INVESTIGATION OF BLACKOUTS / TRANSIENT LOSS OF CONSCIOUSNESS (T-LOC)

KEY POINTS:

1. It is widely assumed that most blackout/T-LOC is due to a neurological cause, and this is quite wrong. Most instances of blackout/T-LOC are probably due to Reflex Syncope, and misdiagnoses are common.
2. Syncope is commonly associated with abnormal movements, (and even urinary and faecal incontinence), and these are mistaken for the generalised convulsions of epilepsy. This misunderstanding leads to a major problem of the misdiagnosis of epilepsy, that may affect over 100,000 patients in the UK alone, and costs the NHS nearly £200m each year.
3. Arrhythmias are an important cause of blackout/T-LOC at all ages and also commonly mimic epilepsy, similarly leading to a misdiagnosis. In children and young adults, life-threatening arrhythmias may present with a blackout/T-LOC. Many such patients are referred to neurological services, and in the UK, they do not routinely get an ECG and appropriate report. In some cases this has lead to a missed-diagnosis of the congenital Long QT syndrome and subsequent sudden cardiac death.
4. Patients with structural heart disease and blackout/T-LOC may be at high-risk for sudden cardiac death, and should be referred urgently to a cardiologist.
5. Patients with a blackout/T-LOC during exercise may be at high-risk for sudden cardiac death and should be referred urgently to a cardiologist.
6. Elderly patients who fall may have had blackout/T-LOC, but experience retrograde amnesia and only recall the fall. The precipitating cause, such as an arrhythmia may therefore go untreated, leading to recurrences. Falls cost the NHS over £1bn each year.
7. With Government initiatives in Falls, Epilepsy and Arrhythmias, there is a danger that services for patients with blackout/T-LOC will be fragmented and duplicated. At secondary and tertiary care levels services should be 'joined-up' for all patients with blackout/T-LOC, to ensure rapid correct diagnosis and treatment, efficiency and cost-effectiveness. This should also help ensure that no patient gets 'trapped' in an inappropriate care-pathway.

INTRODUCTION

T-LOC is a very common symptom, affecting up to 50% of the population at some stage of life. It causes 3% of casualty attendances, and 1% of all admissions to hospital [1]. T-LOC has many causes, and patients with T-LOC often have a prolonged stay in hospital. More and more costly investigations typically yield fewer and fewer diagnoses [2]. Conditions causing T-LOC include syncope, such as occurs with cardiac arrhythmia or reflex syncope. Another, very different and important cause of T-LOC is epilepsy.

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DEFINITION OF TRANSIENT LOSS OF CONSCIOUSNESS

Transient loss of consciousness (often referred to by patients as a "blackout", or more correctly, T-LOC*), is defined as *"spontaneous, transient, complete loss of consciousness with complete recovery".*

CAUSES OF BLACKOUT/T-LOC

- syncope is due to **dysfunction of the cardiovascular system**, causing by transient global cerebral hypoperfusion [3]
- epilepsy is due to **dysfunction of the brain**, caused by primary inappropriate discharge of cerebral neurones, or a neurological disorder, which results in recurrent seizures [4]
- psychogenic blackouts, and these are due to a **dysfunction of the psyche**, with T-LOC produced or caused by psychic or mental factors rather than organic factors [5]

In these three causes:

- 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 T-LOC

Syncope frequently masquerades as epilepsy, because abnormal limb and facial movements are quite common with syncope, (convulsive syncope). Other phenomena such as tongue biting and urinary incontinence, often associated with epilepsy, also occur with syncope. It is also clear that doctors commonly believe that T-LOC usually indicates a primary brain dysfunction, whereas the large majority of T-LOC episodes are probably due to Reflex Syncope. Such misunderstandings can lead to a misdiagnosis.

IMPORTANCE OF A CORRECT DIAGNOSIS

T-LOC occurs across the full age spectrum of the population. Critical to the cost-effective management of T-LOC is a correct diagnosis of the underlying cause, but up to 50% of patients with T-LOC leave hospital without a diagnosis [2], and many have recurrences thereafter [6-7]. Further, there is a strong evidence-base to show that there are high rates of misdiagnosis of transient loss of consciousness [8-9]. This is so for all age groups but is particularly relevant at extremes of age. In childhood there may commonly be a misdiagnosis of 'epilepsy' [10], and old age misdiagnosis of transient loss of consciousness as a 'fall' [11]. Both of these situations are of specific concern to NICE at present, in the Guidelines for Epilepsy and the Guidelines for Falls. However, neither draft guideline has so far sufficiently emphasised the diagnostic difficulties, and the common problem of misdiagnosis. Misdiagnosis may occur with rates up to nearly 40% [12-13].

SIGNIFICANCE OF A MISDIAGNOSIS

Misdiagnosis results in ineffective treatment, subsequent symptom recurrences, and high cost, with an annual cost in the UK of up to £189m [14]. A misdiagnosis of epilepsy occurs in 20-30% of 'epilepsy' patients [9]. This misdiagnosis potentially carries a very high social cost, and drug treatment may damage the unborn child [13]. Sudden death is a relatively high risk in epilepsy, and some cases of SUDEP, (sudden unexpected death in epilepsy), have been due to unsuspected cardiac arrhythmias [15]. The overall

risk of sudden death in epilepsy is estimated to be 3 times normal, and is probably up to 15x higher in younger patients, and appears to be seizure-related, with poorly-controlled seizures conferring a 23-fold increase in the risk of sudden death [16]. Risk factors include poorly-controlled seizures, where drugs are being taken, but not working well, and poor drug-compliance, (where epilepsy drugs are not actually being taken when they should be).

