New-onset seizure in adult and adolescents management

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Definitions

Seizure: A transient occurrence of signs and symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

Unprovoked Seizure: Occurring in the absence of precipitating factors and may be caused by a static or progressive injury.

Acute Symptomatic Seizure: In close temporal association with a transient central nervous system or systemic insult presumed to be an acute manifestation of the insult.

Focal Seizure: Initial onset originates within 1 part of a cerebral hemisphere.

Generalized Seizure: Initial activity is consistent with rapidly engaging networks distributing in bilateral cerebral hemispheres.

Epilepsy: Disorder of the brain characterized by an enduring predisposition to generate epileptic seizures. Has been defined as 2 or more unprovoked seizures occurring more than 24 hours apart or 1 unprovoked seizure and a high risk (at least 60%) of recurrent unprovoked seizures over the next 10 years.

Introduction

- Seizure are a common occurrence 8-10% of population over a life time[1-2]
- 1-2% of all emergency department visit ,1/4 of them will be a first seizure [3]

1.Annegers JF , Hanser WA, Lee Jr , Rocca WA.Epilepsia 1995:36:327,
2.Hansa WA,Annegers F,Kurland LT, .Epilepsia 1993 :34:453
3.Huff SS , Monis DL ,Kothari RU,at at al .acad emerg Med.2001; 8:622.

Outline of talk

1. Is this a seizure?
2. Is this the first seizure?
3. What is the cause: provoked or unprovoked?
4. What are the investigations needed?
5. Is this epilepsy—what is the epilepsy or syndrome syndrome?
6. What is the risk of seizure recurrence?
7. Should this patient be treated with AEDs? What are the risks and benefits of antiepileptic drug (AED) treatment?
8. What are the instructions on safety and lifestyle?
9. Common Question from parent and PEW.
10. First aid in SZ
11. Quiz

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- **Is this a seizure?**

Differential diagnosis of seizures

- Syncope and cardiac causes (arrhythmia, reduced cardiac output)
- Psychogenic non-epileptic seizures
- Physiological sleep related phenomena: hypnic myoclonus
- Sleep disorders: parasomnias, rapid eye movement (REM)
- Sleep behavior disorder, cataplexy, micro sleeps, daytime
- sleepiness, periodic limb movement disorder (PLMD)
- Panic attacks
- Complex migraine
- Transient global amnesia
- Metabolic: recurrent hypoglycemia
- Movement disorders: paroxysmal dyskinesia
- Transient ischemic attacks (TIA): "limb shaking TIA"
- Acute rise in intracranial pressure

