapid and intensive investigations.[20]

'One year mortality following cardiac syncope may be up to 30% and therefore requires rapid and intensive investigations'

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key points

SELECTED BY

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Syncope is defined as a transient loss of consciousness (T-LOC) and postural tone due to global cerebral hypoperfusion with rapid onset, brief duration and prompt spontaneous recovery. Around 40% of people experience a syncopal event during their lifetime. Syncope accounts for 1% of emergency department attendances and 6% of hospital admissions. The incidence increases with age, with two peaks in the second and eighth decades. Syncope can be classified into three primary groups: reflex (neurally mediated), orthostatic hypotension and cardiac syncope. Reflex syncope is the most common cause of syncope, accounting for 50% of all episodes of T-LOC.

Cardiac syncope accounts for 10% of presentations. Incidence rises significantly with age. A drop in cardiac output and subsequent cerebral hypoperfusion results from either an arrhythmia (tachycardia or bradycardia) or from an anatomical obstruction to cardiac output (aortic stenosis, pulmonary embolism, hypertrophic cardiomyopathy). Syncope may occur at rest or supine with arrhythmia or on exertion with obstructive causes.

Assessment should be systematic: a thorough history, physical examination including lying and standing BP and 12-lead ECG. The medical history and physical examination are key components which, when used in combination, can distinguish a syncopal event from other causes of T-LOC in 60% of cases and identify the probable cause of syncope in a quarter of cases.

Although an ECG has a low diagnostic yield, it can identify several abnormalities such as conduction disturbances, arrhythmias, ischaemic changes, pre-excitation and prolonged QT interval and must be performed routinely. A 'normal' ECG has a very high negative predictive value (> 99%) for a serious underlying cardiac cause. A routine transthoracic echocardiogram is not recommended unless initial assessment suggests structural heart disease or there is a known cardiac disorder.

Prolonged ECG monitoring should be employed when there is a high pretest probability of capturing an arrhythmia. The value lies in correlating the heart rhythm with the presence of symptoms. It can therefore be diagnostic but also confidently rule out arrhythmic aetiology if no abnormalities are observed during typical episodes. Monitors should be selected according to the frequency of syncope and the likelihood of recording the events.

If following initial assessment cardiac syncope is suspected patients should be referred for urgent specialist cardiovascular assessment or emergency department admission. NICE recommends referral within 24 hours in patients with T-LOC and any of the following features: any ECG abnormality; heart failure; heart murmur or dyspnoea; syncope on exertion; family history of sudden cardiac death. The treatment of cardiac syncope is mainly directed at the underlying cardiac disease.

ADDITIONAL TESTING AND INVESTIGATION

Additional investigations should be tailored to suspected aetiology. It is important to bear in mind that in many cases, especially in the elderly, syncope is multifactorial, arising from an interaction of various coexisting conditions, rather than a single cause and results of a test must be interpreted with caution.

Tilt testing is an orthostatic challenge to assess susceptibility for vasovagal response and determine the haemodynamic pattern (cardioinhibitory, vasodepressive, mixed). It is a safe procedure but has suboptimal reproducibility, sensitivity and specificity.[1,2] Importantly, a positive response only demonstrates a tendency for vasovagal response, also known as hypotensive susceptibility, and does not imply causality. Indeed, one study reported that around half of patients with cardiac syncope have a positive tilt test.[21] Thus, correlation with presenting symptoms is paramount to reduce false-positive rates and it is more appropriate in patients with suspected reflex syncope or orthostatic hypotension.[1,2] Indeed, in both the American and European guidelines the recommendations on tilt testing have been downgraded.

Exercise testing should be performed under close supervision in patients presenting with exertional presyncope or syncope. This stress test may unmask arrhythmias or ischaemia, however, postexertional syncope may also be observed which is most commonly reflex-mediated.[22]

Prolonged ECG monitoring should be employed when there is a high pretest probability of capturing an arrhythmia. The value lies in correlating the heart rhythm with the presence of symptoms. It can therefore be diagnostic but also confidently rule out arrhythmic aetiology if no abnormalities are observed during typical episodes. Monitors should be selected according to the frequency of syncope and the likelihood of recording the events.