Primary cardiac arrhythmias may cause syncope, which may be mistaken for epilepsy. This often occurs when syncope is accompanied by abnormal movements, which are caused by a temporary lack of blood flow to the brain. Typically, in adults, these movements are jerking and myoclonic, rather than the tonic-clonic movements seen in true epilepsy. However, young patients with Reflex Anoxic Seizures (RAS)[21] have been described as having tonic/clonic movements. Nevertheless, it can be very difficult to distinguish an epileptic seizure from convulsive syncope caused by cerebral anoxia, both for professional or lay people. In reality, however, the underlying mechanisms are completely different. In epilepsy there is a primary disorganised action of brain cells that causes T-LOC with preserved blood flow to the brain. In convulsive syncope, there is T-LOC due to transient global cerebral hypoperfusion, and abnormal movements are due to the irritant effect of cerebral anoxia. Misdiagnosing epilepsy in such cases, and prescribing anticonvulsants, is unlikely to lead to any real pharmacological response, although placebo effects and random variation in seizure frequency could lead to apparent responses. Equally, in Reflex Syncope, many patients exhibit a spontaneous resolution of symptoms, just with investigation, diagnosis and reassurance alone [17]. However, resolution of syncope could be misconstrued as a response to epilepsy drugs, and a failure to respond could be misconstrued as resistant epilepsy. In these cases, multiple drug regimes are likely to be commoner, as is the use of newer and more expensive anticonvulsants. Poor drug-compliance may also be commoner, as patients perceive no benefit to weigh against side effects.

Another common clinical problem is that doctors often assume that ***any*** T-LOC must have a neurological basis, even when the episodes are not convulsive. In reality, reflex syncope is probably far more common than true epilepsy.

In old age, evidence suggests that T-LOC often leads to collapse, but many elderly patients often do not report a blackout prior to falling [18]. Often this is due to retrograde amnesia for the moments leading up to the collapse. Some elderly patients also exhibit reluctance to admit to a more frightening or embarrassing collapse, rather than a trip or fall. Consequently, a patient may be treated for a fall when the precipitating T-LOC remains undiagnosed and untreated. A misdiagnosis of falls in the elderly may result in recurrent fractures, loss of independence and high costs of hospital and social care, as well as high morbidity and mortality [20]. Falls are thought to cost £1bn per annum in the UK. In children, T-LOC is routinely considered to be caused by epilepsy, but Reflex Syncope, again, is probably more common. Epilepsy Action, a patient group, has stated that 40% of epilepsy in children is misdiagnosed. Reflex syncope in children commonly manifests as “reflex anoxic seizures”, now more correctly referred to as ‘reflex asystolic syncope’ (RAS) with prolonged cardiac asystolic pauses, and as other phenomena, such as “white breath-holding attacks” [21]. However, such attacks are not epilepsy, because they are a primary cardio-respiratory disturbance, not a primary disturbance of the brain.

Unfortunately, the cause of T-LOC in children, adults and the elderly is often very difficult to determine. This is because episodes typically occur when there is no objective physiological monitoring of brain and cardio-respiratory activity. In patients diagnosed with epilepsy, up to 70% have a normal electroencephalogram (EEG) between seizures [22]. Non-specific EEG abnormalities may be reported, and there is a

**T LOC is the preferred terminology of the European Federation of Neurological Societies working group on terminology*

danger that these will be over-interpreted to arrive at a diagnosis of epilepsy. The vast majority of patients with T-LOC will have a normal brain scan, but equally, innocent incidental anatomic abnormalities may be found and used to support a diagnosis of epilepsy.

By avoiding a misdiagnosis of epilepsy, other savings may accrue in primary care drug budgets by avoiding inappropriate use of costly anti-convulsants. In patients with a misdiagnosis of epilepsy where simpler drug therapy is ineffective, the newest and most expensive anti-convulsants are often prescribed, frequently in multi-drug regimes. A good example of such inappropriate management exists in the Hulton case from Leicester. Staffing levels for neurology in the UK are very low compared to Western Europe. In the UK there is a shortage of neurologists, with just five per million. Germany has 12 per million, France 15, Spain 23 per million and Italy 71 per million.

Other patients found to have Reflex Syncope, not epilepsy, may respond to cardiac pacing [23], (see Chapter 12). This costs £300-£600 per annum, where treatment with a single newer anti-convulsant may cost £1,600-£2,000 per annum. A correct diagnosis and effective treatment may control recurrent admissions that often prompt repeated investigation but no definitive diagnosis. Even without injury, such re-admissions are costly. One prospective study showed that unexplained T-LOC cost £2,500 per patient over an average 9-day admission to hospital, or £10,000 at today's prices, while 50% of these patients were discharged without a diagnosis [2]. The cost of investigation where the diagnosis was unclear after simple bedside investigation was x10 higher [2]. Patients diagnosed with epilepsy have to cope with problems in education, employment, childbearing, driving and life-insurance. The health and social costs of epilepsy are very high, and the costs of a misdiagnosis of epilepsy are unnecessarily high.

Of crucial importance is the exclusion of the Long QT syndrome in causing T-LOC. Long QT Syndrome is usually an inherited condition has at least 6 genotypes, (patterns of abnormal heart genes) with 3 syndromes commonly recognised. The abnormal genes disturb the smooth recovery of the heart muscle after each beat, by upsetting the way that small charged chemicals, or ions, travel to-and-fro across the muscle cell membranes with each beat. This can lead to electrical blips that can trigger rapid firing of the muscle cells and lead to a tachycardia. This tachycardia is commonly disorganised and very dangerous because it easily leads to ventricular fibrillation, which causes death within minutes if not immediately treated by shock therapy. Episodes of the malignant tachycardia are often induced by an emotional shock, such as the sudden ringing of a door-bell in the middle of the night. This is because the ion-channel abnormalities are very influenced by the autonomic nervous system, a network of nerves that influences the heart and other organs. This tachycardia, which can be torsades des pointes or polymorphic ventricular tachycardia, is quite often self-terminating. This is probably because the ion-channels get tired before ventricular fibrillation can occur. Because of all these factors occurring together, Long QT Syndrome is an important cause of T-LOC, and it occurs in young people. There may commonly be a history of sudden cardiac death at a young age in the patient's extended family. It is often missed if it is not considered, and the minimum investigation is at least 3 12-lead ECGs, appropriately reported, at different times where the condition is suspected.

MANAGING T-LOC

T-LOC patients present to primary care, secondary care electively and through the ambulance service and Emergency departments, and tertiary care.

