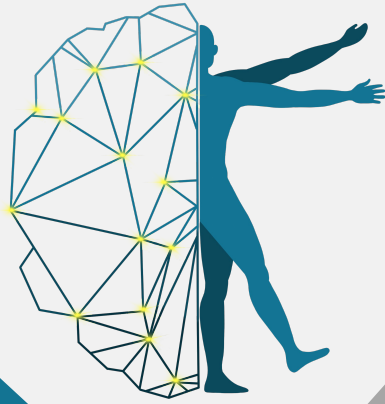
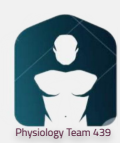


Revised & Approved



Pathophysiology of Epilepsy



Objectives:

- ❖ Define epilepsy
 - ❖ Types of epilepsy
 - ❖ Etiopathology of epilepsy
 - ❖ Manifestations
 - ❖ Role of genetic in epilepsy
 - ❖ Role of Electrophysiological tests in the diagnosis of Epilepsy
-



First Aid in epilepsy

what to do if someone has a seizure?

Summary from Osmosis

Color index:

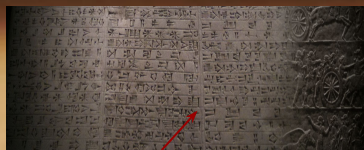
- ❖ Important.
- ❖ Girls slide only.
- ❖ Boys slide only.
- ❖ Dr's note.
- ❖ Extra information.



Editing File

EXTRA

History of epilepsy



The oldest detailed account of epilepsy is on a Babylonian tablet in the British Museum. This is a chapter from a Babylonian textbook of medicine comprising 40 tablets dating as far back as at least 2000 BC. The tablet accurately records many of the different seizure types we recognize today. It emphasizes the supernatural nature of epilepsy, with each seizure type associated with the name of a spirit or god - usually evil. Treatment was, therefore, largely a spiritual matter.

The Babylonian view was the forerunner of the Greek concept (5th century BC) of "The Sacred Disease," as described in the famous treatise of that title by Hippocrates. However, Hippocrates believed that epilepsy was not sacred, but a disorder of the brain - a revolutionary view. He did not believe "that a human could be invaded by a god, the basest by the most pure." He recommended physical treatments and stated that if the disease became chronic, it was incurable.

The word "epilepsy" is derived from the Greek "epilepsia" which means "to take hold of" or "to seize." Hippocrates' view of epilepsy as a brain disorder did not begin to take root until the 18th and 19th centuries.



A seventeenth-century epileptic being restrained by another man is brought before a priest, to be blessed. Epilepsy was long associated with the supernatural and hence the Church.

الصرع في العصر الذهبي للحضارة الإسلامية

ألف ابن سينا (980 م - 1037 م) كتابه "القانون في الطب" وتحدث عن الأعراض والأمراض ومختلف الأدوية المستعملة في وقته، وقد تناول مرض الصرع وقُصّل فيه تفصيلاً وأشار إلى نشوئه من الدماغ حيث قال: "الصرع علة تمنع الأعضاء النفسية عن أفعال الحس والحركة والانتصاب منعاً غير تام وذلك لسدة تقع، وأكثره لتشنج كلي يعرض من أفة تصيب البطن (الجهة) المقدم من الدماغ، فتحدث سدة غير كاملة فيمنع نفوذ قوة الحس والحركة فيه، وفي الأعضاء نفوذاً تاماً من غير انقطاع بالكلية، ويمنع عن التمكن من القيام، ولا يمكن الإنسان أن يبقى معه منتصب القائمة".

وتكلم في كتابه عما يحدث للمصاب قبل النوبة من بوادر الصرع حيث قال "و يتقدمه ضعف في حركة اللسان و أحلام رديئة ونسيان، أو فزع وخوف وجبن، وحديث النفس وضيق الصدر وغضب وحدة".

وقد تحدث ابن سينا أيضاً عن بعض الأسباب التي تقع للمصاب بالصرع فقال "والدفع إنما يتأتى بالانقباض والانعصار، وكل تشنج مادي فإنه ينتفع بالحمى، والصرع تشنج مادي فهو ينتفع بالحمى والأورام إذا ظهرت به (يقصد أنه قد يكون مرتبط بالحمى والأورام فهي تغذيه أو تزيد أو تسببه) والصرع يصيب الصبيان كثيراً بسبب رطوبتهم (وصف الانتشار وهو فعلاً أكثر ما يصيب الصغار اليافعين بينما قد يصيب الكبار prevalence) فربما ظهر بهم أول ما يولدون وقد يكون بعد الترعير".

وأما العالم والطبيب المسلم أبو بكر الرازي (864 م - 923 م) فقد ألف كتابه الكبير "الحواي في الطب" وذكر الصرع مبرراً المنشأ الدماغى له حيث قال "الصرع تشنج" في جميع البدن إلا أنه ليس بدائم لأن علته تنقضي سريعاً وما ينال فيه الأعضاء التي في الرأس مع جميع الجسد من المضرة بدل على أن تولد العلة إنما هي الدماغ".

Definitions

1

Seizure (Convulsion)

- **Clinical manifestation of synchronised electrical discharges of neurons.**
- Seizures are symptoms of a disturbance in brain function, which can be due to epilepsy or other causes.
- A seizure is a sudden surge in electrical activity in the brain that causes an alteration in sensation, behavior, or consciousness. **or motor activity**

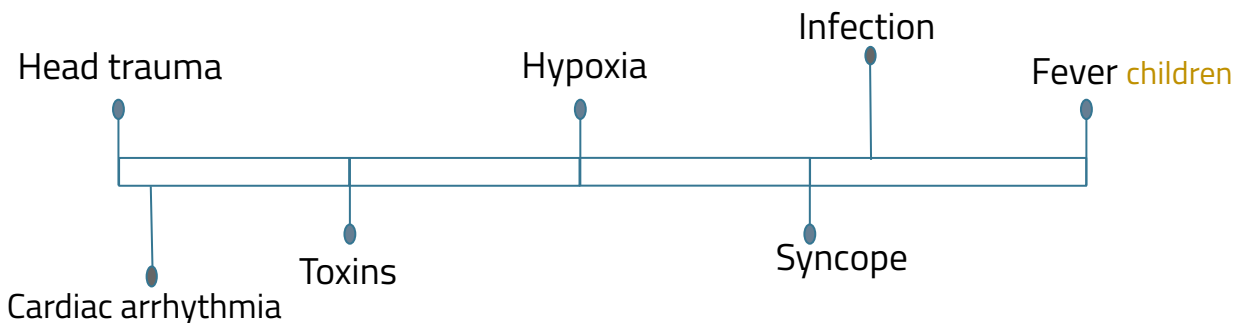
2

Epilepsy

- Present when 2 or more unprovoked seizures occur at an interval greater than 24 hours apart.
- When a person has recurrent (2 or more) **unprovoked** **without a known cause** seizures .
- Seizures is a symptom of epilepsy.

Provoked seizures Girls slide only

induced by somatic disorders originating outside the brain.



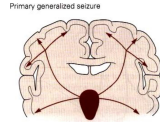
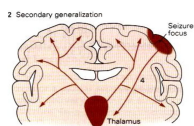
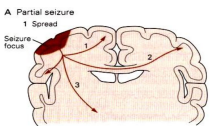
Seizure is a symptom of epilepsy. It could be due to:

- Abnormal electrical activity in the brain.
- Excessive electrical discharge of a group of neurons within the brain.
- A clinical seizure occurs when the electrical discharges of a large number of cells become abnormally linked together, creating a storm of electrical activity in the brain.
- Seizures may then spread to involve adjacent areas of the brain or through established anatomic pathways to other distant areas.
- Decreased threshold level of neurons, meaning that only slightly increased excitement will cause them to have a seizure.
- Increased firing rates in a group of neurons at the same time, unlike healthy brain.
- Abnormality in excitatory neurotransmitter (glutamate) or inhibitory neurotransmitter (GABA) or their receptors.

Classification of seizures

Seizures

Seizures affect all ages, most cases of epilepsy are identified in childhood, and several seizure types are particular to children



1

Partial (focal):
Involves only one part of cerebral hemisphere

2

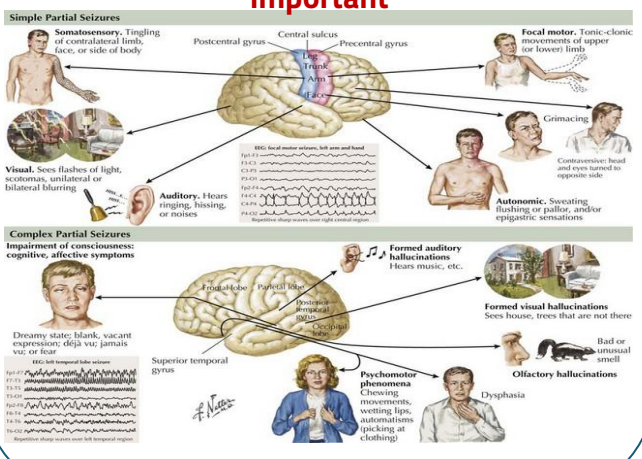
Primary Generalized:
Involves the entire cerebral cortex. (whole of it)

A) Simple:
Awareness is retained

B) Complex:
Altered consciousness **subconsciousness**

C) Partial with secondary generalization:
Seizures may spread to involve adjacent areas of the brain and progress to complex partial seizures, and complex partial seizures can secondarily become generalized.

important



A) Tonic-clonic: Stiffness followed by violent contractions & relaxation (1-2 minute).

B) Tonic: Muscle stiffness

C) Clonic: Spasms of contraction & relaxation

D) Atonic (loss of tone): Patients legs give under him & drop down

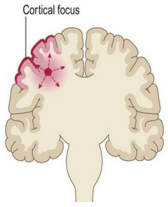
E) Myoclonic: Jerking movement of the body

F) Absence (Petit mal): Brief loss of consciousness with minor muscle twitches and eye blinking

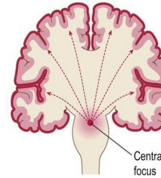
- Typical in typical absence seizures there is a characteristic pattern in EEG, unlike atypical absence seizures
- Atypical

G) Status epilepticus: Recurring tonic-clonic seizure (30 min or more), or two or more seizures within a five-minute period without the person returning to normal between them. "life-threatening condition"

Classification of seizures



partial seizures
(Focal)



Generalized seizures

Type of seizure

Definition

their onset (start) is limited to only one **part of the cerebral hemisphere**
-manifest a +/- of consciousness

those that involve the **entire cerebral cortex** diffusely from the beginning.
-manifest a **loss of consciousness**
-Convulsive or non-convulsive

Subtypes

Simple partial seizures

based on where the focus is

Complex partial seizures

same symptoms as simple partial seizures but with loss of consciousness

Generalized tonic-clonic seizures main type in epilepsy

(Grand Mal epileptic seizure)

Grand Mal Literally "great illness".

Absence seizures

(Petit mal epileptic seizures)

petit mal literally "little illness"

Manifestations

-motor
tonic clonic movements of upper limb or lower limb.
-psychomotor
Chewing movements-Wetting lips
Automatisms (Picking at clothing)
-somatosensory
tingling of one side of face or body
symptoms **without impairment of consciousness**

impairment of consciousness with or without simple partial symptoms
(motor-somatosensory-psycho sensory)

-**Aura(+/-)** It's like a warning sign
peculiar sensation or dizziness; then sudden onset of seizure **with loss of consciousness.**
like an abnormal smell

-**Tonic phase** : مرحلة التصلب
Rigid muscle contraction in which clenched jaw and hands, eyes open with pupils dilated, **lasts 30 to 60 seconds**
in tonic phase there might be an epileptic cry or/and cyanosis due to spasm of respiratory muscles

-**Clonic phase**: مرحلة الانقباض والانبساط
Rhythmic, jerky contraction and relaxation of all muscles in with incontinence and frothing at the lips; may bite tongue or cheek, lasts **several minutes.**
any seizure with biting of the tongue is usually epileptic in origin

-**Postictal state**: مرحلة الراحة والتعافي
Sleeping or dazed for up to **several hours.** depression of CNS

The postictal state is the altered state of consciousness after an epileptic seizure. It usually lasts between 5 and 30 minutes or more

-Loss of contact with environment for 5 to 30 seconds.

-Appears to be day dreaming or may roll eyes, nod head, move hands, or smack lips.

-Resumes activity and is not aware of seizure.
usually affects children and it doesn't involve muscle tone or posture

Very difficult to diagnose

what does it look like?



Boys slide only

Other types of focal (partial) seizure

Partial psychomotor (temporal lobe)

- Epileptic seizures which originate in the temporal lobe of the brain.
- The seizures involve sensory changes, for example smelling an unusual odour that is not there, and disturbance of memory.
- Visual , auditory , olfactory or visceral hallucinations, déjà vu (over familiarity), feelings of unreality (jamais vu)
- The most common cause is mesial temporal sclerosis **deep scarring of the temporal lobe**

ملاحظة مالها فائدة

ديجا فو ؟ ظاهرة الشعور بأن حدث حاضر قد حدث في الماضي من قبل وينص التفاصيل، مثل إجراء محادثة مع شخص فجأة يجيكم شعور أن هذه المحادثة مألوفة (والرود كذلك مألوفة ومتوقعة وكأنكم شاهدتم الموقف في بعد آخر من قبل، وبالفرنسي الكلمة تعني (شاهد من قبل (بينما جامي فو تعاكسها بالمعنى تمامًا حيث يكون المشهد مألوف لكن الشخص لا يتعرف عليه وكأنه لم يره من قبل، وبالفرنسي تعني (لم يشاهد من قبل كان يكون في منزله ثم تأتيه حالة مفاجئة بالغرابة وعدم الإلتناء، يبدو منزله فجأة مكثًا مختلفًا عن ذلك الذي نشأ فيه وكل شيء حوله غير مألوف

Jacksonian epilepsy

- Focal motor seizures begin in motor areas of cerebral cortex, usually begins with twitching of the thumb or finger , toe or the angle of the mouth.
- Spreading to involve the limbs on the side opposite the epileptic focus.
- Clinical evidence of this spread of activity is called the march of the seizure.

Jacksonian March is a phenomenon where a simple partial seizure spreads from the distal part of the limb toward the ipsilateral face (on same side of body).

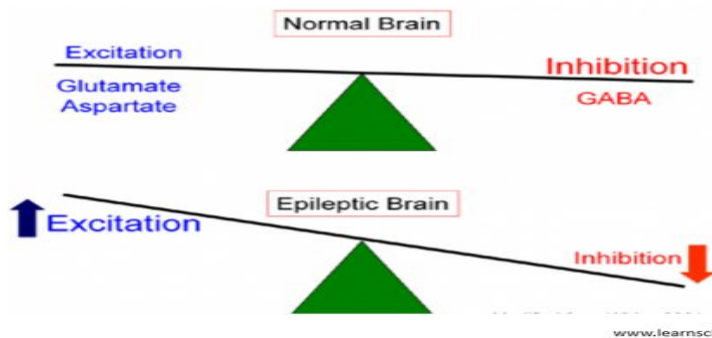
Aetiology of seizures:

Epileptic <i>usually with recurrent seizures</i>	Non-epileptic <i>no tendency for recurrence</i>
Idiopathic (70-80%)	Febrile convulsions <i>usually with children</i>
Cerebral tumour	Metabolic Hypoglycemia, HypoCa, HypoMg, HyperNa, HypoNa
Neurodegenerative disorders (Alzheimer, Multiple sclerosis)	Head trauma
Secondary to cerebral damage: e.g. congenital infections, intraventricular haemorrhage	Meningitis/Encephalitis
Secondary to cerebral dysgenesis malformation: e.g. hydrocephalus	Poisons/toxins <i>like in drug withdrawal</i>

Pathophysiology of Epilepsy (at molecular level)

Cortical cell membrane level:

- 01 Instability of the nerve cell membrane
- 02 Polarization abnormalities (excessive polarization , hypopolarization , or lapses in repolarization)
- 03 Allowing the cell to be more susceptible to activation
- 04 Hypersensitive neurons with lowered thresholds for firing and firing excessively , related to
 - 4.1 **Excess of Excitatory** (acetylcholine- or Glutamate- related activity)
 - 4.2 **Decreased inhibitory** (GABA -related activity)
- 05 Both or any one of 4.1 & 4.2 can lead to instability of cell- membrane & lowered threshold for excitation
- 06 Excessive polarization, hypopolarization allowing the cell to be more susceptible to activation spontaneously or by any ionic imbalances in the immediate chemical environment of neurons



Clinical Features of seizure

- The clinical manifestations of a seizure reflect the area of the brain from which the seizure begins (i.e., seizure focus) and the spread of the electrical discharge.
- Clinical manifestations accompanying a seizure are numerous and varied, including:

1	Indescribable bodily sensations	6	Momentary jerks or head nods
2	"pins and needles" sensations	7	Déjà vu (over familiarity) <small>تذكرون المعنى صح ؟ مأوف ؟ بن هالمرة فعلا شفتوه من قبل</small>
3	Smells or Sounds	8	Staring with loss of awareness like in petit mal seizures
4	Fear or depression	9	Convulsions i.e., involuntary muscle contractions) lasting seconds to minutes.
5	Hallucination auditory or visual		

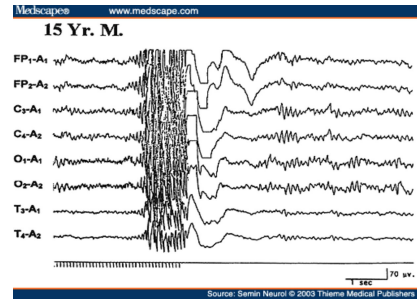
Genetic Factors:

- Some types linked to genes (run in families)
- Genetic abnormalities → increasing a person's susceptibility to seizures that are triggered by an environmental factor
- Several types of epilepsy have now been linked to defective genes for **ion channels** the "gates" that control the flow of ions in to and out of cells and that regulate neuron signaling.
- Genetic factor plays at least 20 %
- Some examples
 - Benign neonatal convulsions--20q and 8q channelopathy affecting K channels
 - Juvenile myoclonic epilepsy--6p
 - Progressive myoclonic epilepsy--21q22.3

Dr's note : we won't ask you about genes or numbers

Electroencephalogram (EEG)

to diagnose epilepsy with EEG it has to be done during the seizure, not before or after



EEG HELPFUL IN: diagnosis, classifying seizures therapeutic decisions.

- In combination with appropriate clinical findings, epileptiform EEG patterns termed spikes or sharp waves strongly support a diagnosis of epilepsy

Focal epileptiform discharges indicate

Focal epilepsy.

Generalized epileptiform indicates

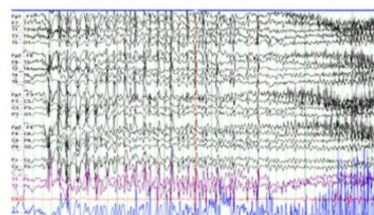
Generalized epilepsy.

- Most EEGs are obtained between seizures, and interictal abnormalities alone can never prove or eliminate a diagnosis of epilepsy
- Epilepsy can be definitely established only by recording a characteristic ictal discharge during a clinical attack.
- 3Hz spike-and-wave (spike and dome pattern) activity occurs specifically in petit mal

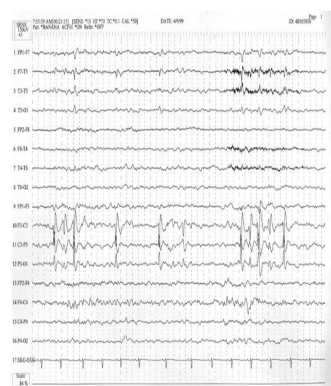
Normal EEG Awake



Generalized Tonic Clonic



EEG: Partial Seizures



Q1: Simple seizures do not include

- A. Motor symptoms
- B. Loss of consciousness
- C. Psychomotor symptoms
- D. Somatosensory symptoms

Q3: Seizures can be triggered by

- A. Head trauma
- B. Intense light
- C. Fever
- D. All the above

Q4: Which epileptic condition involves a postictal depression period lasting from several minutes to perhaps as long as several hours?

- A. Grand mal seizure
- B. Petit mal seizure
- C. Jacksonian seizure
- D. Temporal lobe seizure

Q2: A 27-year-old man with severe epilepsy, characterized by major convulsions and lapses of consciousness every few minutes, underwent experimental neurosurgery to help relieve his seizures. The operation had a significant, beneficial effect on the epilepsy, but led to a devastating memory deficit. He had normal procedural memory, maintained long-term memory for events that occurred prior to surgery, and his short-term memory was intact, but he could not commit new events to long-term memory (loss of declarative memory). Which of the following areas of the brain was bilaterally resected in this patient? **High caliber question ;**

- A. Cerebral cortex
- B. Hypothalamus
- C. Parietal lobe
- D. Temporal lobe

Q5: Non-epileptic seizure can be caused by all of these except:

- A. Hypoglycemia
- B. Hyponatremia
- C. Hyperglycemia
- D. Hypernatremia

Q6: Seizures occur when :

- A. There is a Decrease Glutamate neurotransmitters
- B. There is a Increase in GABA neurotransmitters
- C. Both A&B
- D. Cell membrane have high sensitivity

6: D
5: C
4: A
3: D
2: D
1: B
key:
answer

1- What is the difference between epilepsy and seizure in brief ?

2- Describe the manifestations of grand mal seizure ?

3-List three clinical features can accompany seizures

4- EXPLAIN the pathophysiology of epilepsy in a cellular level.

A1: Slide 4

A2: slide 6

A3: slide 9

A4: slide 8

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