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MANAGEMENT OF SEIZURES DISORDER

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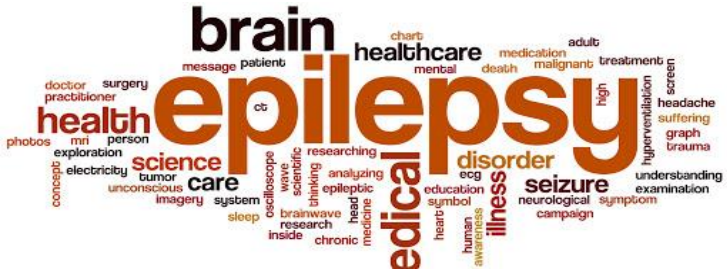
EPILEPSY IS A GLOBAL HEALTH PROBLEM AFFECTING APPROXIMATELY 50 MILLION PEOPLE WORLDWIDE. IT IS ONE OF THE MOST COMMON CHRONIC NEUROLOGICAL DISEASES IN THE WORLD AND HAS SERIOUS PHYSICAL, ECONOMIC AND DISCRIMINATORY CONSEQUENCES IN SOME PARTS OF THE WORLD. HOWEVER, THE HEALTHCARE BURDEN AND FINANCIAL COST OF TREATING EPILEPSY CAN BE REDUCED WITH APPROPRIATE, PROMPT INTERVENTIONS.

1. A **"seizure"** is a paroxysmal alteration of neurologic function caused by the excessive, hypersynchronous discharge of neurons in the brain.
2. **"Epileptic seizure"** is used to distinguish a seizure caused by abnormal neuronal firing from a nonepileptic event, such as a psychogenic seizure.
3. **"Epilepsy"** is the condition of recurrent, unprovoked seizures. Epilepsy has numerous causes, each reflecting underlying brain dysfunction .A seizure provoked by a reversible insult (e.g., fever, hypoglycemia) does not fall under the definition of epilepsy because it is a short-lived secondary condition, not a chronic state.
4. **"Epilepsy syndrome"** refers to a group of clinical characteristics that consistently occur together, with similar seizure type(s), age of onset, EEG findings, triggering factors, genetics, natural history, prognosis, and response to antiepileptic drugs (AEDs). The nonspecific term "seizure disorder" should be avoided.



* ***In order to understand the basic concepts of seizures, epilepsy and epileptogenesis, please refer basic anatomic and electrophysiologic properties of the cerebral cortex, and the factors that determine the level of neural activity at the cellular and cell network level.*** ***https://youtu.be/mGxomKWfJXs*** ***and*** ***https://youtu.be/e_Eb32Eq_fw***

OVERALL PATHOPHYSIOLOGY OF SEIZURES:

* A seizure can be conceptualized as occurring when there is distortion of the normal balance between excitation (E) and inhibition (I) in the brain . This E/I imbalance can result from an alteration at many levels of brain function, from genes and subcellular signaling cascades to widespread neuronal circuits.

* The factors that alter E/I balance can be genetic or acquired. Genetic pathologies leading to epilepsy can occur anywhere from the circuit level (e.g., abnormal synaptic connectivity in cortical dysplasia) to the receptor level (e.g., abnormal γ-aminobutyric acid [GABA] receptor subunits in Angelman syndrome) to abnormal ionic channel function (e.g., potassium channel mutations in benign familial neonatal epilepsy [BFNE]).

* Given that the basic mechanism of neuronal excitability is the action potential, a hyperexcitable state can result from increased excitatory synaptic neurotransmission, decreased inhibitory neurotransmission, an alteration in voltage-gated ion channels, or an alteration of intra- or extra-cellular ion concentrations in favor of membrane depolarization. A hyperexcitable state can also result when several synchronous subthreshold excitatory stimuli occur, allowing their temporal summation in the post synaptic neurons.

* Action potentials occur due to depolarization of the neuronal membrane, with membrane depolarization propagating down the axon to induce neurotransmitter release at the axon terminal. The action potential occurs in an all-or-none fashion as a result of local changes in membrane potential brought about by net positive inward ion fluxes. Membrane potential thus varies with activation of ligand-gated channels, whose conductance is affected by binding to neurotransmitters; or with activation of voltage-gated channels, whose conductance is affected by changes in

transmembrane potential; or with changes in intracellular ion compartmentalization.