- The first principle of managing T-LOC is to maintain an open mind and not to assume that all T-LOC is due to a primary neurological dysfunction. Indeed, most T-LOC is probably caused by Reflex Syncope, and many classic features of epilepsy, such as urinary incontinence, thrashing limbs and tongue-biting also occur in convulsive syncope

Primary Care Questioning:

- Are there typical epilepsy features? For example; generalised convulsions with tonic-clonic movements, cyanosis due to impaired breathing, incontinence, lateral tongue biting and prolonged confusion upon waking
- Are there typical Reflex Syncope features? For example; faintness prior to blackout, extreme pallor, random jerking of limbs and face, (myoclonus), and rapid recovery of orientation upon waking. There may also be nausea, vomiting, violent intestinal movement, sweatiness and flushing before/during/after the episode. A very pale colour is common, hence witnesses think the patient has died. RAS is also known as Pallid Syncope
- Do symptoms suggest a cardiac arrhythmia? For example; a very brief T-LOC with a collapse and an immediate recovery. Arrhythmias don't have a vasodepressor component like Reflex Syncope, and hence they may recover more quickly
- Have other family members had 'childhood epilepsy' or "only ever had an attack if they hurt themselves"
- Is there a history of underlying heart disease?

Primary Care Investigation:

- ECG & chest X-ray looking for evidence of structural heart disease
- Further cardiac tests, such as echocardiography should be obtained if there are any doubts about the presence of structural heart disease
- T-LOC during exercise may be due to an underlying cardiac disease and/or an arrhythmia, and warrants prompt investigation at secondary or tertiary level to exclude structural heart disease and to attempt to reproduce symptoms during supervised controlled exercise

A resting 12-lead electrocardiogram, with appropriate report, is mandatory.

Secondary Care Investigation:

- All the principles of management of T-LOC in primary care hold true for secondary care through outpatients, inpatients and Emergency Departments
- Secondary care may be better equipped to exclude electrocardiographic abnormalities, such as the Long QT Syndromes, or heart muscle diseases such as the cardiomyopathies. These may give rise to arrhythmias that cause T-LOC. Many salutary cases exist where epilepsy has been diagnosed and treated but an underlying cardiac disease has been missed
- Secondary care settings are an easier environment for investigation of possible intracerebral pathology, such as brain tumours in new cases of T-LOC without a history of brain injury.
- Secondary care settings offer an opportunity to refer onward for a specialist opinion which, currently in the UK, usually involves neurological evaluation but seldom involves cardiological evaluation. Since most T-LOC is probably due to Reflex Syncope this may not be the best use of resources, and reflects the widespread misunderstanding of the common causes of T-LOC, and the overlap of clinical features between epilepsy and Reflex Syncope
- Most patients with T-LOC *will not* have an obvious arrhythmia or arrhythmic substrate, *will not* have had a brain injury, and *will not* have a reliable eye-

witness account of their T-LOC that can absolutely rule-in or rule-out a definite underlying cause.

- Most investigations undertaken after a T-LOC has completely recovered *will not be diagnostic*, including an ECG, an EEG, a 24hr ambulatory ECG tape and brain scanning
- Triage of T-LOC patients in primary, secondary and specialist care will often depend on clinical evaluation without the aid of diagnostic technology to remove significant doubt
- A presumptive diagnosis of epilepsy, followed by a trial of anticonvulsants should be avoided, unless epilepsy seems very likely
- A trial of anticonvulsants imprints a diagnosis of epilepsy, and should be avoided until ***all other*** investigation/care pathways have been exhausted
- Up to 30%, possibly more, of patients with a diagnosis of epilepsy are misdiagnosed, others may have a spontaneous resolution of T-LOC falsely attributed to anticonvulsant therapy
- T-LOC during exercise may be due to an underlying cardiac disease and/or an arrhythmia, and warrants prompt investigation to exclude structural heart disease and to attempt to reproduce symptoms during supervised controlled exercise

A resting 12-lead electrocardiogram, with appropriate report, is mandatory.

Specialist/Tertiary Care:

- Specialist evaluation should be sought for patients in whom the cause of T-LOC is in any doubt, rather than a diagnosis being made when there are significant doubts thereby avoiding imprinting a false diagnosis.
- NICE guidelines will require such referrals to neurologists to be seen within one month
- Cardiologists will aim to exclude underlying significant structural heart disease that makes an arrhythmia more likely
- Cardiologists will have access to more prolonged ECG monitoring for arrhythmias, including implantable ECG monitors, (Implantable Loop Recorder - ILR)
- Cardiologists will have access to tilt-table testing which may be useful in confirming a cause of T-LOC, and can be shared
- Neurologists may have access to video-telemetry for the diagnosis of T-LOC
- T-LOC during exercise may be due to an underlying cardiac disease and/or an arrhythmia, and warrants prompt investigation to exclude structural heart disease and to attempt to reproduce symptoms during supervised controlled exercise

Accident & Emergency Care:

The temptation is always to admit patients with T-LOC to hospital when they present to casualty departments, as many do. Patients who are obtunded, for example, patients with known epilepsy, may be incapable of being discharged safely. Some elderly patients may need admission primarily for social reasons, even if there is no evidence of an ongoing threat from discharge. The overwhelming majority of patients admitted to casualty departments with T-LOC who have a diagnosis made, have it made “at the bedside” by simple thorough clinical evaluation and inexpensive tests, particularly an ECG, if accompanied by an appropriate report. Published series show that patients who are admitted in the absence of a diagnosis made this way have an average hospital stay of 9 days, and have a low yield of costly investigations such as brain scanning, electroencephalography and cardiac electrophysiological study [2 37]. The average cost of a diagnosis made by complex tests, (which have a low yield anyway), is ten times the average costs of admission for all such patients [2]. Furthermore, many

series have showed that a substantial proportion of patients admitted to hospital for T-LOC are discharged from hospital with no diagnosis. This was 50% of patients in one series [2].

In T-LOC, most diagnoses are made clinically or with simple tests. Admission and costly investigation is often unhelpful. In the absence of an unsafe reason for discharge, significant social of other reason for admission, or injury, the value of admission should be questioned in the absence of a diagnosis made simply. Rapid access to nurse-led T-LOC clinics, with medical backup and early specialist review, may reduce the number of unhelpful and unnecessary admissions.

