Syncope

Syncope and its causes

SYNCOPE is defined as an episode of sudden loss of consciousness and postural tone, with spontaneous recovery. It affects about 3-3.5% of people during their lifetime and recurs in 30%. Presyncope refers to symptoms of faintness or lightheadedness without loss of consciousness.

Any condition that leads to loss of nutrient supply (oxygen, glucose) to the brain can lead to syncope. Excluding the extremely remote possibilities of transient and self-correcting hypoxaemia or hypoglycaemia, all causes of true syncope result from loss of cerebral blood flow. Even syncope secondary to hyperventilation results from hypocapnia-induced cerebral vasoconstriction.

Although other disturbances such as epilepsy or cerebral trauma can also cause sudden loss of consciousness and postural tone with spontaneous recovery, in practice the term syncope is retained for transient reduction in cerebral blood flow, while other causes are considered syncope mimics (table 1). Older studies have shown that syncope will ensue when effective blood flow has been removed for about six seconds.

It is important to remember that in up to one-third of cases, no diagnosis is made despite investigation. It is very likely that most of these undiagnosed cases are due to reflex-mediated syncope or orthostatic hypotension.

Reflex-mediated syncope

It is likely that reflex-mediated syncope (also referred to as

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Table 1: Causes of syncope

Reflex-mediated
- Vasovagal syncope
- Carotid sinus hypersensitivity
- Situational syncope (cough, micturition, swallowing, defecation)
- Receptor stimulation (cranial nerve irritation, bladder distension, airway stimulation, neck tumour)

Orthostatic hypotension
- Drug induced
- Hypovolaemia/haemorrhage
- Deconditioning
- Autonomic dysfunction
  - — Primary (pure autonomic failure, multiple system atrophy, etc)
  - — Secondary (diabetic, paraneoplastic neuropathies, amyloidosis)

Cardiac electrical
- Bradycardias (sinus node dysfunction or AV-conduction-system disease)
- Tachycardias (supraventricular or ventricular)

Cardiac mechanical
- Valvular disease (aortic, mitral or pulmonary stenosis)
- Hypertrophic obstructive cardiomyopathy
- Aortic dissection
- Pulmonary embolus
- Pericardial disease/cardiac tamponade
- Primary pulmonary hypertension
- Cardiac tumours
- Critical myocardial ischaemia

Non-cardiac (predominantly syncope mimics)
- Neurological/cerebrovascular
  - — Seizure
  - — Migraine
  - — Subarachnoid haemorrhage
  - — Subclavian steal syndrome
  - — Vertebrobasilar insufficiency
- Metabolic disturbances
  - — Hypoglycaemia or hypoxaemia
  - — Phaeochromocytoma, Addison's disease
  - — Drug intoxication, including alcohol
  - — Hyperventilation (via hypocapnia)
- Psychogenic pseudo-syncope

INSIDE

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neurally-mediated or neurocardiogenic syncope) accounts for at least one-third of syncopal episodes. As these terms imply, the nervous system is the root cause of the problem, rather than the heart (see figure1).

Vasovagal syncope

Reflex-mediated syncope is the mechanism of the common faint (vasovagal syncope), for example, fainting at the sight of blood or after standing for a long time. Vasovagal events are relatively common in childhood and adolescence, usually settling by early adulthood. However, a small number of people will suffer repeated faints, both in response to typical triggers and in the absence of apparent triggers.

In a very small number this pattern will continue throughout life. In others, recurrent vasovagal events begin for the first time in adulthood, or settle in early adult life, only to return in late middle age. Vasovagal syncope is the most common form of syncope in all age groups. Typical characteristics are listed in table 2.

Carotid sinus hypersensitivity

This uncommon variant of reflex-mediated syncope occurs in the elderly. The trigger is pressure on one or other of the carotid arteries, which can be precipitated by tight collars, turning the head or looking upwards, or by direct digital pressure.

Situational syncope

Uncommonly, some people present with recurrent syncope triggered by certain manoeuvres, such as coughing, straining while micturating or defecating, or after swallowing foods. The mechanism of syncope may differ from reflex-mediated events in certain cases. It is likely that swallowing-induced syncope is neurally mediated, while cough syncope may result from transient cessation of cerebral venous blood flow secondary to markedly raised intrathoracic pressure.

Receptor stimulation

In addition to the carotid and aortic arch baroreceptors, several other receptors (stretch- or pressure-sensitive) scattered throughout the body can trigger a vasovagal response when activated sufficiently, sometimes enough to cause syncope. These receptors are concentrated in the larger airways of the lung, the postero-inferior wall of the heart, the gut and the bladder. Irritation of the cranial nerves by conditions such as trigeminal and glossopharyngeal neuralgia or tumours (particularly those affecting nerves IX to XII) can also trigger vasovagal responses.

Orthostatic hypotension

Orthostatic hypotension is probably the second most common cause of syncope, accounting for 10-15% of cases. Orthostatic hypotension is defined as a fall in systolic blood pressure ≥20mmHg or a fall in diastolic blood pressure ≥10mmHg within 2-5 minutes of standing from a supine position. Symptoms of dizziness with standing, associated with a lesser reduction in pressure, are referred to as orthostatic intolerance.

Orthostatic hypotension can be symptomatic or asymptomatic but to cause syncope the drop in pressure must be quite significant. Patients can experience symptoms on standing, sometimes shortly after arising, at other times taking 30 minutes or more before symptoms develop. Although in extreme situations symptoms may develop with sitting, the cardinal feature of this form of syncope is that it is posturally dependent.

Orthostatic hypotension is a particularly common contributing factor to syncope in the elderly for three reasons:

- Multiple orthostatic hypotension-inducing medication use is prevalent, eg, antihypertensives, antianginals and antidepressants;
- Protective baroreceptor reflex mechanisms are impaired by the combination of age and acquired autonomic disease;
- Awareness of impending syncope is blunted due to the combination of age and autonomic disease.

Drug-induced orthostatic hypotension (table 3)

Most antihypertensive and anti-anginal agents, but particularly the vasodilators (eg, calcium-channel blockers, prazosin and nitrates) and diuretics (via volume depletion) can lead to orthostatic hypotension, particularly in the elderly. Beta blockers do not directly cause orthostatic hypotension but, by impeding the normal baroreceptor response, can aggravate the effects of age, autonomic dysfunction, or other antihypertensives. Antidepressants are a commonly overlooked cause; however, this side effect is much less likely with the newer agents such as SSRIs.

Hypovolaemia/haemorrhage

Orthostatic hypotension from marked hypovolaemia or haemorrhage is usually apparent; however, dehydration can develop insidiously in the elderly, as the thirst response is blunted. Some metabolic conditions may cause syncope via hypovolaemia, for example, Addison's disease, uncontrolled diabetes mellitus, and salt-wasting conditions of the kidneys.

Deconditioning

Prolonged bed rest (more than a day) can lead to orthostatic hypotension through a number of mechanisms, including:

- Diminished vasomotor tone;
- Deactivation of the renin-angiotensin-aldosterone system and ADH release, leading to salt and water loss;
- Effects of the condition leading to the prolonged bed rest, eg, fever-induced peripheral vasodilatation.

Autonomic dysfunction (table 4, facing page)

Dysfunction of the autonomic nervous system can lead to orthostatic hypotension and syncope by affecting baroreceptors and their connections to the brainstem (the afferent limb), central processing, or the autonomic outflow (the efferent limb). Sometimes there is evidence of a widespread process, such as bladder, bowel and/or sexual dysfunction.

