SEIZURES AND STATUS EPILEPTICUS IN ADULTS:

EPILEPSY IS A CLINICAL CONDITION IN WHICH AN INDIVIDUAL IS SUBJET TO RECURRENT SEIZURES → DOES NOT REFER TO THOSE WITH A REVERSIBLE CAUSE OF SEIZURE (ALCOHOL WITHDRAWAL, POISONING, HYPOGLYCAEMIA OR OTHER METABOLIC DERANGMENTS)

SEIZURE CLASSIFICATION:

TWO MAJOR GROUPS → GENERALISED AND PARTIAL (FOCAL):

Table 165-1 Classification of Seizures
Generalized seizures (consciousness always lost)
Tonic-clonic seizures (grand mal)
Absence seizures (petit mal)
Others (myoclonic, tonic, clonic, or atonic seizures)
Partial (focal) seizures
Simple partial (no alteration of consciousness)
Complex partial (consciousness impaired)
Partial seizures (simple or complex) with secondary generalization
Unclassified (due to inadequate information)

GENERALISED SEIZURES:

- Thought to be caused by nearly simultaneous activation of the entire cerebral cortex
- Begins with ABRUPT LOSS OF CONSCIOUSNESS (may be only manifestation e.g. in absence attacks, where patients become unaware, without losing postural tone, they appear confused, detached or withdrawn, no postictal phase → daydreaming)
- GENERALISED TONIC-CLONIC SEIZURES → the most dramatic form, in a typical attack, the patient suddenly becomes rigid, trunk and extremities are EXTENDED and the patient falls to the ground
    - Often apnoeic during this period and appear deeply cyanotic
    - Often urinate and vomiti
    - As the rigid (tonic) phase subsides → increasing coarse trembling that evolves intoa symmetric, rhythmic (clonic) jerking of the trunk and extremities
    - As the attack ends → patient is left flaccid and unconscious
    - Typically last 60-90 seconds, which is often overestimated by bystanders

- Consciousness returns gradually and postictal confusion and fatigue may persist for hours

PARTIAL SEIZURES (FOCAL):

- DUE TO ELECTRICAL DISCHARGE IN A LOCALISED REGION OF THE CORTEX → MAY REMAIN LOCALISED OR SPREAD TO INVOLVED NEARBY CORTEX → SECONDARY GENERALISATION
- In simple partial seizures → seizure remains localised and consciousness and mentation are not affected
- COMPLEX PARTIAL SEIZURES → focal seizreus in which consciousness or mentation is affected → often misdiagnosed as psychiatric conditions as symptoms are so bizarre → automatisms, hallucinations, memory disturbances, distorted perception and affective disorders

<u>CLINICAL FEATURES OF SEIZURES:</u>

HISTORY:

- Presence of preceding AURA
- Abrupt or gradual onset
- Progression of motor activity
- Loss or bowel or bladder control
- Whether activity was local or generalised
- Post-ictal confusion/lethargy
- COMMON PRECIPITATING FACTORS:
  - Missed anticonvulsants
  - Recent alterations in medications
  - Sleep deprivation
  - Alcohol or substance withdrawal
  - Infection
  - Electrolyte disturbance
  - Substance abuse

Table 165-2 Common Causes of Secondary Seizures
Trauma (recent or remote)
Intracranial hemorrhage (subdural, epidural, subarachnoid, intraparenchymal)
Structural CNS abnormalities
Vascular lesion (aneurysm, arteriovenous malformation)
Mass lesions (primary or metastatic neoplasms)
Degenerative neurologic diseases
Congenital brain abnormalities
Infection (meningitis, encephalitis, abscess)
Metabolic disturbances
Hypo- or hyperglycemia
Hypo- or hypernatremia
Hyperosmolar states
Uremia
Hepatic failure
Hypocalcemia, hypomagnesemia (rare)
Toxins and drugs (many)
Cocaine, lidocaine
Antidepressants
Theophylline
Alcohol withdrawal
Drug withdrawal
Eclampsia of pregnancy (may occur up to 8 weeks postpartum)
Hypertensive encephalopathy
Anoxic-ischemic injury (cardiac arrest, severe hypoxemia)

- Persistent, severe or sudden headache suggest intracranial pathology

PHYSICAL EXAMINATION:

- Check for injuries → posterior shoulder dislocation easy to overlook
- TRANSIENT FOCAL DEFICIT (USUALLY UNILATERAL) → **TODD'S PARESIS** → SHOULD RESOLVE WITHIN 48 HOURS

DIFFERENTIAL DIAGNOSIS:

Table 165-3 Paroxysmal Disorders: Differential Diagnosis
Seizures
Syncope
Pseudoseizures
Hyperventilation syndrome
Migraine headache
Movement disorders
Narcolepsy/cataplexy