The new generation of ambulatory monitor, such as the Zio™ XT patch, uses a water-resistant adhesive patch with a 1-lead ECG which reduces artefacts. After completing the 14 days of monitoring, patients send the device by post to the company where it is

Table 4

Low-risk and high-risk features (Adapted from the ESC syncope guidelines)[2]

Low-risk features	High-risk features
Syncope	**Syncope**
● Features suggestive of vasovagal syncope or orthostatic hypotension	● New onset of chest pain, dyspnoea, abdominal pain or headache ● Preceded by palpitation ● Supine or exertional
Past medical history	**Past medical history**
● Long history of similar syncope ● Structurally normal heart	● Severe structural heart disease or coronary artery disease
Physical examination	**Physical examination**
● Normal	● Unexplained systolic BP < 90 mmHg ● Persistent bradycardia (< 40 bpm) ● Undiagnosed systolic murmur ● Severe injury
ECG	**ECG**
● Normal	● Ischaemic changes ● Atrial fibrillation with slow ventricular response ● Mobitz type II, 3rd degree atrioventricular block ● Ventricular tachycardia ● Bundle branch block, intraventricular conduction delay, left ventricular hypertrophy ● QTc > 460 ms ● Brugada type I pattern

analysed, and a report generated. The Zio™ is smaller, more comfortable and has higher compliance and detection rates than the Holter.[23, 24]

Implantable cardiac monitors (ICM) are small injectable devices with a battery longevity of 3 to 5 years. Several studies demonstrate a higher diagnostic yield when compared with conventional measures and, although more expensive, they are cost effective.[25,26] An ICM is indicated in recurrent syncope of unknown origin or syncope with high-risk features and likely arrhythmic cause.

The role of electrophysiology studies (EPS) has diminished due to expanding non-invasive technology. A positive EPS can uncover an arrhythmic aetiology, but a negative test does not exclude it. Currently indications include unexplained syncope despite investigations in patients with prior myocardial infarction or bifascicular block on a 12-lead ECG.[2]

MANAGEMENT

The cornerstone of management in reflex syncope is reassurance and lifestyle modifications: avoidance of triggers, stopping hypotensive medications and increasing hydration and salt intake. Pharmacological treatments may be considered in selected cases. Permanent pacing is almost never indicated, the exception being profound cardioinhibitory reflex syncope with injury.

Drug-induced autonomic failure is the main culprit in orthostatic hypotension. A careful review of the medications with elimination of the offending drugs, education and adequate hydration and salt intake are all helpful in most cases.

Patients who present with no high-risk features, and have a clear or probable diagnosis of vasovagal syncope, orthostatic hypotension or situational syncope have an excellent prognosis and need reassurance.[2,27]

If following initial assessment cardiac syncope is suspected, patients should be referred for urgent specialist cardiovascular assessment or emergency department admission. NICE recommends referral within 24 hours in patients with T-LOC and any of the following features:[27]

