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## REVIEW ARTICLE

# Approach to transient loss of consciousness and syncope in children

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**Abstract:**

*Transient loss of consciousness (TLOC) encompasses a group of disorders with four common presenting features which include loss of consciousness, that is transient in nature, self-limited, and not due to a trauma of the head and brain, when no probable cause can yet be identified. There are three main categories of TLOC in children and young people. The first is syncope: TLOC resulting from a sudden and reversible lack of oxygenated blood supply to the brain, often caused by transient impairment of cardiac output or systemic arterial hypotension. Secondly, TLOC due to an epileptic seizure, i.e. typically due to excessive and hypersynchronous cortical neuronal electrical activity in the brain. Thirdly "Unexplained TLOC" which includes cases not yet diagnosed fully and those for which a pathophysiological mechanism has not been identified despite thorough investigation, it includes episodes that may be due to emotional or psychogenic mechanisms or abnormal illness behaviour. This review will describe an approach to the diagnosis and management of children and young people with TLOC, and especially syncope.*

**Keywords:** TLOC, Syncope, Reflex Asystolic Syncope, Reflex Anoxic Seizure, Breath holding, Expiratory Apnoea Syncope, investigations

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## Introduction

Transient loss of consciousness (TLOC) encompasses a group of disorders with four common presenting features which include loss of consciousness, that is transient in nature, self-limited, and not due to a trauma of the head and brain, when no probable cause can yet be identified (1). More commonly used terms are 'fainting', 'blacking out', 'collapse', or 'passing out'. It is a very common symptom occurring in all age groups and affecting up to 50% of the population at some stage of life. It causes 3% of Emergency Department attendances, and 1% of all hospital admissions (2).

There are three main categories of TLOC in children and young people. The first is syncope: TLOC resulting from a sudden and reversible lack of oxygenated blood supply to the brain, often caused by transient impairment of cardiac output or systemic arterial hypotension. Secondly, TLOC due to an

epileptic seizure, i.e. typically due to excessive and hypersynchronous cortical neuronal electrical activity

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in the brain. Thirdly “Unexplained TLOC” which includes cases not yet diagnosed fully and those for which a pathophysiological mechanism has not been identified despite thorough investigation, it includes episodes that may be due to emotional or psychogenic mechanisms or abnormal illness behaviour.

Although the underlying mechanisms are quite different, the history from a patient, and the observations of a witness, may be similar in these different causes of TLOC. Patients may require prolonged investigations and ambulatory monitoring and even hospital admissions to ascertain the correct diagnosis. Critical to the cost effective management of TLOC is elucidating the correct diagnosis of the underlying mechanisms and cause. However the diagnosis is often difficult, sometimes impossible and recurrences following hospital admission for investigation (3) and misdiagnosis rates in children are high (4). This review will describe an approach to the diagnosis and management of children and young people with TLOC, and especially syncope.

### Classification

The literature on TLOC, syncope and associated conditions can be very confusing because of a lack of consistency in the use of terms, rendering them uncertain (1). For some, an originally clear meaning has become obscured over time, because the term was later used in a different context or in a different meaning.

### Definitions

**Seizures** are paroxysmal abnormalities of motor, sensory, autonomic, or cognitive function due to transient brain dysfunction. The causes include *epileptic*, *syncopal* (anoxic), *brainstem* (hydrocephalic, coning), *emotional* (psychogenic) and undetermined. They can manifest as alterations in mental state, responsiveness, tonic or clonic or complex movements or convulsions, autonomic signs and symptoms, and various other sensory or psychic symptoms, alone or in combination or sequence. **Convulsions** are episodes of excessive, abnormal muscle contractions, usually bilateral, which may be sustained or interrupted. The episodes may include *tonic* or *dystonic* spasms (stiffening), *clonic* or *myoclonic* (jerking), *hyper-motor* (complex thrashing) movements and causes may include

*epileptic*, *syncopal*, *brainstem*, *emotional* or *be undetermined*. **Epileptic Seizure** is a paroxysmal abnormality of motor, sensory, autonomic, or cognitive function due to transient dysfunction of cerebral cortical neuronal electrical activity (excessive and or hyper-synchronous). There are many clinical, electrical and pathological varieties and these will not be discussed further in this article.

**An Epilepsy** is a medical syndrome of recurrent, unprovoked epileptic seizures, due to an abnormality in the brain in the control of cortical neuronal synchrony. **Syncope** (derived from the Greek words, ‘syn’ meaning ‘with’ and the verb ‘kopto’ meaning ‘I interrupt’) is a symptom, defined as a transient, self-limited loss of consciousness, usually leading to falling. The onset of syncope is relatively rapid, and the subsequent recoveries are spontaneous, complete and usually prompt (5). The underlying mechanism is a transient global cerebral hypoperfusion. Gastaut’s definition of syncope, “an abrupt cutting off of the energy substrates to the cerebral cortex,” is preferable in early childhood as the mechanism involved are not clearly defined and in a common form of syncope, the so called cyanotic breath-holding spell there may be hypoxia without impairment of cerebral circulation (6). **Drop attacks** ‘Drop attacks’ was originally used to indicate a very specific and benign syndrome, describing patients, who suddenly fell to their knees without loss of consciousness. Later use included grouping all possible causes of falls with or without loss of consciousness under this heading. Over time, the term has become so unclear that its use is now more likely to cause confusion than to increase understanding.

