

## CONGENITAL HEART DISEASE

## Dizziness and syncope in adolescence

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“The only difference between syncope and sudden death is that in syncope you wake up”—*G L Engels*<sup>1</sup>

**S**yncope is a common problem in adolescence, with up to one in five experiencing an episode of syncope before adulthood.<sup>2</sup> Whereas the vast majority of syncope is benign, a minority is caused by something potentially more serious or even life threatening. For this reason and also because syncope has such a death-like quality, it often generates extreme anxiety and is often extensively, inappropriately, and unfruitfully investigated.

### Classification

There are many causes of syncope and therefore it can be helpful to categorise them. One way of categorising syncope is to divide the causes into three main groups.<sup>2</sup> Neurally mediated syncopes occur when there is a disturbance in the autonomic nervous system's control of heart rate and blood pressure. Generally they can be considered as benign. Cardiovascular causes of syncope are rare in adolescence, but it is important to be aware of them, as they are potential causes of sudden death. Non-cardiovascular syncopes can broadly be divided into the epilepsies and the psychogenic causes. In the latter the child actually fakes the syncope. It is beyond the scope of this article to discuss all the causes of syncope and the aim will be to concentrate on the most common form of syncope, the neurally mediated syncopes.

### Neurally mediated syncopes

Although neurally mediated syncope can occur at any age in childhood, the peak age groups are in toddlers and in adolescents. Neurally mediated syncopes are a heterogeneous group of autonomic disorders, which result in orthostatic intolerance. Grubb suggests dividing them into four main groups: the reflex syncopes, postural orthostatic tachycardia syndrome, pure autonomic failure, and multiple system atrophy.<sup>3</sup>

Neurocardiogenic syncope is a form of reflex syncope and also the most common type of syncope in adolescence. A typical history is of syncope that occurs when the child is upright, either sitting or standing. Characteristically the child will experience a prodrome such as dizziness, nausea and pallor, before loss of tone and consciousness. It is important to remember that following loss of consciousness there may

### Classification of syncope in adolescence

- Neurally mediated syncopes
  - reflex syncopes
  - postural orthostatic tachycardia syndrome (POTS)
  - pure autonomic failure
  - multiple system atrophy
- Cardiovascular causes
  - arrhythmic
  - structural
  - vascular
- Noncardiovascular
  - epileptic
  - psychogenic

be a period of retrograde amnesia and, despite a prodrome, the child might claim “I went straight down without warning”. Depending on the duration and severity of cerebral hypoxia secondary to hypotension or profound bradycardia, or both, the child may have an anoxic seizure and may be incontinent. An anoxic seizure is often mistaken for an epileptic seizure but in reality is quite different. During an anoxic seizure the electroencephalogram (EEG) is flat and rather than tonic-clonic movements, there tends to be stiffening, opisthotonos, and fine twitching.<sup>4</sup> On recovery the child will often complain of feeling tired and “washed out” for some time afterwards.

The mechanism of neurocardiogenic syncope is not entirely understood. It has been proposed that in response to being in the upright position, there is peripheral pooling of blood.<sup>2</sup> This results in reduced venous return and an empty heart. The empty heart contracts overvigorous, stimulating so called “C fibres”. The brain interprets this as *hypertension*, resulting in sympathetic withdrawal. There is initially pallor, sweating, often with hyperventilation and tachycardia, followed by relative bradycardia, hypotension, and loss of consciousness.

A type of reflex syncope that has only been recognised relatively recently is cerebral vasoconstrictive syncope.<sup>5</sup> In this condition syncope occurs as a result of cerebral vasoconstriction in the absence of hypotension and bradycardia. The diagnosis is made by showing that cerebral vasoconstriction occurs during symptoms. This can be done by measuring cerebral blood flow with techniques such as transcranial Doppler or near infrared cerebral spectrophotometry.<sup>3,5</sup> Cerebral vasoconstrictive syncope is probably uncommon in adolescence, but probably also underdiagnosed. As blood pressure and heart rate are not significantly altered during symptoms, it can be mistaken for psychogenic pseudosyncope. This mistake can usually be avoided by recording an EEG or measuring cerebral blood flow during tilt testing in individuals who have symptoms despite normal blood pressure and heart rate.

