

# Management of a first unprovoked epileptic seizure in adolescence and adulthood

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**ABSTRACT** – An epileptic seizure is one of the causes of so-called “transient neurological events” (TNEs). The differential diagnosis of a TNE relies mainly on history and physical examination. Laboratory markers are less frequently useful. After diagnosing an epileptic seizure, a distinction must be made between an acute symptomatic and an unprovoked seizure, since they have different treatments and prognosis. History, physical examination and other examinations (laboratory and imaging) are paramount in this distinction. After the diagnosis of a first unprovoked seizure, an EEG should be requested which may aid in establishing the diagnosis, evaluating the recurrence risk or ascertaining the self-limited nature of the seizure. 3T-MRI with an epilepsy protocol can be considered when CT has not clarified the aetiology. The decision to treat should be discussed with the patient/relatives, taking into account the risk of recurrence, the clinical characteristics (aetiology, seizure type, age, job, epileptic seizure schedule, comorbidities and polymedication), probability of AED side effects, and stigmatization. Nowadays, the chosen regimen is usually monotherapy with a second-generation AED that better suits the patient’s characteristics, comorbidities and concurrent medication. Counselling should include first aid, precipitating factors, sport and physical exercise in order to avoid possible driving restrictions, the need for therapy compliance, and risk of recurrence and SUDEP.

**Key words:** first unprovoked epileptic seizure, diagnosis, recurrence, treatment



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## ILAE Curriculum

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Epileptic seizures are one of the most frequent causes of so-called “transient neurological events” (TNEs). About up to 10% of people will experience a seizure during their lifetime but only 2% to 3% will develop epilepsy [1]. A first unprovoked epileptic seizure (FUES) is a troublesome event for people who experience it and close relatives. Therefore,

there is a need for the diagnosis to be as fast and accurate as possible. A lot of questions will probably arise in relation to the event, such as: “are you sure that it was really a seizure?”, “will it recur?”, “is it epilepsy?”, “do I need to take drugs?”, “for how long?”, and “what is going to happen in the future?”. Furthermore, the word “epilepsy” is usually linked to significant social, personal and professional stigmatization.

In this article, the authors aim to guide the reader through this topic in a practical way. The authors will offer some suggestions, stemming from our current practice, of how to act in this situation. However, each case is unique and, as such, there will be room for subjective decisions, either by the neurologist, the patient or relatives.

## Was “this” TNE an epileptic seizure?

There is a broad differential diagnosis to consider when facing a TNE, including the following: transient ischemic attacks, migraine auras, paroxysmal movement disorders, (pre-)syncope, sleep disorders, intracranial hypertension and psychogenic non-epileptic seizures (PNES). By definition, an epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain [2]. And yet, precise diagnosis is frequently not an easy task (*table 1*). Indeed, like most TNEs, an epileptic seizure is very rarely seen by the physician and the patient is frequently an unreliable source of information, especially if consciousness is altered. Neurological examination and ancillary examinations may not always be of great help in this setting. However, two case series have shown that history and physical examination yield a diagnosis in approximately 85% of cases [3]. A witness to the event can provide valuable information on history and semiology, but description should be interpreted carefully. While features such as muscle tone during seizure, drooling and gaze deviation are more

frequently correctly reported [4], others such as eye closure are more unreliably reported [5]. A video is rarely available for a first seizure, but should be sought because it increases diagnostic accuracy [6]. A more rudimentary but practical and often effective solution, especially when the witness cannot accurately describe the event, is to ask the person to mimic what has been observed. The presence of previous neurological phenomena may be useful for the differential diagnosis, especially if additional information on semiology can be obtained. While some patients may present an unequivocal seizure, many patients describe more of a “spell”, with a seizure as only one of the possible TNEs. There is a lack of validated diagnostic criteria to help the physician in diagnosing a TNE [7]. The Sheldon questionnaire [8] may be useful for the differential diagnosis of syncope. As for PNES, a review-of-system questionnaire [9] may aid in the different diagnosis, although it should not be used as the sole clinical tool. The Frontal Lobe Epilepsy and Parasomnias (FLEP) scale can be useful in differentiating nocturnal frontal lobe epilepsy from parasomnias [10]. It is certainly not practical to have the questionnaires at hand, but if the clinician is familiar with the questions, they can help to direct the clinical history

▼ **Table 1.** Difficulties in diagnosing a first epileptic seizure.

### I. Reliability of testimony

1. The physician rarely witnesses a seizure
2. The patient is not the best person to describe the event because most seizures are accompanied by a disturbance of consciousness
3. A witness may be present during the event (for instance, for a seizure in a street)
4. A witness of the seizure may have difficulty in describing it due to:
  - (a) significant nervousness and anxiety with respect to the unexpected event
  - (b) not seeing the very beginning of the seizure (for instance, the aura)
  - (c) considering the seizure too complex to be properly described
  - (d) seizures occurring at night

### II. Biomarkers for seizure detection in the emergency setting for generalized-onset or focal-to-bilateral tonic-clonic seizures (usually with low specificity and sensitivity)

1. Prolactin secretion
2. Changes in serum adrenocorticotrophic hormone and cortisol levels
3. Increased levels of ammonia
4. Troponin I elevation
5. Creatine kinase elevation
6. Anion gap > 10 mEq/L within the first 2 hours

### III. Ancillary examinations (either in the emergency setting or outpatient clinic)

1. EEG is seldom performed in the emergency setting.
2. Neurophysiological markers (e.g. interictal EEG) show high specificity but low sensitivity.
3. The interictal, or even prolonged EEG or video-EEG may be normal.
4. Imaging, mainly MRI, may be normal or show abnormalities that are not seizure-related.

▼ **Table 2.** Physical examination findings that can aid in the differential diagnosis of a TNE (adapted from [41]).

System	Finding	Potential significance
General appearance	Poor cooperation with examination; exaggeration/dramatization of features	Psychiatric co-morbidities with PNES
Vitals	Bradycardia or tachycardia	Cardiogenic syncope
Head and neck	Scalp or facial laceration	Fall from loss of consciousness
Cardiovascular system	Drop in systolic BP of $\geq 20$ mmHg or diastolic BP of $\geq 10$ mmHg on standing	Syncope from orthostatic hypotension
	Irregular cardiac rhythm	Cardiogenic syncope (e.g. sick sinus syndrome)
	Heart murmur	Cardiogenic syncope (e.g. aortic stenosis)
	Drop in BP of $\geq 50$ mmHg or asystole $>3$ s with carotid massage	Syncope from carotid hypersensitivity
Respiratory	Cough	Syncope from increased intrathoracic pressure
Cutaneous	Linear scars from "cutting"	Psychiatric co-morbidities with PNES

and examination. Lateral tongue biting may be indicative of epileptic seizures with low sensitivity but high specificity [11]. Posterior shoulder dislocation in the absence of direct trauma favours an unwitnessed GTCS [12]. Some findings in the physical examination may aid in the differential diagnosis of an epileptic seizure. However, they should not be used as the only tool (table 2).

Laboratory markers can help to determine whether an unwitnessed event was more likely to be epileptic or non-epileptic. Prolactin testing helps differentiate epileptic seizures from PNES in adults and adolescents, and is associated with high specificity and moderate sensitivity [13], but not recommended as a diagnostic test for epileptic seizures [14,15]. Elevation in creatine kinase (CK) level is common after generalized tonic-clonic seizures (GTCS) with high specificity and moderate sensitivity. Metabolic markers such as ammonia, lactate and increased anion gap (typically driven by increase in serum lactate) may have diagnostic potential for postictal blood tests [16,17]. However, no laboratory test can reliably diagnose or exclude an epileptic seizure [18].