### Classification of TLOC

The two most common causes of TLOC are syncope and epileptic seizures. TLOC can be divided into two broad categories of syncope and non-syncopal attacks.

### Categories of syncope

Syncope can be categorised descriptively from the history: was it *reflex* (i.e. triggered by a stimulus e.g. a sudden pain or sight of blood); was it *convulsive* (with abnormal postures and movements comprising a convulsion); was it *sudden* (with no warning and so a risk of injury, or of gradual onset with *pre-syncopal symptoms* and behaviours; was it *mild* (with prompt recovery and no post-ictal confusion or drowsiness)

**Table I. Classification based on mechanism of syncope*****Neurally Mediated (reflex) Syncope (NMS)***

- Vasovagal syncope
- Reflex Asystolic Syncope or Infantile Vaso/Vagal Syncope (typically causing a Reflex Anoxic Seizure)
- Carotid sinus syncope
- Situational syncope: acute haemorrhage, cough, sneeze, gastrointestinal stimulation (swallow, defaecation, visceral pain), micturition (post-micturition), post-exercise, post-prandial, adolescent stretch syncope, G-LOC (due to excessive G-force), others (e.g., pain, brass instrument playing, weightlifting)

***Orthostatic hypotension***

- Autonomic failure: primary and secondary autonomic failure syndromes
- Post-exercise, post-prandial
- Drug (and alcohol)-induced orthostatic syncope
- Volume depletion, haemorrhage, profound anaemia, diarrhoea, Addison's disease
- Anaphylaxis, septic shock

***Cardiac arrhythmias and structural cardiac or cardiopulmonary disease***

- Sinus node dysfunction (including bradycardia/tachycardia syndrome), atrioventricular conduction system disease, Paroxysmal supraventricular and ventricular tachycardias, inherited syndromes (e.g., long QT syndrome), implanted device (pacemaker, ICD) malfunction and drug-induced arrhythmias
- Cardiac valvular disease, acute myocardial infarction/ischaemia, obstructive cardiomyopathy, acute aortic dissection, atrial myxoma, pericardial disease/tamponade, pulmonary embolus/pulmonary hypertension, vascular steal syndromes.
- Resuscitated cardiac arrest

***Hypoxic contribution*** (this is important in children & young people, even if excluded from the current ESC definition of "Syncope" (1))

- Inspired Hypoxia (as in aviation, diving, mountaineering, or anaesthetic mishaps)
- Expiratory Apnoea Syncope / cyanotic breath-holding spells (there may be a compromised cardiac output from impaired venous return with this as well as hypoxia from intra pulmonary shunting and apnoea)
- Transient upper airway obstruction (e.g. foreign body; Imposed Upper Airway Obstruction / Fabricated and Induced Illness)

or *severe* (with post-ictal drowsiness or confusion). It can also be classified by mechanism, but this is not always evident and is often inferred from the history and other clues (Table 1)

**Epidemiology of Syncope**

The incidence of syncope coming to medical attention in childhood and adolescence was

126/100,000 population in the single available population based study (7). However, as many as 15 percent of children may experience at least one episode before the age of 18 (8). Moreover, up to 5% of toddlers experience Reflex Anoxic Seizures, or "breath-holding spells" in North American usage, including Reflex Asystolic Syncope (RAS), called Infantile Vaso/vagal Syncope in the ESC

**Table 2. Causes of non-syncopal attacks (commonly misdiagnosed as syncope)**

<i>Disorders without any impairment of consciousness</i>	<i>Disorders with partial or complete loss of consciousness</i>
Falls	Epilepsy
Cataplexy	Intoxications
Drop attacks	Vertebro-basilar TIA
Psychogenic pseudo-syncope	Head injury
Transient ischaemic attacks (TIA) of carotid origin	Metabolic disorders, including hypoglycaemia, hyperventilation with hypocapnia

classification (1), and prolonged Expiratory Apnoea Syncope (EAS) or “cyanotic breath-holding spells” (9).

The reported incidence peaks in 15-19 year olds and is more common in females than males. NMS is by far the most frequent (61–71%); followed by cerebrovascular; and “psychogenic pseudo syncope” or more accurately psychogenic or unexplained TLOC (11–19%); and cardiac syncope (6%) (7). However, the majority of these individuals probably do not seek medical evaluation.

### **Pathophysiology of Syncope**

With a sudden temporary decrease in blood pressure, or arrest of cardiac output, the brain is hypoperfused and deprived of sufficient oxygen. If mild this will temporarily cause diverse “pre-syncope” symptoms such as “dizziness” or a faint feeling or perceptual distortions of vision or hearing, nausea, flushing, sweating etc. If more significant, the impaired cerebral perfusion will cause syncope proper.

