Neurology

**Acute stroke syndromes**

* General information:
	+ Strokes/CVA are 3rd MCC of death in USA (MCC of neurological disability)
	+ Differential DDx of stroke:
		- ***Ischemic stroke (85%)***
			* **Thrombotic** (atherosclerosis)
* Large vessel or small vessel
	+ - * **Embolic:**
* Cardiogenic (AF, post-MI, valvular)
* Artery (Aorta, CAROTID artery)
* Air, fat, PARADOXICAL
	+ - * **Global** ischemia:
* MI, VT, HF, hypotension/sepsis
	+ - * Other **intrinsic vessel disease**:
* Vasculitis
* Vasospasm
* Compression
* Dissection
* Hypercoagulable states (thrombophilias, SCD, polycythemia, homocystinuria, etc.)
	+ - ***Hemorrhagic stroke (15%)***
			* **ICH**
* **HTN** (bouchard microaneurysms)
* Trauma
* Others (**Amyloid angiopathy**, **AVM**, **bleeding diasthesis**)
	+ - * **SAH**
* **Trauma**
* **Berry aneurysm** rupture
* **AVM**
* Others (amyloid angiopathy, bleeding diasthasis)
	+ - **Venous sinus thrombosis**
		- **Stroke mimics** (DIMS)
			* Drug intoxication
			* Infections (mycotic aneurysms)
			* Metabolic (hypoglycemia, renal failure, MELAS, hepatic encephalopathy)
			* Migraines
			* Seizures
			* Structural (tumors, subdural hematoma)
	+ About the causes:
		- **Large vessel stroke**
			* MC due to atherosclerosis and overlying thrombosis (like in ACS)
			* Typically occurs in at the **bifurcation of the common carotid artery** (but also middle cerebral artery stem, origin of the vertebral arteries or in the basilar artery)
		- **Small vessel stroke**
			* Occur in the **penetrating arteries** (capsular branches) of the anterior, middle and posterior cerebral and basilar arteries
				+ **Lenticulostriate** branch of the **MCA** = MC site (“**Artery of catastrophe**”)
			* Can result in **lacunar stroke**:
				+ Thickened small vessel wall that gets blocked
				+ **HTN is a very important risk factor**
				+ ****Locations: basal ganglia, thalamus, internal capsule, pons
		- **Cardiac sources of emboli:**
			* LA (atrial fibrillation, CHF, valvular disease)
			* LV (post-MI true aneurysm)
			* Valvular diseases (endocarditis) or mechanical valves
		- Hypotension (global ischemia):
			* Sudden drop in BP by >40 mm Hg can result in stroke in the boundary zones (**watershed stroke**)
	+ **Risk factors:**
		- **AGE** = **independent risk factor** of **thrombotic** stroke (e.g. those with TIAs)
		- Common to most causes:
			* **Smoking**
			* **DM**
			* **Dyslipidemia**
			* **HTN**
			* **Family history**
		- Thrombotic:
			* HISTORY OF **TRANSIENT ISCHEMIC ATTACKS (TIA)**
		- Embolic:
			* History of **heart disease** (valvular, AF, endocarditis, recent MI)
		- Hemorrhagic:
			* HTN, trauma, bleeding diasthesis, AVM, blacks, Asians

* **Transient Ischemic Attacks (TIAs)**
	+ Definition = **transient neurological deficit** lasting **<24 hours** (by rule), but most commonly **lasts <1 hour** (in actuality <30 minutes, < 15 minute)
		- Reperfusion occurs either because of collateral circulation or breaking up of the embolus – so there is not enough time for permanent damage to occur (ischemia NOT infarction)
	+ **Risk of stroke following an TIA is high**
	+ Causes:
		- Embolic (MC) from a atherosclerotic source (e.g. the carotid artery)
	+ DDx:
		- Hyperviscosity syndromes, vasculitis (true TIAs can result)
		- Hypoglycemia, MS, migraine aura, focal epilepsy
	+ Risk factors:
		- **AGE** (independent risk factor) and HTN
		- Smoking, hyperlipidemia, CAD, DM, AF, previous TIA/Stroke, family history
	+ **Presentations:**
		- **Carotid system** 🡪 **amaurosis fugax** (loss of vision in a **drop down CURTAIN pattern**), loss of speech, **paresis** on contralateral limb
		- **Vertebrobasilar system** 🡪 **double vision**, vertigo, **facial numbness, dysarthria**, vomiting, dysphagia, **drop attacks**, headache, ataxia
		- Signs: **CAROTID BRUIT**, high BP, heart murmur, AF, etc.
	+ **Scoring: What to do with a patient who had a TIA?**
		- **ABCD2 Score**:
			* **A** = Age (>60) – 1 point
			* **B** = Blood pressure (>140/90) – 1 point
			* **C** = Clinical features (**unilateral weakness** – **2 points** OR speech disturbance only – 1 point)
			* **D** = DM (1 point)
			* **D** = Duration of symptoms (**>1 hour – 2 points** OR < 1 hour – 1 point)
		- **Interpretation:**
			* **Low risk (0 – 3)** ~ **outpatient ok** (unless has new AF)
			* **Moderate risk (4 – 5)** ~ **inpatient** observation
			* **High risk (6 or more)** ~ **inpatient**, investigate immediately/**within 24 hours** (risk of stroke in 2 days is about 8%)
		- What steps will you take to prevent stroke in TIA patient?
			* CXR, **ECG, echo, carotid Doppler**
			* **Control risk factors** (**cautiously lower BP** [aim <140/85], DM, hyperlipidemia)
			* **Antiplatelet drugs** (**clopidogrel/Plavix** > aspirin)
			* Anticoagulants only if needs it (e.g. AF, valvular disease)
			* If **carotid stenosis >70%** and **symptomatic** 🡪 carotid **endartectomy** (other options include **endovascular stenting**, which has ADR)
* Entities/terms to be aware of:
	+ **Stroke in evolution:**
		- Unlike TIA, stroke in evolution refers to **worsening of S&S after 24 hours**
	+ **Subclavian steal syndrome**:
		- Stenosis of the subclavian artery before the origin of the vertebral artery results in a backflow of blood from the vertebral artery to fill the vessels distal to the stenosis – reduced cerebral blood flow results
		- Signs: lower BP and pulse in the affected arm + claudications
* **Clinical features of strokes:**
	+ Based on which artery involved (remember the homunculus and territories of the cerebral vessels):
		- **Anterior cerebral artery:**
			* Branch of ICA; capsular branch is recurrent artery of Heubner
			* **Lower limb motor** **and sensory deficits**
			* **Frontal release signs** (primitive reflexes such as grasp, snout, rooting and suckling reflex returns)
			* **Gait apraxia**
			* **Personality changes**
		- **Middle cerebral artery:**
			* Most people are left hemisphere dominant (even most left handed people)
			* **Aphasia** (Broca or Wernicke or global)
			* **Contralateral hemiparesis** (and **suprabulbar**) and **sensory loss** (for all, **UL, face > LL**)
			* Right parietal lobe 🡪 left hemispatial neglect
			* Left parietal/temporal lobe 🡪 **left homonymous hemianopia** (but if Meyer’s loop in temporal lobe is involved, then upper/superior quadrant part)
			* **Impaired conjugate gaze** (FEF; ipsilateral deviation)
		- **Deep (subcortical/lacunar):**
			* **Pure motor** stroke (**internal capsule**)
			* **Pure sensory** stroke (**thalamus**)
			* **Ataxic hemiparesis**
			* **Clumsy hand dysarthria**
			* NO abnormalities in cognition, language or vision (unless specific areas involved)
		- **Posterior cerebral artery:**
			* Capsular branch is thalamogeniculate artery (supplies thalamus)
			* Homonymous hemianopia with macular sparing
			* Visual hallucinations or perservations
			* **Thalamic pain syndrome** (hyperaesthesia/spontaneous pain)
		- **Vertebrobasilar involvement** (brainstem involvement):
			* Motor and sensory loss in all 4 limbs (locked in syndrome)
			* Crossed signs
			* Ataxia, dysarthria, dysphagia
			* Syndromes based on involved vessels (PICA, AICA, SCA, pontine arteries)
* Weber syndrome (medial midbrain; PCA or basilar perforating branches)
* Benedikt syndrome (midbrain tegmentum)
* Medial pontine syndrome (Foville) and lateral pontine syndrome (Millard-Gubler)
* Lateral medullary syndrome (Wallenburg syndrome [PICA/ASA]) or medial medullary syndrome
* Based on type of stroke:

|  |  |  |  |
| --- | --- | --- | --- |
| Feature | Thrombosis | Embolism | Hemorrhage |
| Age | Old age | Any age | Commonly old age |
| Onset | **Rapid (hours)** | **Sudden (seconds)** | **Abrupt/dramatic** |
| Prodomata | TIA | Absent | Absent |
| Vomiting | Absent  | Absent | **Common** |
| Consciousness | Usually preserved | Usually preserved | **Lost with coma** |
| Convulsions | May occur | May occur | **Frequently**  |
| Pupils | Normal, equal | Normal, equal | **Dilated, irreactive** |
| Fever | Absent  | Absent  | May be present |
| BP | May be high | Normal  | Usually high |
| Heart | CAD | Valvular lesion, AF | LVH |
| CSF | - | - | **Xanthochromia**High RBCs |
| CT scan/MRI | Hypodense(better with MRI) | Hypodense (better with MRI) | **Hyperdense** (white) |

* **Thrombotic stroke**:
	+ Patient classically wakes up from sleep with neurological deficits (tells you about its progressive nature)
* **Embolic stroke:**
	+ Very rapid (within seconds), deficits occurring maximally initially
* Hemorrhagic (see later)
* **Management of stroke:**
	+ **A, B, C and in patient care**
		- Check airways, protect airways, O2, IV fluids
		- Put them on NPO in the mean time
		- RAISE THE HEAD OF THE BED (prevent aspiration, etc.)
		- Sliding scale if DM (this is not A,B,Cs sorry)
	+ **Investigations:**
		- **CT scan without contrast** (first important thing)
			* Classify as **hemorrhagic or non-hemorrhagic**
			* Can identify ICH and SAH (yes) and any other findings
			* Hemorrhagic stroke appears as a **hyperdense (white) area on CT**
			* Ischemia may or may not be apparent, but if so, it will be hypodense – it **may take 24 – 48 hours for ischemia to be apparent**
			* It **cannot effectively identify bleeding <1 cm**
			* MCA infarction 🡪 **hyperdense middle cerebral artery** sign, **loss of gray-white differentiation**, **sulcal effacement**
		- **Brain MRI**
			* **FLAIR** sequence or **diffusion sequence or SWI**
			* Gold standard in identifying **ISCHEMIC stroke** (after you did CT scan) – not preferred in emergency setting
		- **ECG**
			* Identify acute MI or atrial fibrillation (which can lead to stroke)
		- **Carotid duplex ultrasound/doppler**
			* Note and estimate the degree of carotid stenosis
		- **CXR**
		- **Echocardiography**
			* Identify mural thrombi or valvular disease or vegetations
		- In the case of hemorrhagic stroke, an **MRA** can be done to identify aneurysm/bleeding site – useful for surgical need
		- **Lab investigations:**
			* CBC, BUN & Cr, electrolytes, glucose, cardiac markers, coagulation profile, lipid profile (HDL, LDL, cholesterol)
	+ **Thrombolytics (tPA, IV, per body weight)**
		- Once hemorrhagic stroke has been ruled out, it is considered
		- Rules:
			* **<4.5 hours** (originally <3 hours) from onset of **ischemic stroke** (if CT shows non-hemorrhagic stroke)
		- **Contraindications**:
			* History:
* **Unknown time of onset**
* **Prior history of ICH**
* Head trauma/**stroke**/MI within last 3 months
* **Major surgery recently**
* Arterial puncture in non-compressible site
* Coagulopathies/bleeding diasthesis
	+ - * Clinical:
* Rapidly improving stroke symptoms (getting better)
* Minor/isolated symptoms (not worth it)
* **SEVERE stroke** (clinically or radiologically involved **>1/3rd of a hemisphere**)
* **Seizure at onset of stroke** and now postictal
* **Suspicious of SAH**
* **Persistent HTN >185/110**
	+ - * Lab/imaging:
* **Thrombocytopenia** (<100 x 109/L)
* **Hypoglycemia or hyperglycemia**
* **Prolonged PTT** (coagulopathy)
* CT scan shows hemorrhagic stroke
* You have to make it clear to the patient and his family that this **does NOT treat stroke** but we are trying to **prevent FURTHER DAMAGE or ANOTHER STROKE** (the infarcted areas are GONE for GOOD)
* Complications:
	+ **Hemorrhagic transformation** (rarer, usually minute)
* Alternatives routes?
	+ **4.5 – 6 hours** 🡪 **intra-arterial thrombolytic instillation** (by femoral catheter)
* **Antiplatelets:**
* **Clopidogrel (Plavix) or aspirin** or ticlopidine
* May be begun **after 24 hours if thrombolytics given**
* If thrombolytics CI or unsuitable or >4.5 hours passed 🡪 start
* **Anticoagulants:**
* Generally not given unless embolic with a known cardiac source (e.g. AF with mural thrombi found)
* May be given later in hospital stay because of risk of DVT & PE
* **BP control in stroke:**
* In ischemic stroke, ONLY lower BP if it is EXTREMELY HIGH (**>220/120 mm Hg**) or there is evidence of **hypertensive encephalopathy** (AND MUST BE DONE SLOWLY)
	+ IV, labetalol or nitroprusside to lower **BP <185/110 mm** Hg
	+ Why? It can worsen the ischemia
* In hemorrhagic stroke, aggressive control of BP is ok
* Patients receiving thrombolytics should also take anti-hypertensives
* **Neurosurgical consult:**
* May be required if intracranial hemorrhage suspected or if there is **“malignant” MCA stroke** 🡪 massive infarct can cause cerebral edema that causes mass effect 🡪 **decompression craniectomy** (**SAME side** as infarcted area!)
* **Others:**
* **Cerebral edema management** (e.g. raise bed, hyperventilate, mannitol, acetazolamide)
* Nimodipine for vasospasm that occurs after SAH (See later)
* **What’s next?**
	+ **Rx underlying cause** or **manage risk factors** to prevent future risk
		- Control BP, blood glucose, electrolyte disturbances
		- Reduce risk factors & if TIAs in history, use carotid Doppler and assess if you need to do endarterectomy or stenting
	+ Managing a patient with hemiplegia (**STROKE REHABILITATION**):
		- **DVT/PE prophylaxis** (LMWH can help with this)
		- Ask daily about **feeding, bowel, bladder & breathing** control
			* May need tube feeding
			* May need to be catheterized and need daily enemas
			* May need care for respiration (nasal/pharyngeal secretion suctioning, O2 mask, tracheostomy)
		- Monitor for and prevent pressure sores (**decubitus ulcers**)
		- **Physiotherapy for early mobilization** and to **depress spasticity** and prevent contractures
		- **Speech therapist** (assess for aphasias, dyslexias, dysarthrias, etc.)
		- **Post-stroke depression management** (anti-depressants?)
		- **Occupational therapist** (can lose their jobs or can’t work)
		- Activity of daily living assessment
	+ **Complications**
		- Progression of stroke or new stroke (**re-infarction, hemorrhagic transformation**) – clinically: reduced LOC or other side begins to develop weakness too
		- Cerebral edema/**mass effect with herniation** (e.g. malignant MCA)
		- **Permanent neurological deficits** (e.g. paralysis), **bed ridden**, **coma**, **death**
* Details:
	+ **Hemorrhagic stroke:**
		- **Intracerebral hemorrhage (ICH)**
			* High mortality and morbidity rate
			* Can raised ICP
			* Causes:
* **HTN** (sudden increase in BP) – rupture of **charcot-bouchard microaneurysm**
* Ischemic stroke with hemorrhagic conversion
* Amyloid angiopathy, AVM, anticoagulants/antithrombolytic use, brain tumors
	+ - * Locations:
* Basal ganglia, pons, cerebellum
	+ - * Clinical features:
* Abrupt onset, quickly worsens, pupillary changes
* **Headache, vomiting, seizures**
* **Altered level of consciousness**/coma
	+ - * Investigations:
* CT without contrast
* Coagulation profile
	+ - * Complications:
* Seizures, rebleeding, **VASOSPASM**, hydrocephalus, SIADH
	+ - * Management:
* **ICU admission**, **ABCs, may require intubation** (altered mental status and reduced respiratory drive)
* **BP reduction** (gradual)
* Rx raised ICP (raise head of bed, mannitol, diuretics, hyperventilation)
* **Surgical evacuation ONLY IF CEREBELLAR** hematoma/cortical (*not* in other locations) and there is mass effect
	+ - **Subarachnoid hemorrhage (SAH):**
			* Causes:
* **Trauma**
* Rupture of saccular **berry aneurysm**
* AVM, amyloid angiopathy (near brain surface)
	+ - * **Locations:**
* Berry aneurysms most commonly occur in the **PCom to ICA** or **ACom to ACA**
* Berry aneurysms occur in **ADPKD**, **Marfan** syndrome, Ehler Danlos, hereditary hemorrhagic telangiectasia and VHL syndrome
	+ - * Clinical features:
* Sudden, severe, **thunderclap** excruciating (typically **occipita**l) headache – **“worst headache of my life”**
* Sudden, transient **loss of consciousness** or collapse
* **Vomiting**
* **Meningism** (neck stiffness, photophobia, +ve kernig)
* **Retinal hemorrhage** (30%)
* **CN3 palsy** (PCom aneurysm) -
* **Death** (patients either die when it ruptures or survive and regain consciousness)
	+ - * **Diagnosis:**
* **CT scan** (>90% are detected)
* If CT scan –ve, **lumbar puncture** (if *no* papilledema/raised ICP) – check for **xanthochromia** (yellowish color on gross exam after standing [initially it is obviously bloody])
	+ - * **Complications:**
* ***Rerupture/rebleeding*** (very high risk)
* ***Vasospasm*** (leading to ischemic stroke)
* ***Communicating hydrocephalus*** (fibrosis/damage to the arachnoid granulations)
* ***Seizures***
* SIADH
	+ - * **Management:**
* **A, B, C (IV fluids)**
* **Analgesics,** bed rest, stool softeners
* **BP control** (gradual, but more aggressive/lower threshold than ischemic stroke)
* **Neurosurgery (ALWAYS CONSIDER):**
* **CT angiography** to **locate** bleeding site
* **Neurosurgical clipping** is performed
* **Endovascular coiling** (SAH –ve, but high risk)
* **CCB (Nimodipine) to prevent vasospasm** (only effective in 20%) – PO, 3 weeks
	+ **Venous infarction/intracranial venous thrombosis:**
		- Problem?