Electrocardiogram should be performed in all adults with loss of consciousness, to identify features suggesting cardiac arrhythmia and syncope, which may mimic epilepsy [15,19].

### If the TNE was an epileptic seizure, was it an acute symptomatic seizure (ASS) or an unprovoked epileptic seizure?

Unprovoked epileptic seizures are defined as seizures occurring in the absence of a potentially causal

clinical condition or beyond the interval estimated for the occurrence of ASS. Unprovoked seizures differ from ASS in terms of risk of seizure recurrence and mortality, related to several aetiologies [20]. For these reasons, the therapeutic approach is also different.

ASS often occur when systemic (metabolic, toxic or other systemic illness) or brain (traumatic brain injury, cerebrovascular, infectious, tumour or inflammatory/demyelination disease) insults are documented [20]. In general, the gap between the insult and the seizure occurrence may be as long as seven days. Suggestions have been made to define ASS as events that occur within one week of a stroke, traumatic brain injury, anoxic encephalopathy, intracranial surgery, or at first identification of subdural hematoma, in the presence of an active central nervous system (CNS) infection, or during an active phase of multiple sclerosis or other autoimmune diseases. In addition, a diagnosis of ASS should be made in cases of severe metabolic derangements (documented within 24 hours based on specific biochemical or haematological abnormalities), drug or alcohol intoxication and withdrawal, or exposure to well-defined epileptogenic drugs [20]. The incidence of ASS is about 29 to 39 per 100,000 per year and predominates in the youngest ages [21]. Clinically, ASS may be focal or bilateral tonic-clonic. Electrolyte disturbances may themselves cause focal seizures [22]. Physical examination may provide some clues as to the aetiology of the ASS, such as fever (infection, e.g. encephalitis), hypertension (e.g. posterior reversible encephalopathy syndrome), papilledema (intracranial hypertension), hepatomegaly, jaundice, scleral icterus, ascites, palmar erythema or gynecomastia (chronic alcoholism) or track marks (illicit drug use). New-onset seizures are frequently encountered in community and hospital settings, with different

▼ **Table 3.** Proposed cut-off values for acute symptomatic seizures in common metabolic disorders (adapted from [20]).

Biochemical parameter	Value
Serum glucose	<36 mg/dL (2.0 mM) or >450 mg/dL (25 mM) associated with ketoacidosis (whether or not there is long-standing diabetes)
Serum sodium	<115 mmol/L (<5 mM)
Serum calcium	<5.0 mg/dL (<1.2 mM)
Serum magnesium	<0.8 mg/dL (<0.3 mM)
Urea nitrogen	>100 mg/dL (>35.7 mM)
Creatinine	>10.0 mg/dL (>884 μM)

aetiologies and prognoses, requiring different approaches for investigation and treatment [23].

Most laboratory abnormalities are predicted based on history and physical examination, and the yield resulting from laboratory evaluations in patients which have returned to baseline is low [24]. Laboratory evaluations which should be considered in the evaluation of a first seizure include electrolytes, glucose, calcium, magnesium, complete blood count, renal function tests and liver function tests [15]. Laboratory tests, which are recommended even in healthy adults who have returned to baseline, include serum glucose and sodium, based on literature reports of unsuspected hypoglycaemia and hyponatremia [24]. The International League Against Epilepsy has proposed cut-off values for ASS in cases of common metabolic disorders (table 3), however, these are only partially evidence-based [20]. Other non-specific laboratory abnormalities may be present after a generalized tonic-clonic seizure, including elevated leukocyte count, creatine phosphokinase, cortisol, lactate dehydrogenase, and neuron-specific enolase. Screening for drug abuse should be considered, although there is no compelling evidence for routine screening of drugs [24]. The probability of seizure occurrence varies between specific drugs –high (cocaine, crack, normeperidine, meperidine, methaqualone, glutarimide; stimulants), fair (hallucinogens; angel dust [PCP, phencyclidine], quatadine) and low (heroin, marijuana).

In the emergency department (ED), the main role of brain imaging is to exclude immediately treatable intracranial pathology. Not surprisingly, the neuroimaging yield is higher in the presence of a focal neurological deficit on physical examination [25-27]. However, significant intracranial abnormalities are found in 10-22% of patients with a first seizure and normal neurological examination [27]. Recommendations vary on whether neuroimaging should be performed in the ED. In the acute setting, unenhanced head CT is an appropriate initial neuroimaging study [15,25,28]. Some guidelines recommend immediate head CT in all adult patients presenting with a first

seizure [27], based on data suggesting that emergency head CT leads to an acute change in management in 9-17% of patients [25,26]. Other recommendations allow deferred neuroimaging [26], particularly in patients who have returned to normal baseline when reliable follow-up is available [24]. In the experience of the authors, all adult patients presenting with a first seizure undergo unenhanced head CT in the ED. Depending on its availability in the ED, some clinical situations may merit urgent brain MRI, such as cerebral venous thrombosis [29] and viral encephalitis [30], as the diagnosis may have direct and urgent impact in the patient's management.

Lumbar puncture (LP) is not routinely recommended as part of the diagnostic evaluation of the patient presenting with a first epileptic seizure [15,24,31]. However, it should be performed if there is clinical suspicion of an acute infectious process involving the central nervous system. There is some evidence supporting LP in otherwise asymptomatic immunocompromised patients [24,32]. In this context, LP should only be performed after a neuroimaging study has excluded mass lesions or other causes of increased intracranial pressure.

It has been clearly shown that ASS are associated with higher early mortality but a lower risk of subsequent unprovoked epileptic seizures, *i.e.* epilepsy [33]. Control of ASS requires treatment of the underlying aetiology although, when prolonged, as in status epilepticus [34], or recurrent, further efforts to control ASS with antiepileptic drugs (AED) should be put in place [35,36]. Indeed, although different in aetiology, it is well known that ASS increase the risk of posterior development of remote symptomatic seizures or epilepsy [37].

### An unprovoked epileptic seizure has been accepted as the most likely diagnosis

An initial assumption that the epileptic seizure is a FUES is most frequently based on the work-up performed in the ED which should include the clinical

history, general and neurological examination, blood tests and imaging, most frequently brain CT. An acute EEG is seldom performed in this setting if the patient has fully recovered. Comprehensive further work-up should be performed in the setting of an outpatient epilepsy clinic, to be performed within two weeks [38] However, patients with abnormal imaging, prolonged or recurrent seizures or incomplete recovery may benefit from a brief admission for more urgent medical and neurological assessment [39].