NMS is frequently caused by a combination of factors or circumstances. One example could be the child who is chronically anaemic, dehydrated with gastroenteritis, exhausted by lack of sleep and hungry, who, when seeing the child in the next hospital bed undergoing a rather painful or unpleasant venepuncture, attempts to stand up, becomes ‘dizzy’ and nauseated...

Cerebral blood flow represents about 12–15% of resting cardiac output and cerebral perfusion pressure is largely dependent on systemic arterial pressure.

Thus, any factor that decreases either cardiac output or total peripheral vascular resistance diminishes systemic arterial pressure and cerebral perfusion pressure. In regard to cardiac output, the most important physiological determinant is venous filling (pre-load).

Cardiac output may also be impaired due to arrhythmias (SVT, VT with Long QT syndromes or Brugada syndrome especially, or heart block) or valvular disease. In terms of peripheral vascular resistance, widespread and excessive vasodilatation will play a critical role in decreasing arterial pressure, and is the commonest mechanism in NMS. Impaired capacity to increase vascular tone during standing is the cause of orthostatic hypotension and syncope in patients with autonomic neuropathies.

A sudden cessation of cerebral blood flow for 6–8 seconds has been shown to be sufficient to cause complete loss of consciousness. Experience from head-up tilt testing showed that a decrease in systolic blood pressure to 60 mmHg or less was associated with syncope. Further, it has been estimated that as little as a 20 percent drop in cerebral oxygen delivery is sufficient to cause loss of consciousness.

However, when severe and frequent, advice and treatment can be guided by whether the syncope is primarily hypotensive (vasodepressor), bradycardic / asystolic (cardio inhibitory), or mixed.

### **Neurally-mediated / Reflex Syncope (NMS)**

NMS is the most common form of syncope. It has

also been known as VasoVagal Syncope, neurocardiogenic syncope, reflex syncope or fainting. It is caused by an abnormal autonomic response (10). NMS is characterized by peripheral vasodilation, decrease in blood pressure and or a slow heart rate. The changes in heart rate and blood pressure are due to an increase in parasympathetic tone and concomitant inhibition of sympathetic outflow. The triggering factor for NMS varies widely and includes orthostatic stress, emotional stress, urination, coughing, swallowing, physical exercise, pain and stimulation of the carotid sinus in susceptible persons. Nausea, vomiting is associated with syncope and can occur during or after a meal, prolonged standing in crowded, hot places and following exertion. VasoVagal Syncope applies especially to NMS in which pain, emotional distress, and instrumentation or prolonged standing trigger syncope. Neurocardiogenic syncope is used for a putative type of reflex syncope in which the reflex trigger originates in the heart (1).

### **Convulsive syncope**

Syncope accompanied by convulsive movements such as tonic and dystonic posturing, jerking, waving or thrashing and other involuntary movements. The term does not imply epilepsy. The pathogenesis of involuntary jerking movements of the limbs during syncope is unclear. There is no evidence that distinguishing between syncope with and syncope without movements helps refine the diagnosis or helps guide treatment. Convulsive syncope is often interpreted as an epileptic seizure, especially when the history is taken quickly and there is no video record. The EEG during convulsive syncope as during any syncope will demonstrate high amplitude slow waves (e.g. after 5 or 6 seconds of arrested cerebral perfusion) and in severe syncope a flat EEG trace at normal amplitude gain (e.g. after 9 or 10 seconds of arrested cerebral perfusion), followed by slow waves during the post-ictal recovery phase. Stiffness and jerking can occur during the flat EEG phase.

To complicate matters further, reflex epileptic seizures / acute symptomatic epileptic seizures can be precipitated by a severe syncope: the patient has a real epileptic seizure at the end of a convulsive or non-convulsive syncope. These have been called "Anoxic Epileptic Seizures" (AESs) (11). Although

such attacks do include an epileptic seizure, the patient does not have epilepsy. The role of antiepileptic drugs in AES is controversial.

### **Pre-syncope**

It is a descriptive term for all sensations directly preceding syncope whether or not they are followed by complete loss of consciousness. When cerebral blood flow stops or diminishes, patients may be aware that something is amiss before consciousness is lost altogether. They may describe light-headedness or dizziness, loss of control over eye and other movements, blurring of vision, and constriction of the field of vision. Symptoms of another kind may also occur before syncope that are related to the mechanism causing syncope rather than to decreased cerebral blood flow itself. These may include pain in the head and shoulder region in autonomic failure, sweating and nausea in reflex syncope, and tingling in hyperventilation. These sensations occur close in time to syncope, although they are only indirectly linked to the loss of consciousness.

### **Orthostatic syncope**

Orthostatic syncope can occur after prolonged standing especially in crowded, hot places, after exertion and occasionally there may be a temporal relationship with start of medication leading to hypotension. Orthostatic syncope is diagnosed, when there is documentation of orthostatic hypotension associated with syncope or presyncope. Orthostatic blood pressure (BP) and heart rate (HR) measurements are recommended after 5 minutes or more of lying supine relaxed at rest, followed by BP and HR measurements after standing for up to 3 minutes. Measurements may be continued for longer, if blood pressure is still falling at 3 minutes. If the patient does not tolerate standing for this period, the lowest systolic blood pressure during the upright posture should be recorded. A decrease in systolic blood pressure 20 mmHg or more, or a decrease of systolic blood pressure to less than 90 mmHg is defined as orthostatic hypotension regardless of whether or not symptoms occur (10).

### **Postural Orthostatic Tachycardia Syndrome (POTS)**

POTS is clinically defined as a HR increase of 30 beats per minute or more or a HR of more than 120 bpm, from the supine to the standing position within

ten minutes or less with symptoms of syncope. It typically occurs in teenagers and young adults. It is caused by body's inability to make the necessary adjustments to counteract gravity when standing up. Patients with POTS may have recurrent episodes of VasoVagal Syncope, which may result in injuries, embarrassment, anxiety, urinary incontinence and social withdrawal. Patients more typically experience pre-syncope symptoms e.g. weakness, "dizziness", nausea, and typically have fatigue, headaches, exercise intolerance and exercise avoidance. POTS may be acquired from autonomic de-conditioning associated with prolonged bed rest e.g. in orthopaedic and trauma patients and in children and young people with Chronic Fatigue Syndrome (CFS/ME). POTS is also a differential diagnosis of CFS/ME and its recognition and treatment can prove helpful in patients with chronic fatigue (12).

### **Reflex Asystolic Syncope / Infantile Vaso / Vagal Syncope (IVS) and Reflex Anoxic Seizures (RAS)**

Most syncope's in childhood and adolescence are reflex syncope / NMS (13). IVS is a paroxysmal disorder, which typically occurs in a neuro-developmentally intact preschool child. Syncopal attacks are associated with convulsive movements often triggered by sudden pain or surprise. Any unexpected stimulus, such as pain, shock, fright, causes the heart and breathing to stop, the eyes to roll up, the complexion to become deathly white/grey, often blue around the mouth and under the eyes, the jaw to clench and the body to stiffen, sometimes the arms and legs jerk. After 30 seconds or so, the body relaxes, the heart and breathing resume and the person is unconscious in a post-ictal state. One or two minutes later the person may regain consciousness but can remain unconscious or sleepy for well over an hour. On recovery the person may be very emotional and then fall into a deep sleep for one to three hours and looks extremely pale. IVS attacks may occur several times per day (rarely), per week, or per month (more usually), or per year. The attacks appear to cluster. The trigger causes the heart to stop or slow down dramatically (reflex asystole vagally mediated), which in turn reduces the flow of blood to the brain. Diagnosis of IVS is based on detailed description of the attack. Some attacks have no trigger and some children may present with end-expiratory apnoea and as *near misses*.

Reflex Anoxic Seizure (RAS) meaning reflex convulsive syncope, refers to the clinical syndrome as described above, which although in the majority will be due to reflex asystolic syncope i.e. IVS, as documented with ocular compression testing (14), can sometimes be indistinguishable on history or video record from EAS. In North America the term breath holding spells is used to describe both EAS and IVS / RAS. The use of 'seizure' in 'reflex anoxic seizures' was never intended to imply an epileptic seizure, but simply to describe an 'attack' without any pathophysiological connotation. However, for many physicians the word 'seizure' is strongly associated with epilepsy, and such attacks in children are often mistaken for epilepsy.

### **Expiratory Apnoea Syncope (EAS)/ cyanotic breath-holding spells**

These are common reflex syncope's of infants and toddlers (9). The typical "breath-holding" episode begins when a child becomes upset, and then begins to cry. Crying may be brief or prolonged, but typically, after a few cries, the child becomes silent and apnoeic in expiration, unable to catch their breath. This stage is quickly followed by a dramatic change in skin colour. The skin becomes cyanotic or blue / grey. Subsequent loss of consciousness, change in postural tone and sometimes a dramatic axial extensor spasm as described above for the typical reflex anoxic seizure can occur, even without asystole. The entire episode, which lasts from several seconds to more than a minute, may end with a sudden, deep inspiration or with the return of normal breathing.

### **Diagnosis**

#### ***Initial evaluation***

A major issue in the use of diagnostic tests is that syncope is a transient symptom and not a disease. Typically patients are asymptomatic at the time of evaluation and the opportunity to capture a spontaneous event during diagnostic testing is rare. Most investigations undertaken after TLOC has completely recovered will not be diagnostic. The key questions are:

- Is loss of consciousness attributable to syncope or not?
- Is heart disease present or absent?

- Is loss of consciousness attributable to epileptic seizures?
- Are there important clinical features in the history that suggest the diagnosis?

