Neurological disorders -III

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Epilepsy

Definition

- Epilepsy implies a chronic brain disorder of various etiologies.
- Characterized by recurrent seizures, due to excessive discharge of cerebral neurons
- Associated with a variety of clinical and laboratory manifestations.
- Epilepsy is labeled after the child had two or more unprovoked seizures.

Introduction

- **What is a Seizure?**
- is a transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain.
- **What is Epilepsy?**
- Greek word: seized by forces from Without
- A condition of ***recurrent*** and ***unprovoked*** seizures
    - 2 or more seizures without a clear cause (e.g. alcohol withdrawal or poisoning)
    - "Seizure Disorder" = Epilepsy

- Seizures can be many things – depending on
- **where** in the brain and
- **how much** of the brain is affected
- Seizures can manifest as:
- • *Motor event*
- • *Sensory hallucinations*

  smell, sight, sound, touch, taste)
- • *Autonomic symptoms*

  sweating, incontinence, drop in blood pressure, sluggish pupil reaction, change in heart rate, funny feeling in stomach
- • *Psychic symptoms*

  Intense emotions (fear, panic, impending doom)

  Language or perceptual distortions

Eileen “Peggy” Vining, MD

Johns Hopkins University(USA)

“**Anything** your brain can do normally,
it can do abnormally as a seizure.”

Did you know that:

- Epilepsy is not contagious.
- The tongue **cannot** be swallowed during a seizure.
- Most seizures are **Not** medical emergencies.
- Epilepsy is not a form of mental illness.
- Epilepsy can begin at any age from birth to 99+
- Epilepsy can & does affect memory and learning.
- ***NOTHING*** should be put **in the mouth** of a person having a seizure
- Medication does not stop all seizures .

The International Classification of Epileptic Seizures(2 Large categories):

- Focal
- Generalized

International classification of epileptic seizures

Partial seizures

- Simple partial (retained consciousness)
  - Motor
  - Sensory
  - Autonomic
  - Psychic
- Complex partial (impaired consciousness)
  - Simple partial followed by impaired consciousness
  - Consciousness is impaired at onset.
- Partial seizures with secondary generalization.

International classification of epileptic seizures

Generalized seizures

- Absence (petit mal)
- Tonic-clonic seizures
- Clonic seizures.
- Myoclonic seizures
- Atonic seizures
- Infantile spasms

Unclassified seizures

Types of Epileptic Seizures(ILAE Classification):

Self- limited seizures types

- Focal seizures
- Generalized seizures
- Unknown
- Epileptic spasm

Continues Seizures

- Generalized Status Epilepticus
- Focal Status Epilepticus

Focal Seizures

- **Focal sensory seizures**
  - With elementary sensory symptoms (e.g., occipital and parietal lobe seizures)
  - With experiential sensory symptoms (e.g.,temporoparietooccipital junction seizures)
- **Focal motor seizures**
  - With elementary clonic motor signs
  - With asymmetrical tonic motor seizures (e.g., supplementary motor seizures)
  - With typical (temporal lobe) automatisms (e.g., mesial temporal lobe seizures)
  - With hyperkinetic automatisms
  - With focal negative myoclonus
  - With inhibitory motor seizures

- Gelastic seizures
- Hemiclonic seizures
- Secondarily generalized seizures
- Reflex seizures in focal epilepsy syndromes

Generalized Seizures

- Tonic-clonic seizures (includes variations beginning with a clonic or myoclonic phase)
- Clonic seizures
  - Without tonic features
  - With tonic features
- Typical absence seizures
- Atypical absence seizures
- Absence with special features
  - Eyelid myoclonia
  - Myoclonic absence

- Tonic seizures
- Myoclonic seizures
- Myoclonic atonic seizures
- Negative myoclonus
- Atonic seizures
- Reflex seizures in generalized epilepsy syndromes

Generalized Status Epilepticus

- Generalized tonic-clonic status epilepticus
- Clonic status epilepticus
- Absence status epilepticus
- Tonic status epilepticus
- Myoclonic status epilepticus

Focal Status Epilepticus

- Epilepsia partialis continua of Kojevnikov
- Aura continua
- Limbic status epilepticus (psychomotor status)
- Hemiconvulsive status with hemiparesis

