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# Detailed history the cornerstone of epilepsy diagnosis

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Dr William Stern
MA MBBS MRCP
Consultant Neurologist,
Department of Neurology,
Guy's and St Thomas' NHS Foundation Trust,
London, UK

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**AUTHOR**
**Dr William Stern**
MA MBBS MRCP
Consultant Neurologist, Department of Neurology, Guy's and St Thomas' NHS Foundation Trust, London, UK

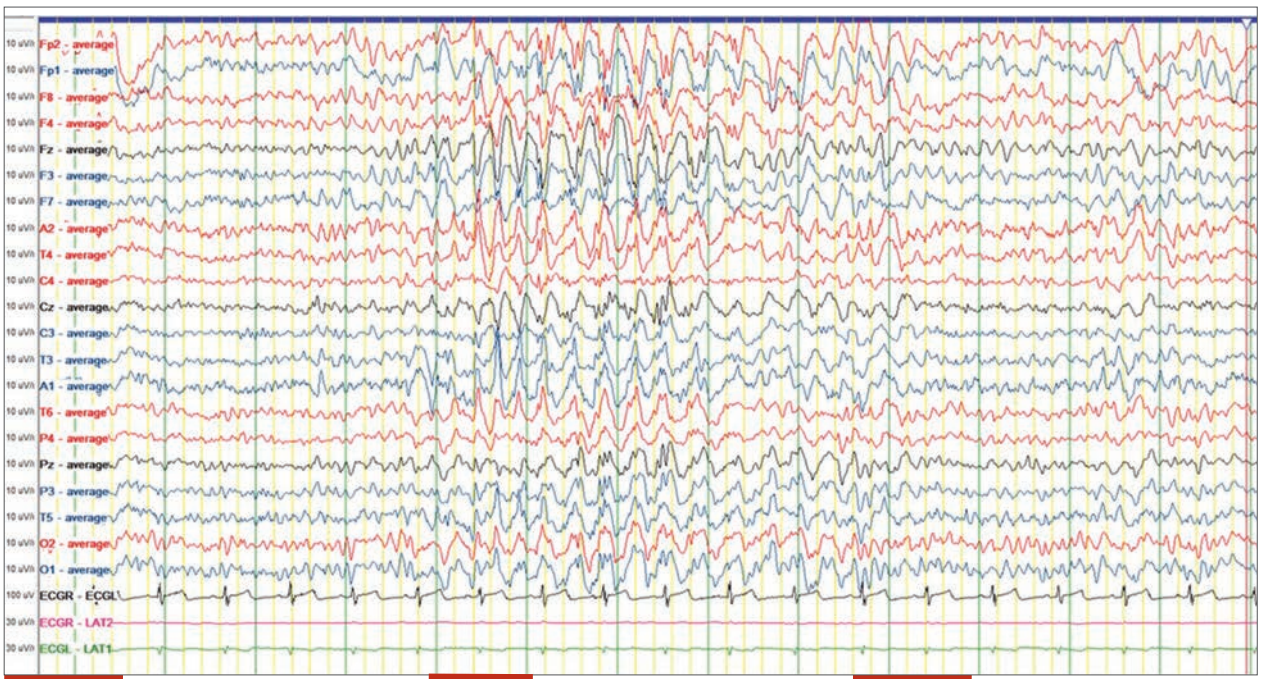


**FIGURE 1**
An EEG trace from a patient presenting with a first seizure in adulthood, showing a generalised spike-wave discharge suggestive of generalised epilepsy

## What are the differential diagnoses?

**A SEIZURE IS THE TRANSIENT OCCURRENCE OF SIGNS OR SYMPTOMS CAUSED BY ABNORMAL EXCESSIVE** or synchronous neuronal activity in the brain.

For a diagnosis of epilepsy, a patient would usually have two unprovoked seizures more than 24 hours apart. The definition of epilepsy also includes a single seizure with a higher than 60% chance of recurrence based on investigations, or an identifiable epilepsy syndrome.[1]

Up to 5% of people will experience at least a single seizure at some point in their lifetime.[2] It is estimated that there are between 362,000 and 415,000 people with epilepsy in England. The estimated UK incidence is 50 per 100,000 per year and up to 1% of the population have active epilepsy at any time.[2]

Epilepsy is arguably not one condition but an umbrella term encompassing multiple conditions causing seizures, with diverse causes, some genetic and others acquired.

## How should patients be investigated?

### DIFFERENTIAL DIAGNOSIS

Most patients with a first seizure will have experienced loss of consciousness. The cause of loss of consciousness is not necessarily neurological. Aside from a seizure, the differential diagnosis will include syncope, a temporary drop in blood supply to the brain leading to loss of consciousness. Syncope has a range of causes including reflex vasovagal, cardiogenic or postural. Another important differential diagnosis is psychogenic non-epileptic seizures (PNES), also referred to as dissociative seizures or non-epileptic attacks. The differential diagnosis for nocturnal episodes includes sleep disorders such as parasomnias.[3]

A seizure does not necessarily imply loss of consciousness, and focal seizures can present with diverse neurological symptoms depending on the brain area affected (see below). Other important causes of transient neurological symptoms without loss of consciousness include transient ischaemic attack (TIA) and migraine.

## What are the treatment options?

Depending on the suspected diagnosis, the patient may need onward referral. The diagnosis of epilepsy will usually be made in a neurology clinic.

### HISTORY AND EXAMINATION

A detailed history remains the cornerstone of epilepsy diagnosis. For each seizure type, the first symptoms and their subsequent progression should be recorded.

A generalised seizure as part of a generalised epilepsy syndrome may give no warning but may be preceded by blank spells or myoclonic jerks.

A generalised seizure with focal onset may be preceded by an aura, which gives clues as to the site of onset. The most common is temporal lobe onset, classically causing a burning smell or metallic taste, déjà vu or jamais vu, or a rising feeling in the stomach.

Occipital onset may be associated with a visual aura, frontal onset may present with unilateral motor symptoms and parietal aura can cause paraesthesia or pain. »

Not all seizures result in loss of consciousness, and all of the above situations may occur without proceeding to a generalised seizure, although these patients are perhaps less likely to present to a first seizure clinic.

A focal onset seizure typically lasts seconds to minutes and is usually briefer than a migraine or TIA. There may not be a postictal period. Myoclonic jerks are sudden uncontrolled and unpredictable muscle jerks, typically occurring late at night and in the early morning. Absences may be reported as daydreaming or feeling that the world around them has skipped forwards.

A 'first seizure' may not in fact be the first, and it is crucial to explore milder past episodes which may not have seemed significant at the time.

**'A 'first seizure' may not in fact be the first, and it is crucial to explore milder past episodes which may not have seemed significant at the time'**

If there is loss of consciousness, the history should continue from the moment the patient regains awareness. A generalised seizure is commonly followed by postictal confusion, and there may be myalgia, tongue biting or incontinence.

For the period of unconsciousness a witness account, if available, is crucial. A generalised tonic-clonic seizure may be preceded by a loud cry, with generalised muscle stiffness with open eyes, and rhythmic convulsions. There may be a colour change, including cyanosis, as breathing is interrupted. As the convulsion stops, there will be deep unconsciousness with wet stertorous breathing, which a witness will often call snoring. The duration of the shaking is typically only a minute or two but may seem longer to a non-medical observer. If attacks occur in a public space, there may be CCTV footage.

A history should include relevant triggers such as alcohol, sleep deprivation or stress. Photosensitivity is relatively rare but may be apparent from the history.[4]

Seizure markers in the history could include injuries such as tongue biting, urinary incontinence and myalgia. Significant injuries are rare after PNES,[5] but may be seen after syncope if it occurs without warning. A generalised seizure often leads to a prolonged period of unconsciousness or amnesia, such that it is common for people to report waking in an ambulance or with paramedics present, which is uncommon after a syncopal episode which is typically briefer. A prolonged episode of shaking with eyes closed, and waxing and waning of the attack would be more typical of PNES.[6]

Risk factors for epilepsy include:

- Family history
- Significant head injury
- Stroke
- Brain infection such as meningitis or encephalitis

Examination rarely contributes to the diagnosis, but any unexplained neurological signs would be a cause for concern and prompt urgent investigation.