### ***History and physical examination***

History and physical examination are the most specific and sensitive ways to evaluate TLOC and syncope. Data from population based studies showed that the history and physical examination identified a potential cause of syncope in 45% patients whose primary disorder can be diagnosed (15). No single laboratory test has greater diagnostic efficacy. The diagnosis of TLOC should be made by clinical history with the objective being to elicit a sequence which, replayed in the mind's eye, is as good as or better than a split-screen recording with full photography (16). A detailed account of the event must be obtained from the patient and from any available witnesses, which can aid the clinician in differentiating among syncope, epileptic seizures and other causes of TLOC. The account must include the circumstances surrounding the episode: the precipitant factors, the patient's activity involved in prior to the event and the patient's position when it occurred. Activity prior to syncope may give a clue as to the aetiology of symptoms. Assessing whether the patient was standing, sitting, or lying supine when the TLOC occurred may help. Symptoms of nausea or diaphoresis prior to the event may suggest syncope rather than epileptic seizures when the episode was not witnessed. Also the description of an aura may suggest an epileptic seizure or syncope depending on the details. The duration of symptoms preceding a syncopal episode has been reported to be an average of 2-3 minutes. The syncope duration averaged 12 seconds (range 5–22) in one video-telemetry study (17). However, sometimes syncope can last for several minutes. Features typical of an epileptic seizure include generalised convulsion with tonic-clonic movements, cyanosis due to impaired breathing, incontinence, and tongue biting for several minutes, with prolonged confusion on waking. Unfortunately many of these features will occur in severe syncope and the epileptic seizure may be induced by a syncope (see AES above).

A sudden but brief TLOC with collapse and an immediate recovery may suggest an arrhythmia, as they do not have a vasodepressor component of

reflex syncope. Syncope during exercise may be NMS but warrants further investigation looking especially for Long QT syndromes.

Up to 30-40% of children diagnosed with epilepsy do not have the condition (19), the commonest misdiagnosed condition being syncope. The anxiety of clinicians that the diagnosis of epilepsy may be missed contributes to the misdiagnosis of epilepsy (19). Presumptive diagnosis of epilepsy with a trial of anticonvulsants should be avoided. This mistake is probably because syncope can appear like an epileptic seizure, with random jerking of the limbs and even incontinence. It can be difficult, even for experts, to tell apart. It is essential to get a good history, and if possible a video, of the TLOC. Smith et al found that incomplete history taking is one of the principal reasons for misdiagnosis of epilepsy, especially in attacks which are characteristically provoked and / or there were initial or warning symptoms unlike those commonly encountered in epileptic seizures (20). The symptoms surrounding the loss of consciousness can discriminate between epileptic seizures and syncope more confidently in adults than children (21). The clinical context, pattern, evolution and clear detailed account of proceeding, ictal events and ictal recordings can help in differentiating the various causes of TLOC.

A complete physical examination is requisite for all patients presenting with TLOC. Analyse the vital signs. Fever may point to a precipitant of syncope, such as a urinary tract infection (UTI) or pneumonia. Measure the Blood Pressure (BP) and Heart Rate (HR) lying down at rest then on standing up. Both should be normal and the mean BP should rise on standing. It is usual for the HR to rise too but should be less than 120 and should not rise by more than 30 beats per minute or more: such excessive orthostatic tachycardia suggests Postural Orthostatic Tachycardia Syndrome (POTS). Postural falls in blood pressure (BP) and heart rate may point toward an orthostatic cause of syncope. A glucose level, by rapid finger-stick, should be evaluated in any patient with TLOC if they are not fully recovered when seen. Hypoglycaemia can produce a clinical picture identical to syncope, including the prodromal symptoms, absence of memory for the event, and spontaneous resolution.



Clinical findings that suggest the diagnosis		
	Seizure likely	Syncope likely
<b>Symptoms before the event</b>	Aura (such as funny smell)	Nausea, vomiting, abdominal discomfort, feeling of cold sweating (neurally mediated) Lightheadedness, blurring of vision
<b>Findings during loss of consciousness (as observed by an eyewitness)</b>	Tonic-clonic movements are usually prolonged and their onset coincides with loss of consciousness Hemilateral clonic movement Clear automatisms such as chewing or lip smacking or frothing at the mouth (partial seizure) Tongue biting Blue face	Tonic-clonic movements are always of short duration (<15 s) and they start after the loss of consciousness
<b>Symptoms after the event</b>	Prolonged confusion Aching muscles	Usually of short duration Nausea, vomiting, pallor (neurally mediated)
<b>Other clinical findings of less value for suspecting seizure (low specificity)</b>		
Family history		
Timing of the event (night)		
'Pins and needles' before the event		
Incontinence after the event		
Injury after the event		
Headache after the event		
Sleepy after the event		
Nausea and abdominal discomfort		

A detailed cardiopulmonary examination is essential. Arrhythmias may be detected. Auscultation of heart sounds may reveal murmurs indicating high-grade valvular defects.

A detailed neurological examination assists in establishing a baseline as well as defining new or worsening deficits. The patient should have a detailed neurological examination, including head circumference, evaluation for carotid bruits, cranial nerve deficits, motor deficits, deep tendon reflex asymmetries, and sensory deficits.

The patient must be examined for signs of trauma. Tongue trauma is thought to suggest an epileptic seizure. Remember to consider antecedent head trauma resulting in loss of consciousness as opposed to syncope with resultant trauma if the history or findings are unclear.

The Hall pike manoeuvre may be performed in patients who describe short, intermittent prodromes

with primarily vertiginous components to assess for benign paroxysmal positional vertigo.