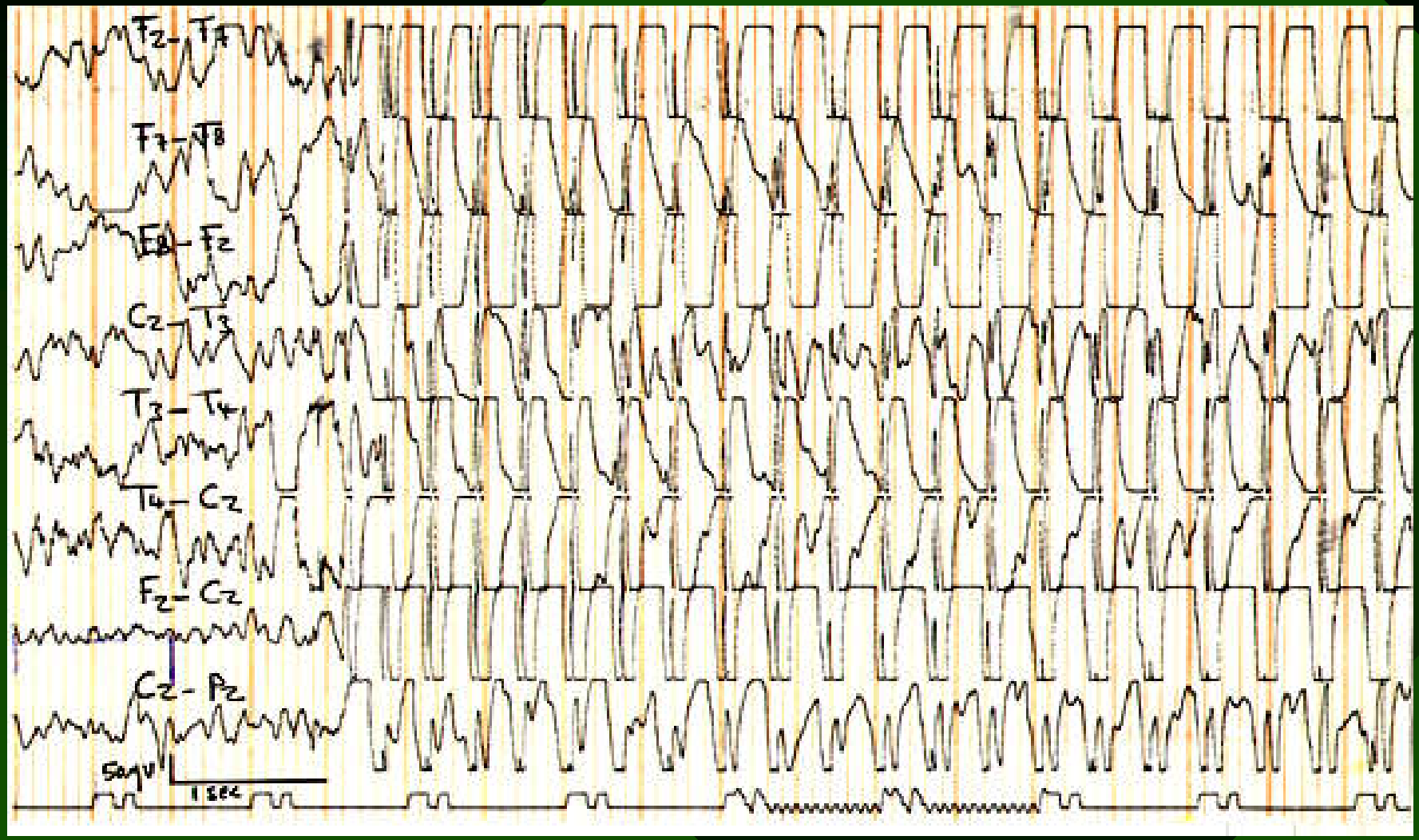
PRECIPITATING STIMULI FOR REFLEX SEIZURES

- **Visual stimuli**
- Flickering light—color to be specified when possible Patterns
  - Other visual stimuli

✓ Thinking
✓ Music
✓ Eating
✓ Praxis
✓ Somatosensory
✓ Proprioceptive
✓ Reading
✓ Hot water
✓ Startle

1-Absence seizures

- The attacks consist of impaired consciousness without falling or involuntary movements.
- The child stops all activities and looks vacant for 5-20 seconds and then continues what he was doing.
- The EEG characteristically shows bursts of generalized 3 per second spike and wave discharges.