Table 1. Differential Diagnosis of New-Onset Seizure

Clinical Entity	Clinical Features	Tools for Diagnosis	Patient Account	Bystander Account
Transient ischemic attack	Results from temporary interruption of blood supply in the distribution of a cerebral vessel. This produces rapid onset of negative symptoms such as numbness, weakness, and aphasia, and is typically not associated with stiffness or jerking. Occasionally a transient ischemic attack may present with a stuttering course.	Risk factors for cerebrovascular disease. Brain magnetic resonance imaging and magnetic resonance angiogram looking at blood vessels of the head and neck.	Fully aware of deficits and typically only is limited in his or her ability to report the presentation due to language impairment.	Same as patient account unless the patient has language impairment preventing accurate reporting.
Migraine	Aura present with visual aura, unilateral pulsating headache, nausea, and vomiting. However, atypical migraines can present with isolated neurological symptoms or without associated headache. The duration and intensity of migraines typically last hours to days with a slow progression of aura and neurological deficits.	A history of migraines and family history of migraines may be helpful.	Does not lose awareness during a migraine and can accurately report his or her presentation. However, confusional and basilar migraines can result in inattention and decreased levels of consciousness.	Similar to patient account unless there is associated confusion or inattention as can be seen in basilar or confusional migraines.
Syncope	A transient loss of consciousness with complete return to preexisting neurological function. Vasovagal syncope typically has a situational trigger such as fear, pain, medical procedures, coughing, micturition, defecation, or Valsalva maneuver. Orthostasis can aggravate a vasovagal reaction or bring out a syncope from hypovolemia or structural heart disease.	Electrocardiography, cardiac telemetry, and echocardiography are recommended to exclude cardiac etiologies. Tilt table testing may help reproduce typical events.	Typically is preceded by feelings of dizziness, fullness in ears, nausea, and blurry vision. Patients are usually pale and have cold and clammy skin and flaccid muscle tone. Patients will not have recollection of events that occur after loss of consciousness, although this period is brief. There is typically no postictal state.	May notice brief myoclonic jerks or tonic posturing at the end of the event. This may be described by witnesses as "convulsive" activity.
Psychogenic nonepileptic seizures	Typically are associated with emotional events or stressors, last longer than epileptic seizures, and often have a waxing and waning quality. Clinical features such as eye closure, pelvic thrusting, vocal stuttering, and partial awareness during whole-body motor movements are typical.	Continuous electroencephalographic monitoring is recommended to capture events in question and ensure no epileptic changes are seen.	May claim awareness of bilateral shaking movements, which in epileptic seizures are typically associated with amnesia and unresponsiveness.	May report clinical features of the event such as those most typical for psychogenic nonepileptic seizures (eye closure, pelvic thrusting, waxing and waning of motor movements).
Focal seizure	May start with an aura followed by loss of awareness, unilateral sensations, or motor activity. This may progress to a generalized tonic-clonic seizure in some cases (evolving to bilateral convulsive activity). This progression is faster than seen with migraine.	An electroencephalogram may show focal epileptiform discharges. Brain magnetic resonance imaging should be performed to look for structural abnormalities.	May report an aura (déjà vu or an epigastric aura with temporal lobe epilepsy), contralateral paresthesia in parietal lobe seizures, and visual distortions in occipital lobe seizures. If awareness is not affected, he or she may report progression of symptoms to unilateral motor or sensory symptoms. If loss of awareness or generalized tonic-clonic activity, will not be able to report event.	Report probably more reliable and may include patient staring, frequent eye blinking, semipurposeful movements of hands and feet, and characteristics of tonic-clonic seizure activity. May also report open eyes, urinary incontinence, focal or whole-body stiffening, postevent lethargy or confusion, and a stereotyped progression with recurrent events.
Generalized seizure	Typically no warning. Seizures characterized by brief staring spells, generalized tonic-clonic activity, myoclonic jerks.	An electroencephalogram may show generalized epileptiform discharges and confirm a specific epilepsy syndrome.	Frequently have no awareness of event, except for myoclonic jerks, but may report postictal findings such as tongue bite or incontinence (if generalized tonic-clonic seizures).	Crucial to understand the clinical presentation.

2

Is this the first seizure?

- - At 2 yrs, risk of recurrence after a first unprovoked seizure = 30-50%

  - After two or more unprovoked seizure = 70-80%

- Preceding minor seizures (myoclonus, absence, aura, CPS) are often time under recognized

Berg AT and Shinnar S Neurology 1991
Camfield PR et.al Neurology 1985
Hauser WA et.al NEJM 1998

3

What is the cause: provoked or unprovoked?

- Different in risk of recurrence and management between provoked and unprovoked seizure
- Provoking factors: acute systemic or CNS insults
- **Unprovoked seizure** ; indicates intrinsic brain epilepto-genicity

- fever, sleep deprivation and photic stimulation

- Remote symptomatic pathology (onset of CNS insult > 1 week before the seizure)

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What are the investigations needed?

Neurology®

Practice Parameter: Evaluating an apparent unprovoked first seizure in adults (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society

A. Krumholz, S. Wiebe, G. Gronseth, et al.

Neurology 2007;69;1996-2007
DOI 10.1212/01.wnl.0000285084.93652.43

- **Apparent** unprovoked first seizure in adults 2007
- Patients returned to baseline function

- **Recommendations;**

1. **EEG** should be considered (Level B) (high yield, risk of recurrence); if possible within 24-48 h

2. **Either a CT or MRI** should be considered (Level B) (significant abnormal 10%, some value in determining risk of recurrence)

3. **Lab studies** blood glucose, electrolyte, blood counts, lumbar puncture (fever), toxicology screening (Level U)

Guided by specific clinical circumstances

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- 300 consecutive adults and children presented with first unexplained seizure

Is this epilepsy- what is the epilepsy syndrome?