- **Neurotransmitters** are substances that are released by the presynaptic nerve terminal at a synapse and subsequently bind to specific postsynaptic receptors for that ligand. Ligand binding results in channel activation and passage of ions into or out of the cells. The major neurotransmitters in the brain are glutamate, gamma-amino-butyric acid (GABA), acetylcholine (ACh), norepinephrine, dopamine, serotonin, and histamine. Other molecules, such as neuropeptides and hormones, play modulatory roles that modify neurotransmission over longer time periods.

Please refer this link to understand seizures pathophysiology ***https://youtu.be/YlxGbsDiSRw***

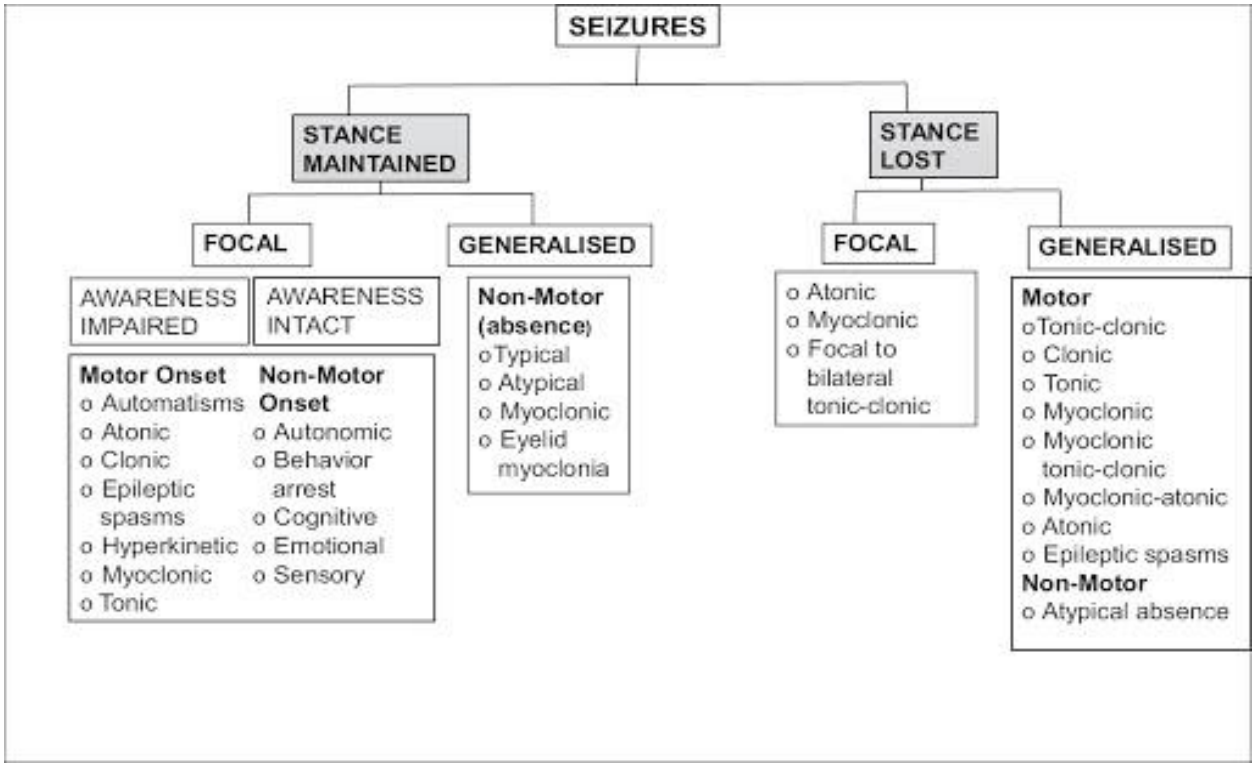
DIAGNOSTIC EVALUATION

History and Examination

The history and neurologic examination are the cornerstones of the diagnosis of seizures and epilepsy, whereas laboratory evaluations serve as adjunctive tests. Important historical features include the clinical context in which the seizure occurred, including premonitory signs, details of the seizure itself, such as phenomenology, responsiveness, focal features, and the **postictal state**. Further inquiry centers on whether an epilepsy syndrome is present, guides the nature and extent of the evaluation, and determines treatment and prognosis.

The neurological examination assesses focal signs that might implicate or localize cerebral pathology. For example, increased tone on one side of the body could indicate pathology in the contralateral hemisphere, such as a cortical dysplasia. The general physical examination is also important to determine whether the patient has an underlying condition. For example, abnormal skin markings could indicate a neurocutaneous disorder in which epilepsy is common, such as tuberous sclerosis or neurofibromatosis.

