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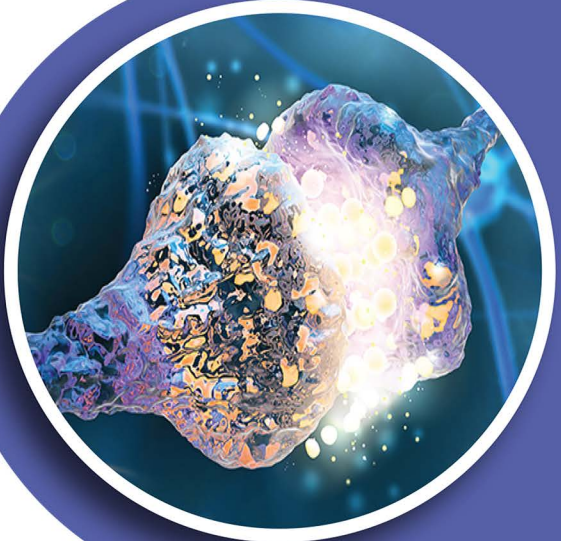
ICP-IAN 100 Questions in Neurological Practice



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SECTION 1

Epilepsy

Section Editors: Sita Jayalakshmi, Mrinal Kanti Roy
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Q1. What is the difference between seizure and epilepsy?

Ans.

Seizure: It is transient occurrence of signs and/or symptoms (either convulsive, nonconvulsive, psychic, etc.) due to abnormal excessive or synchronous neuronal activity in the brain.[1] An epileptic seizure starts and terminates abruptly but sometimes the latter is less evident. Greek meaning of seizure—"to take hold" relates that the person is like under someone else's possession for the time being.

Epilepsy: It is a disease of the brain defined by any of the following conditions.[2]

One unprovoked or reflex seizure and a probability of further seizures (due to presence of other risk factors) match the general recurrence risk after two unprovoked seizures, occurring over the next 10 years (at least 60%) suggests the diagnosis of epilepsy. Examples of risk of recurrence may be a structural brain lesion in brain imaging and an epileptiform discharge in electroencephalogram (EEG) presents in a patient of single unprovoked seizure. This patient may qualify for the diagnosis of epilepsy.

So, all patients of epilepsy have seizures. But all patients with seizures may not develop epilepsy. This is important from the treatment viewpoint. There is no need to give preventive antiseizure medication (ASM) treatment to each and every patient after first seizure if there is no possibility of developing epilepsy.

Q2. What are the clinical symptoms and signs (semiology) of seizures?

Ans. The semiology of seizures can be divided into the following parts—Prodrome, aura, ictal, and postictal phase. The International League Against Epilepsy (ILAE) task force has elaborated various seizure-related descriptive terminology.[3]