### Diagnostic work-up

Intervention is indicated, when episodes are severe, disabling, handicapping or frequent. In a recent study the cause of syncope could not be determined in 20% of cases (range 17.5–26%) (22).

### Video-recording of the event

Video recording with attention to the detail of the episode may be a helpful in identifying the cause for TLOC (23). Video recording coupled with physiological recording increase the yield.

### Electrocardiogram (ECG)

Every patient presenting with an unexplained TLOC should have a 12-lead ECG to analyse the heart rhythm (24). If there is uncertainty about diagnosis the ECG should be reviewed by a paediatric cardiologist, especially if long QT seems possible (25). The diagnostic yield of ECG and rhythm

**Table 3. Modified blackout checklist (18)*****Questions about circumstances just prior to the attack:***

- Position (supine, sitting or standing)
- Activity (rest, change in posture, during or after exercise, during or immediately after urination, defecation, cough or swallowing)
- Did something trigger your attack? (e.g., bump or fright, not eating, post-prandial period, alcohol, lack of sleep, stressful situation, crowded or warm places, prolonged standing, fear, intense pain and neck movements)
- Do you have a warning that something is about to happen?
- Did you have early symptoms like light-headedness, sweating, and nausea, pale?

***Questions about onset of the attack:***

- Nausea, vomiting, abdominal discomfort, feeling of cold, sweating, aura, pain in neck or shoulders, blurred vision, dizziness
- Do you definitely lose consciousness or do you collapse whilst remaining conscious
- Do you remember everything that happens during your attack? How long were you unconscious? Were you confused on coming around and for how long?

***Questions about frequency of the attacks and its affects on daily activities and quality of life.******Questions about the attack (eyewitness): clear description of the episode from eyewitness from trigger to complete recovery:***

- Way of falling (slumping or kneeling over), skin colour (pallor, cyanosis, flushing), duration of loss of consciousness, breathing pattern (snoring), movements (tonic, clonic, tonic-clonic or minimal myoclonus, automatism) and their duration, onset of movement in relation to fall, tongue biting
- Did the limbs move whilst unconscious: jerk randomly or rhythmically, where the eyes open or closed, if open did they move?

***Questions about the end of the attack:***

- Nausea, vomiting, sweating, feeling of cold, confusion, muscle aches, skin colour, injury, chest pain, palpitations, urinary or faecal incontinence

***Questions about the background:***

- Family history of sudden death, heart disease, epilepsy or loss of consciousness
- Previous cardiac disease, neurological history (epilepsy, narcolepsy), metabolic disorders (diabetes, etc.), medication
- Information on recurrences such as the time from the first episode and on the number of spells

recordings obtained in the emergency department is low but significant, ranging between 1% and 11% (mean 7%) (26).

**Lightweight external cardiac monitors** allow heart rhythms to be captured. They are helpful in detecting

cardio inhibitory NMS e.g. with a systole and also useful in cases, where repeated episodes of TLOC are caused by imposed upper airway obstruction / intentional suffocation (27). If there are “Red Flags” it will be prudent to seek advice from a paediatric cardiologist or paediatrician with cardiological

**Table 4. Seizure Differential Diagnosis**

Epileptic seizures	Migraine, cluster-like headache
Syncopal seizures	Movement Disorders
Brainstem seizures	Behaviours & Habits
Emotional seizures / Psychogenic non-epileptic attacks	Factitious or Induced Illness
Sleep disorders	Undetermined / unexplained seizures

**Table 5. Red flag symptoms and signs**

Chest pain, dyspnoea, palpitations or structural heart disease.
Syncope during exercise, with swimming, or in or from sleep is typical of the much rarer but potentially fatal, long QT syndromes.
Low back pain, severe headache, focal neurological deficits, diplopia, ataxia, or dysarthria prior to the syncope
Family history of deafness
Family history of sudden unexpected death.

expertise, an echocardiogram, exercise ECG, prolonged ECG monitoring (Holter, external or implantable digital loop ECG recorder as appropriate).

**Holter monitoring:** This is indicated in paediatric patients with recurrent syncope, although the yield of true pathology is probably about 10%. A 24-hour heart rate monitor is very unlikely to identify any problems if TLOC occur once a week or less. Wireless Holter transmission is less invasive and has given promising results in evaluation of syncope (28).

**Loop recording:** Continuously applied digital loop ECG event monitors capture the cardiac rhythm into memory. They are particularly useful if symptoms occur every week or two. After that period, compliance with wearing the device often decreases and the skin can be sensitive to the electrode stickers after a few days when attacks are less frequent; they can be captured with an implantable digital loop recorder (ILR), which can constantly monitor the heart for a period of up to 18 months.

**Exercise ECG:** The specific indications for and utility of exercise testing in paediatric syncope are not identified. Certainly, patients with events that appear to be related to stress or exercise should undergo an exercise evaluation if the patient is capable.

**Specialist / Paediatric Cardiology** referral will be needed for:

**Echocardiography** is indicated in patients with abnormal ECG findings, abnormal physical examination findings, or other features suggestive of structural heart disease. **Electrophysiology studies** should be performed in patients with aborted sudden death if the diagnosis remains unclear. It may be considered in patients who have recurrent syncope not diagnosed based on non-invasive means.