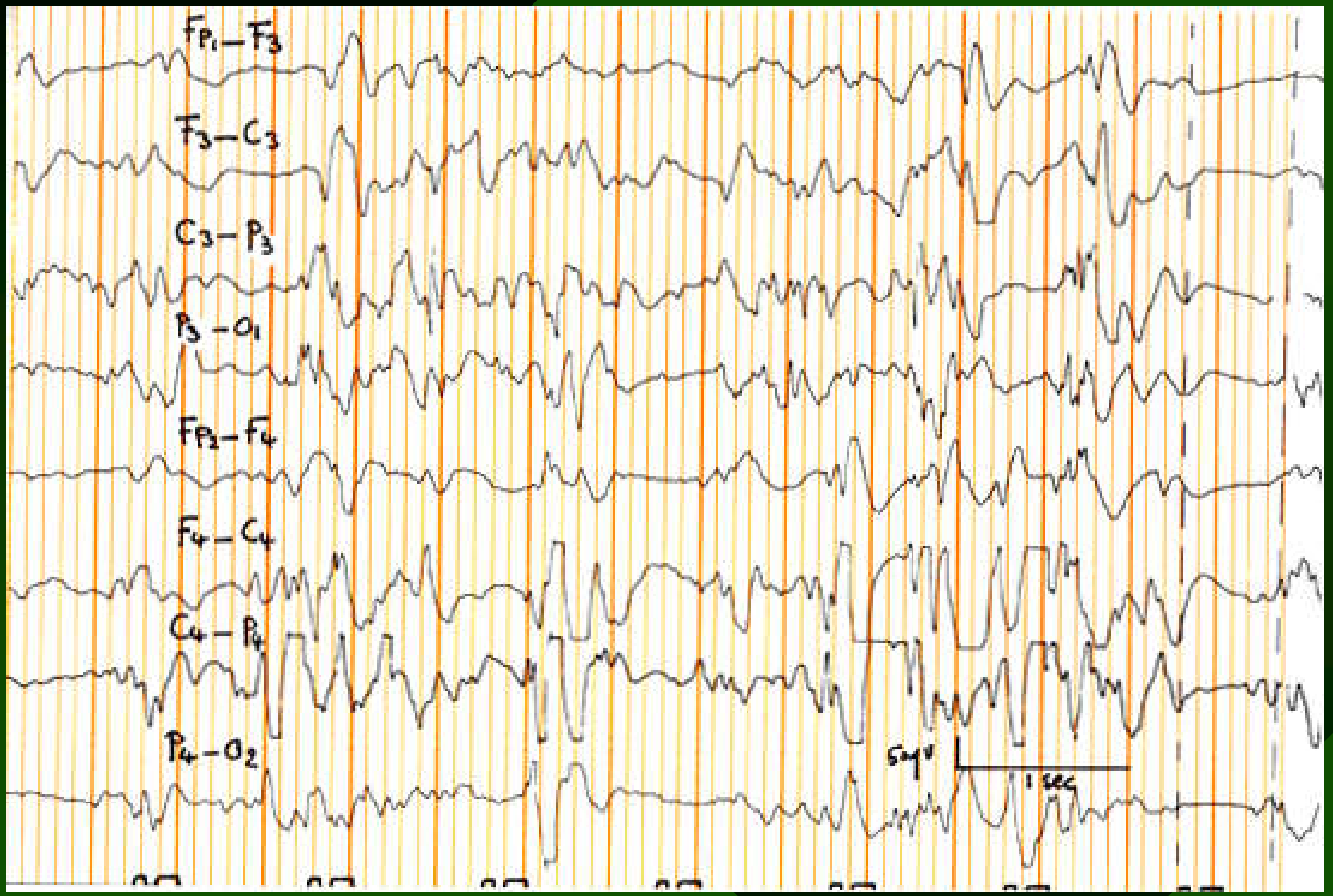
EEG of a 6 years old girl with staring spells showing three per second spike and wave discharges typical of absence