**Which elements of the clinical history and physical examination can aid in the diagnosis?**

**● Clinical history**

Regarding generalized tonic-clonic seizures (GTCS) or the generalized phase of focal to bilateral tonic-clonic seizures, video analysis has identified a consistent pattern of five phases (onset, pre-tonic clonic, tonic, early clonic, clonic) with a mean duration of one minute [40]. GTCS can be accompanied by other brief seizure types such as myoclonus (*i.e.* <one-second muscular jerk) or absence (typically <10 seconds of staring and unresponsiveness with retained postural tone) events [41]. Focal-onset seizures are accompanied by retained or altered consciousness. The so called “auras” are focal seizures with retained consciousness of subjective sensations that cannot be seen by the outside observer. The patient experiences a sensation related to the area of cortex involved. Some patients may even have had these events before but not given them a second thought. Temporal lobe auras may include an epigastric rising sensation, unpleasant olfactory sensation, palpitations or complex psychic manifestations such as *déjà-vu* or *jamais vu*, fear, elation or autoscopy. Occipital and parietal

lobe auras can be characterized by somatosensory (paresthetic, painful, thermal, disturbances of body image) or visual (amaroutic, elementary and complex hallucinations, illusions) [42] characteristics. Objective seizure manifestations can also occur, depending on the location of the cortex involved, and are usually the reason why patients seek help. These symptoms are part of the symptomatogenic zone [43] and do not necessarily indicate that the seizure arises from that region. These objective manifestations may include: focal clonic limb jerking, dystonic posturing, an explosive onset of hypermotor features, bilateral motor activity and likely nocturnal occurrence, sudden onset of lack of movement and unresponsiveness, and automatisms (*i.e.* repetitive behaviours that do not meaningful interact with the environment) such as swallowing, chewing, lip-smacking, and repetitive movements such as picking at clothing or objects, or more complex behaviours such as waking up, running and undressing. Symptoms that follow a seizure can be equally important, namely disorientation, anterograde amnesia, transient somnolence or fatigue and sore limb muscles. Post-ictal aphasia or hemiparesis should also be sought during history taking, since these are helpful towards the diagnosis of a (focal) seizure and may not be present during the physical examination. These and other objective manifestations can have some lateralizing and localizing value but such a detailed discussion is beyond the scope of this paper [44,45].

**● Physical examination**

Physical examination is unremarkable in most patients with FUES. However, some findings may provide clues as to the aetiology of the epileptic seizure (*table 4*). Epilepsy is currently defined as a brain disturbance including any of the following:

▼ **Table 4.** Physical examination findings and their potential significance in first-seizure patients (adapted from [41]).

System	Finding	Potential significance
Cutaneous	Café au lait spots, axillary or inguinal freckling, cutaneous neurofibroma	Neurofibromatosis
	Hypomelanotic macules, shagreen patches, subungueal fibromas, adenoma sebaceum	Tuberous sclerosis
	Facial capillary haemangiomas (“port wine stain”)	Sturge-Weber syndrome
	Skin and mucosal telangiectasias	Hereditary haemorrhagic Telangiectasia
	Macular hypopigmented whorls or patches	Hypomelanosis of Ito
Nervous system	Focal neurological deficits (motor, sensory, visual)	Structural cerebral lesions as cause of seizure
	Limb hemiatrophy	<i>In utero</i> or paediatric cerebral insult as cause of seizure

- (1) at least two unprovoked, or reflex seizures occurring more than 24 hours apart;
- (2) one unprovoked, or reflex seizure with a risk of further seizures similar to that of recurrence typically after two unprovoked seizures (at least 60%), occurring over the next 10 years;
- (3) and diagnosis of an epilepsy syndrome [46].

For the second point, for a lesion that is believed to generate an enduring predisposition for unprovoked seizures, the patient is considered to have epilepsy. In this setting, aetiology of the epilepsy and seizure type(s) should be determined as accurately as possible. The decision to treat or not to treat, the choice of the most appropriate AED for a given patient, treatment duration, and prognosis are all important topics that must be considered and discussed with the patient/relatives (*table 5*).

### The role of EEG in the management of a FUES

EEG is the gold standard for identifying different biomarkers of epileptogenesis and ictogenesis. In fact, EEG is an essential neurophysiological examination in the evaluation of patients with epileptic seizures, status epilepticus and/or epilepsy, both for diagnosis and classification, as well as for prognostication and establishment of an appropriate management plan [38].

#### • Why request an EEG after a FUES?

##### *To aid diagnosis*

Although EEG is frequently used as a tool to help clinical diagnosis, the sensitivity reported for EEG as a diagnostic test for epilepsy ranges from only 26% to 56% [38]. Different clinical recommendations state that an EEG should be performed only to support a diagnosis of epilepsy when the clinical history suggests that the neurological event is likely to be epileptic. It should not be used to exclude the diagnosis of an epileptic

seizure when the clinical presentation supports a non-epileptic event [19,38]. Therefore, whenever in doubt about the epileptic nature of a transitory neurological event, referral to a specialized epilepsy centre is of paramount importance [38]. A normal EEG does not exclude the diagnosis of epilepsy.

Although the general predictive value of EEG for diagnosis is low, EEG should be requested after an epileptic seizure, especially in young people, to aid syndromic classification [19]. The presence of a specific type and the location of epileptiform activity will enable the diagnosis of an epileptic syndrome, and thus a diagnosis of epilepsy (even after only one epileptic seizure) [47]. Additionally, the presence of a photoparoxysmal response on EEG implies important daily-life recommendations [19].

##### *To evaluate the risk of recurrence*

The EEG demonstrates predictive value in determining the risk of seizure recurrence with Class 1 evidence [48]. Unequivocal epileptiform activity shown on EEG can be used to assess the risk of a FUES [38], estimated on average in 51% cases [49]. In fact, seizure aetiology and EEG are the strongest recurrence predictors and can be used to distinguish patient subgroups with risks as low as 24% and as high as 65% [49] or more. The finding of epileptic discharges has been associated with a risk of recurrence of 83% (95% confidence interval [CI]: 69-97%) vs 41% (95% CI: 29-53%) in patients with non-epileptic abnormalities [50]. Antiepileptic drug treatment after a first seizure should therefore be recommended in cases with unequivocal epileptic discharges on EEG [19].

##### *To ascertain the self-limited nature of a seizure*

Another indication for EEG after an epileptic seizure is to ensure that it was in fact a self-limited event. This is of utmost importance in patients with previous neurological structural lesions, and consequently neurological deficits, for whom neurological examination cannot confidently assure that the patient will return to his previous neurological status. Furthermore, in

▼ **Table 5.** What must be discussed with the patient/relatives at the time of diagnosis of a FUES.

1. The decision to treat/or not to treat with AEDs, taking the wishes of the patient/relatives into account
2. Medication (including decision to treat, role of medication, side effects, expected treatment duration, relapse rate)
3. Seizure first-aid
4. Purpose of tests and procedures (including blood tests, EEG, brain imaging studies)
5. Lifestyle considerations (including sleep deprivation, alcohol, bathing, work-related activities)
6. Driving constraints
7. Counselling about sudden unexplained death in epilepsy (SUDEP)
8. Psychological issues (including stigma, psychiatric comorbidity)

patients with an apparently increased post-seizure deficit (such as aphasia or hemiparesis), EEG will help to distinguish between the presence of persistent epileptic activity and a post-ictal deficit.

● **When should EEG be performed?**

Although EEG is available in most hospitals, it is not available in the majority of EDs (not even in some epilepsy outpatient clinics). As such, a broad spectrum of possible critical decisions regarding EEG request and patient management must be taken by the clinician facing a first-seizure patient.

**After a few days or weeks**

In the case of a self-limited FUES, there are recommendations for performing an EEG soon after the event [38]. According to NICE Guidelines, 'soon' means within four weeks. In fact, the likelihood of finding epileptiform activity on EEG seems to decrease over time after a paroxysmal event [51], but can be increased by recordings during sleep or following sleep deprivation [52-54]. Therefore, when a standard EEG has not contributed to diagnosis or classification after a FUES, a sleep EEG should be performed [38]. Repeat EEG can also be useful when the diagnosis of epilepsy is not clear [38,55,56]. Furthermore, as discussed, an EEG carried out within the first few weeks after a first epileptic seizure carries prognostic value, as patients with epileptiform abnormalities are more likely to have a second epileptic seizure [50].

**After a few days or weeks under antiepileptic medication**

As mentioned above, in certain cases, epilepsy diagnosis can be made after a FUES, including a reflex epileptic seizure (or reflex) [47]. Although the chance of recurrence is unknown for the majority of seizure aetiologies, evidence suggests an elevated risk in the case of post-stroke unprovoked seizures occurring at least one month after a stroke [33]. Therefore, after an unprovoked post-stroke epileptic seizure, AEDs should be prescribed immediately in the ED along with postponement of EEG based on the risk of recurrence.