**Catheter laboratory investigations** including hemodynamic assessment, ventricular angiography, aortic angiography, coronary angiography, and endomyocardial biopsy should be considered and scheduled as indicated, along with the electrophysiological procedure.

#### **Electroencephalography (EEG)**

Analyses the brain activity during the episode. It is potentially hazardous to request an interictal EEG, when the diagnosis is syncope. Misinterpretation of EEG is one of the major reasons for misdiagnosis of epilepsy (20). "Epileptiform" abnormalities on EEGs, which include spikes or sharp waves or spike and wave discharges, can occur in healthy children who do not have epilepsy (29) and rolandic spikes may be seen in children with syncope (30). An ECG channel added to an EEG recording will help in identifying

rhythm abnormalities resulting in TLOC (31). Investigation for suspected epilepsy will not be discussed in this article but has been well reviewed (32). Ictal EEG does have a useful role in the assessment of TLOC especially in the diagnosis of syncope and can be used during Head-up tilt testing, to confirm syncope (by the ictal slow waves or slow-flat-slow pattern) and to demonstrate that the brain ictal physiology is normal in unexplained and psychogenic TLOC.

### **External Ocular Compression**

Oculocardiac reflex, which is predominantly a trigeminovagal reflex, which is elicited by 10 seconds of bilateral digital ocular compression, is a measure vagal reactivity and not vagal tone (33). It has been used in the evaluation of syncope and explores the developing autonomic nervous system in infants and young pre-school children. It is diagnostic test for RAS when the attacks are so frequent or incapacitating that therapy e.g. atropine or cardiac pacing, would be considered if asystole was confirmed. The procedure is painful but completely safe and is particularly useful in those under 3 years of age. However, with the advent child-friendly digital loop ECG monitors its use as a diagnostic test has declined recently. The test is positive if an asystole of 5 or 6 seconds or longer is recorded (16). Combined Video, ECG, EEG is required.

### **Head-up tilt testing**

It is widely used, particularly by adult cardiologists in the evaluation of syncope. This provocative test is usually not possible in children younger than six years. The patient is gently strapped on to a tilting bed with foot-plate, and after a period of relaxation (e.g. 15 minutes), is head-up tilted to 60 to 70° upright position for approximately 30 or 45 minutes while ECG, HR, and BP (ideally beat to beat BP) are monitored. Other physiological data can be gathered at the same time including video, EEG (see above), respiratory function, oxygen saturation, cardiac output etc. A positive tilt test is the induction of the typical symptoms AND physiological confirmation of a cardio inhibitory syncope, vasodepressor syncope or mixed syncope. A negative but symptomatic result will precipitate the typical symptoms without physiological correlates of syncope. Such episode could be due to cerebral syncope e.g. adolescent stretch syncope, hypoxia, or psychogenic or unexplained TLOC (with no

abnormalities in physiological recordings including EEG).

The use of vasodilators is not that helpful in children as so many will have syncope during the test some of whom will not be presenting with syncope.

**Mortality / Morbidity:** The morbidity and mortality rates of syncope depend on the underlying cause. A mortality and sudden death rate in young patients without heart disease and normal ECG is low (34). Essentially, no mortality is associated with NMS, however there is morbidity when the NMS is frequent and severe (35). This can be related to injury from sudden loss of consciousness and psychological problems related to altered parenting in children with frequent RAS, and low self esteem and social anxiety and isolation in teenagers with frequent attacks, e.g. with convulsive syncope, associated incontinence and post-ictal drowsiness. Syncope may result in injury to the patient or to others such as may occur when a patient is driving. Over 70% of the sufferers endure depression or anxiety because of their attacks and a similar number alter their daily activities to avoid the risk of blacking out in embarrassing or dangerous circumstances. Cardiac causes of syncope are associated with mortality. Patients with syncope are often admitted to hospital and undergo expensive and repeated investigations, many of which do not provide a definite diagnosis (1). Concerns that well-appearing patients are at risk for sudden death often fuel extensive clinical evaluations or hospital admissions. Many studies have demonstrated the low yield of nondirected diagnostic testing and from the available literature, it is unclear whether admitting asymptomatic syncope patients for observation and inpatient evaluation affects patient outcome (36).

### **Referrals**

“Dizziness”, pre-syncope and syncope may be symptoms of depression, anxiety, panic disorder, somatization, and substance abuse. Unexplained frequent syncope with multiple somatic symptoms is likely to have a psychological or psychiatric etiology. Furthermore, a psychiatric or psychology assessment may be very helpful as part of a multidisciplinary package of care to families of children and young people with severe and frequent syncope. It may also be helpful in those with unexplained TLOC, if accepted by the young person and their family, to try and make an underlying psychiatric or psychological

**Table 6. Burden of TLOC, Syncope & RAS**

To the child	To the family	To health
Frequency, duration & severity	Child looks dead Emotional toll	Cost of false diagnosis high
Avoidance behaviour	Social isolation	Cost of correct diagnosis low
Physical injuries	Protection & restrictions	Loss of trust
Depression and anxiety	Anger at health workers	Prolonged hospital stays

diagnosis e.g. post traumatic stress disorder, somatisation, dissociative state etc. and provide supportive therapy related to the underlying psychological diagnosis. Treatment of these psychiatric illnesses results in lower rates of symptom recurrence.

