Syncope

4

Mark D. Carlson

Syncope is defined as transient loss of consciousness due to reduced cerebral blood flow associated with postural collapse and rapid spontaneous recovery. It may occur suddenly, without warning, or be preceded by faintness ("presyncope"). Symptoms and signs that precede syncope may include pallor, diaphoresis, a feeling of warmth, nausea, persistent and often progressive generalized weakness, fatigue, cognitive slowing, leg buckling, visual blurring occasionally proceeding to blindness, and the "coat hanger" headache (a triangular headache at the base of the neck due to trapezius ischemia). These may vary in duration and increase in severity until loss of consciousness occurs or may resolve prior to loss of consciousness if the cerebral ischemia is corrected. It is important, but sometimes challenging, to differentiate syncope from seizure. Syncope may be benign when it occurs as the result of normal cardiovascular reflex effects on heart rate and vascular tone and is preceded by symptoms that enable the individual to take actions that prevent injury or serious when it occurs abruptly or is due to a life-threatening arrhythmia. Syncope may occur as a single event or may be recurrent. Studies report syncope prevalence to be as high as 41% and recurrent syncope to be 13.5%. The incidence follows a trimodal distribution, with first episodes common around ages 20, 60, or 80 years and the third peak occurring 5–7 years earlier in males. Recurrent, unexplained syncope, particularly in an individual with structural heart disease, is associated with a high risk of death (40% mortality within 2 years).

Causes

Transiently decreased cerebral blood flow is usually due to one of three general mechanisms: (1) disorders of vascular tone or blood volume, (2) cardiovascular disorders including cardiac arrhythmias, or (3) cerebrovascular disease. Often, the cause of syncope is multifactorial.

Disorders of Vascular Tone or Blood Volume

Disorders of autonomic control of the heart and circulation share common pathophysiologic mechanisms: a cardioinhibitory component (e.g., bradycardia due to increased vagal activity), a vasodepressor component (e.g., inappropriate vasodilatation due to sympathetic withdrawal), or both.

M. D. Carlson (✉)
Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, OH, USA

K. L. Roos (ed.), *Emergency Neurology*, https://doi.org/10.1007/978-3-030-75778-6_4

Neurocardiogenic (Vasovagal and Vasodepressor) Syncope

The term *neurocardiogenic* encompasses both vasovagal and vasodepressor forms of syncope. Vasovagal syncope is associated with both sympathetic withdrawal (vasodilatation) and increased parasympathetic activity (bradycardia), whereas vasodepressor syncope is associated with sympathetic withdrawal alone. These types of syncope account for about one-half of syncopal episodes including the common faint that may occur in the absence of disease. Neurocardiogenic syncope is frequently recurrent and is commonly precipitated by a hot or crowded environment, extreme fatigue, severe pain, hunger, alcohol ingestion, prolonged standing, and an emotional or stressful event. The syndrome usually occurs when individuals are in the standing position and rarely occurs when supine. Although often preceded by weakness, nausea, diaphoresis, light-headedness, or blurred vision, in some individuals, syncope may occur abruptly, without warning.

The unconscious patient usually lies motionless with skeletal muscles relaxed, but clonic jerks of the limbs and face may occur. In contrast to a seizure, individuals rarely lose sphincter control. The pulse and blood pressure may be undetectable, and breathing is almost imperceptible. The duration of unconsciousness is rarely longer than a few minutes if the conditions that provoked the episode are reversed. When placed supine, most individuals recover rapidly. Although commonly benign, neurocardiogenic syncope can be associated with prolonged asystole and hypotension, resulting in injury.

In the setting of increased peripheral sympathetic activity and venous pooling, vigorous myocardial contraction of a relatively empty left ventricle activates myocardial mechanoreceptors and vagal afferent nerve fibers that inhibit sympathetic activity and increase parasympathetic activity. The resultant vasodilatation and bradycardia induce hypotension and syncope. Although most investigators have credited the drop in systemic vascular resistance and subsequent vasodilation as the primary cause of vasodepressor syncope, recent articles have focused attention on decreased cardiac output (up to 50%) during presyncope as an important contributor to the syndrome.

