

Management of blackouts and misdiagnosis of epilepsy and falls

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‘Collapse?cause’ is a colloquial term that is widely used, especially in acute and emergency medical practice in the UK. Patients with ‘collapse?cause’ can be defined as having suffered ‘a physical collapse due to an abrupt loss of postural tone’. There may or may not have been accompanying loss of consciousness. Some patients with ‘collapse?cause’ will have suffered a stroke, others may have an acute metabolic disorder, such as hypoglycaemia, and others may have collapsed due to the effects of drugs. However, very many such patients with collapse will have suffered a ‘blackout’ (ie transient loss of consciousness (T-LOC)), with consequent collapse. It is these patients who most frequently present a diagnostic problem, since there will often be no symptoms, signs or laboratory findings of stroke, metabolic disorder or drug effect; they may have completely recovered upon admission; all the admitting doctor has to rely on is a second-hand ‘word-of-mouth’ description of the features of the blackout and collapse from bystanders, who are usually lay observers. It seems to be commonly assumed that T-LOC represents a primary neurological disturbance, and the differential diagnosis often focuses on epilepsy versus syncope. It is poorly understood that syncope is quite often convulsive, and may feature limb twitching and sometimes urinary incontinence.

Syncope, defined ‘as transient loss of consciousness due to global impairment of cerebral perfusion’,¹ is very common, with up to 50% of the population having syncope at some stage in life. Syncope is the sixth most common cause of emergency admission in the UK,² accounting for 3% of all attendances to the emergency departments and 1% of all hospital admissions. In contrast, epilepsy affects about 0.5–1% of the population.³ Syncope is probably far more common than epilepsy, but this seems to go unrecognised. As a consequence, the misdiagnosis of epilepsy is very common, with 20–30% of adults misdiagnosed with epilepsy, and a greater percentage of children.³ The misdiagnosis of epilepsy is thought to cost the NHS about £200m per annum, and recent settlements for compensation in misdiagnosed and mistreated cases will further add to this cost. Misdiagnosis has been a feature in children,⁴ but a major problem also exists with misdiagnosis in older patients.

Falls in the elderly are very common and cost the

NHS about £1 billion per annum. An aging population means these costs will rise. Frequently syncope is overlooked as the cause of a fall, or not reported by patients, due to embarrassment, anxiety or retrograde amnesia for the precipitating fall.⁵ It has been demonstrated that syncope is a frequent cause, that investigation for syncope is fruitful and cost-effective, and that treatment, eg cardiac pacing,⁶ is effective.

Blackouts, or T-LOC, are therefore a major cause of morbidity, and are very costly, poorly understood and often misdiagnosed (Fig 1). Major concerns exist over management in respect of the misdiagnosis of epilepsy and the tendency to overlook syncope as the precipitating cause of a fall in the elderly. The theme of this conference was to emphasise the correct clinical evaluation, investigation and treatment of patients with definite or likely blackouts/T-LOC. Emphasis was placed on the underlying pathophysiology, described simply as:

- a primary disorder of the global circulation to the brain – syncope
- a primary disorder of the brain – epilepsy
- a disorder of the psyche – ‘psychogenic seizures’ or ‘non-epileptic attack’.

Strategies were presented that might help prevent a misdiagnosis of epilepsy or oversight of the underlying cause of a fall in an elderly patient.

Syncope

Definition and terminology

Syncope has been defined by the European Society of Cardiology as ‘a symptom with transient, self-limited loss of consciousness usually leading to collapse. The onset of syncope is relatively rapid, and the recovery is spontaneous, complete, and usually prompt. The underlying mechanism is transient global cerebral hypoperfusion.’¹ One of the most common clinical errors is to consider a transient cerebral ischaemic episode (TIA), as a cause of T-LOC. In fact T-LOC *excludes* TIA as a cause of the episode. T-LOC is ‘a transient loss of consciousness without neurological deficit, and a TIA is a transient neurological deficit (<24-h duration), without T-LOC’. Many patients are unnecessarily investigated for carotid disease

after an episode of T-LOC, and some may have unnecessary operations for incidental carotid stenoses.

