

Family medicine approach to seizures

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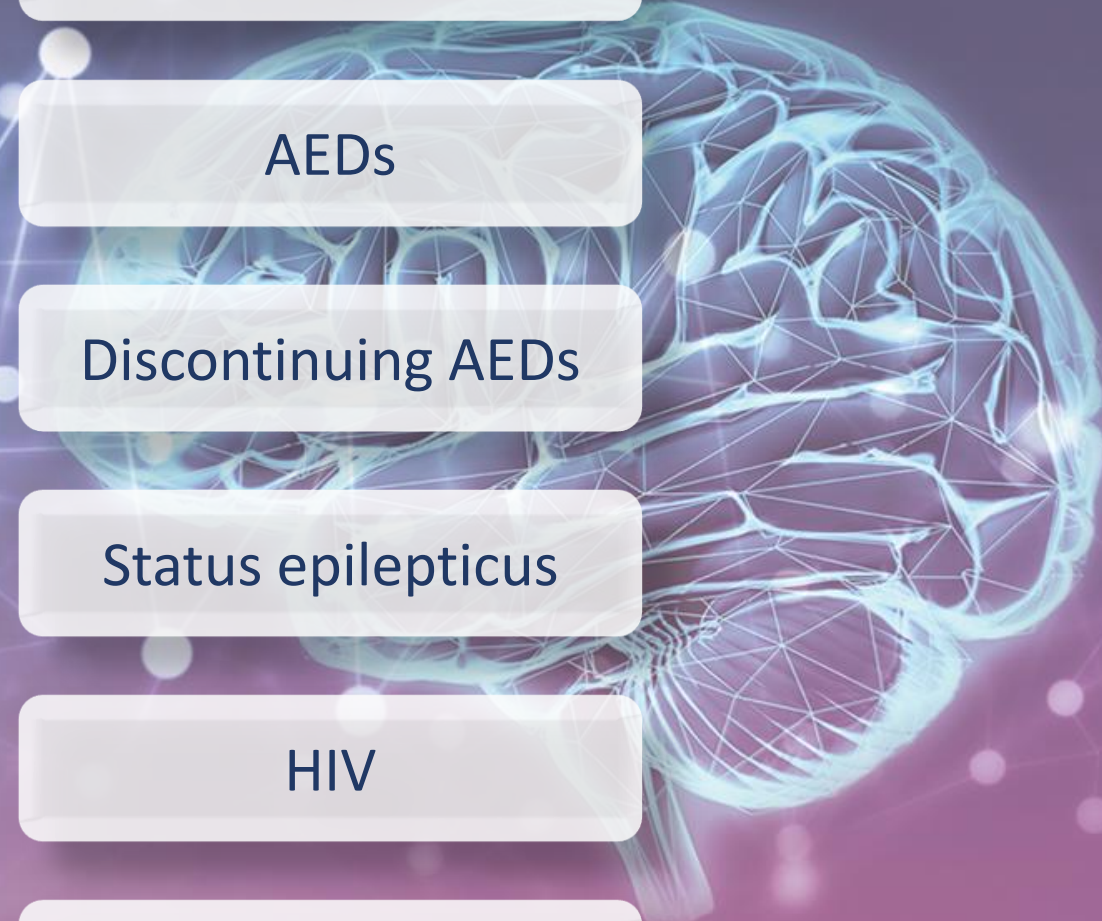
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Quick Reference

Classifications

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What is?

What is epilepsy?

Is a seizure a disease?

What is also on the differential for seizures?



Classification?

What are the classifications of seizures?



Goals?

What are the goals of seizure diagnosis and management?



What happened?

Was it a seizure, what is typical for a seizure presentation?



History?

What are pertinent portions of the history?



Investigations?

What investigations should be performed if the suspicion is high for a seizure?



Management?

What portion of the population will have an unprovoked seizure?

What factors should be considered when deciding to treat an unprovoked seizure?

When is treatment warranted for a first-time seizure?

Should a first provoked seizure receive treatment?



Anti-epileptic drugs (AEDs)?

