PRIMARY HEADACHE

Headache-introduction 00:02:46

Pain sensitive cranial structures
Dura
Scalp
middle meningeal artery \( i, ii, xi, x \)
Falk cerebri
Ependyma
Choroid Plexus
Pial veins
Brain parenchyma

\( \{ \) pain insensitive structures \( \} \)

Headache classification 00:08:23

Primary
- Benign
- Recurrent
- No organic disease
  \( \downarrow \)
1. Tension type (mc)
2. Migraine
3. Trigeminal autonomic cephalalgias
   - Cluster headache

Secondary
- Malignant
- Organic disease
  \( \downarrow \)
1. Systemic infection (mc)
2. Head injury
3. Vascular disorder
4. Hemorrhage
5. Brain tumor (0.1%)
  \( \downarrow \)
due to ↑ intracranial pressure.
  "Dangerous headache"

Tension headache 00:11:17

mc type primary headache
Female>>Male (middle aged female)
30-45 years
One third of cases associated with depression
Fullness or tightness or pressure band
  \( \downarrow \)
doesn't affect activities of daily living
Headaches

- Sinus: pain is usually behind the forehead and/or cheekbones
- Cluster: pain is in and around one eye
- Tension: pain is like a band squeezing the head
- Migraine: pain, nausea, and visual changes are typical of classic form

No vomiting
- Photophobia
- Phonophobia

Patient is never disturbed from sleep due to headache

Migraine

- Episodic headache
- Started during school (10-15 yrs)
- Downward trend in frequency and severity over time
  - 60% common
  - 20% classical (aura+)
  - No aura
  - Visual > Auditory > Sensory

- Zigzag lines
- Fortification spectra
- Scintillating scotomas

2-3 days prior to attack
- Mood changes
- Irritability
- Depression

Fundus → No papilloedema (↑ ICT)

Treatment
1. Acute attack - NSAIDS
2. Chronic TTH - prophylaxis with Amitriptyline (TCA)
Migraine headache features

Aura → visual (20-30 minutes)
   ↓ auditory, sensory

Typical headache
W/L (sometimes become holocranial)

↓

Site - Frontotemporal > orbital

↓

Nature - Throbbing / pounding

↓

Nausea + or - vomiting

4-72hrs per episode

Photophobia / Phonophobia / Osmophobia

Aggravated by movement

↓

After headache patient feels lethargic, depressed

O/E - normal

Migraine theories

↓

Vascular theory

↓

Blood vessel dilation

Vasocstruction - "aura"

↓

Vasodilation - "headache"

Triggers

- Stress
- Hormonal fluctuations during menses
- Bright lights
- Lack of or excess sleep
- Sounds
- Alcohol
- Hunger (or other chemical stimulation)
- Excess stress

Pathology - CGRP (calcitonin gene related peptide)

Centre - Trigemino vascular complex
Rare types of migraine

1. Ophthalmoplegic migraine - transient w/ L 3rd N Palsy
   Completely reversible
2. Basilar migraine - Transient posterior circulation symptoms
   ataxia/vertigo/diplopia
3. Hemiplegic migraine - Transient weakness on one side
4. Retinal Migraine - Transient monocular visual loss
   Familial hemiplegic migraine - Ca2+ channelopathy

Episodic disabling headache of > 6 months duration with
normal neurological examination is migraine until proven
otherwise

Acute migraine Management

- mild
  Paracetamol
  or
  NSAIDs
  - Naproxen 550 mg bd
  - Ibuprofen 200 – 400 mg Q 4h
- moderate - severe
  - Triptans
  - SHT 1B/1D agonists
  - Oral RizatRIPTAN 5mg- 30mg
  - Eletriptan
    40mg - 80 mg
  - sumatriptan (oral, nasal, sc)
  - Zolmitriptan (oral or nasal)

Severe attack
- 6mg s/c sumatriptan
- Other drugs
- Ergot alkaloids - Dihydroergotamines
- Issues with triptans
  1. Triptan ineffective in classical migraine
  2. CAD/CVA patient contraindicated
  3. Clinical efficacy depends on T max
  4. Headache recurrence is least for Ergotamines

Newer treatment modality
- monoclonal Antibody against CGRP
  - Erenumab
Prophylaxis of migraine

First line - Propranolol
   TCA - Amitriptyline
   Topiramate

Second line - Telmisartan
   Venlafaxine
   Valproate

Third line - Pizotifen (5HT1 antagonist)
   Flunarizine (CCl6)
   Clonidine

Other modalities of treatment
1. Greater Occipital nerve block
2. Onabotulinum toxin A
3. supraorbital transcutaneous stimulation
4. CGRP antagonists
   Differential diagnosis - sinusitis

Trigeminal autonomic Cephalgia

1. Cluster headache (MC)
2. Paroxysmal hemicrania
3. SUNCT
   (Short lasting unilateral neuralgic headache with conjunctival congestion & tearing)
4. Hemicrania continua