- Syncope usually accompanied by premonitory symptoms → light-headedness, diaphoresis, nausea, tunnel vision. However, cardiac syncope can occur suddenly without any warning
    - Recovery is usually rapid without post-ictal phase
- PSEUDOSEIZURES (psychogenic, non-epileptiform seizures):
    - Extremely difficult to distinguish from true seizures

    - Often associated with conversion disorder, impulse control or panic attacks
    - Occur regularly in response to emotional upset or occur ONLY WHEN WITNESSES ARE PRESENT
    - Attacks are often bizarre
    - Often able to protect themselves from noxious stimuli during an attack
    - Characteristic movements:
        - Side-to-side head thrashing
        - Rhythmic pelvic thrusting
        - Clonic extremity movements that are alternating rather than symmetric
        - Incontinence and injury are uncommon
        - Absence of postictal confusion
        - Absence of lactic acidosis on bloods taken at time of attack
- Narcolepsy → brief attacks of uncontrollable daytime sleepiness
- Cataplexy → sudden brief loss of postural tone that is often triggered by emotional upset, laughter or crying
- Seizures are suggestive if:
    - Onset and termination are abrupt → view with suspicion if developed over "minutes to hours". Most seizures only last 1-2 minutes unless in status
    - Lack of recall
    - Purposelss movements or behaviour during the attack
    - Postictal confusion (unless absence attack)

LABORATORY EXAMINATION:

- Need for laboratory evaluation should be individualised → in a patient with a well-established seizure disorder, all that may be needed are glucose and anticonvulsant level
- In case of adult with first seizures or unclear history → BSL, electrolytes, EUC, CMP, pregnancy and toxicology screen
- ABG → wide anion gap lactic acidosis → clears within 30 minutes of seizure cessation
- The therapeutic level of a drug is that which provides adequate seizure control without unacceptable side effects
    - A marked change in previously stable drug levels → non-compliance, change in medications, malabsorption, ingestion of competing drug

RADIOGRAPHIC STUDIES:

- CT head should be obtained with first seizure or change in usual pattern to identify a structural lesion
- CXR → primary or metastatic malignancies or aspiration

LUMBAR PUNCTURE:

- Indicated if patient is febrile or immunocompromised or if SAH is suspected

<u>TREATMENT OF UNCOMPLICATED SEIZURES</u>:

PATIENTS WITH ACTIVE SEIZRUES:

- Little intervention required if seizure is uncomplicated, other than to protect patient from injury
- Turn on side to protect from aspiration
- No indication for anticonvulsants
- Airway protection once subsided

PATIENTS WITH A HISTORY OF SEIZURES:

- Identify and correct potential precipitants that may lower seizure threshold
- Missing a dose of anticonvulsants is a common cause of seizures → especially as many have very short half-lives, hence missing one dose can lead to subtherapeutic levels → OBTAIN A DRUG LEVEL PRIOR TO ADMINISTERING A SUPPLEMENTAL OR LOADING DOSE TO AVOID DRUG TOXICITY
- If anticonvulsant levels are adequate and the patient has had a single attack, specific treatment may not be needed
- Patients should be discharged with a reliable family member or friend, with medical follow-up arranged

PATIENTS WITH A FIRST SEIZURE:

- In general, patients with a first seizure who have a normal neurologic exam, no acute or chronic medical comorbidities, normal tests (including imaging) and who have normal mental state can be discharged → initiation of antiepileptic medications can be deferred to follow up
- Patients with secondary seizures due to identifiable condition should be treated as recurrence is high
- Ideal initial regimen is a single agent that controls seizures with minimum toxicity → newer agents (carbamazepine, valproate, levetiracetam) are preferred to phenytoin, phenobarbitone
- POST-SEIZURE ADVICE → AVOID:
    - Swimming
    - Working with hazardous tools or machines
    - Working at heights
    - Driving (until cleared by a neurologist)

SPECIAL POPULATIONS:

- **HIV POSITIVE PATIENTS:**
    - **Mass lesions, HIV encephalopathy, meningitis are seen more commonly**
    - Extensive ED evaluation required → include LP to exclude meningitis and CT brain

Table 165-5 Causes of Seizures in the Human Immunodeficiency Virus Patient
Mass lesion
Toxoplasmosis
Lymphoma
Meningitis/encephalitis
Cryptococcal
Bacterial/aseptic
Herpes zoster
Cytomegalovirus
Human immunodeficiency virus encephalopathy/acquired immunodeficiency syndrome dementia complex
Progressive multifocal leukoencephalopathy
CNS tuberculosis
Cysticercosis
Neurosyphilis