Classically, when the patient stands (in the most extreme forms sitting may also cause symptoms) there is a steady progressive fall in blood pressure without any increase in heart rate. As the pressure falls, cerebral blood flow is maintained by the cerebral autoregulatory system until a critical feeding pressure is crossed, after which syncope rapidly ensues.

In some patients with autonomic dysfunction and postural hypotension, cerebral blood flow may be maintained while standing

Table 2: Characteristics of vasovagal syncope

Triggers
- Prolonged standing
- Overcrowding/heat
- Pain
- Emotional stress
- After eating
- Vigorous exercise
- Unexplained

Prodrome
- Weakness
- Headache and visual disturbances
- Sweating
- Nausea and abdominal discomfort, vomiting
- Light-headedness
- Seconds to minutes
- Can be aborted by lying down

Unconsciousness
- Typically brief (seconds)
- Pallor or ashen complexion
- Sweating
- Dilated pupils
- Often tonic-clonic convulsive movements
- Occasional incontinence

Recovery
- Extreme fatigue, prolonged (often hours)
- Sweating, nausea, vomiting
- Headache
- Weak and drained, not confused
- May faint again if stand too quickly

Figure 1: Reflex-mediated syncope. A wide variety of triggers ultimately lead to syncope by a final common pathway via the vasomotor centre of the brainstem. Activation of this centre leads to varying degrees of enhancement of vagus nerve activity, reduction of cardiac sympathetic nerve activity, and release of adrenaline, which together lead to the pathognomonic signs of this form of syncope — hypotension, bradycardia and pallor. Other typical features are sweating, nausea and a prolonged recovery time, sometimes many hours (see table 2).

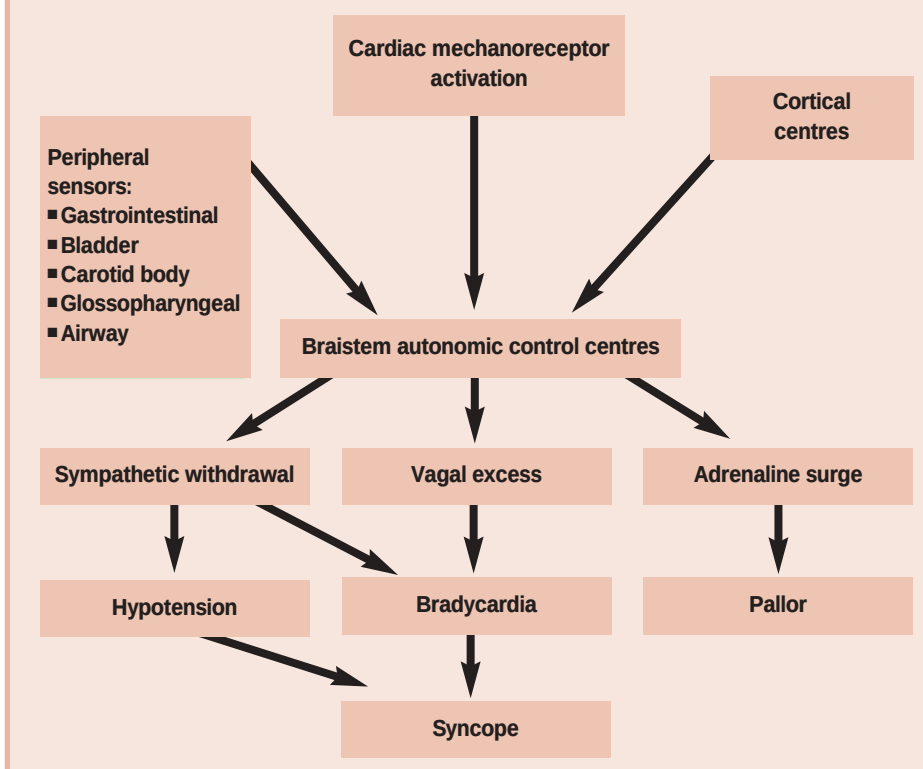


Figure 2: Tachy-brady syndrome. The top two strips show a run of atrial fibrillation with relatively rapid ventricular response, ending abruptly and followed by sinus pauses of >7 seconds, during which the patient lost consciousness. The third strip down shows a period of extreme sinus bradycardia and the fourth strip shows how even a brief run of atrial tachycardia can lead to profound suppression of the sinus node in this patient.

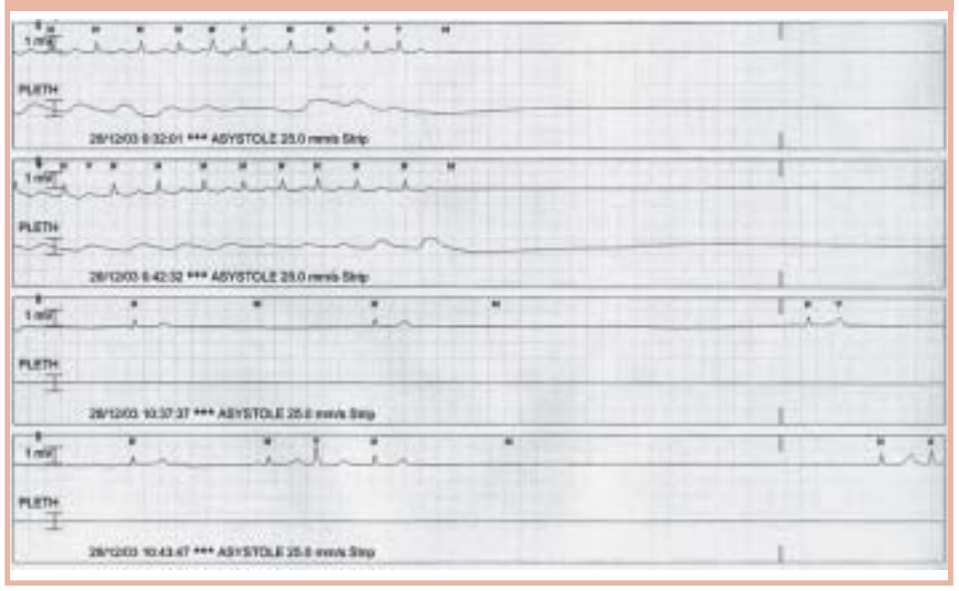


Table 3: Drugs causing orthostatic hypotension
- Antihypertensives and antianginal medications
  - — Nitrates
  - — Vasodilators (calcium-channel blockers, prozosin, hydralazine, minoxidil)
  - — ACE inhibitors and angiotensin-II-receptor antagonists
  - — Others (clonidine, methyldopa, reserpine, ganglionic-blocking drugs)
- Diuretics
- Antidepressants (tricyclic antidepressants, MAOIs)
- Antipsychotics (phenothiazines, clozapine, risperidone, etc)
- Anticholinergics (antihistamines, antispasmodics and some antiemetics)
- Antiparkinsonian medications (levodopa, bromocriptine)
- Miscellaneous (alcohol, vincristine)

Table 4: Causes of autonomic dysfunction

Primary autonomic disorders

Acquired

- Acute pandysautonomia
- Pure autonomic failure
- Multiple system atrophy (Shy-Drager syndrome)
- Parkinson's disease

Inherited

- Familial dysautonomia (Riley-Day syndrome)
- Dopamine β-hydroxylase deficiency
- Noradrenaline transporter deficiency

Secondary autonomic failure

Central/spinal

- Demyelinating conditions
- Tumours
- Syringobulbia (syringomyelia)
- Infections

Peripheral neuropathies

- Diabetes
- Renal failure
- Paraneoplastic syndromes
- Guillain-Barré syndrome
- Amyloidosis
- Autoimmune/collagen vascular diseases
- Infections
- Alcoholic neuropathy

Figure 3: Complete heart block leading to syncope. Tracing obtained from a 75-year-old man with a King of Hearts event monitor. The initial rhythm is sinus, with 1:1 conduction to the ventricles with a left bundle-branch block pattern. Suddenly complete heart block occurs (note the gradual acceleration in the sinus rate after this), and after about 10 seconds the patient hits the ground (impact electrogram) followed by an escape beat. It takes a further 30 seconds before the next escape beat, then gradually a regular escape rhythm emerges.

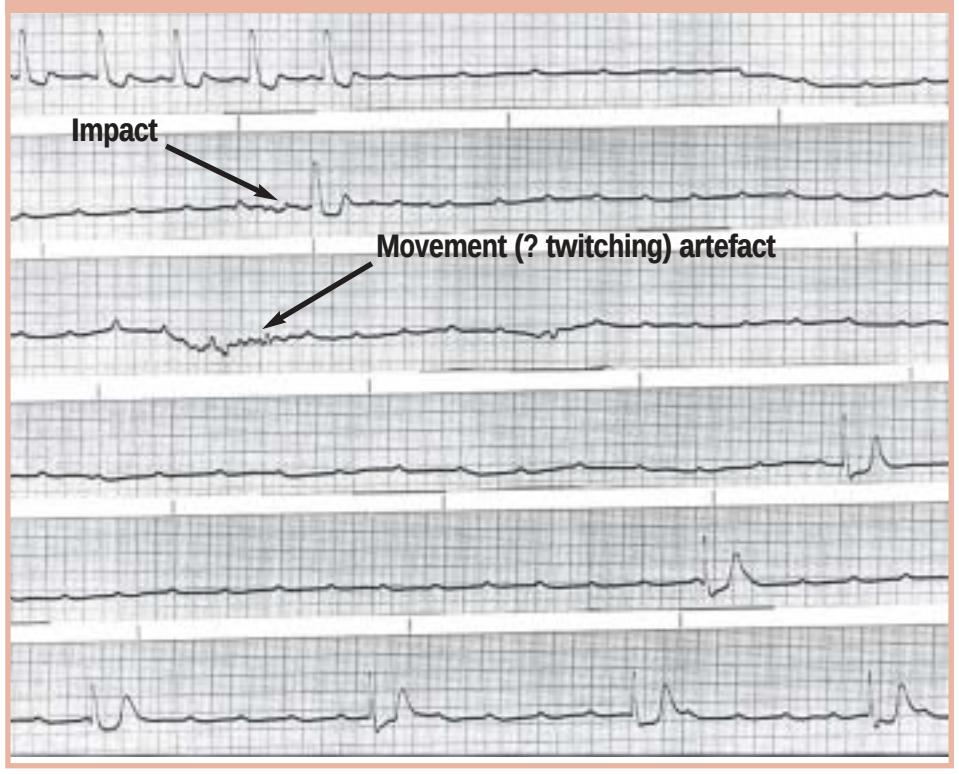
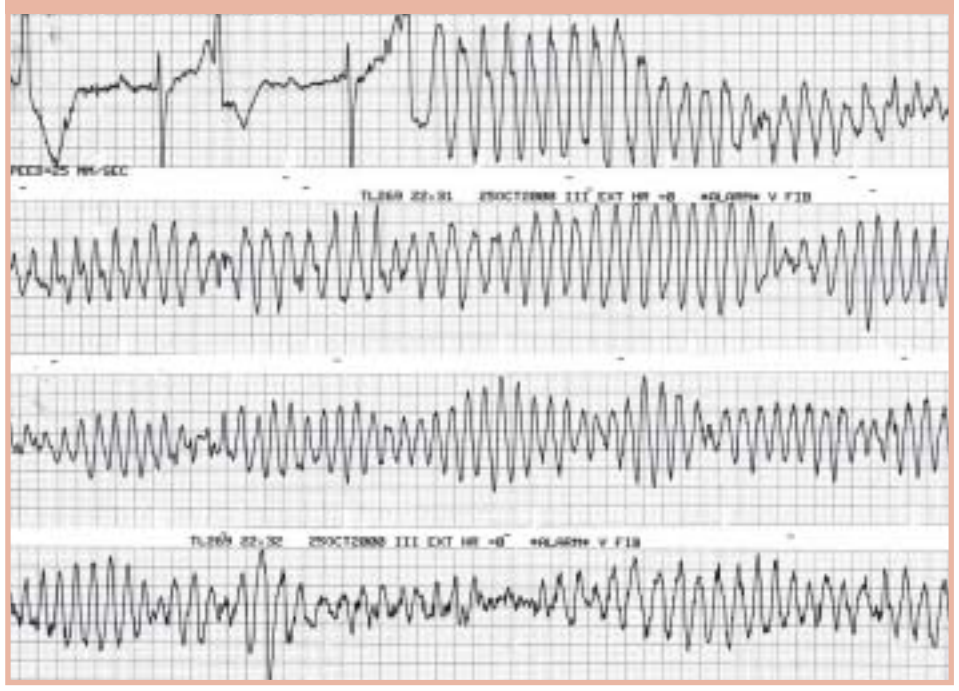


Figure 4: Syncope secondary to torsade de pointes. The initial rhythm is complete heart block with a narrow junctional escape rhythm and frequent ventricular ectopics, produced by the excessively prolonged QT interval. Finally, one of these ectopics triggers sustained polymorphic ventricular tachycardia (torsade de pointes).



despite systolic pressures of close to 60mmHg. Typically, despite the marked hypotension, there is no sweating (reflecting the dysfunctional autonomic system) and few or no warning symptoms. However, the particular manifestations will vary according to the cause of the autonomic dysfunction.

Supine hypertension is common (because of defective baroreceptor reflexes) and treatment with antihypertensives is likely to exacerbate the postural hypotension. An aggravation of postural hypotension after meals is well recognised (postprandial hypotension) and probably due to inadequate sympathetic compensation to meal-induced pooling of blood in the splanchnic circulation.

Cardiac electrical

Arrhythmias account for about 10% of causes of syncope. When loss of consciousness occurs it is sudden with, at the most, very brief premonitory symptoms. Awareness of palpitations before the episode is the exception rather than the norm. The duration of unconsciousness varies but is generally less than 30 seconds. Recovery is typically quick, particularly if the arrhythmia has completely resolved. An arrhythmia should be high on the list of possible causes of syncope in the elderly, especially in those with underlying cardiac disease or with electrocardiographic abnormalities, particularly evidence of AV-conduction disease (eg, bundle-branch block).