2-Myoclonic seizures

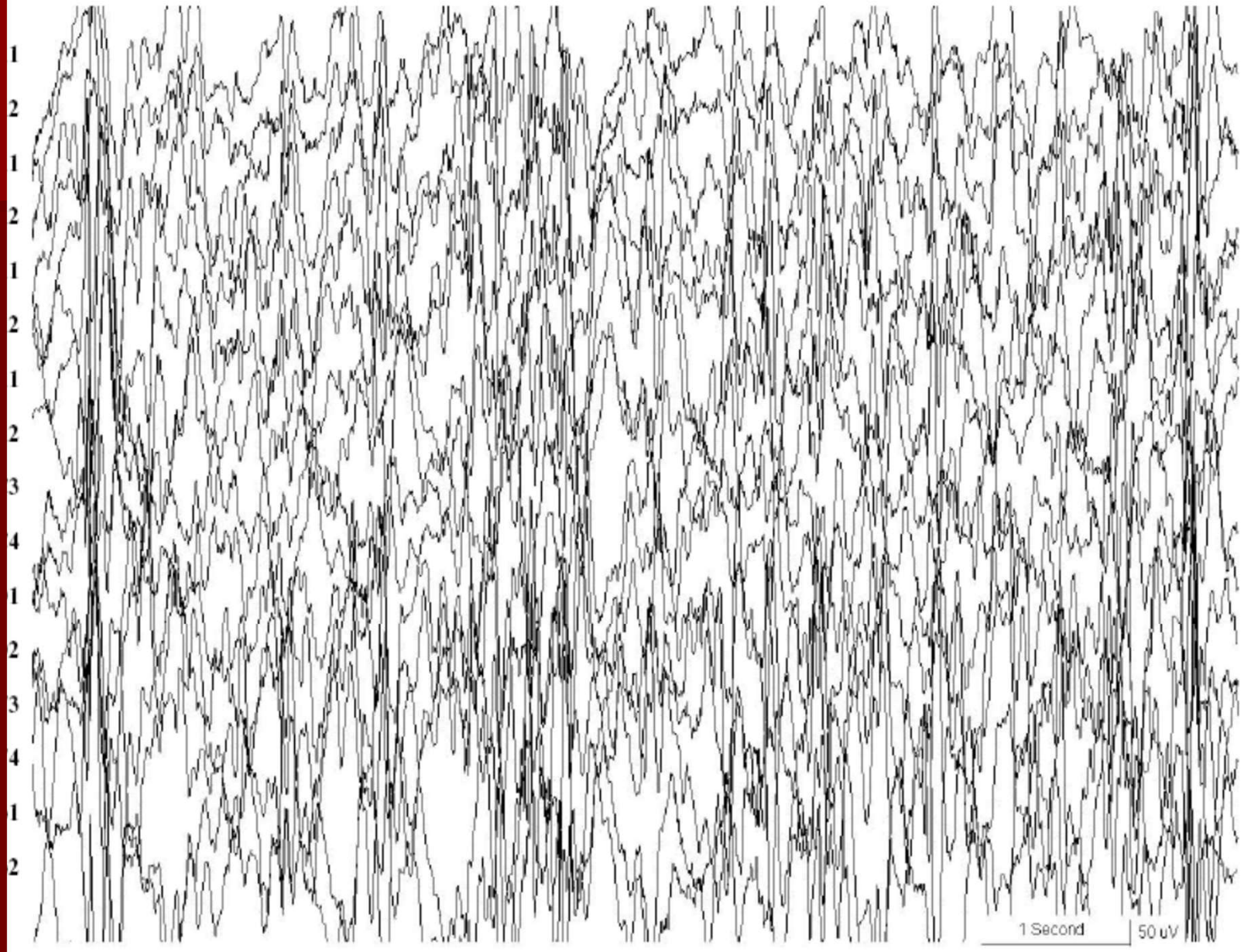
- Take the form of sudden shock-like jerks affecting one part or the whole of the body, usually bilateral and symmetrical.
- They may be flexor or extensor.
- Mild attacks take the form of sudden head drops but severe attacks can lead to throwing the child forwards or backwards and head injury.

3-Infantile spasms

- A kind of myoclonic epilepsy, relatively rare but serious type of epilepsy seen in young children starting between 3-8 months of age.
- The majority of children show typical flexion spasms which may occur several hundred times a day at their most frequent.
- The spasm involves sudden flexion of the neck and limbs and lasts 1-3 seconds only but usually occur in clusters lasting 15-30 minutes.



EEG of an 8 months old baby with infantile spasms shwoing hypsarrhythmic pattern. Note the abnormal background activity containing high amplitude irregular delta waves and multifocal spike discharges. A brief interval of electo-decrement can be seen between the dotted lines.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4-Tonic-clonic seizures

- The attacks start with sudden loss of consciousness, falling and often an initial tonic phase in which the limbs are extended and the back arched.
- This soon gives way to the clonic phase associated with generalized jerking during which micturation and salivation may occur.
- Respiration ceases during the tonic phase but recommences in an irregular fashion during the clonic phase.
- When the clonic phase ceases the child gradually regain consciousness but usually remain sleepy for an hour or so afterwards.