TYPES OF SEIZURES



CAUSES OF SEIZURES

METABOLIC CAUSES:

1. HYPOGLYCEMIA
2. HYPONETREMIA/HYPERNETREMIA
3. HYPOCALCEMIA/ HYPERCALCEMIA
4. RENAL FAILUERE/ COMPLICATION DURING DIALYSIS
5. HIGH ANION GAP ACIDOSIS
6. THYROID DISORDERS

INFECTIOUS CAUSES:

1. MENENGITIS
2. ENCEPHALITIS

3. SYPHILIS
4. TAXOPLASMOSIS
5. NEUROCYSTICARCOSIS
6. CNS ABSCESS(IN GENERAL)
7. HIV
8. HYPERPYREXIA

DEGENERATIVE CAUSES:

1. ALZHIMERS DISEASES
2. NEUROFIBROMETOSIS
3. TUBEROUS SCLEROSIS
4. MULIPLE SCLEROSIS

DRUGS AND TOXINS:

1. NONCOMPLINCE OF ANTICUONVULSANTS
2. WITHDRAWAL OF SEDATIVES/HYPNOTICS
3. ANTICOLINERGETIC AGENTS
4. SALICYLATES
5. LITHIUM
6. QUINOLONES
7. METHAMPHETAMIES
8. LITHIUM
9. COCAINE

ANATOMIC CAUSES:

1. POST TRAUMATIC
2. CNS NEOPLASMS
3. CNS VASCULITIS(SLE, POLYARTHRITIS)
4. ARTEIO VENOUS MALFORMATION
5. CEREBRO VASCULARACCIDENTS (STROKES)

MISCELLANEOUS:

1. FEBRILE SEZIURES

2. ECLAMPSIA
3. CEREBRAL ARTERIAL GAS EMBOLISM
4. PSEUDOSEIZURES
5. PSYCOLOGICAL DISORDERS

HISTORY TO BE ASKED:

1. PRIOR HISTORY OF SEIZURES?
2. HOW LONG TDID THE SEIZURES LASTS?
3. HOW MANY TIMES?
4. ANY RECENT CHANGE IN YOUR SEIZURE PATTERNS?
5. ANY HISTORY OF MEDICINES/ DRUG INTAKE (OLD ONES, RECENTLY STARTED, LOOK FOR SUICIDAL ACTIVITY)
6. ANY AURA OR PREMONITATION PRIOR THE SYMPTOMS?
7. ASK IF THE PATIENT REMEMBERS WHAT HE WAS DOING WHEN HTHE SEIZURES OCCURRED
8. WAS THERE ANY TOUNGUE BITE/ URINE OR STOOL INCONTINENCE?
9. CONFUSED STATE IMMEDIETLY AFTER THE SEIZURES?
10. LOOK FOR POST ECTAL PARALYSIS(TODD'S PALSY)
11. ALCOHOL HISTORY/ RECREATIONAL DRUGS INTAKE
12. HISTORY OF
    1. ALCOHOLIC LIVER DISEASE
    2. DIABETES MILITUS
    3. HYPERTENSION
    4. THYROID DISORDERS
    5. ISCHEMIC HEART DISEASE/ HISTORY OF MI/ POST CABG
    6. CHILHOOD HISTORY OF SEIZURES
13. POST HISTORY
14. FAMILY HISTORY
15. PREGNANCY

DETAILED EXAMINATION

One should always do complete examination of all the system .

INVESTIGATION

1. Complete blood count
2. Erythrocyte sedimentation rate
3. RBS
4. LFT
5. RFT
6. ELECTROLYTES
7. FASTING BLOOD SUGAR/POST PRANDIAL BLOOD SUGAR
8. CPK
9. CRP
10. URINE PREGNENCY TEST (IF SUSPECTED)
11. CT
12. MRI
13. EMG
14. USG

NOTE:

- An EEG is a recording of the brain's electrical activity. It can detect abnormal electrical activity, such as focal spikes or waves (consistent with focal epilepsy), or diffuse bilateral spike waves (consistent with generalized epilepsy). A routine EEG will, preferably, include wakefulness, drowsiness, and sleep because the prevalence of epileptiform abnormalities varies in these different states of consciousness. Hyperventilation and photic stimulation are activation procedures performed during an EEG to increase the yield of epileptic activity.
- Computed tomography (CT) and magnetic resonance imaging (MRI) scans are important adjuncts to the clinical examination and EEG in the evaluation of a person with seizures. Neuroimaging techniques are especially sensitive for central nervous system (CNS) structural lesions. Focal neurologic findings on examination (e.g., unilateral weakness, asymmetric reflexes) mandate neuroimaging.