Bradyarrhythmias

There are two types of bradycardia: sinus node dysfunction and AV-conduction block. Both are much more common in the elderly because of age-related cardiac fibrosis and the increased prevalence of acquired heart disease. Sinus node dysfunction, sometimes referred to as sick sinus syndrome, has various manifestations: sinus bradycardia with blunted response to exercise, intermittent sinus pauses or sinus arrest of varying duration, and the combination of either of these manifestations with intermittent atrial fibrillation accompanied by rapid ventricular response (the so-called tachy-brady syndrome). Symptoms of presyncope or syncope are more likely to be caused by sinus pauses or arrest occurring either spontaneously or at the termination of an episode of atrial fibrillation (figure 2).

Similarly, AV-conduction disease is more likely to cause syncope at the onset of complete heart block when there is a period of asystole before the junctional or ventricular escape rhythm emerges (figure 3). Lesser forms of block are usually associated with milder symptoms such as exercise limitation, dyspnoea, weakness or dizziness. Established third-degree AV block does not cause syncope unless there is intermittent failure of the escape rhythm or supervention of torsade de pointes (figure 4).

Tachyarrhythmias

Both supraventricular and ventricular tachycardias may lead to syncope but this is much less common than bradycardia-induced syncope. Syncope may result from ineffective cardiac output or from a reflex-mediated mechanism (ie, a vasovagal faint). Awareness of palpitations before syncope is distinctly uncommon (usually due to the progressive hypotension); however, in people with tachycardia-induced vasovagal reactions, awareness of palpitations after regaining consciousness is common.

Table 5: Features suggesting seizures rather than syncope

Prodrome

- Aura such as deja vu or certain smell

Period of unconsciousness

- Longer than a minute
- Unresponsive, without loss of postural tone or with semi-purposeful movements
- Violent epileptiform movements
- Tongue biting, clenched jaw, stertorous breathing, frothing at the mouth

Post-episode

- Confusion
- Extreme somnolence
- Neurological signs
- Fever and leucocytosis

Cardiac mechanical

This group comprises several serious, potentially lethal cardiovascular disorders that may cause syncope. The fundamental mechanism is obstruction to cardiac flow, but other mechanisms may play a role in some cases. For example, syncope in patients with hypertrophic obstructive cardiomyopathy may be secondary to severe obstruction, cardiac arrhythmia (usually ventricular tachycardia), or a vasovagal reflex-mediated mechanism (activation of cardiac mechanoreceptors in response to high intracavitary pressure).

Presentation will vary somewhat according to the particular condition but often the syncopal event will be profound and recovery may be slow and incomplete until the underlying condition is relieved. Because of their life-threatening nature, these disorders should be considered in anyone presenting with syncope. In particular it is important to think about pulmonary embolism and aortic dissection, as these are easily overlooked even with echocardiography.

Non-cardiac

Non-cardiac conditions, particularly those of neurological or psychogenic aetiology, account for 10-20% of apparent cases of syncope.

Neurological/cerebrovascular

Seizures may mimic syncope. There may be few or no tonic or clonic movements during the seizure, the patient may appear pale and sweaty and may even develop vasomotor disturbances such as bradycardia and hypotension in some circumstances. Similarly, syncope may mimic epilepsy: it is not uncommon for the syncopal event to be associated with gross twitching of the limbs lasting a few seconds; profound reduction in cerebral blood flow may be associated with urinary and faecal incontinence; and the prolonged recovery time after some reflex-mediated syncopal episodes may be mistaken for post-epileptic drowsiness.

A detailed history is usually the most helpful way of distinguishing between the two alternatives (table 5). Atherosclerotic cerebrovascular disease is a rare cause of syncope and almost invariably other neurological signs will accompany the syncopal episode. This also applies to the unique variant known as subclavian steal syndrome. Metabolic disturbances will usually be suggested by the history.

Psychogenic pseudo-syncope, seen predominantly in adolescent or young-adult girls, is not uncommon. Typically the episodes are very frequent, of sudden onset and not associated with injury.

One of the most helpful investigations in establishing the mechanism is the tilt table test (see Head-up tilt table testing page 38), as almost without exception those with this condition will suffer an event during the test. This allows direct observation of the episode and correlation with blood pressure and heart rate or rhythm. Usually, the diagnosis is quite obvious — syncope occurs within seconds of being tilted, there is no change in colour, the patient resists movement and there is no change in heart rate, rhythm or blood pressure.

Investigating syncope

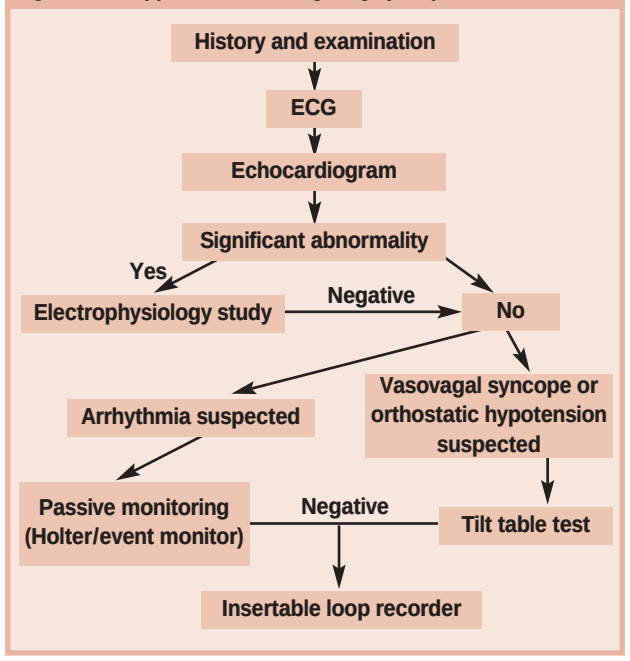
INVESTIGATING syncope can be a frustrating process. The syncopal events are usually quite infrequent and unpredictable, and capturing a spontaneous episode, which is the best way of making the diagnosis, is difficult. Patients often have multiple, expensive and sometimes repeated investigations without a firm diagnosis ever being reached.

When interpreting the various tests it is important to distinguish between a presumptive diagnosis and the actual diagnosis. Unless the investigation is performed during a spontaneous event, the suggested cause may not be the real cause. For example, the finding of repeated sinus pauses of 2-3 seconds during a Holter monitor recording raises the possibility of more prolonged pauses causing syncope, but this is not proven. As a result patients can end up receiving unnecessary treatments, which are not only ineffective, but also costly and potentially harmful.

Also, the cause for the patient's presyncope might be quite different from the cause of their syncope. Therefore, the finding of an arrhythmia on Holter monitor at the time of presyncope may indicate the cause for the patient's syncope, but equally it may not.

Finally, provocative tests (eg, electrophysiology study or tilt test), may also simply evoke a range of possibilities that have nothing to do with the real cause, and all tests need to be interpreted carefully (See Author's case study, page 40).

Figure 5: An approach to investigating syncope.



Initial assessment

A detailed history (including eyewitness accounts) is the most helpful tool when investigating a patient with syncope. In occasional cases the diagnosis is obvious and no additional investigation is necessary, eg, the history of person passing out whenever they see blood. Even when the diagnosis is not obvious, the list of possible causes can usually be narrowed down by a careful history, accordingly directing and limiting the investigative process. However, occasionally, even after a detailed history, the list of possibilities remains large and a structured approach to investigation can be helpful (figure 5).

The initial assessment should not only include the history but also an examination of the cardiovascular system. In particular the heart rate and rhythm should be noted and blood pressure measured with the patient supine then after standing for two minutes.