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- *Prodrome*: It is a preictal subjective or objective clinical alteration in the form of ill-localized sensation, headache, agitation, etc., that precedes the seizure-onset but does not form part of the seizure.
- *Aura*: It is a subjective ictal phenomenon which patient can remember, and it usually occurs preceding an observable seizure. Aura can be sensory (elementary and experiential) or dyscognitive. In *elementary sensory aura*, patient has a single unformed phenomenon comprising one primary sensory modality, like *somatosensory* (tingling, numbness, and electric-shock sensation), *visual* (flashing or flickering lights, spots, simple patterns, scotomata, or amaurosis), *auditory* (buzzing, drumming sounds, or single tones), *olfactory* (usually disagreeable odor), *gustatory* (acidic, bitter, salty, sweet, or metallic taste), *epigastric* (abdominal discomfort including nausea, sensation may rise to chest or throat), *cephalic* (sensation in the head such as light-headedness, tingling, or headache), and *autonomic* (including cardiovascular, gastrointestinal, sudomotor, vasomotor, and thermoregulatory functions). In *experiential sensory aura*, patient feels illusory or composite hallucinatory events alone or in combination which are similar to those experienced in life, but the patient experiences them as happening outside of actual contexts. Experiential sensory aura can be *affective* (fear, depression, joy, and anger), *mnemonic* (reflect ictal abnormal cognition such as feelings of familiarity or déjà-vu and unfamiliarity or jamais-vu), *hallucinatory* (without corresponding external stimuli involving visual, auditory, somatosensory, olfactory, and/or gustatory phenomena), and *illusory* (an alteration of actual percepts involving the visual, auditory, somatosensory, olfactory, or gustatory systems).[3]
- *Ictal phase*: It is the sudden external manifestation during a seizure. It may be either sustained increase in muscle contraction lasting a few seconds to minutes *(tonic)*, or sudden, brief (<100 ms) involuntary single or multiple contraction(s) of muscles(s) or muscle groups (*myoclonic*) or repeated myoclonia regularly for a prolonged period and involving the same muscle groups at a frequency of 2–3 cycles per second (*clonic*). *Jacksonian march* indicates the spread of clonic movements through contiguous body parts unilaterally. *Tonic-clonic* denotes a sequence of a tonic followed by a clonic phase.[3] *Focal seizure* denotes initial activation of only part of one cerebral hemisphere. On the contrary, *generalized seizure* denotes more than minimal initial involvement of both cerebral hemispheres.[4]
- *Automatism*: A coordinated, repetitive, motor activity usually occurs when cognition is impaired and for which the subject is usually amnesic afterward. Automatism often looks like a voluntary movement and may have inappropriate continuation of an ongoing preictal motor activity. It is an ictal phenomenon.[3]
- *Postictal phase*: After the termination of ictal phase, a transient clinical abnormality of central nervous system (CNS) appears or accentuates, called postictal phenomena. It can be of two types: (1) *Lateralizing* (Todd's

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or Bravais' phenomena—any unilateral postictal dysfunction relating to motor, language, sensory, and/or integrative functions including visual, auditory, or somatosensory neglect phenomena) and (2) *nonlateralizing* (impaired cognition, amnesia, and psychosis). Postictal nose-wiping is found in temporal lobe epilepsy (TLE) and has lateralizing value also.

Q3. How do we classify seizures and epilepsies?

Ans. Seizures are classified according to the mode of onset by the ILAE in 2017 as per following **Figure 1**.[5] One eyewitness or video recording is required to describe the onset of the seizures.

Epilepsies are classified in following three tiers according to level to specialized medical environment[6]—(1) seizure type, (2) epilepsy type, and (3) epilepsy syndrome.

1. *Seizure type*: If the patient has only a single seizure or no facility of EEG, video, or brain imaging then clinician can reach up to the level of seizure-onset type which is described in the previous section (focal onset, generalized onset, and unknown onset).
2. *Epilepsy type*: Generalized epilepsy, focal epilepsy, combined generalized and focal epilepsy, and unknown. The diagnosis of *generalized epilepsy* is made on the clinical grounds in the form of absence, tonic, tonic-clonic, myoclonic, and atonic, which is supported by interictal generalized epileptiform discharges in EEG. In the case of a normal EEG, supportive evidence in the form of myoclonic jerks of relevant family history is required to make the diagnosis of a generalized epilepsy. Similarly, the diagnosis of *focal epilepsy* is also made on the clinical grounds in the form of focal motor seizures, focal nonmotor seizures, focal aware seizure, focal