Dural venous sinus thrombosis: hemorrhage or ischemic infarction or BOTH?

When the venous drainage is blocked, there is cerebral edema and blockage of blood flow, leading to ischemia but also tiny hemorrhages that merge to form a hematoma. As you will see later, dural venous sinus thrombosis is the only condition where we give anticoagulants even though there is possible sign of hemorrhage.

* + - * Thrombosis in vein can cause an infarction within a venous territory (which overlies several arterial territories – so if you suspect stroke and see it affects multiple territories of arterial supply, consider venous thrombosis)
		- Causes:
			* **Pregnancy** (***any new neurological event in 3rd trimester of up to 40 days post-partum is venous sinus thrombosis until proven otherwise***)
			* **Oral contraceptive use**
			* Blood dyscrasias/**thrombophilias** (e.g. SCD, myeloma, leukemias, PND, SLE, APL, polycythemia, homocystinuria, etc.)
			* Interesting causes: IBD and Behcet’s disease
			* Infectious causes (meningitis, TB, cerebral abscess, **OTITIS MEDIA**, cerebral malaria)
		- **Dural venous sinus thrombosis:**
			* **Sagittal sinus thrombosis (MC)** or transverse sinus thrombosis (2nd MC); others (sigmoid sinus, cavernous sinus, inferior petrosal sinus)
			* Symptoms occur **GRADUALLY** (over days or weeks)
* ***Headache***, vomiting, ***seizures***, reduced vision, papilledema, slowly evolving neurological deficits
* Inferior petrosal sinus involvement 🡪 5th and 6th cranial nerve palsy + temporal and retro-orbital pain = Gradenigo’s syndrome
* Cavernous sinus thrombosis 🡪 2ndry to folliculitis and facial pustule spreading into venous system 🡪 headache, edematous eyelids, proptosis, ophthalmoplegia, fever
* **Investigations:**
* CT scan (first thing as usual)
* **MRI venography** (will help visualize hemorrhage [dark color] and infarction [lighter color])
* Lab investigations (CBC, coagulation profile, thrombophilia screen, serology, etc.)
* Management:
	+ **ANTICOAGULATION (heparin)**
		- *THE ONLY TIME YOU GIVE ANTICOAGULATION IN A HEMORRHAGE IS IN CEREBRAL VENOUS SINUS THROMBOSIS*
	+ Rx underlying cause (search for cause and treat)
* **Hematomas:**
	+ **Epidural hematoma:**
		- Blood collection in epidural space following head injury as a result of damage to the middle meningeal artery (MC) – branch of maxillary artery - over the pterion
		- Clinical features:
			* LOC and regaining it (lucid interval)
			* Suspect in any head injury with gradual reduction in level of consciousness
			* Severe headache, vomiting, confusion, seziures, hemiparesis can follow (rising ICP)
			* Ipsilateral pupil dilation (CN3 palsy from external compression), weakness becomes more severe
			* In the end, coma becomes more deep and breathing becomes irregular and then is arrested (compression of medulla by herniation)
			* Cushing’s triad (Raised BP, irregular breathing, bradycardia)
		- Investigations:
			* Head CT finding of epidural hematoma is that of a LENS shaped opacity (it DOES NOT cross suture lines)
			* Midline shift may be seen
		- Management:
			* A, B, C (stabilize patient)
			* Neurosurgery 🡪 burr hole craniostomy OR craniotomy
			* Prognosis is excellent if diagnosed and operated on early (poor if diagnosed late with coma, pupil abnormality, etc.)
	+ **Subdural hematoma:**
		- Damage to the bridging veins secondary to acceleration-deceleration injury - results in blood collecting in the subdural space (above arachnoid mater, below dura mater)
			* THE TRAUMA IS USUALLY NOT RECENT/FORGOTTEN (typically minor trauma in old patients because they have brain atrophy making the veins more vulnerable)
			* Risk factors include falls and anticoagulants
		- GRADUALLY rising ICP causing midline shift with herniations (“chronic subdural hematoma”)
		- Clinical features:
			* Fluctuating level of consciousness
			* Unsteadiness, headache, personality changes, sleepiness
			* Signs occur later (seizures, localizing neurological symptoms)
			* DDx: stroke, IC masses (tumor, abscess, neurocysticercosis)
		- Investigations:
			* CT scan 🡪 Sickle/crescent-shaped (not confined to suture lines)
		- Management:
			* Evacuation by burr hole craniostomy OR craniotomy (especially if clot has organized)
* **DDx of LOC/SYNCOPE:**
	+ **Syncope = transient loss of consciousness**
	+ Blackout = general term that varies in meaning:
		- Syncope OR collapse OR drop attacks
	+ Causes:
		- **Vasovagal syncope (“neurocardiogenic”) - MCC**
			* Most people have one episode
			* Onset is over **SECONDS** (not instantly)
			* Triggers: emotional stress, pain, fear, claustrophobic situations
			* **Symptoms before syncope include pallor, sweating, lightheadedness, nausea, diming of vision**
			* It **CANNOT occur when patient is lying down**
			* Normally, when standing we have sympathetic drive to cause vasoconstriction and raised HR because we need blood in the brain as gravity pools blood in LL…Result of stressor is transient reflex bradycardia and peripheral vasodilation resulting in hypoperfusion of brain 🡪 faints
			* Rapid recovery expected (lay down, raise legs)
			* **Tilt-table test can be +ve**
		- **Seizure disorder**
			* Suspect epilepsy if there is tonic phase and then a clonic phase, with tongue biting, incontinence, change in complexion (cyanosis), a preceding aura and a post-ictal phase of confusion, muscle aches, sleepiness/tiredness
			* The period of unconsciousness in seizures is typically longer than the general syncope
		- **Cardiac causes:**
			* Typically sudden and without prodromata or with EXERTION
			* **Arrhythmias** (sick sinus syndrome, ventricular tachycardia, rapid SVT, AV block [complete])
			* **Outflow obstruction** (HCM, aortic stenosis, MVP, atrial myxoma, pulmonary HTN)
			* **Massive MI**
			* **Stokes-Adams attack** = syncope secondary to arrhythmias like **complete heart block** and **V. tachycardia** – low COP and LOC result without warning (palpitations are felt) – recovery is within seconds with the patients pulse speeding up and there is flushing
		- **Orthostatic hypotension**:
			* **Old age, DM, drugs** (ganglionic blockers, nitrates, first dose hypotension in diuretics and antihypertensives, a-blockers)
			* Drop in BP >20 mm Hg when standing
			* Tilt-table test is +ve
		- **Cerebrovascular disease**:
			* ***Vertebrobasilar*** circulation TIA
			* Hemorrhagic stroke (SAH)
			* Trauma to the head (subdural hematoma, etc.)
		- **Hypovolemia** (massive hemorrhage)
		- **Metabolic causes** (hypoglycemia)
		- **Hyperventilation/anxiety**
		- Choking/asphyxiation
		- Situational syncope:
			* Cough syncope (after paroxysm)
			* Effort syncope (exercise)
			* Micturition syncope (reduction in venous return)
			* Hypersensitive baroreceptors/**carotid sinus syncope** (**tight collar**, turning the head, **shaving**)
		- Factitious syncope
		- Drop attacks does NOT involve LOC (sudden weakness of both legs causes person to collapse – benign condition)
	+ **Approach:**
		- Ask a witness if the pt is recovering and cannot answer or does not remember
		- Take a full history about the event (what occurred before, during and after)
		- **P/E** (focus on differentiating cardiac and non-cardiac etiologies):
			* Pulse, BP (sitting and standing)
			* Mental status (post-ictal state)
			* Mumurs (AS, HCM)
			* Carotid pulses – auscultate for bruits
			* Test for hypersensitive carotid sinus (watch reflex bradycardia, hypotension)
		- Investigations:
			* **ECG (ALL patients)** – some may require Holter monitor (24 hr ECG)
			* CBC, blood glucose, metabolic panel
			* **Tilt-bed test** (for orthostatic hypotension)
			* Further tests based on suspected diagnosis (echo, EEG/CT)
* **Meningitis:**
	+ Route of infection:
		- Direct
			* Otitis media, mastoiditis
			* Osteomyelitis
		- Indirect:
			* Hematogenously (e.g. septicemia, URTI, endocarditis, osteomyelitis, dental procedures)
			* Retrograde travel up nerves (e.g. HSV, VZV)
		- Neurosurgical/traumatic setting:
			* Traumatic head injuries
			* CSF leakage/fracture of base of skull
			* Ruptured meningomyelocele
			* Shunt operations
			* Post-operative
	+ **Causes:**
		- Infectious (bacterial, viral, fungal)
		- Non-infectious (SLE, medications, sarcoidosis, carcinomatosis)
	+ **Infectious causes:**
		- ***Aseptic* meningitis**
			* **Viral meningitis (MCC)**
* Enteroviruses
* Arboviruses
* HSV, VZV
* HIV and lymphocytic choriomeningitis virus
	+ - * Fungal meningitis (Cryptococcus, candida, histoplasma,)
		- ***Bacterial* meningitis**
			* **Neonates** (up to 3 months):
1. GBBHS (Strep. agalactiae)
2. E. coli
3. Listeria monocytogenes
	* + - **Children** (>3 months):

Streptococcus pneumoniae

Neisseria meningitidis

H. influenzae (loves base of the brain)

* + - * **Young adults** (teenagers):
1. Neisseria meningitidis
2. Streptococcus pneumonaie
	* + - **Adults** (18 – 50):