Postural orthostatic tachycardia syndrome (POTS) probably is a heterogeneous group of

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**Diagnosis of syncope—history, history, history!**

- Eye witness?
- Onset and frequency?
- Circumstances: relation to exercise? posture? precipitating factor?
- Prodrome: dizziness? nausea? pallor? aura?
- Altered consciousness: complete loss? partial impairment? duration?
- Abnormal movements: tonic-clonic? anoxic? fine repetitive?
- Incontinence, injury?
- Recovery: tired? “washed out”? post-ictal? rapid return to normal?
- Family history: fits? faints? sudden death in young person?

conditions.<sup>3</sup> Although not common in adolescence, it is almost certainly underdiagnosed. POTS is defined as an excessive tachycardia, either a rise of > 30 beats per minute (bpm) or an increase to > 120 bpm, in response to being upright.<sup>6</sup> In some, the heart rate may be persistently greater than 160 bpm. Symptoms include fatigue, dizziness, and exercise intolerance.<sup>7</sup> POTS is probably a mild form of chronic autonomic failure, such that there is failure of the peripheral vasculature to vasoconstrict adequately in response to upright posture. This results in a compensatory tachycardia. There is a danger of misdiagnosing POTS as inappropriate sinus tachycardia. Radiofrequency modification of the sinus node will usually make symptoms worse.

Pure autonomic failure and multiple system atrophy are very rare in adolescence and are accompanied by other signs of autonomic failure, including loss of sweating, thermoregulatory problems, and bladder and bowel dysfunction.

**Diagnosis of syncope**

History, history, history!

The key to the diagnosis of syncope is to take a careful and detailed history. If a good history is taken, the physician will obtain a very good idea which of the three categories the syncope is likely to fall into. It is important to be alert for any “warning bells” from the history that would point towards a potentially more serious or life threatening cause of syncope. Neurally mediated syncope can occur before or following exercise, but syncope that occurs during exercise raises the possibility of a cardiac structural or arrhythmic cause of syncope. Syncope that occurs secondary to a loud noise, fright or extreme emotional stress raises the possibility of the long QT syndrome. Syncope that occurs when supine is of concern

**Syncope “warning bells”**

- Syncope in response to loud noise, fright or extreme emotional stress
- Syncope during exercise
- Syncope while supine
- Syncope associated with tonic clonic or abnormal movements
- Family history of sudden death in young person < 30 years old
- Syncope with an “odd” history

as this would be very unusual for neurally mediated syncope. A family history of sudden death in a young person raises the possibility of a hereditary cardiovascular cause such as long QT syndrome or hypertrophic cardiomyopathy. Tonic-clonic or fine repetitive movements suggest a possible epileptic cause. One caveat is that in some susceptible individuals, an anoxic seizure can result in a secondary epileptic seizure, leading to an incorrect diagnosis of primary epilepsy.<sup>8</sup> A careful history should help prevent this mistake.

**Investigation of recurrent syncope**

Investigations for syncope in adolescents will almost always be normal. The most important investigation is a 12 lead ECG, primarily to exclude a long QT interval. Pre-excitation, heart block or ventricular hypertrophy can also be diagnosed from an ECG. If symptoms are related to exercise, an exercise test should be performed in the hope of inducing symptoms. In reality, they rarely occur during the test. Holter monitoring is usually unhelpful, as symptoms almost never occur in the 24–48 hour period while the monitor is worn. This also tends to be true for cardiac event monitoring. Unless the child has other cardiac signs or symptoms, or any of the warning bells from the history, an echo will almost certainly be normal. Although an EEG is often performed on children with syncope to “exclude epilepsy”, this is rarely helpful for even in children with epilepsy the EEG will usually be normal between attacks. Intracerebral causes of syncope are very rare in childhood and would usually be associated with other neurological signs or symptoms; thus magnetic resonance imaging (MRI) or computed tomographic (CT) scan is usually an expensive waste of time.

It is our practise to perform a 12 lead ECG in all adolescents referred with recurrent syncope. If there are any of the “warning bells” from the history or if there are any other cardiac or neurological signs or symptoms, appropriate cardiac or neurological investigations are undertaken. If there is a good history for neurally mediated syncope and the ECG is normal, usually no further investigation is required. For those who have very severe or frequent attacks,

