MEDICINE

432 Team

52 Epilepsy

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COLOR GUIDE: • Females' Notes • Males' Notes • Important • Additional

Objectives

Guess what! We have objectives

1. Definition of epileptic seizure, provoked seizure and epilepsy.
2. Status epilepticus.
3. Frequent causes of seizure and risk factors.
4. Triggers of seizures in epileptic patient.
5. Epilepsy classification and seizure semiology.
6. DDX of SZ
7. Approach to seizure disorder (Hx, Ex,Inx)
8. Medical and surgical management of epilepsy.
9. How to select antiepileptic medications.
10. When to stop antiepileptic medications,

Extra sources: Kumar

What is epilepsy?

Epileptic seizure:

Transient occurrence of signs and symptoms of **sudden** changes in neurological function due to **abnormal excessive, synchronous** discharge of cortical neurons.

Provoked seizures:

Is occur in the setting of acute medical and neurological illnesses in people with no prior history of seizures. (e.g. patient with hypoglycemia developed a seizure. Can we consider him epileptic? NO, his seizure is provoked; when you remove the etiology, he's fine)

Epilepsy:

Recurrent (two or more) **unprovoked (epileptic)** seizures. (Even if a long interval separates attacks) - (How to tell if it's unprovoked? Complete lab work is normal, Electrolytes are normal, no evidence of infection, everything's normal, or you might say no clear underlying cause)

Difference between seizure and epilepsy:

Seizure is not a diagnosis; it's a symptom of other diseases like epilepsy.

Status Epilepticus

Status epilepticus (SE):

defined as recurrent persistent convulsions that last for more than 20-30 minutes and are interrupted by only brief periods of partial relief. (Prolonged seizures) OR recurrent seizure with no regain of consciousness in between.

It is a serious, potentially life-threatening.

Any type of seizure can lead to SE, the most serious form of status epilepticus is the generalized tonic-clonic type.

Epidemiology and course

- 5% of the population suffer a single seizure at some time.
- 0.5-1% of the population have recurrent seizure: diagnosed epileptic.
- 70% of the 1% well controlled with drugs (prolonged remissions).
- 30% epilepsy at least partially resistant to drug treatments = Intractable (farmacoresistant) epilepsy. (thier management will be discussed later on).

Note(s):

Mechanisms and definitions: (from Kumar)
Spread of electrical activity between neurons is normally restricted and synchronous discharge of neurons takes place in confined groups, producing normal EEG rhythms. During a seizure, large groups of neurons are activated repetitively, unrestrictedly and hypersynchronously; synaptic inhibition between them fails. High-voltage spike-and-wave activity is the result, epilepsy's EEG hallmark.

Risk Factors for Epilepsy

- Febrile convulsion (it's a convulsion caused by fever in the pediatric age group from **6 months to 6 years** – should be a prolonged convulsion or a recurrent attack of febrile convulsion to be considered as a risk factor)
- Perinatal insult (trauma, or natal -during delivery- hypoxia)
- CNS infection (e.g. encephalitis, at first you consider it a provoked seizure, you treat the patient and send him home. Later on, he might comes with a seizure without any underlying cause, it's probably caused by the infection)
- CNS mass lesion
- Family history of epilepsy - well known
- Head injury (with loss of consciousness for > 30 minutes, also frontal penetrating trauma)
- Abnormal gestation or delivery
- Developmental delay
- Stroke (ischemic or hemorrhagic)

Frequent causes

Unknown etiology	vascular cause	Frontal lobe penetrating accident	Focal lesion: inflammation, tumor, etc... can cause cortical irritation	Infections
65%	10 %	6%	4%	3%

Triggers for seizure: *(not causes, but those factors associated with high chance of developing a seizure for already diagnosed epileptic patients)*

- Poor compliance
- Sleep deprivation (commonest and well known)
- Stress
- Alcohol
- Infection (e.g. tonsillitis)
- Menstrual cycle