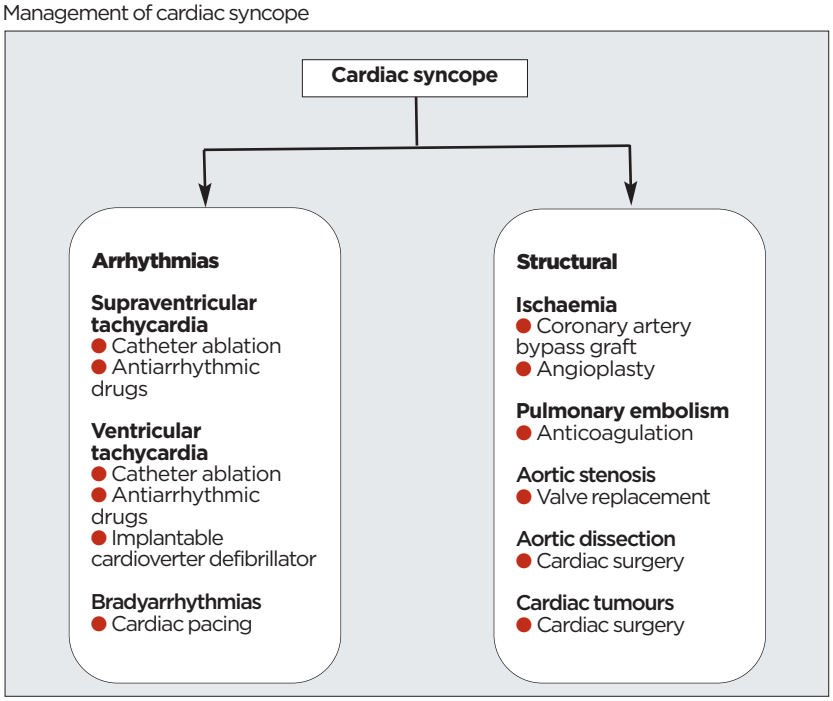
- Any ECG abnormality
- Heart failure
- Heart murmur or dyspnoea
- Syncope on exertion
- Family history of sudden cardiac death

The treatment of cardiac syncope is mainly directed at the underlying cardiac disease (see figure 2, below).

Potential reversible causes of arrhythmias (drugs, electrolyte imbalances) should be investigated in the first instance and treated if present.

Critical obstruction such as severe aortic stenosis or hypertrophic cardiomyopathy may be amenable to surgical intervention. Cardiac pacing is recommended for treatment of bradycardia-induced syncope resulting from significant conduction disease.

FIGURE 2
Management of cardiac syncope



Catheter ablation and drugs are potential treatment options for tachycardia-induced syncope.

Implantable cardioverter defibrillator therapy might be indicated in the case of ventricular tachycardia with structural or electrical heart disease and in the case of unexplained syncope (suspected as arrhythmic) in patients with high-risk conditions including severely depressed left ventricular systolic function (LVEF < 35%), hypertrophic cardiomyopathy, Brugada syndrome and long QT syndrome.

The goal of treatment of syncope secondary to structural heart disease is treatment of the underlying disease with reduction of the associated risk of death.

Specialist input is also warranted for recurrent traumatic syncope or frequent episodes which cannot be controlled by simple avoidance of triggers. If epilepsy is suspected after initial assessment patients should be reviewed by neurology within two weeks.

DRIVING

T-LOC while driving can cause injuries to the driver and others. In a large Danish cohort, the incidence of road traffic accidents almost doubled in patients with syncope.[28] Patients should be counselled regarding driving restrictions they may incur depending on the nature of their syncope and driving licence category. Patients have a duty to notify the DVLA. If the aetiology of syncope is unclear, they should not drive until specialist assessment is undertaken. Extensive recommendations are available on the DVLA website, (see useful information box, p20).

Competing interests: Professor Tim Betts has received speakers' honoraria from Pfizer, Boston Scientific and Abbott Medical. Dr Andre Briosa e Gala has no competing interests

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Useful information

Arrhythmia Alliance
www.heartrhythmcharity.org.uk

STARS (Syncope Trust And Reflex anoxic Seizures)
www.stars.org.uk

DVLA guidance for medical professionals
www.gov.uk/government/publications/assessing-fitness-to-drive-a-guide-for-medical-professionals

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Prompt diagnosis can improve outcomes in multiple sclerosis

