SEIZURE:
- 9% of population and 1/3 people with fever will experience seizures
- Transient occurrence resulting from disturbances in brain electrical activity
  - Results in abnormal and excessive synchronization of cortical neurons
- Clinical manifestations are determined by brain region where the abnormal electrical activity is located
  - Leads to changes in movement, sensation, behavior and/or awareness

SEIZURE INDUCTION BY NON-EPILEPTIC FACTORS:
- Metabolic and electrolyte imbalance
- Stimulant/other proconvulsant intoxication
- Sedative or ethanol withdrawal
- Sleep deprivation
- Antiepileptic medication titration/ pharmacoresistance
- Hormonal variations
- Stress
- Fever or systemic infection
- Concussion and/or closed head injury

SEIZURE IMITATION:

Loss of consciousness (LOC)	• Cardiac (HF, heart attack, arrhythmia) • Hypoglycemia (fasting, excess insulin) • Hypovolemia (dehydration) • Hypoxia (lung disease) • Panic attack (vasovagal response) • Syncope (orthostatic)
Syncope	Decreased delivery of oxygenated blood to brain resulting in LOC • Very common with many etiologies • Sudden and unpredictable • Recurrent • Stereotypic • Premonitory symptoms (nausea, sweating) • "Convulsive"-type movements
Confusion	• Cerebrovascular (TIA, stroke TGA) • Endocrine (hypo/hyper-glycemia, thyroid disease) • Migraine headaches (complicated) • Metabolic (hepatic or renal encephalopathy)
Motoric or behavioral change	• Movement disorders (Tics, Tremors, RLS) • Panic attacks • Sleep Disorders (night terrors/sleep walking, benign myoclonus, sleep apnea)

PSYCHOGENIC NON-EPILEPTIC SEIZURES (PNES)

Description	• Resemble epileptic seizures but lack EEG correlate
	  ○ Presumed diagnosis of intractable epilepsy
	• 25% of pts referred to video-EEG monitoring
	  ○ Difficult to distinguish clinically from epileptic seizures

Characteristics	• Variable responsiveness or preserved awareness • Out of phase movements of extremities • Discontinuous motor activity • Pelvic thrusting • Side-to-side head movements • Eye closure/eye flutter • Varied character of events • Suggestibility • Emotional triggers • Prompt recovery (absence of post-ictal state) • Poor response to AEDs

COMMON STAGES IN SEIZURE:

Prodrome	Changes in behavior, mood, or feelings that may occur hours or days before a sz
Aura	Sx correspond to area of brain having abnormal electrical activity
Ictus	What is seen/felt during abnormal electrical activity
Postictal	What is seen and felt as brain returns to baseline

ILAE SEIZURE CLASSIFICATION:

Partial • Common, begins in certain brain • May begin with aura • Asymmetric or focal motor movements • Alteration of awareness	Simple partial	• AURA • Remain conscious • Have memory of incident • Interact with others
	Complex partial	• Loss of consciousness • No memory • Unable to communicate
	Secondarily generalized	• Spreads to other hemisphere
Generalized: • Less common, involves both hemispheres • Sudden onset with no warning or aura • Symmetrical movements • Loss of consciousness	Absence	• No movements
	Myoclonic	• Rhythmic movements
	Atonic	
	Tonic	
	Tonic-Clonic	• AURA

EPILEPSY:
- Electrical disorder of the brain caused by enduring predisposition to generate spontaneous seizures

PRINCIPAL CAUSES OF EPILEPSY BY AGE:

Infancy and childhood	• Birth injury • Metabolic errors • Congenital malformations
Childhood and adolescents	• Epilepsy of unknown cause (idiopathic genetic epilepsy) • Syndromic epilepsies • Severe infection/high fever
Adolescents and young adults	• Trauma and infection • Drug intoxication/ withdrawal/ overdose
Adult and geriatric	• Stroke, tumor • Metabolic disturbances