Reflex syncope (aka vasovagal, neurocardiogenic, vaso-depressor, neurally-mediated hypotension and bradycardia syndrome, emotional fainting, pallid breath-holding spells, pallid infantile syncope, reflex anoxic seizure, reflex asystolic syncope, malignant vasovagal syncope, etc) is probably by far the most common cause of syncope. Its origin is unknown, but the afferent arc synapses with the brain stem cardioinhibitory and vasodepressor centres to cause T-LOC by vasodepressive hypotension and a variable degree of bradycardia or asystole.⁵

Prevalence

The reported prevalence of syncope varies widely, with approximately 15% of children before 18 years of age and a similar percentage of middle-aged men and women experiencing an episode.¹ The prevalence rises significantly in the elderly population, with approximately a quarter of all patients over the age of 70 years experiencing an attack, of which one-third will have a recurrent blackout in the next 2 years. Unfortunately, falls are also common in this age group, with about 30% of blackouts in the over 65-year age group presenting as falls as there is amnesia to the event.⁵ Around 70% of blackouts in this age group are unwitnessed. Thus, getting the management of blackouts right in this age group can be very challenging. For those patients who are hospitalised, the average length of stay varies from 5 to 17 days and accounts for most of the cost involved in caring for these patients.²

Causes

Syncope is a *cardiovascular* disorder. Causes can be divided into:

- 1 Cardiac causes:
 - i due to underlying structural heart disease, eg:
 - aortic stenosis

- hypertrophic cardiomyopathy
- arrhythmogenic right ventricular dysplasia
- ischaemic left ventricular dysfunction
- some forms of congenital heart disease
- left atrial myxoma
- pulmonary embolism
- ii due to an arrhythmia, eg:
 - tachyarrhythmias, eg ventricular tachycardia, ventricular fibrillation, polymorphic ventricular tachycardia, Brugada syndrome, long QT syndrome, pre-excited atrial fibrillation, supraventricular tachycardia
 - bradyarrhythmias, eg atrioventricular block, sinus node disease

- 2 Vascular causes:
 - i reflex causes:
 - vasovagal syncope
 - carotid sinus hypersensitivity
 - ii situational causes:
 - cough syncope
 - micturition syncope, etc
 - iii postural causes:
 - orthostatic hypotension
 - postural orthostatic tachycardia syndrome (POTS).

Evaluation

The aims of evaluation of a patient with syncope are to identify any underlying structural heart disease, identify the reason or mechanism of syncope, define any risk of sudden cardiac death and identify any treatment options.

All patients presenting with syncope should be subjected to a detailed history taking, a physical examination (including lying and standing blood pressure) and an electrocardiogram (ECG). Syncope implies that there has been T-LOC. Important features include precipitating factors, injury sustained and specific situations in which syncope occurs, eg micturition, cough and swallowing. A description from any witness to the episode is essential, if not always possible. T-LOC is a story, with a beginning, middle and end. The history should focus on any premonitory symptoms, the features during unconsciousness and symptoms during recovery.

Cardiac syncope may occur in the setting of structural heart disease, during exertion, may be associated with palpitations and presyncope, and there may be a history of sudden cardiac death in the family. Consequently, a family history of sudden cardiac death should be sought in all patients and may be helpful in suspected Brugada syndrome, long QT syndrome or an inherited cardiomyopathy, eg hypertrophic cardiomyopathy, familial

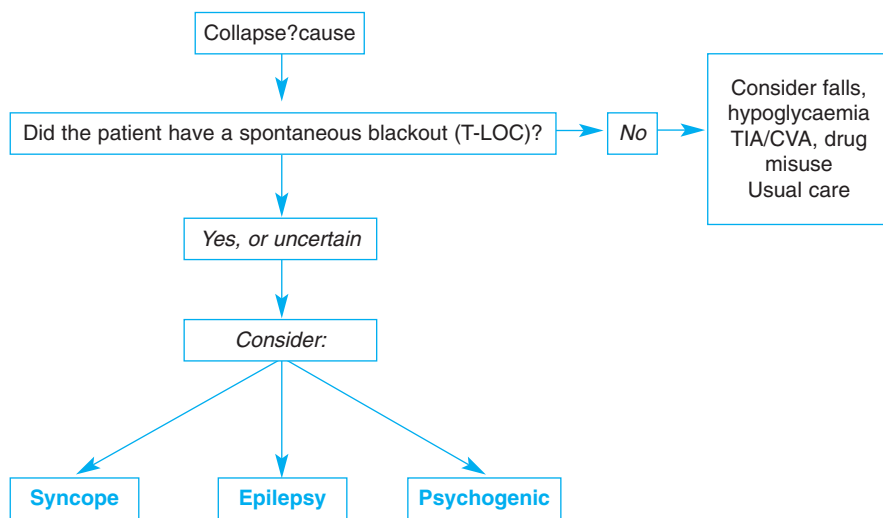


Fig 1. Differential diagnosis of blackout. CVA = cerebrovascular accident; ECG = electrocardiogram; TIA = transient ischaemic attack.

dilated cardiomyopathy or arrhythmogenic right ventricular dysplasia. In contrast, reflex syncope usually occurs in the absence of cardiac disease, is associated with autonomic symptoms like nausea, vomiting and sweating, and the patient is noted to go pale during the episodes, with quick recovery of consciousness. Often, patients have a long history of syncope. Frequently there are precipitating causes like emotional stress as can be experienced at the time of a phlebotomy, reduced plasma volume during prolonged standing or dehydration, low blood pressure due to low salt intake, and raised intrathoracic pressure impeding venous return in cough syncope and carotid sinus pressure or after exercise.

Studies have shown that syncope occurring in the setting of structural heart disease is associated with a poorer prognosis, and investigations should be aimed at demonstrating or excluding structural heart disease. Every syncopal patient should have at least one 12-lead ECG, and many will need echocardiography if this is not completely normal.

Infrastructure for evaluation

The European Society of Cardiology recommends a cohesive, structured care pathway either delivered within a single syncope facility or as a more multifaceted service for the assessment of the patient with syncope. Many models exist. The important principles are speed of access and a multidisciplinary approach, so that patients cannot get 'stuck' in one care pathway and

instead can easily access other disciplines if a particular diagnostic or treatment pathway appears unhelpful. As well as expert opinion, which is by far the most important resource, access to echocardiography, stress testing, electroencephalography (EEG), MRI/CT scans and electrophysiology studies is needed.

Epilepsy

Epilepsy is a common neurological condition. Approximately 30,000 new cases of epilepsy (50 per 100,000 population) are seen every year in the UK.³ At any one time 0.7–1.0% of the UK population or 400,000–600,000 individuals have epilepsy.³

Epilepsy is an excessive asynchronous discharge of cerebral neurones leading to a clinical event.³ Patients with epilepsy present with a T-LOC, but may not have collapsed. In some forms of epilepsy postural tone is preserved, eg in some complex partial seizures. The clinician should be wary of making a diagnosis of epilepsy after a single T-LOC. When seizures are recurrent, and specialist clinical opinion, backed up by corroborative tests, deem it likely, it may be appropriate to diagnose epilepsy.

Causes

The etiology of epilepsy varies with age and geographical location. Congenital, developmental and genetic conditions are the cause of epilepsy in childhood, adolescence and young adults. A history of brain injury, brain infection or neoplasm may occur at any age, although tumours are more likely over the age of 40 years. In the elderly population, cerebrovascular disease can cause epilepsy, while malaria, neurocysticercosis, paragonomiasis, schistosomiasis and American trypanosomiasis are the cause in various geographical areas around the world.

All seizure disorders start in the cortex of the brain. The clinical manifestations of epilepsy depend on where in the cortex it begins and the extent and speed of spread. All seizures evolve and activate some parts of the brain, disrupt physiological function and terminate due to activation of inhibitory mechanisms. The latter results in what is known as the postictal state. Seizures can be classified as generalised (involving both cerebral hemispheres) or focal/partial. Generalised seizures can be further classified as absence seizures, myoclonic seizures, atonic seizures, tonic seizures or tonic clonic seizures. Partial seizures can be further subdivided into simple partial and complex partial seizures with secondary generalisation. Generalised absence seizures are brief in duration, lasting for <30 s. They usually manifest as a blank stare with cessation of motor activity. There may be many attacks during the day, which are seen on EEG as a 3-s spike-and-wave pattern.