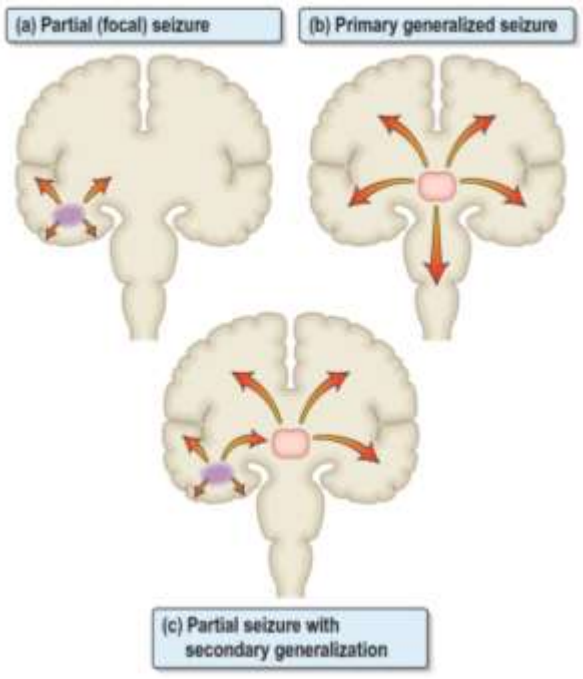
Danger of epileptic seizures:

- Drowning
- RTA – road traffic accidents
- Status epilepticus
- Sudden death (mechanism is not very clear but it's believed to be caused by arrhythmia or suffocation)

Seizure Classification

(imp.) 👇

- **Focal seizures** (partial) – *account for 80% of adult epilepsies*
  - Simple partial seizures: preserved consiousness. e.g. one limb jerking (Jacksonian seizure)
  - Complex partial seizures: altered level of consiousness
  - Partial seizures turns into generalised



- **Generalised seizures:** the whole brain fires at the same time → complete loss of consiousness
- **Unclassified seizures:** seizures that do not fit a category above

Note(s):

Focal seizures:
- Symptoms differ according to the site (temporal lobe, occipital lobe, frontal etc…)
A partial seizure is epileptic activity confined to one area of cortex with a recognizable clinical pattern this activity either remains focal or spreads to generate epileptic activity in both hemispheres and thus a generalized seizure. This spread is called secondary generalization. The focal nature of a seizure may not be apparent clinically because of rapid secondary generalization.

An apparent generalized tonic–clonic seizure may either have started as a focal seizure or be a primary generalized convulsion.

Aura (single: auras) means a stereotyped perception caused by initial focal electrical events before a partial seizure, such as a smell, tingling in one limb, or strange recognizable inner feelings.

NEW ILAE Classification of seizures

1. Generalized seizures: bilateral abnormal electrical activity, with bilateral motor manifestations and impaired consciousness.

- Tonic-clonic (in any combination) Tonic: Following a vague warning, the tonic phase commences. The body becomes rigid, for up to a minute. The patient utters a cry and falls, sometimes suffering serious injury. The tongue is usually bitten. There may be incontinence of urine or faeces. The clonic phase then begins, with generalized convulsing, frothing at the mouth and bilateral, rhythmic jerking of muscles. This lasts from a few seconds to several minutes. Seizures are usually self-limiting, followed by drowsiness, confusion or coma for several hours.
- Absence
  - Typical: almost invariably begins in childhood. The patient stares and pales slightly for a few seconds. The eyelids twitch; a few muscle jerks may occur. After an attack, normal activity is resumed. Typical absence attacks are never due to acquired lesions such as tumors. They are a developmental abnormality of neuronal control. Children with typical absence attacks tend to develop generalized tonic–clonic seizures in adult life (known as primary generalized epilepsy).
  - Atypical (mimics complex partial)
  - Absence with special features
  - Myoclonic absence
  - Eyelid myoclonia

- Myoclonic (jerks): seizures describe isolated muscle jerking. Juvenile myoclonic epilepsy is one variety. Seen in adolescence.
  - Myoclonic atonic
  - Myoclonic tonic
- Clonic (repetitive movements)
- Tonic: intense stiffening of the body.
- Atonic (loss of power at once)