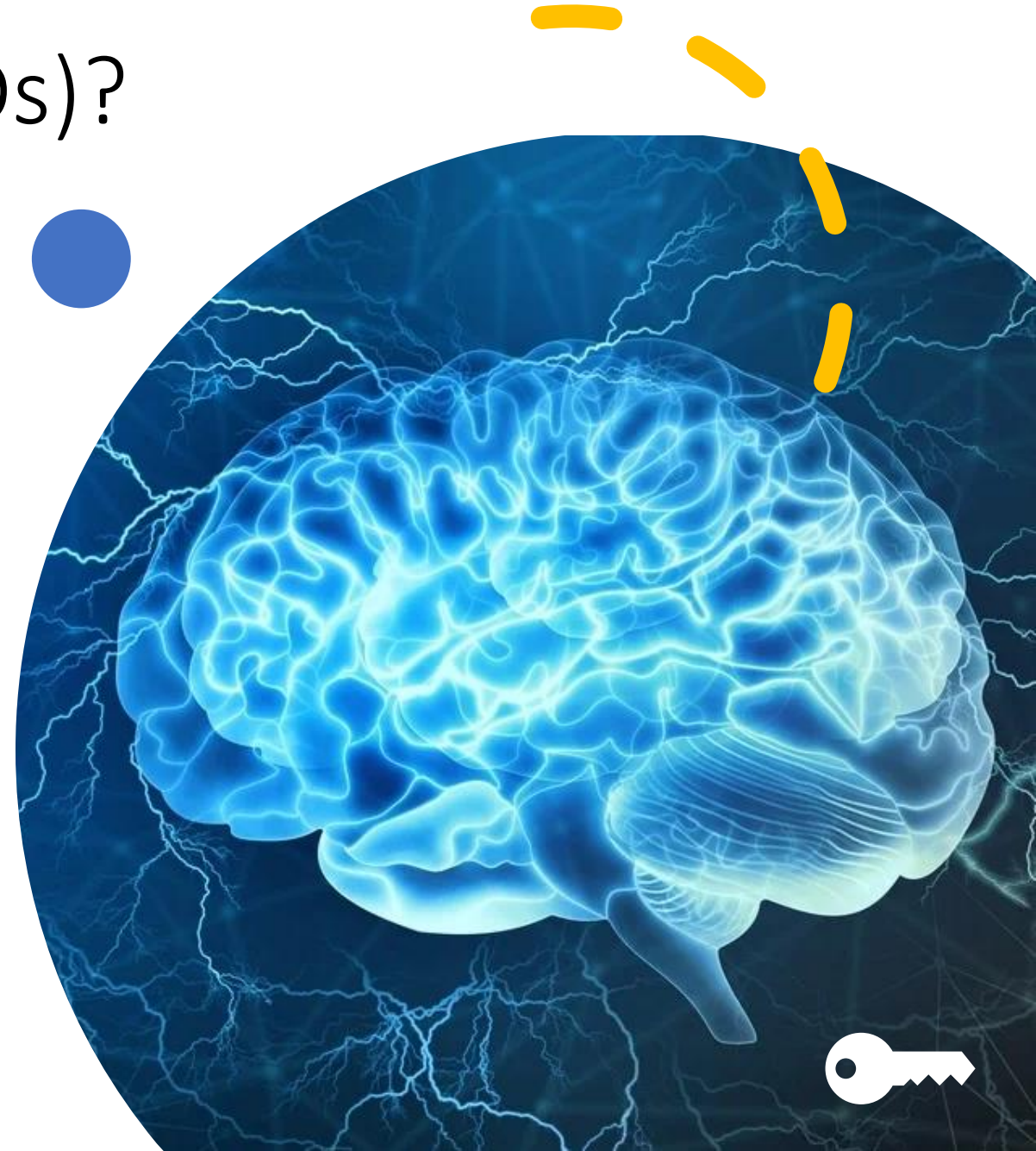
What percentage of patients on controlled on their initial AED?

Which AED is optimal for all patients?

What should be considered when choosing an AED?

When do you add on a second medication?

What if the patient develops a rash?