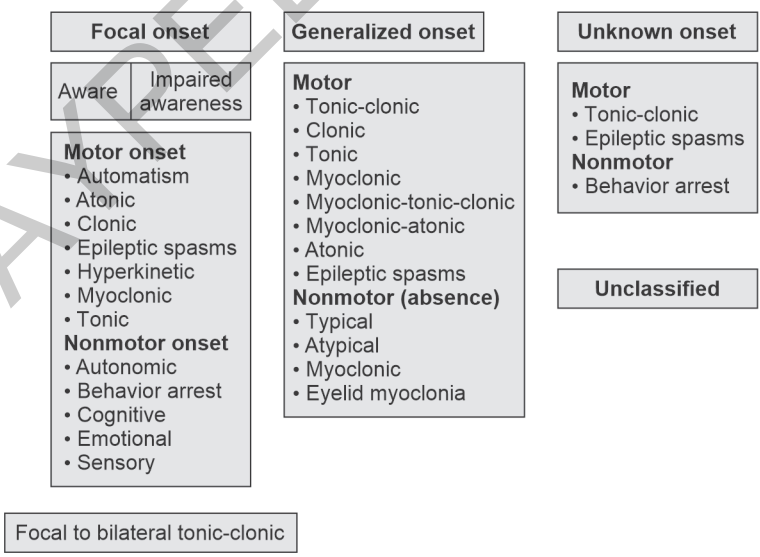

FIG. 1: International League Against Epilepsy (ILAE) classification of seizures (2017).

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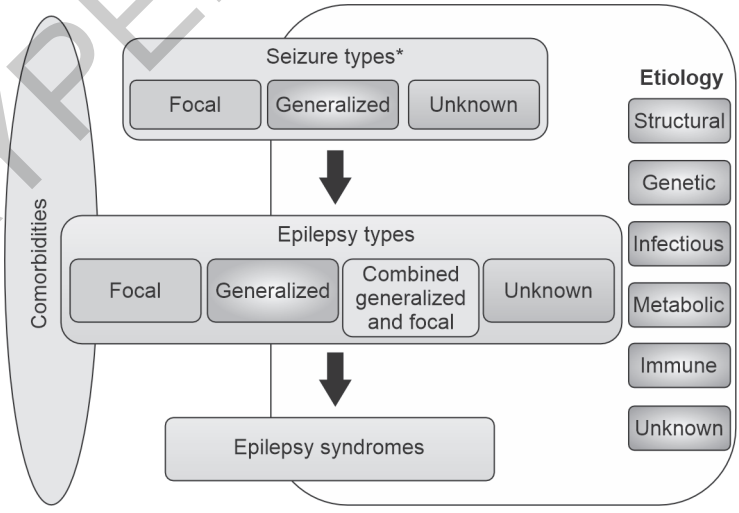
impaired awareness seizure, and focal to bilateral tonic-clonic seizures. EEG will show a focal epileptiform change. A new group of *combined generalized and focal epilepsy* patients have both generalized and focal-onset seizures. Examples of such conditions are Dravet syndrome and Lennox–Gastaut syndrome. The fourth variety is *unknown* type. The epilepsy type is denoted unknown if there is insufficient information about the seizure type or is no concordance between the seizure semiology and the EEG features. For example, if the patient is having generalized tonic-clonic seizures (GTCS) with a normal EEG, it will be unknown epilepsy till further studies are available. The diagnosis up to the epilepsy type may be the maximum achievable diagnosis if the clinical features and EEG findings cannot be suitably placed in the known epilepsy syndromes discussed subsequently. Etiological diagnosis also to be done with brain MRI (structural etiology), whole exome sequencing (genetic etiology), cerebrospinal fluid analysis (infectious etiology), tandem mass spectrometry and urine abnormal metabolites (metabolic etiology), autoimmune encephalitis antibodies (autoimmune etiology), and many other individualized tests (in respective scenarios) in combination.

3. *Epilepsy syndromes*: Epilepsy syndromes are a complex of signs and symptoms defining a unique epilepsy condition with different etiologies **(Fig. 2)**.[4]
   i. Benign familial neonatal epilepsy: Seizures since day 2–3 of life, typically clonic, but often preceded by tonic, often unilateral, remit within 2–6 months, slight risk of later epilepsy.
   ii. Early myoclonic encephalopathy and Ohtahara syndrome: Onset at neonatal age group, severe seizures, and EEG burst suppression. Early myoclonic encephalopathy has frequent limb or face



*Indicates onset of seizure.