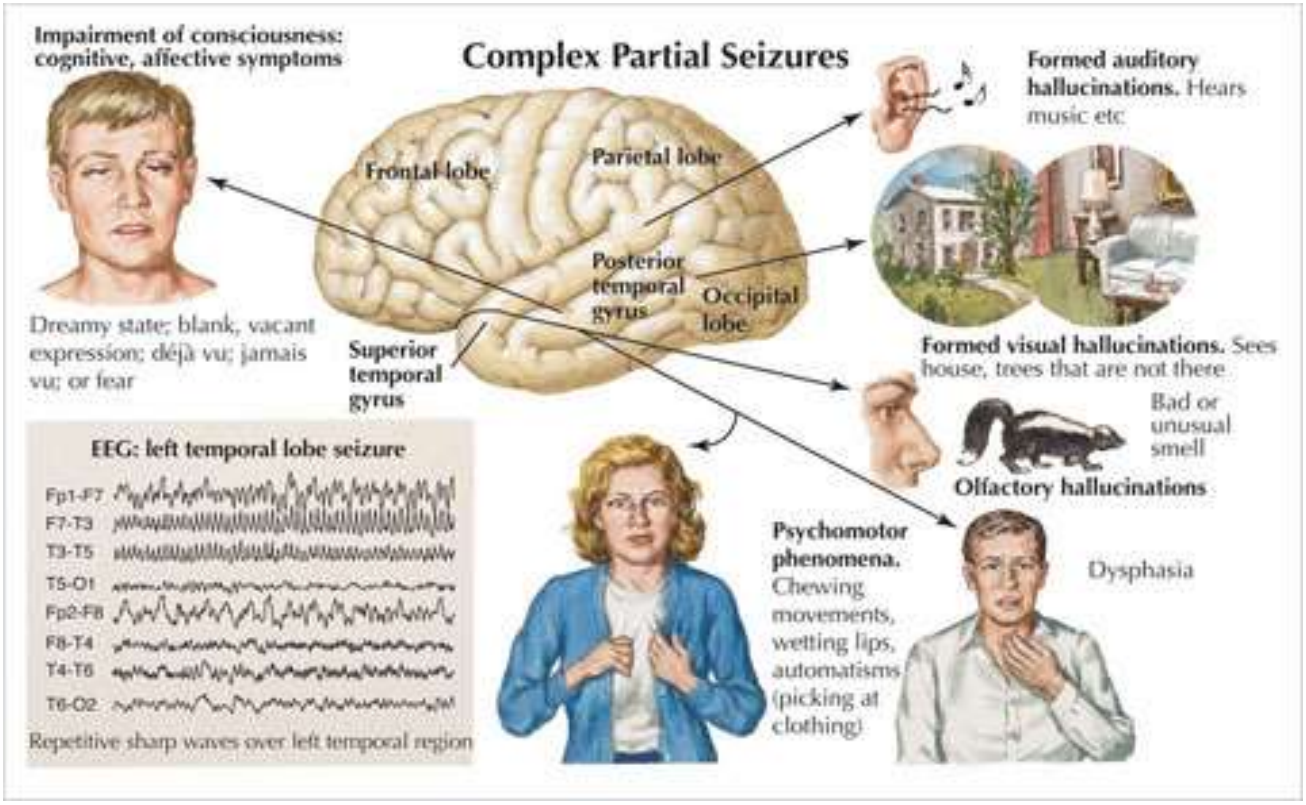
2. Focal seizures (most common auras: temporal lobe → either simple or complex, can produce feelings of unreality (jamais vu) or undue familiarity (déjà vu) with the surroundings. Blank episodes of staring, vertigo, visual hallucinations)
3. Unknown