VALUE OF LABORATORY INVESTIGATIONS & USE OF TECHNOLOGY TO MAKE A DIAGNOSIS

At all levels of care the mainstay of diagnosis in T-LOC/blackouts is a thorough clinical evaluation, and a willingness to question a diagnosis and seek help from others where a diagnosis is in some doubt. Some patients, and eyewitnesses to episodes, may give a history that leaves little doubt that the episodes are caused by Reflex Syncope, by epilepsy, or indeed are genuinely due to a fall without T-LOC in elderly patients. However, in most patients there is doubt, especially because of growing awareness that "classic" features of Reflex Syncope or epilepsy are increasingly recognised to occur with another phenomenon. Examples include urinary incontinence and tongue-biting that may occur in convulsive syncope. Abnormal movements usually associated with epilepsy also commonly occur in syncope where cerebral anoxia, (lack of oxygen to the brain because of lack of blood flow to the brain), causes irritation to motor neurones and myoclonic jerking of the limbs, eyes and face.

When syncope is clearly the cause of T-LOC, the European Society of Cardiology Guidelines on Syncope, produced by the ESC Task Force on Syncope [17], provide good guidelines about the use and value of technology and laboratory investigations.

Where epilepsy is clearly the cause of T-LOC, the UK NICE Epilepsy Guideline, currently in preparation, should provide guidance for investigation and management [14].

Problems with laboratory investigations and the use of investigative technologies arise when the cause of T-LOC is unclear. The "grey-area" is probably substantially the largest group, when patients are considered overall, managed at all levels of care, and bearing in mind that many patients are discharged from hospital after acute admission with T-LOC, without a clear diagnosis [2].

Three types of investigative data can be gained:

- Spontaneous recordings of physiological data during an episode
- Recording of physiological data during a provoked episode
- Recording of background physiological data without symptoms

KEY PHYSIOLOGICAL MEASURES

The key physiological signals are:

- The electrocardiogram, giving heart rate and rhythm
- Blood pressure
- The electroencephalogram

RECORDING OF SPONTANEOUS EPISODES

With conventional technology, the chance co-incidence of recording of some or all of the key physiological data during a typical episode of T-LOC is very unusual.

A 24-hour continuous ambulatory ECG recording in T-LOC has a very low yield and a very low cost-effectiveness. Published work suggests that the yield is <1% [25]. The inter-ictal EEG is commonly non-diagnostic between seizures [10]. Blood pressure may be taken and recorded by a bystander by chance if they have the necessary equipment, time and presence of mind, but this combination is rarely present. Video-telemetry may capture an episode. With this technique a patient is admitted to hospital, continuously connected to an electroencephalograph and ECG, and continuously video-taped in a their room. Whilst this may capture and confirm epilepsy, periods of up to 6 weeks hospital admission may be needed, and it is very onerous for staff and patient, and very costly with limited availability.

By far the most effective form of monitoring is with the implantable ECG loop-recorder. This is implanted under the skin near the heart, and has an 18 month battery-life, and continuously monitors the heart rate and rhythm. The device is implanted under local anaesthetic in a 10 minute procedure. In one single centre experience of over 350 implants, over 85% of patients had symptom/ECG correlation in under 6 months. The device has a continuous rolling ECG memory, unless the device is activated by automatic or patient-activation. Automatic activation occurs when the heart rate goes below or above certain pre-programmed rate limits, and is prone to false activation by artefact. Much more valuable is patient-activation using a small external hand-held activator. Because the device has a rolling retrospective memory for up to 42 minutes, patients are usually able to recover from a blackout and activate their device. This freezes the memory for the last 42 minutes of ECG in a solid-state memory. This remains in the memory until the patient has the episode downloaded, or the battery runs out. Downloading is with a standard pacemaker programming computer, and the final product is a high-quality ECG recording for up to 42 minutes prior to activation and 2 minutes after activation.

There are three important limitations of this technology:

- There is no information about blood pressure and the electroencephalogram.
- The second limitation is that doctors dealing with T-LOC patients have been reluctant to part with their trusted methods of working up T-LOC patients, and embrace an implantable technique.
- The third is the apparent high cost.

Because the ILR cannot give information about blood pressure and the EEG, many causes of T-LOC will not be proven. Negative ECG results are valuable, however, because they rule out an arrhythmia as the cause of spontaneous T-LOC. However, the device is very ***cost-effective***.

In one unpublished series of 350 patients implanted, ILR results were compared to a similar number of patients studied with conventional external ECG monitoring. Conventional ECG monitoring was approximately 4.5 times as costly as the implanted device. This was because although the ILR was expensive to buy and implant, (about £1,500), but much more effective at capturing a symptom/ECG correlation, it was therefore very cost-effective. External ECG monitoring, (approximately £75 per tape), was cheap to perform, but has a very low yield, and therefore was very ***cost-ineffective***.

Major strides have been taken forward as a result of the ILR used in specific research studies. In one study it was made very clear that in patients with bundle branch block (BBB) and syncope, paroxysmal complete heart block was very commonly recorded by the ILR at the time of recurrences. This should now lead to patients with BBB and syncope receiving a pacemaker instead of many other unnecessary, costly and ineffective investigations [36].