An electrocardiogram is indicated, not only for examining the heart's rate, rhythm and AV-conduction properties but also because it gives evidence of other cardiac structural conditions (such as ischaemic heart disease and hypertrophy), as well as a variety of uncommon electrical disturbances capable of causing sudden death (table 6).

To complete the assessment, perform routine blood biochemistry (electrolytes, urea and creatinine, LFTs, fasting glucose and FBC and blood film) to look for evidence of other medical abnormalities that may impact upon the patient's management is reasonable.

Primary investigations

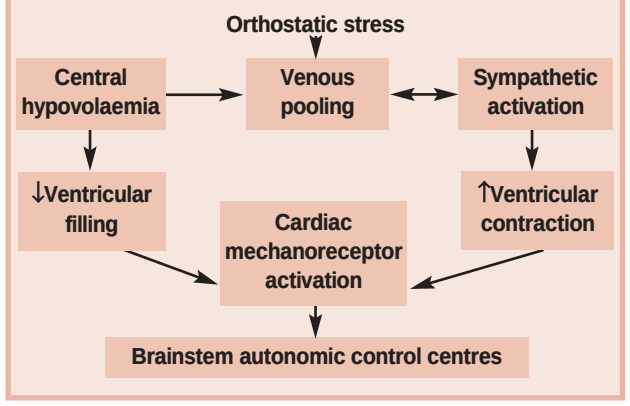
Echocardiography

One of the most helpful investigations is the echocardiogram. It is non-invasive, relatively inexpensive and helpful in directing further investigations. Although it rarely gives the diagnosis by itself, the echocardiogram excludes uncommon but serious, potentially life-threatening, cardiac obstructive conditions (eg, severe valve stenosis, myxoma) and stratifies patients into those with or without significant cardiac structural and/or functional abnormalities (eg, left ventricular dysfunction, infarction, hypertrophy, cardiomyopathy, ventricular non-compaction, etc).

Patients with abnormal ventricular structure or function have a much greater risk of malignant forms of ventricular tachycardia and should be considered for diagnostic electrophysiological testing to rule out this arrhythmia. On the other hand, the combination of a normal electrocardiogram and echocardiogram effectively rules out a life-threatening cardiac cause for the syncope. Apart from pulmonary embolism, there are very few serious potential conditions not excluded by these tests, and these are exceedingly rare.

Figure 6: Head-up tilt table test. The patient is strapped to a table capable of being tilted to 70°. The duration and angle of tilt vary depending on the protocol used. At our institution we tilt patients to 70° for 30 minutes. During this time, the patient's blood pressure and heart rate and rhythm are recorded continuously. Blood pressure is measured using a device capable of measuring beat-to-beat differences in pressure, as well as with cuff measurements every two minutes. We do not insert an IV cannula, to avoid provoking vasovagal reactions before the tilt has begun. After 10 minutes (the passive phase) a 400μg spray of glyceryl trinitrate is administered (in the past, IV isoprenaline was used) and the patient observed for a further 20 minutes (the active phase).

Figure 7: Mechanism of tilt-induced vasovagal syncope.



Head-up tilt table testing

Tilt table testing (figure 6) has been used to investigate the effects of orthostatic stress for many years. Only a few centres in Australia use it as a tool for investigating syncope but in our opinion it is perhaps the single most helpful investigation in recurrent syncope because it is capable of provoking two of the most common causes of syncope — vasovagal syncope and orthostatic hypotension.

On assuming the upright posture, 500-1000mL of blood pools in the lower limbs and splanchnic circulation. This leads to a rapid decrease in venous return to the heart, which causes a reduction in cardiac output and fall in blood pressure. The reduction in blood pressure and thoracic volume is sensed by the aortic and carotid baroreceptors, leading to a reflex increase in sympathetic, and decrease in vagal, activity. This increases peripheral vascular resistance, venous return and cardiac output, thereby limiting the fall in blood pressure.

Overall, in healthy people, there is a small (5-10mmHg) fall in systolic pressure, a slight rise (5-10mmHg) in diastolic pressure and a small increase (10-25 beats/min) in heart rate. With continued standing, the renin-angiotensin-aldosterone system is activated and antidiuretic hormone released, resulting in salt and water retention and enhanced peripheral vascular tone.

The head-up tilt test assesses the adequacy of these normal responses. Orthostatic hypotension can be readily documented and quantified and, with the addition of some simple tests (eg, mental arithmetic, ice-water test, and Valsalva manoeuvre), the cardiovascular autonomic reflexes can be adequately tested.

However, the primary role of the tilt test is assessing vasovagal syncope. The exact mechanism through which tilting provokes this reflex is not completely understood. Patients prone to this form of syncope usually have a completely normal initial response to tilting, indicating intact cardiovascular autonomic reflexes. However, at some point during the tilt there is sudden failure of these com-

Treating syncope

IF the diagnosis can be established, the treatment options are often clear-cut, eg, pacemaker implantation for bradycardia or valve replacement for severe aortic stenosis, and a referral to the relevant specialist is appropriate.

Managing vasovagal syncope

Reassurance

The first step in managing this condition is that of reassurance. It should be explained to the patient that, although it is often a significant problem, it is a benign condition that will not cause stroke, heart attack, or shorten their lifespan. In almost all patients it simply represents an abnormal sensitivity of a normal reflex. In addition, in most younger patients with this condition there is spontaneous improvement with time.

Conservative measures

In elderly patients, use of medication such as vasodilators and diuretics can precipitate this form of syncope and should be minimised wherever possible. Similarly, any known precipitants, such as prolonged standing on a hot day, should be avoided.

By improving venous return to the heart, an increase in the circulating blood volume can protect the susceptible individual from an event. We advise the patient to ensure they drink at least two litres of fluid a day and to add some salt to their meals if they do not suffer from hypertension.

One of the characteristic features of this condition is the ability to abort an episode by lying down. So if the prodrome is long enough, the patient should lie — or at the very least sit — as soon as the warning symptoms are recognised. Lying with the feet elevated on a chair or bench, which further enhances blood return to the heart, is even more effective. Isometric tensing of the upper limbs (abducting the arms while holding the hands together) has also been shown to successfully abort syncope in some people.

In particularly refractory individuals, 'tilt training' can be attempted. This is performed by the patient standing with their back to a wall, leaning their shoulders against the wall with their feet about 15cm out from it (hence mimicking the tilt test). The patient should do this surrounded by soft padding such as mattresses, in a place where they can avoid damage if they fall. The duration of standing is gradually increased as tolerance improves. In one trial performing this manoeuvre for up to 40 minutes twice a day, syncope was prevented for as long as the manoeuvre was continued. However, in our experience it is the rare patient who has the patience and commitment to adhere to such a time-consuming ritual.

Medications

In a small number of patients conservative measures are not sufficient and certain medications may be helpful. Few of these have been tested in prospective, randomised, double-blind placebo-controlled trials, or, if they have, they have not been found to be any more effective than placebo.

Beta blockers (both β_1-selective and non-selective) have been the most popular choice for first-line medication and, theoretically, they should be helpful. However, the evidence to date suggests they are no more effective than placebo and in some cases may exacerbate the problem.

Fludrocortisone (Florinef) causes salt and water retention, as well as enhancing peripheral vasoconstriction. It is generally well tolerated in small doses but is contraindicated in patients with hypertension.