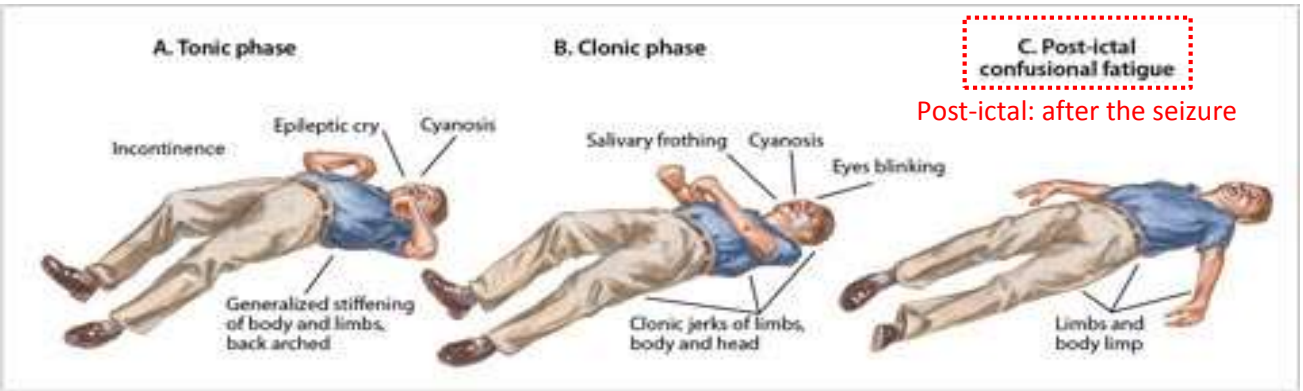
- Epileptic spasm

Seizure Semiology *(discretion of the seizure)*

Depends on the location:

- Frontal lobe: hyper-motor, patient might present with strange smells.
- Occipital lobe: loss of vision, blurred vision, flashes of light
- Temporal lobe: epigastric rising sensation, Déjà vu
- Parietal lobe: numbness, sensory disturbances





Post-ictal phase: Not seen in myoclonic & absence seizures

Differential diagnosis:

- TIA (transient ischemic attack) patient present in a situation that might be mistaken as post-ictal phase. To clarify ask if the patient had any jerk movements.
- Syncope very common.
- Migraine (Auras: mimics temporal lobe seizure)
- Movement disorders (Hemiballismus https://www.youtube.com/watch?v=hqg2GTUq1k4)
- Panic attack
- Psychogenic - non-epileptic - seizure

Seizure vs syncope

Comparison of clinical features in cardiogenic syncope versus seizure disorders

Clinical features	Cardiogenic syncope	Seizure disorders
Loss of consciousness	Typical	Common
Episode duration	Seconds	Minutes
Involuntary movements	Common	Typical
Amnesia	Yes	Yes
Arrhythmia	Common	Rare*
Electroencephalogram	Slow waves Flattening	Focal or general spike activity
Responsive to AEDs	No	Often
Short term mortality†	High	Low

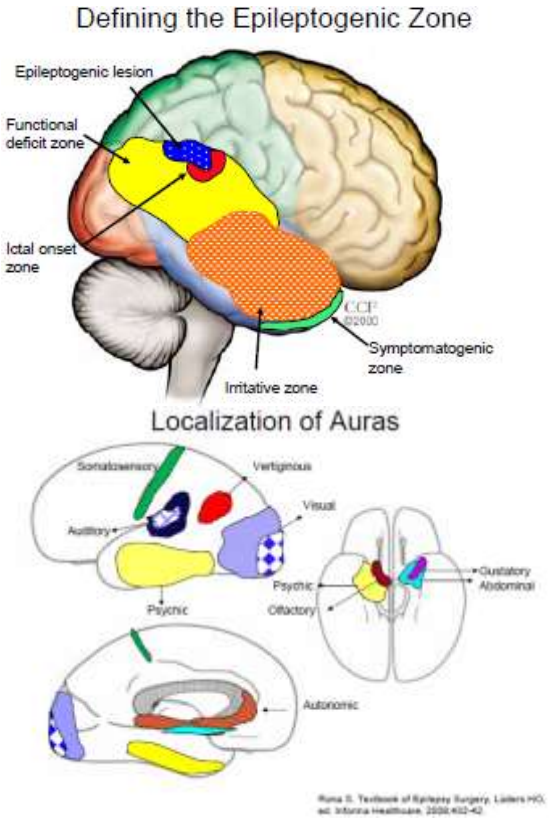
Seizure approach

- Non-invasive tests
  - Clinical history (most important) and examination
  - MRI
  - Video EEG
  - Neuropsychological evaluation
  - Nuclear medicine
- Invasive monitoring
  - Intracranial electrodes
  - Intraoperative corticography
  - Cortical stimulation.

Clinical history

Questions that help clarify the type of seizure include the following:

1. Was any warning noted before the spell? If so, what kind of warning occurred? Generalized or partial.
2. What did the patient do during the spell? To know the type of the seizure.
3. Was the patient able to relate to the environment during the spell? To evaluate the level of consciousness.
4. How did the patient feel after the spell? How long did it take for the patient to get back to baseline condition? Did he face any post-ictal phase? Prolonged post-ictal phase is associated with a high risk of sudden death.
5. How long did the spell last? 20-30 min → Status epilepticus.
6. How frequent do the spells occur? For the management.
7. Are any precipitants associated with the spells?