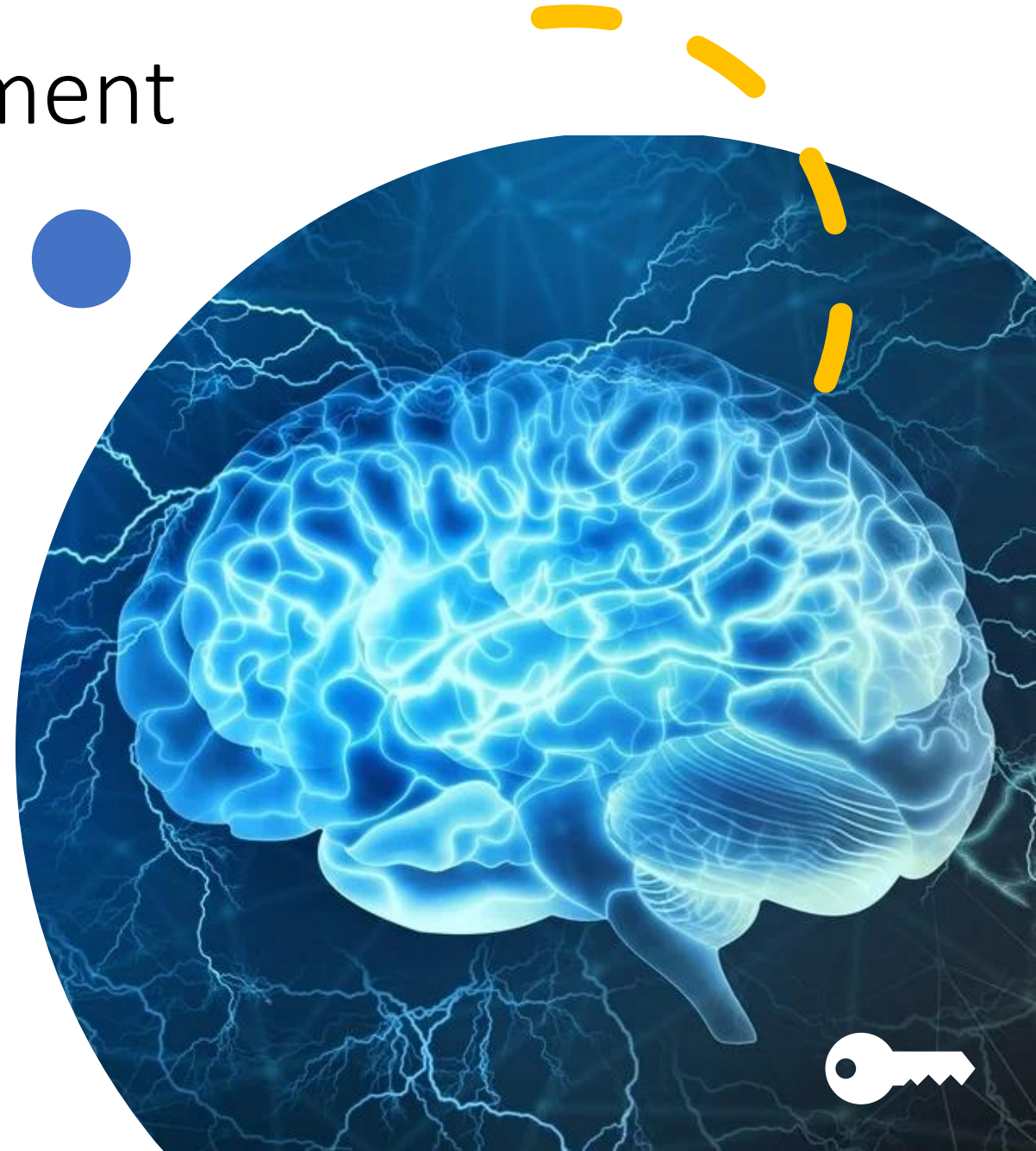


Discontinuing AED treatment

When should discontinuation be considered?

What are the benefits of discontinuing treatment?

What are factors associated with recurrence after discontinuation?



Status Epilepticus?

What is considered status epilepticus?

How is status treated?

What should be done if seizures continue beyond 20 minutes?



HIV?

What etiologies should be considered if a patient with HIV has a seizure?

Which AEDs have significant interactions with ARVs?



Women?

What care should be taken with reproductive aged women?

What types of contraceptives are preferred?

What should be done if a woman on AEDs becomes pregnant?

If a woman who is pregnant develops seizures (non eclampsia) which AEDs should be avoided?