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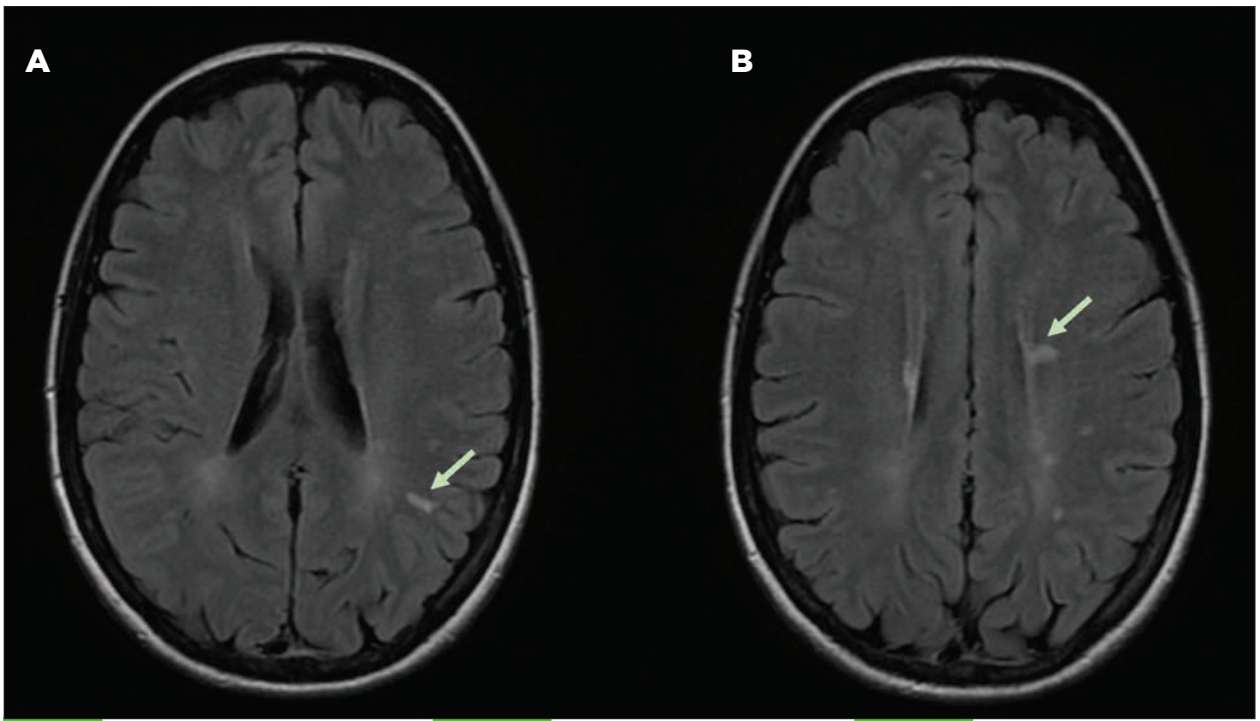


FIGURE 1
MRI scan of an MS patient at diagnosis showing two typical examples of MS lesions:
A A juxtacortical lesion and
B A periventricular lesion perpendicular to the corpus callosum (Dawson's fingers)

How do patients with MS present in primary care?

MULTIPLE SCLEROSIS (MS) IS THE LEADING CAUSE OF NON-TRAUMATIC NEUROLOGICAL DISABILITY in young adults.[1,2]

Diagnosis is based on the evidence of neurological symptoms, and aided by magnetic resonance imaging (MRI), e.g. white and grey matter changes in the brain and spinal cord, and CSF analysis, e.g. presence of oligoclonal bands.[3] Once diagnosed, people with MS require lifelong management usually involving a range of healthcare professionals.[4]

In the UK, MS prevalence increased by 28%, from 1990 to 2016, due to earlier diagnosis and increased survival.[2,5] Public Health England estimates that the 2018 prevalence in England was 190 cases per 100,000, with 105,800 affected individuals.[6]

The female to male ratio is 2:1, and patients have a minimally reduced life expectancy.[1,2]

What are the different phenotypes?

CLINICAL PRESENTATION

Over the past few decades, the natural history of MS has progressively become milder,[7] mainly as a result of advances in diagnosis and treatment. In particular, early recognition of MS symptoms and referral to MS specialists has contributed to improved long-term prognosis, and better management before irreversible disability accrues.[8]

In most cases, clinical presentation is characterised by recurring episodes of neurological deficit i.e. relapses. A relapse is defined as the acute-subacute onset of neurological symptoms lasting at least 24 hours, in the absence of infections, fever or other symptoms of systemic disease.[9]

In relapsing patients, the most common symptoms at onset are loss of power and/or sensation in one or more limbs, visual defects, or a combination of multiple symptoms.[1] In the early phase of MS, patients generally recover from relapses fully, without treatment, within days or weeks. However, over time, neurological deficits from relapses can accumulate, resulting in irreversible disability.[10]

In a minority of patients with subtle clinical progression at onset, symptoms may consist of gradual loss of power in the lower limbs, often accompanied by sensory disturbances and bladder/bowel dysfunction.[11] Symptoms progressively worsen over months or years, and patients are often unable to pinpoint the actual starting date.

In clinical practice, symptoms are generally investigated across different neurological systems:

- Visual (e.g. changes in visual acuity and/or visual field)
- Brainstem (e.g. nystagmus, diplopia, trigeminal neuralgia, dysarthria, dysphagia)
- Pyramidal (e.g. reduced power and mobility, spasticity)
- Cerebellar (e.g. tremor, ataxia, problems with balance)

»

What are the management approaches?

- Sensory (e.g. changes in superficial, vibration or position sense, pain)
- Bowel/bladder (e.g. urinary urgency, urinary retention, bowel dysfunction, sexual dysfunction)
- Cerebral (e.g. changes in mentation, depression, fatigue)

Based on a combination of these systems, an overall disability level can be scored with the Expanded Disability Status Scale (EDSS), which uses an ordinal scale of increasing severity from 0 (absence of neurological symptoms and signs) to 10 (death related to MS), with 0.5 unit increments.[12] Generally, EDSS steps 1.0 to 3.5 indicate unrestricted walking, while EDSS steps 4.0 to 7.5 indicate progressive reduction in walking ability.[12]

The classification of MS phenotypes is shown in table 1, opposite. Following the first relapse, the condition is termed either clinically isolated syndrome (CIS) or relapsing-remitting MS (RRMS), depending on whether additional tests (e.g. MRI, CSF analysis) suggest dissemination in time (DIT) and space (DIS).[3,9,13]

On the occasion of a second clinical relapse, the condition inevitably falls within RRMS.[3,9,14] Following this initial relapsing-remitting course, patients can develop progressive disability, independently from relapses; this disease stage is named secondary progressive MS (SPMS).[13,15]

In around 10% of patients, a gradual worsening of disability can occur from the start of the disease, which is termed primary progressive MS (PPMS).[13]

Of note, patients diagnosed with PPMS and SPMS may also experience periods of symptom remission (and sometimes improvement), within an overall declining trajectory, and can still present with inflammatory activity (e.g. clinical relapses or evidence of MRI activity). As such, PPMS and SPMS have been reclassified as different parts of the same progressive spectrum, and more attention is actually given to the detection of clinical and/or MRI evidence of disease activity.[13,16]

DIAGNOSIS

A diagnosis of MS requires that clinical, radiological and laboratory signs of MS are disseminated in both time and space, as originally described in the 2001 McDonald criteria and subsequently revised in the 2017 Thompson revision (see table 2, opposite).[3,9,17,18] This revision has been specifically implemented in order to facilitate an earlier and more accurate diagnosis.[3,9,17,18] Overall, MS diagnosis is based on the combination of clinical features (relapses and clinical progression), MRI findings (T2 and T1 gadolinium-enhancing lesions in periventricular, cortical/juxtacortical, infratentorial and/or spinal cord areas), and CSF analysis (the presence of oligoclonal bands in the CSF indicates disseminated inflammatory activity within the central nervous system).[3]

Because of the variability of clinical presentation and the existence of different phenotypes, on the first assessment, frequently carried out in primary care, blood tests should be ordered to exclude any alternative diagnoses which may mimic MS symptoms. These include: full blood count, inflammatory markers (e.g. ESR, CRP), liver function, renal function, calcium, glucose, thyroid function, vitamin B_{12} and HIV serology.[19] Subsequently, if blood test results are within normal limits, a brain MRI without a contrast enhancing agent (gadolinium) is generally ordered.