who are in need of reassurance or where the history is not entirely clear, tilt testing is probably the most productive investigation.<sup>9</sup> Unfortunately there is no standardised protocol for tilt testing in either children or adults, and protocols vary in terms of duration of tilt, degree of tilt, and whether or not drugs, including isoprenaline or glyceryl trinitrate, are given.<sup>10</sup> The specificity or sensitivity of any given protocol will therefore vary. Our own protocol at The Royal Hospital for Sick Children in Glasgow is very simple and tolerated by most children, as it does not involve any intravenous cannulae or drugs. We rest the child supine for 15 minutes. The child is then tilted to 60° head-up for a maximum of 45 minutes. During this time the blood pressure is continuously but non-invasively monitored using the Finapres system, and a three lead ECG continuously recorded. We always warn the children (and those supervising) that the test is likely to be one of the most boring things they have ever done! Using this protocol, approximately 50% of children with a good history for neurally mediated syncope will have a positive tilt test. The use of drugs increases the sensitivity of the test but reduces its specificity and makes the test more unpleasant for the child. Whatever tilt test protocol is chosen it seems important to have a period of supine rest before tilting, to tilt to between 60–80° to reduce false positive and negative responses, and to tilt for at least 40 minutes of drug-free period.

The most common positive tilt test response is a combination of hypotension and bradycardia before syncope. Hypotension with no significant change in heart rate is the next most common positive response. The least common positive response is asystole before syncope.

In children with suspected psychogenic pseudosyncope it is important to include EEG monitoring or measurement of cerebral blood flow during tilt in order not to miss the diagnosis of cerebral vasoconstrictive syncope. In situations where it is claimed that syncope is occurring several times a day every day, admission to hospital for observation with continuous ambulatory ECG and EEG monitoring is usually the best approach. With this history the ECG, EEG, and measured blood pressure will almost always be normal during the “syncope” and a diagnosis of psychogenic pseudosyncope can be confirmed.

In situations where the distinction between neurally mediated syncope and potentially serious arrhythmia remains unclear—for example, in a child with a borderline QT interval or slightly worrying history—our approach is now to implant a Reveal monitor (Medtronic Inc, USA). The monitors are extremely easy and quick to implant. Most adolescents find them considerably more acceptable than the non-invasive monitors in that they are less conspicuous and do not restrict activities. The manufacturer recommends that the monitors be implanted in the left parasternal region to reduce artefact from muscle activity. We have found that a pocket made medial to the left axilla is better cosmetically, and although there can be some artefact on the ECG from muscle



**Figure 1.** The Reveal Plus monitor (A) is easy to implant and tends to be more acceptable to adolescents than the more traditional non-invasive cardiac event monitors. The Reveal Plus can be activated using an external activator or programmed to recognise and record significant bradycardias, tachycardias or pauses. The quality of ECG recording is usually very good (B). Although there may be some artefact from muscle activity, it is rarely sufficient to affect ECG interpretation.

activity, we have not found this to be enough to impair ECG interpretation (fig 1). The new Reveal Plus monitors have automatic functions and can be programmed to recognise and record significant pauses, bradycardias, and tachycardias even if the patient does not activate the monitor with the external activator. This is a distinct advantage in the adolescent population where there are the inevitable excuses of forgetting the activator or forgetting to use it to record an event.

### Management of neurally mediated syncope

The mainstay of treatment is reassurance, specifically that the episodes are not caused by epilepsy or a cardiac problem.<sup>11</sup> Advice should be given to drink plenty (with the exception of caffeine containing drinks as they tend to dehydrate) such that the urine always looks clear. Many families now restrict the amount of salt in the diet because of concerns about future hypertension. We advise an increase in dietary salt to what might be termed a “normal” salt diet. Advice on posture when prodromal symptoms are experienced can be helpful. Manoeuvres such as crossing the legs and folding the arms especially when standing help to maintain blood pressure. Often with the above simple measures of reassurance, fluid, posture and salt, symptoms will improve significantly.

**Management of neurally mediated syncope**

- Reassurance
- Fluid, posture, salt
- Drugs: fludrocortisone,  $\beta$  blocker, others
- Biofeedback techniques
- Pacemaker

The likelihood of further syncopal attacks depends on the number of episodes of syncope before presentation.<sup>12</sup> For those who present with frequent syncope or continue to have syncope despite the above simple measures, drug treatment should be considered. There are many pharmacological agents available, which no doubt testifies to our lack of understanding of the mechanisms of neurally mediated syncope and probably also reflects a likely placebo effect of drugs. No drug has been adequately evaluated by randomised clinical trials, but fludrocortisone and  $\beta$  blockers are the most favoured first line drugs, with relatively few side effects.<sup>13</sup> My own preference is for fludrocortisone at a dosage of 100  $\mu$ g daily in the first instance. This seems to be effective in most adolescents in reducing frequency and severity of syncope. Occasionally the drug is not tolerated because of problems of fluid retention and weight gain. If symptoms continue despite fludrocortisone, then the addition of a  $\beta$  blocker can be helpful. Serotonin reuptake inhibitors such as fluoxetine hydrochloride and vasoconstrictors such as midodrine are currently under clinical review. Initial studies suggest they might prove beneficial for some forms of neurally mediated syncope, but the use and safety of the drugs in children has not been established. It would be wise, therefore, to reserve them for those who continue to have symptoms despite first line treatments. Serotonin reuptake inhibitors are thought to act by inhibiting sympathetic neural outflow and reducing susceptibility to certain neurally mediated events.<sup>14</sup> Midodrine is an  $\alpha_1$  agonist which causes peripheral vasoconstriction but with minimal cardiac and neurological effects.<sup>15</sup>