FIG. 2: International League Against Epilepsy (ILAE) classification of epilepsies (2017).

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myoclonus, generalized massive myoclonus, later epileptic spasms, floppy child, and abnormal neurological examination. Ohtahara syndrome predominantly has epileptic spasm which is associated with generalized EEG attenuation, severe mental and psychiatric handicap, and high mortality.

iii. West syndrome: Onset between 3 and 7 months; characterized by a clinical triad of epileptic spasms, arrest or deterioration of psychomotor development, and a characteristic EEG pattern called hypsarrhythmia; seizures in clusters; multiple times per day; abnormal psychomotor development; cognitive disability; and epileptic spasms (symmetric or asymmetric). Hypsarrhythmia is characterized by high-voltage disorganized EEG activity with slow waves and multifocal spikes and sharp waves punctuated by periods of generalized attenuation. When a spasm occurs, it is usually during a period of attenuation.

iv. Dravet syndrome: Severe myoclonic epilepsy of infancy (SMEI), sodium voltage-gated channel alpha subunit 1 (SCN1A) or gamma-aminobutyric acid type A ($GABA_A$) mutation, previously normally developing infant having febrile status epilepticus (SE), multiple seizure type, exacerbated by sodium channel blockers such as carbamazepine (CBZ) and lamotrigine (LTG), poor prognosis, intellectual disability, ataxia, and spasticity.

v. Genetic epilepsy with febrile seizure plus: Autosomal dominant, *SCN1A*, *SCN1B*, or $GABA_A$ mutation, most of them remit by 6-year age, others denoted as febrile seizure plus.

vi. Panayiotopoulos syndrome: Onset 1–14 years, autonomic manifestation, ictal vomiting, and seizures can be very prolonged (>30 minutes), predominate during sleep, EEG posterior predominant multifocal spikes, good prognosis, and remission by 3 years.

vii. Doose syndrome: Onset between 18 and 60 months of age, myoclonic, myoclonic-atonic seizures, and tonic-clonic seizures also, nearly half of them has poor cognition.

viii. Autosomal dominant nocturnal frontal lobe epilepsy: Onset before 20 years, typically during sleep, hypermotor seizures, short duration (30 seconds), and mutation in neuronal nicotinic acetylcholine receptor. CBZ is mostly effective.

ix. Epilepsy with myoclonic absence: Onset 1–12 years of age, myoclonic absence, 10–60 seconds, several times a day, and 3-Hz generalized rhythmic spike-and-wave activity. Myoclonic absence disappears but GTCS persists.

x. Lennox–Gastaut syndrome: A triad of several seizure types including generalized tonic, generalized atonic, and atypical absence seizures, a characteristic interictal EEG abnormality of generalized slow spike-and-wave discharges (<2.5 Hz) in waking and bursts of paroxysmal fast activity (10 Hz) in sleep, and cognitive dysfunction. Onset 3–10 years, resistant epilepsy.

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xi. Continuous spike-and-wave during sleep and Landau–Kleffner syndrome (LKS): Cognitive decline, EEG shows continuous spike-wave activities in slow-wave sleep (CSWS). LKS has acquired epileptic aphasia, onset in first decade, verbal auditory agnosia, and classical ASM ineffective. Steroid, immunoglobulin, and multiple subpial resections are helpful. CSWS has preexisting neurological illnesses, global cognitive regression, and motor impairments.
xii. Childhood absence epilepsy: Onset in first decade, absence seizures many times a day, normal development and neurological status, and EEG have generalized spike-wave discharges around 3 Hz, single gene mutation or polygenic inheritance, ethosuximide (ETS) drug of choice, 12% cases may have glucose transporter type 1 (GLUT1) deficiency if onset before 4 years age.
xiii. Juvenile absence epilepsy: Onset in second decade, seizures are less frequent, very similar to childhood absence epilepsy.
xiv. Juvenile myoclonic epilepsy: Very common (10% of all epilepsies), onset first decade, generalized myoclonic seizures—specially in early morning after sleep deprivation (100%), GTCS (90%), generalized absence seizure (65%), EEG—generalized irregular 4–6 Hz spike-wave bursts, a lifelong condition, polygenic, and seizures aggravate by ASMs meant for focal epilepsies.
xv. Autosomal dominant epilepsy with auditory features: Begin at adolescence or adulthood, have elemental auditory aura such as buzzing, ringing, even hearing loss, seizure may start with aphasia if onset from dominant temporal lobe.