What is

Seizure

- A clinical sign or symptom and not a disease
- A transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain, is identified based on clinical findings
- EEG is supportive rather than diagnostic

Epilepsy

- At least two unprovoked (or reflex) seizures occurring > 24 hours apart
- One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years

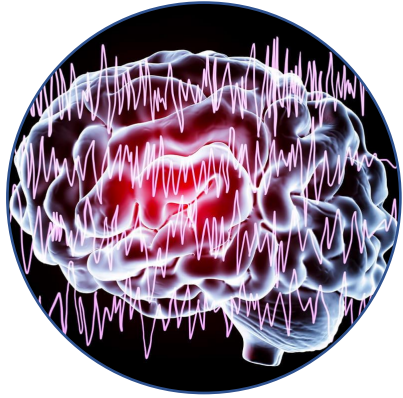
Differential

- Sudden loss of consciousness: syncope, intracranial hemorrhage, drug intoxication
- Sudden neurologic deficit: stroke, TIA, intracranial hemorrhage, migraine
- Psychological/psychiatric: functional disorder



Classifications

ILAE 2017 Classification of Seizure Types Expanded Version ¹



Focal Onset

Aware

Impaired
Awareness

Motor Onset

automatisms
atonic ²
clonic
epileptic spasms ²
hyperkinetic
myoclonic
tonic

Nonmotor Onset

autonomic
behavior arrest
cognitive
emotional
sensory

focal to bilateral tonic-clonic

Generalized Onset

Motor

tonic-clonic
clonic
tonic
myoclonic
myoclonic-tonic-clonic
myoclonic-atonic
atonic
epileptic spasms

Nonmotor (absence)

typical
atypical
myoclonic
eyelid myoclonia

Unknown Onset

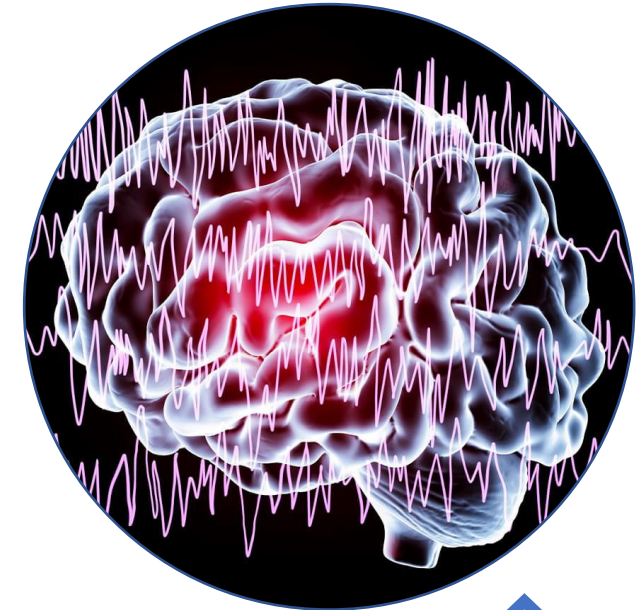
Motor

tonic-clonic
epileptic spasms

Nonmotor

behavior arrest

Unclassified ³



Goals

1

Determine if the event described was a seizure

2

Determine and treat cause if applicable (infection, metabolic, etc)

3

Control seizures



Was it a seizure?

- Warning with an aura prior to onset
- Stereotyped, attacks are almost identical or have minimal variation
- Impaired consciousness, eyes open
- Automatism
- Deja-vu or Jamais-vu
- Repetitive movements or behaviors
- Jerking of limbs
- Post-ictal confusion
- Urine or stool incontinence, tongue biting
- Provoked or unprovoked



History

Question whether this was a seizure

Is the cause known

Characteristics – what happens, in what chronicity, how long, number and frequency of events

Similar history: are events new or recurrent?

Triggers of events

Time of day, alcohol/drug use/withdrawal OR other acute causes.

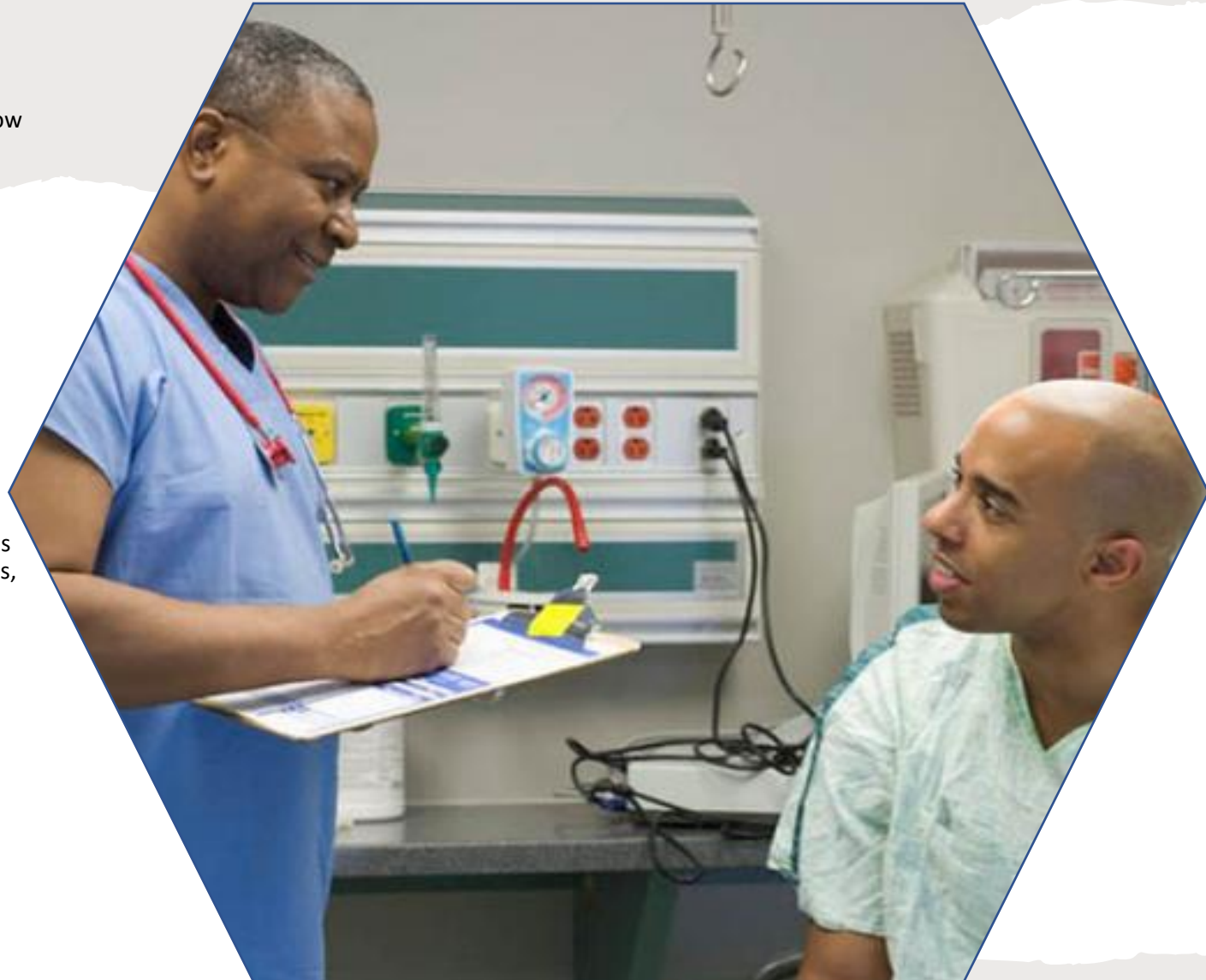
Is patient completely normal when not having seizures or has developed any neurologic problems (headaches, weakness, visual changes, psychiatric changes)?

If patient has ever taken medication, did it help? If stopped, why it was stopped.

Birth and developmental history

Family history (any others with seizures?)

Remote history of head trauma



Investigations

- HIV
- EEG
 - most helpful during an event to determine if events are seizures and can be normal between seizures
- Brain imaging
 - CT or MRI



Management

About 10% of the population will have an unprovoked seizure at some point (no cause determined)

Once AEDs are started, they have lifelong consequences, need to carefully assess the risks vs benefits.