## INVESTIGATIONS

A screening set of blood tests including full blood count, renal and liver function, and blood glucose will exclude some causes of loss of consciousness and act as a baseline in case treatment is required.

All patients should have a 12-lead ECG. This is important if a cardiac cause of collapse is suspected, and also because patients with epilepsy have an increased prevalence of early repolarisation pattern and QTc prolongation, which are treatable and can have serious consequences if missed.[7] If a cardiac cause is suspected, then further cardiac investigations such as prolonged ECG monitoring and an echocardiogram may be helpful, with a low threshold for specialist cardiology referral.

Neurological investigations for seizures commonly include an EEG to look for aberrant electrical activity in the brain suggestive of epilepsy. An EEG should not be requested unless there is a suspicion of epilepsy. Brain electrical activity varies over time. Hence a normal EEG cannot exclude epilepsy, but an abnormal EEG in the appropriate clinical context may be diagnostic. The yield of an EEG can be increased by recording for a prolonged period, or by depriving the patient of sleep prior to recording. An EEG will typically include screening for photosensitivity, which is widely known about but relatively rare, affecting 3% of patients with epilepsy.[4]

Brain imaging is required in almost all cases where epilepsy is suspected, the only possible exception being people with generalised epilepsies proven on EEG. CT scanning is often performed in the emergency department, which can exclude some structural lesions.[8] However, MRI is the imaging modality of choice with a much higher yield for smaller and more subtle brain lesions.[9]

Neuropsychological assessment can be helpful in identifying areas of focal cognitive weakness linked to particular brain regions, or in quantifying subjective memory impairment.

**'A normal EEG cannot exclude epilepsy, but an abnormal EEG in the appropriate clinical context may be diagnostic'**

Rarely, a seizure may be part of an acute illness such as encephalitis. A seizure without full neurological recovery should always prompt admission and urgent investigation, which may then include lumbar puncture and autoimmune antibody screening. Such patients require specialist input.

## CAUSES

Adult onset epilepsy occurs in two main peaks with higher incidence in those under 20 and those over 65.[10] Younger people with epilepsy are more likely to have genetic (idiopathic) epilepsies but may also present with new onset focal seizures arising from congenital or acquired brain lesions, or without a detectable lesion. Older adults are more likely to have acquired or symptomatic epilepsies from accumulated brain insults such as vascular disease or neurodegenerative conditions[11]

**'Between 20 and 40% of patients with a brain tumour have a seizure as their presenting symptom'**

A seizure may be the presenting symptom of an underlying illness requiring prompt treatment. For example, between 20 and 40% of patients with a brain tumour have a seizure as their presenting symptom,[12] and early diagnosis can improve treatment prospects. In older people, a seizure may be a sign of otherwise asymptomatic cerebrovascular disease, requiring treatment of risk factors.

## key points

SELECTED BY

**Dr Phillip Bland**
Former GP, Dalton-in-Furness, UK

**The incidence of epilepsy in the UK is estimated to be** 50 per 100,000 per year and up to 1% of the population have active epilepsy. Most patients with a first seizure will have experienced loss of consciousness. The differential diagnosis includes syncope, and psychogenic non-epileptic seizures, also referred to as dissociative seizures or non-epileptic attacks. The differential diagnosis for nocturnal episodes includes sleep disorders such as parasomnias. Depending on the suspected diagnosis, the patient may need onward referral. The diagnosis of epilepsy will usually be made in a neurology clinic.

**A generalised seizure as part of a generalised epilepsy** syndrome may occur without warning but may be preceded by blank spells or myoclonic jerks. A generalised seizure with focal onset may be preceded by an aura. The temporal lobe is the most common site of onset, producing symptoms such as a burning smell or metallic taste, déjà vu or jamais vu, or a rising feeling in the stomach. Seizure markers in the history may include tongue biting, incontinence and myalgia. A generalised seizure often leads to a prolonged period of unconsciousness or amnesia; it is common for patients to report waking in an ambulance or with paramedics present.