Conference programme

■ Introduction: The challenge of the blackouts patient

Professor John Camm, St George's Hospital Medical School

■ Terminology in transient loss of consciousness

Professor Gert van Dijk, University of Leiden, The Netherlands

■ Pathogenesis of syncope

Dr Adam Fitzpatrick, Manchester Heart Centre, Manchester Royal Infirmary

■ Pathogenesis of epilepsy

Dr Matthew Walker, National Hospital for Neurology and Neurosurgery, London

■ Clinical evaluation

Dr Neil Sulke, Eastbourne General Hospital

Dr Paul Cooper, Greater Manchester Neurosciences Centre

■ Investigations

Dr Derek Connelly, Glasgow Royal Infirmary

Dr David Smith, Walton Centre for Neurology, Liverpool

■ Infrastructure for best practice

Professor Rose Anne Kenny, University of Newcastle

Professor Christopher Mathias, Imperial College London

■ Treatment

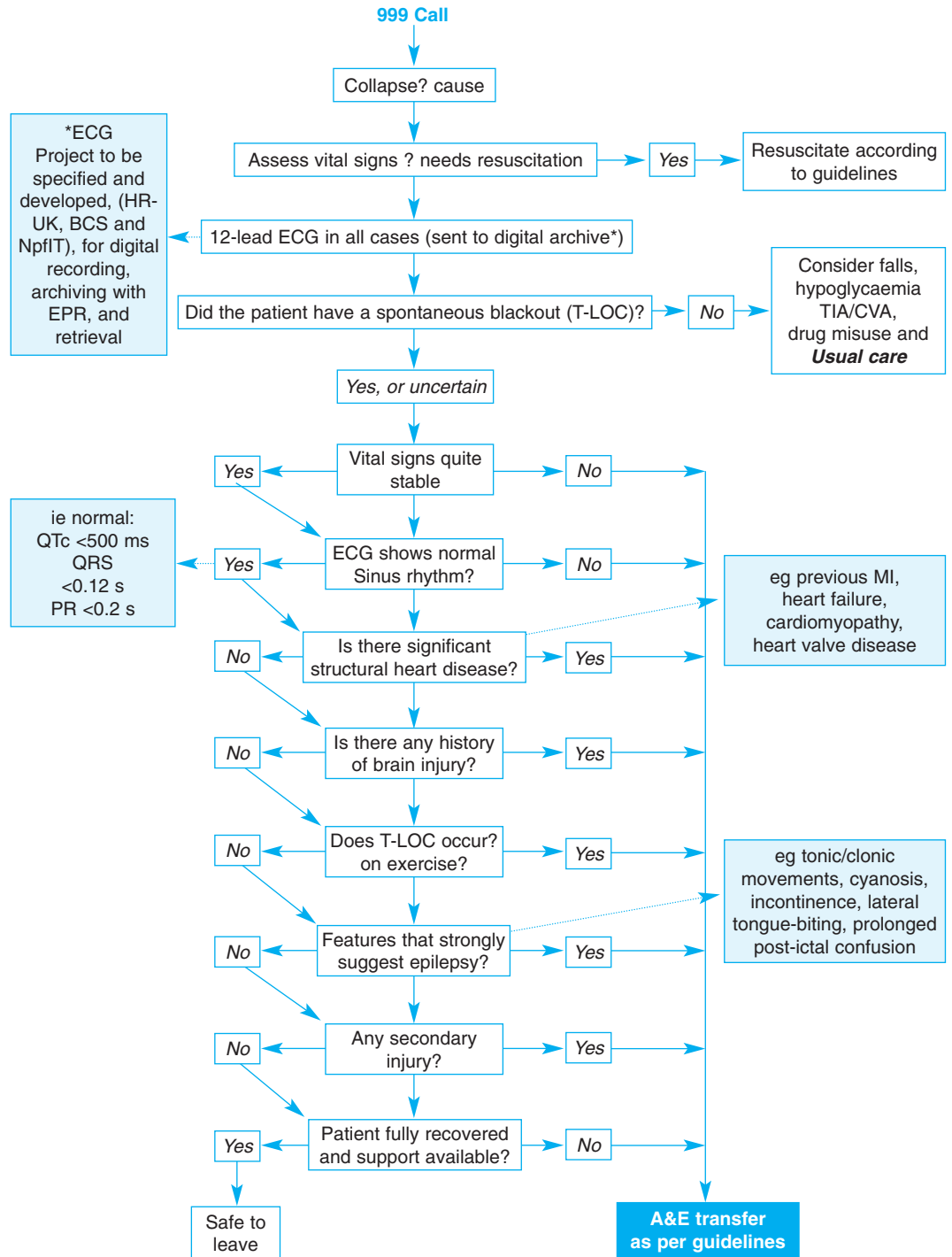
Dr John Morgan, Wessex Cardiac Centre, Southampton

Dr Margaret Jackson, Royal Victoria Infirmary, Newcastle upon Tyne

■ Managing non-responders, social and driving impact

Professor David Chadwick, Walton Centre for Neurology

Fig 2. Point of care: ambulance service.⁷
 BCS = British Cardiac Society; CVA = cerebrovascular accident; ECG = electrocardiogram; EPR = electronic patient record; HR-UK = Heart Rhythm-UK; MI = myocardial infarction; Npfit = National Programme for Information Technology; SCD = Sudden cardiac death; TIA = transient ischaemic attack.

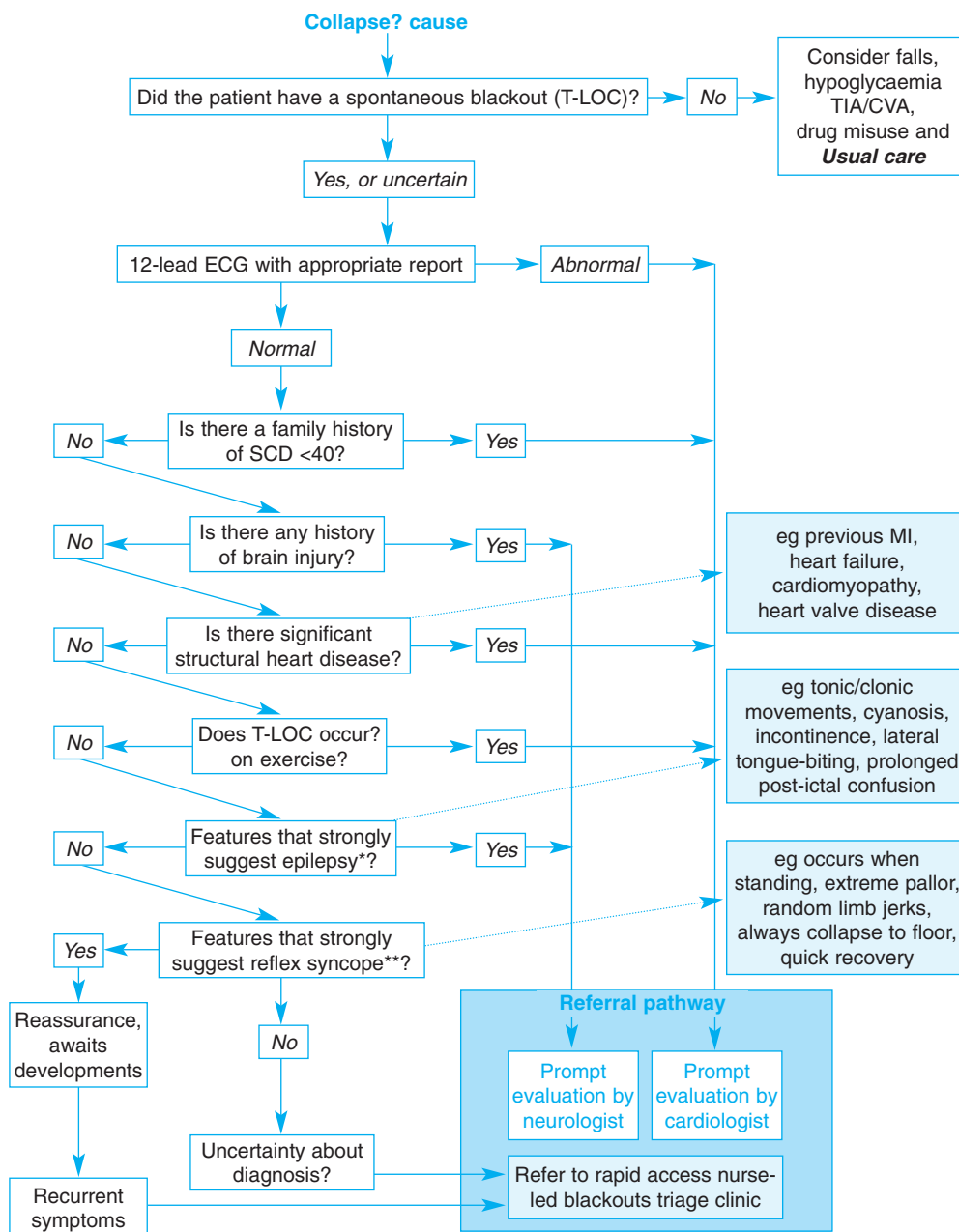


Myoclonic jerks are brief movements of one or many, usually distal, muscle groups and can originate from the cortex, brain stem or the spinal cord. Importantly, consciousness is preserved in these cases as opposed to myoclonic jerks in syncope, when consciousness is lost. While myoclonus is seen in epilepsy, it is also commonly seen in syncope, where cerebral anoxia, secondary to global impairment of cerebral blood flow, causes neuronal irritation and myoclonic twitching of the limbs. This is easily mistaken for epilepsy.