Indeed, although the reflexes described above are generally thought to be responsible for neurocardiogenic syncope, other reflexes may also be operative. Patients with transplanted (denervated) hearts have experienced cardiovascular responses identical to those present during neurocardiogenic syncope, which, unless the heart has become reinnervated, should not be possible if the response depends solely on the reflex mechanisms described above. Moreover, neurocardiogenic syncope often occurs in response to stimuli (fear, emotional stress, or pain) that may not be associated with venous pooling in the lower extremities, which suggests a cortical component to the reflex. Thus, a variety of afferent and efferent responses may cause neurocardiogenic syncope. The central nervous system (CNS) mechanisms responsible for neurocardiogenic syncope are uncertain, but a sudden surge in central serotonin levels may contribute to the sympathetic withdrawal. Endogenous opiates (endorphins) and adenosine are also putative participants in the pathogenesis.

Syncope with Normal Heart and ECG and Without Prodrome

Syncope without or with a short prodrome (<5 s) in an individual with a normal heart and electrocardiogram is a recently described phenomenon that is to be differentiated from the typical neurocardiogenic syncope described above. These individuals often present with abrupt asystole due to atrioventricular block, and their plasma adenosine levels are lower than the affinity constant for high – affinity A1 adenosine receptors (<0.7 microM). Theoretically, the A1 adenosine receptors in the sinus and atrioventricular nodes are upregulated which renders them to be very susceptible to cause atrioventricular block or sinus arrest in the setting of even a modest increase in adenosine plasma levels.

Postural (Orthostatic) Hypotension

This occurs in patients who have chronic or episodic instability of vasomotor reflexes. Systemic arterial blood pressure falls on assumption of upright posture due to loss of vasoconstriction reflexes in lower extremity resistance and capacitance vessels. Although the episode differs little from vasodepressor syncope, the effect of posture is critical. Sudden rising from a recumbent position or standing quickly may precipitate episodes. *Orthostatic hypotension may be the cause in up to 30% of elderly individuals who experience syncope; antihypertensive or antidepressant drugs often contribute to syncope in these patients.* Postural syncope may occur in otherwise normal persons with defective postural reflexes. Patients with *idiopathic postural hypotension* may be identified by a characteristic response to upright tilt. Initially, the blood pressure diminishes slightly before stabilizing at a lower level. Thereafter, compensatory reflexes fail and arterial pressure falls precipitously. Orthostatic hypotension, often accompanied by disturbances in sweating, impotence, and sphincter difficulties, also occurs in patients with autonomic nervous system disorders. The most common causes of neurogenic orthostatic hypotension are chronic diseases of the peripheral nervous system that involve postganglionic unmyelinated fibers (e.g., diabetic, nutritional, and amyloid polyneuropathy). Much less common are the multiple system atrophies; CNS disorders in which orthostatic hypotension is associated with (1) parkinsonism but the autonomic dysfunction predominates (Shy–Drager syndrome), (2) olivopontocerebellar atrophy when progressive cerebellar degeneration is a predominant feature, or (3) striatonigral degeneration when parkinsonian features, such as bradykinesia and rigidity, predominate. A rare, acute postganglionic dysautonomia may represent a variant of Guillain–Barre' syndrome. There are several additional causes of postural syncope: (1) after physical deconditioning (such as after prolonged illness with recumbency, particularly in elderly individuals with reduced muscle tone) or after prolonged weightlessness, as in space flight; (2) after sympathectomy that has abolished vasopressor reflexes; and (3) in patients receiving antihypertensive or vasodilator drugs and those who are hypovolemic because of diuretics, excessive sweating, diarrhea, vomiting, hemorrhage, or adrenal insufficiency.

Carotid Sinus Hypersensitivity

Syncope due to carotid sinus hypersensitivity is precipitated by pressure on the carotid sinus baroreceptors, located just cephalad to the bifurcation of the common carotid artery. Carotid sinus hypersensitivity occurs predominantly in men over 50 years old, typically in the setting of shaving, a tight collar, or turning the head to one side. Activation of carotid sinus baroreceptors gives rise to impulses carried via the nerve of Hering, a branch of the glossopharyngeal nerve, to the medulla oblongata. These afferent impulses activate efferent sympathetic nerve fibers to the heart and blood vessels, cardiac vagal efferent nerve fibers, or both. In patients with carotid sinus hypersensitivity, these responses may cause sinus arrest or atrioventricular (AV) block (a cardioinhibitory response), vasodilatation (a vasodepressor response), or both (a mixed response). The mechanisms responsible for the syndrome are not clear and validated diagnostic criteria do not exist.