**Immediately in the ED**

Prompt recognition of specific EEG patterns can justify immediate and appropriate therapeutic decisions, leading to rapid resolution of the clinical picture [57]. When a patient has not returned to his/her previous neurological state, due to either the persistence of altered mental status (including confusion, lethargy, memory disturbances and even coma), subtle involuntary movements (myoclonus and unusual behaviour, anxiety, agitation, delirium and hallucination) or apparent persistent neurological deficits (e.g. speech disturbance, paresis), non-convulsive status epilepticus (NCSE) [58] should be suspected. Patients who present with "de novo" status epilepticus present

unique challenges in therapeutic management [61], and in these cases, EEG is mandatory [59,60] for diagnosis. The discussion on NCSE is, however, beyond the scope of this paper.

● **Which investigations should be performed in a patient with a FUES?**

● **Laboratory testing**

Laboratory testing is indicated to identify not only causes of ASS, but also systemic comorbidities affecting both diagnostic testing and the choice and dosing of antiepileptic drug therapy. In women of childbearing age, a pregnancy test is recommended, since pregnancy may affect testing and initiation of antiepileptic drug therapy [24].

● **Neuroimaging**

At this point, head CT performed in the ED might have already identified a remote symptomatic cause, such as stroke, trauma or infection, associated with a 10-year recurrence risk of over 60% [28], meeting the criteria for epilepsy [47]. If the topography of the lesion is congruent with seizure semiology, it is our opinion that further neuroimaging is not essential in the setting of a first epileptic seizure.

When head CT is non-contributory, MRI is indicated. The sensitivity of MRI is much higher than that of CT for a variety of pathologies causing epilepsy, including infarcts, tumours, mesial temporal sclerosis, and cortical malformations, and is the modality of choice in the outpatient setting, where it is fundamental for the diagnostic assessment of a patient with a first epileptic seizure [15,27,31]. In one study, 23% of patients who underwent MRI at the time or soon after a first epileptic seizure had a potentially epileptogenic lesion [62]. The American Academy of Neurology recommends neuroimaging, preferably MRI, as one of the eight epilepsy measures for all patients with epilepsy, with the exception of confident diagnoses of idiopathic generalized epilepsy syndromes that are known to lack neuroimaging abnormalities [63]. In the latter case, neuroimaging should not be routinely requested [15,19,31]. The ILAE Neuroimaging Task Force also recommends MRI soon after the first seizure, with the same exception for genetic generalized syndromes [64]. An epilepsy protocol should be used based on the ILAE recommendations for the use of the Harmonized Neuroimaging of Epilepsy Structural Sequences (HARNES-MRI) protocol in order to standardize neuroimaging of epilepsy [64].

● **Additional testing in select cases**

Though most metabolic diseases begin in childhood, some, including porphyria and urea cycle disorders,

▼ **Table 6.** Factors influencing the medical decision to treat a FUES.

1. Relative risk of seizure recurrence
2. Aetiology of the epilepsy
3. Seizure type
4. Age
5. Gender
6. Seizure schedule (if predictable)
7. Occupation
8. Comorbidities
9. Polymedication
10. Possible side effects associated with long-term AED treatment

can appear in adulthood. In the appropriate clinical setting, urine porphobilinogen and porphyrins may be assessed for porphyria, or serum ammonia and urine organic acids for urea cycle defects. If there is clinical suspicion of an autoimmune encephalitis, such as cognitive and psychiatric deterioration that develops contemporaneously with seizures, detection of specific autoantibodies establishes a definitive diagnosis of autoimmune or paraneoplastic encephalitis. Both serum and cerebrospinal fluid antibody testing should be performed. Importantly, the absence of antibodies does not rule out an autoimmune mechanism. Chronic infections, such as neurocysticercosis and tuberculosis, may lead to epilepsy, and evaluation of infectious diseases may be needed in such cases. However, neuroimaging will usually provide a clue to the diagnosis. Genetic testing still has limited clinical utility, and its yield is greater in adults with learning disability and developmental and epileptic encephalopathies. Its role is mainly in the setting of refractory epilepsy [65], and as such, outside the scope of this paper.

### Deciding to treat

When deciding on whether to treat a patient with a FUES, several main points must be taken into account

and discussed with the patient and relatives, when appropriate: the risk of recurrence, the patient's preferences and characteristics, and the long-term impact of the diagnosis and treatment (tables 6, 7).

#### ● **Risk of recurrence**

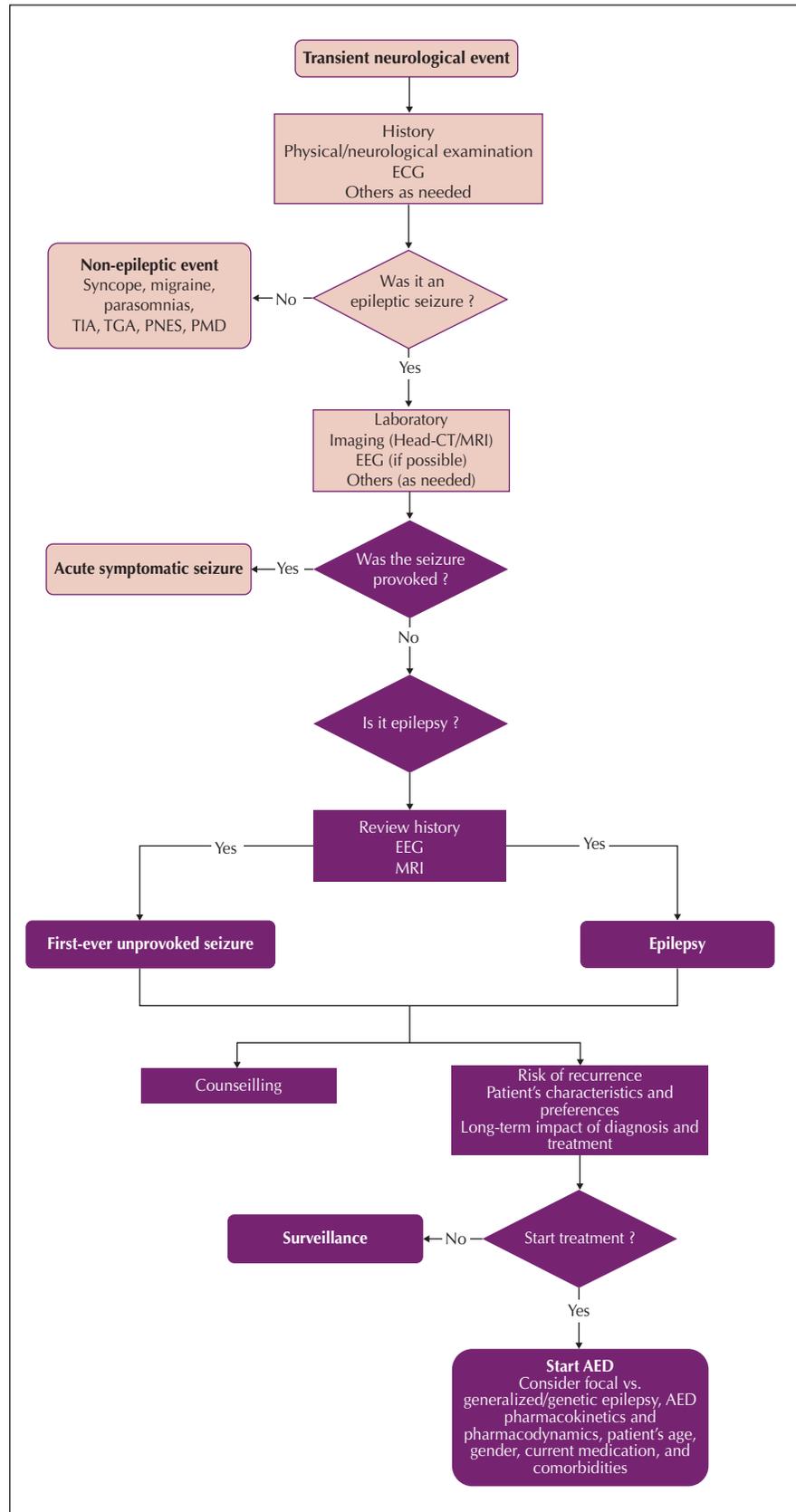
Overall, in untreated individuals with a FUES, 40-50% can expect a recurrence. As mentioned earlier, history is crucial in determining whether an epileptic seizure is really a FUES (if the patient has had an epileptic seizure in the past) or whether there are additional findings which might increase the recurrence risk above >60% after a FUES, such as a significant brain imaging abnormality as the cause of the seizure or an EEG with epileptiform abnormalities, which might fulfil the ILAE definition of epilepsy [47]. The risk of recurrence following a FUES is highly time dependent, rapidly falling with increasing duration of epileptic seizure freedom. Most recurrences can be expected in the first two years.[66,67]. Patients must be made aware that treatment decreases the risk of epileptic seizure recurrence but does not change the long-term prognosis of epilepsy [68]. Talking to the patient about seizure recurrence risk is crucial in making an informed decision. Even in patients without a recurrency risk >60% (epilepsy), seizure recurrence might be unacceptable such that the patient opts for starting treatment.