Evaluation

Just as with suspected syncope, evaluation of every patient suspected of having epilepsy starts with a detailed history taken from the patient and an eyewitness (if available) by an experienced clinician. If an eyewitness is not available in person, a telephone consultation should be sought. The history is all important, as investigations are often unhelpful and are rarely diagnostic.⁷ Nevertheless, all patients should have a 12-lead ECG,

Fig 3. Point of care: accident and emergency or general practice.⁷ CVA = cerebrovascular accident; SCD = Sudden cardiac death; TIA = transient ischaemic attack.



currently only provided for about 4% of patients with suspected epilepsy in the UK. All too commonly, potentially life-threatening cardiac arrhythmias, eg those associated with the long QT syndrome, present as T-LOC misdiagnosed as epilepsy.

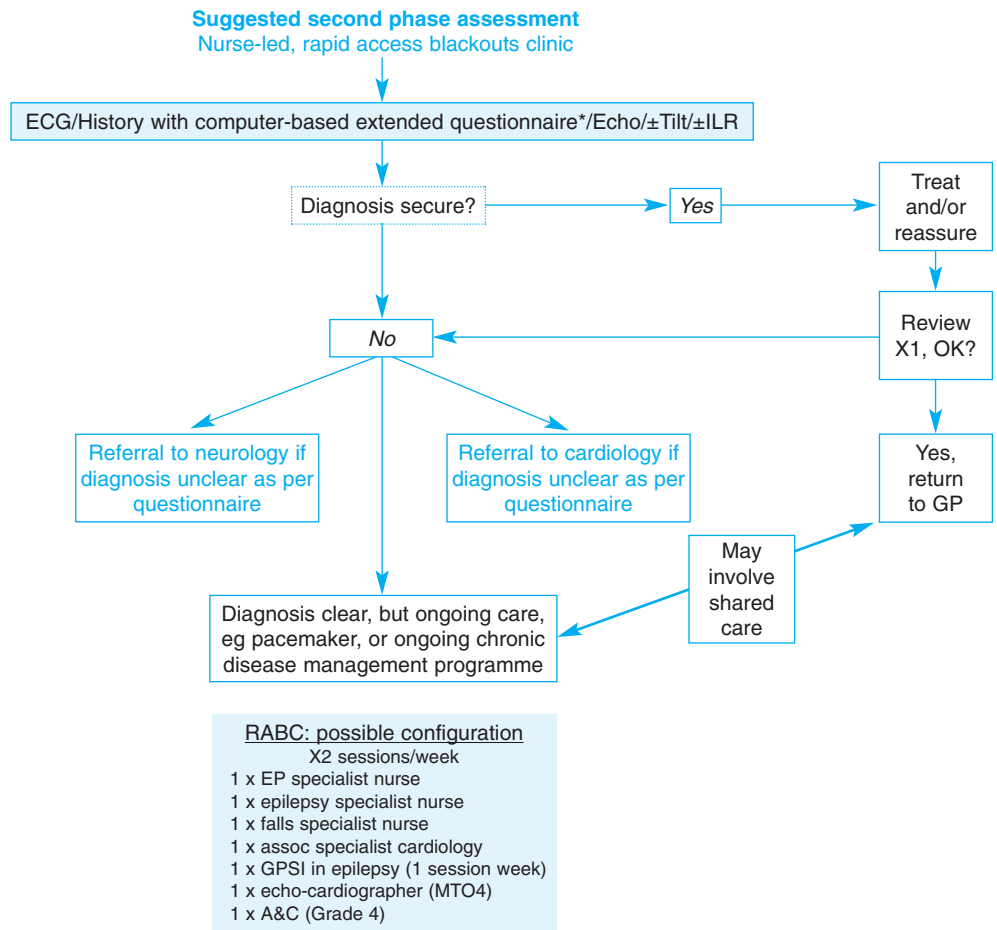
EEG is commonly requested in suspected epilepsy. However, it is not a diagnostic test, since the yield from an interictal EEG is low. It is more helpful in diagnosing epilepsy in the younger population (<35 years),⁷ and when undertaken within 48 h of an epileptic attack. All adults should undergo imaging of the brain. An MRI of the brain is the investigation of choice and should particularly be undertaken when there is suggestion that the epilepsy may be focal in onset or is not responding to first-line therapy. Mesial temporal sclerosis is the most common cause for seizures in adults and can be easily diagnosed on an MRI scan.