Investigations:

1. MRI
    - Lesional
        - Tumor
        - Vascular
        - Trauma
        - Developmental
        - Mesial Temporal Sclerosis
    - Non lesional
2. EEG (shows the epileptic spikes and focal lesion)
3. Nuclear Medicine
4. Cognitive Testing – Neuropsychology
    - Intelligence
    - Memory
        - Verbal
        - Visual
    - Language

Treatment (IMPORTANT)

1. Medical:

Anti-Epileptic drugs list:

- Phenobarbital 1912
- Phenytoin 1938
- Valium 1960s -diazepam
- Carbamazepine 1974
- Valproate 1978
- New AED 1990s: (preferred for newly diagnosed patients)
  - Keppra
  - Lamictal - lamotrigine
  - Clobazam
  - Topamax - topiramate(drug of choice for migraine patients)

(For both partial and generalized seizures, monotherapy with an established first-line AED is the initial choice)

Mechanism of Action:

Current antiepileptic drugs are thought to act mainly by two main mechanisms:

- Reducing electrical excitability of cell membranes, possibly through inhibition of sodium channel.
- Enhancing GABA. This may be achieved by an enhanced pre- or post- synaptic action of GABA, by inhibiting GABA-transaminase, or by drugs with direct GABA-agonist properties.

Clinical Uses of Antiepileptic Drugs (MCQ!!!!)

- **Tonic-clonic** *(grand mal)* seizures: **phenytoin**, **valproate** (valproic acid or depakine) (it covers almost all the types of seizure). Use of single drug is preferred when possible, because of risk of pharmacokinetic interactions.
- **Partial (focal) seizures**: **carbamazepine**, **valproate**; **clonazepam** or **phenytoin** are alternatives.
- **Absence seizures (petit mal):** **ethosuximide** or **valproate**. Valproate is used when absence seizures coexist with tonic-clonic seizures, since most drugs used for tonic-clonic seizures may worsen absence seizures.
- **Myoclonic seizures:** **valproate** or **clonazepam**.
- **Status epilepticus:** must be treated as an emergency (it has it's own protocol).
  - Drug of choice for pregnant patients: Lamictal (you can replace the previous medication with Lactimal only if you know that she's planning to be pregnant in the coming months. If patient is already pregnant, don't change the already prescribed drug)
  - Phenytoin, carbamazepine: both will worsen the juvenile myoclonic epilepsy
  - Valproate: not preferred for pregnant and young patients, it's associated with high risk of teratogenicity, and might cause obesity, hair loss, and polycystic ovary.
  - Try to take a very accurate Hx (to know which type of seizure)

- The majority of patients respond to drug therapy (anticonvulsants).
- In intractable cases (drug-resistants) surgery may be necessary. The treatment target is seizure-freedom and improvement in quality of life.
- The commonest drugs used in clinical practice are:
  - Carbamazepine, Sodium valproate, Lamotrigine (first line drugs)
  - Levetiracetam, Topiramate, Pregabaline (second line drugs)
  - Zonisamide, Eslicarbazepine, Retigabine (new AEDs)

Basic rules for drug treatment

- Drug treatment should be simple, preferably **using one anticonvulsant** (monotherapy). "Start low, increase slow".
- Add-on therapy (adding another drug) is necessary in some patients.
- If patient is seizure-free for three years, withdrawal of pharmacotherapy should be considered. It should be performed very carefully and slowly! 20% of pts will suffer a further seizure within 2 years.

Epilepsy treatment and pregnancy

- The risk of **teratogenicity** is well known (~5%), especially with **valproates**, but withdrawing drug therapy in pregnancy is more risky than continuation. (patient might have epileptic attacks during pregnancy)
- Epileptic females must be aware of this problem and thorough family planning should be recommended.
- Over 90% of pregnant women with epilepsy will deliver a normal child.