Situational Syncope

A variety of activities, including cough, deglutition, micturition, and defecation, are associated with syncope in susceptible individuals. These syndromes are caused, at least in part, by abnormal autonomic control and may involve a cardioinhibitory response, a vasodepressor response, or both. Cough, micturition, and defecation are associated with maneuvers (such as Valsalva and straining) that increase intrathoracic pressure and increase intracranial pressure both of which can contribute to decreased cerebral blood flow. Cough syncope typically occurs during or immediately after prolonged coughing fits in men with

chronic bronchitis or chronic obstructive lung disease. Micturition syncope occurs predominantly in middle-aged and older men, particularly those with prostatic hypertrophy and obstruction of the bladder neck; loss of consciousness usually occurs at night during or immediately after voiding. Deglutition syncope and defecation syncope occur in men and women. Deglutition syncope may be associated with esophageal disorders, particularly esophageal spasm. In some individuals, particular foods and carbonated or cold beverages initiate episodes by activating esophageal sensory receptors that trigger reflex sinus bradycardia or AV block. Defecation syncope may occur secondary to a Valsalva maneuver in older individuals with constipation.

Glossopharyngeal Neuralgia

Syncope due to glossopharyngeal neuralgia is preceded by pain in the oropharynx, tonsillar fossa, or tongue. Loss of consciousness is usually associated with asystole rather than vasodilatation. The mechanism is thought to involve activation of afferent impulses in the glossopharyngeal nerve that terminate in the nucleus solitarius of the medulla, and via collaterals that activate the dorsal motor nucleus of the vagus nerve.

Cardiovascular Disorders

Cardiac syncope results from a sudden reduction in cardiac output, caused most commonly by a cardiac arrhythmia but also by structural abnormalities that obstruct blood flow.

Arrhythmias

In healthy individuals, heart rates between 30 and 180 beats/min do not reduce cerebral blood flow, especially when the person is supine. As the heart rate decreases, ventricular filling time and stroke volume increase to maintain normal cardiac output. At rates less than 30 beats/min, stroke volume can no longer increase to compensate adequately for the decreased heart rate. At rates greater than 180 beats/min, ventricular filling time is often insufficient to maintain adequate stroke volume. Upright posture; cerebrovascular disease; anemia; loss of atrioventricular synchrony; and coronary, myocardial, or valvular disease, all reduce the tolerance to alterations in rate. Bradyarrhythmias may occur as a result of an abnormality of impulse generation (e.g., sinoatrial arrest) or impulse conduction (e.g., AV block). Either may cause syncope if the escape pacemaker rate is insufficient to maintain cardiac output. Syncope due to bradyarrhythmias may occur abruptly, without preceding symptoms, and recur several times daily. Patients with *sick sinus syndrome* may have sinus pauses (>3 s), and those with syncope due to high degree AV block (*Stokes–Adams–Morgagni syndrome*) may have evidence of conduction system disease (e.g., prolonged PR interval, bundle branch block). However, the arrhythmia is often transitory, and the surface electrocardiogram or the continuous electrocardiographic monitor placed later may not reveal the abnormality. The *bradycardia–tachycardia syndrome* is a common form of sinus node dysfunction in which syncope generally occurs as a result of marked sinus pauses, some following termination of an atrial tachyarrhythmia. Drugs are a common cause for bradyarrhythmias, particularly in patients with underlying structural heart disease. Digoxin, adrenergic receptor antagonists, calcium channel blockers, and many antiarrhythmic drugs may suppress sinoatrial node impulse generation or slow AV nodal conduction.

Syncope due to a *tachyarrhythmia* is often preceded by palpitation or light-headedness but may occur abruptly without warning. *Supraventricular tachyarrhythmias* are unlikely to cause syncope in individuals with structurally normal hearts but may do so if they occur in patients with (1) heart disease that also compromises cardiac output, (2) cerebrovascular disease, (3) a disorder of vascular tone or blood volume, or (4) a very rapid ventricular rate. These tachycardias result most commonly from paroxysmal atrial flutter, atrial fibrillation, or reentry involving the AV node or accessory pathways that

bypass part or all of the AV conduction system. Patients with the *Wolff–Parkinson–White syndrome* may experience syncope when a very rapid ventricular rate occurs due to reentry across an accessory AV connection. In patients with structural heart disease, ventricular tachycardia is a common cause of syncope, particularly in patients with a prior myocardial infarction. Patients with aortic valvular stenosis and hypertrophic obstructive cardiomyopathy are also at risk for ventricular tachycardia. Individuals with abnormalities of ventricular repolarization (prolongation of the QT interval) are at risk to develop polymorphic ventricular tachycardia (*torsades de pointes*). Those with the inherited form of this syndrome often have a family history of sudden death in young individuals. Genetic markers can identify some patients with familial long QT syndrome, but the clinical utility of these markers remains unproven. Drugs (i.e., certain antiarrhythmics and erythromycin) and electrolyte disorders (i.e., hypokalemia, hypocalcemia, hypomagnesemia) can prolong the QT interval and predispose to torsades de pointes. Antiarrhythmic medications may precipitate ventricular tachycardia, particularly in patients with structural heart disease.

Structural Disorders

In addition to arrhythmias, syncope may also occur with a variety of structural cardiovascular disorders. Episodes are usually precipitated when the cardiac output cannot increase to compensate adequately for peripheral vasodilatation. Peripheral vasodilatation may be appropriate, such as following exercise, or may occur due to inappropriate activation of left ventricular mechanoreceptor reflexes, as occurs in aortic outflow tract obstruction (aortic valvular stenosis or hypertrophic obstructive cardiomyopathy). Obstruction to forward flow is the most common reason that cardiac output cannot increase. Syncope occurs in up to 10% of patients with massive pulmonary embolism and may occur with exertion in patients with severe primary pulmonary hypertension. The cause is an inability of the right ventricle to provide appropriate cardiac output in the presence of obstruction or increased pulmonary vascular resistance. Loss of consciousness is usually accompanied by other symptoms such as chest pain and dyspnea. Atrial myxoma, a prosthetic valve thrombus, and, rarely, mitral stenosis may impair left ventricular filling, decrease cardiac output, and cause syncope. Pericardial tamponade is a rare cause of syncope.

Cerebrovascular Disease

Cerebrovascular disease alone rarely causes syncope but may lower the threshold for syncope in a patient with another cause. In such cases, the vertebrobasilar arteries, which supply brainstem structures responsible for maintaining consciousness, are usually involved. An exception is the unusual patient with tight bilateral carotid stenoses and recurrent syncope, often precipitated by standing or walking. Most patients who experience light-headedness or syncope due to cerebrovascular disease also have symptoms of focal neurologic ischemia, such as arm or leg weakness, diplopia, ataxia, dysarthria, or sensory disturbances. Basilar artery migraine is a rare disorder that can cause syncope in adolescents.

Differential Diagnosis

Anxiety Attacks and the Hyperventilation Syndrome

Anxiety, such as occurs in panic attacks, is frequently interpreted as a feeling of faintness or dizziness resembling presyncope. The symptoms are not accompanied by facial pallor and are not relieved by assuming a recumbent position. The diagnosis is made on the basis of the associated symptoms, such as a feeling of impending doom, air hunger, palpitations, and tingling of the fingers and perioral region. Attacks can often be reproduced by hyperventilation, resulting in hypocapnia, alkalosis, increased cerebrovascular resistance, and decreased cerebral blood flow.

The release of epinephrine also contributes to the symptoms.

Seizures

Unlike syncope, a seizure may be heralded by an aura, which is caused by a focal epileptogenic discharge and hence has localizing significance. The aura is usually followed by a rapid return to normal or by a loss of consciousness. Injury from falling is frequent in a seizure and rare in syncope, since only in generalized seizures are protective reflexes abolished instantaneously. Sustained tonic-clonic movements are characteristic of convulsive seizures but brief clonic, or tonic-clonic, seizure-like activity can accompany fainting episodes. The period of unconsciousness tends to be longer in seizures than in syncope. Urinary incontinence is frequent in seizures and rare in syncope. The return of consciousness is prompt in syncope, slow after a seizure. Mental confusion, headache, and drowsiness are common sequelae of seizures, whereas physical weakness with a clear sensorium characterizes the postsyncopal state. Repeated spells of unconsciousness in a young person at a rate of several per day or month suggest epilepsy rather than syncope.

Hypoglycemia

Severe hypoglycemia is usually due to a serious disease such as a tumor of the islets of Langerhans; due to advanced adrenal, pituitary, or hepatic disease; or to excessive administration of insulin.

Acute Hemorrhage

Hemorrhage, usually within the gastrointestinal tract, is an occasional cause of syncope. In the absence of pain and hematemesis, the cause of the weakness, faintness, or even unconsciousness may remain obscure until the passage of a black stool.

Hysterical Fainting

The attack is usually unattended by an outward display of anxiety. Lack of change in pulse and blood pressure or color of the skin and mucous membranes distinguishes it from the vasodepressor faint.

Approach to the Patient

The diagnosis of syncope is often challenging. The cause may only be apparent at the time of the event, leaving few, if any, clues when the patient is seen later by the physician. The physician should think first of those causes that constitute a therapeutic emergency. Among these are massive internal hemorrhage or myocardial infarction, which may be painless, and cardiac arrhythmias. In elderly persons, a sudden faint, without obvious cause, should arouse the suspicion of complete heart block or a tachyarrhythmia, even though all findings are negative when the patient is seen. Figure 4.1 depicts an algorithmic approach to syncope. A careful history is the most important diagnostic tool, both to suggest the correct cause and to exclude important potential causes. The nature of the events and their time course prior to, during, and after an episode of syncope often provide valuable etiologic clues. Loss of consciousness in particular situations, such as during venipuncture, micturition, or with volume depletion, suggests an abnormality of vascular tone. The position of the patient at the time of the syncopal episode is important; syncope in the supine position is unlikely to be vasovagal and suggests an arrhythmia or a seizure. Syncope due to carotid sinus syndrome may occur when the individual is wearing a shirt with a tight collar, turning the head (turning to look while driving in reverse), or manipulating the neck (as in shaving). The patient's medications must be noted, including nonprescription drugs or health store supplements, with particular attention to recent changes. Heart rate and blood pressure should be evaluated in the supine, sitting, and standing positions. In patients with

