- Seizure: abnormal electrical discharge in the brain
- Etiology
    - Idiopathic aka Unprovoked aka Cryptogenic (called epilepsy if also recurrent)
    - Symptomatic
        - Extrinsic
            - Medications
                - Intoxications: uppers, carbapenems, lidocaine, theophylline, penicillins, cipro, isoniazid, meperidine, tricyclics
                - Withdrawal: downers, opiates, AED noncompliance
            - Metabolic
                - Hypo/Hypernatremia
                - Hypoglycemia
                - Hypocalcemia
                - Uremic Encephalopathy
                - Hepatic Encephalopathy
                - Thyrotoxicosis
                - Eclampsia
            - Trauma (phenytoin reduces short r/o seizures but no proven to decrease long term risk therefore only given prophylactically acutely after trauma)
            - High Fever
            - Sleep Deprivation
        - Intrinsic
            - CNS Mass (primary and mets)
            - CNS Infections (meningitis and encephalitis)
            - CNS Vascular (hemorrhage and infarcts)
            - CNS Increased ICP
        - Pediatric Syndromes (refer to Peds notes)
        - DDx
            - Syncope: a large percentage of syncopes have auras (but usually different S/S like diaphoresism, nausea, etc), convulsions (but usually lasting <30sec), incontinence, tongue biting, etc but NO post-ictal period,
            - Psychogenic Seizure & Conversion Disorder (suggestive if female w/ h/o abuse/depression, head turns side-to-side not just one side… "no, no, no I am NOT having a seizure", eyes clinched shut, torso extension, large amplitude low frequency movements not small amplitude high frequency movements, diffuse movements but no LOC, lasts longer than 5min, follow an emotional/stressful event)
            - Parasomnias
            - Hyperventilation
            - Movement Disorders
            - Migraines

Approach (important to note that many times seizures can be very unimpressive aka subtle eye/fingertip movements or just even alteration of consciousness can be a seizure thus do not assume that a pt is not seizing b/c of lack of tonic-clonic movements)

- Assess RFs above
- Pre-Ictal: precipitating factors, prodrome
- Ictal: aura (visual, auditory, olfactory, tactile), consciousness, motor (w/ or w/o Jacksonian March, head/eye deviation) , focality (localized, starts in one part of body and generalizes, generalized), tongue/cheek/lip bites, urinary/bowel incontinence, duration
- Post-Ictal: duration/degree of consciousness, aphasia, amnesia, Todd paralysis (always r/o CVA w/ CT/MRI)
- Labs: BMP, Ca, Phos, Mg, CBC, LFTs, UTox, AED levels, Lactic Acid, Hemoglobinuria/emia
- PEx: tongue bite, head trauma, other trauma from fall, neuroectodermal changes
- MRI (if emergent then resort to CT)
- LP (rarely indicated unless suspecting infection, hemorrhage, or inflammation)
- ECG
- EEG
    - Classic Finding: Spike & Slow Wave Complex which occurs not during the seizure but interictal and represents abnormal hyperactive neurons
    - Method: awake and asleep, w/o activation and w/ activation (hyperventilation, sleep deprivation, photic stimulation) b/c increases yield
    - Nl EEG does not rule in/out seizures and 10% of the population has focal findings but no seizures
    - CCTV-EEG (closed circuit television) to accurately characterize seizure
    - Do a 24hr EEG to rule out sub-clinical seizures in ICU pts that are not waking up when off sedation and no evidence of permanent brain damage

Epileptic Classification

<table>
<tr><td colspan="2">Partial
Activity in one region w/ variable degree of spread based on EEG not necessarily clinical findings aside from no complete LOC but consciousness can be affected</td><td>Generalized
Consciousness Lost b/c the entire brain is affected resulting in complete amnesia and LOC</td></tr>
<tr><td>Simple
Consciousness Preserved b/c only a small part of hemisphere is affected such that they do NOT have amnesia (Ask pt a word during the seizure s/he remembers it)
Depending on location can be motor, sensory, autonomic (flushing, pallor, sweating, etc) or psychic (déjà vu, illusions, hallucinations, etc)
Weird sensory, autonomic, psychic manifestations are usually localized to temporal lobe and are often explored as pysch problems
If motor then always note w/ or w/o “Jacksonian March” (activity starts at one spot and then spreads)</td><td>Complex
Consciousness Impaired b/c a large part of one hemisphere is affected such that they have amnesia but NO true LOC
For some reason usually temporal lobe resulting in hallucinations
Can begin complex or begin simple and progress to complex
Pt often performs “automatisms” repetitive movements like lip smacking, chewing, etc</td><td rowspan="2">Tonic-Clonic (Grand Mal)
Tonic Phase (increase in tone of entire body with everything in extension and rigid, jaw clinches and bites tongue, diaphragm contract resulting in “ictal cry”, apnea, cyanosis)
Clonic Phase (follows clonic phase, muscles contract and relax rhythmically, breathing appears labored, at end pt becomes flaccid)
EEG: 10Hz (tonic) Slow Waves (clonic)
There can also be just tonic, clonic, myoclonic (millisecond brief such that pt does not even know s/he had LOC) or atonic</td></tr>
<tr><td colspan="2">Secondarily Generalized
either simple or complex can secondarily generalize
typically tonic-clonic</td></tr>
</table>