- MRI is more likely to show an abnormality in a patient with focal seizures, abnormal neurologic findings, or focal discharges on EEG. MRI is more sensitive than CT and is therefore preferred, especially for the detection of cortical malformation, dysgenesis, or hippocampal sclerosis. Quantitative, computer-assisted volume analysis of the temporal lobes may detect asymmetries that are not readily apparent on visual analysis of the scan. CT is valuable in the acute setting to detect hemorrhage, calcification, or tumors.
- Positron emission tomography (PET) images the brain's regional use of glucose with asymmetries suggesting areas of interictal or ictal abnormality.
- Single-photon emission-computed tomography (SPECT) compares local blood flow discrepancies, information that is most useful when recorded during a seizure.
- Magnetoencephalography (MEG) assesses the brain's dynamic electromagnetic fields and can better localize epileptic dipoles, including those tangential to the scalp, which can be missed by conventional EEG
- These advanced modalities are used mainly in epilepsy centers for presurgical evaluations
- Geetic testing: As the genetic basis of epilepsies becomes progressively unraveled, clinical testing will occupy an increasingly pivotal role in the clinic .At this point, genetic testing is available for several single genes, as well as complex genetic disorders.

MANAGEMENT

The management of patients with epilepsy is focused on three main goals:

1. Controlling seizures
2. Avoiding treatment side effects.
3. Maintaining or restoring quality of life. Clinicians should assist in empowering patients with epilepsy to lead lifestyles consistent with their capabilities

The optimal treatment plan is derived following an accurate diagnosis of the patient's seizure type(s), an objective measure of the intensity and frequency of the seizures, awareness of medication side effects, and an evaluation of disease-related psychosocial problems. A working knowledge of available antiseizure drugs, including their mechanisms of action, pharmacokinetics, drug-drug interactions, and adverse effects, is essential.

Its Doctors decision to begin one seizure medication over another is based on seizure type, age, other medical conditions, and potential side-effect profile. Often, a wide-spectrum medication is used as seizure description by a witness may be lacking. (**Levetiracetam** has become very popular in recent years as first-line therapy because of its efficacy, easy titration, and well-recognized side-effect profile. Previously, **carbamazepine** was the first choice for focal seizures, whereas **valproic acid** was the first choice for generalized seizures.)

As a general principle, medication should be started at a low dose to avoid side effects. Dose increases can be performed at regular intervals if needed. The goal is to control seizures with the lowest dose.

Lifestyle adjustment is a crucial aspect of epilepsy management. Optimizing sleep, improving medication compliance, and reducing stress can significantly improve epilepsy outcome.

Here are some Antiepileptic drugs.

Mechanism	**Antiepileptic drugs**
Block repetitive activation of sodium channels	Phenytoin, carbamazepine, oxcarbazepine, lamotrigine, topiramate
Enhance slow inactivation of sodium channels	Lacosamide, rufinamide

Enhance activity of γ-aminobutyric acid ($GABA_A$) receptors	Phenobarbital, benzodiazepines, clobazam
Block *N*-methyl-D-aspartate (NMDA) receptors	Felbamate
Block α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptors	Perampanel, topiramate
Block T-calcium channels	Ethosuximide, valproate
Block N- and L-calcium channels	Lamotrigine, topiramate, zonisamide, valproate
Modulate H-currents	Gabapentin, lamotrigine
Block unique binding sites	Gabapentin, levetiracetam
Inhibit carbonic anhydrase	Topiramate, zonisamide
Open potassium channels (KCNQ [Kv7])	Retigabine
Inhibit GABA transaminase	Vigabatrin

Inhibit GABA reuptake	Tiagabine

EMERGENCY MANAGEMENT:

1. First line of treatment: Benzodiazepines (CLONAZEPAM, DIAZEPAM, LORAZEPAM, CLOBAZAME) IV/IM

(these enchance GABA medicated inhibition and are effective I 80-90%)

2. Second line of treatment:

- Phenytoin (suppress neuronal activity / recruitment around the seizures focus) but care should be taken since it causes the cardiac arrhythmia and hypotension.
- Phenobarbital (Barbiturate)

DOES: DIAZEPAM ORALLY/ RECTALY- 5-10MG IV EVERY 5-10 MIN

PHENYTOIN IV 1GM IV LOAD AT 50MG./MIN

PHENOBARBITAL 10-20 MG/KG IV AT 60-100 G/MIN

3. IF NO RESPONSE THEN ISOGLURANE INHALATION ANAESTHESIA.
4. AT LAST TREAT THE CAUSE.