Clinical history and MRI findings could be sufficient to make a diagnosis of MS in particular in the presence of lesions with topography and morphology typical of MS. If not, following neurology consultation, other tests could be considered, such as spinal cord MRI, repeated brain/spinal cord MRI with gadolinium, and/or CSF examination.

The incidental finding of MS-like lesions on brain MRI in individuals without any clinical history of neurological dysfunction is called radiological isolated syndrome (RIS).[7] RIS is seen by many as potentially the initial stage of MS.[20]

Referral to an MS team is helpful to confirm the MS-like nature of MRI findings and to exclude any subtle symptoms (e.g. defects in specific cognitive functions). Additional tests (e.g. CSF analysis, visual evoked potentials) can be considered to estimate the likelihood of future conversion to MS, though no specific treatment is currently indicated in RIS.

MANAGEMENT

Disease modifying treatments

MS is currently not curable. Disease modifying treatments (DMTs) can reduce the risk of new neurological symptoms, severe ambulatory impairment (EDSS 6.0), and death in people with RRMS, compared with no treatment or placebo.[21-23] As such, patients with MS undergo regular neurological consultations, blood tests, and MRI scans for disease and DMT monitoring.[1,4]

More than ten DMTs have been developed and approved for RRMS and CIS over the past 20 years, but only three for progressive MS (interferon beta 1b and siponimod for SPMS, and ocrelizumab for PPMS).[24-27] DMTs for RRMS and CIS mainly target inflammatory cells (e.g. lymphocytes) and mechanisms (e.g. cytokine production, CNS permeability to inflammatory cells); by contrast, to treat progression effectively, DMTs need to target neurodegeneration through neuroprotection and repair, which is much more challenging in light of the complexity of underpinning pathology.[28,29]

For each DMT, MS teams will recommend specific follow-up protocols including regular blood tests and MRI scans, to monitor both treatment response and side effects. Although follow-up and monitoring are generally carried out at MS clinics, patients may present to their GP with side effects from DMTs.

Most side effects are mild and easy to deal with (e.g. flu-like syndrome, gastrointestinal problems, flushing, injection site reaction, infusion-related reactions). However, some side effects are potentially life-threatening and need to be detected early and treated effectively.

Some DMTs increase the risk of infections (e.g. respiratory tract, urinary tract, herpes virus infections), while others can cause autoimmune diseases (e.g. immune thrombocytopenia, thyroid disease, kidney damage), requiring immediate diagnosis and treatment.

More recently, cardiovascular problems (e.g. myocardial ischaemia, myocardial infarction, cerebral haemorrhage, cervico-cephalic arterial dissection, pulmonary alveolar haemorrhage and thrombocytopenia) have been reported in alemtuzumab-treated patients, and the risk of progressive multifocal leukoencephalopathy (PML), a rare but potentially life-threatening disease of the CNS, caused by activation of the John Cunningham virus (JCV), has been extended from natalizumab to dimethyl fumarate and fingolimod.[24,25,30]

Treatment of relapses

Patients with established MS may consult their GP with new, acute onset neurological symptoms. First, the presence of infections (e.g. respiratory and urinary) should be ruled out, since they can cause disease worsening mimicking a neurological relapse.[31] Also, it is important to establish, before

referral to the MS team, that new symptoms (or worsening of existing symptoms) have persisted for more than 24 hours.

Treatment for relapses of MS should be offered if there is an impact on daily activities and, ideally, as early as possible, within 14 days from the onset of symptoms. Standard treatment is oral methylprednisolone 0.5 g daily for 5 days.[31] Of note, steroid treatment does not affect the overall outcome of the relapses and/or the long-term disease progression, but only shortens the time to recovery.[32] Thus, potential benefits should be carefully weighed in relation to risk (e.g. worsening of mental health conditions, hypertension, poor glucose »

Table 1

Classification of MS clinical phenotypes. Adapted from Lublin FD et al. Neurology 2014[14]