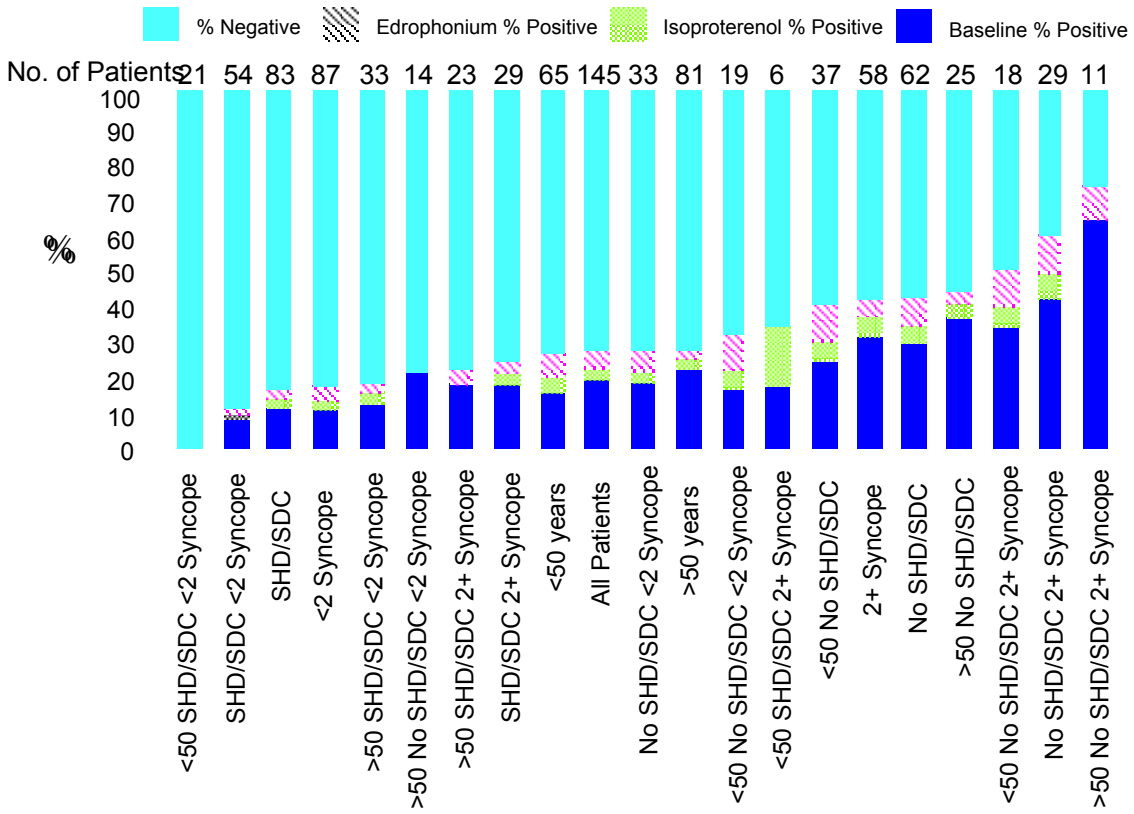
In laboratory testing in T-LOC, the best and most reliable data are obtained where there is a spontaneous recurrence of typical symptoms during the recording.

RECORDING OF PROVOKED EPISODES

More useful information may be obtained by undertaking provocative laboratory testing. Tilt-table testing has become one of the mainstays of investigation over the last 20 years. In suspected Reflex Syncope, this may be useful [26 27], and increasingly it is common for neurological workup to include head-up tilting. However, early series reported widely different yields of tilting, ranging from 20 to 75%, and many different protocols were introduced to try and increase the sensitivity of the test [28-32]. Tilt-table testing has important limitations that are not always fully appreciated. As with any provocative test, there is a limited specificity and sensitivity, and therefore a limited positive and negative predictive value of the test in indicating the true cause of a spontaneous event. This value is dependant upon the pre-test likelihood of achieving a positive or negative result. Tilt-table testing provokes a dramatic reflex syncopal response in some patients, which commonly has a component of very low blood pressure due to dilatation of peripheral arterioles, mediated by sympathetic nervous withdrawal, (vasodepression), and slowing of the heart, mediated by activation of the vagus nerve. In about 15% of positive tests, there is complete cardiac standstill, (cardiac asystole) for a period of seconds. A schedule has been drawn up to classify these different reactions, (VASIS), but this has limitations [33]. Tilt-table testing is not very reproducible over time, and the type of positive response is not reliable, making it difficult to use as a guide for treatment [33]. However, false positive rates, when syncope is induced during a tilt test in patients used as control subjects, who clearly have another reason for their blackouts, are about 10%[34].

In “all-comers” with T-LOC, the overall diagnostic yield of tilt-table testing is around 25-35% [35 36]. In patients with T-LOC and a very low pre-test likelihood, tilt-test positive responses are very low. In patients with a high pre-test likelihood of a positive test tilt-test, tilt-induced syncope is much more likely [36]. This is illustrated in Figure 1. The added yield of drug provocation over prolonged baseline tilt-testing without drug provocation is probably 10-15% across a variety of groups with both low and high pre-test likelihood of a positive test [36]. Some of these responses may be false positives. The number of true negative responses to tilt-testing, (where the tilt-test is negative because patients have another cause for their T-LOC), is unknown, because there is no “Gold Standard” laboratory test for diagnosing Reflex Syncope with which tilt-testing can be compared.

Figure 1. Yield of head-up tilt-testing. 'All-comers', (145 patients with blackout/T-LOC), had an overall yield of 20% for provoked Reflex Syncope during baseline tilt, which was increased to about 27% by additional drug-provocation. Patients with a low pre-test likelihood of a provoked Reflex Syncopal response, (left side of graph), had a low yield from the test. Patients with a high pre-test likelihood of a provoked Reflex Syncopal response, (right side of graph), had a high yield from the test. Additional yield of drug provocation was similar in all groups. (From Fitzpatrick A P et al HEART 1996; 76: 406-411)



In laboratory testing in T-LOC, ECG, blood pressure and EEG data recorded during a provoked episode should be treated with caution. Provocative testing in patients who are likely to have a positive test will have a high yield, and provocative testing in patients who are unlikely to have a positive test will have a low yield. Attempts to increase the yield of provocative testing always increases the risks of a false-positive result. Such a false-positive result could lead to a misdiagnosis and inappropriate treatment.

RECORDING OF BACKGROUND DATA

The greatest danger in laboratory testing in syncope is that innocent or incidental findings on testing might be over-interpreted in the absence of corroborative simultaneous recurrence of syncope at the time of the test. With ambulatory ECG monitoring, arrhythmias may be found that suggest a cause, but these may be over-interpreted. ***This can lead to a misdiagnosis and inappropriate treatment***. Arrhythmias on ECG monitoring should be accompanied by a recurrence of typical symptoms, (i.e. T-LOC), in order to influence management, unless the findings are very striking and repetitive, or the presence of co-morbidity, e.g. heart failure, makes treatment sensible for other good reasons. Arrhythmias in normal hearts are commonly found on ECG monitoring. Sinus pauses are found in 4% of normal healthy medical students [38], and non-sustained ventricular tachycardia is found in 2% of healthy elderly patients [39]. Worse still, it should never be assumed, in any patient, that the absence of significant arrhythmias on 24hour ECG monitoring indicates that the cause of T-LOC is not an arrhythmia. This is especially true of patients at risk of arrhythmias, for example, patients with T-LOC, previous myocardial infarction and

impaired left ventricular function, who are at risk of life-threatening ventricular arrhythmias. Rather, it should be realised that a short period of ECG monitoring without recurrent symptoms is an inadequate diagnostic technology.