Epilepsy	Clinical data only	Clinical+EEG data	Clinical+EEG+MRI data
Generalised	25 (8%)	69 (23%)	68 (23%)
Partial	116 (39%)	163 (54%)	175 (58%)
Unclassified	159 (53%)	68 (23%)	57 (19%)

81%

King MA et.al The Lancet 1998

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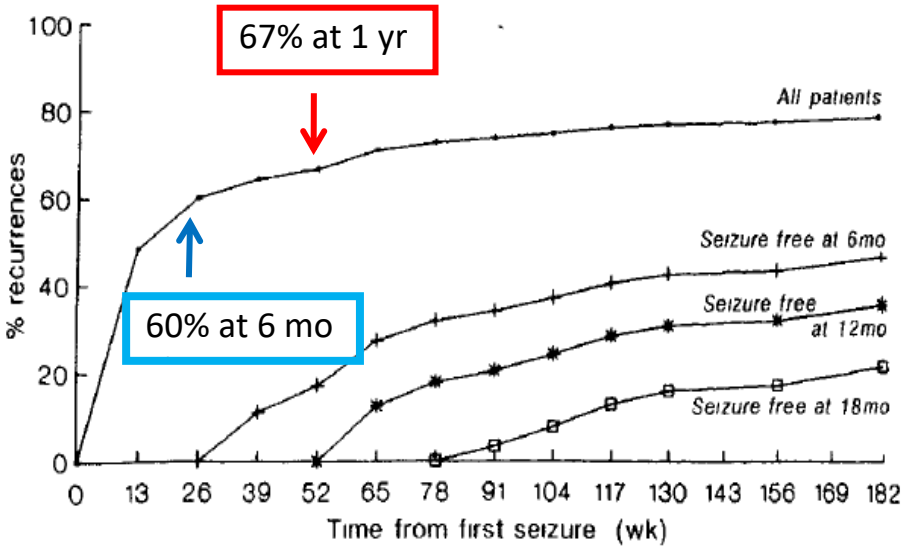
- **What is the risk of seizure recurrenc ?**