Phenotype classification for relapsing patients

CIS	Clinical relapses, and/or new/enlarging T2 lesions, and/or T1-enhancing lesions?	**Yes** Active **No** Not active	→	**Active CIS*** **Not active CIS**
RRMS	Clinical relapses, and/or new/enlarging T2 lesions, and/or T1-enhancing lesions?	**Yes** Active **No** Not active	→	**Active RRMS** **Not active RRMS**

*Active CIS is classified as RRMS

Phenotype classification for progressive patients

PPMS (from disease onset)	Clinical relapses, and/or new/enlarging T2 lesions, and/or T1-enhancing lesions?	**Yes** **No**	→ →	**Active and with progression** **Not active but with progression**
Progressive MS (after a relapsing phase)	Clinical progression on annual review?	**Yes** **No**	→ →	**Active but without progression** **Not active and without progression**

SPMS

CIS = clinically isolated syndrome RRMS = relapsing-remitting MS PPMS = primary progressive MS SPMS = secondary progressive MS

Table 2

2017 Thompson revisions of McDonald criteria for MS diagnosis. Adapted from Thompson AJ et al. Lancet Neurology 2018[3]

Clinical, radiological and laboratory criteria for MS diagnosis in different clinical presentations

Clinical presentation	2017 Thompson revision of McDonald criteria
≥2 relapses and objective clinical evidence of ≥2 lesions or of 1 lesion with reasonable historical evidence of a prior relapse	None
≥2 relapses and objective clinical evidence of 1 lesion	DIS demonstrated by: ≥1 T2 lesion in at least 2 of 4 MS-typical regions, or further relapse implicating a different CNS site
1 Relapse and objective clinical evidence of ≥2 lesions	DIT demonstrated by: simultaneous presence of T1-enhancing and T2 lesions, or a new T1-enhancing or T2 lesions on follow-up, or further relapse, or CSF-specific oligoclonal bands
1 Relapse and objective clinical evidence of 1 lesion (CIS)	● DIS demonstrated by: ≥1 T2 lesion in at least 2 of 4 MS-typical regions, or further relapse implicating a different CNS site ● DIT demonstrated by: simultaneous presence of T1-enhancing and T2 lesions, or a new T1-enhancing or T2 lesions on follow-up, or further relapse, or CSF-specific oligoclonal bands
Insidious neurological progression suggestive of MS (PPMS)	One-year disease progression and 2 of the following 3 criteria: ● ≥1 T2 lesions in periventricular, cortical/juxtacortical or infratentorial areas ● ≥ 2 T2 lesions in the spinal cord ● Positive CSF (CSF-specific oligoclonal bands)

key points

SELECTED BY

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Multiple sclerosis (MS) is the leading cause of non-traumatic neurological disability in young adults. Between 1990 and 2016, the UK prevalence increased by 28%, as a consequence of both earlier diagnosis and increased survival. The 2018 prevalence in England was estimated to be 190 cases per 100,000, with 105,800 affected individuals. The female to male ratio is 2:1, and patients have a minimally reduced life expectancy.

Diagnostic criteria require that clinical, radiological and laboratory signs of MS are disseminated in both time and space. Diagnosis is based on a combination of clinical features (relapses and clinical progression), MRI findings, and CSF analysis. When patients first present to primary care, blood tests should be ordered to exclude alternative diagnoses which may mimic MS symptoms. A full blood count, ESR, CRP, liver and renal function tests, calcium, glucose, thyroid function tests, vitamin B_{12} and HIV serology are recommended.

In most cases, clinical presentation is characterised by relapses. A relapse is defined as acute-subacute onset of neurological symptoms lasting at least 24 hours, in the absence of infections, fever or other symptoms of systemic disease. In relapsing patients, the most common symptoms at onset are loss of power and/or sensation in one or more limbs, visual defects, or a combination of multiple symptoms. In the early phase of MS, patients generally recover fully from relapses without treatment, within days or weeks. However, over time, neurological deficits from relapses can accumulate, resulting in irreversible disability. In the minority of patients with subtle clinical progression at onset, symptoms may consist of gradual loss of power in the lower limbs, often accompanied by sensory disturbances and bladder/bowel dysfunction.