S. pneumonaie

N. meningitidis

* + - * **Old age** (>50):
1. S. pnuemoniae
2. N. meningitidis
3. Listeria monocytogenes
	* + - Others:
				* TB (tuberculoma)
				* S. aureus (neurosurgical setting)
				* Syphilis
				* Lyme disease (borrelia) – look for facial palsy
	* Notes:
		+ Meningitis is a **medical emergency** (needs prompt recognition and antibiotic coverage when suspected)
		+ Complications of meningitis:
			- Seizures, septic shock!
			- Progression to brain abscess or subdural empyema
			- CN8 deafness
			- Brain damage
			- SIADH/DI
			- Communicating hydrocephalus (scarring of the arachnoid granulations)
	* **Clinical presentation:**
		+ Symptoms:
			- Headache (especially when supine)
			- Neck stiffness/pain
			- Fever
			- Photophobia
			- Nausea and vomiting
			- Altered mental status, irritable
			- Seizures
		+ Signs:
			- Neck stiffness/nuchal rigidity
			- Rashes:
* Maculopapular rash
* Purpuric rash (not a good sign – purpura fulminans can occur - meningococcemia, does not blanch with glass test, and could have Waterhouse Frederichsen)
* Vesicular rash (varicella, HSV)
	+ - * Signs of increased ICP (papilledema, seizures)
			* Brudzinski’s sign
			* Kernig’s sign (others? Lassauge sign/straight leg test)
			* If you see facial nerve palsy, consider lyme disease
	+ Investigations:
		- CBC + ESR/CRP
		- Pharyngeal swab and culture
		- Blood culture
		- CT scan (note raised ICP)
		- Lumbar puncture for CSF analysis (R/O raised ICP by FIRST doing fundoscopy [papilledema] then CONFIRM using CT SCAN):
			* Opening pressure
			* Gross appearance (may be turbid/purulent)
			* Gram and AFB stain and microscopy (fastest way)
* Gram –ve diplococci in PMNs = N. meningitis
* Gram +ve diplococci, lancet shaped = Strep. pneumoniae
* Gram –ve bacilli: E. coli/H. influenza
	+ - * Culture and sensitivity (Best way, takes days)
				+ Latex agglutination can also be useful for cryptococcal meningitis and niesseria and pnuemococcus
			* PCR for viral RNA/DNA
			* Cell count (WBC, RBC)
			* Biochemistry (glucose, protein, Ig)
* WBC normal < 5 cells/mm3 (*NO* PMNs)
* Glucose >50% of serum (1/2 or 2/3)
* Protein <60 mg/dL
* RBC:WBC ratio (> 500:1 ~ think traumatic LP)
* High protein, low glucose, high PMN 🡪 bacterial
* High protein, low glucose, high LØ 🡪 fungal, TB
* High protein, normal glucose, high LØ 🡪 viral
* DON’T DEPEND on CSF culture maaaan! It can be sterile! Which could either mean the patient has a partially treated bacterial meningitis or the yield is too low
	+ Management:
		- **A, B, Cs** (maintain airway, IV access, fluid resuscitation)
			* When the opportunity arises, collect blood for investigations
			* Supportive care is important
		- **Symptomatic Rx**
			* **Analgesia** for pain
			* **Rx convulsions** if necessary (lorazepam)
		- **IV corticosteroids** (***Dexamethasone***)
			* In the case of MARKED cerebral edema in **BACTERIAL meningitis ONLY** (given with initial antibiotics or 15 minutes before it)
			* Has been shown to **lower mortality in TB** and **deafness by H. influenzae**
			* However, some argue that because it reduces inflammation it reduces penetration of antibiotics across BBB
		- **Empirical antibiotics (*IV*)**
			* *In ALL cases* only AFTER blood culture/CSF ***samples*** taken
			* It is done ASAP (**don’t delay** it for CSF C&S results and CT scan!)
			* *Neonates and elderly* 🡪 **cefotaxime + vancomycin + ampicillin** (for listeria)
* Ceftriaxone maybe preferred if >50 years
* Same group for immunocompromised, but consider ceftazidime for pseudomonas coverage
	+ - * *Other age groups* 🡪 **cefotaxime + vancomycin**
			* *Neurosurgical setting* 🡪 **ceftazidime + vancomycin**
			* Note: viral meningitis typically have a benign, self-limiting course that lasts 4 – 10 days (no serious sequelae unless there is also encephalitis)
		- Definitive **antibiotics based on C&S results**
			* May yield no infectious cause
			* Tuberculoid meningitis requires TB Rx for **12 months** (not 6 months) and with **adjuvant corticosteroids** – **high mortality** even with treatment (60%)
			* Syphilis 🡪 IM benzathine penicillin G, or IV penicillin G
			* **Cryptococcus 🡪 amphotericin B**
			* Anaerobes 🡪 clindamycin/metronidazole
			* HSV 🡪 acyclovir
		- Prophylaxis and Rx of close contacts:
			* **Meningococcal and H. influenzae** 🡪 Must Rx close contacts with:
				+ Rifampin, OR
				+ Ciprofloxacin, OR
				+ Ceftriaxone IM (if pregnant or child)
			* **VACCINATIONS:**
				+ Pneumovax (PPV) if >65 years old or immunocompromised or SCD or asplenic
				+ Meningococcal (ACYW) and H. influenza also for asplenics and SCD
				+ ALSO GIVE WHEN GOING ON RISKY TRIPS LIKE HAJJ!!
* **ENCEPHALITIS:**
	+ Causes:
		- Viral (MCC)
			* **HSV (MCC)** – bilaterateral frontotemporal lobe (HSV1>HSV2) – Kluver-Buchy syndrome
			* **Arboviruses, enteroviruses**
			* CMV, EBV, VZV, **HIV**
			* **Measles (SSPE)**, mumps, rabies
		- **Non-viral** (includes encephalopathy causes)
			* **Prions** (Cruetzfelt-Jakob disease)
			* **Protozoal** (**toxoplasmosis**, naegleria, acanthomeba)
			* **Fungal** (Cerebral aspergillosis)
			* **Encephalopathies** (MELAS, hepatic and uremic, Wernicke-Korsakoff, behcet’s, hypertensive)
			* T Cell lymphomas
			* Autoimmune encephalitis (paraneoplastic encephalitis seen in small cell carcinoma of the lung 🡪 Anti-Hu and anti-Ma2 and typically PRECEDES the diagnosis of cancer!)
	+ **Clinical presentation:**
		- Headache, fever, neck stiffness (like meningitis)
		- **Altered mental status**, **seizures** (more marked), photophobia
		- **Neurological deficits**, hemiparesis and coma
	+ **Investigations:**
		- ***Find source of infection:***
			* CBC
			* CXR, blood culture, urinalysis and culture
			* If not CI, LP 🡪 CSF analysis including PCR (shows viral combo – high/normal protein, normal glucose, high lymphocytes)
		- Toxicology scan, serum biochemistry
		- **Imaging:**
			* CT or MRI (note: toxoplasmosis shows ring enhancing lesions or intracranial calcifications, multiple vs lymphoma)
			* HSV encephalitis best seen on T2 weighted **MRI**
	+ **Management:**
		- **A, B, Cs** (supportive care, fluids)
		- **Symptomatic Rx** (analgesia, seizures and cerebral edema Rx)
		- **IV acyclovir** (2 – 3 weeks) **empirically** if HSV is suspected until imaging or CSF analysis confirms it is HSV
			* If found to be CMV 🡪 ganciclovir
			* Alternatives = foscarnet
			* Toxoplasmosis = sulfapyridine + pyramethamine + folinic acid (alternative = spiramycin)
		- Most other viral causes are SELF-LIMITING
		- Rx underlying cause if not infectious
* **Brain abscess:**
	+ Causes = **POLYMICROBIAL**
		- Streptococcus
		- **Anaerobes** (bacteroides)
		- **Enterobacteriaceae** (gram negatives)
		- **Staphylococcus aureus**
	+ Presentation:
		- Headache, fever, seizures, focal neurological deficits
		- You’d initially Rx as meningitis or encephalitis
	+ Investigations:
		- You would typically do all the investigations as above
			* Avoid LP if you suspect abscess because of cerebral edema risk of herniation
		- But you’d know that it’s an abscess when seen on imaging:
			* Head CT scan with contrast/ MRI (ring-enhancing lesion with surrounding edema)
		- **Diagnostic/therapeutic stereotactic aspiration**
			* RARELY do you need to do surgical excision
			* But in all cases, you need to **consider drainage**
	+ **Management:**
		- A, B, Cs
		- Symptomatic Rx
		- If HIV +ve (suspect toxoplasmosis or lymphoma)
			* Consider giving trial of pyramethamine + sulfadiazine and if they respond, diagnostic
		- IV steroids for cerebral edema
		- Antibiotics:
			* Pencillin + metronidazole + ceftazidime
			* For toxo 🡪 you know what
		- Neurosurgical consult for drainage (stereotactic aspiration)
* **DDx of altered mental status and fever in adults:**
	+ **Septicemia** (urosepsis/pyelonephritis, pneumonia, liver abscess, etc.)
	+ **Meningitis/encephalitis/brain abscess**/intracranial empyema
	+ **Delirium tremens** (alcohol withdrawal)
	+ **Thyroid storm**
	+ **Neuroleptic malignant syndrome** (haloperidol)
* **DDx of Coma:**
	+ Nowadays we classify altered consciousness by the GCS (instead of the stepwise manner of drowsiness/lethargy 🡪 stupor 🡪 semi-coma 🡪 coma)
	+ SMASHED:
		- S: structural
			* Stroke
			* Hematomas (Subdural or epidural)
			* Tumors
			* Hydrocephalus
			* Herniation (tonsillar, uncal/transentorial)
			* Brain abscess
		- M = Meningitis
		- A = Alcohol and Acidosis
		- S = Seizures (epilepsy, post-ictal state)
		- H = Hypers and Hypos:
			* Hypers (hypercapnia, hyperglycemia, hyperthermia)
			* Hypos (Hyponatremia [cerebral edema], hypoglycemia, hypoxia, cerebral hypoperfusion, hypothermia)
		- E = Endocrine, Encephalitis and Encephalopathy and Electrolyte disturbances
			* Endocrine (Thyrotoxicosis, hypothyroidism [myxedema coma], addisonian crisis)
			* Encephalopathies (most importantly uremic, hepatic or hypertensive)
			* Extreme disturbances in Ca, PO4 and Mg
		- D = Drugs, Dangerous compounds and Deficiency
			* Opiates, benzodiazepines, barbiturates, sedatives
			* Dangerous stuff: Carbon monoxide poisoning, cyanide, methanol
			* Deficiency = thiamine deficiency
	+ Can also be divided into:
		- Intracranial causes (with lateralizing signs)
			* Traumatic
			* Inflammatory (infectious)
			* Vascular (SAH, ICH, cerebral venous thrombosis, encephalopathy)
			* Neoplastic
			* Epilepsy
		- Extracranial causes (without lateralizing signs)
			* Toxic (barbiturates, opiates, atropine, salicylates, alcohol, CO poisoning, BZ, sedative hypnotics)
			* Hypoxic (and CO2 narcosis/type 2 RF)
			* Ischemic (cardiac arrest, MI, hypotension, arrhythmias)
			* Metabolic
			* Endocrine
			* Fevers (cerebral malaria, septicemia, status typhosus)
		- Hysterical (psychiatric)
	+ Approach to coma:
		- A, B, Cs + assess vitals
			* Assume trauma, so stabilize cervical spine and assess for signs of trauma
		- History from family
		- P/E:

Vitals:

- Low C: hypothyroidism, hypopituitarism, barbiturate, opiate poisoning, CHF

- low BP: addisonian crisis, alcohol and barbiturate poisoning

- high BP: HTN encephalopathy

- Kussmaul breathing: DKA, uremic acidosis

- Slow, deep: Barbs, morphine tox

- Cheyne-Stokes breathing (fast, then apnea, then fast)

- Apneustic (pontine) and ataxic breathing (irregular deep and shallow in medullary problem)

Inspection of skin:

- injuries/bruises

- dry skin (DKA, atropine poisoning)

- moist skin (hypoglycemic coma)

- cherry-red (CO poisoning)

- needle marks (drug toxicity)

- rashes (meningococcemia, endocarditis, exanthems)

Breath:

- acetone: DKA

- ammonia/fetor hepatic: hepatic encephalopathy, RF

- Alcoholic odor

Pupillary changes:

- Dilated irreactive to light:

 > uni (CN3 compression)

 > bi (atropine poisoning)

- Constricted:

> uni (Horner’s)

 > bi (reactive to light? Metabolic coma; not reactive? Pontine hemorrhage and opioid tox)

* + - * Inspect patient body and skin
			* Pay attention to patient breathing and its pattern
				+ If patient breathing on their own = brainstem is ok, but pay attention to breathing pattern
				+ Check the odor of the patient’s breath
			* Do a quick motor exam
				+ If asymmetry is noted = mass effect (think intracranial causes)
				+ Metabolic and systemic causes result in bilateral motor abnormalities
			* CNS examination with brainstem reflexes:
* Light reflex
* Oculocephalic test (Doll’s eye)
* Fundoscopy and meningeal signs
	+ - Investigations:
			* CBC, electrolytes and osmolarity, BUN & Cr, glucose, ABG, ECG, toxicology scan of blood and urine, head CT/MRI, LP if meningitis/SAH suspected
		- Management:
			* Rx underlying cause
			* General care of a comatosed patient:
* Skin, pressure points, respiration (and suctioning of secretions), nutrition and fluid balance, bowel and bladder

**SEIZURES & EPILEPSY:**

* Seizures:
	+ Result of sudden abnormal discharge of electrical impulse in the brain
	+ Lifetime risk of a seizure is 5%
	+ Seizure ≠ epilepsy
		- Epilepsy = recurrent episodes of seizures (at least 2 times) whose true cause is usually unknown
		- Convulsions = the motor signs of a seizure
	+ Causes:
		- Metabolic and electrolyte disturbances
			* Hyponatremia, water intoxication, hypoglycemia and hyperglycemia, hypoCa, thyroid storm, hyperthermia
		- Mass lesions (\*\*\* big DDx for epilepsy)
			* Brain tumors, hemorrhage and brain mets
		- Missing drugs
			* Non-compliance with AED or rapid withdrawal of AED (MCC of seizures in epileptics)
			* Acute withdrawal of alcohol, BZ, barbiturates
		- Miscellaneous
			* Pseudoseizures (hysterical)
			* Eclampsia
			* Hypertensive encephalopathy
		- Intoxications
			* Cocaine, lithium, theophylline, metal poisoning, CO
		- Infections
			* Septic shock, meningitis, brain abscess
		- Ischemia
			* Stroke, TIA
			* Note: venous thrombosis can present with seizures
		- Increased ICP
		- EPILEPSY!
* Elements of a seizure:
	+ Prodrome (rare)
		- Hours or days (not the same as aura)
		- Not part of seizure itself but noticeable change that can precede it (mood, behavior)
	+ **Aura**
		- Part of the seizure
		- It is one of the features of partial seizures (preceding the complex partial seizure)
		- Includes:
			* Strange feeling in gut
			* Déjà vu (sense of familiarity)
			* Jamais vu (unfamiliarity)
			* Strange smell (uncal stimulation in temporal lobe)
			* Flashing lights (occipital)
	+ **Ictal state**/seizure
	+ **Post-ictal state**
		- Headache, confusion, **myalgias**, sore tongue, temporary weakness after a motor cortex focal seizure (**Todd’s palsy**), sleepiness, **impaired memory**
* **Epilepsy:**
	+ 1% of the population has epilepsy (A LOT)
	+ Causes:
		- 2/3rd 🡪 idiopathic
		- Structural causes:
			* **Mesial temporal sclerosis** (MTS) – said to occur after multiple febrile convulsions
			* **Cortical scarring**
		- **Tuberous sclerosis** (infantile spasms/West syndrome)
		- SLE, vasculitis
	+ How to distinguish epilepsy/seizure from a hysterical seizure (pseudoseizure)? Real seizures:
		- Have **facial involvement**
		- Can **occur at night**
		- Involves tongue biting (specially **LATERAL tongue bite marks** – not anterior bite marks)
		- **Incontinence** can occur
		- **Eye can be opened without resistance**
		- When arm is held up and allowed to drop over the face, it will (**patient will not protect themselves**)
		- Movements are **stereotypical**
		- **Plantar reflex is upgoing** (Babinski sign is present)
		- **BP & HR will be elevated**
		- **EEG findings** can be seen
	+ Types:
		- ***Partial seizure* (70%)**
			* Typically begins in one region (temporal lobe most commonly) and then can set off and spread to other parts of the brain

Localizing features of partial (focal) seizures:

**TEMPORAL LOBE:**

**- AUTOMATISMS** (focal complex motor phenomenon with no recall of it):

 > lip smaking, chewing, swallow

 > manual movements

 > singing, driving, violent acts

- Jamais vu, déjà vu, emotional disturbances (sudden terror, panic, anger, derealization)

- Uncal hallucinations (abnormal smell, taste, dream-like state, music, conversations)

**FRONTAL LOBE:**

- **motor** (posturing, leg peddling, **JACKSONIAN MARCH** [retained awareness, spreading from thumb or face])

- dysphasia, speech arrest, behavioral disturbances

- **post-ictal Todd paralysis**

**PARIETAL LOBE:**

**Sensory disturbances** (tingling, numbness, pain)

**OCCIPITAL LOBE:**

**Visual phenomena** (spots, lines, flashes)

* + - * ***SIMPLE* partial seizure:**
* **Consciousness is INTACT**
* Can progress to a complex partial seizure
* May involve transient **UNILATERAL** tonic-clonic movements (**automatisms** are purposeless, involuntary, repetitive movements, which lasts 1 – 3 minutes with patients becoming aggressive when restrained)
* Basically they can get **FOCAL motor, sensory (olfactory, visual), autonomic or psychic symptoms**
	+ - * ***COMPLEX* partial seizure:**
* **IMPAIRED AWARENESS/CONSCIOUSNESS**
* May have a **preceding aura**
* Most commonly arises from temporal lobe
* May have a **SECONDARY GENERALIZATION** (it spreads to involve rest of cortex) 🡪 generalized seizure (typically tonic-clonic)
* **Generalized seizure:**
* ***Tonic-clonic (Grand Mal) seizure***
* **Loss of consciousness** (fall to the ground)
* **Tonic phase** (rigid/extension of limb, neck, trunk - may release a scream/become apneic)
* **Clonic phase** - bilaterally symmetric convulsions without focal onset
* Patient becomes flaccid and comatosed before regaining consciousness (passing into a **post-ictal phase**, lasting for 10 – 30 minutes up to hours)
* Patient can have **incontinence, tongue biting, frothing of the mouth, upwards eye-rolling**
* ***Absence (Petit mal) seizure***
* School-age young children
* Random, short (< or = 10 seconds) but frequent (100 times a day or so) pause and staring into the distance (confused with day-dreaming)
* Continue as nothing has happened (continues talking, drawing)
* No LOC or postictal states and very minor motor features (eye blinking)
* ***Myoclonic seizures***
* Jerky movements only occur (no tonic phase)
* Types to be aware of include **juvenile myoclonic epilepsy (JME)** and **progressive myoclonic epilepsy**
* It starts off typically as benign myoclonus (like simple partial) that people tend to ignore (if caught at this stage = good prognosis)
* Patients report random hand movements like throwing spoons or continued brushing of teeth
* When it becomes worse and becomes a generalized myoclonic epilepsy, as in JME, it requires LIFE-LONG Rx with valproate ☹
* Tonic seizures
* Atonic seizures (no LOC, but falls)
* Triggers for seizures in epilepsy (not causes of seizures):
	+ **Poor compliance with medications**
	+ Alcohol
	+ Stress
	+ Fevers
	+ Certain sounds
	+ **Flickering lights/strobe lights**/contrasting patterns
	+ **Hyperventilation**
	+ Lack of sleep/**insomnia**
	+ **Fasting**
* **Sudden unexpected death in epilepsy (SUDEP)**
	+ More common in uncontrolled epilepsy
	+ May be related to nocturnal seizure associated apnea or asystole
* Investigations:
* ***Known patient with seizure disorder?***
* Check **serum AED levels**
* ***New patient with seizures*** (**admit** them and **investigate for 24 hr**)
* CBC
* **RFTs** (**BUN**, Cr)
* **Glucose** & **electrolyte panel** & **CK** (may be raised after convulsions)
* **LFTs** (with coagulation profile)
* **Tox-scan** (and other tests depending on what you suspect it is.. e.g. TFTs, LP or blood culture)
* **IMAGING = CT scan** (immediately), **MRI** (later and for FOLLOW UP, helpful to find out if MTS present, which is amenable to surgery)
* **EEG**
* **Management:**
	+ **Non-acute setting:**
		- If has an underlying cause for seizure, Rx underlying cause
		- If ***no* cause found** and **first seizure 🡪 DO NOTHING**
			* If they have a strong family history, or has obvious structural brain lesion (MTS) or EEG findings, or they have a dangerous job 🡪 manage
		- If **SECOND** seizure and you think epilepsy, begin AED:
			* **MONOTHERAPY** by **ONE DOCTOR**
			* Start with the lowest dose and continue to increase until the tolerable maximum if seizure still not controlled
			* If still seizures occur OR if there is ADR 🡪 begin a second drug and wait till it becomes efficacious and then stop the first drug (so only during bridging do we use two drugs at once, but **in general ONLY ONE DRUG**!)

**Lifestyle changes** are necessary in epilepsy:

**- NO driving** (license given back if 6 months seizure free)

- **NO swimming, specific jobs** (heights involved)

- Needs counseling for job, sports, insurance and pregnancy

- **Counseling for depression** (high risk of suicide in epileptic patients)

* + - * **WE DO NOT STOP THE DRUG BASED ON SERUM LEVELS** (we typically may make it reach above toxic levels sometimes!) – we stop if it doesn’t work and if there ADR (So we need ***CLINICAL monitoring***)
			* TELL YOUR PATIENT TO **NEVER STOP THE DRUG SUDDENLY** (it is a trigger for a severe epileptic attack)
			* ADJUVANT THERAPY NOW HAVE A ROLE
		- ***When to stop?***
			* If the patient is **seizure free for ≥ 2 years** ***AND***
			* Has **normal EEG findings** ***AND***
			* Normal CNS examination AND
			* NOT JME (needs lifelong Rx)
		- ***Alternatives?***
			* **Surgery for MTS**
			* **Vagal nerve stimulation**
	+ **WHICH DRUGS TO USE?**
		- Partial seizures (+/- 2nd gen):

When a Dr. asks you for a backup drug, you can’t go wrong with valproate and lamotrigine – this is in general, because in REAL LIFE, every patient is different with differing comorbidities, necessitating the **selection of a drug with the least ADR.**

* + - * **1= Carbamazepine**
			* **Valproate (Depakene)**
			* **Lamotrigine**
			* Gabapentin?

Other uses of AED and AED combos:

- Valproate for BIPOLAR DISORDER (mania) and used in MIGRAINES

- Carbamazepine for trigeminal neuralgia (neuropathic pain)

- Lamotrigine for neuralgia, Lennox Gustaut, and even bipolar disorder

- Gabapentin for neuropathic pain (especially post-herpetic neuralgia, diabetic neuropathy)

* + - **Grand mal:**
			* **1 = valproate or lamotrigine**
			* Carbamazepine, topiramate
			* Levetiracetam (Keppra)
		- **Absence (petit mal) seizures:**
			* **1= Ethosuximide**
			* Valproate
			* Lamotrigine
		- **Tonic, atonic and myoclonic:**
			* Same as grand mal, BUT***avoid* carbamazepine** (will make it WORSE!)

**Pregnancy and AED:**

- No absolute drug has been shown to be safe in pregnancy, however **avoid valproate** because it causes NTD and phenytoin because it causes fetal hydantoin syndrome and NTD. Whatever drug you were giving them (except the above), you may continue them at a low dose that protects them from seizures. **Increasing the pre-pregnancy and pregnancy doses of folic acid** is recommended (1 – 4 mg, instead of 0.4 mg). Some drugs I’ve heard mentioned are **levetiracetam and lamotrigine**, but the research is lacking and are on small groups. Carbamazepine causes cleft lip and palate (☹).

**CONTRACEPTION:**

Be sure to warn mothers who take AED that INDUCE CYP450, that **CONTRACEPTIVES MAY NOT BE AS EFFECTIVE**, because OCPs are substrates of CYP450 (just like warfarin). Which are enzyme inducers? Phenytoin, carbamazepine, phenobarbital.

Unlike in other conditions, use of the trade name drugs are preferred, because most studies are done with them. (I read this somewhere but I’m NOT sure).

* + - **Levetiracetam:**
			* Approved for partial (alone) and adjuvant Rx for myoclonic and tonic clonic
			* **No drug-drug interactions** (useful in elderly)
	+ ADR:
		- **Common to all:**
			* **Dizziness**
			* **Nausea, vomiting,** fatigue
			* **Incoordination, ataxia, diplopia**
			* **Suicidal tendencies** increase
		- **Valproate (Depakene) –** CYP450 inhibitor
			* **Nausea** (MC)
			* ***Weight gain*** (PCOS, obesity associations)
			* Irritability
			* **Hepatotoxicity** (MUST check LFTs)
			* **Teratogenic** (spina bifida, in considering conception avoid valproate – use lamotrigine)
			* **Thrombocytopenia**
			* **Pancreatitis**
			* Suicidal tendencies
		- **Carbamazepine** – CYP450 inducer
			* **Agranulocytosis** (aplastic anemia)
			* **SJS/TEN**
			* Dilutional hyponatremia (SIADH) 🡪 **EDEMA**
			* Suicidal tendencies
			* Teratogenic (risk of **cleft lip and palate**)
		- **Phenytoin** – CYP450 inducer (not used as often nowadays)
			* **Gingival hyperplasia**
			* Megaloblastic anemia (impairs folate absorption in GIT)
			* **Arrhythmias** (it is an anti-arrythmic – class IB)
			* **Hirsutism**
			* CI in porphyrias, pregnancy (NTD) and watch carefully if patient taking aspirin
		- **Lamotrigine**
			* Blackbox warning for **DRESS syndrome**, **SJS/TEN**
		- **Topiramate:**
			* **Weight LOSS**
			* **Word finding difficulties**
			* Renal stones
		- **Levetiracetam (Keppra)**
			* **Suicidal tendencies** (avoid in depression)
* **ACUTE SEIZURE MANAGEMENT:**
	+ ***Status epilepticus***:
		- Seizures **lasting for >30 minutes** OR
		- Seizures **without intervening consciousness**
		- Increased risk of mortality and permanent brain damage
		- If it is the 1st presentation, the chance of a structural brain lesion is high (>50%)
		- If seen in pregnant women 🡪 eclampsia 🡪 obstetrician for delivery/MgSO4
	+ **Management:**
		- **A, B, Cs**
			* **Open and secure airway**
			* Lay in **recovery position** (**to the side**, **one knee bent** [prevent rolling on stomach and support position], **one arm bent** tosupport head and mouth, head tilted back)
			* **Give O2**, **suction secretions** (when required), intubate if required
			* **Gain IV access** (**can be difficult at first**) for blood collection for investigations (e.g. **AED levels**, **tox screen**, **U&E**, **CBC**, **LFT**, **glucose**, **Ca2+**)

qIn America, you would most probably want to consider giving naloxone if you consider a drug intoxication to be a cause.

* + - * Finger stick **glucose low**? **Give thiamine + D50W IV**
			* Seizure may or may not stop, if it doesn’t continue
		- Make sure to have a full resuscitation team and facility ready and go according to below (move further down when seizure continues):
		- 1 = **Slow IV bolus of BZ** into ***large vein*** OR ***rectally***:
			* **Lorazepam** (2 – 4 mg), give **2nd dose if no response** in 10 minutes
			* Buccal midazolam or rectal diazepam are alternatives
		- **2 = IV infusion of fosphenytoin** or **phenytoin** (under ECG & BP monitoring)
			* 15 – 20 mg/kg (max 2 g), must be in a **DIFFERENT line than that of diazepam** (they don’t mix)
		- 3 = IV infusion of **phenobarbital**
			* Monitor respiration and make sure ventilator present (causes respiratory depression)
			* This should control it really, if it doesn’t good luck
		- **4 = last case = General anesthesia – rapid sequence induction** (thiopental, propofol, midazolam)
		- NOTE: Pt with convulsions **can develop AKI** (ATN) because of **high CK and myoglobin** as a result of rhabdomyolysis
* **Multiple Sclerosis (MS):**
	+ Autoimmune (**T cell mediated**) **demyelinating** condition of the CNS
	+ The demyelination occurs at multiple CNS sites (seen as MRI plaques) at different times

NOTES:

- Involved are **GENETIC** FACTORS (RF: female, **HLA-DR2**) and **ENVIRONMENTAL** FACTORS (low vitamin D and infections)

Demyelination is initially reversible, but repeated attacks can result in eventual irreversible demyelination.

* + - Loves involving the optic nerve, MLF, cerebellar, pyramidal tracts and posterior columns
	+ Epidemiology:
		- **Women > men (3:1)**
		- **30 years old** = mean age of onset
		- Cause is unknown, but **vitamin D deficiency** (or lack of sun exposure) is thought to have a role (environmental factors)
	+ Clinical course (presentation):
		- **Relapsing-remitting (85%)** – average about **1 attack/year**
		- **Primary progressive (15%)**
		- **Secondary progressive** – (after relapsing-remitting period)
		- **Progressive-relapsing** (each relapse becomes worse and worse)
		- In most cases, normal life span is expected (good prognostic signs include initial presentation of optic neuritis or sensory and if MRI is normal)
		- **Severe disability/poor prognosis is suspected if:**
			* **Frequent attacks** early in disease course (>2/year)
			* **Onset is at an older age** (>40 years)
			* **Progressive course**
			* **Early cerebellar or pyramidal tract** involvement
	+ **Clinical features:**
		- ***Fatigue***
		- **Transient *sensory* deficits**
			* **MC initial presentation**
			* Paresthesia, dysthesia, hyperesthesia
			* **Neuropathic pains** – *bilateral* trigeminal neuralgia, **Lhermitte’s sign** (lightening bolt radiating down neck with flexion, also seen in cervical spondylosis, SCD of B12 deficiency, cord tumors)
			* **Useless hand syndrome** (loss of discriminatory function and proprioception)
			* **“Cold water” trickling** feeling along limb
			* **Pseudoathetosis** (eyes closed 🡪 athetosis)
		- ***Motor* symptoms**
			* **Spasm spells** that can be painful
			* Spontaneous **clonus**
			* **UMN spasticity/weakness** (will show hyperreflexia), **stiff lower limbs that impairs walking**
			* **Cerebellar signs** (loss of balance, incoordination [ataxia], intention tremors, scanning/staccato speech)
		- **Visual disturbances**
			* **Optic neuritis** (**PAINFUL eye movement**, monocular visual loss/**temporary blindness** or reduced acuity, decreased pupillary reaction to light); no findings obvious on fundoscopy because it is a retro-bulbar pathology); 1 – 21 days
			* **Marcus Gunn pupil** (Relative afferent pupillary defect or **RAPD**) – tested by swinging light test
			* Bilateral **internuclear ophthalmoplegia (INO)** as a result of demyelination of the medial longitudinal fasciculus (**MLF**) – can converge but cannot conjugate gaze to either side
			* **Diplopia, visual hallucinations** of faces, flashes, **Uhthoff’s phenomenon** (reduced vision during exercise, hot meals, hot baths)
		- **Autonomic disturbances**
			* Incontinence (bladder and bowel)
			* Erectile dysfunction in men
			* Anorgasmia
		- **Cognitive disturbances**
			* Depression, anxiety, emotional lability, personality changes
			* Inattention, slowed information processing
			* Memory loss, difficulties with abstract concepts and complex reasoning
			* Major cause of unemployment and accidents
		- **Specific entities:**
			* Transverse myelitis
			* Longitudinal myelitis
			* **Devic’s syndrome** (neuromyelitis optica) – MS variant with transverse myelitis + optic atrophy + NMO-IgG Ab

To summarize the features:

- Sensory

-Motor (pyramidal & cerebellar)

- Visual (optic neuritis, INO, occipital)

-Autonomic

-Cognitive (all kinds)

They can also get BILATERAL trigeminal neuralgia… R/O other causes if you find patients with headaches or seizures.

Poor prognostic signs = Male, extreme of ages, motor deficits as initial presentation, high frequency of attacks

* + - The **most common presenting features are sensory deficits, optic neuritis and one-sided weakness**
		- It may take a really long time for some features to subside (the longer it takes for motor/cerebellar, the poorer the prognosis)
			* They may become irreversible
	+ **Investigations:**
		- **Diagnosis is clinical**, but certain investigations can help
			* **MRI head/spine for MS plaques:**
				+ **T2 weighted**/**FLAIR sequence MRI** with **Gadolinium** contrast

Clinically isolated syndrome (CIS) = features of MS occurring only once without MRI findings, which requires no DMD therapy (diagnosis of MS is not made). Many of these patients develop MS.

Radiologically isolated syndrome (RIS) = incidental MRI finding of plaques suggestive of MS, however, no Rx indicated, make them come again in 6 months for another MRI. Should fulfill 3/4 of Barkhof criteria. Many of these patients also go to develop MS.

DDx?

Behcet, sarcoidosis, sjogren, MCTD, ADEM.

* + - * + Common sites: **periventricular, juxtacortical, infratentorial or SC** (not grey-white junction or cortex)
				+ NOT necessarily proportional to disease severity or speed of progression
			* **Lumbar puncture:**
				+ **≥ 2 IgG oligoclonal bands**
				+ **High IgG index**
				+ **Mild lymphocytosis**
				+ **Mildly raised protein levels**
			* **Evoked potential studies** (will be **slow** because newly myelinated fibers are much slower)
	+ **Diagnostic criteria:**

Dissemination in TIME and SPACE:

If patient develops what appears to be a CIS, then check for dissemination in SPACE radiologically (≥1 T2 lesion in ≥2 classical locations) or clinically (another attack but different neurological deficit)

Or check for dissemination in TIME radiologically (you see asymptomatic gadolinium enhancing and non-enhanching at same time, or a new lesion on a F/U visit) or clinically (new clinical attack)

* + - Must have lesions disseminated in **time** and **space**, unattributable to other causes
		- Attacks must last **>1 hour**, and **>1 month between attacks**
		- Criteria includes:
			* **Poser criteria**
* **≥ 2 attacks**
* ***Clinical*** or ***lab*** evidence of **≥ 2 CNS lesions**
	+ - * **McDonald criteria** (more emphasis on MRI findings)
* Very complicated, but it tries to implement the idea of the poser criteria with the occurrence of a MRI plaque
	+ **Management:**
		- **Attacks/exacerbations:**
			* **IV methylprednisolone** (3 – 5 days)
* DOES NOT change progression of disease
* **SHORTENS acute attacks**
	+ - * Treatment of acute attacks does not affect outcome of or course of MS
			* Other options: plasmapharesis
		- **General Rx (immunomodulators) – usually for RRMS:**

IFN therapy is associated with pain at injection site, flu like symptoms (severe! Reduce dose by ½ and give symptomatic Rx), raised LFTs and eventual reduced efficacy after prolonged use because of auto-Ab against it (“neutralizing Ab”). Fingolimod is associated with bradycardia (need to admit patient for ECG) and macular edema. Natalizumab is associated with JC virus activation and PML (JC virus serological testing required). You are NOT suppose to give them more than ONE DMD at one time. If they don’t respond to one (wait for 6 months) then you can gradually change it to another drug.

Devic’s syndrome is important to distinguish because management is plasmapharesis and rituximab (anti-CD20, because it caused by anti-NMO IgG Ab).