If there are “Red Flags” (table 5) it will be prudent to seek advice from a paediatric cardiologist or paediatrician with cardiological expertise, an echocardiogram, exercise ECG, or prolonged ECG monitoring (Holter, external or implantable digital loop ECG recorder as appropriate).

The role of a children’s and young people’s TLOC clinic, similar to adult “Black-out” or “Falls” clinics is unproven. However it could enable the close cooperation of general paediatrician, paediatric neurologist and paediatric cardiologist; development of expertise in managing difficult diagnostic and therapeutic challenges; facilitate the access to specialist investigations; allow clinical nurse specialist development; facilitate medical training; encourage consumer involvement in service and research development; and facilitate research.

### Treatment

NMS with RAS rarely requires medication or cardiac pacing in childhood. As with NMS in older school aged children and teenagers, it is often manageable with advice on preventative maneuvers, general information and referral to the excellent patient and family information and support group STARS ([www.stars.org.uk](http://www.stars.org.uk)).

**Prevention:** A patients should be encouraged to lead as normal and full a life as possible. If having to stand up for a long time they should wiggle their toes to assist venous return. They should be informed

about lifestyle issues that will increase the risk of NMS such as skipping meals, not drinking enough fluids, exhaustion, smoking and alcohol. The most important initial step is to reassure the patient and to provide instructions regarding avoidance of both dehydration and postural hypotension.

<i>Abort syncope</i>	<b>Improve orthostatic tolerance / BP</b>
Drink water	Fitness training
Calf muscle pump	Drink enough
Squat	Stockings
Buttock-clench	Avoid drugs, alcohol, smoking

### Specific treatments for syncope

However specific therapy will sometime be necessary. This may be achieved by increasing intravascular volume with an increased daily fluid intake (encourage the patient to drink enough keep urine colorless), dietary salt intake or slow release sodium preparations, e.g. Slow Sodium 50 mmol (5 tablets) twice a day in a teenager. If these measures fail, Fludrocortisone 0.1 mg once or twice daily increasing to maximum tolerated dose or no more than 1 mg/day may be prescribed, in which case initial periodic measurements of BP and plasma electrolytes are recommended. Alternatively, or additionally peripheral venous pooling may be treated with Midodrine 2.5 mg three times a day, increasing to 10 mg four times a day at most. The last dose of the day is best taken in the early evening rather than just before bedtime, to reduce the risk of hypertension.

For proven cardio inhibitory NMS, e.g. with RAS

(Reflex Asystolic Syncope / Infantile Vaso/Vagal Syncope), or NMS in the teenage years with documented asystole / profound bradycardia, Atropine Sulphate at 20-40 micrograms/kg twice, three time or four times a day can be curative. If this fails or is not tolerated cardiac pacing should be suggested, if attacks are frequent and severe enough to warrant the intervention.

There are no specific treatments for EAS / “cyanotic breath holding spells”, but the literature highlights the role of anaemia or iron deficiency which can be corrected. We would emphasise that if severe and frequent the possibility that there is asystole during the attacks should be considered, i.e. that the patient actually has RAS.

The treatment of cardiac diseases causing (cardiac) syncope will not be discussed in this article and generally will be managed by a paediatric cardiologist.

**Medically Unexplained TLOC:** is a useful designation when ictal recording has excluded syncope or other identifiable physiological derangement e.g. epileptic seizures, hydrocephalic attacks, sleep attacks, hypoxia etc, and a psychiatric diagnosis or psychological explanation has either not been made or is not accepted by the patient and their family. In this situation general advice as for NMS will help as some have a mixture of attacks or started with NMS. Reassurance and establishing rapport with the young person and their family, who may feel doctors have not taken them seriously in the past, will help. Once they feel the team are on their side and understand that many diseases are thankfully ruled out they may be ready to take on behavioural advice such as not calling an ambulance or not sending her home from school but letting her sleep it off and then return to class. Patients incapacitated by frequent unexplained TLOC will benefit from general fitness training, encouraging increasing participation in school and social activities and sport or other hobbies. The patient will need to have access to further confidential support e.g. through Child Line or members of the clinical team, so help can be provided if requested. Further offers of psychological or psychiatric support can be made periodically as indicated, and follow-up and periodic clinical reassessment are recommended, but may be refused.

Some patients will develop CFS/ME and further management can then be organized.

### Conclusions

TLOC is a useful concept and the vast majority of children and young people presenting with it will have NMS. Convulsive syncope however continues to be misdiagnosed as epilepsy, even though the most powerful diagnostic tool is the detailed history by some one knowledgeable about not just epilepsies but all the differential diagnoses, especially syncope. Adoption of appropriate medical terminology for the range of syncope's in children (7) would help.

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