Seizure Freedom with AED use:

- 1st drug: patients will be seizure free (47%) means when using monotherapy
- 2nd drug: patients will be seizure free (14%) (when adding another drug, it's indicated only if the monotherapy was not effective)
- 3rd drug-: patients will be seizure free (3%) (never use 3 drugs at the same time! it's useless, patient will suffer from contraindications without any benefit)
- Medication resistant 36%

Elderly and epilepsy:

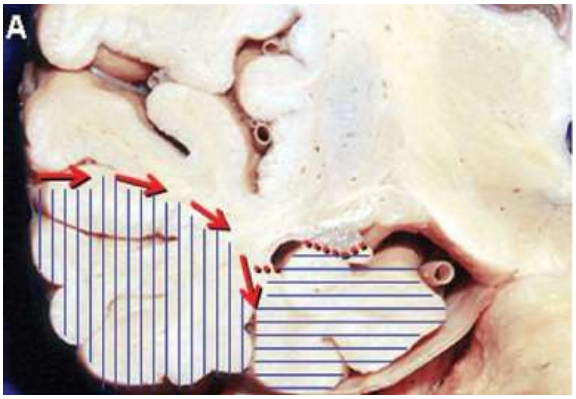
- More cautious dosing
- Monotherapy preferred
- More frequent SEs
- Comorbid medical problems/meds
- Osteoporosis
- Cognitive decline
- Risk of falls/injury
- Drug-drug interactions

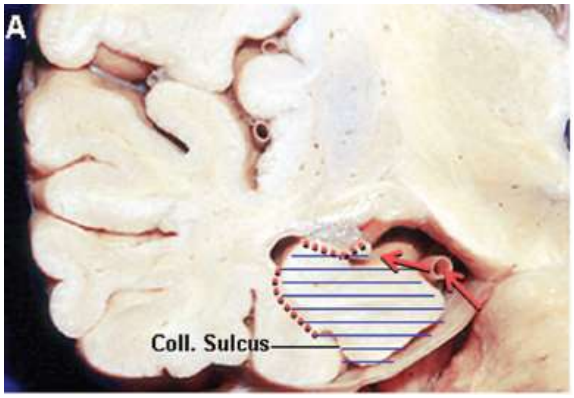
Note(s):

Unwante deffects of drugs:
Intoxication with all AEDs causes ataxia, nystagmus and dysarthria. Chronic phenytoin causes gum hypertrophy, hypertrichosis, osteomalacia, folate deficiency, polyneuropathy and encephalopathy. A wide range of potential unwanted effects are known.

2. Surgical:

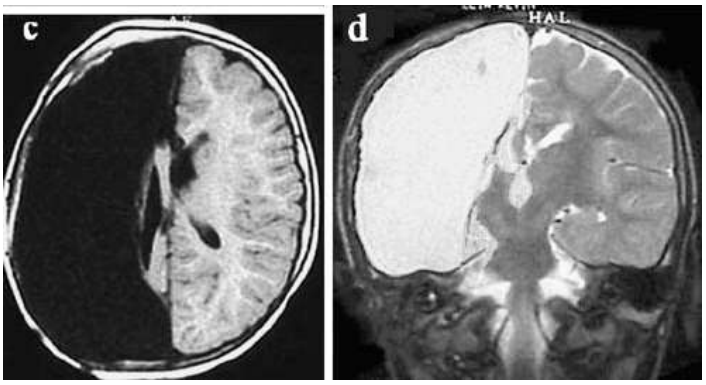
- Indicated if patient is drug resistant: patients are admitted to the unit to localize the focal lesion and remove it. (Seizure freedom up to 68%)



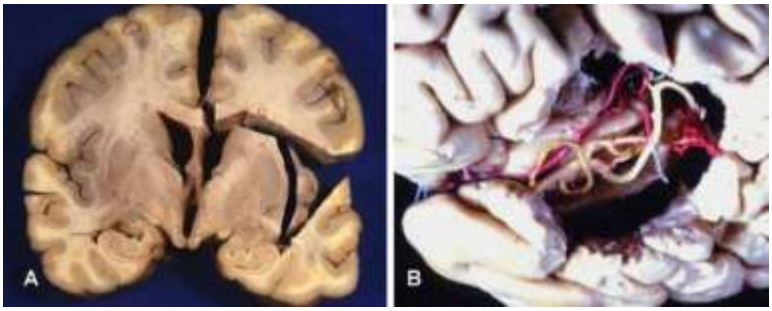


Types of surgeries:

- Hemispherectomy (complete removal of one hemisphere e.g. muse encephalitis, no surgery means patients will continuously suffer from status epilepticus) complications: partial hemiparesis.



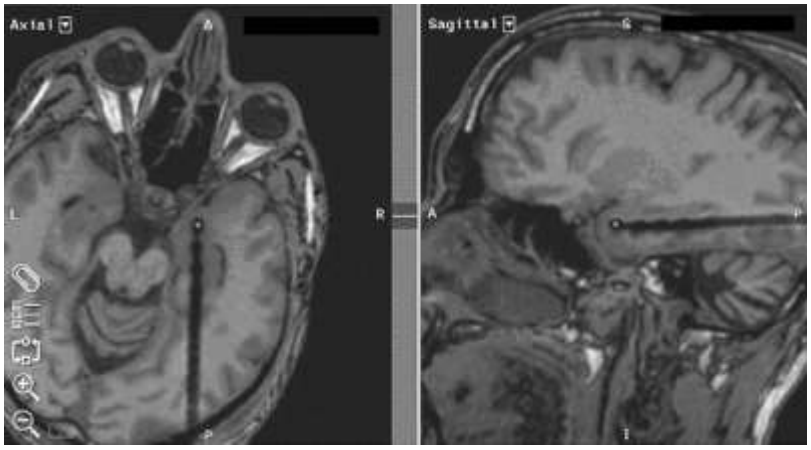
- Hemispherotomy (disconnect the two hemispheres by cutting the carpus callosum)



What if the patient is not a candidate for surgery? (e.g. the affected area is responsible for an important function to the patient like speech)

- VNS (vagus nerve stimulation - decrease the seizure by 50%)

- DBS (deep brain stimulation - electrode inside the brain to suppress any abnormal electrical activity)



SUMMARY

1. Epilepsy:
   - Recurrent (two or more) unprovoked seizures.

2. Status epilepticus:
   - Recurrent persistent convulsions that last for more than 20-30 minutes. OR recurrent seizure with no regain of consciousness in between.

3. Classification of seizures and the appropriate drug for each one:

- Focal (partial):
  - Simple, complex, partial turns into generalized
  - Drug of choice: Carbamazepine
- Generalized:
  - Tonic-clonic: Valproate
  - Absence: Ethosuximide
  - Myoclonic: Valproate
  - Tonic
  - Clonic
  - Atonic

4. Types of surgeries for drug-resistant patients
   - Hemispherectomy
   - Hemispherectomy

Questions

1. The patient recalls having episodes when he smells a pungent odor, becomes sweaty, and loses consciousness. His wife describes a period of motor arrest followed by repetitive picking movements that last about a minute. The patient does not fall or lose muscle control.
   What's the appropriate diagnosis?
   a. Absence seizure
   b. Complex partial seizure
   c. Simple partial seizure
   d. Atonic seizure
   e. Myoclonic seizure

2. The teacher of a 14-year-old child recounts episodes where the child stares into space and does not respond to verbal commands for a few seconds. These episodes occur several times per day. An EEG shows 3-per-second spike and slow wave discharges.
   What's the appropriate diagnosis?
   a. Absence seizure
   b. Complex partial seizure
   c. Simple partial seizure
   d. Atonic seizure
   e. Myoclonic seizure

3. 68 years old male is seen in the ER after an unwitnessed syncopeal episode. His wife heard a strange noise and found him confused on the floor. His wife tells that he has no ongoing medical problems, does not take any medications, and does not use alcohol or drugs. On examination the patient is drowsy and has toungue laceration, and his pants are wet with urine serum electrolytes are normal,
   Which of the following the best next step in evaluation?
   a- MRI of the brain
   b- Lumber puncture
   c- Holter monitor
   d- CT of the head
   e- ECG

All questions are taken from: PreTest Medicine 13th edition (Qs: 367, 382 & 383)

Good Luck <3

432 Medicine Team Leaders

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For mistakes or feedback: *medicine341@gmail.com*

Answers:

1st Q: **B**

2nd Q: **A**

3rd Q: **A**