* + - * **Interferon therapy** (IFN-ß1a, ß1b, ..)
* Many ADR, but **FLU-LIKE SYMPTOMS** can be severe and persistent
* Should be started early before disability can become irreversible
	+ - * **Monoclonal Ab** (Natalizumab [against VLA-4 receptors], Alemtuzumab [against T cells])
			* Others (Mitoxantrone, glatiramer acetate, Fingolimod)
			* Start immunotherapy early in relapsing-remitting type
			* Drug failure = >1 attack in 6 months or new MRI lesion
		- **Symptomatic Rx**
			* Fatigue (amantadine)
			* **Spasticity** (**physiotherapy**, baclofen, BZ)
			* **Hypertonic bladder** (fluid restriction, timed voiding, oxybutynin, intermittent catheterization)
			* May need to use **wheelchair** if significant motor symptoms occur
		- Others (**VITAMIN D**!!!!); make sure to do annual MRI
* ABNORMAL MOVEMENTS:
	+ **Fasciculations** (lower motor neuron lesions)
		- Flicker muscle movements, often best observed using EMG
	+ **Tremors** (see below)
		- Shaking of the limbs
	+ **Chorea**
		- Non-rhythmic, jerky, purposeless movements flitting from one place to another
		- Causes include:
			* Huntington’s disease (Huntington’s chorea)
			* Sydenham’s chorea (Rheumatic fever)
			* Choreoathetoid cerebral palsy occurs 2ndry to kernicterus
	+ **Hemiballismus**
		- Large-amplitude, flinging hemichorea
		- Whole limb does a crazy movement
		- Result of lesion to the **contralateral subthalamus**
	+ **Athetosis:**
		- Wringing, slow, sinuous confluent movements (especially affecting digits, hands, face and tongue)
		- Choreoathetoid and athetosis is seen in cerebral palsy
		- May occur also in severe deficit of conscious proprioception (when patients close their eyes, their hands begin to do this) – “pseudoathetosis” – this is seen in MS
* **DDx of tremors**
	+ **Physiologic tremor**
		- **Anxiety**, fear, fatigue
		- Metabolic causes (increased sympathetic drive):
			* **Hypoglycemia**
			* **Hyperthyroidism**
			* Pheochromocytoma
		- **Toxic causes:**
			* **CAFFEINE** and methylxanthines (COFFEE and TEA!)
			* **Alcohol withdrawal** (delirium TREMENS)
			* Drugs (valproate, lithium, beta 2 agonists)
	+ **Essential tremors (benign essential tremors)**
		- Autosomal dominant (and common)
		- Induced or exacerbated by intentional activity (intention tremor)
		- Improves with alcohol ingestion
		- Rx ~ propranolol
	+ **Neurological tremors:**
		- **Intention tremors**
			* Worse with actions/activity, not present at rest
			* Seen with cerebellar disease (primary or secondary to stroke, drugs [phenytoin], Wernicke-korsakoff, Wilson’s disease)
		- **Resting tremors**
			* Seen in extrapyramidal tract disorders like PD
			* Pill-rolling, slow tremors only occurring at rest
			* Associated with bradykinesia, rigidity (hypertonia), shuffling/festinating gait
* **Delirium vs. Dementia (both organic cognitive disorders)**
	+ **Delirium = acute confusional state**
		- Acute period of cognitive dysfunction secondary
		- Clinical features:
			* Rapid deterioration in mental status (hours to days) that is waxing and waning
			* Fluctuating level of awareness/consciousness (disoriented)
			* Memory deficits, inattention, hallucinations (VISUAL > tactile > auditory [think of psychosis]), impaired language (repetitive and disruptive)
			* Mood may be labile; irritable patient
			* Tremors may be present (delirium tremens in alcohol withdrawal, asterixis)
			* Most likely will have abnormal vitals of some kind
			* Reversal of sleep wake cycle (sun-downing)
		- Causes:
			* Systemic infections (pneumonia, UTI, malaria, wounds, IV line infection, sepsis, etc.)
			* Intracranial infections (encephalitis, meningitis)
			* Drugs (opiates, AED, levodopa, sedatives, post-GA, corticosteroids, anticholinergic)
			* Alcohol (delirium tremens, 2 – 5 days after admitting) and BZ withdrawal
			* Metabolic (uremia, liver failure, high or low Na+ and glucose)
			* Hypoxic (respiratory or cardiac failure)
			* Vascular (stroke, myocardial infarction)
			* Head injury (space occupying lesions, raised ICP)
			* Epilepsy (non-convulsive status epilepticus)
			* Nutritional (thiamine (B1), NAD (B3) and B12 deficiency)
		- Investigations:
			* CBC
			* RFTs (BUN, Cr, electrolyte panel), LFTs
			* Septic workup (urinalysis + C&S, blood culture, CXR)
			* Blood glucose, B12, thiamine levels, tox scan
			* ABG, ECG, head CT/MRI
		- Management:
			* Keep in a dimly lit quiet room, use same nurse staff, DO NOT try to restrain them, remove/replace catheters
			* Rx underlying cause
			* Haloperidol if agitated/disruptive or show psychotic behavior
	+ **Dementia**
		- **PROGRESSIVE deterioration of cognition** (it is also an organic disorder of cognition)
			* **Level of consciousness/awareness is PRESERVED** (at least early in disease)
			* Usually no tremors, hallucinations
		- **Major risk factor is increasing age**
		- Features:
			* Typically begins with memory loss that has increased over months to years (days = infection, stroke; weeks = depression)
			* In AD, the memory loss is then accompanied with visuospatial (resulting in wandering), speech and mood disturbances
			* Eventually all motor and cognitive functioning fails and they may become bed-ridden requiring assistance for almost everything
		- **Causes:**
			* **Alzheimer’s disease (MCC)**
			* **Vascular/multi-infarct dementia (2nd MCC)**
			* **Lewy body dementia (3rd MCC)**
			* Fronto-temporal dementia (**Pick’s disease**) – deficits in executive functioning and personality changes are seen
			* **Alcoholism** associated **thiamine deficiency** (Korsakoff syndrome and Wernicke’s encephalopathy)
			* Parkinson’s disease, **Huntington’s disease**, **normal pressure hydrocephalus** (wet, wacky and wobbly – urinary incontinence, dementia, ataxia), **intracranial masses** (e.g. chronic subdural hematoma)
			* Infections: HIV (AIDS-dementia complex), neurosyphilis, cryptococcal infection, neurocysticercosis, **PRION DISEASES** (Creutzfeldt-Jakob disease), **PML** (JC virus)
			* Metabolic: **hypothyroidism**, B12 deficiency, thiamine deficiency (alcoholics)
			* **Repeated head trauma**/boxing
			* **Pseudodementia** (depression, especially in elderly)
		- Investigations:
			* CBC
			* RFTs,LFTs, TFTs
			* B12 levels, folate, thiamine, syphilis serology
			* CT/MRI
		- **Management:**
			* Reversible causes – Rx underlying conditions:
				+ Hypothyroidism, neurosyphilis, deficiencies (B12, folate, thiamine), depression, NPH, intracranial masses
			* Delay progression with medications (e.g. in AD)
			* Avoid drugs that impair cognition (e.g. sedatives, anticholinergics, neuroleptics, corticosteroids, opiates, etc.)
			* Family education and planning – develop ROUTINES, manage comorbid conditions and depression..
* **Alzheimer’s disease:**
	+ **Onset ~ 40s** (**earlier in Down syndrome** patients)
	+ Inherited forms are **AD**
	+ Risk factors:
		- **AGE**
		- **Family history** (1st degree relative)
		- **Down syndrome**
		- Homozygosity for apo(E) e4 allele
		- Smoking may accelerate onset
	+ Cause:
		- Unknown, but it has been linked to **chromosomes 14, 19, 21**
		- Pathologically, it is believed there to be impaired clearance of **Aß amyloid**, which is a breakdown product of **amyloid precursor protein (APP)**, builds up and produces **senile plaques** around the neuron… and which are selectively **neurotoxic in the Hippocampus** and result in inflammation, but other parts of the CNS are affected (**frontal cortex**, subcortical nuclei [**nucleus basalis of meynert**])
		- As a result of this reaction, **hyperphosphorylation of tau** proteins results in tangles within the neuron (**NFTs**)
		- There is a **reduction in ACh producing neurons**
		- With time, imaging will show **cerebral atrophy**, widening of the sulci and narrowing of the gyri, **widened ventricles**
		- The amyloid (stains with **Congo red**) deposits can result in **amyloid angiopathy**, which can result in **ICH**
		- Diagnosis is confirmed on autopsy, which shows:
			* **Senile plaques (SP)** – specific to AD
			* **Neurofibrillary tangles (NGT)** – non-specific to AD
	+ **Clinical features:**
		- ***Early stage:***
			* **Mild forgetfulness**, **anterograde memory problems** (can’t learn new things), poor performance at work, **poor concentration**, **impaired judgment**
		- ***Intermediate stage:***
			* Progressive memory impairment + **Anosognosia** (lack of insight into patient’s own condition, may be in denial)
			* **Visuospatial disturbances** begin to manifest (getting lost at home, difficulty following directions), repeating questions/**echolalia**
		- **Later stage:**
			* **Executive functioning becomes impaired** along with progressive deterioration of memory
			* **Needs assistance for ADL** and may **forget names** of relatives/friends; may become delusional and show behavioral and mood changes
		- **Advanced disease:**
			* **Completely dependent** on others, **incontinence, bed-ridden, little interest** in anything
			* **Death is usually secondary to infections** (e.g. **pneumonia**)
	+ **Management:**
		- It cannot be reversed, but it **can be slowed down**
		- GOALS: **raise ACh, lower glutamate**
		- ***AChE inhibitors*** (brain-selective ones):
			* **Donepezil**
			* **Rivastigmine**
			* Galantamine
			* Metrifonate
			* ADR = nausea, vomiting, diarrhea, incontinence, cramps, rarely worsens heart block and peptic ulcer disease (give omeprazole? **Do ECG** before starting)
		- ***Anti-glutamate:***
			* **Memantine** (NMDA antagonist)
* **Parkinson’s disease:**
	+ **Cardinal triad** of parkinsonism:
		- ***Resting tremors***
			* **Pill-rolling** of thumb over fingers
			* **Slow frequency** (4 – 6 cycles)
		- ***Hypertonia of rigidity***
			* Includes **leadpipe rigidity** and **cogwheeling** (when with tremors)
		- ***Bradykinesia***
			* **Slow to initiate movements**
			* **Monotonous hypophonic speech**
			* **Micrographia**
			* Reduced blink rate (but also low habituation in glabellar reflex 🡪 **myerson’s sign**)
			* **Expressionless (mask) facies**
			* **Shuffling gait** that becomes **festinating** [lack of arm swinging] (Parkinsonian gait)
		- **Other features:**
			* Depending on type, but some forms can include dementia, gaze palsy, incontinence, motor and sensory deficits
	+ **Parkinsonism includes:**
		- ***PD*** (idiopathic parkinsonism)
		- ***Drug-induced parkinsonism*** (***dopamine antagonists*** such as **neuroleptics** and **antiemetics**)
		- **Acquired parkinsonism** (MPTP intoxication, repeated trauma/boxing)
	+ **Pathology & cause:**
		- Idiopathic as to why the following pathological changes occur
		- **Lack of dopaminergic neurons** arising from the **substantia nigra pars compacta (SNPC)** in the **midbrain** results in an imbalance in the activity of the extrapyramidal system (chiefly the basal ganglia) – **high ACh vs. low dopamine** = low activity
			* Autopsy will show depigmentation of SNPC, reduced number of DA neurons and the remaining neurons may show **lewy bodies**
			* Proteins involved include **a-synuclein** and tau proteins
			* Ubiquitinization of a-synuclein results in LEWY BODIES (classic finding) = synucleinopathy
		- Typical age of onset: **65 years**
	+ **Parkinson-Plus syndromes:**
		- **Worse prognosis** as they **respond poorly to medications**
		- **Progressive supranuclear palsy (PSP)**
			* Vertical **gaze palsy**
			* **Pseudobulbar palsies**
			* Postural instability
		- **Multisystem atrophy (MSA)** – AKA ***Shy-Drager syndrome***
			* Early **autonomic dysfunction** (incontinence, impotence, postural hypotension)
			* Cerebellar and pyramidal signs
		- **Diffuse Lewy Body Dementia (DLBD)**
			* PD + AD
			* PD symptoms appear first, but dementia occurs rapidly after this
		- **Corticobasal ganglionic degeneration (CBGD)**
			* **PD + pyramidal signs** (asymmetrical) + **sensory deficits (KEY)** + cognitive decline
			* Name signifies that it affects the cortex too (frontal cortex, parietal cortex and prefrontal cortex respectively)
	+ **Management:**
		- Patient and family education about the progressive course of the condition and that it **cannot be cured**, but, however **it can be slowed down** (delay progression)
		- Goals of medical therapy = **increase dopamine, lower ACh**
			* Start with **dopamine receptor agonists** (non-ergot alkaloids like **pramipexole and ropinirole**; ergots like cabergoline and bromocriptine) to delay the use of levodopa and carbidopa
			* **MAO-B inhibitor** (**Rasigiline** > **selegiline**) and **AMANTADINE** are also useful initial agents
			* **Anticholinergic agents** are the best drugs to **alleviate tremors** (**trihexyphenidyl, benztropine**)
			* **COMT inhibitors** have a role in late disease but are hepatotoxic (entacopone)
		- Use of **carbidopa-levodopa (Sinemet)**
			* **DOC for PD**, but has a lot of ADR, so **reserve for advanced disease**
			* Levodopa crosses BBB and increases dopamine levels in SNPC, but because it can be broken down to dopamine outside the CNS before reaching BBB (which also increases the ADR), **carbidopa blocks peripheral carboxylases** to increase the amount of levodopa that reaches BBB
			* ADR:
				+ **GI upset (nausea, vomiting)** – activates CTZ!
				+ Hypotension
				+ Arrhythmias
				+ **Hallucinations/psychotic features**
				+ **ON/OFF phenomenon** (try to prevent this by keeping the drug use for advanced disease, try using **controlled release pills** [Sinemet-CR])
			* Don’t forget to Rx any other associated conditions (depression) + provide respite care
		- **Non-medical therapy (last resorts):**
			* **Deep brain stimulation**
			* **Surgical ablation of subthalamic nucleus**
		- Warning:
			* Do not operate heavy machinery
			* Drugs must be discontinued gradually (sudden stoppage is linked to neuroleptic malignant syndrome)
* **Huntington’s disease:**
	+ AD disease with a trinucleotide repeat expansion of CAG, located in chromosome 4
		- Shows anticipation (every successive generation has an earlier onset of disease)
		- Typical age of onset is 30 – 50 years of age
	+ Clinical features:
		- Chorea
		- Altered behavior (irritability, personality changes, antisocial behavior, depression, suicidal tendencies, psychosis)
		- Impaired mentation (dementia develops)
		- Extrapyramidal symptoms and gait disturbances
		- Incontinence
	+ Investigations
		- MRI shows atrophy of the head of the caudate nucleus
		- DNA testing confirms the diagnosis
	+ Management is symptomatic (no curative Rx ☹)