**Examination rarely contributes to the diagnosis, but any** unexplained neurological signs would be a cause for concern and prompt urgent investigation. All patients should have a 12-lead ECG. Patients with epilepsy have an increased prevalence of early repolarisation pattern and QTc prolongation, which are treatable and can have serious consequences if missed. A normal EEG cannot exclude epilepsy, but an abnormal EEG in the appropriate clinical context may be diagnostic. Brain imaging is required in almost all cases where epilepsy is suspected, the only possible exception being people with generalised epilepsies proven on EEG. MRI is the imaging modality of choice. Between 20 and 40% of patients with a brain tumour have a seizure as their presenting symptom.

**Following a first seizure, many patients present directly to** an emergency department. For patients presenting to primary care, NICE still recommends emergency admission for assessment. Patients presenting to primary care after a delay may prefer a direct referral to a first seizure clinic with appropriate safety netting. After a first seizure, most clinicians favour a watchful waiting approach, unless investigations suggest a high risk of recurrence. More than half of such patients will not go on to have further seizures. After more than one seizure, treatment should be offered immediately, without waiting for investigations.

**Patients should avoid recognised triggers for their seizures,** which commonly include sleep deprivation, alcohol excess and stress. Patients should be given lifestyle safety advice and driving must always be covered. Sudden unexpected death in epilepsy should be discussed with all patients with epilepsy, or their carers.

## MANAGEMENT

Following a first seizure, many patients present directly to an emergency department. For patients presenting to primary care, NICE still recommends emergency admission for assessment.[13] Patients presenting to primary care after a delay may prefer a direct referral to a first seizure clinic with appropriate safety netting. After a first seizure, most clinicians favour a watchful waiting approach, unless investigation results suggest a diagnosis of epilepsy. More than half of such patients will not go on to have further seizures.[14]

Treatment would be considered after a second seizure, or after a single seizure if investigations reveal a high risk of recurrence. After more than one seizure, treatment should be offered immediately, without waiting for investigations, since investigation findings are unlikely to alter this decision and a delay carries risk of further seizures.

### Antiepileptic drugs

Most people with epilepsy are treated with antiepileptic medication. Choice of medication depends on the specific epilepsy diagnosis and will usually be initiated with guidance from a specialist.

A comprehensive review of antiepileptic medications is beyond the scope of this article, but first-line broad spectrum antiepileptic medications include lamotrigine and levetiracetam.

Patients starting lamotrigine should be counselled about the risk of allergic reactions including Stevens Johnson syndrome, and should start at a low dose which is gradually increased.

Levetiracetam carries a risk of causing or exacerbating depression or irritability. Sodium valproate is very effective for generalised epilepsies but should normally be avoided in women of childbearing age because of its teratogenicity.

Carbamazepine remains a first-line choice for focal epilepsies but can exacerbate some types of generalised epilepsy. It is an enzyme inducer and should be used with caution in Han Chinese patients for whom it carries a risk of severe allergic reaction.[13]

### Other treatments

Surgical treatments may be necessary if an underlying tumour is discovered, but can also be extremely effective for patients with drug resistant epilepsy caused by a benign lesion that can be safely resected.[15] Vagus nerve stimulators may reduce seizure frequency but rarely lead to seizure freedom.[16]

A ketogenic diet is useful in some metabolic epilepsies, but is rarely used in adults, and requires close monitoring by a specialist metabolic service.[17]

Catamenial epilepsy can occasionally be helped by hormone treatment.

### Avoiding triggers

Patients should avoid recognised triggers for their seizures, which commonly include sleep deprivation, alcohol excess (seizures often occur the following day) and stress. In people with photosensitive epilepsy, wearing dark glasses or closing one eye may reduce the likelihood of a flashing light causing a seizure.

## PROGNOSIS

Treatment with antiepileptic medication leads to seizure freedom in around two thirds of patients.[18] Depending on investigation results, careful withdrawal of medication can be considered after a period of 2-5 years of seizure freedom, with a proportion remaining seizure free off medication.[19]

Poor response to treatment should prompt the clinician to revisit the diagnosis and confirm adherence to treatment, but a third of people with epilepsy have drug resistance, defined as ongoing seizures despite adequate treatment trials of two or more antiepileptic medications.[20] This group remains challenging to treat despite therapeutic advances.[18]

The majority of seizures cause no significant injuries, although tongue biting and urinary incontinence are common. More major injuries such as fractures or joint dislocations may occur. Seizures occurring in dangerous situations may lead to more significant injuries; seizures while cooking can lead to burns, seizures while at heights can lead to falls, and seizures while cycling or driving can cause high speed crashes. A seizure while swimming or taking a bath may lead to drowning.