- **PREGNANT PATIENTS:**
  - Risks of uncontrolled seizures to mother and foetus warrant continuation of seizure medications despite risks of neural tube defects, facial dysmorphism etc → splitting drugs, addition of folate and vitamin K
  - Because pregnancy is a hypercoagulable state → consider stroke or cerebral sinus thrombosis in a first episode of seizure
  - When a woman beyond 20 weeks gestation develops seizures in the setting of preeclampsia → ECLAMPSIA and can occur up to 3 weeks post partum
    - Treat with MAGNESIUM SULPHATE (more efficacious than diazepam and phenytoin in treating seizures in pregnant women)
- **SEIZURES IN THE ALCOHOL ABUSER:**
  - Classic alcohol withdrawal seizures occur 6-48 hours post cessation (or reduction) of alcohol, but may occur up to one week later
  - GENERALISED
  - Do NOT require chronic anticonvulsant therapy
    - Use benzodiazepines, usually in high doses

STATUS EPILEPTICUS:

- CONTINUOUS OR INTERMITTENT SEIZURES FOR MORE THAN 5 MINUTES WITHOUT RECOVERY OF CONSCIOUSNESS
  - After 5 minutes, seizures become less likely to spontaneously terminate
  - Treatment for status epilepticus should be initiated in all patients with continuous seizure activity lasting more than 5 minutes
- Animal models suggest permanent neurological damage could occur after 20 minutes of seizure activity → after 20 minutes hypotension, hypoxia, metabolic acidosis, hyperthermia and hypoglycaemia can develop
  - Neuroexcitatory amino acids, calcium are released → cardiac dysrhythmias, rhabdomyolysis and pulmonary oedema can all develop

- NON CONVULSIVE STATUS → patient is comatose or has fluctuating abnormal mental status or confusion but no overt seizure activity

TREATMENT:

- GOAL IS SEIZURE CONTROL AS SOON AS POSSIBLE
- SIMPLE RESUSCITATIVE MEASURES SHOULD BE INSTITUTED IN THE INTERIM
    - Intubation is recommended in most cases
    - IV antibiotics should be given prior to LP if meningitis is suspected as the cause
- TREATMENT ALGORITHM SHOWN BELOW
- Lorazepam is used in the US, as it has longer duration of action
- Phenytoin is mixed with a propylene glycol diluent → direct myocardial suppressant
- Phenytoin should not be used in those with second or third degree AV block → infusion site reactions, hypotension and dysrhythmias are among complications. Do not mix with glucose containing fluids and do not give IM as absorption is erratic
- For those with refractory status → consider IV keppra, valproate or barbiturates (thiopentone coma) should be considered. IV midazolam/propofol infusions for 24 hours may be considered
- Ketamine is an agent of last resort
- EEG monitoring is mandatory if neuromuscular blockers are being used

Immediate treatment of convulsive status epilepticus involves simultaneous protection of the airway, maintenance of oxygenation and termination of seizure activity using:

1 **clonazepam 1 mg (child: 0.25 to 0.5 mg) IV, over 2 to 5 minutes, not exceeding 0.5 mg/min. Repeat once 15 minutes later if status epilepticus continues**

OR

1 **diazepam 10 to 20 mg (child: 0.1 to 0.25 mg/kg up to 20 mg) IV, over 2 to 5 minutes, not exceeding 5 mg/min. Repeat once 15 minutes later if status epilepticus continues**

OR

1 **midazolam 5 to 10 mg (child: 0.15 to 0.2 mg/kg up to 10 mg) IM or IV, over 2 to 5 minutes**
or midazolam 5 to 10 mg (child: 0.2 to 0.3 mg/kg up to 10 mg) buccally or intranasally. Repeat once 15 minutes later if status epilepticus continues [Note 1].

The above benzodiazepines have a short duration of anticonvulsant effect, so each drug should be **followed immediately** by:

1 **phenytoin (adult and child) 15 to 20 mg/kg IV, not exceeding 50 mg/min (25 mg/min in children, elderly patients and those with comorbidities). Continuous monitoring of the electrocardiogram and blood pressure is essential [Note 2] [Note 3]**

OR

2 **phenobarbitone 10 to 20 mg/kg (child: 15 to 20 mg/kg) IV, not exceeding 100 mg/min**

OR

2 **sodium valproate 10 mg/kg up to 800 mg (child: 15 to 30 mg/kg up to 800 mg) by slow IV injection over 3 to 5 minutes, usually followed by continuous infusion of 1 to 2 mg/kg/hour to a maximum of 2500 mg/day (child: 40 mg/kg/day up to 2500 mg/day), according to the patient's clinical response.**

If seizures continue (refractory status epilepticus), the patient should be transferred to the intensive care unit, where an infusion of clonazepam, midazolam, propofol or thiopentone may be used. Other antiepileptic drugs with intravenous formulations (eg lacosamide, levetiracetam) may also be used, although there is little well-controlled evidence for their efficacy in status epilepticus.