In just the same way, non-specific findings of an EEG could be over-interpreted by non-experts as indicative of a likely diagnosis of epilepsy, and a misdiagnosis could result. Equally, many patients with epilepsy may have a normal or near normal inter-ictal EEG [10].

Background physiological laboratory data recorded in T-LOC patients in the absence of spontaneous recurrence of symptoms should be treated with great caution, and never used alone to make a diagnosis.

STRUCTURING RESOURCES TO GET THE BEST RESULTS

The differential diagnosis of T-LOC very often depends upon clinical evaluation without corroborative, objective evidence. Emphasis needs to be placed on collaborative working between professionals in clinical care. A great deal of benefit can be derived from collaboration between cardiologists, neurologists and doctors investigating Falls in secondary and tertiary care.

NICE guidelines are being developed in two keys areas, the management of epilepsy and the management of falls, and the NSF for Heart Disease is now addressing Arrhythmias. However, patients with T-LOC may come under the care of disparate clinicians following guidelines for epilepsy, falls and arrhythmias. Joined-up thinking is needed to derive a correct underlying diagnosis quickly, efficiently and cost-effectively, and tailor a management plan to suit the true diagnosis.

Medical and nursing resources will be provided through doctors, Trusts and commissioners following the guidance of these different documents. These agencies need to work together to share resources, collaborate in clinical evaluation and make decisions together. Some resources, such as tilt-table testing, may be useful to cardiologists, neurologists and Falls Clinics, and where this is the case, shared resources should be set up, and specialist nurses and medical staff should team-up.

At consultant level, it is desirable to have a colleague with the fresh perspective of a different specialty to see a difficult diagnostic problem in T-LOC. This is much better than to resort to a trial of drug treatment that might unwittingly impart a false diagnosis.

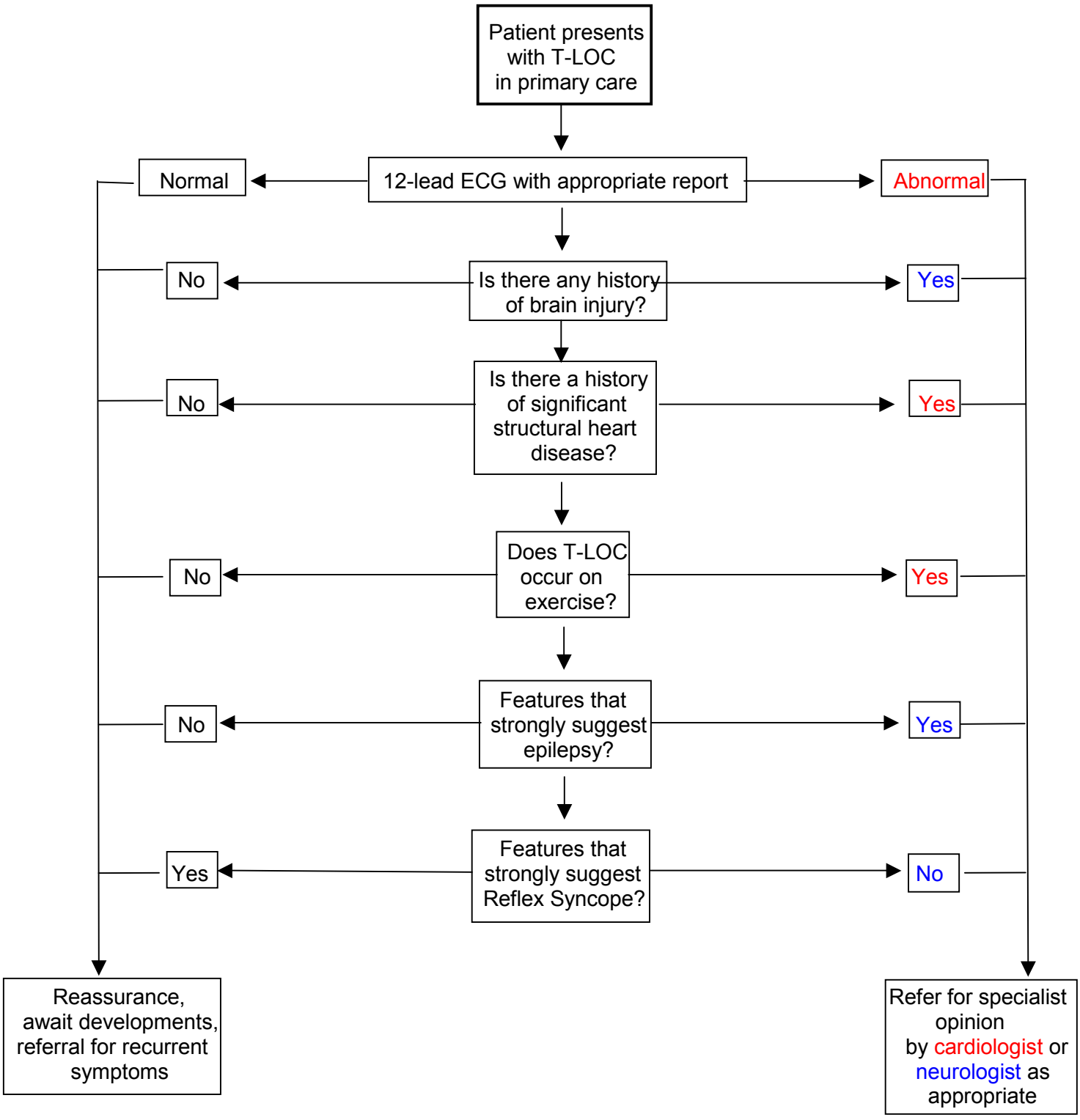
T-LOC Teams:

- Doctors and nurses looking after T-LOC patients should seek to collaborate with other doctors and nurses with similar patients in other disciplines.
- Resources set aside for managing epilepsy, falls and cardiac arrhythmias could be much more effective if they were shared, and a structure was in place for regular interaction in clinics, case-conferences, CPD and clinical audit.
- Primary care and emergency care systems should be encouraged to access such a T-LOC team where triage could be undertaken by specialist nurses to facilitate the most appropriate initial specialist opinion according to structured interview techniques, and schedule testing to try and establish a true diagnosis more rapidly and reliably.
- A DGH pilot scheme of specialist blackout/T-LOC nurse-triage has yielded good results and helped foster a collaborative interaction between local cardiologists and neurologists, and a further scheme is being planned to foster collaboration

between a PCT, A&E, cardiology, epilepsy and falls clinics, particularly fostering collaborative working between specialist nurses in cardiac electrophysiology, epilepsy and falls.

- One large city is trying to establish a "hub-and-spoke" network between local DGH teams of cardiologists and neurologists and a tertiary T-LOC team for more difficult cases.

A CARE-PATHWAY FOR PATIENTS WITH BLACKOUTS/T-LOC



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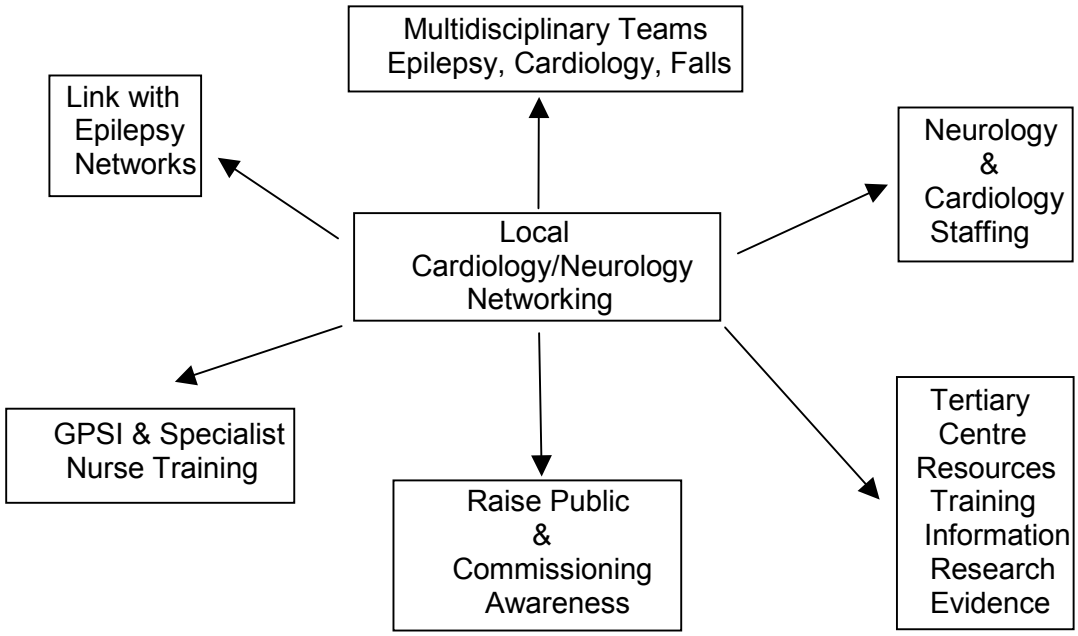
FOSTERING BETTER CARE FOR PATIENTS WITH BLACKOUTS

Improving clinical care for patients with blackouts depends upon:

- establishing collaborative clinical systems
- developing care-pathways for improved T-LOC diagnosis,
- providing readily available alternate care-pathways for T-LOC patients who are difficult to diagnose, to avoid patients "getting stuck" in the wrong care-pathway
- providing readily available alternate care-pathways for T-LOC patients in whom a diagnosis is in doubt
- providing readily available alternate care-pathways for T-LOC patients who still have on-going symptoms despite appropriate treatment

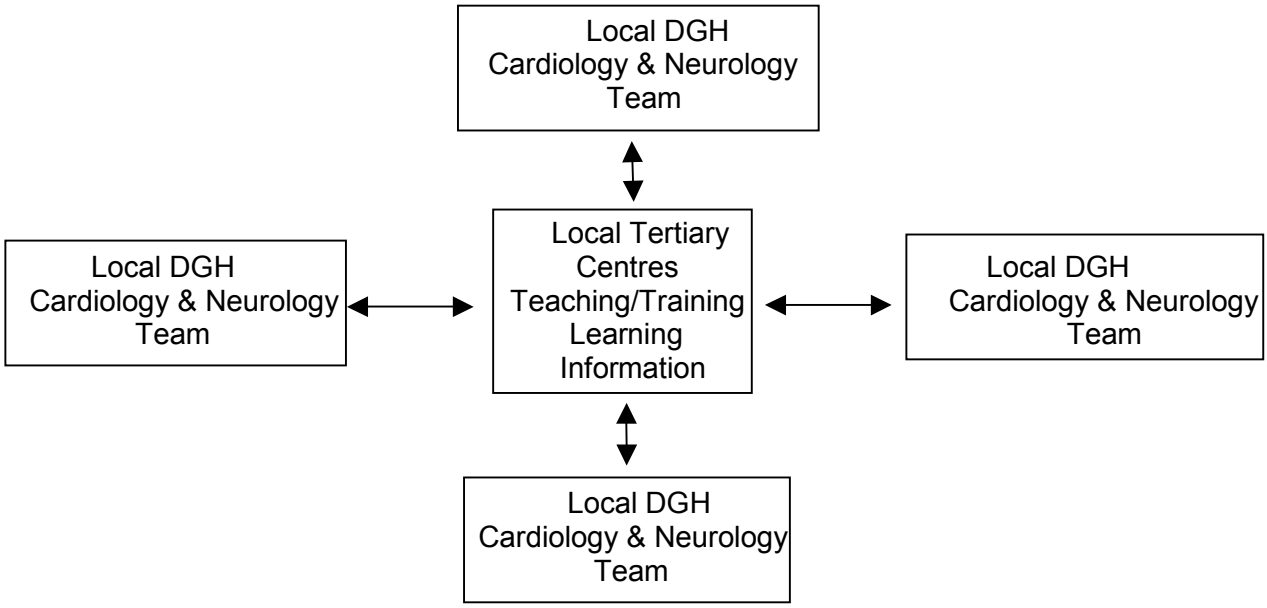
Good guidelines exist for the management of syncope, (European Society of Cardiology Task Force on Syncope Guidelines [17].), and the UK will soon have NICE Guidelines for Epilepsy [14]. These provide direction for care pathways once a diagnosis is secure. Links and networks should help create multi-disciplinary, multi-specialty teams and systems to arrive at a secure diagnosis more quickly, cost-effectively and successfully. These must develop at local level using the resources of General Practitioners with Special Interests, (GPSIs), Specialist Nurses and growth in the consultant workforce as available.

STRATEGIC ELEMENTS FOR IMPROVED BLACKOUTS CARE



LOCAL ELEMENTS FOR IMPROVED BLACKOUTS CARE

Local PCTs, primary care groups, secondary and tertiary care Hospital Trusts should endeavour to encourage local neurologists and cardiologists, GPSIs and Specialist Nurses in epilepsy, cardiology and falls, to share investigative resources, (e.g. tilt-table testing, electrocardiography and long-term ECG monitoring). They should establish mechanisms for triage of emergency admissions and elective referrals to the most optimum specialist opinion. Care pathways should be established, and no patient should fail to cross disciplines where a diagnosis is uncertain or symptoms continue despite treatment.



IMPROVING ACCESS, AWARENESS AND PATIENT INFORMATION

Patients deserve reliable, readily available information about their condition and how to access services to get help for symptoms and assessment of risks. This should be available in the form of leaflets and booklets, internet sites and help-lines. Patient advocacy groups and charities are at the forefront of Government thinking, and may take an increasing role in delivery of public services [24]. Patient advocacy and support groups and their websites, leaflets and help-lines should receive support in the form of public funding. Such groups should be encouraged to work closely with professional and allied professional groups. These include UKICES, (www.ukices.org), and BPEG. Such groups should also work on local implementation of services, with local professional groups, to assist audit, evaluate unmet need, and facilitate teaching and training in the Regions. These groups include NWREPG (www.nwrepg.com), SMEG, TPEG, LEPG. Charities such as STARS, (www.stars.org.uk) have made a huge contribution to advocacy for patients and families, and deserve the full backing of the Department of Health and the Government in taking on a more formal role in public service delivery.

STANDARDS FOR INVESTIGATION AND MANAGEMENT OF BLACKOUTS/T-LOC

Standard 1. Patients with blackouts and:

- no features of epilepsy
- no history of brain injury
- no underlying structural heart disease
- no T-LOC during exercise
- features suggesting reflex syncope

Should have reassurance and be referred to a Rapid Access Specialist Nurse-Led Blackouts Triage Clinic if symptoms become recurrent and interfere with normal life, education employment etc.

Such clinics should be established in every DGH and tertiary centre to pool resources required by NICE Guidelines for Falls and Epilepsy. These should underpin consultant-led specialist services in cardiology, neurology and care of the elderly, and ensure their most-efficient use within current workforce constraints.

Standard 2. Patients with blackouts and:

- a history suggesting epilepsy
- a history including brain injury
- no features of reflex syncope

Should be referred straight away to the Rapid Access Specialist Nurse-Led Blackouts Triage Clinic, or to a neurologist directly if local circumstances allow an early clinical evaluation.

Standard 3. Patients with blackouts and:

- underlying structural heart disease
- T-LOC during exercise
- Features suggesting a cardiac arrhythmia

Should be referred immediately to the Rapid Access Specialist Nurse-Led Blackouts Triage Clinic or to a cardiologist directly if local circumstances allow an early clinical evaluation.

Standard 4. Patients with definite syncope should be managed according to the Guidelines of the European Society of Cardiology Task Force Guidelines on Syncope.

Standard 5. Patients with definite epilepsy should be managed according to the NICE Guideline for Epilepsy.

Standard 6. Patients with suspected psychogenic blackouts should be investigated by head-up tilt-testing with continuous ECG, phasic blood pressure using digital plethysmography, and EEG. In patients with a blackout induced by tilting without disturbance of heart rate and rhythm, blood pressure and EEG, a psychogenic cause can be inferred.

Standard 7. Patients with blackouts should have at least one, high-quality, 12-lead resting ECG with an appropriate report. A computerised “normal” report is acceptable. Otherwise, the ECG should be reported by an experienced doctor.

Dr Adam P Fitzpatrick, Manchester Heart Centre

LAY SUMMARY

Not all blackouts (T-LOC) are due to a primary dysfunction of the brain, most blackouts are probably due to syncope, (sin-co-pee). Syncope occurs when the blood flow to the brain falls below a level where brain cells can continue to function normally. Brain cells become starved of oxygen and glucose and stop functioning. Patients then fall unconscious and typically fall to the ground. The cause of poor blood flow may be the triggering of reflexes in the circulation. These can cause the heart to slow right down or stop. They also cause blood vessels to open up suddenly. Pooling of blood then causes the blood pressure to drop, abruptly. Another cause of syncope is a heart rhythm abnormality. This may occur suddenly without warning, and can be due to the heart racing too fast, or beating too slow. In either case, the pumping action may become so inefficient that blood pressure falls very low as above, and patients can become unconscious. The commonest heart rhythm abnormality causing this is probably the heart going too slowly, (bradyarrhythmia). This is because of a transient fault in the electrical system that makes the heart pump work.

The treatment is the fitting of a permanent pacemaker under the skin near the collar-bone, with local anaesthetic in a short procedure. The UK puts in about 440 pacemakers per million, while Western Europe manages 900 pacemakers per million. In the UK the lower rates probably reflect in part, a shortage of trained doctors who can investigate blackouts and determine that they are due to a transient slow heart beat. Obvious problems of slow heart beat, for example those discovered in a casualty department, always receive a pacemaker in the UK, but a patient with a slow heart beat that is only transient, may not.

The treatment of a fast heart beat (tachyarrhythmia), depends upon whether a patient also has other significant problems with the heart, for example a previous heart attack. Patients with no other significant heart problems, whose only problem is a short-circuit causing a rapid heart beat, can be treated with simple drugs. Better still, if available, or if there are any problems with the drugs, patients should be referred to a heart rhythm specialist, (cardiac electrophysiologist). He/she will usually offer patients a catheter ablation procedure. This involves passing fine wires to the heart through the veins, identifying and the short circuit, and cauterising it through the skin. Catheter ablation is very safe and may cure about 95% of fast heart rhythms, avoiding the need for drugs treatments and restoring a normal life.

Patients with blackouts often have features that mimic epilepsy, such a twitching and even incontinence of urine. However, between 20% and 30% of patients with epilepsy are wrongly diagnosed. Patients in whom there is a doubt about epilepsy, or in whom epilepsy drugs are not working, should be referred to a cardiologist who should consider whether the blackouts are due to reflex syncope or a cardiac arrhythmia.

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