Risk of recurrence after first unprovoked seizure

✓ Pooled estimate of 2 year recurrence risk = **42% (30-50%)**



78% at 3 yrs

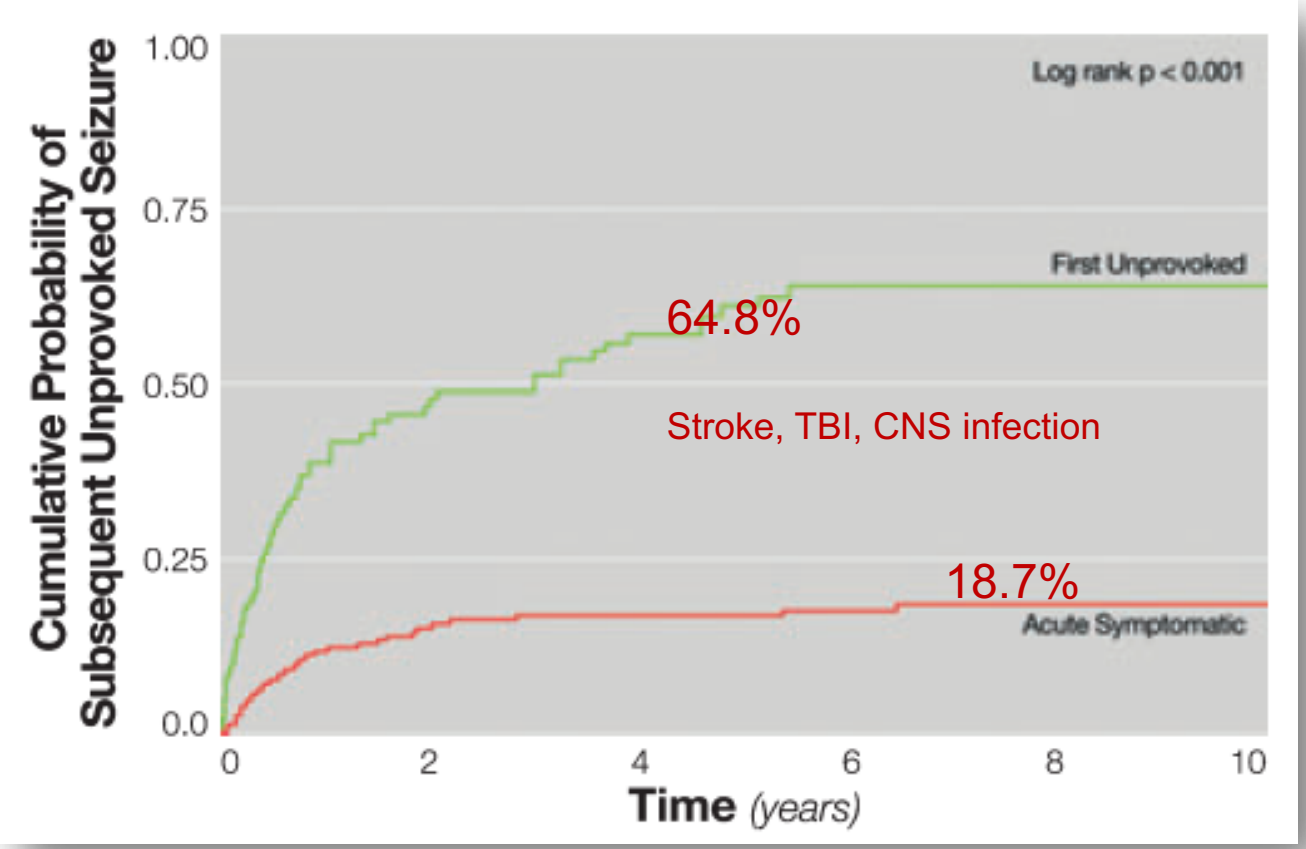
44 % at 3yrs

32 % at 3yrs

17 % at 3yrs

Berg AT and Shinnar S Neurology 1991
Hart YM et.al; The Lancet 1990

Risk of recurrence after First unprovoked vs Acute symptomatic seizure



Hesdorffer DC et.al; Epilepsia 2009

Recurrence risk after first seizure

1. First unprovoked seizure risk recurrence Sz. In first 2 yr. (21-45%) (LevelA)
2. Prior brain insult risk recurrence Sz. in first 1-5 yr. 2.35 times (LevelA)
3. EEG with epileptiform abnormalities in 1-5 yr =2.16 times (levelA)
4. A significant brain imaging abnormal = 2.44 time (levelB)
5. Nocturnal seizure risk recurrence Sz. in first 1-4 yr. 2.1 times (Level b)
6. Immediate AEDs therapy can delay of second Sz with in 2 yr (LevelB) with out improved QOL (level C) when compare delay AEDs

Risk of recurrence after multiple seizures within 24 h and status epilepticus (SE)

- Multiple seizures occurring within 24 h and SE are usually treated as a single event since they do not carry a greater risk of recurrence

- Individuals who present with SE as a first seizure are at a high risk of experiencing SE as the recurrence (risk of SE recurrence = 25% over 10 years)

Kho LK et.al Neurology 2006
Shinnar S et.al Pediatrics 1996
Berg AT et.al Neurology 2004

What are the predictors of recurrence?

Abnormal neurological status and abnormal EEG

Predictor	Pooled RR of recurrence	Pooled risk of 2 year recurrence (%)
Abnormal neurological status	1.8	57
Normal EEG		27
Epileptiform abnormalities in EEG	2.0	58
Non-epileptiform abnormalities in EEG	1.3	37
Aetiology and EEG combined		
Idiopathic + normal EEG		24
Idiopathic + abnormal EEG	1.9	48
Remote symptomatic + normal EEG		48
Remote symptomatic + abnormal EEG	1.4	65

EEG, electroencephalogram; RR, relative risk.

Camfield P and Camfield C Epilepsia 2000

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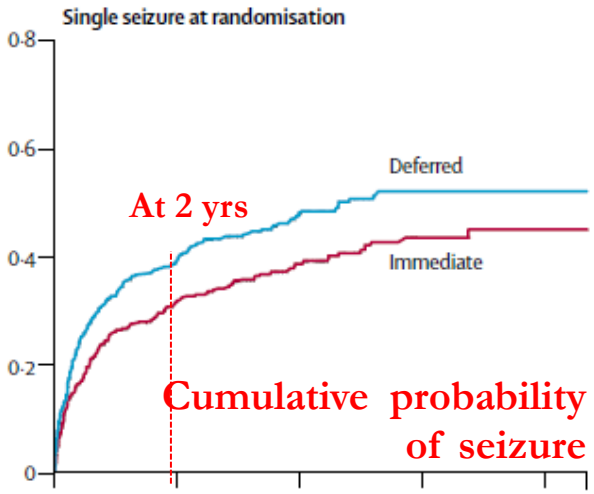
- **Should this patient be treated with AEDs?**
  - **What are the risks and benefits of antiepileptic drug (AED) treatment ?**