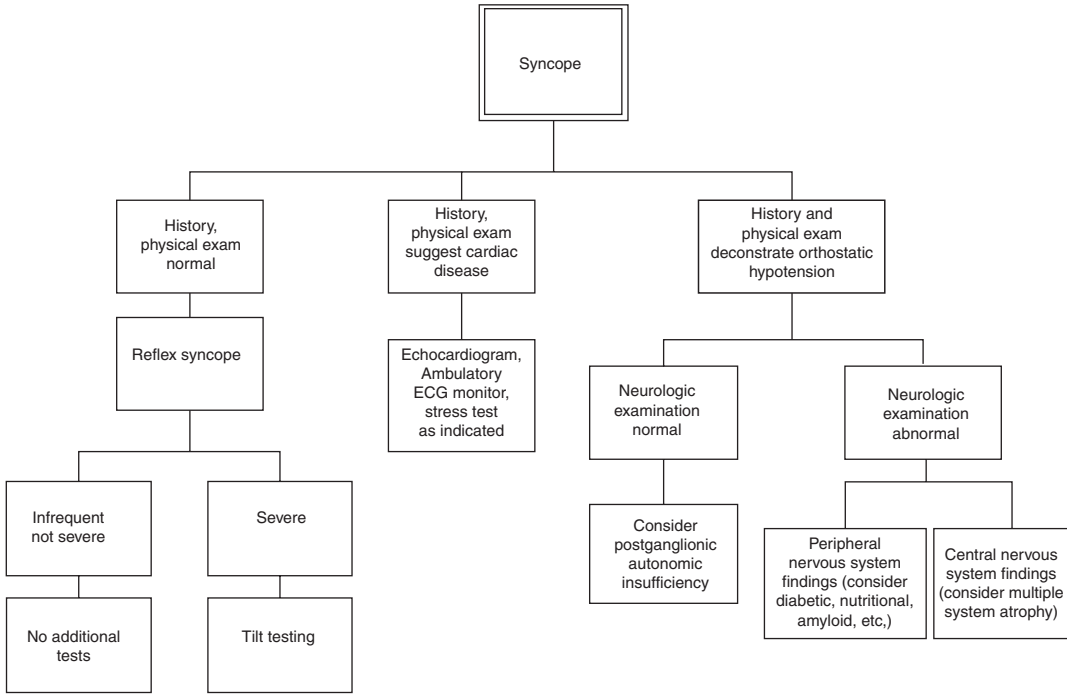

Fig. 4.1 Approach to diagnosing the cause of syncope

unexplained recurrent syncope, an attempt to reproduce an attack may assist in diagnosis.

Anxiety attacks induced by hyperventilation can be reproduced readily by having the patient breathe rapidly and deeply for 2–3 min. Cough syncope may be reproduced by inducing the Valsalva maneuver. Carotid sinus massage should generally be avoided, even in patients with suspected carotid sinus hypersensitivity; it can cause a transient ischemic attack (TIA) or stroke in individuals with carotid atheromas.

Diagnostic Tests

The history and physical examination guide the choice of diagnostic tests. Although unlikely to provide a definitive diagnosis, a surface 12-lead electrocardiogram may provide clues to the cause of syncope *and should be performed in almost all patients*. The presence of conduction abnormalities (PR prolongation and bundle branch block) suggests a bradyarrhythmia, whereas pathologic Q waves or prolongation of the QT interval suggests a ventricular tachyarrhythmia. The approach to heart rhythm monitoring depends on the frequency of the episodes, the likelihood of an arrhythmic cause, and the patient's risk for morbidity or mortality. Inpatients should undergo continuous electrocardiographic monitoring; outpatient monitoring may depend on the frequency of episodes. Holter monitors, which record continuously for 24–48 h, may be useful for patients with frequent episodes. Newer external monitors are able to monitor surface ECG leads for several weeks. In patients with infrequent episodes that are suspected to be due to an arrhythmia, an implantable cardiac monitor, which monitors the heart rhythm continuously for up to 3 years, is useful and cost-effective. Regardless of the monitor type, symptoms should be correlated with the occurrence of arrhythmias. Cardiac event monitors may be useful in patients with infrequent symptoms, particularly in patients with presyncope.

Measurements of serum electrolytes, glucose, and the hematocrit are usually indicated, and cardiac enzymes should be evaluated if myocardial

ischemia is suspected. Blood and urine toxicology screens may reveal the presence of alcohol or other drugs. In patients with possible adrenocortical insufficiency, plasma aldosterone and mineralocorticoid levels should be obtained.

Invasive cardiac electrophysiologic testing provides diagnostic and prognostic information regarding sinus node function, AV conduction, and supraventricular and ventricular arrhythmias. Continuous electrocardiographic monitoring is usually more effective for diagnosing sinus node disease. However, invasive electrophysiologic testing is useful for detecting His–Purkinje disease, and in patients who have experienced a myocardial infarction, ventricular arrhythmias may be responsible for syncope.

Upright tilt table testing is indicated for recurrent syncope or a single syncopal episode that caused or could cause injury were it to recur, particularly if the patient is likely to be in a "high-risk" setting (pilot, commercial vehicle driver, etc.). In susceptible patients, upright tilt at an angle between 60° and 80° for 30–60 min induces a vasovagal episode particularly when accompanied with administration of drugs that cause venous pooling or increase adrenergic stimulation (isoproterenol, nitroglycerin, edrophonium, or adenosine). The sensitivity and specificity of tilt table testing are difficult to ascertain because of the lack of validated criteria. Moreover, the reflexes responsible for vasovagal syncope can be elicited in most, if not all, individuals given the necessary stimulus. The reported accuracy of the test ranges from 30% to 80%, depending on the population studied and the techniques used. Whereas the reproducibility of a negative test is 85–100%, the reproducibility of a positive tilt table test is only between 62% and 88%. Importantly, all three recent international guideline and consensus documents recommend that tilt testing be performed only in patients for whom a history, and therefore prodromal symptoms, did not provide a diagnosis.