## EPILEPSY COUNSELLING

After a first seizure or a new epilepsy diagnosis, patients should receive lifestyle safety advice. Patients should take showers rather than baths, avoid heights, and generally try to avoid situations where losing awareness would cause increased risk. It is impossible to counsel patients about every possible situation, but occupation and social history are crucial here as the advice offered to an office worker will differ from that offered to a bus driver or a deep sea diver.

NICE recommends that patients should have a regular structured review with their GP at least annually.[13] »

### Driving

Driving is a topic that must always be covered. For a standard driving licence, after a single seizure, there will be a driving ban of 6 months in the UK, with a similar ban for a loss of consciousness without a clear diagnosis.

Syncope is not subject to a driving ban if there is an avoidable trigger or if it only occurs from standing, but syncope from sitting can trigger similar restrictions to a seizure. If there are multiple seizures, or a diagnosis of epilepsy is reached by another means, the ban will be 12 months. More stringent rules apply to those with a group 2 licence, such as bus and lorry drivers. Rules are periodically updated, and it is best to consult the Driver and Vehicle Licensing Agency (DVLA) guidance (see Useful information box, below, right).

The patient is responsible for informing the DVLA of their diagnosis, and the clinician would only do so in exceptional circumstances, but the discussion about driving should be well documented for medicolegal reasons.

### Sudden unexpected death in epilepsy

Sudden unexpected death in epilepsy (SUDEP) is defined as the sudden and unexpected death of a person with epilepsy, in normal and benign circumstances, without an obvious alternative cause of death,[21] and has an estimated incidence of 0.1% per year in people with epilepsy.[22] Although the mechanisms are uncertain and difficult to research, risk factors include ongoing uncontrolled convulsive seizures, living and sleeping alone, male sex, early onset and long duration of epilepsy, psychiatric comorbidity and alcohol excess.

NICE advocates discussion of SUDEP with all patients with epilepsy, or their carers.[13] It is a particularly important topic for discussion when patients make choices that will increase their risk, for example poor adherence to medication, alcohol excess, or recurrent sleep deprivation.

## PREGNANCY

There are specific concerns regarding pregnancy, breastfeeding, and contraception which should be discussed with a specialist where appropriate.

Enzyme-inducing antiepileptic medication such as carbamazepine, phenytoin, phenobarbital and topiramate may reduce the effectiveness of the oral contraceptive pill.

Most women with epilepsy who become pregnant will have a normal pregnancy, labour, and birth, with a healthy child. High-dose folic acid (5 mg daily) is recommended for all women with epilepsy considering pregnancy.

Lamotrigine and levetiracetam are considered first-choice medication for women in pregnancy, with observational data suggesting that they have little impact on the fetus.[23] Generally, the lowest effective dose of a single safe medication is chosen. Combinations of epilepsy medications are best avoided if possible, as data on the safety of polypharmacy in pregnancy is lacking.

**'Women of childbearing age on valproate should be enrolled in the MHRA pregnancy prevention programme'**

Valproate should be avoided in pregnancy because of the risk of teratogenicity, and women of childbearing age on valproate should be enrolled in the MHRA pregnancy prevention programme.[24]

## CONCLUSIONS

Epilepsy is an umbrella term for many conditions, with seizures the thread connecting them. It is common, and for the majority of people with epilepsy the prognosis is excellent, with a high chance of seizure freedom with first- or second-line medication. Drug resistant epilepsy remains very challenging to treat. Underlying causes requiring urgent treatment, such as brain tumours, make up a small proportion of cases but must be excluded. Patients should be counselled on lifestyle and driving.