Immediate vs deferred treatment after a first unprovoked seizure



MESS studies

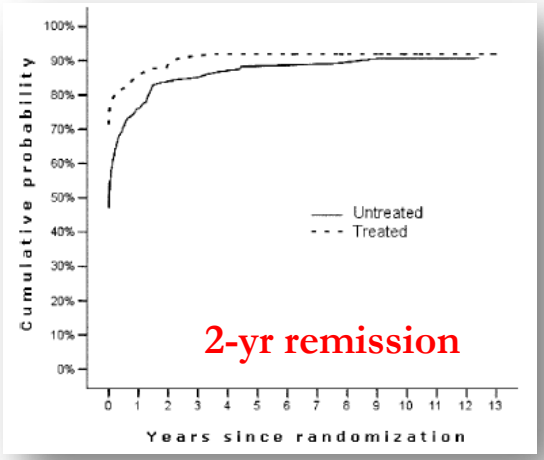
- 2 yr-remission: 69% vs 61%
  At 3 yrs: 1-3 yrs sz remission: 74% vs 71%
  At 5 yrs: 3-5 yr sz remission: 76% vs 77%

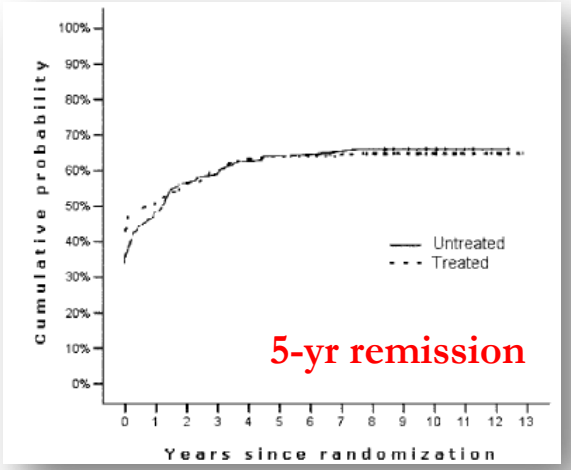
"Immediate antiepileptic drug treatment reduces the occurrence of seizures in the next 1–2 years, but does not affect long-term remission in individuals with single or infrequent seizures"

Marson A et.al The Lancet 2005

Immediate vs deferred treatment after a first unprovoked seizure

FIR.S.T. (First Seizure Trial) studies





- Treatment of the first seizure increased the probability of a 2-year remission in the first 3 years; however, the difference disappeared after a longer period of follow-up

(only patients with GTCs were included)

Maurizio AL et.al Neurology 2006

Prediction of risk of seizure recurrence

	Prognostic index
Starting value	
One seizure prior to presentation	0
Two or three seizures prior to presentation	1
Four or more seizures prior to presentation	2
Add if present	
Neurological disorder or deficit, learning disability, or developmental delay	1
Abnormal EEG	1
Risk classification group for seizure recurrence*	**Final score**
Low risk	0
Medium risk	1
High risk	2–4

*See table 3 for probabilities of no seizure recurrence at specific time points for each of these subgroups.

Table 4: Prognostic index, with integer values

MESS studies

"There is little benefit to immediate treatment in patients at low risk of seizure recurrence, but potentially worthwhile benefits are seen in those at medium and high risk"

Kim LG et.al The Lancet 2006

Indications to consider antiepileptic drug treatment after the first seizure

- High risk of recurrence
  - abnormal EEG
  - abnormal neurological status
  - prior seizures (previously unreported)
  - possibly: partial seizure with remote symptomatic aetiology
  - possibly: first seizure in sleep
- High risk of complications with recurrence
  - when first seizure presents as status epilepticus
- High risk of injuries with recurrence
  - osteoporosis
  - anticoagulant treatment
  - elderly living alone
- Socioeconomic reasons
  - employment
  - driving

Pohlmann-Eden B et.al BMJ 2006
Seneviratne U Postgrad Med J 2009

Epilepsia, 54(3):551–563, 2013
doi: 10.1111/epi.12074

SPECIAL REPORT

Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes

*Tracy Glauser, †Elinor Ben-Menachem, ‡Blaise Bourgeois, §Avital Cnaan, ¶Carlos Guerreiro, #Reetta Kälviäinen, **Richard Mattson, ††Jacqueline A. French, ‡‡Emilio Perucca, §§Torbjorn Tomson for the ILAE Subcommission on AED Guidelines