- Risk of recurrence in unprovoked seizures:
 - First unprovoked seizure – 46% (30-50%) chance of recurrence in 2 years.
 - Second unprovoked seizure - >70% (70 - 80%) chance of recurrence.
 - Hence recommendation to treat if ≥ 2 unprovoked seizures

Treat

- Single unprovoked seizure but with increased risk of recurrence:
 - epileptiform abnormalities on EEG
 - previous brain injury (remote symptomatic seizure) – brain tumour, brain malformation, head injury with LOC, stroke, meningitis, brain surgery.
 - abnormal neurological examination – focal findings
 - first seizure occurring during sleep (nocturnal seizure).
- Single seizure but with focal brain findings (provoking factor ongoing):
 - neurocysticercosis granulomas etc
 - mesial temporal sclerosis
 - brain tumour

First provoked seizure by factors that resolve e.g. drug intoxication, hypoglycaemia, HTN encephalopathy should not receive treatment



Anti Epileptic Drugs

~ 50% of patients are controlled on the initial AED

No single AED is optimal for every patient, trial and error

- Broad vs narrow spectrum

Factors to consider when choosing AED:

- Drug effectiveness for the seizure type or types
- Potential adverse effects of the drug
- Interactions with other medications
- Comorbid medical conditions, especially, hepatic and renal disease
- Age and gender, including childbearing plans
- Lifestyle and patient preferences
- Cost

Use minimal dose of medication to have decreased (or ideally zero) seizures at tolerable (or ideally zero) toxicity.

Maximize dose of one medication before determining if medication is not working or need to add another medication

Instruct patient to stop new medication *immediately* if rash develops – especially carbamazepine, lamotrigine, phenytoin, phenobarbitone



Discontinuing AED treatment



Discontinuation might be considered after two to four years of seizure freedom

Benefits of discontinuing treatment

- Patients get a sense of being “cured” as opposed to being chronically disabled if still on treatment
- Adverse effects associated with chronic therapy may take years to become evident
- Cognitive and behavioural side effects of AEDs may be subtle and only recognized once drugs are discontinued
- AEDs are expensive and pose a significant financial burden for many patients
- There may be special circumstances, such as pregnancy or serious coexisting medical conditions, in which outcomes may be improved and management simplified in the absence of unnecessary AED therapy

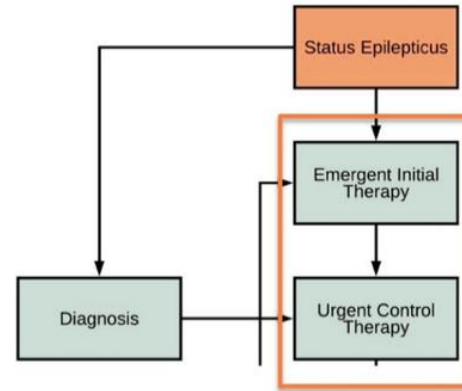
Factors associated with seizure recurrence after discontinuation

- Epilepsy duration before remission (longer duration associated with higher risk)
- Seizure-free interval before antiseizure drug withdrawal (shorter interval associated with higher risk)
- Age at onset of epilepsy (onset in adulthood associated with higher risk)
- History of febrile seizures
- Number of seizures before remission (≥ 10 associated with higher risk)
- Absence of a self-limiting epilepsy syndrome (e.g. absence epilepsy, benign epilepsy with centrotemporal spikes)
- Epileptiform abnormality on EEG before withdrawal



Status epilepticus

- 5 min or more of continuous clinical and/or electrographic seizure activity or recurrent seizure activity without recovery (returning to baseline) between seizures
- *Lorazepam* 4mg IV over 2 minutes, may repeat in 5-10 minutes (8mg max)
 - alternatives
- Investigate and treat possible cause
- Prevent seizure recurrence once SE controlled by keeping patient on adequate doses of AEDs
- If seizures continue beyond 20 minutes after initiation of treatment, intubate and initiate advanced treatment of refractory status epilepticus



Checklist

- Fingertick glucose
- Obtain IV access
- Pulse oximetry, BP, cardiac monitoring; supplemental O₂ and fluid as needed
- Labs: CBC, BMP, Ca, Mg, HCG in females of childbearing age
- Head CT
- Continuous EEG (if available); notify EEG tech if available (as soon as available unless patient returns to pre-status epilepticus baseline)



Exclude CNS opportunistic infections

Cryptococcus

Tuberculosis

Toxoplasmosis

Primary CNS Lymphoma

PML

Drug interactions between AEDs and ARVs

Phenytoin *decreases* levels of LPV/r (lopinavir/ritonavir)

Valproic acid *increases* levels of AZT (zidovudine)

ATV/r (atazanavir/ritonavir) appears to *decrease* lamotrigine levels

HIV





Women

Pregnancies should be planned and monitored thereafter

- Risk is likely dose-dependent
- Depends on number of AEDs

Folic acid supplementation for all reproductive women on AEDs

Contraceptives

- consider non-hormonal options for women on liver-inducing AEDs. Efficacy of hormonal contraception lowered.