A variety of other tests may be useful to determine the presence of structural heart disease that may cause syncope. The echocardiogram with Doppler examination detects valvular, myocardial, and pericardial abnormalities. The echocardiogram is the "gold standard" for the diagnosis of hypertrophic cardiomyopathy and atrial myxoma. Cardiac cine magnetic resonance (MR) imaging provides an alternative noninvasive modality that may be useful for patients in whom diagnostic-quality echocardiographic images cannot be obtained. This test is also indicated for patients suspected of having arrhythmogenic right ventricular dysplasia or right ventricular outflow tract ventricular tachycardia. Both are associated with right ventricular structural abnormalities that are better visualized on MR imaging than by echocardiogram. Exercise testing may detect ischemia or exercise-induced arrhythmias. In some patients, cardiac catheterization may be necessary to diagnose the presence or severity of coronary artery disease or valvular abnormalities. Ultrafast computed tomographic scan, ventilation–perfusion scan, or pulmonary angiography is indicated in patients in whom syncope may be due to pulmonary embolus.

In cases of possible cerebrovascular syncope, neuroimaging tests may be indicated, including Doppler ultrasound studies of the carotid and vertebrobasilar systems, MR imaging, MR angiography, and CT angiography of the cerebral vasculature. Electroencephalography is indicated if seizures are suspected.

Decision support algorithms and specialized syncope evaluation units have been used and advocated by some to reduce health service use. However, currently the data are insufficient to demonstrate their efficacy in making patient disposition decisions or that they are financially feasible.

Treatment

The treatment of syncope depends on the underlying cause. With respect to the disorders of autonomic control, certain precautions should be taken regardless of the specific cause of syncope. Patients with frequent episodes, or those who have experienced syncope without warning symptoms, should avoid situations in which sudden loss of consciousness might result in injury (e.g., climbing ladders, swimming alone,

operating heavy machinery, driving, etc.). At the onset of symptoms, patients should take steps to avoid injury should they lose consciousness, lowering their head and preferably lying down. Lowering the head by bending at the waist should be avoided because it may further compromise venous return to the heart. Family members or other close contacts should be informed of the problem in order to ensure appropriate therapy and prevent delivery of inappropriate therapy (chest compressions associated with cardiopulmonary resuscitation) that may inflict trauma. Patients who have lost consciousness should be placed in a position that maximizes cerebral blood flow, offers protection from trauma, and secures the airway. Whenever possible, the patient should be placed supine with the head turned to the side to prevent aspiration and the tongue from blocking the airway. Assessment of the pulse and direct cardiac auscultation may assist in determining if the episode is associated with a bradyarrhythmia or tachyarrhythmia. Clothing that fits tightly around the neck or waist should be loosened. Patients should not be given anything by mouth or be permitted to rise until full consciousness has returned.

Patients with vasovagal syncope should be instructed to avoid situations or stimuli that have caused them to lose consciousness and to assume a recumbent position when premonitory symptoms occur. This alone may be sufficient therapy for patients with infrequent and relatively benign episodes of vasovagal syncope, particularly when episodes occur in response to a specific stimulus. Tilt training (standing and leaning against a wall for progressively longer periods each day) has been used with limited success, particularly for those patients who have profound orthostatic intolerance. Episodes associated with intravascular volume depletion may be prevented by salt and fluid loading prior to provocative events.

Prescription drug therapy may be necessary when vasovagal syncope is resistant to these measures, when episodes occur frequently, or when syncope is associated with a significant risk for injury. Adrenergic receptor antagonists (metoprolol, 25–50 mg bid; atenolol, 25–50 mg qd; or nadolol, 10–20 mg bid; all starting doses), the most widely used agents, mitigate the increase in myocardial contractility that stimulates left ventricular mechanoreceptors and also block central serotonin receptors. Serotonin reuptake inhibitors (paroxetine, 20–40 mg qd; or sertraline, 25–50 mg qd) appear to be effective for some patients. A recent meta-analysis indicated that norepinephrine transport inhibitors (sibutramine, reboxetine, and atomoxetine) prevents vasovagal reactions and syncope during head-up tilt testing and is promising for treatment of recurrent syncope. Bupropion SR (150 mg qd), another antidepressant, has also been used with success. Adrenergic receptor antagonists and serotonin reuptake inhibitors are well tolerated and are often used as first-line agents for younger patients. Hydrofludrocortisone (0.1–0.2 mg qd), a mineralocorticoid, promotes sodium retention, volume expansion, and peripheral vasoconstriction by increasing receptor sensitivity to endogenous catecholamines. Hydrofludrocortisone is useful for patients with intravascular volume depletion and those who also have postural hypotension. Proamatine, an alpha agonist, has been used as a first-line agent for some patients. In a randomized controlled trial, proamatine was more effective than placebo in preventing syncope during an upright tilt test. However, in some patients, proamatine and hydrofludrocortisone may increase resting supine systemic blood pressure, a property that may be problematic for those with hypertension.