Q4. What are seizure mimics? How do we differentiate each one of them from seizures?

Ans. Seizures necessarily indicate transient neurological events (TNEs) with episodic paroxysmal loss of awareness with stereotypic motor or sensory accompaniments. Often nonepileptic events may be misdiagnosed as seizures due to same presenting features leading to overtreatment and missed diagnosis. The gold standard for diagnosing epilepsy is to record a seizure with video EEG (VEEG). Again, the stereotyped nature of seizures (perhaps more than for other types of events) may be a big pointer to their diagnosis.[7,8]

- *Syncope*:
  - Reflex: Vasovagal, micturition, swallow, carotid sinus, orgasmic, and laughing
  - Cardiac:
    - Arrhythmogenic
    - Elderly: Scar-related ventricular tachycardia
    - Young: Long QT syndrome, short QT syndrome, arrhythmogenic right ventricular cardiomyopathy.
    - Structural, aortic stenosis, and hypertrophic cardiomyopathy

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- *Orthostatic*: Autonomic failure
- *Psychogenic nonepileptic attack disorder*:
  - Panic disorder (especially in people with epilepsy)
  - Dissociative
  - Factitious and malingering
- *Sleep disorders*:
  - Narcolepsy syndrome and cataplexy
  - Parasomnias
- *Paroxysmal symptoms of structural brain disease*:
  - Multiple sclerosis
  - Tumor, e.g., brainstem glioma
- *Vascular*:
  - Migraine (hemiparetic, occipital, and "basilar artery")
  - Shaking transient ischemic attack (critical bilateral stenosis)
  - Subclavian steal syndrome
  - Moyamoya (combination of TIA and seizures)
  - Not vertebrobasilar insufficiency
- *Hypoglycemia*:
  - Behavior disturbance
  - Hemiparesis
- *Movement disorder*:
  - Paroxysmal kinesigenic dystonia/dyskinesia
  - Myoclonus following hypoxia
- *Hydrocephalus*:
  - Colloid cyst
  - Chiari malformation
- *Drop attacks*:
  - Postural instability
  - Psychogenic

Q5. What is the role of neuroimaging in epilepsy? If so, what is the best modality?

Ans. Neuroimaging is indicated in new-onset seizures or epilepsy to identify structural causes. After the first unprovoked seizure, neuroimaging gives clinically relevant significant positive finding in only 10% of cases. Magnetic resonance imaging (MRI) brain is the modality of choice as computed tomography (CT) brain misses temporal lobe details and other smaller details.[4] However, in remote villages of our country, MRI may not be available. If CT is available in nearby areas, it can be utilized to exclude gross intracranial abnormalities.

Magnetic resonance imaging brain is to be done in children with new-onset seizures under conscious sedation or general anesthesia (GA). If the child has cognitive or motor impairment or any other neurological examination abnormality, focal-onset seizures, EEG does not show any benign focal or generalized epilepsy, or age < 1 year, MRI brain is mandatory.

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The Neuroimaging Task Force recommends use of the Harmonized Neuroimaging of Epilepsy Structural Sequences (HARNESS-MRI) protocol with isotropic, millimetric 3D T1 and fluid-attenuated inversion recovery (FLAIR) images, and high-resolution 2D submillimetric T2 images.[9]

Q6. What is the role of EEG in the diagnosis of epilepsy?