Fertility may be affected by AEDs

In a woman with epilepsy who has become pregnant, if on antiepileptics, keep on medication, dose increase may be necessary, start folic acid 2-4mg daily

New seizure in pregnancy avoid valproate, topiramate. Lamotrigine, levetiracetam, carbamazepine relatively safe



Differential Diagnosis

	Loss of consciousness	Motor features	Preceding	Following	Incontinence	Self-injury
Generalised Seizure*	Yes (seconds to minutes)	Rhythmic bilateral jerking	May have aura	Post-ictal confusion/ depressed level of consciousness	Common	Common (tongue bite), soreness, even fractures
Syncope	Yes, very brief (seconds)	May have brief twitching	May have presyncope	Immediately alert	Uncommon	May have head injury from fall
TIA	No (unless basilar)	Paralysis	None	Deficits generally < 2 hours	No	No
Migraine	No	Can have weakness in rare cases	May have aura (20%)	Headache	No	No
Psychogenic spell	Variable	Often erratic, non-rhythmic, asymmetric movements	Variable	Variable	Possible	Possible



Causes of Provoked Seizures

Metabolic derangements

- Hypo or hyperglycemia
- Hyponatremia
- Hypocalcemia
- Hypomagnesemia

Medications

- Bupropion
- Tramadol
- Fluoroquinolones
 - ciprofloxacin
- Cephalosporins
- Carbapenems
 - Imipenem
- Isoniazid

Drugs/drug withdrawal

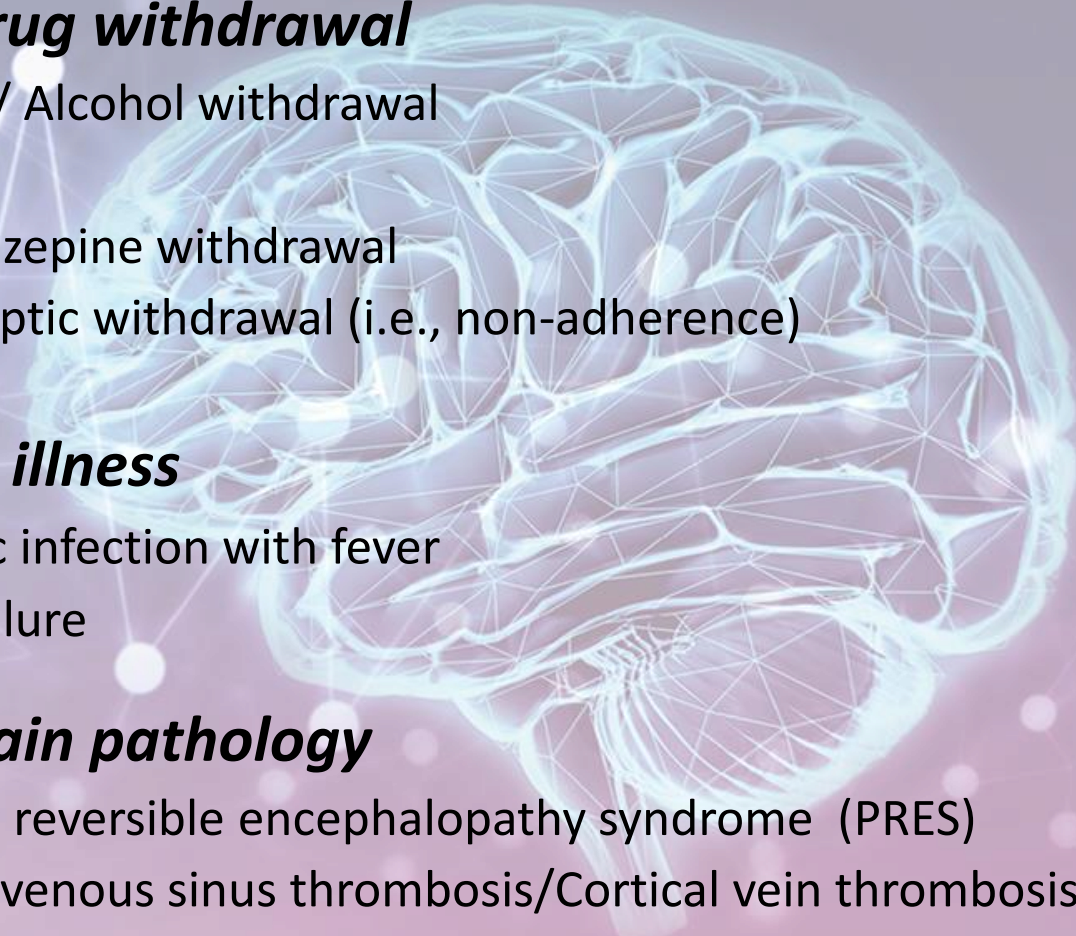
- Alcohol / Alcohol withdrawal
- Cocaine
- Benzodiazepine withdrawal
- Antiepileptic withdrawal (i.e., non-adherence)