#### ● **Patients' characteristics and preferences**

Other, but also important, considerations must be given to seizure type (disturbances of consciousness increase the risk of traumatic injuries), age (a seizure occurrence in an older, retired patient may be different in terms of social or professional consequences to an epileptic seizure occurring in an active adolescent or adult), gender (women of childbearing age, for instance), occupation (a professional or retired patient), and presence of comorbidities and/or poly-medication (meaning a further increase in medication). In women of childbearing age, this discussion must take into account possible teratogenic effects [69-71].

▼ **Table 7.** What the patient/relatives should know about the decision to treat a first unprovoked seizure (adapted from [67]).

1. In untreated individuals with a first unprovoked seizure, 40-50% can expect a recurrence.
2. Most recurrences can be expected within the first 2 years.
3. Immediate treatment reduces recurrence in the next 1-2 years, but does not affect long-term remission in those individuals with a single epileptic seizure or infrequent seizures.
4. The likelihood of seizure recurrence is greater when associated with a prior lesion as the cause of the seizure, an EEG with epileptiform abnormalities, a significant brain imaging abnormality, or a nocturnal seizure.
6. The risk of AED adverse events ranges from about 10 to 30%, but these are usually mild and reversible.



■ **Figure 1.** Flowchart with the steps to consider when dealing with a transient neurological event.

### • Long-term impact of diagnosis and treatment

Being on medication may increase the stigma that a patient feels. This is a matter that the patient is frequently reluctant to discuss and may affect adherence. Finally, patients must be informed that the risk of AED adverse events ranges from about 10% to 30%, but these are likely to be predominantly mild and reversible [67]. In our experience, when patients are presented with the evidence, they feel more confident in taking part in the decision to initiate medication and deal with the situation.

### Choosing the appropriate AED

A large arsenal of AEDs is currently available. In the case of an actual FUES and after a decision has been made to start therapy, a monotherapy regime should be the natural choice. Furthermore, one should be as certain as possible regarding its aetiology (genetical/generalized vs structural/focal seizures). When in doubt, a broad-spectrum AED is a safer choice. When history, EEG, imaging and/or post-ictal deficits point to a focal seizure, more narrow-spectrum AEDs may also be used. In general, the usual decision is to start medication with a second-generation AED. However, one must keep in mind that, although presenting better pharmacodynamic and pharmacokinetic profiles (hence less interactions and side effects), second-generation AEDs fail to provide superior efficacy relative to first-generation agents [72]. Considerations regarding AED choice must also include pharmacokinetic properties, safety and tolerability profile, as well as how the drug relates to comorbidities (psychiatric, renal failure and hepatic dysfunction, for example) and possible interactions with the patient's current medication. Women of childbearing age require special consideration due to teratogenicity associated with some AEDs. A detailed description of AEDs is beyond the scope of this paper [72,73]. In practice, when prescribing an AED, several online and offline tools are readily available which allow the clinician to review the above-mentioned topics when deciding which drug to choose. The authors recommend these tools to be used often as it is impossible to keep in mind the specific details of all AEDs and their possible drug interactions.

### Counselling after a FUES

A FUES can be a terrifying event, and counselling is an important aspect of its management. It is essential to explain what an epileptic seizure is and how to recognize it, seizure first aid, and the importance of reporting further attacks [15]. Additionally, counselling should include seizure precautions, including

common precipitating factors and general safety measures, and patients must be informed about eventual driving restrictions prior to discharge from the ED. Topics that must be discussed with the patient and caregivers are presented in *table 5*, and a recent review regarding counselling adults who experience a first seizure is available [74].

### Conclusion

Diagnosing a TNE as an epileptic seizure may not be easy and relies on careful history taking and examination of the patient, as well as use of the right ancillary tests. Using this step-by-step approach explained above, we have attempted to provide an overview of the decisions that remain following the diagnosis of a first epileptic seizure. Careful investigations are needed to exclude causes that might suggest an ASS, especially since these are more frequent than unprovoked epileptic seizures. Investigations also help predict the risk of recurrence; a >60% risk after 10 years constitutes a diagnosis of epilepsy. When diagnosing a FUES, pharmacological treatment should always be adjusted to the patient's specific demographic and clinical factors, and this decision should be shared with the patient and his/her caregivers (*figure 1*). ■

### Case 1

A 21-year-old woman, a waitress, presented to the epilepsy clinic for a second opinion for a diagnosis of epilepsy that was made a year ago. She was taking valproate at 1,500 mg/day.

The patient described a seven-year history of episodes of yellow/white flashes of light, followed by a headache with photophobia, sonophobia, cinesophobia and nausea without vomiting. When the headache was very intense, she felt light-headed and a loss of consciousness followed. Friends described "rigid arms" followed by very brief movements considered as myoclonic jerks. She recovered very quickly. There was occasionally sphincter incontinence but never tongue biting.

She had 10 episodes of flashes with headache per month and about two to three of these were followed by loss of consciousness. These episodes were especially frequent and intense around menses. There was some improvement regarding the frequency of episodes with valproate, but seizures worsened when she tried to stop it.

She had already undergone head CT, EEG, echocardiogram and 24-hour Holter which were unremarkable.

A diagnosis of probable migraine with aura was made and she was started on propranolol at up to 120 mg/day. There was a significant improvement in headache frequency and intensity, and at last follow-up visit, she no longer experienced any further episodes of loss of consciousness.

*Case notes:*

This is an interesting case of differential diagnosis of focal epilepsy vs migraine with aura. Several factors can confound the diagnosis: response to valproate (which can be effective in both disorders), prevalence around menses, and loss of consciousness with involuntary movements. Propranolol was started since this is only effective for migraine, unlike other migraine-preventative drugs (ex: topiramate, lamotrigine). Evaluation at an epilepsy clinic is important in such cases in order to avoid long-term medication with AEDs. In this case of a young woman of child-bearing age, it is important to limit unnecessary stigma and restrictions associated with epilepsy, and ascertain accurate treatment of the underlying disorder.