- Review of all 64 **randomized controlled trials** from 1940 – 2012
- "For patients with newly diagnosed or untreated epilepsy, which AEDs have the best evidence for long-term efficacy (=seizure control) or effectiveness (=retention) as initial monotherapy?"
- Failed superiority studies were reanalysed to evaluate non-inferiority
- Not meant to be a treatment guideline since other potential parameters in choosing an AED (e. g. interactions, specific side effects, cost) not considered

ILAE report on monotherapy 2013

Table 4. Summary of studies and level of evidence for each seizure type and epilepsy syndrome

Seizure type or epilepsy syndrome	Class I studies	Class II studies	Class III studies	Level of efficacy and effectiveness evidence (in alphabetical order)
Adults with partial-onset seizures	4	1	34	Level A: CBZ, LEV, PHT, ZNS Level B: VPA Level C: GBP, LTG, OXC, PB, TPM, VGB Level D: CZP, PRM
Children with partial-onset seizures	1	0	19	Level A: OXC Level B: None Level C: CBZ, PB, PHT, TPM, VPA, VGB Level D: CLB, CZP, LTG, ZNS
Elderly adults with partial-onset seizures	1	1	3	Level A: GBP, LTG Level B: None Level C: CBZ Level D: TPM, VPA
Adults with generalized onset tonic–clonic seizures	0	0	27	Level A: None Level B: None Level C: CBZ, LTG, OXC, PB, PHT, TPM, VPA Level D: GBP, LEV, VGB
Children with generalized-onset tonic–clonic seizures	0	0	14	Level A: None Level B: None Level C: CBZ, PB, PHT, TPM, VPA Level D: OXC
Children with absence seizures	1	0	7	Level A: ESM, VPA Level B: None Level C: LTG Level D: None
Benign epilepsy with centrotemporal spikes (BECTS)	0	0	3	Level A: None Level B: None Level C: CBZ, VPA Level D: GBP, LEV, OXC, STM
Juvenile myoclonic epilepsy (JME)	0	0	1	Level A: None Level B: None Level C: None Level D: TPM, VPA

ILAE report on monotherapy 2013

Table4 .Summary of studies and level of evidence for each seizure type and epileptic syndrome

SZ type &epileptic syndrome	class I study	Class II study	Class III study	level of efficacy and effectiveness evidence (in alphabetical order)
Adult with partial onset seizure	4	1	34	level A : CBZ,LEV,PHT,ZNS B : VPA C : GBP,LTG,OXC,PB,,TPM, VGB D : CZP,PRM
Elderly adult with partial onset seizure	1	1	3	level A : GBP, LTG B : none C : CBZ D : TPM,VPA
Adult with generalized onset tonic- clonic seizure	0	0	27	level A : none B : none C :CBZ,LTG,OXC,PB,PHT, TPM, VPA D : GBP,LEV,VGB

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What are the instructions on safety and lifestyle?

- No rational/evidence-based approach to restrictions after a first seizure for children and adolescence (ILAE Commission report 1997)

- If there are to be restriction, they ***should not be imposed for more than 6-12 months*** after the first seizure since nearly all recurrences will have happened by then

- **Driving**:

- Non-commercial ?? Sz freedom 3 to 12 months

- Commercial ?? at least 2 years without medication

?? 10 years with medication

- **Working**: dangerous machine ?? at least 6 months
- **High-risk activities**: ?? At least 3-6 months
- **Take a shower rather than a bath**

Seneviratne U Postgrad Med J 2009
Camfield P and Camfield C Epilepsia 2008

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Common questions from the parents and the patients

- **Will it happen again ?**

  30-50%

(may be varied; 20% in generalized sz, normal EEG, no concomitant neurological deficits vs 80% if focal sz and presence of IEDs and neurological deficits)

- **How long might it be before we can be sure that the patient will not have a recurrence?**

Recurrences may be delayed for 2 years or more, but most recurrences are within 6 months of the first seizure

- **Could the patient die during a recurrence?**

The risk of the patient dying during a recurrent seizure is miniscule

(The risk of death during a first recurrent seizure has not been reported; however, children with established epilepsy have a tiny risk of SUDEP)

- **Could there be brain damage with a recurrence?**

A robust literature shows that clinically significant brain injury does not result from a few recurrent unprovoked seizures

Austin JK et.al Epilepsia 2000
Bourgeios BF et.al Ann Neurol 1983

- **If medication treatment is delayed will there be any long-term change in the chance of a permanent remission?**

The chance of remission is not altered by delaying daily AED treatment after a first seizure

Do I call 1669?