5-Simple partial seizures

- Twisting or jerking of one side of the face, one arm, or one leg.
- Consciousness is usually retained or only slightly impaired and the child doesn't usually fall.
- A simple partial seizure may proceed to generalized tonic-clonic seizures with loss of consciousness, falling and generalized convulsive movements.

6-Complex partial seizures

- Consist of altered or impaired consciousness, usually without falling and associated with strange sensations or complex semipurposeful movements.
- The strange sensations may be visual (objects may look too big, too small or distorted), auditory sounds or voices appeared too loud or two quiet), gustatory, olfactory or emotional.
- Commonly there may be chewing, sucking or swallowing movements.
- The attack commonly lasts few minutes and the child on coming round has little recollection of what has happened.

Assessment

- Careful and detailed history from persons have witnessed the attacks

- General examination with special emphasis on developmental and neurological aspects.

Assessment

- EEG help to decide if doubtful attacks are epileptic or not and give help in deciding the kind of epilepsy present like

  hippsarrythmia in infantile spasms

  cortical spike foci in partial epilepsy

  bilateral spike –wave discharge in primary generalized epilepsy.

- CT or MRI head may be required if structural lesion of the brain is suspected.

Management

A-Anticonvulsant drugs

i-Sodium valproate:

- It is a broad-spectrum anticonvulsant
- indicated, mainly in generalized tonic-clonic seizures, absence and Myoclonic epilepsy.
- The dose is started with 15-20 mg/kg/24 hours
- increased by 10 mg/kg/week till 40mg/kg/24 hours.
- The therapeutic serum level should range from 50 to 100 ug/ml.

i-Sodium valproate:

Side effects include

- mild GIT troubles (anorexia and' vomiting),
- alopecia or curly hair,
- hyperplasia leading to weight gain and tremors.
- Mild elevation of liver transaminases can be found.

ii-Carbamazepine

- This is the drug of choice in partial seizures although it can be used in generalized seizures as an add-on drug.
- The usual dose is 10-30 mg/kg/24 hours. The therapeutic serum level is 8-12 ug/dl. It is the best tolerated anticonvulsant.

Side effects include

- reversible leucopenia,
- dizziness or skin rash.
- Hepatoxicity may occur idiosyncratically.

iii-Phenobarbital

- This is the anticonvulsant of choice in infants in generalized and partial seizures.
- The dose is 3-5 mg/kg/24 hours. The therapeutic serum level is 10-30 ug/dl.

The main side effects include

somnolence

behavioral changes,

decrease cognitive performance

rarely rashes, agranulocytosis or aplastic anemia.

:iv-Phenytoin

- It can be used in generalized tonic-clonic seizures as well as partial seizures
- The dose is 5-8 mg/kg/24 hours. The therapeutic serum level is 10-20 ugldl.

Side effects include

skin rash,

lymphadenopathy,

ataxia

gum hyperplasia,

hirsuitsm,

rickets.

:v-Clonazepam

- It is indicated in myoclonic seizures and infantile spasms.
- The usual dose is 0.05-0.1mg/kgl24 hours.
- The therapeutic serum level is 0.01-0.02 ugl dl.

The main side effects are

- drowsiness, irritability,
- behavioral abnormalities,
- excessive salivation or depression.

vi-Ethosuximide

- It is used in absence and myoclonic seizures.
- The dose is 20 mg/kgl24 hours that can be increased to 40 mg/kgl24 hours.

The main side effects are

- abdominal discomfort,
- skin rash, liver dysfunction
-
- leucopenia.

vii-Diazepam

- It is used in all types of epilepsy especially status epilepticus.
- The dose is 0.3 mg/kg IV or rectally
- The main side effect is respiratory depression.

Recently approved anti epileptic drugs

i-Vigabatrin:

1-Vigabatrin appears to be mainly effective against partial seizures and infantile spasms.

2-The recommended dose is 40-85 mg/kgl24 hours.

3- The most frequent side effects are agitation and insomnia.

4-toxicity to the visual system, include reports of severe, persistent visual field defects

ii-Lamotrigine:

1-It appears to have activity against partial and generalized tonic-clonic seizures in addition to its efficacy against refractory partial seizures.

2-Lamotrigine also has been shown to be useful in the Lennox-Gastaut syndrome juvenile myoclonic epilepsy, and typical and atypical absence seizures.