Ans. Electroencephalography is an important tool to delineate the epileptogenic cortex. Although the most commonly used bedside method, its sensitivity and specificity depend on many factors including patient age, recording techniques, use of activation procedures (hyperventilation and photic stimulation), etc. There are prototypical EEG findings in several epilepsy syndromes. As also, sometimes epileptiform discharges may be recorded in healthy, especially young individuals and should not misled into overtreatment. It is important to recognize that a normal EEG does not exclude epilepsy, as around 10% of patients with epilepsy never show epileptiform discharges. As also, an abnormal EEG demonstrating interictal epileptiform discharge (IED) does not in itself indicate that an individual has a seizure disorder, as IEDs are seen in a small percentage of normal subjects who never develop epilepsy, and IED may also be found in patients with neurological disorders which are not complicated by epilepsy. VEEG recording helps in associating the clinical features with corresponding EEG changes. Careful analysis of the clinical signs and symptoms and seizure symptomatology including the triggering factors can provide important localizing clues. Surface EEG recordings are less sensitive than invasive studies but provide the best overview to determine the localization of the epileptogenic zone. Further invasive recordings are used among those where epileptogenic zone either cannot be located with noninvasive diagnostic methods or is adjacent to eloquent cortex. Invasive electrodes include stereotactically implanted depth electrodes and subdural strip or grid electrodes. These are subject to sampling errors, if misplaced hence should be used only after thorough clinical evaluation formulating a working hypothesis of seizure origin and propagation.[8] Additional risks associated with invasive recording are justifiable only if there is a good chance of obtaining essential localizing information and on a potentially resectable area. Some representative EEG patterns are:

- Anterior to mid temporal spikes and temporal intermittent rhythmic delta activity associated with mesial TLE.
- Generalized 3-Hz spike–wave complexes accentuated with hyperventilation characteristic of absence epilepsy.
- Fast 3–4.5-Hz spike–wave complexes, generalized polyspikes aggravated with slow photic stimulation associated with juvenile myoclonic epilepsy.
- Generalized slow <2.5-Hz spike–wave complexes, rhythmic fast activity associated with Lennox–Gastaut syndrome.
- *Regional (extratemporal) polyspikes or focal rhythmic spikes*: Focal cortical dysplasia
- Hypsarrhythmia seen in West syndrome

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Q7. What are the indications for VEEG during the evaluation of a person with seizures and/or epilepsy?

Ans. Initial diagnosis is typically based on a description of clinical paroxysmal events (seizures) and medical history provided by the individual or observers. Supporting information may be obtained from routine outpatient electroencephalography or neuroimaging. When additional diagnostic information is needed, however, inpatient admission for continuous EEG monitoring may be indicated. Although, the most common reason is to capture a typical clinical event or "spell", a generic term for paroxysmal symptoms. VEEG allows for behavioral observation through a video recording that is time-locked with the EEG, providing the gold standard for diagnosis and presurgical planning. Because spells and seizures are transient events, they are rarely witnessed by medical personnel during outpatient visits or recorded on routine outpatient EEG testing. Although epileptic seizures are the prototypical spell, there are many other medical problems that present with transient symptoms that can be diagnosed or differentiated from seizures only by capturing an episode.

The most common indications for elective inpatient admissions are to:[10]

- Determine whether spells are epileptic seizures (spell classification or differential diagnosis).
- Identify the type of seizures occurring in individuals with known epilepsy (seizure/syndrome classification).
- Localize the seizure focus for consideration of epilepsy surgery (presurgical evaluation).
- Perform ictal single photon emission CT (SPECT).
- Monitor seizure frequency (seizure quantification).
- Adjust medications to control seizures (medication adjustment).
- Differentiate between seizures and medication side effects.

Q8. What are the etiologies for epilepsy? Is it different at different ages?

Ans. Determining the etiology of epilepsy is the next important step after the confirmation of diagnosis of epilepsy. The major etiological subgroups of epilepsy as defined by ILAE 2017 consensus include[6]—structural, genetic, metabolic, immune-mediated, infectious, and lastly, cryptogenic. Epilepsy may be classified into more than one etiologic category based on onset, age, and other circumstances. For example, tuberous sclerosis has both a structural and a genetic etiology. The structural etiology is important for epilepsy surgery, while the genetic etiology guides genetic counseling and targeted therapies.[11]

- *Structural*: A structural abnormality in a person has a significant risk of being associated with observed epilepsy. These may be acquired such as stroke, trauma, and infection, or genetic such as malformations of cortical development and tuberous sclerosis.

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- *Genetic*: This category includes epilepsy resulting directly from a known or presumed genetic mutation causing seizures as a core symptom of the disorder. Often there are diverse and multiple associated genes and, in most cases, the underlying genes are not yet determined.
- *Infectious*: An infectious etiology refers to a patient with epilepsy resulting as a consequence of an infectious disorder. It does not encompass seizures occurring in the setting of acute infection such as meningitis or encephalitis. Examples include neurocysticercosis, CNS tuberculosis, human immunodeficiency virus (HIV), cerebral malaria, subacute sclerosing panencephalitis (SSPE), cerebral toxoplasmosis, and congenital infections such as Zika virus, Herpes simplex, and cytomegalovirus.
- *Metabolic*: It results directly from a known or presumed metabolic disorder in which seizures are a core symptom of the disorder. There could be a well-delineated metabolic defect with subtle biochemical changes or manifestations throughout the body such as porphyria, uremia, aminoacidopathies, or pyridoxine-dependent seizures.
- *Immune*: This includes epilepsy resulting from autoimmune-mediated CNS inflammation or systemic immune-mediated disorders leading to neurological changes causing epilepsy.
- *Unknown/Cryptogenic*: Despite thorough evaluation cause of the epilepsy may remain equivocal in certain cases. It is not possible to make a specific diagnosis apart from the possible origin such as frontal lobe epilepsy or remain uncertain as generalized epilepsy with uncertain onset.

Structural-metabolic epilepsy and perinatal insults were the leading causes of epilepsy in the children and adolescents. Whereas disturbances of brain development dominated in the youngest age groups (≤4 years). Among the ≥60 years old, stroke was the most common cause of epilepsy (44%). Despite recent advances in research and technology, many patients in all age groups (including the youngest) still have an unknown cause of epilepsy.[6]

Q9. Discuss the approach to the management of first unprovoked seizure.

Ans. Epilepsy should not be immediately diagnosed after a single seizure. The average risk of developing another unprovoked seizure following the first one is about 35–40%. Many individuals if untreated may not even have a second seizure. The risk of a third seizure following two unprovoked seizures is, however, much higher. Often, the first seizure need not be treated. The individual and family members can be explained about the possible risk of recurrence, necessary precautions, and need for regular follow-up. There are certain situations in which even the first seizure may merit treatment.[12,13]

- Prolonged focal seizure or focal SE
- First seizure itself presenting with SE
- Associated severe neurological deficit such as hemiparesis, mental retardation, and cerebral palsy.

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- Family history of seizures among parents, siblings, or children
- Abnormal EEG with features typical of epilepsy syndromes
- Abnormality on brain imaging
- An unrecognized previous seizure brought out only by a careful history.
- High-risk jobs (professional or other activities that may endanger life during a seizure).
- When either the individual or family does not accept the expected risk of recurrence.

Q10. What are the mechanisms of action of various anti-seizure medications?