EPILEPSY SYNDROMES: group pts that share similar:
- Seizure type(s)
- Age of onset
- Natural history/prognosis
- EEG patterns
- Genetics
- Pathophysiological cause
- Response to treatment

DIAGNOSIS OF EPILEPSY:
1. At least 2 unprovoked (or reflex) seizures occurring more than 24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 y
3. Diagnosis of an epilepsy syndrome

- Detailed hx and physical examination
- EEG, video EEG
- Imaging (CT, MRI, PET)

HISTORY:
- Precipitating factors; aura
- Area of body first involved, progression of activity
- Specific activity observed (head/eye deviation, type of movement or posturing)
- Level of consciousness
- Incontinence
- Apnea or cyanosis
- Duration of seizure
- Postictal sx (confusion, hemiplegia, aphasia)

SEIZURE TRIGGERS:
- Missed dose of medication
- Sleep deprivation, illness
- Stress, anxiety, overstimulation
- Hormonal changes
- Alcohol and drugs of abuse
- Hyperventilation
- Flashing lights
- Temperature extremes
- Dehydration

PSYCHOSOCIAL EFFECTS OF EPILEPSY:
- Stigma of epilepsy
- Compromised quality of life
- Lower self-esteem
- "Vulnerable child"
- High incidence of depression, anxiety, ADHD & learning problems
- Adverse effects of medications
- Parenteral

GENERALIZED SEIZURES:

Absence	• Results in brief period of staring (5-10 seconds) • Patient is usually unaware of his surroundings • Sometimes accompanied by eye blinking or chewing movements • Prompt recovery • Commonly seen in childhood and may be mistaken for day-dreaming	
Myoclonic	• Brief jerk like contractions which can be localized or generalized	
Atonic	• Drop attacks	
Tonic/ Clonic	• Electrically the entire brain is affected all at once	
	AURA	• 50% patients for 5-15 seconds • Sensory: autonomic sx, pain, lights, HA, stereotypical ictal YELL • Followed by loss of consciousness (pt falls)
	TONIC	• Generalized muscle contracture starting in trunk and moving to extremities • Cyanotic apnea is common
	CLONIC	• Muscles relax in synchronous waves in jerking motion • Less violent through time as muscle hypertonia subsidies • Check/tongue biting, sphincter voiding as enter atonic phase
	ATONIA	• Muscle contractions cease and body relaxes
	POSTICTAL	• Coma state lasts from 1-5 mins up to 20-25 mins where patient becomes quiet and breathing resumes

STATUS EPILEPTICUS:

- Prolonged sz state (continuous epileptic activity)
  - Serial seizures without return to normal state of consciousness between seizures (no post-ictal phase)
- Cause
  - Prolonged febrile seizure (most common)
  - Idiopathic status epilepticus
    - Non-compliance to anti-convulsants
    - Sudden withdrawal of anticonvulsants
    - Sleep deprivation
  - Symptomatic status epilepticus
    - Encephalitis, meningitis
    - Encephalopathy, congenital brain malformations
    - Electrolyte disturbances, drug/lead intoxication, extreme hyperpyrexia, brain tumor

ELECTROENCEPHALOGRAPHY (EEG):

- Measurement of voltage fluctuations (charge movement across neuronal membranes) recorded from the scalp that allows visualizations of activity in cerebral cortex
  - Each channel is made up of 2 electrode site pairs – the voltage recorded at one electrode site is subtracted from its neighbour (gives polarity and amplitude of signal)
- EEG measures current flow during afferent synaptic excitation onto dendrites of pyramidal neurons = SUM of excitatory & inhibitory post-synaptic potentials in cerebral cortex x
  - Irregular cellular activation: summed EEG consists of low-amplitude irregular waves
  - Regular & equal activation: large, regular, "synchronized" waves = EEG rhythm
    - EPILEPTIC BRAIN
- EEG waves (Hz = cycles/second)
  - Beta: > 14 Hz Alpha: 8-13 Hz Theta: 4-7 Hz Delta: < 4 Hz
  - Sleep spindles: 7-14 Hz