Midodrine, an α_1-agonist (vasoconstrictor) is popular overseas but is only available in this country after application to the TGA on a case-by-case basis. Although it has been shown to be effective over the short term, it is uncertain whether it retains its potency over the long term, and a longer-term trial of a similar substance (etilefrine) failed to show any long-term benefit.

The SSRIs fluoxetine and sertraline have been shown to be beneficial in about 50% of patients with recurrent vasovagal syncope and positive tilt tests.

Pacing

There is some evidence from small non-blinded trials that by pacing the heart at a higher rate the vasovagal

Figure 8: External event monitors. A. The 'RhythmCard' (top and bottom). It is slightly larger than a credit card. B. The 'King of Hearts' event monitor.

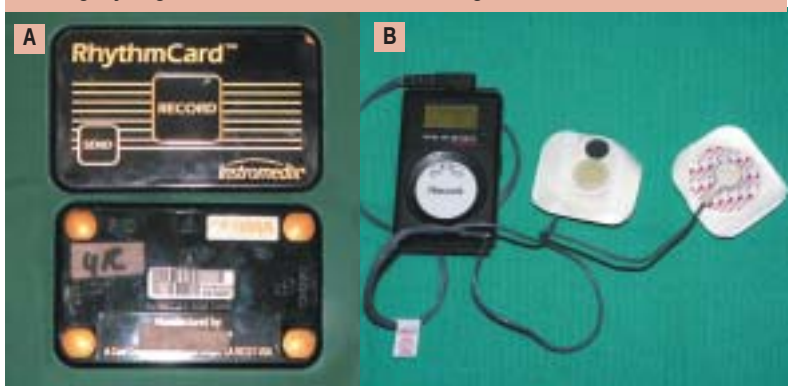
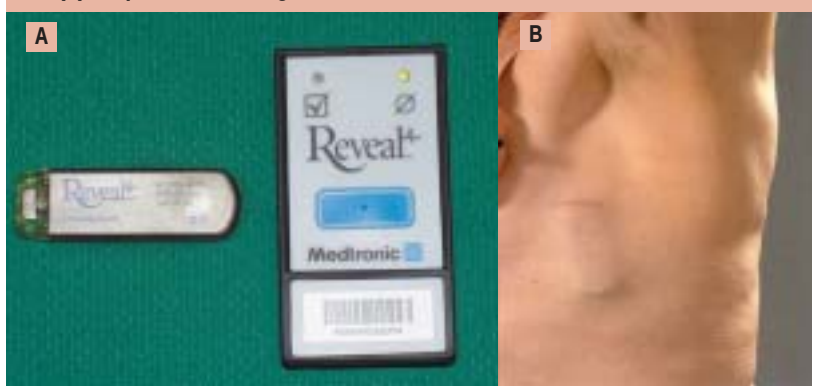


Figure 9: The insertable loop recorder. A. The insertable loop recorder device and (B) the patient activating the device.



pensatory reflexes, with paradoxical sympathetic withdrawal and vagal enhancement.

It is believed that the combination of reduced cardiac filling secondary to reduced venous return, coupled with increased cardiac contractility and rate secondary to enhanced sympathetic tone, leads to vigorous contraction of relatively empty ventricles. This may be sufficient to activate the cardiac mechano-receptors, which then feed back to the vasomotor centre in the brainstem to provoke the vasovagal response (figure 7).

The tilt test needs to be interpreted carefully. There is a false-positive rate of about 10% when active agents (eg, glyceryl trinitrate or isoprenaline) are used. A variety of mechanisms can cause patients to faint, eg, vasovagal syncope, exaggerated response to glyceryl trinitrate, autonomic-dysfunction-induced syncope, and pseudo-syncope. There is also a significant false-negative rate (patients with typical vasovagal syncope having a normal test), so a negative test does not exclude this diagnosis. As with any test, the sensitivity and specificity are highest when it is applied to the appropriate population (in those with suspected vasovagal or orthostatic-hypotension-related syncope).

Despite these limitations, when properly interpreted the tilt test is an extremely helpful investigative tool. In particular, when syncope is induced by a specific mechanism and the patient's symptoms are accurately reproduced, this is strong corroboration of the mechanism for the syncope.

Cardiac rhythm testing

Passive electrocardiographic monitoring

To prove an arrhythmic aetiology in the patient with recurrent syncope it is necessary to obtain a symptom-rhythm correlation. Because of the unpredictable and usually infrequent nature of the episodes, this can be very difficult. Several types of constant recording devices are available.

Holter monitor. Because this test is easy to order, non-invasive and cheap, it is one of the most overused tests in the investigation of syncope. On the negative side, the chance of detecting a significant arrhythmia is very low. The likelihood of the patient passing out while wearing the recorder is even lower.

Arrhythmias unrelated to the syncope (eg, non-sustained atrial tachycardia, atrial and ventricular ectopics, atrial fibrillation, sinus irregularities with brief pauses of up to two seconds, and lesser degrees of AV block) are common in elderly patients and potentially misleading. Even if a symptom-rhythm recording is obtained during a presyncopal episode, there is no guarantee that the aetiology of the syncope is the same as that of the presyncope.

On the positive side, it is a helpful screening test, giving a brief snapshot of the arrhythmic milieu. Even in the absence of symptoms, some arrhythmias are worth pursuing (eg, frequent ventricular ectopics, ventricular tachycardia, prolonged supraventricular tachycardia and second- to third-degree heart block). Also, although the doctor cannot completely rely on the rhythm during presyncope, it is certainly a significant pointer, and the weight that can be attached to it increases with the severity of the presyncopal episode.

External event monitors (figure 8). The external event monitor gives a much higher yield than Holter monitoring, but access to this test is limited to some public teaching hospitals and individual cardiologists and it requires more patient cooperation. There are two basic types of external event monitor. The first type (eg, RhythmCard) is applied to the skin over the chest when symptoms are present. It gives no recording before its application to the chest wall and is clearly inappropriate in investigating syncope or presyncope.

The second type is a loop recorder similar in size to the Holter monitor. ECG electrodes are applied each morning by the patient and connected to the recording device. When an event occurs the patient pushes a button, enabling a recording of variable duration of the rhythm before and after activation. This is suitable as long as the duration of pre-event recording is at least two minutes and the patient is capable of complying with the instructions. The main limit to the use of this type of recorder is sensitivity to the ECG electrodes and the patient having to commit to the device long enough to capture an event (most patients will not tolerate it for more than two weeks).

Insertable loop recorder (figure 9). This recently developed device is inserted under the skin in the left pre-pectoral area, just like a pacemaker but with no leads — instead it senses and records cardiac electrical events via exposed metal parts at each end that act as cathode and anode.

Because of the cost it tends to be reserved for use in patients with recurrent syncope (or a single worrisome event) that remains unexplained after other investigations. However, it can be a very helpful device identifying or ruling out an arrhythmia as the cause (figure 5).

Electrophysiological testing

Diagnostic electrophysiological testing should be considered in patients with unexplained syncope and cardiac dysfunction or structural abnormalities, especially those with underlying ischaemic heart disease, as they are at increased risk of malignant ventricular tachyarrhythmias. This test is also helpful in those suspected of having syncope secondary to other forms of tachycardia; however, it is not a reliable test for picking up or ruling out bradycardic causes of syncope.

Further testing

Exercise stress testing

Stress testing is of value when patients have recurrent exercise-induced syncope. It should be performed only after excluding significant cardiac obstructive lesions by echocardiography and usually after excluding malignant ventricular arrhythmias by electrophysiological testing. Not all stress-testing centres will be set up to perform the test for this indication.

Neurological testing

Tests of neurological function (including EEG, carotid Doppler studies, CT and MRI of the brain) are among the other most over-ordered tests in the investigation of syncope. Assuming a history suggestive of syncope, epilepsy and other neurological conditions remain very uncommon causes. Furthermore, a normal EEG does not rule out the possibility of epilepsy, neither does an abnormal one definitely identify it as the cause for apparent syncope. If you suspect a neurological cause for the apparent syncopal episode, referral to a neurologist may be more appropriate than a battery of neurological tests.

Table 6: What to look for on the ECG in syncope

Rate and rhythm

Evidence of AV-conduction disorder
- Prolonged PR interval
- Left anterior or posterior fascicular block
- Left or right bundle-branch block
- Prolonged QRS duration indicative of intraventricular conduction delay
- Mobitz I (Wenckebach) or II; second-degree AV block
- Complete (third-degree) AV block

Evidence of underlying cardiac disease
- Significant left or right axis deviation
- Significant ST or T wave changes
- Left or right ventricular hypertrophy
- MI

Conditions associated with increased risk of sudden death
- Hypertrophic cardiomyopathy
- Long QT syndrome
- Ventricular pre-excitation (Wolff-Parkinson-White syndrome)
- Arrhythmogenic right ventricular dysplasia
- Brugada syndrome
- Short QT syndrome

response could be attenuated. However, a larger, randomised double-blind trial failed to demonstrate any significant benefit. Pacing is reserved for the rare patient with refractory recurrent vasovagal syncope and documented profound asystole.

Managing orthostatic hypotension

The first step in managing orthostatic hypotension is the disentangling of the various contributory factors. Any condition that can cause postural hypotension is more likely to do so in the elderly because of age-related decreased sensitivity of baroreceptors. Similarly, those with any underlying predisposing condition such as diabetic autonomic dysfunction are much more likely to develop orthostatic symptoms when exposed to an additional orthostatic stressor such as vasodilators, dehydration, etc.

Often, when the patient presents with symptomatic orthostatic hypotension it is because of some new stress. For example, the elderly patient with diabetes and mild, asymptomatic postural hypotension may develop significant orthostatic hypotension (with or without symptoms) after starting an ACE inhibitor-diuretic combination for hypertension, but only present with syncope after having lunch on a hot day.

Having ascertained the possible contributors to postural hypotension, address the treatable factors. In the example above, treatment may include removal or change of the antihypertensive, and education about avoiding or taking adequate precautions in the face of orthostatic stresses such as postprandial hypotension, heat, alcohol and dehydration. Almost all patients with postural hypotension can be successfully managed by removing or correcting the orthostatic stressors, which are most commonly medications.

Table 7: Principles of management of postural hypotension secondary to autonomic dysfunction

Non-pharmacological

To be avoided
- Sudden standing (especially in the morning)
- Prolonged recumbency
- Straining during micturition and defecation
- Hot environments
- Extreme exertion
- Large meals (especially with refined carbohydrate)
- Alcohol
- Drugs (see table 3)

To be introduced
- Head-up tilt at night
- Small frequent meals
- High salt intake
- Regular mild-to-moderate exercise

To be considered
- Elastic stockings
- Abdominal binders

Pharmacological
- Starter drug: fludrocortisone (Florinef)
- Sympathomimetics: midodrine, ephedrine
- Specific targeting: octreotide (Sandostatin), desmopressin (Minirin), erythropoietin

Adapted from: Mathias CJ, Bannister R. *Management of Postural Hypotension in Autonomic Failure: a Textbook of Clinical Disorders of the Autonomic Nervous System*. 4th edn. Oxford University Press, Oxford, 1999.

However, patients with underlying autonomic dysfunction may remain symptomatic even after the removal of external factors. Some principles to bear in mind when managing such patients include:
- Many patients with chronic autonomic dysfunction and significant postural hypotension can tolerate systolic blood pressures as low as 60mmHg without symptoms;
- Many patients have supine hypertension owing to defective baroreceptors, which can greatly complicate the pharmacological treatment;
- Maintenance of adequate circulating blood volume is central to any treatment strategy.

All methods of treatment aim either at reducing the degree of pooling of blood that occurs on standing or increasing the circulating blood volume. Principles of management are summarised in table 7.

Concluding comments

Syncope is a common and difficult problem. It is responsible for numerous GP visits, hospital emergency room presentations and hospitalisations. The investigation process can be frustrating and often patients end up requiring multiple tests.

The patient who suffers recurrent syncopal events can become quite disabled, as the condition affects their self-confidence and limits their ability to travel, drive and work. Their quality of life has been found to be as poor as that of patients with chronic debilitating diseases such as rheumatoid arthritis.

Nevertheless, effective therapies exist for almost all causes, so a cause should be sought wherever possible.

Author's case study

First syncopal episode

STANDING outside feeding birds one evening, a 53-year-old teacher suddenly felt lightheaded, then passed out. Her daughter noticed that she was pale and unconscious for about one minute, and a little vague for about one minute afterwards, with no other sequelae. Examination disclosed no abnormalities other than some ectopics.

The cardiologist's report was as follows:

- ECG: left bundle-branch block, '?' ventricular preexcitation;
- Echocardiogram: normal;
- Electrophysiology study: no evidence of ventricular preexcitation; left bundle-branch block with normal AV-conduction time; no cause for syncope identified;
- No treatment indicated.

Continuing presyncopal episodes

The patient continued experiencing presyncopal spells over the next 18 months, typically occurring on exertion and characterised by weakness, trembling, pallor lasting seconds, and recovery within minutes. Examination was unchanged but frequent ectopics were again noted.

A second referral to a cardiologist included a head-up tilt test, which induced vasovagal syncope with symptoms similar to the patient's presyncopal spells. The patient's spells were attributed to vasovagal syndrome (figure 10).

Figure 10: Symptoms of presyncope occurred with runs of atrial tachycardia

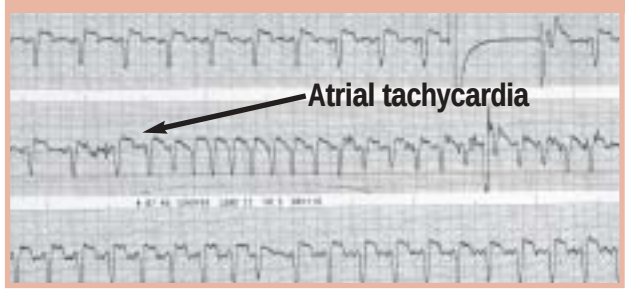
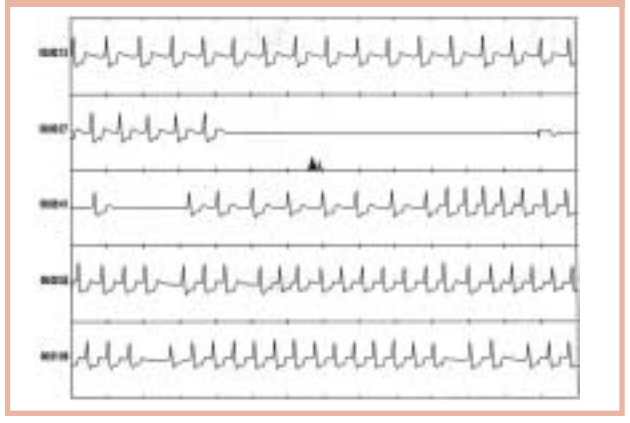


Figure 11: Trace from an insertable loop recorder, showing a 10-second period of ventricular asystole due to complete AV block.