## Case 2

A 20-year-old male, with a past medical history of migraine without aura, was observed in the emergency department. His mother described an episode at around 6 a.m. in which she had heard a noise coming from his room; when she got there, the patient made a choking sound and had rhythmic jerking of the entire body which lasted for 1-2 minutes, followed by a deep sleep. He gradually woke up, returning to his usual state after 30 minutes.

He denied ingestion of alcohol or other drugs, fever, or any systemic symptoms. He also denied any recent illness or sleep deprivation. He denied previous episodes of loss of consciousness, muscle jerks or behavioural arrest. He had no history of febrile seizures, severe head trauma, or central nervous system infections. There was no family history of epilepsy.

Neurological examination, laboratory workup, ECG, and plain head CT were all unremarkable. The diagnosis of a single unprovoked seizure was explained to the patient and his mother. Both denied the possibility of this diagnosis, and the patient refused any treatment.

One month after, he returned to the emergency department after a similar episode, also on awakening. At this time, a diagnosis of epilepsy was made, and he was started on sodium valproate. Later, at

the outpatient clinic, sleep-deprived EEG and brain MRI were ordered, and both were unremarkable.

*Case notes:*

After the first episode, only a diagnosis of a single unprovoked seizure could be made. Since this was a first seizure that occurred during sleep, the risk of recurrence was increased, and this factor should be included in the patient discussion. By the end of the vignette, the patient fulfils a single criterion for epilepsy: two unprovoked seizures occurring at more than 24 hours apart. He does not fulfil criteria for diagnosis of an epilepsy syndrome since the diagnosis of IGE with generalized tonic-clonic seizures cannot be made in the absence of generalized spike-wave discharges on EEG.

## Key points

- About up to 10% of people will experience an epileptic seizure during their lifetime but only 2-3% will develop epilepsy.
- An epileptic seizure is one of the causes of so-called “transient neurological events” (TNEs). The therapeutic approach for a first unprovoked epileptic seizure (FUES) should be based on the following reasoning: is this first TNE an epileptic seizure? If so, is it a provoked seizure or an FUES? If it is an FUES, how should you investigate further? Should you treat the patient or not? Which antiepileptic drugs should you choose?
- The occurrence of an FUES is troublesome for people who experience it and their relatives. Therefore, there is a need for fast and accurate diagnosis and to provide those involved with as much information as possible.
- Diagnosing a FUES may be challenging given that the physician rarely witnesses an epileptic seizure, the patient is not the best person to describe the event, and no witness may be present during the event, or, if present, able to describe it properly.
- Although most FUES are first seen in the emergency room, usually it is only later that a detailed investigation is established in the outpatient clinic. This investigation includes, in general, re-examination of the clinical history and general and neurological examination, an EEG (with several modalities), and brain MRI, if necessary.
- Several matters must be discussed with the patient and relatives: decisions concerning treatment initiation and its duration, relapse rate after stopping treatment, the risk of SUDEP, the need for medication compliance, avoidance of

alcohol intake, sleeping properly, avoidance of any dangerous activities (including driving), and stigmatisation.

- Overall, 40 to 50% of untreated people with a FUES can expect a recurrence. This risk is time-dependent, and the majority can expect recurrence within the first two years.
- The most well-known risks associated with FUES recurrence include: a prior brain insult or lesion as the cause of the epileptic seizure, an EEG with epileptiform abnormalities, a significant abnormality on brain imaging, or nocturnal ES.
- When deciding to treat or not to treat an FUES, many factors should be taken into account and discussed with the patient/relatives: the relative risk of recurrence, aetiology, seizure type, age, seizure schedule, patient's occupation, and comorbidities or poly medication.
- When choosing a first antiepileptic drug regimen, one should keep in mind the aetiology of the epilepsy, the patient's age and gender, as well as comorbidities or poly medication.

#### Supplementary material.

Summary slides accompanying the manuscript are available at [www.epilepticdisorders.com](http://www.epilepticdisorders.com).

#### Disclosures.

The authors have no conflicts of interest to disclose.

#### References

1. Hauser WA, Beghi E. First seizure definitions and worldwide incidence and mortality. *Epilepsia* 2008; 49: 8-12.
2. Fisher RS, Van Emde Boas W, Blume W, Elger C, Genton P, Lee P, et al. Response: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 2005; 46: 1701-2.
3. Angus-Leppan H. Diagnosing epilepsy in neurology clinics: a prospective study. *Seizure* 2008; 17: 431-6.
4. Thijs RD, Wagenaar WA, Middelkoop HAM, Wieling W, van Dijk JG. Transient loss of consciousness through the eyes of a witness. *Neurology* 2008; 71: 1713-8.
5. Syed TU, Arozullah AM, Suci GP, Toub J, Kim H, Dougherty ML, et al. Do observer and self-reports of ictal eye closure predict psychogenic nonepileptic seizures? *Epilepsia* 2008; 49: 898-904.
6. Tatum WO, Hirsch LJ, Gelfand MA, Acton KE, La France Jr WC, Duckrow RB, et al. Assessment of the predictive value of outpatient smartphone videos for diagnosis of epileptic seizures. *JAMA Neurol* 2020; 77: 593-600.
7. Wardrope A, Newberry E, Reuber M. Diagnostic criteria to aid the differential diagnosis of patients presenting with transient loss of consciousness: a systematic review. *Seizure* 2018; 61: 139-48.
8. Sheldon R, Rose S, Ritchie D, Connolly SJ, Koshman M-L, Lee MA, et al. Historical criteria that distinguish syncope from seizures. *J Am Coll Cardiol* 2002; 40: 142-8.
9. Kerr WT, Janio EA, Braesch CT, Le JM, Hori JM, Patel AB, et al. Diagnostic implications of review-of-systems questionnaires to differentiate epileptic seizures from psychogenic seizures. *Epilepsy & Behavior* 2017; 69: 69-74.
10. Derry CP, Davey M, Johns M, Kron K, Glencross D, Marin C, et al. Distinguishing sleep disorders from seizures: diagnosing bumps in the night. *Arch Neurol* 2006; 63: 705-9.
11. Brigo F, Nardone R, Bongiovanni LG. Value of tongue biting in the differential diagnosis between epileptic seizures and syncope. *Seizure* 2012; 21: 568-72.
12. Gosens T, Poels PJE, Rondhuis JJ. Posterior dislocation fractures of the shoulder in seizure disorders - two case reports and a review of literature. *Seizure* 2000; 9: 446-8.
13. Malkowicz DE, Legido A, Jackel RA, Sussman NM, Eskin BA, Harner RN. Prolactin secretion following repetitive seizures. *Neurology* 1995; 45: 448-52.
14. Shukla G, Bhatia M, Vivekanandhan S, Gupta N, Tripathi M, Srivastava A, et al. Serum prolactin levels for differentiation of nonepileptic versus true seizures: limited utility. *Epilepsy Behav* 2004; 5: 517-21.
15. *Epilepsies: diagnosis and management (NICE)*. London: National Institute for Health and Care Excellence (NICE); 2021. PMID: 32027473.
16. Albadareen R, Gronseth G, Landazuri P, Jianghua H, Hammond N, Uysal U. Postictal ammonia as a biomarker for electrographic convulsive seizures: a prospective study. *Epilepsia* 2016; 57: 1221-7.
17. Li Y, Matzka L, Maranda L, Weber D. Anion gap can differentiate between psychogenic and epileptic seizures in the emergency setting. *Epilepsia* 2017; 58: e132-e5.
18. Nass RD, Sassen R, Elger CE, Surges R. The role of postictal laboratory blood analyses in the diagnosis and prognosis of seizures. *Seizure* 2017; 47: 51-65.
19. SIGN. Diagnosis and management of epilepsy in adults. *Scottish Intercollegiate Guideline Network* 2018; 143: 1-101.
20. Beghi E, Carpio A, Forsgren L, Hesdorffer DC, Malmgren K, Sander JW, et al. Recommendation for a definition of acute symptomatic seizure. *Epilepsia* 2010; 51: 671-5.
21. Annegers JF, Hauser WA, Lee JR, Rocca WA. Incidence of acute symptomatic seizures in rochester, minnesota, 1935-1984. *Epilepsia* 1995; 36: 327-33.
22. Nardone R, Brigo F, Trinka E. Acute symptomatic seizures caused by electrolyte disturbances. *J Clin Neurol* 2016; 12: 21-33.
23. Foster E, Holper S, Chen Z, Kwan P. Presentation and management of community-onset vs hospital-onset first seizures. *Neurol Clin Pract* 2018; 8: 421-8.
24. Physicians E, Committee P, Subcommittee CP. Clinical Policy: critical Issues in the evaluation and management of adult patients presenting to the emergency department with seizures. *Ann Emerg Med* 2004; 43: 605-25.

