Neurology Summary

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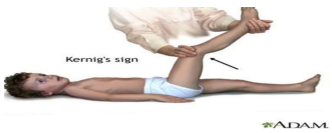
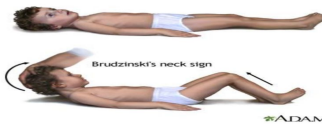
Bacterial meningitis

Definition

- Inflammation of the (meninges) pia mater and the arachnoid mater (dura mater is usually spared),with suppuration of the cerebrospinal fluid

Signs and Symptoms

- **Classic triad: fever, neck stiffness and confusion.**
- **Severe Headache, Photophobia** (intolerance of light) and Phonophobia (intolerance to loud noises) can be specific to bacterial meningitis.
- Bulging fontanel in infants, sometimes with hydrocephalus

Kernig's sign	Brudzinski's neck sign
While patient is lying supine, with the hip and knee flexed to 90 degrees pain limits passive extension of the knee.  The Kernig sign	Flexion of the neck causes involuntary flexion of the knee and hip.  Brudzinski sign

What's the most useful sign?

- **Jolt accentuation maneuver:** ask patient to rapidly rotate his or her head horizontally: Headache worsens, In healthy individuals it might be uncomfortable but a pt with meningitis will avoid doing it.
- **Sensitivity of 100%, specificity of 54% (Low, unlike kernig and Brudzinski signs),**

Management (Based on Dr notes)

How to manage a patient with meningitis?

- **Step 1:** Give empirical therapy!! Whenever you suspect meningitis or encephalitis, start empirical therapy! (In real life the pt will be started on empirical therapy in the ER, before you see him)
- **Step 2: CT** (To exclude herniation, supratentorial tumor, bleeding, pus collection (Subdural empyema) before doing LP bc it may kill the pt). **NEVER do LP before CT.**
- **Step 3:** LP.
  - **Contraindications to LP:** Herniation, Infection at the site of LP (e.g. Cellulitis), bleeding disorders, Low platelet count <100, anticoagulants . If one of these contraindication is present you can delay LP but **NEVER delay the treatment**

What antibiotics should be given?

- **Ceftriaxone + Vancomycin (**to cover highly penicillin resistant pneumococcus)
- Add ampicillin if there's suspicion of listeria

  Note: **Dexamethasone should be given** concomitant with 1st dose Abx to block TNF production

EXTRA

Typical CSF changes in viral, pyogenic and TB meningitis

	Normal	Viral	Bacterial	Tuberculosis
Appearance	Crystal clear	Clear/turbid	Turbid/purulent	Turbid/viscous
Mononuclear cells	<5/mm^3	10-100/mm^3	<50/mm^3	100-300/mm^3
Polymorph cells	Nil	Nil	200-300/mm^3	0-200/mm^3
Protein	0.2-0.4 g/L	0.4-0.8 g/L	0.5-2.0 g/L	0.5-3.0 g/L
Glucose	⅔ - ½ blood glucose	> ½ blood glucose	< ½ blood glucose	< ½ blood glucose

Special cases of bacterial meningitis

Meningococcal meningitis (Emergency)

Meningococcal meningitis and meningococcaemia: emergency treatment

Suspicion of meningococcal infection is a medical emergency requiring treatment immediately.

Clinical features:

- Petechial or nonspecific blotchy red rash
- Fever, headache, neck stiffness.

All these features may not be present – and meningococcal infection may sometimes begin like any apparently non-serious infection.

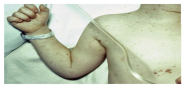
Immediate treatment for suspected meningococcal meningitis at first contact before transfer to hospital or investigation:

- Benzylpenicillin 1200 mg (adult dose) slow i.v. injection or intramuscularly
- Alternative if penicillin allergy – cefotaxime 1 g i.v.

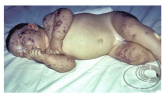
In meningitis, minutes count: delay is unacceptable. On arrival in hospital:

- Routine tests including blood cultures immediately
- Watch out for septicaemic shock.

- Fulminate meningococcemia with purpura caused by **Neisseria meningitidis**
  - Overwhelming sepsis, DIC
- **Classic: Meningitis with rash (Petechiae) + Headache + Fever**



- Lumbar puncture **should not be performed** if meningococcal sepsis is suspected because coning of the cerebellar tonsils may follow – the organism is confirmed by blood culture.



- **Treatment and prophylaxis:**
  - **Droplet Isolation:** 48h post Abx
  - **Treatment: Ceftriaxone or Pen G** 7 days
  - **Eradicate nasopharyngeal carriage:**
    - House hold contact
    - Health care providers who examined patient closely
  - **Prophylaxis (Not done routinely):** Rifampin 600 mg for 2 d or Ciprofloxacin 500mg once or Ceftriaxone 125mg I.M once

Recall: Ceftriaxone is C.I in neonates, give cefotaxime instead.

Listeria Monocytogenes meningitis

- **Pathology:** It causes brain stem, cerebellum inflammation (Rhombencephalitis) and meningitis
- **Risk groups:**
  - Age <1y or >50y
  - Alcoholics
  - Pregnancy: up to 30%
  - Immunocompromised 70 %
- **Routes of transmission:**
  - **Mainly food borne:** survives refrigeration
    - linked to poultry, hotdogs, cold cuts, coleslaw, ice-cream
  - **Cheeses,** particularly soft cheeses, have been implicated in listeriosis outbreaks worldwide.
  - Inform micro lab: special media **(Mueller-Hinton agar)**

Note: Whenever you see a pt with changing signals in brain stem and cerebellum MRI , think of Listeria.

- **Treatment:**
  - **Ampicillin** 2gm IV Q4h +/- Gentamicin 2mg/kg loading dose then 1.7mg/kg Q8h
  - **21 day** duration
  - Penicillin allergy patients: **TMP-SMX or Meropenem**

Neuro Brucellosis

- **Treatment:**
  - **Doxycycline**
  - **Plus** Rifampin
  - **Plus** Ceftriaxone 2gm IV q12h

What's the most common organism in neonates?

- Group B Streptococci (occurs ONLY in neonates)

What's the most common organism in older infants and children?

- Streptococcus pneumonia

What's the most common organism in adults?

- Streptococcus pneumonia

What's the most common complication?

- CN palsies (esp. deafness)

L53- CNS infections *(cont.)*

Aseptic meningitis

Definition

- Inflammation of meninges with sterile CSF
- **CSF: pleocytosis 100s,** Normal Glucose, Protein normal, Neg Culture

Note: Pleocytosis is the hallmark of aseptic meningitis, since it's sterile inflammation usually it has **neutrophilic** pleocytosis (there might be some lymphocytes, but the main cells are neutrophils)

Causes

- **Enteroviruses:** most common cause 80%
- HSV-2 (HSV-1 can cause it but it usually causes encephalitis)
- **Partially treated bacteria** (Think of it when the pt has taken abx in the past 2-3 days. When you suspect viral meningitis it is important to verify that the patient has not received antibiotics (for whatever cause) prior to the lumbar puncture, as CSF lymphocytosis can also be found in partially treated bacterial meningitis.)
- **Drugs: Metronidazole**, TMP-SMX, NSAIDs, carbamazepine (Given to epileptic pts), **IVIG-** headache is very common (Given to pts with myasthenia gravis and Guillain barre syndrome (GBS))

Viral encephalitis

General info

- **Encephalitis**: means acute infection/inflammation of brain parenchyma, and is often seen simultaneously with meningitis, usually viral.
- **Meningoencephalitis:** inflammation of brain + meninges
- In viral encephalitis, fever (90%) and meningism are usual; in contrast to meningitis, however, the clinical picture is dominated by brain parenchyma inflammation.
- **Personality and behavioural change** is a common early manifestation, which progresses to a reduced level of consciousness and even coma.
- **Seizures** (focal and generalized) are very common and focal neurological deficits, such as speech disturbance, often occur (especially in herpes simplex encephalitis).

What's the most common organism?

- **Most common: Herpes simplex (Either type 1 or 2)**:
  - How to confirm? Perform LP and PCR. MRI is also helpful (**The limbic system** and the medial temporal are its favourable place)
  - Treat with Acyclovir

Cerebral abscess

General info

- Bacteria may enter the cerebral substance through penetrating injury, by direct spread from paranasal sinuses or the middle ear, or secondary to sepsis. **Untreated congenital heart disease** is a recognised risk factor.
- Initial infection leads to local suppuration followed by loculation of pus within a surrounding wall of gliosis, which in a chronic abscess may form a tough capsule.
- **Organisms:**
  - **Streptococci (60-70%),** Bacteroides (20-40%), Enterobacteriacea (25-33%),
- **S&S:**
  - Fever, Headache, Meningism, Drowsiness
  - Seizures, raised intracranial pressure and focal hemisphere signs occur alone or in combination.

Management

- Lumbar puncture is potentially hazardous in the presence of raised intracranial pressure **and CT should always precede it.**
- **CT with contrast:** reveals single or multiple low-density areas, which show ring enhancement with contrast and surrounding cerebral oedema
- **CT brain:** If abscess more than 2.5cm then **surgical drainage**. And if patient neurologically unstable or decrease LOC drain regardless of size
- **Antimicrobials:** empirically Ceftriaxone with metronidazole, otherwise according to susceptibility

L54- Epilepsy

◄ Definitions:

- **Epileptic seizure:** **Transient** occurrence of signs and symptoms of sudden changes in neurological function due to **abnormal excessive** and **synchronous** discharge of cortical neurons
- **Epilepsy:** recurrent (two or more) **unprovoked** seizures.
- **Provoked seizures:** occurs in the setting of acute medical and neurological illnesses in people with no prior history of seizures

◄ Risk Factors:

- Febrile convulsion
- Family history
- CNS mass lesion and infection
- Perinatal insult, abnormal gestation or delivery
- Developmental delay
- Head injury
- Stroke

◄ Triggers for seizures:

- **Poor compliance**
- **Stress**
- **Infection**
- **Alcohol withdrawal**
- **Sleep deprivation**
- **Menstrual cycle**

Types of Seizures

Focal Seizures
preceded by warning "Aura"

- Simple partial seizures → **preserved** consciousness
- Complex partial seizures → **Altered** consciousness **but not** complete loss
- Partial seizures secondarily generalised

Generalized seizures
comes with **no aura** (no warning) and leads to **complete loss of consciousness**.

Unclassified seizures

Generalized Seizures

Absence (petit mal)	• Always start in **childhood**. They are mistaken for daydreaming or poor concentration in school. • Characterized by **fast recovery** from seizure (No post-ictal phase), and can be **provoked by hyperventilation**
Tonic-clonic "grand mal"	• **Rigid (tonic) and unconscious**, falling heavily if standing and risking facial injury. During this phase, breathing stops and central cyanosis may occur. • followed by **jerking (clonic)** movements emerge for 2 minutes at most. • Afterwards, there is a **flaccid state** of deep coma, which can persist for some minutes • During the attack, **urinary incontinence and tongue-biting** may occur. • Subsequently, the patient usually feels unwell and sleepy, with headache and myalgia.
Atonic "drop seizures"	Involving **brief loss of muscle tone,** usually resulting in heavy falls with or without loss of consciousness.
Myoclonic	Typically **brief, jerking movements,** predominating in the arms.

◄ Seizure approach

- **Non Invasive tests:**
  - Clinical history
  - MRI and Nuclear medicine
  - Neuropsychological evaluation
  - Video EEG
- **Invasive monitoring**

L54- Epilepsy *(cont.)*

Typical EEG Sign	Localizes to	Typical EEG Sign	Localizes to
Oral Automatismes	Temporal lobe	Tonic arm elevation	Supplementary motor area
Hypermotor automatism	Frontal lobe	Epigastric Aura	Temporal lobe
Manual picking automatismes	Temporal lobe	Throat tightening Sensation	Insula
Visual Hallucinations	Occipital lobe	Ictal pain	Parietal lobe
Auditory Hallucinations	Temporal neocortex (Heschl's Gyrus)	Somatosensory sensations	Postcentral gyrus or Supplementary motor area
Olfactory Hallucinations	Mesial temporal lobe	Clonic activity	Precentral gyrus
Nystagmus, eye blinking, eye pulling sensation	Occipital lobe	De-ja-vu or jamais vu aura	Mesial / Medial temporal lobe
Ictal amaurosis		Fear	Most often temporal, but also frontal lobe

◄ Medical Treatment (first line):

MOA	1. **Reducing electrical excitability of cell membranes: by inhibition of sodium channel.** 2. **Enhancing GABA:** By inhibiting GABA-transaminase or direct GABA-agonist properties.
Clinical uses of Antiepileptic drugs	1. **Tonic-clonic (grand mal) seizures: phenytoin or valproate** (drugs of choice) 2. **Partial (focal) seizures: carbamazepine** (drug of choice) • valproate; clonazepam or phenytoin are alternatives. 3. **Absence seizures (petit mal): ethosuximide** (drug of choice) or valproate 4. **Myoclonic seizures: valproate** or clonazepam
Basic rules for drug treatment	• Drug treatment should be simple, preferably using one anticonvulsant (**monotherapy**). "Start low, increase slow" • **Add-on therapy** is necessary in some patients • If patient i**s seizure-free for three years, withdrawa**l of pharmacotherapy should be considered. Should be performed very carefully and **slowly!**
Drug resistant epilepsy	• Failure of at least **TWO** antiepileptic medications to completely control seizures ○ **Appropriately chosen for seizure type** . ○ Taken as prescribed ○ Well tolerated (not failed due to side effects)

◄ Surgical Treatment (second line):

- **Hemispherectomy:** one of the two cerebral hemispheres is removed.
- **Hemispherotomy:** disconnects the cortex of a hemisphere from the other cutting the corpus callosum.
- **Temporal lobectomy**

➔ **If the patient is not a good candidate for surgery?**

- ◆ Vagus nerve stimulation (NS)
- ◆ Deep Brain Stimulation (DBS)

◄ Status epilepticus

- **Definition:** recurrent convulsions that last for more than **30 minutes** **(5 min in the last update)** and are interrupted by only brief periods of partial relief.
- **Rhabdomyolysis** is a complication of SE that may lead to acute kidney injury
- **Treatment:**
  - Early status (up to 30 min): **lorazepam IV**
  - Established status (30–90 min): Phenytoin
  - If ongoing seizures: Phenobarbital, and Valproate
  - Refractory status (>90 min): general anaesthesia

◄ Epilepsy treatment in pregnancy

The **risk of teratogenicity** is well known, especially with **valproates**, but withdrawing drug therapy in pregnancy is more risky than continuation.

- All antiepileptic medications are not safe, however **lamotrigine** is the **safest**. .

◄ Seizures vs Syncope:

	Cardiogenic Syncope	Seizure Disorders
Loss of Consciousness	Typical	Common
Aura	-	+
Cyanosis	-	+
Episode Duration	Seconds	Minutes
Involuntary movements	Common	Typical
Amnesia	Yes	Yes
Postictal delirium & headache	-	+
Arrhythmia	Common	Rare
Electroencephalogram	Slow waves Flattening	Focal or General Spike
Responsive to AED	No	Often
Short Term Mortality	High	Low

L55- Peripheral neuropathies

	Weakness				Sensory symptoms	Severe proprioceptive loss	UMN signs	Autonomic symptoms/ signs	Diagnosis
	Proximal	Distal	Asymmetric	Symmetric					
Pattern 1: symmetric proximal and distal weakness with sensory loss	+	+		+	+				GBS, CIDP
Pattern 2: Distal Sensory loss with/ without weakness		+		+	+				CSPN[1], metabolic, drugs, hereditary: (CMT, Amyloidosis)
Pattern 3: Distal weakness with sensory loss		+	+		+				- Multiple: vasculitis, HNPP[2], MADSAM, infection (leprosy, lyme, sarcoid, HIV) - Single: Mononeuropathy, radiculopathy
Pattern 4: Asymmetric Proximal and distal weakness with sensory loss	+	+	+		+				Polyradiculopathy, plexopathy
Pattern 5 : Asymmetric distal weakness without sensory loss		+	+				±		- **LMN and UMN** - ALS - **Pure UMN** - PLS - **Pure LMN** - MMN[3]. PMA[4], BAD[5], LAD[6], MAMA[7]
Pattern 6 : Symmetric sensory loss and upper motor neuron signs		+		+	+	+	+		b_{12} deficiency, copper deficiency, friedreich ataxia, adrenomyeloneuropathy
Pattern 7: Symmetric weakness without sensory loss	±	+		+					- Proximal and distal SMA - Distal Hereditary motor neuropathy
Pattern 8: Focal midline proximal symmetric weakness	+ Neck/extensor + Bulbar			+ +			+ +		ALS
Pattern 9: Asymmetric proprioceptive loss without weakness			+		+	+			Sensory Neuropathy (Ganglionopathy)
Pattern 10: Autonomic dysfunction								+	HSAN[9], Diabetes, GBS, amyloid, poryphyria, Fabry's

L55- Peripheral neuropathies *(cont.)*

Ulnar nerve mononeuropathy	• **system involved: sensory and motor** • **clinical features: numbness of medial hand (fourth and fifth digits). weakness of abduction and adduction,** atrophy of intrinsic muscles of the hand, wartenberg and froment signs will be evident there will also be grip weakness • finger extensors are not involved (sign of radial nerve) •
carpal tunnel syndrome	• **system involved: sensory and motor** • **clinical features: wasting of thenar eminences. weak thumb abduction, reduced sensation over thumb, index, middle and ring fingers.** • **the most common focal neuropathy** • **it is usually asymmetrical, however, it can occur bilaterally.**
Hereditary neuropathy	• they might deny family history • sensory problems may not be present in the history but it can be present in the physical because it's chronic. • **clinical features: Deformities e.g. high arched foot (Pes cavus), symmetric weakness, distal more than proximal. absent reflexes. decreased proprioception, vibration, heat and pinprick.**
Diabetic neuropathy	• history of Diabetes • Clinical features: decreased sensation, numbness, and tingling that is progressive for a very long time (e.g 2 years) and pain • usually symmetrical. • most common Asymmetric neuropathy in Diabetics is Carpal tunnel syndrome • most common symmetric is Distal symmetric polyneuropathy.
S1 Radiculopathy	• **clinical features: Weakness of hip extension**, Weakness of knee flexion, Weakness of ankle plantar flexion, Absent ankle reflex. **sensory over lateral and plantar surfaces** • **How to differentiate sciatic from S1? by sensory distribution and the presence of hip extension.**
Common peroneal nerve damage	• **clinical features: Foot drop (difficulty in dorsiflexion). parasthesia in teh dorsum of the foot. toe dorsiflexion weakness. ankle eversion is also affected. inversion is NORMAL.** • **loss of sensation is well demarcated. over the dorsum extending over the lateral calf.**

Guillain barre syndrome	• **Paralysis follows 1-3 weeks after an infection**
	• signs and symptoms include:
	  ○ weakness of the **distal** limb muscles and/or **distal** numbness. (usually **symmetrical**)
	  ○ The weakness and sensory loss progress proximally, over several days **(acute)**
	  ○ Could be Motor, sensory, autonomic or combination
	  ○ **Loss of tendon reflexes**
	LP will show cytoalbuminologic dissociation (normal cells with high proteins)
	• **treated with IVIG or plasmapheresis NOT steroids**
	• **regularly motor pulmonary functions**
	• **CIDP is the chronic variant of the same presentation**

L56- Ischemic stroke

Stroke :

- Ischemic (blockage) → 80-85% of all strokes
- Hemorrhagic (bleeding) → 15-20% of strokes

Ischemic stroke :

- **Persisting neurologic deficit after 24 hours** and/or
- **infarct on CT or MRI.**

Transient ischemic attacks :

stroke-like symptoms that last for a very short time(<1hr) with complete recovery (most are <5 min) with the **absence of infarct** in neuroimaging study.

Risk factors:

Modifiable :

- **Hypertension. (Most important one)**
- **Diabetes mellitus.**
- **Hyperlipidemia.**

Non- modifiable:

- **Age**
- **Sex** young women are at higher risk than men due to pregnancy, hormonal changes.

Subtypes:

- **Blood vessels**
  - **Atheromatous (most common)**
  - Non-atheromatous
    - Vasculitis
    - Dissection of blood vessels (common in young patient "50 and less").
- **Heart**
  - Cardio Embolic
    - Atrial fibrillation
- **Blood**
  - Haemoglobinopathies
    - Sickle cell disease
  - Coagulopathy
    - Thrombophilia

Clinical presentation :

Middle cerebral artery occlusion:

- Hemiparesis: **Arm + face (UE) more than leg weakness (LE)**
- Hemisensory loss
- Higher cerebral dysfunction:
  - **Aphasia** if affecting the **dominant (left)** hemisphere.
    - **Broca's (expressive, anterior) aphasia: Damage in the left inferior frontal lobe** causes reduced speech fluency with relatively preserved comprehension
    - **Wernicke's (receptive, posterior) aphasia: Left temporo-parietal damage** leaves fluency of language but words are muddled. This varies from insertion of a few incorrect or non-existent words
    - **Nominal (anomic, amnestic) aphasia:** difficulty naming familiar objects
    - **Global (central) aphasia:** combination of the expressive problems of Broca's aphasia and the loss of comprehension of Wernicke's with loss of both language production and understanding. Writing and reading are also affected.
  - Neglect if affecting the **non-dominant** hemisphere.
- homonymous hemianopia

L56- Ischemic stroke *(cont.)*

Anterior Cerebral Artery (ACA) occlusion :
Symptoms :

- **Weakness LE more than UE**
- Emotional disturbance.

Internal carotid occlusion:
Symptoms : above and ophthalmic
Posterior cerebral artery :
Symptoms:

- Vision - visual field (homonymous hemianopia)
- memory

Vertebrobasilar
Symptoms

- Cranial nerve syndrome with crossed motor
- cerebellum (cerebellar syndrome)
- altered LOC.
- homonymous hemianopia

Midbrain
Symptoms:

- CN III: signs of complete CN III palsy:
  - dilated pupil
  - Unilateral complete ptosis (levator weakness)
  - Eye deviated **down and out** (unopposed lateral rectus and superior oblique
- **Weber's syndrome:** Ipsilateral IIIrd nerve palsy with contralateral hemiplegia

Pons
Symptoms: CN V ⟶ Sensory:

- **CN VI ⟶ lateral rectus palsy**
- CN VII ⟶ facial weakness.

Medulla
Symptoms:CN VIII ⟶ vertigo, hearing loss.

- CN IX, X ⟶ dysphagia.
- CN XII ⟶ tongue weakness.

Small penetrating arteries (Lacunar syndrome)
Symptoms **:**
arms and face will be affected to the same degree.
no higher cerebral dysfunction or hemianopia
Pathophysiology :

- **Core:** area of irreversible damage.
- **Penumbra:** tissue at risk (ischemic but still viable cerebral tissue)
- Reduced blood blow (20-30cc) ⟶ tissue is still viable but stops functioning (penumbra) ⟶ needs to be saved ASAP
- A drop to 10 cc in blood flow ⟶ severe ischemia

History taking in Ischemic stroke :

- Onset (Last time seen normal)
  - Symptoms: FAST
  - Headache
  - Neck pain/ trauma in case of dissection
- Past Medical history
  - Oral contraceptives
  - Antithrombotics

L56- Ischemic stroke *(cont.)*

Physical examination in ischemic stroke : :

- keep it neurological (focused) and quick, use **National Institution of Health Stroke Scale (NIHSS)**
- ABC (sometimes they add D for dextrose)
- BP Will be high (in both ischemic and hemorrhagic strokes)
- CN involvement and crossed motor typical presentation of brainstem strokes (ipsilateral CN involvement & contralateral weakness)
- Tone : **decreased** on side of weakness early on, **later on increased**
- Reflexes: hyperreflexia on side of weakness, with upgoing toe.

Investigations of ischemic stroke :

- Coagulation profile
- Chemistry : Fasting glucose
- Imaging
  a. CT scan : non-contrast CT is the only way to differentiate between ischemic and hemorrhagic strokes
  b. MRI :
    - MRI is **better overall, if immediately available**
    - MRI is used when there is diagnostic uncertainty or delayed presentation, and when more
- Vascular imaging
  a. Carotid U/S the least invasive
  b. CTA: invasive
- Cardiac workup : ECG to detect Afib

Management of ischemic stroke :

- Acute stroke management **code stroke**
  a. ABC
  b. Reperfusion
    - **Intravenous thrombolysis (IV t-PA): Effective up to 4.5 hours from onset.**
      - Exclusion criteria: **Intracerebral hemorrhage ,** stroke in the past 3 months., major surgery 14d,Pregnancy, active bleeding or acute trauma
    - aspirin (300 mg daily) should be started immediately after an ischaemic stroke **if the patient is not a candidate for thrombolysis.** If the patient has already received tPA, withhold aspirin for at least 24 hours.
      - In case of atrial fibrillation → add warfarin.
      - In case of significant carotid stenosis → surgery
      - In case of vasculitis → steroids
    - **Intra-arterial thrombolytic & Mechanical thrombectomy**
      - Only in case of blockage in **large vessels** e.g. MCA, ACA, Internal carotid or basillar
      - you could do for **up to 6 hours.**
    - **Internal carotid endarterectomy:** recommended in TIA or stroke patients with **internal carotid artery stenosis >70%.**
  c. Prevent progression and complications:
    - **BP and glycemic control**
      - **do not lower blood pressure abruptly in first week as it may reduce cerebral perfusion**
      - Control BP before thrombolysis bc of the risk of bleeding
    - **NPO, avoid aspiration.**
    - **Dx and Rx temp**
    - **PT, OT and early rehab.**
    - **DVT prophylaxis**

d. Other components of acute stroke management:

- Nutrition**:**If dysphagia persists for >48 hrs, start feeding via nasogastric
- Temperature: Control with antipyretics, **as raised brain temperature may increase infarct volume**

- **Long term stroke management:**
  a. Long term management of Risk factors (secondary prevention)
     - HTN: Transient hypertension, often seen in the first 24-48 hours following stroke, usually does not require treatment provided (let BP autoregulate) given diastolic pressure does not rise >100 mmHg, because high BP helps the cerebral circulation. unless
       - Patient is candidate for thrombolysis
       - patient has other risk factors that necessitate BP control
     - DM,Lipid , Smoking , A-fib, and Exercise

  b. Anti-platelet: for atherosclerosis Long-term soluble aspirin (75 mg daily)
  Anticoagulant
     - Heparin and warfarin should be given when there is:
       - atrial fibrillation
       - Hypercoagulability
     - Anticoagulants are potentially dangerous in the two weeks following infarction

  c. Rehabilitation

Transient ischemic attack :

- The term TIA traditionally also includes patients with **amaurosis fugax :** sudden transient loss of vision in one eye. the first clinical evidence of internal carotid artery stenosis – and forerunner of a hemiparesis.
- **Duration:** most TIA's **last 5-20 mins**
- **Features depend on: anterior circulation carotid system posterior vertebrobasilar circulation. system**
- **Prognosis: up to ⅓ will have a stroke (usually within 48 hours)**

Clinical findings :

Consciousness is usually preserved in TIA.
There may be clinical evidence of a source of embolus, e.g.:

- Carotid arterial bruit (stenosis)
- Atrial fibrillation or other dysrhythmia

Approach to TIA :

1. Needs **urgent assessment** (ER)
2. **Rule out other causes**
3. **Work up:** (labs, CT scan or MRI)
   - Vascular image of carotid CTA, MRA, US.
   - Cardiac work up: (EKG، echo, +/- holter)
4. **Start stroke prevention measures** (like ischemic stroke)

Hemorrhagic transformation :

- **> 50% of ischemic stroke have some hemorrhage**
- **Risk factors:**
  a. Older age
  b. Larger stroke size
  c. **Anticoagulant use**
  d. **Thrombolytic therapy/recanalization: increases the risk of haemorrhagic transformation**

Prognosis :

- **Why does hemorrhagic stroke carries worse prognosis?** Because the blood can compress the neurons, blood vessels. Also, it will cause edema and herniation

L57- Hemorrhagic stroke

Intracranial hemorrhage (ICH):

- meningeal space hemorrhage:
  - epidural hemorrhage.
  - subdural hemorrhage..
  - subarachnoid hemorrhage.
- intracerebral:
  - brain parenchyma.
  - IVH.

Risk factors:

- Hypertension. - excessive alcohol use. -smoking. -obesity. - physical inactivity. -older age.
- ethnicity/race. - medications (antiplatelet or anticoagulant). -sympathomimetics (cocaine & amphetamine in young age).

Etiology :

- Hypertensive ICH: 1- Essential: rupture of microaneurysms (Charcot-Bouchard aneurysm). 2- Eclampsia.
- Non-hypertensive ICH:
  1- Vascular malformation: aneurysm, cavernous hemangioma, bleeding disorders, venous and cavernous angiomas.
  2- anticoagulant (more than antiplatelets)
  3- Amyloid angiopathy: elderly especially Alzheimer pt. usually in cortical and subcortical areas (lobar area).
  4- Trauma: commonly causes subdural hemorrhage or epidural hemorrhage.
  5- Tumor
  6- Drug abuse: amphetamine, cocaine, and PPA.
- other causes:
  1- Cerebral venous thrombosis (CVT): young female due to OCP use.
  2- Intracranial neoplasm.
  3- Moya Moya.
  4- Vasculitis.

Pathophysiology :

- Primary immediate effect: hemorrhage growth and increase intracranial pressure.
- Secondary effect: downstream effect, edema, and ischemia.
- Site: basal ganglia, lobar regions, thalamus, pons, and cerebellum.

clinical presentation :

- **Alteration in level of consciousness**
- **Nausea and vomiting**
- **Headache**
- **Headache**

Investigations:

- LAboratory studies:
  - **CBC** → looking for thrombocytopenia.
  - coagulogram
- Imaging
  - **CT brain without contrast** (essential to differentiate ischemic from hemorrhagic)
    - Hyperdense signal intensity.
    - Multifocal hemorrhages suggests a traumatic etiology.
    - Hematoma volume can be approximately by (AxBxCx)/2.
  - **CT vessels:** CT angiography screening for AVMs, vasculitis.
- the workup:
  - MRI brain: with gado if looking for neoplasm, MRI diffusion-weighted.
  - MRA/MRV: if allergic to CT dye of if you're looking at venous outfkow.
    - MRA → for AVM and aneurysm.
    - MRV → for cerebral venous thrombosis.
  - Cerebral angiography.

Management of ICH:

- **Medical:**
  - **Control blood pressure:**
    - **Reduction of SBP to 140 is save.** why not less? to preserve blood perfusion to small vessel and preventing ischemia resulted from small blood vessel compression. in the area around the hemorrhage.
    - Use labetalol and/or nicardipine drip to titrate blood pressure.

L57- Hemorrhagic stroke *(cont.)*

Intracranial hemorrhage (ICH):

Management of ICH:

- **Medical:**
  - **Control blood pressure:**
    - Evidence-based practice nursing care:

- Watch for neuro decline -Type and cross with your labs -Head of bed > 30o elevation -Head midline
-Treat hyperthermia -Prevent vagal maneuvers -Control SBP (120-140) -Treat hyperglycemia
-Treat hyperthermia -Seizure prophylaxis -DVT prophylaxis only after 48hrs & no haemorrhage

  - Cerebral edema: soduim (hypoosmolar hyponatremia) and CO2
    - Use the ventilator to manage CO2.
    - Get the Sodium levels up to 145- 155.
    - Mannitol 3% Given to prevent brain herniation that's caused by the cerebral edema.
      - Give them hypertonic saline e.g. 3% sodium or mannitol to lower edema
- Surgical:
  - Surgery never works except in only two scenarios:
    - Cerebellar hemorrhage if the hemorrhage is small we will observe the patient for any deterioration
    - Labor superficial hemorrhage: if small observe the pt deterioration to take him to the OR.

subarachnoid hemorrhage (SAH):

Etiology:

- Aneurysm rupture: usually **berry aneurysm rupture**, most common sites are: anterior communicating artery, posterior communicating artery, and middle cerebral artery.
  - Can be perimesencephalic SAH.
- Arteriovenous malformation (AVM).

Differential diagnosis of SAH:

- Migraine: presence of neck stiffness usually indicates SAH.
- Acute bacterial meningitis.
- Cervical dissection.

Clinical presentation:

- **Sudden acute severe headache:** thunderclap headache (often occipital), could be followed by vomiting and death.
- Other features: raised PB, neck stiffness or pain, straining, sexual excitement, papilloedema, and loss of consciousness at the onset.
- Physical examination:
  - Distress & Irritability. - Photophobia. -Positive Kernig's sign: (may take hours to develop).
  - Focal hemisphere signs, such as hemiparesis or aphasia.

Investigations:

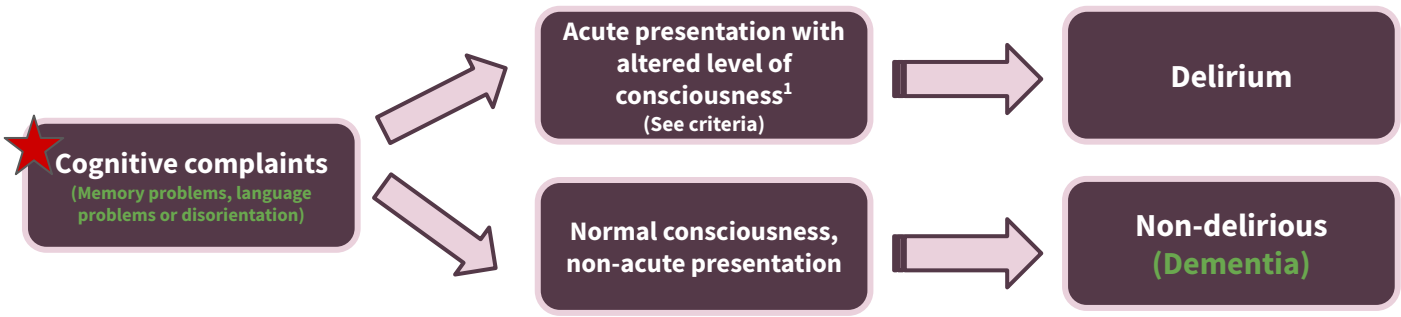
- CT brain scan: negative result does not completely exclude SAH
  - if CT is negative and the presentation is suggestive of subarachnoid hemorrhage then you do spinal tap to look for blood in the CSF.
- Lumbar puncture: performed 12 hr after symptom onset, to allow detection of xanthochromia → yellow CSF.
- CT angiogram: if wither CT of LP is +ve, angiogram is required to determine the optimal approach to prevent recurrent bleeding.

Management:

- Surgery: Coil/Clip
- Medication:
  - NIMOTOP/ NIMODIPINE: all the patient should be given, CCB prevent and treat the vasospasm, given for 21 days.
    - If patient develops vasospasm while on Nimodipine you should do angioplasty of the vasospasm.
- strict BP control.
- Check Sodium Levels → Treat the central Hyponatremia:
  - best managed by fluid restriction & 3% NaCl
- Check Urine output.
- Treat the obstructive hydrocephalus (a complication of SAH) → may require drainage via a shunt

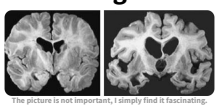
L58- Dementia

Characteristic	Delirium	Dementia
Causes	Metabolic, Toxic, Infectious, Drugs, Surgery & CNS disorders.	Vascular, Neurodegenerative, Infective, Toxic/Nutritional, Traumatic,Hydrocephalus, Inflammatory, Neoplastic & Prion.
Attention	Impaired (fluctuating (**worse at night**))	Usually alert
Onset	Acute (Hours/Days)	Gradual
Course	Fluctuating from hour to hour (waxing and waning)	Progressive deterioration
Consciousness	Clouded	Intact
Hallucinations/ Delusions	Present (often visual or tactile) Delusions of Harm	Rare, only in highly advanced disease
Diagnostic Criteria DSM-V	1) **Disturbance in attention** 2) **Change in cognition** 3) The disturbance develops **over a short period (usually hours to days)** and tends to **fluctuate** during the course of the day. 4) There is evidence from the history, physical examination, or laboratory findings that the **disturbance is caused by a direct physiologic consequence of a general medical condition**	1) **Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains:** - Learning and memory - Language - Executive function - Complex attention - Perceptual-motor - Social cognition 2) The cognitive deficits **interfere with independence** in everyday activities. 3) The cognitive deficits **do not occur exclusively in the context of a delirium.** **4) The cognitive deficits are not better explained by another mental disorder.**
Prognosis	Reversible	Irreversible
Treatment	Treat the underlying cause	Cholinesterase inhibitors



L58- Dementia *(cont.)*

Alzheimer's Disease
(Most common cause of dementia)

Clinical features	Risk factors	Pathophysiology	Diagnosis	Management
• **Decreased memory and new learning** • Language impairment • Apraxia • Unawareness of illness • Delusions • **Passivity** • **Delusions** • Depression, Circadian rhythm disturbances & Weight loss	• **Increasing age** • APOE ε4 • Down Syndrome • vascular risk factors(DM, HTN, Hyperlipidemia & Lack of exercise) • Brain trauma	• Accumulation of amyloid beta > **senile plaques** • Accumulation of hyperphosphorylated tau protein > **neurofibrillary tangles** • **Resultant loss of neurons and synapses, (esp. in basal forebrain leading to cholinergic deficit)**	• **Diagnosis is clinical** • **Brain structure on MRI may demonstrate medial temporal atrophy bilaterally** • **PET scans can demonstrate decreased metabolism in temporal and parietal regions** 	• **Donepezil, rivastigmine and galantamine which increase central nervous system acetylcholine** • Does not stop disease progression, only provides transient clinical stability. • Not a treatment, but education and **physical activity (Most beneficial)**

Lewy body dementia (LBD): dementia and signs of Parkinson's disease.
(Second most common cause of dementia)

Clinical features	Notes	Pathophysiology	Diagnosis	Management
• **Visual hallucinations** • **Parkinsonism** • **Fluctuations in cognitive ability** and **level of consciousness.** • **Visual spatial impairment** • **Sensitivity to neuroleptics** • **REM sleep behavior disorder** • **Autonomic dysfunction**	Parkinson's Disease Dementia (PDD) is similar to LBD, The difference is that a clear history of PD with NO cognitive impairment precedes the development of dementia by at least a year.	• **intracytoplasmic "Lewy Bodies" present in neurons, which are the result of abnormal α-synuclein protein accumulation**	• **Diagnosis is primarily clinical** • **PET scan may show decreased occipital lobe metabolism** • Myocardial scintigraphy may be abnormal due to abnormal cardiac sympathetic innervation	• Same as Alzheimer's Disease.

Frontotempol Dementia:
A number of different syndromes characterised by behaviour abnormalities and impairment of language.

Behavioral Variant	• Associated with personality changes, inappropriate social behavior (**disinhibited**), **lack of insight**, **Binging on certain foods**, **emotional blunting**, rigidity & decreased attention modulation. • MRI: **atrophy in the frontal lobes** (may be asymmetric).
Primary Progressive Aphasia	• Slowly progressive non-fluent aphasia: Patients present **first with a non-fluent type of aphasia.** • MRI : **focal left frontal atrophy**
Semantic Dementia	• Usually have **intact fluency, but comprehension is impaired** and decreased naming ability. • MRI may show focal **left temporal atrophy.**

Vascular Dementia

Clinical features	Risk factors	
• Frequently coexists with Alzheimer's disease	• Hypertension • Hyperlipidemia • DM • Smoking	• A single stroke in a region important to cognition such as **hippocampus or thalamus**, or a large stroke that affects multiple lobes. • **Recurrent strokes** that accumulate over time, there is a **step-wise development of cognitive deficits.** • **Slowly progressing cognitive** deficits due to subclinical progressing of **small vessel disease**.

Normal pressure hydrocephalus (NPH) (Rare)

Clinical features	Notes	Pathophysiology	Diagnosis	Management
Classically triad of: • **Gait impairment "magnetic"** • **Dementia** • **Urinary incontinence**	- In 2ry NPH, there is a history of a previous meningitis, inflammatory disorder, or SAH. - Idiopathic NPH is when there is no preceding explanation for the condition.	• **Impaired CSF absorption at the level of the arachnoid villi**	• **Improvement after a LP that removes 30-50 cc of CSF** • **MRI: dilated ventricles (CSF pressure is normal)**	• **CSF shunting procedure is performed.**

Creutzfeldt-Jakob Disease (CJD) (Rare, 1 in a million)

Clinical features	Notes	Pathophysiology	Diagnosis	Management
• **Rapidly progressing dementia, disease duration (usually 6 months).** • **Myoclonic jerks may occur.**	Prion disorder	• abnormally formed proteins that induce pathological transformations in other proteins leading to leading to spongiform pathology in brain	• **CSF Analysis: ↑ 14-3-3 protein** • **EEG shows characteristic periodic sharp wave complexes** • abnormal signal intensity in the basal ganglia and cortical ribbon	• **No treatment, patients die within a year.**

Feel free to vent here, no one will read it..

L59- Parkinsonism

◀ Types of movement Disorders

- **Hyperkinesia:** Myoclonus, Tremor, Dystonia and Chorea.
- **Hypokinesia:** Bradykinesia.

◀ Parkinsonism

- Clinical syndrome characterised primarily by bradykinesia, with associated increased tone (rigidity), tremor and loss of postural reflexes.
- **Most common cause is idiopathic parkinson's disease.**

◀ Idiopathic Parkinson's disease

Pathophysiology

- Presence of neuronal inclusions called **Lewy bodies** which contains tangles of α-synuclein.
- **Loss of the dopaminergic neurons** from the substantia nigra

Risk Factors

- Older age, men, pesticide exposure, MPTP (potent mitochondrial toxin) and non-smokers.

Clinical features

- Pre-motor → Ansomia, **REMBD**, autonomic dysfunction and Depression/anxiety.
- Motor →
  - **Bradykinesia**; **slowness of movement** and progressive **fatiguing**, **mask like semblance** of the face.
  - **Parkinsonian tremor** "pill-rolling"; rhythmic **oscillatory**, **predominantly at rest, re-emergence with maintained posture.**
  - **Rigidity;** "lead-pipe" "cogwheel", **independent of velocity.**
  - **Postural gait changes;** stooped posture, **shuffling**.
- Quit speech and drooling, **Visual hallucination.**

Diagnosis

- Clinical with normal imaging.

Management

Levodopa/Carbidopa (LD/CD)	Dopamine agonists (Pramipexole, rotigotine)	other drugs
- **Mainstay of treatment** - **Relieving akinesia and rigidity** - Combined with dopa decarboxylase inhibitor (carbidopa). - **ADRs**: ON-OFF phenomenon; ON with dyskinesia happens when the levels of L-dopa are too high.	- Used in combination with levodopa or as **initial monotherapy in younger patients < 65–70** with mild to moderate impairment. - Apomorphine: short-acting DA administered subcutaneously, It is used in advanced PD - **ADRs**: fibrotic reactions, including cardiac valvular fibrosis.	- (MAO)-B inhibitor: Selegiline - COMT inhibitors : Entacapone - Anticholinergic: help tremor, cause **confusion and cognitive impairment in older patients**.

Other management options

- Deep brain stimulation (DBS) → LD/CD responsive patients only) as an adjunct to treatment.

◀ Red flags

If present, suspect conditions other than Parkinson's disease.

- **Neuroleptic or anti-emetic drug use.**
- Early/prominent autonomic dysfunction
- Limited eye movements
- Pyramidal, cerebellar or sensory symptoms
- Cognitive impairment

L59- Parkinsonism *(cont.)*

◄ Other akinetic-rigid syndromes

Drug induced Parkinsonism	- **Metoclopramide** or haloperidol
Progressive Supranuclear Gaze Palsy	- Parkinsonism + the inability to look up & down due to degeneration in the part of the midbrain. - **Path**: Shrunken midbrain "**hummingbird sign**" and Tau deposition.
Multiple System Atrophy	- Cerebellar signs, extrapyramidal system and severe **early autonomic dysfunction.** - **Path**: α-synuclein inclusion and hot cross bun sign".
Vascular Parkinsonism	- Upper motor neuron signs, results from multiple strokes.
Corticobasal degeneration	- Cortical impairment: **Sensory, Astereognosis, Agraphesthesia, Apraxia.**
Wilson's disease	- Copper deposition occurs in the basal ganglia, the cornea and liver causing cirrhosis. - **Young patients <50** - Check serum copper and ceruloplasmin.

◄ Hyperkinetic disorders

Essential Tremor	- Hereditary, benign condition but impairing. - Slowly progressive, bilateral, asymmetric, upper limbs action tremor, that disappears at rest. - There is no bradykinesia, rigidity, or dystonia. - Cerebellar tremor could look exactly like an essential tremor. - Treated with **Propranolol**
Dystonia	- same movement happening persistently or repetitively, usually there's contraction of both agonist + antagonist muscles at the same time. - **Ballismus**: large amplitude choreiform movement, seen after subthalamic strokes usually, botulinum toxin injections or DBS may be useful.
Chorea	- continuous flow of random muscle contractions ('dance-like'). - Can occur in "Sydenham's Chorea" and in Huntington's disease (HD)
Myoclonus	- Involuntary single quick contraction of a muscle group (or its inhibition). Can be repeated but **not rhythmic**
Tics	- stereotyped movements or vocalizations (may be temporarily suppressed)

L60- Myopathies

Inflammatory Myopathies	**Polymyositis (PM):** inflammatory myopathy affecting the proximal skeletal muscles
	Dermatomyositis (DM): inflammatory myopathy that presents similarly to polymyositis, **with the addition of skin involvement**
	Inclusion body myositis (IBM)
	• **Skin features (Specific for DM):** Gottron papules, heliotrope rash, and the shawl sign
	• **Malignancies are associated with DM > PM**
	• Patients with IM typically complain of **muscle weakness** with difficulties reaching overhead, **climbing the stairs**, and/or **standing up**. Advanced disease may present with **dysphagia** and **aspiration** because of oropharyngeal muscle involvement, or even **respiratory failure** if breathing muscles are affected.
	• **DM** is primarily **distinguished** from **PM** by the **characteristic rash.**
	• **The best initial test is CPK and aldolase**
	• **Muscle biopsy is the pivotal investigation (most accurate test)!**
	  ○ **DM:** Perifascicular atrophy
	  ○ **PM:** No Perifascicular atrophy
	• **interstitial lung disease is strongly associated with the presence of antisynthetase (Jo-1) antibodies**
	• **Management: Steroids & screen for underlying malignancies**

Inclusion body myositis	**Inclusion body myositis (IBM):** inflammatory myopathy affecting both the proximal and distal skeletal muscles (mainly **Distal**). Common after **age 50** • **Quadriceps muscle weakness (Thigh):** knees lack support → frequent falling ○ Usually spares rectus femoris muscle • **+/- long finger Finger flexors:** difficulties gripping, e.g., shopping bags or a briefcase • **Severe Oropharyngeal dysphagia** • **Biopsy (most accurate test):** Inflammatory cells invading non-necrotic muscle fibers, Rimmed vacuoles. • Relentless progression, lacks effective therapies

Drug Induced Myopathies	• **Steroid myopathy:** due to chronic exposure to steroids
	  ○ Biopsy: type 2 fiber atrophy and lipid accumulation in type 1 fibers.
	• **Statin Induced Myopathy:** Statins inhibit HMG-CoA reductase, rate-limiting enzyme of cholesterol biosynthesis. Can cause:
	  ○ Discontinuation of the statin → resolution of symptom

Dystrophinopathies	• **They are x-linked recessive disorders** (manifest in males). **Duchenne** (**early** age) and **becker** (**late** age). • **Mutation** in the **dystrophin gene (Xp21)** → **absent** (in duchenne) or **reduced** (in becker) Dystrophin **DMD:** • **Symmetrical progressive (Proximal > distal) muscle weakness** (**Legs** & **Arms**) • **Course:** Onset age **2 to 5 yrs**, **Wheelchair** at **10/** • **Gower's sign, Loss of ambulation** at age 9-13 years, **Muscle hypertrophy: Especially calf** • **Dilated cardiomyopathy:** common after age 15 (usually the cause of death) **Becker:** • Older age at onset, Muscle weakness starts from > 7 yrs. Slowly progressive. "Becker is Better." Loss of ambulation usually in the 4th decade Investigations & Management: • Muscle biopsy: **absent dystrophin staining** (DMD). **Partial loss** of dystrophin staining (BMD)

L60- Myopathies *(cont.)*

Facioscapulohumeral dystrophy	• **Manifestations are Asymmetrical**
	  ○ **Face:** Initial manifestation, 95% you will detect it at the age of 30 with examination
	  ○ **Eyes:** Often early in disease course
	  ○ **Lid closure:** Incomplete
	  ○ **Sleeping:** With eyes open
	  ○ **Shoulder:** Pain in shoulder girdle, scapular winging, triple humb
	  ○ **Ear:** deafness
	• **Screen for:**
	  ○ **Hearing loss**
	  ○ **Retinal vascular disease**
	• **No screening** for cardiac needed unless symptomatic

Emery – dreifuss muscular dystrophy	• **Weakness: Humeroperoneal**
	  ○ Bilateral, Symmetrical
	  ○ Arms: Biceps & triceps; Deltoids spared.
	  ○ Scapular winging
	  ○ Legs: Late
	  ○ Face: Mild weakness or normal
	★ **Contractures occurs before weakness and it is often more limiting to function than weakness.**
	  ○ **in elbow, achilles tendon**
	  ○ **Spine:**
	  ■ Posterior neck (extension), Lower back: Usually later onset, but may present with rigid spine syndrome.
	• **Testing:**
	  ○ CK, EMG, **Cardiac screening for arrhythmia and cardiomyopathy (leads to sudden death)**

Myotonic Dystrophy	• The **most prevalent** inherited neuromuscular disease in **adults** (**Autosomal dominant**). • **Tandem repeats at DMPK gene (Anticipation phenomenon)** • **difficulty releasing hand grip on a doorknob or handle.** • **Frontal balding, Cardiorespiratory weakness** • **EMG:** myopathic plus **myotonic** discharges. Genetic testing (confirmatory test)
Malignant Hyperthermia	• **Triggered:** Anesthetics, Depolarizing neuromuscular blocking agents • **Clinical features:** Tachypnea, tachycardia, Rigidity, Acidosis ,Hyperkalemia Rhabdomyolysis, High CK, Hyperthermia. • **Treatment:** Remove anesthetic agent, Dantrolene sodium

Rhabdomyolysis	• Acute Syndrome of **muscle necrosis** due to extensive **injury** of skeletal muscle with **release of intracellular** muscle materials into the **circulation**.
	• **What is the commonest muscle disorder that causes myoglobinuria? Metabolic myopathies**
	• **Clinical features:**
	  ○ **Cola or tea color "dark" urine (Myoglobinuria)**
	  ○ **Elevated blood and urine myoglobin**
	  ○ Fever, **leukocytosis**
	  ○ Markedly **elevated CK**
	• **Complications: ↑ K+ → arrhythmia → death**
	• **Management: IV hydration** to **avoid** acute tubular necrosis (**ATN**) and **renal failure** !!!

L61- Multiple sclerosis

Multiple sclerosis	

Definition	• A chronic autoimmune, **T-cell- mediated**, inflammatory disorder of the CNS.
	  ○ **Myelin is produced by:**
	  ◆ **Schwann cells:** Peripheral nerves.
	  ◆ **Oligodendrocytes:** CNS
	• The most common chronic inflammatory, demyelinating and neurodegenerative disease of the CNS **in young adults**

Risk factors	• **EBV Infection:** Most common • **Vitamin D: Sun exposure & serum vitamin D are inversely related (**Sunlight may be protective**)** • **Smoking: also increase the severity of MS** • **Obesity & Genetics**
Epidemiology	• The life expectancy of patients **is reduced by 7–14 years.** • MS is the main cause of death in more than 50% of patients. Mostly due to MS complications e.g. aspiration pneumonia or Neurogenic bladder (→ Infections → sepsis)
Patho-physiology	**1.** **Characterized by breakdown of the blood—brain barrier (BBB)** → entry of **activated T lymphocytes &** other inflammatory cells nto the CSF **(1st change in MS)** **2.** Recognise myelin-derived antigens on the surface the microglia → **initiates destruction** of the oligodendrocyte–myelin unit **by macrophages** **3.** Most easily recognized **in the white matter** as focal areas of demyelination, inflammation, and glial (astrocytes) reaction → **Plaques** • Recurrent relapses lead to permanent myelin and axonal damage and oligodendrocytes loss

Pathology	• **Plaques of demyelination**, 2–10 mm in size, are the **cardinal features**.
	• Lesions are most easily recognized **in the white matter.** There has to be multiple lesions, if only one then it's not MS
	• **Plaques occur anywhere in CNS white matter but most commonly sites:**
	  ○ Optic nerves
	  ○ Periventricular region
	  ○ Corpus callosum
	  ○ The brainstem and its cerebellar connections
	  ○ Cervical cord (corticospinal tracts and posterior columns)
	  ■ **Spinal lesions:**
	  • **In MS: short** and **peripheral** (visualized on axial images)
	  • **In NMO: long** and **central** or circumferential.

Clinically isolated syndrome (Pre-MS)	★ **CIS is the first clinical episode that is suggestive of MS** • **Why don't we classify them under MS?** Bc it's only one episode and not all of them develop MS (Many ppl in their 20s may get this attack and then live normal for the rest of their lives) • Monophasic episode with symptoms and objective findings that reflect inflammatory demyelinating event in the CNS. • lasting for at least 24 hrs. (If less than 24hrs then it's NOT an MS attack) • Occurs in the absence of fever or infection • Resembles a typical MS relapse (attack) but occurs in a patient not known to have MS

L61- Multiple sclerosis *(cont.)*

Four main clinical pattern	**Relapsing-remitting MS (RRMS) (85–90%)** • **The typical and most common pattern of MS** • A purely RRMS is characterized by the **absence of worsening** neurological function outside of individual relapses • **The majority will eventually enter a secondary progressive phase** **Secondary progressive (SPMS)** • **Worsening irreversible** neurological function, **preceded by RRMS** that cannot be explained purely by worsening associated with ongoing relapses • This late stage of MS consists of **gradually worsening** disability progressing slowly over years. • Starting early treatment in RRMS can delay the onset of SPMS and hopefully even prevent it. **Primary progressive (PPMS) (10-15%)** • **Irreversibly continuous** worsening neurological function, **without preceding relapses** • Patients older at onset or with PPMS **have shorter survival.** Example: a 40 years old lady presenting with slowly progressing weakness in the lower limb. At first she was able to walk independently, then she depended on a cane to help her walk for months, afterwards she noticed that she needs a walker (bilateral support) to walk, which she kept using for a few months to years, and now she needs a wheelchair. **Relapsing–progressive MS (<5%).** • This is the least common form of MS. • It is similar to PPMS but with occasional supra-added relapses on a background of progressive disability from the outset.
Clinical feature of Multiple sclerosis	
Optic Neuritis ★	• **Blurred vision** usually in one eye. **NOT double vision**, seeing black dots, can't see clear in the dark. • **Pain exacerbated by eyes movement**. • Reduced perception of **colors**. (red desaturation, the color will be pale in the affected eye) • Flashes of light on moving the eyes. • Enlarged blind spot. because the optic nerve is inflamed and swollen **Note: Blurred vision in one eye + Pain on eye movement = Almost always optic neuritis**

Brain Stem Related Symptoms	• **Diplopia** if the nucleus of 3rd,4th and 6th nerves affected (the CNs themselves aren't affected, what's affected is their nucleus)
	• **Trigeminal neuralgia:** is a severe pain that happen when one of the divisions of V CN distribution is touched and lasts for a few seconds, happens if involve trigeminal nerve (sensory).
	• **Vertigo (spinning sensation) and nystagmus,** happens if there is a plaque in the cerebellum
	• **Facial numbness and weakness:** if the facial nerve is involved
	• **Internuclear ophthalmoplegia (INO): Bilateral internuclear ophthalmoplegia is pathognomonic of MS**
	  ○ A Specific gaze abnormality, characterized by impaired horizontal eye movement with weak adduction of the affected eye and abduction nystagmus of the contralateral eye
	  ○ Resulting from a lesion in the **medial longitudinal fasciculus** in the dorsomedial brainstem tegmentum of either the pons or the midbrain.
	  ○ If you see it in young patient almost always MS (If elderly, think stroke)

L61- Multiple sclerosis *(cont.)*

Clinical feature of Multiple sclerosis (Cont)	
Cerebellum Related Symptoms	• **Oscillopsia:** (A visual disturbance in which the object in the visual field appears to oscillate due to nystagmus) • **Dysarthria:** (Slurred speech) • **Imbalance:** (Wide-based gait)
Brain And Spinal Cord Symptoms	• **Lhermitte's sign: electric like sensation induced by neck flexion, very serious almost always indicate spinal cord lesion** (any **cervical** cord lesion, not specific to MS) • **Sphincter dysfunction.** urine incontinence, neurogenic bladder and stool incontinence**,** commonly seen if there is spinal cord lesion • **Cognitive dysfunction: memory, concentration, processing speed. (Uncommon in MS**,and usually does not happen with the first attack**)** • **Sensory loss/numbness/pain** • **Weakness (monoparesis, paraparesis, quadriparesis).**
Transverse Myelitis	• A general term that indicates inflammation of the spinal cord with cord swelling and loss of function. Typically, one or two spinal segments are affected with part or all of the cord area at that level involved • Spinal cord related motor, sensory &/or autonomic dysfunction. transverse in the name means involve more than one area of the spinal cord • **Sensory level,** means the is loss of sensation in a specific level eg. patient has complete loss of sensation from mid abdomen and below, this sign **indicate a spinal cord lesion**
Uhthoff phenomenon ★	• **Temporary worsening of pre-existing symptoms with increases in body temperature**, e.g. after exercise or a hot bath • Less than 24 h, Reversible if last for more than 24h think about relapse • It does not indicate that there's ongoing damage, it only indicates that there was an area of inflammation and demyelination

Diagnosis of MS: To diagnosis of MS you must have both:

Dissemination in time	Dissemination in space
• History of **at least two attacks** separated by at least one month. • **if 2 attacks occur in the same month it's counted as 1**	• Clinical evidence of involvement of **two CNS sites OR** of **one lesion with historical evidence of another site being affected.**

• **The presence of multiple lesions on MRI (dissemination in space) or the demonstration of additional clinical attacks on MRI (by showing lesions of different densities (dissemination in time)) fulfills the criteria for MS despite the presence of one attack in the patient's history** (enhancing are new, non-enhancing are old**)**

- **it is essential to ask about previous episodes of neurological symptoms**
- MRI is both the **best initial test and the most accurate test.**
- **Lumbar puncture and CSF analysis:** if you not sure about the diagnosis another way to confirm it is to do lumbar puncture and look for **oligoclonal IgG bands**, BUT **with presence of relapse and remitting symptoms.** Rarely used anymore

L61- Multiple sclerosis *(cont.)*

Management of MS

Acute treatment of relapses

- **Steroids (IV or orally Methylprednisone)**
- **Most of the time relapses resolve on their own but steroids shorten the relapse episode.**
- Only given when relapse is significant or affecting their life (e.g. a pilot comes with blurred vision = needs immediate attention = use steroids)
- **Plasma exchange** is used for those who don't respond to steroids

Disease modifying treatments

- Low efficacy DMT (eg: interferon, teriflunomide) vs high efficacy DMT (eg: natalizumab)

Examples:

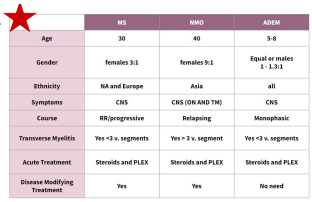
- **Patient with depression:** do not give interferon as it worsens depression
- **Patient with cardiac condition:** do not give fingolimod - causes heart block and seriously arrhythmias
- **Patient came with only tingling, no residual disabilities after the attack, few lesions on MRI→** give low efficacy DMT (interferon or teriflunomide)
- **Patient with only numbness, but had a previous relapse in which she described ataxia and difficulty walking, do we give her low efficacy DMT?** No (if u check MRI, you might find extensive lesions, multiple on spinal cord (very bad prognostic sign)) → start on fingo (medium efficacy DMT) or Natalizumab (high efficacy DMT)
  - **Natalizumab can cause:** Progressive multifocal leukoencephalopathy **PML (fatal) & leukemia**

Other Demyelinating Diseases

Neuromyelitis Optica Spectrum Disorder (Devic's disease)

- Characterized by longitudinally **extensive transverse myelitis (>3 segments)** and bilateral or recurrent optic neuritis.
- **Mean age is 10 years** later than MS.
- Affects mainly the optic nerves and the spinal cord
- **More severe attacks than in MS.** (presenting with **nausea**, **vomiting** and **hiccups** are important red flags in NMO)
- **Usually negative OCB in the CSF. While 90% of MS has positive OCB**
- **Serum antibodies to aquaporin-4 water channels on astrocytes are diagnostic** (should be done for every suspected case)

Acute Disseminated Encephalomyelitis



	MS	NMO	ADEM
Age	30	40	5-8
Gender	females 3:1	females 9:1	Equal or males 1 - 1.3:1
Ethnicity	NA and Europe	Asia	all
Symptoms	CNS	CNS (ON AND TM)	CNS
Course	RR/progressive	Relapsing	Monophasic
Transverse Myelitis	Yes <3 v. segments	Yes > 3 v. segment	Yes <3 v. segments
Acute Treatment	Steroids and PLEX	Steroids and PLEX	Steroids and PLEX
Disease Modifying Treatment	Yes	Yes	No need

- Acute monophasic demyelinating condition.
- **Frequently preceded by vaccination or infection.**
- **More common in children.**
- **Usually a monophasic illness (no relapses).**
- **Pathology:** Wide spread white and gray matter peri venous ''sleeves'' of inflammation and Axons are relatively spared unlike MS and NMO.
- **Symptoms: Encephalopathy, Multifocal neurological deficit, May fluctuates over a 3 months period for one single attack (If more than 3 months, it's not ADEM)**

Behçet's disease

- Behçet's principal features are recurrent **oral and/or genitalulceration**, inflammatory ocular disease (uveitis) and neurological syndromes.
- Brainstem and cord lesions, aseptic meningitis, encephalitis and cerebral venous thrombosis occur.
- There is a predilection for ethnic groups along the ancient 'Silk Road' – Turkey, the Middle East and Asia. Behçet's is associated with the **HLA- B51 allele.**

L62- Neuromuscular junction disorders (NMJ)

Neuromuscular junction physiology :

- This binding of ACh to ACh receptors in the motor end plate causes ion channels to open & so allow the sodium (Na+) ions to flow across (influx) the membrane into the muscle cell , generates a muscle action potential.

Classification of NMJ disorders :

1. According to the mechanism of action or etiology
   a. Immune mediated : Myasthenia gravis and lambert eaton syndrome
   b. Toxic / metabolic : Snake venom, Botulism, Organophosphates and Hypermagnesemia.
   c. Congenital : Congenital myasthenic syndrome
2. According to the location of the disruption:
   a. Presynaptic : decrease in the release of acetylcholine and impair the calcium channels
      - Lambert Eaton Syndrome , Botulism, and Congenital myasthenic syndrome
   b. Synaptic : Organophosphate
   c. Postsynaptic : The highest number of diseases affect the neuromuscular junction postsynaptically. either affects the Na+ channels or the ACh receptors : Immune mediated myasthenia gravis (most common)

Myasthenia gravis Definition :

The hallmark of the disorder is a fluctuating degree and variable combination of weakness in ocular either alone or in combination with , bulbar, limb, and respiratory muscles.

Epidemiology :

- Myasthenia gravis occurs at any age, but there is a bimodal distribution to the age of onset:

Pathophysiology of MG :

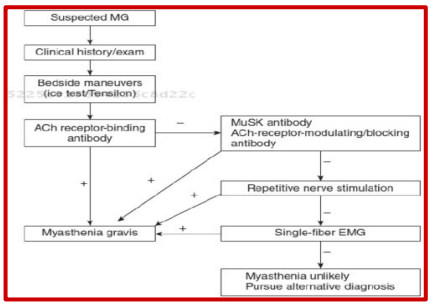
- In MG, there is reduction of postsynaptic AChRs due to production of anti-AChR antibodies that block receptors from binding to Ach and causes damage the postsynaptic membrane.
- Reduction in the number of AChRs available at the muscle endplate and flattening of the postsynaptic folds.
- Patients become symptomatic once the number of AChRs is reduced to approximately 30% of normal.
- Cause of fatigability in MS? **inefficient neuromuscular transmission (pathological) + presynaptic rundown phenomenon (normal)**
- **Which receptors are affected in MS? ONLY nicotinic** (skeletal muscles), while cholinergic (smooth &cardiac) are NOT affected.

Clinical features:

- >50% of patients present with ocular symptoms of ptosis (drooping of eyelids) and/or diplopia .
- half (80%) will develop generalized disease within two years.
- The distinguishing clinical feature in MG is fatigable weakness.
- Ocular myasthenia : The weakness is limited to the eyelids and extraocular muscles. Medial rectus muscle is usually most severely involved extraocular muscle
- Generalized disease : The weakness commonly affects ocular muscles, but it also involves a variable combination of bulbar, limb, and respiratory muscles.
- maximum severity is usually in first year of disease, if After 2 years with no limb symptoms, disease usually remains purely ocular.
- Ocular muscles: **Asymmetric ptosis (fluctuating), binocular diplopia, and Pupils spared**
- Bulbar muscles
  - fatigable- prolonged chewing). Sometimes this can be severe to the extent that it will lead to jaw drop.
  - dysarthria , dysphagia and difficulty clearing secretions, and breathy nasal speech and nasal regurgitation
- Facial muscles
  - expressionless face, **Transverse smile,** and Weak eye closure
- Neck and limb muscles :
  - Neck extensor and flexor (Musk : NE>NF), Dropped head syndrome, Limb weakness: **Proximal > distal,** usually symmetric, and Wrist and finger extensors and foot dorsiflexors.
- Respiratory muscles :
  - orthopnea, and respiratory insufficiency and pending respiratory failure "myasthenic crisis

Investigations:

- Acetylcholine Receptor (AChR) Antibodies. (Best initial) :confirm the diagnosis.
- Anti- MuSK antibodies : If they were seronegative to antiAchR do anti Musk.
- SFEMG. (MOST SENSITIVE TEST)
  - Time required for EPP to reach threshold varies – JITTER
  - Sometimes EPP fails to reach threshold – BLOCKING
- Ocular Cooling/"ice-pack" Test .
- Edrophonium Chloride (Tensilon) Test, causes bradycardia
- Repetitive Nerve stimulation (RNS) :decline in the CMAP amplitude with the first four to five stimuli (characteristic decremental) response
- CT mediastinum : Thymic hyperplasia is most common 85%. **All patients should have a thoracic CT to exclude thymoma**
- Other Autoimmune disorders



Management of MG :

Symptomatic treatment (anticholinesterase agents) :

- Cholinesterase Inhibitors: **Pyridostigmine (Mestinon).**

chronic Immunotherapy:

- Prednisone (Main one), Azathioprine (Imuran),Mycophenolate (CellCept)

MG crisis (Rapid therapy):

- Plasma exchange and intravenous immune globulin [IVIG]

Refractory MG :

- rituximab

Thymectomy::

- Patient has thymoma Or Positive ACh receptor antibodies + Generalised MG + Young patient

Lambert-Eaton Myasthenic Syndrome (LEMS):

- Itis a rare presynaptic disorder of neuromuscular transmission in which quantal release of acetylcholine (ACh) is impaired.

Epidemiology :

associated with a malignancy, mainly **small cell lung cancer (SCLC).**

Pathophysiology :

1. Caused by an autoimmune attack directed against the voltage-gated calcium channels (VGCCs) on the presynaptic motor nerve terminal
2. Parasympathetic, sympathetic, and enteric neurons are all affected Ca++ channels.

Clinical features:

- Weakness/Fatigue (LL>UL) in Limb-Girdle Distribution ,weakness improves with use in LEMS
- slowly progressive proximal muscle weakness, particularly involving the legs
- Autonomic symptoms including **dry mouth**
- Post-tetanic potentiation: Recovery of lost deep tendon reflexes or improvement in muscle strength with vigorous, brief muscle activation is a unique aspect of LEMS

Diagnosis :

1. The diagnosis of LEMS is usually clinical and confirmed by the presence of antibodies to voltage-gated calcium channel (VGCC)
2. High frequency (10, 20 to 50 Hz) **repetitive nerve stimulation (**RNS) or brief (10 seconds) maximal isometric muscle activation result in **significant increment** (>60%, unlike MG in which there's decrement) with a marked **increase in the CMAP amplitude**

Treatment:

1. treat a primary underlying malignancy
2. Symptomatic therapies : These are guanidine hydrochloride, aminopyridines such as 3,4-diaminopyridine (3,4-DAP, aka Amifampridine), and acetylcholinesterase inhibitors such as pyridostigmine
3. Immunologic therapies include intravenous immune globulin (IVIG)

Botulism:

Clinical features:

- **Acute onset (Unlike MG) of bilateral cranial neuropathies associated with symmetric descending weakness.**
- initial GI symptoms (nausea & vomiting)
- Pupils dilated , Ptosis, and EOM
- Bulbar weakness, Limb weakness, and Respiratory weakness.
- **Absence of fever, The patient remains responsive**

Diagnosis:

Repetitive nerve stimulation (RNS) at low frequencies of 2 to 5 Hz causes decremental response.
RNS at high frequencies stimulation or exercise causes incremental response,
The amount of facilitation seen with botulism (40-100%) is usually less than that seen in Lambert-Eaton myasthenic syndrome (200%).

Treatment:

- antitoxin.
- Supportive.
- Equine serum heptavalent botulism antitoxin is used to treat children older than one year of age and adults.

Human-derived botulism immune globulin is used for infants less than one year of age

Tick paralysis:

- inhibits transmission at the neuromuscular junction by blocking influx of sodium ions In the postsynaptic membrane
- Symptoms include anorexia, lethargy, muscle weakness, nystagmus, and an **ascending flaccid**
- **paralysis.**
- The diagnosis of tick paralysis usually relies on the finding of a tick attached to the patient.
- Removal of the tick is the primary treatment of tick paralysis.

Snake venom :

- **Presynaptic junction toxin: beta-bungarotoxin** (krait) / mechanism: inhibit Ach release by inhibiting reformation of the vesicles after exocytosis /management: only supportive, no response to anti venom.
- **Postsynaptic junction toxin: alpha-bungarotoxin** / mechanism: toxins bind irreversibly to the acetylcholine receptor site / management: Antivenom

Clinical features:

- ptosis, ophthalmoplegia, dysarthria, dysphagia, and drooling.
- Weakness of limb muscles.
- **impaired coagulation profile.**
- The postsynaptic toxins produce findings on electrodiagnostic studies identical to those seen in
- myasthenia gravis, Repetitive nerve stimulation produces a decremental response

Organophosphate and carbamates toxicity:

- potent inhibitors of acetylcholinesterase, causing excess acetylcholine concentrations in the synapse.
- Commonly used as pesticides.

Clinical features :

- Both sympathetic and parasympathetic systems are involved.
- Symptoms include muscarinic signs and nicotinic signs .

Management & diagnosis:

- Emergency management (ABC management) often requires endotracheal intubation and volume resuscitation
- **Atropine** is used for symptomatic relief of muscarinic symptoms.
- It does not reverse the paralysis

Hypermagnesemia / hypocalcemia

- Causes inhibition of a acetylcholine release
- Magnesium has a calcium channel blocking effect.
- This produces proximal muscle weakness , ocular muscles are generally spread.