* **Ataxia:**
	+ ***Clinical features:***
		- **Poor coordination** (“point”)
		- **Loss of balance** (“stand”)
		- **Unstable gait** (“walk”)
	+ Depending on the cause of ataxia, there may be other features:
		- Cerebellar ataxia (damage to the spinocerebellar tracts or the cerebellum itself)
		- Sensory ataxia (damage to dorsal column tracts which bring in conscious proprioception)
	+ Causes:
		- Alcohol intoxication and thiamine deficiency
		- Vitamin B12 deficiency (SCD of SC)
		- Cerebellar stroke
		- Drug intoxications (e.g. AED like phenytoin)
		- Tertiary syphilis (tabes dorsalis)
		- Multiple sclerosis
		- Lung cancer (paraneoplastic)
		- Cerebellar tumor
		- Inherited causes (frederich’s ataxia and ataxia telangiectasia)
* **Spinal cord related problems**:
	+ Causes of paraplegia
		- Cord and dural problems:
			* Syringomyelia
			* Anterior spinal artery occlusion
			* Poliomyelitis
			* Transverse myelitis
			* Motor neuron disease
			* Tabes dorsalis (tertiary syphilis)
			* Intramedullary tumors, meningioma
			* Inherited ~ Friedreich’s ataxia
			* Deficiencies ~ B12 deficiency, B3 deficiency and B1 deficiency (B1 deficiency also affects brain [Wernicke- Korsakoff] and, B6 deficiency causes peripheral neuropathy)
		- CNS problems:
			* Encephalitis
			* Acute disseminated (post-infectious) encephalomyelitis
			* Superior sagittal sinus thrombosis
			* Parasagittal meningioma or subdural hematoma
			* Cerebral palsy
		- Vertebral problems:
			* Disc prolapse
			* Spondylolysis and spondylosis
			* Metastasis (prostate, lung, breast)
			* Multiple myeloma
			* Pott’s disease (TB)
		- Presentation:
			* If the cause is ACUTE (vascular, traumatic), there is an initial stage of flaccid paralysis (spinal shock stage) and then a second stage of spastic paralysis (in 2 – 6 weeks)
			* If the cause is GRADUAL (e.g. neoplastic), there is no shock stage
	+ **Syringomyelia and syringobulbia**
		- The central canal of the spinal cord normally communicates with the 4th ventricle
		- In syringomyelia, there is a dilation of the central canal (typically because of blocked CSF circulation)
			* It may be associated with Arnold-Chiari malformations (II = children, cerebellar vermis [and tonsil and associated with lumbosacral meningomyelocele], I = adults, cerebellar tonsils)
			* Most common locations: cervical syrinx > lumbar syrinx
		- May be static for years and suddenly worsen with repeated increase in CNS pressure (sneezing, coughing)
		- Clinical features:
			* Because it initially impinges on the crossing of lateral spinothalamic tracts bearing pain and temperature sensation at a specific level, there is dissociative sensory loss of pain and temperature ONLY
			* The P & T loss levels depends on how large the syrinx is… The tracts themselves do not get disturbed initially, so the loss of P & T is isolated (typically in the upper limbs in the distribution of a cape/jacket)
			* Patient typically will complain of burning hands over fire or stove because they did not feel it
			* Eventually the syrinx grows to involve the anterior horn cells and cause LMNL on the affected levels (small muscles of hand atrophy and so on) 🡪 fasciculations, weakness, atrophy, hyporeflexia, hypotonia
			* Later, the lateral corticospinal tracts become involved and result in spastic paraplegia
			* Also associated with charcot joints, pes cavus
		- Investigations:
			* MRI
		- Management:
			* Decompression may be required (neurosurgery consult)
	+ **Brown Sequard syndrome**
		- Hemisection of the spinal cord (typically at cervical level ☹)
		- Causes:
			* Trauma (fracture, stab wound)
			* Crush injury to one side of the spinal cord
			* Tumors and abscesses that impinge on one side
		- Clinical features:
			* Unilateral anesthesia and muscle paralysis (LMNL) on the dermatomal level of the SC segment (E.g. left T4 = left half of chest as a strip line including the left nipple)
			* Sensory dissociation with loss of dorsal column sensation ipsilateral and below the lesion (E.g. left sided loss of fine touch, pressure, vibration and conscious proprioception below T4) and loss of lateral spinothalamic tract sensations contralateral and further below the lesion (e.g. right sided loss of pain and temperature <<T4)
			* Because of damage to the lateral corticospinal tract (uncrossed), there is ipsilateral UMNL below the level of the lesion (E.g. left sided hypertonia of spasticity, hyperreflexia, Babinski sign, clonus, etc.)
	+ **Transverse myelitis**
		- Tracts are affected across the horizontal aspect of the spinal cord
		- Cause is unknown, but have been associated with:
			* Viral infections
			* Multiple sclerosis variants (Devic syndrome)
		- Clinical features:
			* Depends on level and sites affected (thoracic level MC)
			* Acute or subacute neurological S&S of motor, sensory and/or autonomic dysfunction
		- Imaging:
			* MRI
			* Serum NMO IgG Ab (R/O Devic)
		- Management:
			* Unpredictable course (most patient with idiopathic TM have at least partial recovery, but 40% get some form of permanent disability)
			* High dose steroids and plasmapharesis may play a role in management
	+ **Poliomyelitis**
		- Cause = polio virus
		- Clinical picture:
			* Selectively infects anterior horn cells (results in LMNL)
			* Typically involves the legs (paraplegia)
			* Bulbar involvement (bulbar palsy) of CNIX and CNX can result in respiratory and cardiovascular impairment
		- Management:
			* No Rx available (supportive management, physiotherapy)
			* Prevention is with the polio virus vaccinations (OPV and IPV are available)
	+ **Neurosyphilis**
		- Cause = Treponema pallidum (spirochete)
		- Occurs in TERTIARY SYPHILIS, which includes:
			* **Neurosyphilis**
			* **Syphilitic aortitis** (aortic aneurysm)
			* **Gummas**
		- **Neurosyphilis involves:**
			* Meninges (**aseptic meningitis** picture)
			* **Ocular syphilis** (**optic neuritis**, uveitis, optic atrophy, Argyll-Robertson pupil)
			* **Tabes dorsalis**
			* **General paralysis of the insane** (General paresis) – dementia, personality changes, behavioral changes, psychosis, motor features are seen
		- **Tabes dorsalis:**
			* **Dorsal column and posterior root** involvement and degeneration
			* Results in loss of dorsal column sensation at the lesion and below (with **+ve Romberg sign** when patient closes their eyes; and **pseudoathetosis**)
			* There is also **“LANCINATING PAINS”** which are severe, knife-like, shooting pains at the limbs, back or face lasting for minutes to days
			* Since the afferent fibers don’t make it to the SC properly, there is also diminished reflexes (hyporeflexia)
			* Associated with **Argyll Robertson pupils** (Accommodates but **does not react to light**)
		- **Investigations:**
			* CSF analysis (lumbar puncture) with CSF-VDRL (most commonly), but CSF-FTA/ABS can be done too if VDRL is –ve in CSF and you still suspect it
			* Nonspecific (VDRL/RPR) and specific tests (FTA-ABS) with the latter much better in later syphilis
		- **Rx = Penicillin G** (Now rare in the antibiotic era ☺)
	+ **Cervical spondylosis**
		- It is basically osteoarthrosis of the cervical spine that results in a **myelopathy** (**compression of the cord**) and **radiculopathy** (**compression of the spinal nerve roots**) as a result of degenerative progressive bony changes
		- Because of repeated movement, the cord becomes further damaged by the bony spurs and ligamentum flavum
		- Clinical features:
			* **Limited and painful neck movements** +/- crepitus
			* **Positive Lhermitte’s symptom** (as seen in MS)
			* **Radiculopathy pain** (pain following the supply of the root) and LMN signs because the motor fibers of anterior root join the posterior root to form the spinal nerve
		- Investigations:
			* **MRI** to localize the lesion and R/O DDx (bone or cord tumors)
		- Management:
			* **Neck collar** (restrict movement for healing)
			* **Transforaminal steroid injection**
			* **Surgical options** (surgical root decompression by **laminectomy** or laminoplasty)
	+ **Motor neuron disease**
		- Degenerative disease characterized by **selective loss of motor nerve cells** in the motor cortex, cranial nerve nuclei and anterior horn cells
			* **HALLMARK = UMNL + LMNL** and *no* sensory loss and spares the eyes
			* This distinguishes it from MS and polyneuropathies (former) and myasthenia gravis (latter)
		- **Clinical patterns include:**
			* **Amylotrophic lateral sclerosis (ALS)** – **MC – 50%** -AKA **Lou Gehrig’s disease**
			* Progressive bulbar (medulla) palsy
			* Progressive muscular atrophy
			* Primary lateral sclerosis
		- **ALS:**
			* Motor cortex (UMNL) + anterior horn cells (LMNL)
			* **Worse prognosis if** there is initial bulbar involvement, **diagnosed at an older age** and **low FVC** (yes)
			* **Split hand sign** = atrophy of thenar eminence and sparing of hypothenar eminence
		- **Clinically:**
			* **Look for UMN signs** (Babinski, hyper-reflexia, hypertonia of spasticity) and LMN signs (wasting, fasciculations); look for bulbar palsy signs (impaired speech or swallowing)
			* **LMN + UMN signs in 3 REGIONS = clinical diagnosis**
			* Compromised respiratory and swallowing functions poses many threats including respiratory failure, aspiration and choking
			* *Is there autonomic dysfunction or problems with mentation?* **NO!** The easiest way to recall this is by remembering that Dr. Stephen Hawking has ALS – and he *IS A GENIUS* and *HAS CHILDREN*.
		- Management:
			* Non-medical (Multiple-disciplinary team, end of life care)
			* **Symptomatic Rx** (for drooling, dysphagia [NG tube], joint pains and distress [WHO analgesic ladder], respiratory failure [non-invasive ventilation])
			* Anti-glutamate drugs have been found to prolong life by 3 months, and this includes ***RILUZOLE***, which is EXPENSIVE and has many ADR
	+ **Cauda equina syndrome**
		- Cauda equina is the collection of spinal nerves from the lumbar and sacral spinal cord segments that must travel down to exit below their corresponding vertebra because the spinal cord ends at level L1/L2 in adults
		- The cauda equina lies freely in the lumbar cistern (the dura and arachnoid matter continue down to the S2 vertebral level and so the space between the end of the SC [conus medullaris] and the end of the meninges is filled with CSF – which is the best place to collect CSF in LP)
		- Causes of lesion to the cauda equina:
			* Congenital = spina bifida
			* Traumatic = lumbar vertebral fracture or dislocation
			* Inflammatory = Pott disease of vertebra
			* Neoplastic = meningioma, metastatic, vertebral
			* Degenerative =lumbar spondylosis
		- Manifestations:
			* Cauda equina includes L2 – S5 spinal nerves, which have motor, sensory and autonomic functions, so expect motor, sensory and autonomic dysfunction
			* Motor manifestations = LMN weakness in one or both lower limbs (this includes the knee [L3, L4] and ankle [S1, S2] reflexes and joint movements at the hip, knee, ankle and toes) + loss of anal tone (S3, S4, S5)
			* Sensory manifestations = initially there is radicular pain referred to the lower limbs (either along the femoral distribution [L2 – L4] or sciatic distribution [L4 – S3]… Eventually there is hypoaesthesia and anesthesia (ALL kinds of sensation) in the same areas including the saddle area (S3, S4, S5)
			* Autonomic manifestations (sphincteric manifestations of bladder [overflow incontinence/atonic bladder/autonomic bladder], vasomotor changes and trophic ulcers)
			* *Is there impotence – which is in part mediated by the parasympatethic nerves from the lateral horns of the spinal cord at the level of S2-S4*? IT IS POSSIBLE, but the cause is not a damage to the SC, but the nerve fibers traveling through the roots in the cauda equina
	+ **Conus medullaris lesion:**
		- The conus medullaris is the very tip of the spinal cord
			* It generally comprises the segments of S3 – S5
			* The region above it is known as the epiconus, which comprises the segments L4 – S2
		- Clinical features:
			* Motor problems? *Not really*
			* Sensory problems? *Saddle area loss of sensation*
			* Autonomic problems? *YES,* so expect impotence and bladder control problems (overflow incontinence because PS fibers won’t work)
			* So? Saddle loss of sensation + impotence + overflow incontinence
	+ **Epiconus lesion:**
		- Segments L4 – S2 (above the conus medullaris, S3 – S5)
		- These segments include important motor and sensory portions
		- Clinical features:
			* Motor problem? *Yes, absent ankle reflex* BUT *preserved knee reflex (kinda)* + *lower limb weakness (think of the sciatic nerve supply which is L4 – S3 – so hip extensors, knee flexors and dorsiflexion and plantar flexion of the foot)*
			* Sensory problems? *Yes, L4 – S2 (leg, foot and back of thigh)*
			* Autonomic problem? *Not really, unless late (S2 of S2 – S4) and if there is a bladder problem it will be a “UMNL” so there is a hypertonic bladder (overflow incontinence)*
		- Remember, if you find a “bad” ankle motor function, see if the gluteus muscle extension is fine:
			* If yes, then this is a neuropathy (this would be obvious, because the patient will also complain of sensory problems distally)
			* If not 🡪 could be radicular (cauda equina affecting L2 and below) or segmental/myelopathic (e.g. epiconus affecting L4 – S2)
* **Neuropathies and related conditions:**
	+ Neuropathy can be divided into the distribution or type of nerve affected or pathological findings:
		- Mononeuropathy vs mononeuropathy multiplex vs polyneuropathy
			* Mononeuropathy multiplex = more than one nerve trunk in one limb/location
		- Autonomic neuropathy, motor or sensory neuropathy (but this occurs seldom alone)
		- Axonopathy or demyelination
	+ DDx
		- **Mononeuropathy:**
			* **Trauma:** injection site damage, callus compression
			* **Infective:** leprosy, herpes zoster
			* **Vascular:** PAN, Churg-Strauss (Eosinophilic GPA)
			* **Metabolic:** DM (can cause everything…)
			* Neoplastic?
			* THE MOST COMMON = CARPAL TUNNEL SYNDROME
		- **Polyneuropathy:**
			* **INFECTIVE:** viral (mumps, measles, acute post-infectious), bacterial (**diphtheria, typhoid**, tetanus), mycobacterial (**leprosy**)
			* **TOXIC: Heavy metals** (LEAD, arsenic) and chemicals (alcohol, insecticides)
			* **NUTRITIONAL:** Beri-beri (B1/thiamine deficiency), pellagra (B3 deficiency), B6 (pyridoxine) deficiency, B12 deficiency (SCD)
			* METABOLIC: DM, uremia, porphyria, amyloidosis
			* AUTOIMMUNE: GBS, rheumatological (RA, PAN, systemic sclerosis, SLE)
			* IATROGENIC: INH, sulfonamides
			* NEOPLASTIC: myeloma, lymphoma, lung cancer
	+ **Acute Inflammatory Demyelinating Polyradiculopathy (AIDP)** –***Guillian Barre Syndrome***
		- DDx:
			* Acute transverse myelitis
			* Poliomyelitis
			* ALS
			* Vasculitis
			* Spinal muscular atrophy
		- Typically **preceded by an infection** (URTI or GIT infection) 3- 6 weeks prior (rarely, from vaccinations)
		- Cause?
			* Thought to be an autoimmune cross-reaction secondary to **molecular mimicry** of Ab against the agent causing the infection and the nerves resulting in demyelination of the axons, particularly of MOTOR NERVES
			* **Campylobacter jejuni** > **CMV**, EBV, HIV, hepatitis virus
			* May also occur in lymphomas, SLE and post-op
		- Variants?
			* **Miller-Fischer syndrome:** ophthalmoplegia + ataxia + areflexia
		- **Clinical features:**
			* **ABRUPT ONSET**, **RAPIDLY ASCENDING WEAKNESS** of all four **extremities** + **facial muscles** + **bulbar muscles**
			* Usually **symmetrical** polyneuropathy
			* **Typically begins distally** to proximal (lower limbs > upper limbs), but in 10% it can begin in the arms and facial muscles
			* Generalized paralysis could mean that the **diaphragm is also paralyzed** 🡪 RESPIRATORY ARREST risk
			* Is there sensory loss? *Not commonly, but it is possible* – but there is parasthesias
			* Are there **autonomic features**? ***YES (70%)!*** Arrhythmias, tachycardia (MC) & bradycardia and postural hypotension and they can be dangerous and are associated with sudden death
		- Progression/Course:
			* Usually progresses over the period of two weeks
			* By 4 weeks, >90% of GBS patients have reached the nadir, but to recover 100% to normal takes time and effort
			* If still symptomatic/progressive >8 weeks = CIDP
		- Investigations?
			* **Neurophysiology studies (NCS and EMG)** will show mostly demyelination pattern (low/absent NCV) than axonal injury (Severe cases – NCV amplitude is low)
			* **CSF analysis** will show albuminocytologic dissociation (elevated CSF protein but normal WBC count) in 66% after 1 week of symptom onset and >75% by week 3
			* Millard-Fischer is associated with anti-GQ1b (ganglioside component of nerves)
		- **Diagnosis is clinical** and supported by other findings:
			* Progressive motor weakness
			* Areflexia or hyporeflexia in those weak limbs
		- **Management:**
			* ***Supportive care:***
				+ Initial admission into ICU for monitoring, but then stratify (could be ok in intermediate care unit or general ward)
				+ You must carefully **monitor pulmonary functions** > cardiac and hemodynamic functions
				+ If necessary, **mechanical ventilation is indicated (low FVC <20 ml/kg)**
				+ **Pain control** (gabapentin or carbamazepine)
				+ **Bowel and bladder care** is important
				+ **Physiotherapy and rehabilitation**
				+ For older adults, don’t forget about DVT prophylaxis
			* ***Medical Rx:***
				+ **IVIG** if the patient has significant weakness
				+ If IVIG doesn’t work, **PLASMAPHARESIS**
				+ *DO NOT* give steroids
	+ **Bell’s Palsy**
		- Bell’s palsy = ***IDIOPATHIC*** facial nerve palsy (LMNL)
		- DDx of **unilateral facial nerve palsy?**
			* **Bell palsy** (idiopathic)
			* **Stroke** affecting brainstem
			* **Otitis media** (affects CN7 in the middle ear)
			* **Herpes zoster/VZV** (Ramsay Hunt Syndrome 🡪 facial palsy + ear vesicles + ear pain; here VZV reactivates in geniculate ganglion)
			* Meningitis and brain tumors (e.g. **CPA syndrome**)
			* **MS, GBS (often bilateral)**
			* **Sarcoidosis**
			* **Sjogren’s syndrome, EGPA**
			* **Parotid gland tumor**
			* **LYME DISEASE**
			* Others (diving, **trauma**; from **forceps delivery**)
		- BELL’S PALSY IS A **DIAGNOSIS OF EXCLUSION**
		- **Cause of BELL’S PALSY?**
			* *Idiopathic,* BUT
			* It has been associated with exposure to cold air drafts, edema and compression of the nerve at the stylomastoid foramen or because of a neurotropic virus (e.g. HSV or VZV) or an autoimmune phenomenon (raised Ig found in patients)
		- **Clinical features:**
			* **Abrupt onset** (found **upon waking up**)
			* Onset usually with **acute pain behind the ear**
			* **Unilateral facial paralysis 1 – 2 days later** (LMNL)
			* Expect lack of wrinkling of the forehead, inability to blink/cover the eyes completely, loss of nasiolabial fold, drooping mouth (with drool) on affected side, asking to “show me your teeth” will show the mouth deviating to the unaffected side (rule of 17), and asking them to blow their mouth will show easy air loss on the affected side; saliva will drool over the affected side
			* Speech difficulty (phonation problem), impaired taste in anterior 2/3rd of tongue = ageusia (*sensation* in anterior 2/3rd is intact because it is transmitted by CNV3); food trapped between gum and cheek; probably can’t whistle (orbicularis oris)
			* **Bell phenomenon** = when telling patient to close their eyes, the affected eyes will not close properly and the eyeball may be rolling up in this attempt at closure
			* Complication of reduced eye blinking include ectropion and injury from foreign bodies 🡪 conjunctivitis and scarring
		- **Investigations:**
			* No need, but do it to R/O differential diagnosis
			* Americas 🡪 **borrelia antibodies, VZV Ab titers**
			* Imaging 🡪 MRI
			* Neurophysiology 🡪NCS
		- Management
			* **Prednisolone PO** (**within 72 hours**) for **5 days**
				+ DO NOT use this if you suspect Lyme disease
			* **Supportive** (**protect the eye** [with dark glasses, artificial tears, tape it when asleep at night], massage facial muscles)
			* Surgical management options ~ plastic surgery to help lid closure; surgical decompression
		- Prognosis:
			* In general, **most people will make complete recovery** (few weeks – 4- 6 weeks)
			* Those with axonal degeneration (15% in general, 50% in pregnancy) and delaying in therapy results in **aberrant reconnections** such as **crocodile tears** (gusto-lacrimal reflex, crying when eating) and **synkinesis** (upturning mouth when blinking)
	+ **Trigeminal neuralgia**
		- AKA **Tic Douloureux**
		- Cause? *Idiopathic*
		- **Postulations?**
			* **Compression of the trigeminal nerve root near pons**
			* Classically thought to be due to an **aberrant loop of an artery or vein pressing on the CN5**
		- Clinical features:
			* EXTREMELY EXCRUCIATING brief but frequent attacks of severe, **LANCINATING facial pain** in the CNV2 and CNV3 areas of the face (especially near midline)
			* Patients try to protect anything or anyone from coming near the midline (or face in general), fearful of an impending attack
			* Attacks last from seconds to minutes and are typically described to be one of the most painful conditions known to mankind ☺
			* **TRIGGERS?** Cold air, smiling, chewing, talking, brushing teeth
			* *NO* motor or sensory features
		- Investigations and diagnosis:
			* Clinical diagnosis
			* MRI can be done to R/O CPA masses (e.g. acoustic neuromas) that can compress the CN5
		- Management:
			* Course is relapsing/remitting ☹
			* **DOC = carbamazepine** (other drugs have been used too, such as lamotrigine, baclofen, …)
			* Surgical management in refractory cases = **surgical root decompression**
	+ **Vitamin deficiencies**
		- **Vitamin B1 (Thiamine) deficiency:**
			* **Wet beri-beri** = **heart failure features (DCM)**
			* **Dry beri-beri** = **peripheral sensory neuropathy**
			* Wernicke and Korsakoff syndrome in chronic alcoholics:
				+ **Korsakoff psychosis** (affects mammillary bodies/hypothalamus and cortex):