When patients present to their GP with new, acute onset neurological symptoms, infection (particularly respiratory and urinary) should be ruled out, as infection can cause disease worsening and mimic a neurological relapse. It is important to establish, before referral to the MS team, that new symptoms (or worsening of existing symptoms) have persisted for more than 24 hours. Treatment for relapses of MS should be offered, as early as possible, if there is an impact on daily activities; standard treatment is oral methylprednisolone 0.5 g daily for 5 days.

Disease modifying treatments can reduce the risk of new neurological symptoms, severe ambulatory impairment and death in relapsing-remitting MS. Although follow-up and monitoring are generally carried out at MS clinics, GPs should be aware of potentially life-threatening side effects which need to be detected early and treated effectively. MS patients have high rates of comorbid depression, anxiety, cardiovascular disease, epilepsy, metabolic disease, and autoimmune diseases. A general health review (weight, smoking, access to routine health screening and care of other chronic conditions) should be carried out at least once a year.

control).[31] Ultimately, the MS team should be informed and more active DMTs considered.

Treatment of MS symptoms

Patients with MS require lifelong multidisciplinary management from a range of healthcare professionals (e.g. ophthalmology, urology, psychology, rehabilitation, occupational therapy, speech therapy),[1,4] though the first therapeutic approach is frequently carried out by GPs.

Among the most common symptoms, spasticity can be treated with baclofen or gabapentin as first-line drugs; alternatively, tizanidine, dantrolene or benzodiazepines can be considered. More recently, cannabis-based medicinal products have become available for adults with MS spasticity, though prescription is currently restricted to specialist clinics.[33] Referral to spasticity clinics should be considered in refractory cases.[19]

Pain can be treated as neuropathic pain (e.g. amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment).[34]

Fatigue can be addressed with mindfulness-based training, cognitive behaviour therapy or fatigue management programmes, while pharmacological treatments (e.g. amantadine) are generally less effective.[19,35]

Similarly, in the absence of pharmacological treatments, problems with balance can be addressed by falls management programmes, balance rehabilitation and aquatic exercises.[35] Even in severely disabled patients, rehabilitation including a standing frame programme can be beneficial.[36]

COMORBIDITIES

Patients with MS should have their general health evaluated regularly, at least once a year, (e.g. weight, smoking, access to routine health screening, care of other chronic conditions),[31] all of which can directly and indirectly affect MS relapses and disability.[19,37-40]

Patients with MS have high rates of comorbid depression, anxiety, cardiovascular disease, epilepsy, metabolic diseases, and autoimmune diseases.[41-43] Overall, comorbidities have an adverse influence on MS outcomes and, thus, should be carefully evaluated and treated as in the general population.[44,45]

Vitamin D deficiency has been investigated as a possible determinant of MS risk and progression. To date, there is no evidence supporting the use of vitamin D as a treatment for MS.[46] However, GPs should refer to general recommendations for vitamin D supplements in specific populations at risk of deficiency, for instance MS patients with reduced mobility are inevitably less exposed to sun.[47]

CONCLUSIONS

GPs have a crucial role in seeing people presenting with new neurological symptoms suggestive of MS, and, following initial assessment, in referring them to specialised MS teams. Early diagnosis and treatment are vital to prevent irreversible disability accrual.

Once diagnosis has been established, GPs should work with the MS team within common management strategies and shared care. GPs have a key role in identifying so-called hidden symptoms of MS, especially those symptoms that may be hard to detect in neurology clinical practice but affect patients on a daily basis (e.g. fatigue, bladder and bowel problems, pain, cognitive dysfunction, depression and sexual dysfunction). GPs are at the frontline for the detection of new neurological symptoms and/or potential side effects of DMTs, and onward referral to different specialists to treat MS symptoms. Comorbidities should be carefully evaluated and treated, and a healthy lifestyle should be encouraged, bearing in mind its positive effects on MS.

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MS Trust
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NICE
www.nice.org.uk/guidance/conditions-and-diseases/neurological-conditions/multiple-sclerosis

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