Disopyramide (150 mg bid), a vagolytic antiarrhythmic drug with negative inotropic properties, and another vagolytic, transdermal scopolamine, have been used to treat vasovagal syncope, as have theophylline and ephedrine. Side effects associated with these drugs have limited their use for this indication. Disopyramide is a type 1A antiarrhythmic drug and should be used with great caution, if at all, in patients who are at risk for ventricular arrhythmias. Although several clinical trials have suggested that pharmacologic therapy for vasovagal syncope is effective, long-term prospective randomized controlled trials have yet to be completed.

Permanent dual-chamber cardiac pacing can be effective for patients with frequent episodes of

vasovagal syncope and is indicated for those with prolonged asystole associated with vasovagal episodes. Patients in whom vasodilatation contributes to loss of consciousness may also experience symptomatic benefit from permanent pacing. Pacemakers that can be programmed to transiently pace at a high rate (90–100 beats/min) after a profound drop in the patient's intrinsic heart rate are most effective. Patients with orthostatic hypotension should be instructed to rise slowly and systematically (supine to seated, seated to standing) from the bed or a chair. Movement of the legs prior to rising facilitates venous return from the lower extremities. Whenever possible, medications that aggravate the problem (vasodilators, diuretics, etc.) should be discontinued. Elevation of the head of the bed [20–30 cm (8–12 in)] and use of compression stockings may help. Additional therapeutic modalities include an antigravity or g suit or compression stockings to prevent lower limb blood pooling, salt loading, and a variety of pharmacologic agents including sympathomimetic amines, monoamine oxidase inhibitors, beta blockers, and levodopa.

Glossopharyngeal neuralgia is treated with carbamazepine, which is effective for the syncope as well as for the pain. Patients with carotid sinus syndrome should be instructed to avoid clothing and situations that stimulate carotid sinus baroreceptors. When looking to the side, they should turn their entire body, rather than just their head. Those with intractable syncope due to the cardioinhibitory response to carotid sinus stimulation should undergo permanent pacemaker implantation.

Treatment of the cardiovascular causes of syncope (arrhythmias and structural disorders) is often focused on the underlying cause (myocardial ischemia, valvular disease, etc.). Patients with bradyarrhythmias may benefit from permanent pacing. Those with certain supraventricular arrhythmias may benefit from catheter ablation. An implantable cardioverter defibrillator is indicated for patients with or at high risk for life-threatening ventricular arrhythmias. Surgical replacement is indicated for patients with critical aortic valvular stenosis.

Regardless of the etiology, patients with syncope should be hospitalized with continuous electrocardiographic monitoring when the episode may have resulted from a life-threatening abnormality or if recurrence with significant injury seems likely. Patients who are known to have a normal heart and for whom the history strongly suggests vasovagal or situational syncope may be treated as outpatients if the episodes are neither frequent nor severe.

Further Reading

Brignole M. Mechanism of syncope without prodromes with normal heart and normal electrocardiogram. Heart Rhythm. 2017;14:234–9.

Lei LY. Pharmacological norepinephrine transporter inhibition for the prevention of vasovagal syncope in young and adult subjects. A systematic review and meta-analysis. Heart Rhythm. 2020;17:1151–8.

Shen WK. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope. Heart Rhythm. 2017;14:e155–217.

Sutton R. Pacing in vasovagal syncope: physiology, pacemaker sensors, and recent clinical trials – precise patient selection and measurable benefit. Heart Rhythm. 2020;17:821–8.

Wieling W. Cardiac output and vasodilation in the vasovagal response: an analysis of the classic papers. Heart Rhythm. 2016;13:798–805.