An alternative or adjunct to drugs is biofeedback therapy. Techniques include tilt training and active tension.<sup>16</sup> The latter is best undertaken with the help and supervision of a clinical psychologist.

**Cardiac pacing**

The use of cardiac pacing for neurocardiogenic syncope remains controversial. The rationale is that pacing should eliminate any contribution of bradycardia to the hypotension that results in syncope. There is little direct evidence, however, that significant bradycardia commonly occurs in spontaneous neurocardiogenic syncope even if it is demonstrated during tilt testing. Pacing would not be expected to affect to

any great degree hypotension caused by vasodilation.

An excellent review examining the role of pacing in the treatment of neurocardiogenic syncope is provided by Sheldon.<sup>17</sup> In his summary of clinical studies evaluating the role of permanent pacing for neurocardiogenic syncope, all studies showed a benefit from pacing but only one study successfully addressed the issue of placebo.

The recently published North American vasovagal pacemaker study tested whether dual chamber pacing would reduce frequency of neurocardiogenic syncope.<sup>18</sup> Patients were randomised to pacing or to medical treatment. Pacing did reduce recurrence of syncope by 91% compared with medical treatment, but the important issue of placebo was not addressed.

The only completed study to date that has successfully addressed the problem of placebo was a three way, double blind, randomised, crossover study of dual chamber pacing in 12 children.<sup>19</sup> The children had frequent, severe neurocardiogenic syncopes and a demonstrated asystole of > 4 seconds during a typical attack. The pacemakers were programmed to no pacing, ventricular pacing with hysteresis, and dual chamber pacing with the rate drop algorithm. Each treatment arm lasted four months. Both ventricular pacing and dual chamber pacing with rate drop algorithm were equally effective in preventing syncope, but dual chamber pacing with the rate drop algorithm was more effective in preventing pre-syncope.<sup>20</sup>

It would appear that pacing can be a very effective treatment for children who have severe neurocardiogenic syncope and who have a demonstrated asystole during a typical episode. The question remains as to whether pacing would be effective for the majority of children who have neurocardiogenic syncope but who do not demonstrate prolonged asystole during an event. The vasovagal pacemaker study II might help to answer this question. This study will evaluate adult patients who have had six or more syncopal episodes and who have a positive tilt test with or without bradycardia. All patients will receive a pacemaker and will be randomised to either pacing with the rate drop algorithm, pacing with an escape rate of 45 bpm, or to no pacing. It is expected that the study will be completed by the year 2002.

As cardiac pacing is a significant commitment in a young person it should be reserved for those who have severe, frequent attacks and in whom drug treatment has failed or is declined. Although ventricular pacing with hysteresis should suffice for the younger child, for adolescents who are likely to be more aware of and distressed by symptoms of presyncope, a dual chamber pacemaker with the rate drop algorithm is recommended. Until the question is answered as to whether patients with neurocardiogenic syncope but without demonstrable asystole will benefit from pacing, it seems sensible to reserve pacing for children who have a recorded asystole or profound bradycardia during a typical attack. It is now our practise to

### Syncope in adolescence: key points

- Common
- Usually benign
- Most common cause is neurally mediated syncope
- Diagnosis primarily from history
- 12 lead ECG is most important investigation
- Investigations usually normal
- Mainstay of treatment for neurally mediated syncope is reassurance
- BEWARE OF “WARNING BELLS” FROM HISTORY

implant a Reveal Plus monitor in any young person with frequent neurally mediated syncope in whom we are considering a pacemaker. The Reveal allows us to determine accurately both the frequency of events and whether asystole or profound bradycardia occurs during a spontaneous syncope. It has been our experience that implantation of the Reveal can have an astonishingly curative effect. Perhaps it works as a placebo or perhaps the awareness of the monitor and activator works as a form of biofeedback. Certainly we been impressed enough to wonder whether the manufacturer should recommend it as a treatment for neurocardiogenic syncope!

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