**Competing interests:** None

## REFERENCES

**1** Fisher RS, Acevedo C, Arzimanoglou A et al. ILAE Official Report: A practical clinical definition of epilepsy. *Epilepsia* 2014;55:475-82
**2** Sander JW, Shorvon SD. Epidemiology of the epilepsies. *J Neurol Neurosurg Psychiatry* 1996;61:433-43
**3** Pohlmann-Eden B, Beghi E, Camfield C, Camfield P. The first seizure and its management in adults and children. *BMJ* 2006;332:339-42
**4** Quirk JA, Fish DR, Smith SJM et al. Incidence of photosensitive epilepsy: a prospective national study. *Electroencephalogr Clin Neurophysiol* 1995;95:260-67
**5** Asadi-Pooya AA, Bahrami Z. Dramatic presentations in psychogenic nonepileptic seizures. *Seizure* 2019;65:144-47
**6** Kotsopoulos IAW, de Krom MCTFM, Kessels FGH et al. The diagnosis of epileptic and non-epileptic seizures. *Epilepsy Res* 2003;57:59-67
**7** Lamberts RJ, Blom MT, Novy J et al. Increased prevalence of ECG markers for sudden cardiac arrest in refractory epilepsy. *J Neurol Neurosurg Psychiatry* 2015;86:309-13
**8** Harden CL, Huff JS, Schwartz TH 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
**9** Sidhu MK, Duncan JS, Sander JW. Neuroimaging in epilepsy. *Curr Opin Neurol* 2018;31:371-78
**10** Forsgren L, Beghi E, Oun A, Sillanpää M. The epidemiology of epilepsy in Europe - a systematic review. *Eur J Neurol* 2005;12:245-53
**11** Thijs RD, Surges R, O'Brien TJ, Sander JW. Epilepsy in adults. *Lancet* 2019;393:689-701
**12** Maschio M. Brain tumor-related epilepsy. *Curr Neuropharmacol* 2012;10:124-33
**13** National Institute for Health and Care Excellence. CG137. Epilepsies: diagnosis and management. NICE. London. 2012 Updated Feb 2020 www.nice.org.uk/guidance/cg137 [Last accessed 6 Sep 2020]
**14** Berg AT, Shinnar S. The risk of seizure recurrence following a first unprovoked seizure: a quantitative review. *Neurology* 1991;41:965-72
**15** West S, Nevitt SJ, Cotton J et al. Surgery for epilepsy. *Cochrane Database Syst Rev* 2019;CD010541.pub3
**16** Englot DJ, Rolston JD, Wright CW et al. Rates and predictors of seizure freedom with vagus nerve stimulation for intractable epilepsy. *Neurosurgery* 2016;79:345-53
**17** Martin-McGill KJ, Jackson CF, Bresnahan R et al. Ketogenic diets for drug-resistant epilepsy. *Cochrane Database Syst Rev* 2018;CD001903.pub4
**18** Chen Z, Brodie MJ, Liew D, Kwan P. Treatment outcomes in patients with newly diagnosed epilepsy treated with established and new antiepileptic drugs. *JAMA Neurol* 2018;75:279-86
**19** Lamberink HJ, Otte WM, Geerts AT et al. Individualised prediction model of seizure recurrence and long-term outcomes after withdrawal of antiepileptic drugs in seizure-free patients – a systematic review and individual participant data meta-analysis. *Lancet Neurol* 2017;16(7):523-31
**20** Kwan P, Arzimanoglou A, Berg AT et al. Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia* 2010;51:1069-77
**21** Nashef L, So EL, Ryvlin P, Tomson T. Unifying the definitions of sudden unexpected death in epilepsy. *Epilepsia* 2012;53:227-33
**22** Thurman DJ, Hesdorffer DC, French JA. Sudden unexpected death in epilepsy: assessing the public health burden. *Epilepsia* 2014; 55:1479-85
**23** Veroniki AA, Cogo E, Rios P et al. Comparative safety of anti-epileptic drugs during pregnancy: a systematic review and network meta-analysis of congenital malformations and prenatal outcomes. *BMC Med* 2017;15
**24** Valproate use by women and girls. www.gov.uk/guidance/valproate-use-by-women-and-girls [Last accessed 7 Sep 2020]

## Useful information

**Driver and Vehicle Licensing Agency**
**www.gov.uk/epilepsy-and-driving**

**Epilepsy Society**
**www.epilepsysociety.org.uk/**

**Epilepsy Action**
**www.epilepsy.org**

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