Prognosis

- Cannot drive in Texas for 6mo (1yr for syncope) even if on AED thereafter can drive if seizure free
- following one epileptic seizure the risk of recurrence is 10% if not localizing and not SE to 75% if localizing or SE with second seizure w/in 1st yr
- increased risk: abnl EEG and initially focal/partial seizure
- no increased risk: age, gender, duration, number of seizures in first day
- questionable increased risk: abnl neuro exam, +FHx

Treatment w/ Anti Epileptic Drugs (AEDs)

- Partial w/ or w/o Secondary Generalization: all are effective except ethosuximide VS Generalized: all are effective for tonic/clonic but valproic acid (Depakote), topiramta (Topamax), lamotrigine (Lamictal), levetiracetem (Keppra) work better, NB there are certain ones that are better/worse for other types of generalized seizures
- If 1st seizure and no alarming Sx (status, underlying neuro dz, abnl EEG, >65yo, Todd’s paralysis, FHx) then NO Tx as recurrence is 35%, if second start Tx b/c recurrence is 60%
- No driving for 3-12mo
- check AED levels (Free Dilantin, Tegretol, Keppra)
- decision to initiate AED after first seizure is based on risk for future seizures (higher if idiopathic or structural abnormality) and risk of side effects from AED, in general only 25-40% of pts will have recurrence in 2yrs depending on the number of RFs
- most common kind of drug to cause SJS/TEN
- choice based on seizure type, SEs, women pt, comorbidities drug interactions
- Mechanisms: block Na channels, block Ca channels, increase GABA, decrease glutamate
- after pt has been seizure free for >2yrs AED withdrawal can be contemplated w/ recurrence of seizures in about 25%, obtain an EEG prior to withdrawal to ensure no subclinical activity, TAPER do not stop abruptly
- >1 complex partial seizure per mo or >1 generalized seizure per yr is poor seizure control
- most AEDs decrease folate therefore all childbearing epileptics should take supplemental folate while taking AEDs regardless if they are trying to get pregnant or not (why important b/c AEDs actually induce P450 which in turn reduces OCP effectiveness), the general risk of congenital birth defects is 3% and this increases to 5% with all AEDs except Depakote which is 15% thus the recommendation is that use AEDs (except Depakote) in pregnant pts b/c the risk of seizure to the baby is more significant than the 2% increase risk of congenital defects
- 65% of pts become seizure free w/ first agent, only 15% more become seizure free when a second different agent is added, only 5% more become seizure free when a third different agent is added, (NB also consider if you are using the right AED for the seizure type, most pts hat being on three AEDs b/c $ and they feel like zombies and would rather have a seizure than be a zombie), therefore after three trials you will have 30% of pts not seizure free and these pts should be referred for surgical consultation for anterior temporal lobectomy / localized neocortical resection or if not surgical candidate then vagal nerve stimulation (partial seizures are more likely to be medically refractory than generalized seizures)
- Some also try ketotic high fat diet
- Pts rarely need two AED

- Loss of bone mineral density is especially common therefore when you start AED also start Ca/VitD and check DEXA in future

valproic acid (Depakote)
- best of all of them
- SEs: hepatitis, aplastic anemia, pancreatitis, polycystic ovarian syndrome, hair loss, thrombocytopenia, N/V, general CNS depression, weight gain

lamotrigine (Lamictal)
- less effective
- SEs: dizziness, sedation, HA, diplopia, ataxia, SJS

topirimate (Topamax)
- as effective as valproic acid but more SEs

carbamazepine (Tegretol)
- For Asian pts it is recommended that they undergo genetic testing, if +HLA-B*1502 then they have a 5% r/o SJS/TEN
- Agranulocytosis, aplastic anemia, pancreatitis, hepatitis, ataxia, confusion, many drug interactions