Systemic illness

- Systemic infection with fever
- Renal failure

Acute brain pathology

- Posterior reversible encephalopathy syndrome (PRES)
- Cerebral venous sinus thrombosis/Cortical vein thrombosis
- Acute stroke or intracranial hemorrhage
- Acute head trauma
- Acute meningitis/encephalitis



Causes of Unprovoked Seizures

- ***Idiopathic (genetic) epilepsy syndromes***
 - onset in childhood
- ***Idiopathic***
 - second “peak” in older adults
- ***Any irreversible brain lesion***
 - Congenital brain malformation
 - Prior stroke
 - Prior head trauma
 - Prior CNS infection
 - Prior neurosurgery
 - Current/prior brain tumor



Broad spectrum for focal and generalized seizures

- Valproate (300-500mg BD, max 3000mg per day)
- Levetiracetum (250-500mg BD, max 3000mg per day)
- Lamotrigine (slow titration, 25mg OD/ alt day, up to 100mg BD, max 500mg daily)
- Clonazepam (add-on tx, 0.5mg nocte, titrated to 4-8mg nocte)
- Perampanel
- Clobazam
- Topiramate
- *Zonisamide*
- *Felbamate*



Narrow spectrum for focal +/- secondary generalisation

- Carbamazepine (slow titration, 100-200mg BD, max 1200mg per day)
- Phenobarbitol (usual dose 90mg nocte, 60 -180mg nocte, slow withdrawal)
- Phenytoin (usual 300mg nocte, 200-500mg but needs tight monitoring!)
- Oxcarbazepine
- Gabapentin
- Pregabalin (150mg OD, 300-600mg divided doses)
- Lacosamide
- Vigabatrin



Adult Initial Hospital Treatment

Recommended	Dosing
Lorazepam	4 mg IV over 2 min, may repeat in 5-10 minutes (8 mg max)
Alternatives	Dosing
Diazepam	5-10 mg IV (0.15 mg/kg max) or 20 mg PR
Midazolam	10 mg IM / IV / IN / buccal / IO
Urgent Control Options	Dosing
Phenytoin	20 mg mg/kg IV at maximum rate of 50 mg/min
Fosphenytoin	20 mg PE/kg IV at a maximum rate of 150 mg/min
Phenobarbital	20 mg/kg IV at a rate of 50-100 mg/min (may give additional 5-10 mg/kg)
Levetiracetam	1-3 g IV over 5 minutes or 2-5 mg/kg/min



Treatment of Refractory SE

Recommend	Dosing	Major Side Effect
Midazolam continuous IV infusion	<ul style="list-style-type: none">• Load 0.2 mg/kg IV at 2 mg/min• Repeat 0.2-0.4 mg/kg boluses every 5 min until seizures stop• Maintenance 0.05 – 2 mg/kg/hr	<ul style="list-style-type: none">• Prolonged sedation in patients with hepatic and renal impairment• Tachyphylaxis (within 24-28 hours)
Propofol continuous IV infusion	<ul style="list-style-type: none">• Load 1-2 mg/kg IV over 3-5 min• Repeat boluses every 3-5 min until sz stop• Maintenance 30-200 mcg/kg/min	<ul style="list-style-type: none">• Hypotension• Propofol infusion syndrome
Pentobarbital continuous IV infusion	<ul style="list-style-type: none">• Load 5 mg/kg IV• Maintenance 1-3 mg/kg/hr• May be used more frequently in children than propofol	<ul style="list-style-type: none">• Severe hypotension• Gastric stasis• Prolonged effective half life• Metabolic acidosis