Second syncopal episode

Over the four years between syncopal episodes, the patient developed increasingly frequent presyncope, initially with exercise but later occurring at rest, both standing and sitting. The second syncopal event occurred while the patient was walking to school. She developed sudden light-headedness and within seconds experienced loss of consciousness, sustaining a head injury with scalp and lip laceration.

On this occasion the cardiologist's report indicated:

- ECG: very frequent atrial ectopics, with runs of atrial tachycardia;
- External event monitor: symptoms of presyncope were associated with runs of atrial tachycardia;
- Echocardiogram: mild left atrial enlargement and mild mitral regurgitation;
- Electrophysiology study: no inducible atrial tachycardia, no atrial fibrillation.

The diagnosis of atrial tachycardia-induced presyncope was made, but the cause of the syncope remained unclear (?sinus arrest, ?heart block). Treatment was with atenolol 50mg daily.

Third syncopal episode

Six months after starting atenolol, the patient had had no further syncope and the presyncopal spells had been less frequent. However, one year later, while driving her car, she again developed light-headedness followed by syncope within a few seconds. She came to with the car resting against a guard rail, with only minor car damage. She had headache and felt weak but within five minutes was better and able to drive home.

Her local medical officer organised further tests — an EEG and CT of the brain — which were both normal.

The cardiologist arranged for an insertable loop recorder, which recorded a transient syncopal event one week after insertion, while talking with her friends over coffee (figure 11).

Comments

The case illustrates several points relevant to the investigation of syncope:

- Several diagnoses were entertained — vasovagal syndrome, atrial tachycardia, sinus pauses and AV block — before a final diagnosis of ventricular asystole was made;
- Both the passive monitoring (ECG and external event monitor) and provocative testing (tilt test) suggested diagnoses that were ultimately proven wrong;
- The patient required a large number of investigations, including ECGs, two electrophysiology studies, use of an external event monitor, two echocardiograms, EEG, CT brain scan and use of an insertable loop recorder before the diagnosis was reached;
- Both atrial tachycardia and transient AV block were responsible for the symptoms of presyncope;
- The best way of making the diagnosis is to capture a spontaneous event.

GP's contribution

PROFESSOR TENG LIAW
GP in Shepparton, Victoria

Case study

A MAN aged 40 presented because he fainted while changing a flat tyre. He was not sure what had happened because he was alone. He remembered starting to change the tyre, then found himself keeling over with his face on the ground. It was quite a hot day and he had drunk a couple of glasses of beer with his counter meal at lunchtime. No other history was obtained or symptoms reported.

There was no relevant past history. He had occasionally taken salt tablets for cramps. He had been told by various doctors that his blood pressure was slightly on the high side. When he played football in the past, he had occasional palpitations, especially when he was playing strenuously. When pressed he said that he thought he may have felt faint when he had palpitations. He does not exercise enough to get palpitations now.

He used to smoke until about three years ago. He drinks 1-2 glasses of beer a day, usually after his evening meal. His wife does not do paid work and they have an 11-year-old daughter. He had an insurance medical three years ago, which was normal except for slightly elevated blood pressure.

His father is still alive but had a heart attack and a CABG. A distant cousin suffered from fits. He thinks that his mother may have had a goitre and heart failure.

Examination showed an overweight man in no obvious distress. He had some minor abrasions on his forehead, consistent with his story. Blood pressure was 140/90mmHg lying and 136/90mmHg standing; heart rate was regular at 90 beats/min; body mass index was 29; pulses were all present and palpable; pupils were equal, reacted to light and displayed accommodation, with the full range of ocular movements; the CNS was grossly intact.

Questions for the author

What are the most likely causes of this patient's faint?

The most likely cause is a combination of relative hypotension due to postprandial splanchnic and peripheral vasodilatation secondary to alcohol, heat and exercise, with or without straining-induced reduction of venous return to the heart (due to raised intrathoracic pressure).

How would you manage his faint during this consultation?

Examination of the cardiovascular system, including lying and standing blood pressure.

Does the patient need any investigations at this point in time? If so, which ones?

The patient should have an ECG performed.

How would you reassure him? He is concerned that he may have a heart problem.

I probably wouldn't perform an echocardiogram at this time, as the situation doesn't seem to warrant it, but if I was unable to reassure the patient verbally I would order an echo.

What would you tell him about his faint?

That it is benign and due to the combination of factors on that particular day.

How would you monitor his progress? Over the long term?

If he experiences recurrent presyncope or syncope, I would next perform a tilt test.

General questions for the author

What is the most discriminating history, examination or test finding to help GPs differentiate between the syncope mimics and the real thing?

There is no magic bullet, but documented injury during an episode is pathognomonic of an organic condition.

How would you manage the patient who says they come from a family of fainters?

This is well recognised (vasovagal syncope runs in families), but patients are managed on their own merits (ie, whether they have syncope).

Can the Valsalva manoeuvre cause syncope? If yes, how and under what circumstances?

Yes. A prolonged and strenuous Valsalva manoeuvre, particularly if combined with abdominal compression, can lead to very transient syncope. This is simply due to obstruction to venous return from the abdominal circulation and lower limbs, where the great bulk of the blood volume resides.

Do GPs have to take special precautions with patients with particular chronic diseases to prevent syncope? If yes, which diseases and what precautions?

Yes — the elderly and patients with diabetes and hypertension. The elderly and people with diabetes have varying degrees of autonomic dysfunction, putting them at risk of postural hypotension. They are more likely to be taking vasodilators, diuretics and antidepressants.

How well is the insertable loop recorder device tolerated by patients? What is the yield?

It is extremely well tolerated as far as the device under the skin is concerned. About two-thirds of patients who have the device inserted experience a syncopal event during the 18 months of battery life.

Of these, about half have normal sinus rhythm at the time of syncope, ruling out an arrhythmia, but not establishing the definitive diagnosis.

Of the other half with an 'arrhythmia' at the time, half have bradycardia, one-third have sinus rhythm with a change in rate suggestive of vasovagal syncope, and the remainder have tachycardia.

About 5-10% of patients will have a recurrent event but fail to activate their device.

What sort of adverse reactions have you observed among patients who have used the medications you recommended for syncope?

With fludrocortisone, oedema, hypertension and heart failure. With midodrine, insomnia and chest pains.

What success rates have you obtained treating syncope with medications?

Overall a little disappointing for vasovagal syncope; much better for orthostatic hypotension.

HOW TO TREAT
Editor: **Dr Lynn Buglar**
Co-ordinator: **Julian McAllan**

NEXT WEEK
The next How to Treat addresses social phobia and its treatment. The author, **Dr Lisa A Lampe**, is honorary medical officer, clinical research unit for anxiety and depression, St Vincent's Hospital, Sydney; conjoint lecturer, University of NSW, Sydney; and consultant psychiatrist, Evesham Clinic, Cremorne, NSW.