Treatment

Starting treatment for epilepsy is a major commitment, as once started, it is often difficult to withdraw, and epilepsy treatment cements a diagnosis of epilepsy. Before starting treatment, a diagnosis must be beyond any reasonable doubt, and careful thought must be given to the prognosis of epilepsy in the patient, the risk to the patient from untreated seizures, the effectiveness and side effects of antiepileptic drugs, and the effect of treatment on the patient’s life, eg driving, employment and recreation. All these issues need to be discussed fully with the patient and family if needed. Patients diagnosed with epilepsy need to be given adequate information on what seizures are, trigger factors, the need to record the frequency of seizures, the

Fig 4. Hospital service: rapid access to blackouts triage.⁷

*Computer-based, nurse-administered, structured interview with extended question database and embedded video clips for eye-witnesses. ECG = electrocardiogram; Echo = echocardiogram; EP = electrophysiology; GPSI = General Practitioner with a Special Interest; Tilt = tilt table; RABC = rapid access blackouts clinic.



need for regular medication, the side effects to look for, drug interactions and lifestyle advice, including alcohol, safety and driving. Women especially need to be given information regarding contraception and the effect of antiepileptic drugs in pregnancy.⁷ All information needs to be given in an accessible format and the role of an epilepsy liaison nurse cannot be overemphasised.

Assuming that there is no misdiagnosis of epilepsy, approximately 25–30% of all epileptics will show resistance to drugs. However, the number of these patients who do not have epilepsy is not known. Epilepsy is most common when there is an underlying structural lesion of the brain or in patients with learning difficulties. It is advisable to avoid combinations of two or more antiepileptic drugs. Patients with focal-onset seizures and refractory epilepsy may be suitable for epilepsy surgery and therefore benefit from referral to an epilepsy specialist.

Misdiagnosis

Many studies have highlighted the issue of misdiagnosis of epilepsy.³ Though studies were conducted in different settings – general practice, community-based and hospital outpatients – they show consistently that about 25% of patients diagnosed with epilepsy are misdiagnosed. Usually, it is cardiac syncope

that is misdiagnosed as epilepsy. As the prevalence of epilepsy in the UK is about 0.7%, this means around 100,000 patients who are currently labelled as suffering from epilepsy do not have this condition. Patients with T-LOC and suspected epilepsy rarely need to commence treatment urgently, and it is better to wait for further information, or the results of long-term monitoring, than to make a hurried diagnosis of epilepsy which is difficult to reverse.

Non-epileptic disorders

Non-epileptic attacks occur in approximately 3% of the general practice population, among 13% of referrals with poorly controlled epilepsy and among 50% of referrals with status epilepticus. Most non-organic attacks mimic tonic clonic seizures, more rarely syncope. Truly uncontrolled epilepsy occurs infrequently and is usually encountered in patients with neurological impairments, learning disability, abnormal brain structure, abnormal interictal brain function and where there is a history of neurological injury or insult. Non-epileptic attacks are more prone to occur in females, where there is a history of self harm or self poisoning, in those with a history of childhood abuse or in those who come from a dysfunctional family background. Capturing an actual attack, eg by videotelemetry, reassuring the

patient, withdrawing treatment when it is not needed, offering continued follow-up and getting a well-informed psychological or psychiatric opinion help to solve the problem in the majority of cases.

Conclusion

The diagnosis of a patient with blackouts/T-LOC is challenging. Careful history taking remains the cornerstone of the clinical diagnosis whether the blackout is due to syncope, epilepsy or psychogenic causes. Investigations between episodes may not be helpful in many patients and misdiagnosis of blackouts is common.

Suggested care pathways, depending on which medical or paramedical person is the first point of contact, are shown in Figs 2–4.⁸

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