Seizures do not usually require emergency medical attention. Only call 911 if one or more of these are true:

- The person has never had a seizure before.
- The person has difficulty breathing or waking after the seizure.
- The seizure lasts longer than 5 minutes.
- The person has another seizure soon after the first one.
- The person is hurt during the seizure.
- The seizure happens in water.
- The person has a health condition like diabetes, heart disease, or is pregnant.

First aid for any type of seizure

There are many types of seizures. Most seizures end in a few minutes.

These are general steps to help someone who is having any type seizure:

- Stay with the person until the seizure ends and he or she is fully awake. After it ends, help the person sit in a safe place. Once they are alert and able to communicate, tell them what happened in very simple terms.
- Comfort the person and speak calmly.
- Check to see if the person is wearing a medical bracelet or other emergency information.
- Keep yourself and other people calm.
- Offer to call a taxi or another person to make sure the person gets home safely

First aid for generalized tonic-clonic (grand mal) seizures

When most people think of a seizure, they think of a generalized tonic-clonic seizure, also called a grand mal seizure. In this type of seizure, the person may cry out, fall, shake or jerk, and become unaware of what's going on around them.

Here are things you can do to help someone who is having this type of seizure:

- Ease the person to the floor.
- Turn the person gently onto one side. This will help the person breathe.
- Clear the area around the person of anything hard or sharp. This can prevent injury.
- Put something soft and flat, like a folded jacket, under his or her head.
- Remove eyeglasses.
- Loosen ties or anything around the neck that may make it hard to breathe.
- Time the seizure. Call 911 if the seizure lasts longer than 5 minutes.

Stop! Do NOT

Knowing what **NOT** to do is important for keeping a person safe during or after a seizure.

Never do any of the following things

- Do **not** hold the person down or try to stop his or her movements.
- Do **not** put anything in the person's mouth. This can injure teeth or the jaw. A person having a seizure cannot swallow his or her tongue.
- Do **not** try to give mouth-to-mouth breaths (like CPR). People usually start breathing again on their own after a seizure.
- Do **not** offer the person water or food until he or she is fully alert.

Need to admit

- Patients who have fully recovered, have no neurological deficit, and have normal initial investigations can be discharge from ED.
- Admission should be considered in all patients with alcoholism,poor circumstances or those without a responsible adult to stay with.

Neurologic Consultation (NEJM 2001)

- Change in the type of seizure
- Uncertain diagnosis (e.g. normal EEG)
- Lack of seizure control in 3 months
- Failure of two monotherapies
- Patient is considering pregnancy
- Prolonged post-ictal state
- History of status epilepticus

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Quiz

MCQS

1. What should be considered as part of the routine neurodiagnostic evaluation of adults presenting with an apparent unprovoked first seizure?

A. EEG

B. Head CT or MRI

C. Lumbar puncture

D. Complete blood count, electrolytes and toxicology screen

E. A and B are correct

2. Lumbar puncture is not recommended in the routine evaluation of an adult with an apparent unprovoked first seizure unless there are specific circumstances such as:

A) Presence of focal neurological deficits

B) Presence of Todd's paresis

C) Fever

D) Being comatose

E) Presence of remote symptomatic etiology

TRUE OR FALSE

Question	Answer
1. Abnormal neurological findings and abnormal EEG predict high risk of recurrence	T
2. Epileptiform EEG abnormalities make seizure recurrence twice more likely	T
3. AED treatment after the first seizure improves long term remission rate	F
4. AED treatment after the first seizure decreases the risk of seizure recurrence particularly in the first 2 years	T
5. Lumbar puncture is not indicated in immuno-compromised individuals if they are afebrile	F

TRUE OR FALSE

Question	Answer
6. EEG should be done in all patients	**T**
7. Toxicology screen should be done in selected patients	**T**
8. Urinary incontinence confirms the diagnosis of seizure	**F**
9. Eyes rolling back does not occur in syncope	**F**
10. Family history of epilepsy is a strong predictor	**F**

Summary

- Management after 1st seizure involves lots of discussion with patient about risks/benefits
- Remember impact on driving: tell the ministry!
- When in doubt about management (especially medications), get a neurologist involved

Thank YOU FOR YOUR ATTENTION