3-The dose in monotherapy is 7-15 mg/kgl24 hours and in polytherapy with valproate is 1-4 mg/kgl24 hours.

4-The most frequent side effects are agitation, ataxia and drowsiness.

iii-Topiramate

1-It is useful in patients with Lennox-Gastaut syndrome, infantile spasms, and refractory partial seizures

2-The primary adverse effects of topiramate in clinical trials were somnolence, fatigue, abnormal thinking, headache, diplopia, ataxia, speech difficulties, psychomotor slowing, nystagmus, paresthesia

3-The recommended daily dose is 100 mg or 2 mg/kg per day.

iv-Levetiracetam (Keppra)

1-It was used as adjunctive therapy for partial-onset seizures with or without secondary generalization and other uses include juvenile myoclonic epilepsy, absence seizures.

2-The starting dose is 5-10mg/kg per day and increasing every 2 weeks until reaching the maintenance dose in children which is 30-40mg/kg per day as twice daily regime.

3-Side effects at usual doses: include somnolence or fatigue, incoordination, behavioral changes as anxiety, agitation, emotional liability.

v-Oxacarbazepine (Trileptal)

1-Used as monotherapy and adjunctive therapy for patients with partial or partial-onset seizures, primary and secondary generalized tonic –clonic seizures.

2-The starting dose is 5-10 mg/kg/ bid and maintenance dose is 30mg/kg twice a day.

3-Side effects at usual plasma levels or doses: are; dizziness, drowsiness, double vision; fatigue; nausea, vomiting, abdominal pain; ataxia.

vi-ACTH and corticosteroids:

1-They are indicated in infantile spasm, myoclonic epilepsy and symptomatic intractable seizures.

2-The usual dose is 0.5-4 IU/kg/day IM or SC

3-Side effects are hyperglycemia, hypertension, and electrolyte imbalance. Gastritis, immunosuppression, and transient brain shrinkage observed by CT scanning.

Choice of anticonvulsant

- Used after confirmation of epilepsy diagnosis, not used after the first fit in neurologically normal child.

- **Choice of antiepileptic**: depends on seizure classification both clinically and by EEG. Drug treatment that is supposed to be most safe and which may reduce frequency or severity of seizures is the drug of choice.

- **Monotherapy or poly therapy**: initially, monotherapy should be started since this reduces cost, improves compliance and avoids toxicity.

Initiation of therapy

– : medication is prescribed initially in an average dose for age and size. Gradual increase of dosage may be done till complete seizure control or development of undesirable side effects.

Termination of therapy:

– one should not consider a reduction of medication until at least 2 years have elapsed since the last convulsion. This tapering of the dose should be gradual on 3-6 months.

2- Vagal nerve stimulation:

used as adjunct therapy for patients with refractory epilepsy.

3-Ketogenic diet:

in which calories are provided from fat with restriction of protein and carbohydrate intake.

Can be used in refractory seizures.

- The ketogenic diet is believed to be effective in glucose transporter protein 1 deficiency, pyruvate dehydrogenase deficiency, myoclonic–astatic epilepsy, tuberous sclerosis complex, Rett syndrome, severemyoclonic epilepsy of infancy (Dravet syndrome), and infantile spasms. There is also suggestion of possible efficacy in selected

- mitochondrial disorders—glycogenosis type V, Landau-Kleffner syndrome,
- Lafora body disease, and subacute sclerosing panencephalitis.

- The diet is absolutely contraindicated in carnitine deficiency (primary);other carnitine disorders and fatty acida oxidation

4-Surgery:

Indicated in patients with intractable seizures particularly focal ones, unresponsive to anticonvulsant drugs

- Epilepsy surgery is often used to treat refractory epilepsy of a number of etiologies,
- including cortical dysplasia,
- tuberous sclerosis,
- polymicrogyria,
- hypothalamic hamartoma,
- Landau-Kleffner syndrome, and hemispheric syndromes, such as Sturge-Weber syndrome, hemimegalencephaly, and Rasmussen encephalitis

- Focal resection of the epileptogenic zone is the most common procedure.

- Hemispherectomy is used for diffuse hemispheric lesions;
- multiple subpial transection, a surgical technique in which the horizontal connections of the epileptic focus are partially cut without resecting it, is sometimes used for unresectable foci located in eloquent cortex such as in Landau-Kleffnersyndrome. In Lennox-Gastaut syndrome, corpus callosotomy is used for drop attacks

5-Intrvenous Immunoglobulin (IVIG)


Thank you