Ans. Antiseizure medications prevent the occurrence of seizures; there is no evidence that they have disease-modifying properties. The ASMs act on brain excitability mechanisms to interfere with the generation and spread of epileptic hyperexcitability, however, they do not address the specific defects that cause epilepsies. There are four broad classes of such ASM mechanisms:[14]

1. Modulation of ionic channels such as voltage-gated sodium channels [e.g., phenytoin (PHT), CBZ, and LTG], voltage-gated calcium channels (e.g., ETS), and voltage-gated potassium channels [e.g., retigabine (ezogabine)]
2. Enhancement of GABA-mediated inhibitory neurotransmission [e.g., benzodiazepines, tiagabine, and vigabatrin (VGB)]
3. Attenuation of glutamate-mediated excitatory neurotransmission (e.g., perampanel)
4. Modulation of neurotransmitter release via a presynaptic action [e.g., levetiracetam (LEV), brivaracetam, gabapentin (GBP), and pregabalin (PGB)]

With new advances in understanding genetic epilepsies, attempts are being made to engineer specific small molecule, antisense, and gene therapies that functionally reverse or structurally correct pathogenic defects in genetic epilepsy syndromes. These new targeted therapies might begin a paradigm shift in the treatment of some rare genetic epilepsy syndrome **(Table 1)**.

Q11. What are the guidelines for the management of partial seizures and epilepsies?

Ans. Approximately, two-thirds of epilepsy patients will respond to either ASM monotherapy or combination therapy. There are approximately 30 ASMs available and, in general, drugs have similar rates of efficacy with limited comparative data. Important factors in choosing among various drugs include potential adverse effects, dosing schedules, drug interactions, available formulations, and cost. For focal epilepsies, narrow-spectrum agents are typically effective, although broad-spectrum agents can improve seizure frequency in focal epilepsies as well with variable efficacy. Several

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TABLE 1: Molecular targets of clinically used ASMs.[14]

Molecular target	ASMs that act on the molecular target
Voltage-gated ion channels	
Voltage-gated sodium channels	Phenytoin, fosphenytoin, carbamazepine, oxcarbazepine, eslicarbazepine, lamotrigine, lacosamide; possibly topiramate, and zonisamide
Voltage-gated calcium channels (T-type)	Ethosuximide
Voltage-gated potassium channels (Kv7)	Ezogabine
GABA inhibition	
$GABA_A$ receptors	Phenobarbital, primidone, benzodiazepines, including diazepam, lorazepam, and clonazepam; possibly topiramate, felbamate, and ezogabine
GAT1 GABA transporter	Tiagabine
GABA transaminase	Vigabatrin
Synaptic release machinery	
SV2A	Levetiracetam
$\alpha 2\delta$	Gabapentin and pregabalin
Ionotropic glutamate receptors	
AMPA receptor	Perampanel
Mixed/unknown	Valproate, felbamate, topiramate, zonisamide, rufinamide, and adrenocorticotrophin

(AMPA: α-amino-3-hydroxy-5-methyl-4-isoxazole-propionate; GABA: γ-aminobutyric acid; GAT1: γ-aminobutyric acid transporter 1; SV2A: synaptic vesicle protein 2A)

ASMs, especially those that are inducers or inhibitors of the cytochrome P450 system, may lead to undesirable drug interactions. In childbearing age women, enzyme inducers such as CBZ and PHT can increase the clearance of oral contraceptives and precipitate unwanted pregnancy; oral contraceptives have been shown to also decrease plasma concentrations of LTG. In patients who are on warfarin, enzyme inhibitors such as valproate (VPA) can impair clearance of anticoagulation. In patients with multiple comorbidities, use of LEV, LTG, lacosamide (LCM), and GBP is favored due to limited drug interactions. Finally, use of LTG and VPA in combination may have synergistic effects but a sensitive dosing approach is necessary.

Current guidelines as per Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society suggest:[15]
In patients with new-onset focal epilepsy or unclassified GTCS:

- LTG use should be considered to decrease seizure frequency (level B).
- LTG use should be considered (level B) and GBP use may be considered (level C) to decrease seizure frequency in patients aged ≥ 60 years.

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He is the founder of Clinical Society for Undergraduate Students, SN Medical College, Agra. He celebrates International Epilepsy Day, Brain Awareness Week, World Diabetes Day, World Hypertension Day, and World AIDS Day regularly. He has also received honor from many distinguished clubs and associations of Agra.

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