**Anterograde amnesia**

**Confabulations** (make up shit)

**Apathy**

* + - * + **Wernicke’s encephalopathy** (pons, cerebellum):

**Confusion**

**Cerebellar ataxia**

**Ophthalmoplegia**

* + - * In 80%, both occur together
			* Management = thiamine and supportive management for related conditions (e.g. for HF)
			* ***DON’T GIVE GLUCOSE BEFORE THIAMINE*** in hypoglycemic (or let’s just say, unconscious) alcoholics because the problem is that thiamin is a cofactor for pyruvate dehydrogenase to make acetyl-CoA for TCA cycle, but because there is low thiamine, all the pyruvate is pushed to become lactic acid and with more glucose given this becomes even worse! So **giving glucose before thiamine will WORSEN the ENCEPHALOPATHY**
		- **B3 deficiency (B3 = NAD= niacin)**
			* B**3** deficiency = Pellagra = **3**Ds
			* **D**ermatitis on sun-exposed areas that becomes rough, scaly and pigmented
			* **D**iarrhea and other GI manifestations occur (including HSmegaly)
			* **D**ementia and other neuropsychiatric manifestations (anterograde dementia, suicidal tendencies, depression, peripheral neuropathy, muscle weakness)
		- **B6 deficiency (B6 = Pyridoxine)**
			* B6 is *very* important for decarboxylation reactions as well producing heme, neurotransmitters (dopamine, serotonin, NE & E), histamine and for transamination reactions (AST, ALT) and to produce B3 (you need B2, B6 and tryptophan to make niacin) and last but not least glycogen phosphorylase ☺
			* Most importantly, occurs secondary to INH use in TB Rx
			* Deficiency results in hematological and neurological changes
			* Hematological = SIDEROBLASTIC ANEMIA
			* Neurological = **CONVULSIONS** and **PERIPHERAL NEUROPATHY**
		- **B12 deficiency (cobalamin)**
			* B12 also has many important functions, some of which work together with B9 (Folate)
			* B12 is needed to make methionine from homocysteine (it helps take CH3 from THF [B9])… Menthionine becomes SAM, and SAM gives away CH3 (methyl group) for important anabolic pathways to produce DNA. Then SAH is left, SAH becomes homocysteine again and the cycle continues
			* B12 is also important for converting methylmalonyl CoA to succinylCoA (this is the pathway to break down odd chain fatty acids and make them join TCA)
			* It’s important to know that it comes from animal products (so food only) and it needs IF from the gastric parietal cells (secrete IF and HCl) so it can be absorbed in the terminal ileum – in our body we have a very large reserve pool in the liver, so it would take *years* of no B12 intake for you to get a deficiency
			* Deficiency occurs with poor or vegan diet, D. latum (fish tapeworm) infection, pernicious anemia (autoimmune condition against gastric parietal cells), gastric bypass and anything that impairs terminal ileal absorption (Crohn’s disease, surgical resection)
			* Deficiency results in HEMATOLOGICAL and NEUROLOGICAL changes
			* Hematological changes = Megaloblastic macrocyctic anemia (peripheral smear shows hypersegmented PMNs and bone marrow shows megaloblasts) – BIGGEST DDx is B9 deficiency, HOWEVER, *B9 deficiency DOES NOT HAVE NEUROLOGICAL FEATURES* and in any case, don’t treat megaloblastic anemia with B9 alone, either give B12 or B12 *and* B9 (if you happen to give B9 and it turns out it was B12 deficiency, if the patient has neurological changes it will become WORSE!)
			* B12 anemia is associated with glossitis (beefy red tongue), angular stomatitis and GIT manifestations
			* Btw, labs in B12 deficiency will show high homocysteine and methylmalonic acid levels
			* Neurological changes (related to loss of myelin) = Subacute combined degeneration of spinal cord – Dorsal column tract AND lateral corticospinal/spinocerebellar tracts are affected by demyelination (hence “combined” for dorsal and lateral columns)
			* It is important to note that the patient will have limb weakness with Babinski sign (UMNL as a result of the CST demyelination), parasthesia/sensory disturbances (except to pain and temperature) and ataxic gait
			* Without prompt treatment, neurological disturbances can become permanent
			* Rx = IM vitamin B12, Rx underlying cause
	+ **Inherited *neuropathies***
		- ***C*harcot-*M*arie-*T*ooth disease** (Peroneal muscular atrophy)
			* **MC inherited neuropathy**
			* Starts in puberty, QOL is good
			* Gene involved (you guessed it) is *CMT*1 gene
			* Clinical features include **muscle atrophy** in lower limb (leg and foot) with **foot drop** and **pes cavus**
			* The atrophy results in an “**upside-down champagne bottle**” appearance
* NMJ problems:
	+ **Myasthenia gravis (MG)**
		- Autoimmune disease mediated by **anti-AChR Ab** against ***post-synaptic*** Nm receptors at the **neuromuscular junction** of skeletal muscles [which is supplied by SOMATIC nerves that release ACh (presynaptic) and the receptor is nicotinic (Nm)]
		- MG is associated with **thymoma** or **thymic hyperplasia**
		- Epidemiology:
			* **<50 years old** 🡪 **females** (think autoimmune conditions and thymic hyperplasia)
			* **> 50 years old** 🡪 **male** (think neoplastic or rheumatologic)
		- DDx to worry about? **Lambert-Eaton**, polymyositis, SLE
		- **Clinical features:**
			* Symptoms:
				+ Skeletal muscle weakness and **FATIGUABILITY** in a descending march course
				+ **Order:** **extraocular, bulbar** (swallowing and chewing) **face, neck, limb girdle and trunk**
				+ Weakness is **worsened by activity**, by the **end of the day** and by certain stressful situations
				+ **Ptosis, diplopia and blurred vision** (most common initial symptoms – so first *place* is the *face* – that rhymed!)
				+ Dysphagia, dysphonia are less common
			* Signs:
				+ **Ptosis**
				+ **Myasthenic snarl** (when asked to smile, they look like they’re snarling)
				+ **Peek sign** (inability/weakness to sustain eye closure for long, resulting in appearance of the sclera)
				+ **Tendon reflexes are NORMAL** (*not hyporeflexia*) – Why? This muscle spindle reflex is brief and does not involve much fatigue!
				+ NO muscle wasting or fasciculations (not a LMNL)
				+ **Tensilon test** (give edrophonium, which is an AChE inhibitor 🡪 improve symptoms, but not very nice because of cholinergic ADR – DUMBBELLS)
			* **Myasthenic crisis = medical emergency**
				+ 15% of patients can get **diaphragm and intercostal muscle fatigue** resulting in poor respiration
				+ This can lead to **respiratory failure** (type II), which will need mechanical ventilation
		- Investigations:
			* Serology = **anti-AChR Ab** (90%) 🡪 if –ve 🡪 MUSK Ab
			* Neurophysiology studies:
				+ EMG and NCS (**repetitive nerve stimulation** results in diminished recruitment)
			* Imaging = **CT scan of THYMUS** (R/O thymoma)
		- Management:
			* **AChE inhibitors**
				+ **Py*rido*stigmine** – gets *rid* *of* myasthenia - +/- neostigmine?)
				+ ADR are DUMBBELLS (diarrhea, lacrimation, salivation, sweating = MC)
				+ Careful in ASTHMATICS
			* Immunosuppressive therapy **in relapses**
				+ Prednisolone with vitamin D
				+ Azathioprine or methotrexate
			* **Thymectomy**
				+ If **<50 years old**
				+ Not easily controlled by AChE inhibitors
				+ HAS thymomas? - You MUST do this!
			* **Myasthenic crisis:**
				+ **Supportive**, **monitor FVC**, **ventilator support** if <20 ml/kg (same as GBS)
				+ **IVIG and plasmapheresis** may play a role too (just like? GBS!)
		- Just FYI, there is also neonatal, congenital and secondary myasthenia (SLE, polymyositis and lambert-Eaton syndrome)
	+ **Lambert-Eaton (myasthenic) syndrome**
		- Result of antibodies against ***pre-synaptic*** voltage-gated Ca2+ channels (**VGCC Ab**), which disallows calcium influx for the release of ACh to the synaptic junction
		- Cause:
			* Neoplastic (small cell lung cancer) – may occur earlier than cancer S&S
			* Autoimmune condition (on its own)
		- Clinical features that distinguish it from MG:
			* Muscle weakness **IMPROVES by end of the day** and with **activity** (more Ca2+ builds up)
			* **Gait disturbances occur BEFORE** eye signs
			* There is **HYPOREFLEXIA**
			* DOES NOT respond to Tensilon test
			* Repetitive nerve stimulation causes **increased recruitment** (becomes BETTER) at least by >60%
		- Management:
			* Rx underlying cause
			* Medical? 3,4-diaminopyridine (I swear I read it somewhere in USMLE step 1 ☺)
* **MYOPATHIES** (problems in the ACTUAL muscles):
	+ **Duchenne muscular dystrophy (MC)**
		- **X-linked recessive** disorder (males > females)
		- Frameshift or nonsense mutation results in truncated **dystrophin** (which is important for holding muscle cell cytoskeleton to the muscle cell wall)
		- **Clinical features:**
			* **Progressive muscle weakness** that begins in early childhood (**onset = 1st decade of life**)
			* Begins in the **pelvic girdle muscles** (this results in the ***Gower maneuver*** [need to use arms to help them stand up], ***waddling gait*** and ***calf muscle pseudohypertrophy*** [replaced with fat and fibrous tissue because muscle cells die])
			* Progresses proximally to involve trunk and other muscles, including the diaphragm (respiratory failure/needs assisted ventilation) and the heart (**Dilated cardiomyopathy** = MCC of death)
			* Weak back muscle results in **scoliosis**
			* Eventually they become wheel-chair bound and require mechanical ventilation
			* Death typically occurs **by 2nd to 3rd decade of life**
		- Investigations:
			* Lab 🡪 **high CK levels** (and aldolase?)
			* **Genetic studies**/DNA testing
			* Western blot and **Muscle biopsy**
			* ECG/Echo
		- Management:
			* No cure, supportive care
			* Steroids may be of benefit
			* Surgery may be required for scoliosis correction
	+ **Becker muscular dystrophy**
		- X-linked recessive disorder like DMD (but less common)
		- Partially functional dystrophin is present
		- Clinically less severe than DMD
			* Onset is in adolescence or early adulthood (20s – 30s)
			* Wheel-chair bound at a much later stage
			* NO ECG changes and no skeletal deformities
	+ **Myotonic dystrophy**
		- AD disease due to a CTG trinucleotide repeat expansion
		- Clinical features:
			* DISTAL muscular weakness (vs. DMD, BMD) and wasting
			* Myotonia (hard for them to let go of what they hold; e.g. when you shake their hand they don’t let go)
			* Arrhythmias
			* Cataracts
			* Frontal balding
			* Testicular atrophy
	+ Others (fuck you, I’m not going to explain them, Google them)
		- Facio-scapulo-humeral (Landouzy-Dejerine)
		- Limb-girdle disease (scapulohumeral)
		- Inflammatory myositis (poly and dermatomyositis, inclusion body myositis)
		- Acquired (Cushing, hyperthyroidism, malignancy)
		- Painful myopathy occurring with exercise, think McArdle’s disease (glycogen storage disease type 5)
* **Neurocutaneous conditions**
	+ Tuberous sclerosis
	+ Neurofibromatosis
	+ Sturge-Weber syndrome
	+ Von-Hippel-Landau syndrome
* **Headache and DDx**
	+ **MC neurological complaint** = headache
	+ **Causes:**
		- Tension headache (MC)
		- Cluster headache
		- Migraine headache
		- SAH, venous sinus thrombosis, intracranial hematomas
		- CNS infections (meningitis, encephalitis)
		- Space-occupying lesions (e.g. tumors)
		- Low ICP (e.g. following LP or CSF leak)
		- Acute glaucoma
	+ **Acute single episode of headache DDx?**
		- With **meningism** (neck stiffness), R/O:
			* *Meningitis* (fever, photophobia)
			* *Encephalitis* (fever, seizures, personality changes, etc.)
			* *SAH* (sudden onset, worst headache of my life, thunderclap, occipital, consciousness may be depressed or lost)
			* You MUST admit them and do an **emergency CT scan** and if no findings + no CI to LP, do an LP!
		- **Following head injury**, R/O:
			* *Epidural hematoma* (lucid interval, drowsy, focal signs)
			* *Subdural hematoma*
		- Following seizure/lower limb weakness and signs of high ICP or gave birth recently?
			* Venous sinus thrombosis
		- Elderly patient with constant, aching pain **around one eye**, radiating to the forehead, with **blurred vision and haloes** + **nausea and vomiting**? *ACUTE GLAUCOMA*
	+ **Recurrent acute attacks of headaches DDx?**
		- *Migraines*
		- *Cluster headache*
	+ **Subacute headaches DDx?**
		- *Giant cell temporal arteritis* (exclude in all *>50 years* and *new onset* of headache for weeks, *temporal* pain and *tenderness*, temporal artery is thick, tender and *pulseless*, *jaw claudications*) 🡪 prompt *high dose IV steroids* before investigations
	+ **Chronic headache DDx?**
		- Tension headache
		- Raised ICP (worse when lying on back, coughing; may have vomiting, papilledema, seizures, etc.)
		- Medication overuse (analgesic rebound headache)
	+ **What are the red flags of a headache?**
		- Onset of new headache in someone >50 years old
		- Sudden, severe onset
		- Worst headache of someone’s life
		- Headache after head trauma
		- Headache with fever, neck stiffness and a rash
		- Headache in someone with HIV or cancer
		- Headache with mental status changes
		- Headache with focal neurological deficits
* **Tension Headache:**
	+ Cause?
		- Not sure, but related to STRESS, ANXIETY, DEPRESSION
	+ Clinical feature:
		- Steady, aching, tight band-like headache around the head
			* Most intense around the neck or back of the head
		- Muscle tenderness and tightness may be present (especially in posterior neck muscles)
		- Remember that it is:
			* Bilateral
			* Steady pain
			* NOT accompanied by aura, photophobia or phonophobia
	+ Management:
		- R/O DDx first
		- General measures:
			* Massage muscles
			* Stress relief promotion
		- Symptomatic relief with medications:
			* NSAIDs or acetaminophen
		- Rx underlying depression or whatever
* **Cluster headache**
	+ Cause? Not sure (but more common in males and smokers)
	+ Men > women (5:1!)
	+ Clinical manifestations:
		- Rapid onset of excruciating periorbital pain (around ONE eye)
			* Pain is strictly UNILATERAL!!!!!
			* Almost always affects the same side every time
			* Can last from 15 minutes to 3 hours
			* Can occur once or twice on the same day
		- The affected eye becomes WATERY, INJECTED (very red) with MIOSIS, lacrimation
		- Swelling of the eyelid, ptosis, facial flushing and rhinorrhea can occur
			* So they can present with features of Horner syndrome because they have ptosis, miosis
	+ Management:
		- Acute attack:
			* 100% O2 for 15 minutes by non-rebreather mask (unless COPD patient of course)
			* Sumatriptan SQ
		- Prophylaxis:
			* Of all headaches, most responsive to prophylaxis
			* ***Verapamil*** (CCB) taken daily = DOC
* **Migraine headaches:**
	+ Inherited disorder more common in:
		- WOMEN > MEN
		- Those with family history
	+ Pathogenesis = uncertain
		- Might be related to serotonin
		- Or irritation of the CNV, meninges or cerebral blood vessels
	+ Types:
		- Migraine with aura (classic) ~ 15%
			* Aura precedes headache (1 hour typically)
			* Aura is typically visual disturbances (flashing lights, scotomata, distortions like melting lines or zigzags)
			* Can be neurological (sensory disturbances, hemiparesis, ataxia, ophthalmoplegia, speech disturbance)
		- Migraine without aura (common migraine) ~ 85%
		- Menstrual migraine
		- Status migrainosus (lasting over 72 hours without spontaneous resolution)
	+ Clinical features:
		- Partial triggers:
			* Chocolate (serotonin!)
			* Hangovers
			* Orgasms
			* Cheese (serotonin!)
			* Oral contraceptives
			* Alcohol
			* Exercise
		- Prodrome vs aura
			* Prodrome can precede the attack much longer than an aura, if present
			* These include symptoms of excitation or inhibition of CNS (excitability, increased appetite vs. depression, irritability, sleepiness, fatigue)
		- ***UNILATERAL THROBBING HEADACHE***
			* **Not always on the same side** (vs. cluster headache)
			* **Lasts 4 – 72 hours** (basically can’t do anything for the rest of the day or two)
			* Very **disabling** condition
		- Nausea and vomiting
		- **Photophobia and phonophobia**
		- Interestingly, migraines improve during pregnancy, but if not, it has potential ADR on pregnancy
		- Note that people with migraines without aura are partially CI to take OCPs (with aura, absolute CI)
	+ Management:
		- ACUTE:
			* **NSAID**
			* **Triptans** (sumatriptan)
			* **Dihydroergotamine**
			* General measures (warm/cold packs to the head, breathing into paper bag, dark room with low sound)
		- Prevention:
			* Lifestyle changes (avoid triggers)
			* Medical therapy:
				+ **First line = beta blockers, TCA [amitriptyline], topiramate, CCB**
				+ Second line = **valproate**, gabapentin, pregabalin
		- Interesting notes:
			* Pets can sometimes be aware of an impending attack and begin to become more attentive to their owners
			* In pregnancy, before 30th week, NSAIDs are ok… In 3rd trimester, migraines fade (thank God) – a lot of the drugs are CI in pregnancy
* Other topics:
	+ Hydrocephalus (= high CSF volume 🡪 dilated ventricles +/- raised ICP) & related conditions
		- Communicating hydrocephalus
			* Problem with CSF absorption into the arachnoid granulations
			* So the ventricles communicate freely with the SA space
			* Causes? Post-meningitis or SAH scarring of granulations
			* Head will not appear to be enlarged in adults, but in infants it may manifest as macrocephaly
			* Don’t forget that there are congenital causes of hydrocephalus (e.g. toxoplasmosis)
		- Non-communicating hydrocephalus
			* There is a blockage of exit sites of the ventricles, so that they do not communicate with the SA space
			* Cerebral aqueduct stenosis disallows fluid to pass into the 4th ventricle from the 3rd ventricle resulting in dilated 3rd and lateral ventricles
			* Tumors at any sites along the ventricles might cause obstruction
			* Head will *not* appear to be enlarged
		- Hydrocephalus ex vacuo
			* Not a true hydrocephalus, and ICP is normal
			* Appears that way because of decreased brain tissue (neuronal atrophy) around the ventricles
		- Normal pressure hydrocephalus (NPH)
			* Elderly patient with triad of urinary incontinence, cognitive dysfunction and ataxia (Wet, Wacky and Wobbly) + gait apraxia (feet stuck on floor/magnetic)
			* Result of dilated ventricles stretching the most adjacent corona radiata fibers
			* No increased ICP and CSF pressure only elevates episodically
		- Pseudotumor cerebri (idiopathic intracranial hypertension)
			* Raised ICP without an apparent cause (e.g. no hydrocephalus, bleeding, tumors, infections, etc.)
			* Risk factors: female, obese, childbearing age, ***hypervitaminosis A***, danazol and tetracycline use
			* Findings will show signs of raised ICP (headache, diplopia (CN6 palsy), papilledema)
			* Lumbar puncture 🡪 high opening pressure and provides relief of headache
			* Management = general (weight loss), medical (acetazolamide), surgical/invasive (repeat LP, shunt placement, others)
* **Lumbar puncture:**
	+ Contraindications:
		- Raised ICP (most importantly)
			* Symptoms can help suggest this to be true, such as vomiting, headache, altered mental status, Cushing triad (bradycardia, hypertension, irregular breathing)
			* *You* ***must*** clinically assess for **papilledema** on **fundoscopy** and do a **CT scan** to confirm
			* *Why?* Because sudden drop in ICP can result in coning of the cerebellar tonsil into the foramen magnum and compress the medulla
		- Bleeding diasthesis (bleeding tendency)
		- Cardiorespiratory compromise (unstable patient)
		- Infection at site of needle insertion
	+ Method:
		- Patient’s back is exposed and he lies on his side with his back near the edge of the bed
			* Must be FULLY FLEXED 🡪 knees to chin position
		- Identify the landmarks
			* In adults, the SC ends at L1/L2, while in infants it is at L2/L3 (in in utero life it occupies the whole vertebral canal)
			* We use the iliac crest as the landmark for L4 – our injection site will be centrally, above L4 level in adults and below L4 in children
		- Aspetic technique is established
			* Mask, gloves, gown for the conductor
			* Sterilize the potential injection site and allow to dry
			* Place sterile drapes
		- Inject local anesthetic intradermally (bleb) and then wait for 1 minute before inserting the spinal needle at the site
			* Needle must enter perpendicular to the body, bevel facing up
			* Continue until you feel resistance of the spinal ligaments (including the ligamentum flavum) and then the dura, which will then “give way” to the SA space
			* Withdraw stilette and check if CSF fills needle and attach manometer
			* Catch fluid in 3 bottles (10 drops per tube)
			* Reinsert stiletto and then remove needle
			* Apply dressing
			* Send the 3 bottles for CSF analysis: gross observation, biochemistry (glucose, protein, lactate, Ig, oligoclonal bands), cytology, cell count and microbiology (gram stain and microscopy, culture; VDRL, PCR)
		- Complications:
			* Post-LP headache
			* Bleeding
			* Infection
			* Cerebral herniation (if not checked before)
			* Minor neurological symptoms (parasthesia, radiculopathy) – R/O cauda equina damage, get spinal MRI
		- Managing post-LP headache:
			* Positional headache (worse when upright)
			* Thought to be due to continued CSF leakage from puncture site and intracranial HYPOtension
			* Prevention?
				+ Smallest needles, go perpendicular, use blunt needles (expensive)
			* Management?
				+ Reassurance and rest
				+ In refractory cases, a BLOOD PATCH can be made (injection of autologous venous blood into the adjacent epidural space that can clog up the “hole” with immediate relief experienced in 95% of cases :o)
* **Vertigo, dizziness**
	+ Subjective feeling of the world rotating around you or in other words, feeling dizzy – but you must always investigate to figure out what the patient exactly means by feeling “dizzy”
		- Vertigo = illusion of movement that is often represented as the rotation of the patient’s surroundings
		- Patient can fall because of dizziness, but LOSS OF AWARENESS IS NOT TYPICAL AND SHOULD PROMPT YOU TO INVESTIGATE for other CNS problems (epilepsy, syncope)
	+ Causes:
		- Benign positional vertigo (MCC)
			* Stone/debris in semicircular canals (Canalolithiasis) that moves with head and when it resettles causes transient vertigo
			* Tests: hallpike maneuver (head turned 45 and then laid below the level of the bed at the edge of it)
			* Helpful/symptomatic relief maneuvers? Epley maneuver (helps clear the debris out)
		- Drug toxicity:
			* Gentamicin (AG are ototoxic, nephrotoxic and can cause neuromuscular blockage too!)
			* Furosemide (loop diuretics!)
			* Cisplatin (chemotherapeutic, remember Chemo-man)
		- Acute labyrinthitis
		- Meniere’s disease
			* Blockage in endolymph flow can result in recurrent attacks of vertigo (that are much longer, >20 minutes), associated with nausea and vomiting and sensineural hearing loss and tinnitus
			* Patients may experience drop attacks (but NO LOC)
			* Acute attacks – bed rest and reassurance
			* Long-term management 🡪 low Na diet, betahistine, surgical options or medical ablation of the vestibular organs (with gentamicin!)
		- Acoustic neuroma (schwannomas)
			* Associated with NF2 and arises from the vestibular part of CN8
			* Can result in cerebellopontine (CPA) syndrome, with the growing tumor affecting the cerebellar peduncle, CN8, CN7 and in severe cases CN6 and CN5
			* DDx = meningioma
		- Ramsay Hunt syndrome
			* Herpes zoster reactivation in the geniculate ganglion can result in facial palsy, vesicular lesions in ear, vertigo, hearing loss and tinnitus
* **Hearing loss and tinnitus**
	+ Ohoooo such a long story, go find it somewhere else ☺
		- Rinnie and weber test – use 256 Hz or 512 Hz (128 Hz for vibration)
	+ Btw, drugs that can cause tinnitus?
		- Salicylate (aspirin) – toxicity can start with tinnitus
		- AG, loop diuretics
* **Carpal tunnel syndrome**
	+ Median nerve compression in the carpal tunnel in the wrist
	+ Most common mononeuropathy
		- More common in women
	+ Important causes (“\*\*\*” = you must mention them to examiner):
		- Overuse (typing? Desk job?)?
		- Myxedema (hypothyroidism\*\*\*)
		- Enforced flexion (Colles’ splint)
		- Diabetic neuropathy
		- Idiopathic
		- Acromegaly (\*\*\*)
		- Neoplasms (myeloma)
		- Tumors (benign kinds, like lipomas)
		- Rheumatoid arthritis (\*\*\*)
		- Amyloidosis (\*\*\*)
		- Pregnancy (\*\*\*)
		- Sarcoidosis
	+ Clinical features:
		- Aching pain in the hand and over the wrist
			* Worse when sleeping at night because unpredictable flexion of wrist for hours (flexing the wrist will make the trapping worse)
		- Parasthesias in the median nerve supply areas (thumb, index and middle fingers)
			* Improves when shaking hand (wake and shake)
			* May be accompanied by sensory loss
			* Weakness and wasting of the thenar muscles can occur
		- Clinical signs/tests:
			* Phalen test
			* Tinel’s sign
	+ Investigations
		- Clinical diagnosis, but if underlying cause not obvious, R/O DDx of causes
		- Neurophysiology studies (NCS)
	+ Management:
		- Splinting (in extension/to avoid flexion when sleeping – so especially wear at night)
		- Local steroid injections
		- Decompression surgery
* Space occupying lesions and brain tumors
	+ Go find it somewhere else ☺
* **Brainstem syndromes:**
	+ See PDF entitled brain stem lesions/syndrome
* Paraneoplastic lung cancer serology:
	+ Anti-Hu, anti-Yo, anti-Ri, anti-Ma2, antiamphiphysin, anti-CV2
* More ☺
	+ **Acute disseminated encephalomyelitis (ADEM)**
		- AKA postinfectious encephalomyelitis
		- Autoimmune demyelinating disease of CNS that is acute and rapidly progressive
			* Commonly triggered by viral infections and vaccinations
			* Thought to be due to auto-Ab against viral Ag that cross-reacts with oligodendrocytic myelin materials such as myelin basic protein (*not* major basic protein)
		- Most of the time, it is monophasic – BUT it may recur and can increase risk of developing MS
		- Clinical features:
			* Multifocal neurological symptoms
			* Nonspecific signs such as fever, nausea and vomiting
		- Investigations:
			* R/O differential investigations
			* You’ll see MRI findings suggestive of the diagnosis (add to differential)
		- Management:
			* It is not on top of your differential list, so management is empirical antibiotics (meningitis), acyclovir (encephalitis)
			* Once diagnosis is confirmed, the mainstay is IV steroids > IVIG and plasmapharesis
			* Prognosis: ADEM improves with Rx, but complete recovery ranges from 10 – 46% only (some deficits remain); some people are at risk to develop MS
	+ **WHO analgesic ladder**
		- Start with non-opioid analgesics (**paracetamol, NSAIDs**)
		- Move to weak opioids (codeine, dihydrocodeine, tramadol)
		- Move to strong opioids (morphine; diamorphine; hydromorphone; oxycodone; fentanyl; buprenorphine)
		- IDEA?
			* If one drug from same level fails, don’t attempt with another drug from same level, GO UP!
			* If you must first CLASSIFY the pain into mild, moderate and severe (roughly based on the pain scale of 0 – 10 and/or by the patient’s appearance [subjective])
			* You don’t have to start from zero… If the patient is in moderate or severe pain, go directly to weak opioids then strong opioids (*don’t be a dick* and give them panadol!!!!)
		- Considerations
			* Start regular laxatives and anti-emetics with strong opioids (opioids cause constipation – that’s why we use loperamide for diarrhea!)
			* Best proceeding: oral then IV
			* In morphine resistant cases, consider adjuvants (NSAIDs, steroids, muscle relaxants, anxiolytics)
			* In neuropathic pain, amitriptyline and pregabalin are useful