25. Kotisaari K, Virtanen P, Forss N, Strbian D, Scheperjans J. Emergency computed tomography in patients with first seizure. *Seizure* 2017; 48: 89-93.
26. Harden CL, Huff JS, Schwartz TH, Dubinsky RM, Zimmerman RD, Weinstein S, et al. Reassessment: neuroimaging in the emergency patient presenting with seizure (an evidence-based review): report of the therapeutics and technology assessment subcommittee of the american academy of neurology. *Neurology* 2007; 69: 1772-80.
27. Tranvinh E, Lanzman B, Provenzale J, Wintermark M. Imaging evaluation of the adult presenting with new-onset seizure. *Am J Roentgenol* 2019; 212: 15-25.
28. Crocker CE, Pohlmann-Eden B, Schmidt MH. Role of neuroimaging in first seizure diagnosis. *Seizure* 2017; 49: 74-8.
29. Saposnik G, Barinagarrementeria F, Brown RD, Bushnell CD, Cucchiara B, Cushman M, et al. Diagnosis and management of cerebral venous thrombosis: a statement for health-care professionals from the American Heart Association/American Stroke Association. *Stroke* 2011; 42: 1158-92.
30. Solomon T, Michael BD, Smith PE, Sanderson F, Davies NWS, Hart IJ, et al. Management of suspected viral encephalitis in adults - Association of British Neurologists and British Infection Association National Guidelines. *J Infect* 2012; 64: 347-73.
31. Beghi E, De Maria G, Gobbi G, Veneselli E. Diagnosis and treatment of the first epileptic seizure: guidelines of the Italian league against epilepsy. *Epilepsia* 2006; 47: 2-8.
32. Holtzman DM, Kaku DA, So YT. New-onset seizures associated with human immunodeficiency virus infection: causation and clinical features in 100 cases. *Am J Med* 1989; 87: 173-7.
33. Hesdorffer DC, Benn EKT, Cascino GD, Hauser WA. Is a first acute symptomatic seizure epilepsy? Mortality and risk for recurrent seizure. *Epilepsia* 2009; 50: 1102-8.
34. Hesdorffer DC, Logroscino G, Cascino G, Annegers JF, Hauser WA. Risk of unprovoked seizure after acute symptomatic seizure: effect of status epilepticus. *Ann Neurol* 1998; 44: 908-12.
35. Koppel BS. Treatment of acute and remote symptomatic seizures. *Curr Treat Options Neurol* 2009; 11: 231-41.
36. Leung H, Man CBL, Hui ACF, Kwan P, Wong KS. Prognosticating acute symptomatic seizures using two different seizure outcomes. *Epilepsia* 2010; 51: 1570-9.
37. Herman ST. Epilepsy after brain insult: targeting epileptogenesis. *Neurology* 2002; 12: S21-6.
38. National Institute for Health and Care Excellence (NICE). *Epilepsies: diagnosis and management. Clinical guideline 137*. 2012.
39. Galizia EC, Faulkner HJ. Seizures and epilepsy in the acute medical setting: presentation and management. *Clin Med J R Coll Physicians London* 2018; 18: 409-13.
40. Theodore WH, Porter RJ, Albert P, Kelley K, Bromfield E, Devinsky O, et al. The secondarily generalized tonic-clonic seizure: a videotape analysis. *Neurology* 1994; 44: 1403-7.
41. Nowacki TA, Jirsch JD. Evaluation of the first seizure patient: key points in the history and physical examination. *Seizure* 2017; 49: 54-63.
42. Rossetti AO, Kaplan PW. Seizure semiology: an overview of the "inverse problem". *Eur Neurol* 2010; 63: 3-10.
43. Lüders HO, Najm I, Nair D, Widdess-Walsh P, Bingman W. The epileptogenic zone: general principles. *Epileptic Disord* 2006; 8: 1-9.
44. Loddenkemper T, Kotagal P. Lateralizing signs during seizures in focal epilepsy. *Epilepsy Behav* 2005; 7: 1-17.
45. Ettinger AB, Weisbrot DM, Nolan E, Devinsky O. Postictal symptoms help distinguish patients with epileptic seizures from those with non-epileptic seizures. *Seizure* 1999; 8: 149-51.
46. Fisher RS, Acevedo C, Arzimanoglou A, Alicia Bogacz, Helen CJ, Elger CE, et al. ILAE official report: a practical clinical definition of epilepsy. *Epilepsia* 2014; 55: 475-82.
47. Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Helen Cross J, Elger CE. ILAE official report: a practical clinical definition of epilepsy. *Epilepsia* 2014; 55: 475-82.
48. Tatum WO, Rubboli G, Kaplan PW, Mirsatari SM, Radhakrishnan K, Gloss D, et al. Clinical utility of EEG in diagnosing and monitoring epilepsy in adults. *Clin Neurophysiol* 2018; 129: 1056-82.
49. Berg AT, Shinnar S. The risk of seizure recurrence following a first unprovoked seizure. *Neurology* 1991; 41: 965-5.
50. van Donselaar CA, Schimsheimer R-J, Geerts AT, Declercq AC. Value of the electroencephalogram in adult patients with untreated idiopathic first seizures. *Arch Neurol* 1992; 49: 231-7.
51. Sundaram M, Hogan T, Hiscock M, Pillay N. Factors affecting interictal spike discharges in adults with epilepsy. *Electroencephalogr Clin Neurophysiol* 1990; 75: 358-60.
52. King MA, Newton MR, Jackson GD, Fitt GJ, Mitchell LA, Silvapulle MJ, et al. Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. *Lancet* 1998; 352: 1007-11.
53. Roupakiotis SC, Gatzonis SD, Triantafyllou N, Mantouvalos V, Chioni A, Zournas C, et al. The usefulness of sleep and sleep deprivation as activating methods in electroencephalographic recording: contribution to a long-standing discussion. *Seizure* 2000; 9: 580-4.
54. Fountain NB, Kim JS, Lee SI. Sleep deprivation activates epileptiform discharges independent of the activating effects of sleep. *J Clin Neurophysiol* 1998; 15: 69-75.
55. Scottish Intercollegiate Guidelines Network (SIGN). *Diagnosis and management of epilepsy in adults. A national clinical guideline (SIGN 143)*. 2015.
56. Salinsky M, Kanter R, Dasheiff RM. Effectiveness of multiple EEGs in supporting the diagnosis of epilepsy: an operational curve. *Epilepsia* 1987; 28: 331-4.
57. Raucci U, Pro S, Di Capua M, Di Nardo G, Pia Villa M, Striano P, et al. A reappraisal of the value of video-EEG recording in the emergency department. *Expert Rev Neurother* 2020; 20: 459-75.

58. Trinka E, Cock H, Hesdorffer D, Rossetti AO, Ingrid ES, Shlomo S, et al. A definition and classification of status epilepticus - report of the ILAE task force on classification of status epilepticus. *Epilepsia* 2015; 56: 1515-23.
59. Beniczky S, Hirsch LJ, Kaplan PW, Pressler R, Bauer G, Aurlien H, et al. Unified EEG terminology and criteria for nonconvulsive status epilepticus. *Epilepsia* 2013; 54: 28-9.
60. Leitinger M, Beniczky S, Rohracher A, Gardella E, Kalss G, Qerama E, et al. Salzburg consensus criteria for non-convulsive status epilepticus - approach to clinical application. *Epilepsy Behav* 2015; 49: 158-63.
61. Aguglia U, Sueri C, Gasparini S, Beghi E, Labate A, Gambardella A, et al. Relevance of clinical context in the diagnostic-therapeutic approach to status epilepticus. *Epilepsia* 2016; 57: 1527-9.
62. Hakami T, McIntosh A, Todaro M, Lui E, Yerra R, Meng TK, et al. MRI-identified pathology in adults with new-onset seizures. *Neurology* 2013; 81: 920-7.
63. Fountain NB, Van Ness PC, Swain-Eng R, Tonn S, Bever Jr CT. American academy of neurology epilepsy measure development panel, et al. Quality improvement in neurology: AAN epilepsy quality measures: report of the quality measurement and reporting subcommittee of the American academy of neurology. *Neurology* 2011; 76: 94-9.
64. Bernasconi A, Cendes F, Theodore WH, Gill RS, Koeppe MJ, Hogan RE, et al. Recommendations for the use of structural magnetic resonance imaging in the care of patients with epilepsy: a consensus report from the International League Against Epilepsy Neuroimaging Task Force. *Epilepsia* 2019; 60: 1054-68.
65. Roctus A, Olson HE, Smith L, Keith LG, El Achkar C, Taylor A, et al. Genetic diagnoses in epilepsy: the impact of dynamic exome analysis in a pediatric cohort. *Epilepsia* 2020; 61: 249-58.
66. Donselaar CAV, Geerts AT, Elwes RDC, et al. First seizure in adult life. *Lancet* 1988; 332: 36-7.
67. Krumholz A, Wiebe S, Gronseth GS, Gloss DS, Sanchez AM, Kabir AA, et al. Evidence-based guideline: management of an unprovoked first seizure in adults: report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. *Epilepsy Curr* 2015; 15: 144-52.
68. Shinnar S, Berg AT. Does antiepileptic drug therapy prevent the development of "chronic" epilepsy? *Epilepsia* 1996; 37: 701-08.
69. Reynolds EH, Trimble MR. Adverse neuropsychiatric effects of anticonvulsant drugs. *Drugs* 1985; 29: 570-81.
70. O'Dell C, Shinnar S. Initiation and discontinuation of antiepileptic drugs. *Neurol Clin* 2001; 19: 289-311.
71. Weston J, Bromley R, Jackson CF, Adab N, Clayton-Smith J, Greenhalgh J. Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child. *Cochrane Database Syst Rev* 2016 ; 11(11) : CD010224.
72. Abou-Khalil BW. Update on antiepileptic drugs 2019. *Contin Lifelong Learn Neurol* 2019; 25: 508-36.
73. Glauser T, Ben-Menachem E, Bourgeois B, Avital C, Carlos G, Kälviäinen R, et al. Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. *Epilepsia* 2013; 54: 551-63.
74. Legg KT, Newton M. Counselling adults who experience a first seizure. *Seizure* 2017; 49: 64-8.

## TEST YOURSELF

- (1) Among the approximate 10% of people who will experience a seizure during their lifetime, what percentage will develop epilepsy?
- 20 to 25%
  - 2 to 3%
  - 40 to 50%
  - 80 to 90%
- (2) In general, the gap between a cerebral insult and the occurrence of a provoked symptomatic seizure may be as long as:
- 2 months
  - 6 months
  - 1 week
  - 1 month
- (3) Epilepsy is currently defined as a brain disturbance including one of the following:
- At least two unprovoked seizures occurring more than 24 hours apart
  - At least two symptomatic seizures occurring more than 48 hours apart
  - At least three unprovoked, or reflex seizures with a risk of further seizures similar to that of recurrence typically after four unprovoked seizures (at least 60%), occurring over the next 10 years
  - Diagnosis of a focal, symptomatic, seizure

- (4) Concerning a first unprovoked seizure, which of the following statements is correct?
- A. In untreated patients, roughly 100% can expect a recurrence
  - B. Immediate treatment reduces recurrence within the next 1-2 years, and positively affects long-term remission in those patients with a single or infrequent seizures
  - C. An EEG with epileptiform abnormalities or a prior lesion as the cause of epilepsy does not affect the likelihood of seizure recurrence
  - D. In untreated patients, most recurrences can be expected in the first 2 years.
- (5) Which of the following are not reasons why an EEG should be requested after a first seizure?
- A. To support a diagnosis of epilepsy when the clinical history suggests that the neurological event is likely to be epileptic
  - B. To evaluate the recurrence risk
  - C. To ascertain the self-limited nature of a seizure
  - D. To distinguish seizure from syncope
- (6) Which of the following factors are not expected to influence a medical decision to treat an adult epilepsy:
- A. Stigmatization
  - B. Occupation
  - C. Comorbidities
  - D. The occurrence of only nocturnal seizures
- (7) Which of the following aspects should be avoided when discussing with the patient/relatives at the time of epilepsy diagnosis.
- A. The rate of seizure relapse after stopping treatment is relatively high
  - B. The risk of SUDEP is too low to be a matter of concern
  - C. There is a need to perform EEG in order to weigh the different pharmacological options
  - D. Treatment duration depends on seizure type
- (8) Concerning investigation of an epilepsy, which of the following is correct:
- A. For focal, symptomatic epilepsies, imaging, mainly brain MRI, always displays abnormalities which are related to the aetiology of the epilepsy.
  - B. Once performed in the emergency room, clinical history and general and neurological examination are not to be repeated at the outpatient clinic.
  - C. The interictal EEG may be normal.
  - D. In most centres, EEG is frequently performed in the emergency room.
- (9) Regarding the choice of antiepileptic drugs (AEDs) to start treating an epilepsy, which of the following is correct:
- A. The aetiology of the epilepsy is of utmost importance.
  - B. Comorbidities should not be taken into consideration.
  - C. Regardless of the AED chosen, the risk of adverse events is about 30-40%.
  - D. In general, the current choice is a first-generation AED.
- (10) Regarding the choice of AEDs to start treating an epilepsy, which of the following is correct:
- A. When starting treatment for a patient with significant comorbidities, a first-generation AED provides a better safety profile.
  - B. Second-generation AEDs show superior efficacy to first-generation agents.
  - C. Women of childbearing age are not a matter of concern when choosing an AED.
  - D. When starting treatment for elderly patients, several factors must be taken into account, including comorbidities and current medications, and a second-generation AED is usually chosen as first-line therapy.

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*Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, [www.epilepticdisorders.com](http://www.epilepticdisorders.com), under the section "The EpiCentre".*

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