phenytoin (Dilantin) fosphenytoin (Cerebyx)
- Mechanism
    i. prolongs Na+ channel inactivation such that neurons cannot evoke another AP as quickly therefore slows the brain down preventing seizures
    ii. inhibits adenosine uptake which appears to be an endogenous anticonvulsant properties
- Important Pharmacokinetics
    i. variation in protein-binding capacity accounts for variance seen in relationship between serum concentration and clinical intoxication
    ii. metabolism: liver conjugation
    iii. excretion: t1/2 of ~1d, bile and urine, at level >10mg/dL excretion become zero order 2/2 conjugation saturation
- Common Sequelae/SEs
    i. cognitive slowing
    ii. alters collagen metabolism resulting in gingival hyperplasia
    iii. various endocrine problems: impaired insulin, impaired ADH, impaired TH, impaired sex hormone secretion
    iv. interference with VitB12 absorption resulting in megaloblastic anemia
    v. coarsening of facial features
    vi. teratogenicity
- Difference b/t Phenytoin and Phosphenytoin
    i. CV depression 2/2 to the preparation (propylene glycol) needed to dilute phenytoin does not exist in phosphenytoin
    ii. Phosphenytoin infuses faster then phenytoin b/c thinner and thus better for status epilepticus
    iii. Phosphenytoin can be administered in dextrose-containing solution unlike phenytoin which precipitates
    iv. Phosphenytoin tissue extravasation does not cause tissue necrosis b/c not as alkaline as phenytoin
    v. Phosphenytoin can also be administered IM
- Anticonvulsant Hypersensitivity Syndrome
    i. idiosyncratic reaction phenytoin/phosphenytoin
    ii. Triad: F, rash, LAD along w/ elevated LFTS and lymphocytosis
    iii. Tx: immediate withdrawal
- Toxicity Sx (Normal is 10-20 mg/dL)
    i. 20-30 mg/dL
        1. horizontal nystagmus
        2. mild ophthalmoplegia
        3. sedation
    ii. 30-50 mg/dL
        1. vertical nystagmus
        2. diplopia
        3. ataxia
        4. coarse tremor, opisthotonic posturing (which could explain his fists)
        5. dysarthria
        6. hyperrelfexia (not seen)
        7. AMS
    iii. >50 mg/dL
        1. death (our pt was about 60)
    iv. Toxicity Management
        1. MDAC only in the acute setting
        2. No Antidote
        3. No Benefit from Hemodialysis/Hemoperfusion
        4. Just follow the pt's neurologic exam

Status Epilepticus

- >30min or >2 sequential seizures without full recovery of consciousness between seizures
    - it is absurd to adhere to the 30min rule in clinical practice to make a diagnosis of SE before starting treatment, treatment should be begin when any seizure lasts >2min or the pt has not regained consciousness within 5min
- although any seizure type even non-convulsive can present as status epilepticus generalized tonic-clonic is most common and most important b/c of complications
    - HTN, lactic acidosis, hyperthermia, respiratory compromise, pulmonary aspiration, rhabdomyalysis, self injury, irreversible neurologic damage after 60min of seizuring
- Medical emergency w/ 20% mortality (increasing to 50% if you have to resort to barbiturate coma)
- Treatment

(1) ABCs
(2) Place pt in lateral decubitus position to prevent aspiration, bed rails up, remove sharp dangerous near pt, loosen tight clothing
(3) Vitals Signs Q2min, ECG, iSTAT, 2 Large Bore IVs (BMP, Ca, Phos, Mg, CBC, UTox, EtOH, AED levels), ABG, D-Stick
(4) "DON'T" Therapy
    a. Thiamine 100mg x1
    b. 50% Glucose 50mL push
    c. Naloxone
(5) Neuro Consult
(6) If persists past 5min (70% respond) BENZO

1° Lorezapam (Ativan) 0.1mg/kg @ 2mg/min IV slower onset (3min) but lasts longer (12-24hrs) 2° Diazepam (Valium) 0.15mg/kg @ 5mg/min IV/PR faster onset (2min) but lasts shorter (5-30min) therefore watch for recurrence If fail then repeat If fail again move on to next step

(7) If persists past 10min (80% respond) AED

1° Fosphenytoin (Cerebyx) 20mg/kg PE @ <150 mg/min IV 2° Phenytoin (Dilantin) 20mg/kg @ <50 mg/min IV b/c has to be prepared in alkaline solution = thrombophlebitis If fail then repeat w/ 5mg/kg If fail again then repeat w/ 5mg/kg If fail again move on to next step

(8) If persists past 30min (controversial) COMA

*** the combination above benzos + below barbs requires intubation *** Phenobarbital 20mg/kg @ 50mg/min IV Propofol 3-5mg/kg load then1-5mg/kg/hr IV Midazolam 0.2mg/kg load then 0.05-2mg/kg/hr IV/IM Pentobarbital 5-15mg/kg load then 0.5-10mg/kg/hr IV

(9) Once controlled continue Phenytoin 4-7mg/kg/d