EEG AND SPREAD OF SEIZURES:

- **Focal (partial seizure):** recorded by electrodes 3, 4
  - **Secondary generalization:** spreads to rest of brain (electrodes 1 and 2 lag behind)
- **Generalized seizure:** begins simultaneously in both hemispheres (bilateral synchronous "spike-wave"

EEG AND SEIZURES:

- EEG is the most important neurophysiological study for the diagnosis, prognosis and treatment of epilepsy
  - **Clinical seizure:** a discharge producing subjective symptoms or objective signs
  - **Electrographic (subclinical) sz:** apparent only on EEG

PATHOPHYSIOLOGY OF EPILEPSY:

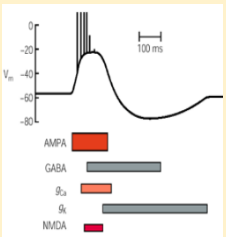
- Epileptogenesis: process where normal brain is biased towards the generation of abnormal electrical activity resulting in chronic seizures
- Epilepsy is due to imbalance:

Increased excitation	• Ionic – inward Na+, Ca++ currents • Neurotransmitter – glutamate, aspartate
Decreased inhibition	• Ionic – inward Cl^-, outward K+ currents • Neurotransmitter – GABA
Changes in ion channels	• Ion channel type, number, and distribution • Post-translational modification of channels (phosphorylation, etc) • Activation of second-messenger systems that affect channel function (ex// G proteins) • Nodulation of gene expression of ion channels
Alteration of ionic concentration	• Changes in extracellular ion concentration • Changes in extracellular space architecture • Modulation of transmitter metabolism • Abnormal uptake by glial cells

EPILEPSY CLASSIFIED BY MECHANISTIC CAUSE:

- Structural-metabolic: a distinct structural or metabolic condition or disease
  - Tumor, trauma, infection
  - Hyponatremia, hypo/hyper K or Mg, hypoglycemia, hyperthyroidism
- Genetic: epilepsy is direct result of a known or inferred genetic defect(s)
  - Does not exclude contributing environmental factors
  - Includes "idiopathic" epilepsies
- Unknown: underlying cause as yet unknown
  - Includes "cryptogenic" epilepsies

PAROXYSMAL DEPOLARIZING SHIFT (PDS):



- Large depolarization triggering a burst of APs
- AMPA and NMDA ligand-gated channel dependent activation is by glutamate (and glycine)
- Depolarization via ionotropic channels activate voltage-dependent Ca^{2+} channels (g_{Ca})
- Cell is then hyperpolarized by activation of GABA receptors (ionotropic Cl channel)
- Afterhyperpolarization by voltage and calcium dependent K+ channels (g_K)

PATHOPHYSIOLOGICAL MECHANISMS OF EPILEPSY:

Normal	Hyperexcitable
• Neuronal firing is regulated by an inhibitory/excitatory synaptic balance • Neurons show regular "spike trains" of action potentials	• Tissue has less synaptic inhibition • Cell becomes more excitable • Increased response to excitatory inputs • Firing rate increases • Shows "BURSTS" of high-frequency spike patterns

SEIZURE PROPAGATION:

1. GABAnergic interneuron inhibition breaks down
2. Focal neurons become synchronous
3. Action potential trains sent to distant neurons
4. Distant neurons propagate seizure activity

PDS IN TONIC-CLONIC GENERALIZED SEIZURE: *no questions*

Tonic phase	Clonic phase
1. Focal neurons depolarize & enter PDS (lasts secs – mins) 2. GABA inhibition fails 3. AMPA/NMDA activity enhanced	4. GABA inhibition gradually returns 5. Focal neurons enter oscillation phase

SPECTRUM OF SEVERITY: