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Case 1

You are working as an intern on your first shift at the ED, 14 year old Lamotri Jean is brought to you having what his mother describes as a ‘sudden collapse at home’.

Lamotri Jean’s mother describes the episode as, he was standing and then suddenly went rigid, fell, and then began to undergo bilateral rhythmic upper limb movements. He felt drowsy on waking and had bitten his tongue throughout the episode.

1. How would you classify Lamotri Jean’s episode and what classification system is commonly used for this type of episode?

Classification system is based on the **ILAE 2017 classification** and you classify it as following:

1. **Where in the brain the seizure starts (e.g. the onset) - focal vs generalised**

- **Focal seizures**

- Abnormal neuronal activity starts in one cerebral hemisphere
- More likely to be caused by focal structural abnormalities
- Symptoms depend on the anatomical location of the lesion or disturbance within the brain
- Can evolve to be generalised seizures

- **Generalised seizures**

- usually start in both hemispheres simultaneously bilateral cerebral cortex disturbance’

2. **If the person is aware or not during the seizure - preserved or impaired awareness**

- Focal seizures – can be either aware or unaware
- Generalised seizures – awareness is almost always affected

3. **Whether the seizure involves movement - motor vs non-motor**

- **motor seizure**

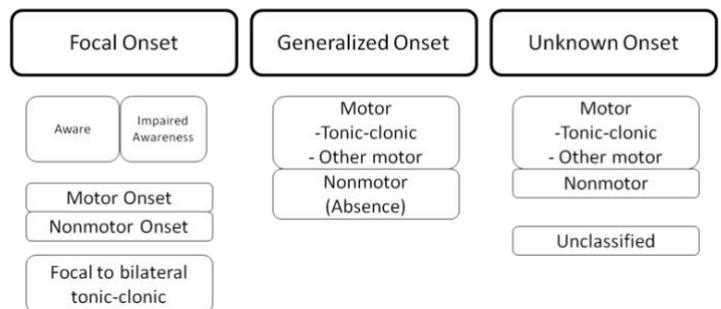
- may involve stiffening (tonic) and jerking (clonic) or other movements

- **non-motor seizure**

- These seizures involve brief changes in awareness, staring, and some may have automatic or repeated movements like lip-smacking.

Flow chart from Australian Therapeutic Guidelines (eTG) Epilepsy classification (dotted lines represent that it can start as one type and evolve to another type)

ILAE 2017 Classification of Seizure Types – Basic Version



Important to note that some seizures onsets are difficult to obtain at first, these are classified as **Unknown onset** and are characterised by **Motor (tonic clonic, epileptic spasms) or Nonmotor** or even **unclassified** if no-one has any idea whats going on

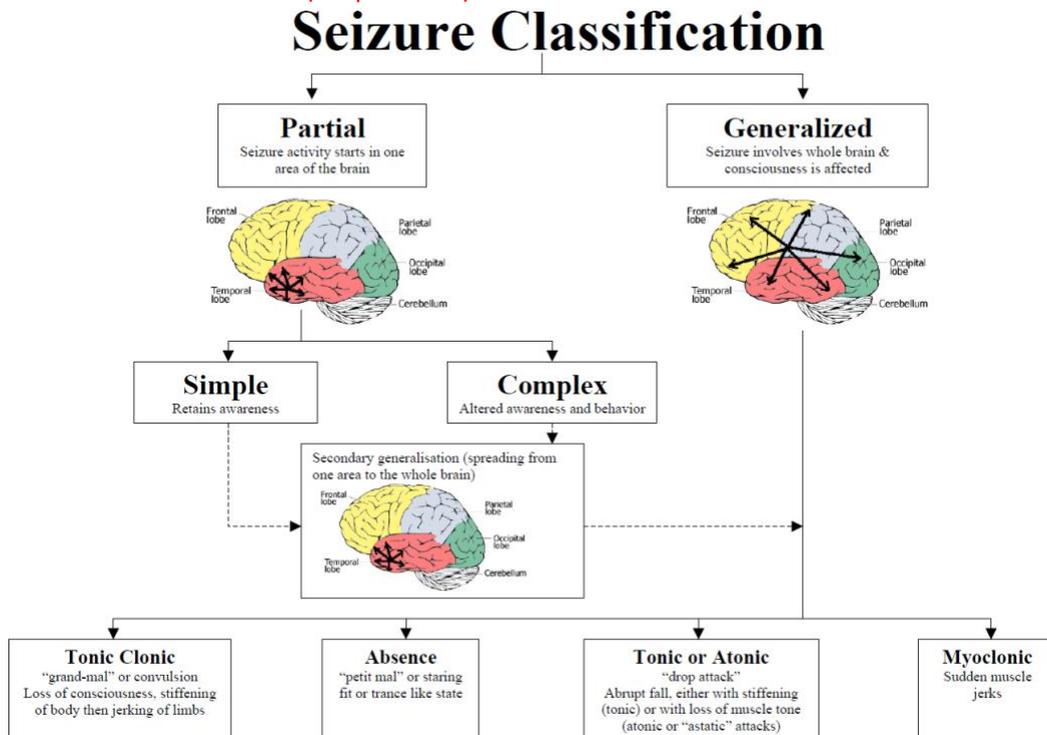
Based on the description, Lamotri Jean has had a **tonic-clonic seizure**

- Stiffing = tonic
- Rhythmic contraction = clonic
- Drowsy + tongue biting confirms the seizure (He may also have experienced urinary incontinence too which is an important thing to ask about)

2. Describe the other types of seizures that are common

Based on the International League Against Epilepsy (ILAE) classification

- **Focal seizures**
 - focal seizures without dyscognitive features (**simple partial**) – consciousness is not impaired
 - focal with dyscognitive features – (**complex partial**) – impaired consciousness
 - focal seizures evolving to **secondarily generalised seizures**
- **Generalised seizures -> These always have impaired awareness**
 - Tonic-clonic seizures (grand mal) - most common type of seizure
 - Absence seizures (petit mal) - most common type of generalised epilepsy in childhood)
 - Myoclonic seizures
 - Clonic seizures
 - Tonic seizures
 - Atonic seizures (drop attacks)





Lamotri Jeans mother becomes curious as to what she saw with her son after his seizure and asks what happens before, during and after a seizure.

3. Describe the different phases of seizures

- **Prodromal phase:**
 - A subjective feeling or sensation that can occur several hours or even days before the actual seizure.
 - The period from when early symptoms begin to before the more obvious, diagnosable symptoms begin.
 - The most common symptoms of a prodrome include confusion, anxiety, irritability, headache, tremor, and anger or other mood disturbances.

- **Ictal phase** (The period of abnormal electrical brain activity when a seizure is occurring)
 - **Early ictal (the aura)**
 - Believed that around 65% of people with epilepsy experience auras
 - Not everyone will have this though
 - symptoms vary depending on seizure type, severity, and affected brain region.
Some common symptoms include:
 - Bitter, acidic taste; Déjà Vu (feeling of familiarity with a person, place, or thing without having experienced it); Dizziness; Flickering vision; Hallucinations; Head, arm, or leg pain; Nausea/stomachache; Numbness; Out-of-body sensation; Ringing or buzzing sounds; Strange, offensive smells; Strong feelings of joy, sadness, fear, or anger; Subtle arm or leg twitching; Tingling; Vision loss or blurring
 - **Ictal phase**
 - Sudden onset
 - Rapid progression of symptoms including: Arm or leg stiffening, Chewing or lip-smacking, Confusion, Difficulty breathing, Distractedness, Drooling, Eye or head twitching movement in one direction, Hearing loss, Inability to move or speak, Loss of bladder and/or bowel control, Memory lapses, Numbness, Pale/flushed skin, Pupil dilation, Racing heart, Sense of detachment, Strange sounds, Sweating, Tremors, Twitching, Unusual physical activity such as dressing/undressing, Vision loss, blurring, flashing vision, Walking/running
 - Duration usually 1-3 minutes
 - the majority resolve spontaneously.
 - Prolonged seizures may be indicative of acute underlying cause or status epilepticus.

- **Postictal phase** - (The phase immediately after the end of a seizure)
 - Can last minutes to hours; some people recover immediately others take longer.
 - Varying degree of confusion, impaired alertness, soreness, drowsiness
 - May have memory loss
 - Neurological symptoms (e.g. Todd's Paralysis) (can mimic stroke)
 - Typically involves confusion, drowsiness, headache, speech impairment, and weakness.

4. You then refer Lamotri jean to a neurologist who makes the diagnosis of epilepsy. How did the neurologist come to this diagnosis (aside from having a big brain), what examinations/investigations would be used here?

- **Primarily a Clinical diagnosis**

- Relies primarily on a description of the seizures during each phase
- Eyewitness account or video can help exclude other causes of loss of consciousness (e.g. syncope)
- Prior events
 - History of epilepsy??
 - History of other potential underlying conditions (e.g., head trauma, stroke, tumor, CNS infection)
- **Physical examination:** attention should be paid to visual inspection (e.g., for bruises from falls, tongue bites, phakomatosis-specific skin manifestations) and evaluation for cardiovascular disorders

- **EEG**

- Can support the diagnosis but a normal EEG does not exclude a diagnosis of epilepsy nor does an abnormal EEG necessarily confirm the diagnosis
- Routine EEG may be of limited use due to difficulty in capturing a seizure in a short period of time
- 24 hour or longer EEG monitoring is frequently more useful and may confirm diagnosis - can be done as an outpatient or as a inpatient with video monitoring
- If used during the Ictal phase you should see Epileptiform discharges (e.g., spikes, sharp waves, spike waves) are usually detected.



- **Brain imaging**

- MRI especially can often be useful in revealing the **cause** but cannot confirm the diagnosis

- **Lab tests**

- Glucose, electrolytes, toxicology screen, Urinalysis, Bacterial cultures, Cerebrospinal fluid analysis, Endocrine studies



- Done to rule out other causes of seizures

5. Describe Epilepsy and why is it important to classify it correctly?

- Epilepsy - A disorder characterised by the tendency to experience recurrent seizures
 - At least two unprovoked (or reflex) seizures occurring more than 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
 - diagnosis of an epilepsy syndrome
- Epilepsy can be the primary problem or a symptom of another brain disorder
- About half the patients who have a seizure for the first time do not have another, and do not have epilepsy.
- It is important to classify epilepsy correctly as:
 - Correct classification = the best chance of achieving seizure remission depends on using the right medication for the right seizure type
 - Anti-Epileptic Drugs (AEDs) are definitely not interchangeable, and vary enormously in efficacy for different seizure syndromes
 - Choosing the wrong AED can **WORSEN** some seizure syndromes, particularly narrow spectrum agents and in Juvenile Myoclonic Epilepsy

The neurologist decides that Lamotri should be put on an anti-epileptic and put him on Sodium Valproate (Epilim) 200mg twice a day.

6. What are some general considerations you need to take into account before starting Lamotri on an Anti-Epileptic Drug?

General steps of epilepsy treatment

- Start treatment with 1 drug only as more does not always equal better - increased side effects/behavioural issues
- Start low and go slow and same for if stopping treatment always taper slowly
- Treat the cause NOT the symptom
- Be clear whether the symptoms being treated are
 - Ictal
 - Post ictal
 - Interictal - part of the other 99% of the patients life
 - Non-epileptic
- All epilepsy is not the same , All seizures are not the same, All people are not the same
 - Treat the person not the disease
 - Go for quality of life not just symptom control (take into account how AEDs side effects may impact a person life)
 - Individuals respond to AEDs differently
 - Special patient populations - pregnancy, children, elderly



General information on AEDS

- AEDs can be classified in multiple ways
 - Historically classified as **old vs new generation** -
 - neither is more effective when used at the right dose for the right indication however side effects and interactions are more common in older generation
 - Can classify according to **target/mechanism of action** -
 - However this can be a bit difficult with AEDs that have multiple targets
 - More useful classification is **narrow-spectrum vs broad-spectrum** -
 - Narrow spectrum only effective for focal epilepsy but often very effective
 - Broad spectrum effect both focal and generalised epilepsies

7. Complete the following table on common Antiepileptic drugs stating the brief mechanism of action and indication

Most important ones for them to know are:

- Sodium Valproate
- Carbamazepine
- Phenytoin
- Benzodiazepines
- Levetiracetam (Keppra)

Agent	Mechanism of action	Indications
Sodium Valproate (Epilim)	Inhibits GABA transaminase > increase in GABA > decreased neuronal excitability Inactivates sodium channels - preventing repetitive neuronal discharge Blocks T-type calcium channels	First line for tonic-clonic generalized seizures and absence and myoclonic seizures Can also be used in atonic seizures and focal (partial) seizures and bipolar disorder
Carbamazepine (Tegretol)	Inactivates sodium channels	First line in focal (partial) seizures And can be first line for tonic-clonic generalised seizures Trigeminal and glossopharyngeal neuralgias
Ethosuximide (Zarontin)	Inhibition of T-type (voltage gated) calcium channels in thalamic neurons	First line for absence seizures
Phenytoin (Dilantin)	Inactivation of sodium channels, may also affect Calcium and chloride channel activity	First line in status epilepticus prophylaxis Can be used in tonic-clonic seizures and focal (partial) seizures



Benzodiazepines - Diazepam - Clobazam - Midazolam - Clonazepam	Indirect GABA _A agonist > increased GABA action	First line for treatment of status epilepticus and acute treatment of seizures
Lamotrigine (Lamictal)	Stabilises presynaptic neuronal membranes by blocking voltage-dependent sodium channels and inhibiting glutamate release.	First line for long term treatment of focal seizures Second line for generalised seizures and absence seizures Can be used as a mood stabiliser for bipolar treatment (depressive episodes)
Phenobarbital (Phenobarbitone)	Barbiturate - GABA _A agonist > increased GABA action	First line treatment in neonates Tonic Clonic seizures Focal seizures
Levetiracetam (Keppra)	Mechanism unknown - may modulate neurotransmission by binding to synaptic vesicle protein 2A	First line treatment for long term treatment of focal seizures Also used in generalised seizures
Topiramate (Topamax)	Blocks voltage gated sodium channels Increases GABA	Focal and generalised tonic clonic seizures Migraine prophylaxis

Lamotri is brought into the ER department 10 weeks later after suffering from multiple seizures in the past hour without gaining consciousness in between. You are the ER intern and you take a history from Mrs Jean, his mum, who reveals that Lamotri stopped taking his sodium valproate 2 days ago due to gaining weight from the medication, without consulting his specialist (stopped abruptly).

8. What has happened to Lamotri
 - Suffered from **Status epilepticus due to abrupt AED withdrawal**
 - Status epilepticus (SE) is a seizure that lasts ≥ 5 minutes or a series of seizures in rapid succession without recovery in the interictal period, which increases the risk of long-term consequences such as neuronal injury and functional deficits.
 - Serious and often life threatening medical condition
 - Can result in neuronal injury/death, alteration of neuronal networks depending on the type and duration of seizures

9. What is the definition of this condition and what are some common causes?
 - A continuous seizure that lasts
 - ≥ 5 minutes for tonic-clonic seizures
 - ≥ 10 minutes for focal seizures with impaired consciousness
 - 10–15 minutes for absence seizures
 - **OR** ≥ 2 seizures where consciousness is not fully regained in the interictal period



- **Causes - anything that lowers 'seizure threshold'**
 - Withdrawal from antiepileptic drugs - taper down slowly
 - Metabolic disturbances (e.g. hyponatremia)
 - Drug toxicity (tricyclic antidepressants)
 - Structural brain lesions/injury (e.g. tumors, trauma, stroke)
 - CNS infections
 - Late-stage neurodegenerative diseases (e.g., Alzheimer disease)
 - Anoxic brain injury

As you are examining Lamotri in the ER, he suffers from another seizure that still hasn't stopped 5 minutes later.

10. What is the treatment for status epilepticus?

- Beware protocols for treatment vary between adults, children and neonate - below is representative:
 - **Provide basic life support**
 - Oxygen
 - Maintain BP and blood glucose concentration
 - **First stage – 5 to 20 mins after seizure onset**
 - Fast acting benzodiazepine to control seizures - Midazolam 5-10mg IM, IV, intranasal or buccal
 - OR clonazepam (IV)
 - **If seizures continue and/or to prevent recurrence give a long acting antiepileptic drug**
 - IV phenytoin, valproate, phenobarbital or levetiracetam
 - **If status epilepticus persists give anaesthetic doses of thiopental, midazolam or propofol**
 - assisted ventilation is usually required because of the risk of severe respiratory depression

WHAT IFs

11. What if Lamotri was a 24 year old female trying to get pregnant, how would this affect her treatment

- **Do NOT give valproate unless last resort due to teratogenicity**
 - If have to give to child bearing age give adequate contraception
 - If patient falls pregnant on valproate the need to change to an alternative agent quickly - absolutely contraindicated
 - A pregnancy test is essential prior to commencing even if using in status epilepticus
- **Educating the patient is really important!!**
 - Do pregnancy counselling BEFORE they are even thinking about conceiving
- Make sure they are taking Folate 5 mg daily (especially with Valproate) BEFORE even thinking about pregnancy



- Do NOT stop all AEDs when they become pregnant: risk of seizures to fetus is high but Try to wean down to monotherapy of the least teratogenic AED for their epilepsy syndrome
- Many pharmacokinetic and dynamic changes of AEDs in pregnancy: need to monitor levels
- Often need to monitor free levels of AEDs as protein binding changes
- **Beware that many AEDs reduce the efficacy of hormonal contraception by inducing hepatic enzymes**
 - Particularly carbamazepine, oxcarbazepine, phenobarbitone, phenytoin, topiramate
 - Effective contraception is provided by depot medroxyprogesterone, intrauterine devices such as mirena (hormonal) or copper IUD
- **lamotrigine and levetiracetam** are the most widely used due to their known safety during pregnancy. Clearance of lamotrigine and levetiracetam doubles during pregnancy compared to before pregnancy.

12. **What if** Lamotri experiences an overwhelming sense of fear, is sweating and has a rapid heart beat around the time of his seizure? What could Lamotri be suffering from?

- He could be experiencing **Ictal Psychiatric symptoms**
- Seizures manifest differently in every person and so if the seizure focus is closely connected to the limbic system than a huge range of psychiatric presentations are possible as seizure manifestations

Feedback – please provide feedback on this PeerBL case here →

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