TAC: Episodic
1. W/L severe headache (sharp stabbing)
2. Restlessness during attack
3. Ipsilateral autonomic symptoms
   Episode: 15 mins - 3 hours

TAC-autonomic features

1. Cluster headache, congestion & lacrimation
2. Nasal congestion & rhinorrhea
3. Eyelid edema
4. Forehead or facial sweating
5. Fullness in ear
6. Flushing
7. Ptosis / meiosis
Cluster headache
1. Episodic, short lasting, U/L, severe
2. Autonomic symptoms
3. Restlessness
Cardinal points
a. Periorbital
b. 15 mins - 3hrs, 1-8 attacks / day
c. 8-10 weeks → symptom free
   of symptoms → interval
d. Stabbing or boring pain
e. Nocturnal pain
f. Precipitated by alcohol
g. Photophobia ± (U/L)
h. Young male
Features
* also: suicide headache

[^20% Chronic
[^80% Episodic

Treatment of cluster headache

- "Reboxetine" 100% O₂ → 10 U/min for 10-15 mins
  or
  1 mg s/c Sumatriptan
Short term ← prophylaxis → Long term
  Prevention
  verapamil or
  Steroids
  Lithium
Paroxysmal hemihemian.
1. Episodic short lasting U/L headache (Severe)
   a) Restlessness
   b) Autonomic symptoms
      Cardinal features
      1. M=F, middle-aged
      2. Stabbing/boring periorbital pain
      3. 5-20 attacks / day
         ↓
         Each attack 2-30 mins (5 min average)
   4. No nocturnal preponderance
   5. Rapid response to Indomethacin
   6. Periodicity not so striking
      Alcohol trigger: no
SUNCT

- Conjunctival congestion ↑ hearing
- Female > male
- ↑ number of attacks
  - Each attack lasts for seconds
- Cutaneous trigger - no refractory periods
  - Acute attacks → IV Lignocaine
- Prevention → Lamotrigine
- No migrainous features
- Alcohol trigger: ± yes
- Hemianopia, continua
- Elderly females
- Continuous, U/L, migrainous features
- Autonomic ++
- Responsive to Indomethacin
- IOC - MRI

Trigeminal neuralgia

- Paroxysms of intense, brief, shock like superficial pain along the distribution of trigeminal nerve
- Few seconds to minutes
- Female > male
- 50 - 60yrs

Nature: v2/v3 (mo)

- Usually ophthalmic division not involved
  - Objective neurological signs absent

Cutaneous trigger

- Brief refractory period
  - U/L (mostly), can be B/L also.

- Compressive
  - Demyelination

- Superior cerebellar artery

multiple sclerosis
Tic douloureux
Diagnosis - 3D MRI
DOC - Carbamazepine > Lamotrigine
  S/C botox
  ↓
  Refractory
  microvascular decompression
HLA B-1502 in carbamazepine causes SJS (Steven Johnson Syndrome)
Eagle's syndrome
  • Enlarged styloid process
  • Glossopharyngeal neuralgia
DANGEROUS HEADACHE

Secondary headache

- Dangerous headache → increase intracranial headache.
- Cerebral Perfusion Pressure (CPP) = mean arterial pressure - intracranial pressure.
- Cerebral autoregulation.
- MAP → 60 - 110 mmHg → normal → CPP normal.

Causes of Dangerous headache:
1. CNS infections
2. Vascular causes
4. Brain tumors (space occupying lesions)
   → tumor, tuberculoma, neurocysticercosis.
5. Hemorrhage

Features of dangerous headache

1. Sudden onset severe headache / time to peak
   → bleed - ‘worst ever’ headache or ‘thunder clap’ headache
2. Subacute onset headache → worsening in severity → associated with vomiting, bending, lifting or coughing
3. Disturbs sleep → early morning headache
4. Any new onset headache with visual blurring or tinnitus
5. Known systemic illness
6. Onset after age 55 → temporal arteritis
7. Fever or unexplained systemic signs.
8. Abnormal neurologic examination
9. Pain associated with local tenderness
   → region of temporal artery.

Investigations:
- Fundal examination → confirms increased ICT.
- Papilledema.
• Early papilledema diagnosed by presence of:
  - Peripapillary halo, with obscuration of borders, elevation of nasal border

• Marked papilledema:
  - Elevation of entire nerve head
  - Obscuration of all the borders
  - Projections
  - Segment of major vessel obscured on the disc.

• Established papilledema:
  - Marked elevation of nerve head with blurring of margins.
  - Engorged tortuous venules.
  - Peripapillary splinter hemorrhages
  - Cotton wool spots.
  - Hard exudates over the disc and macular area.

• Chronic papilledema:
  - Classical champagne cork appearance of disk.
    - Pale disk.
  - Disc hyperemia decreases and disk progressively appears pale in color.
  - Optociliary shunts and drusen-like deposits may be present on the disc.
  - High water mark.

**Signs of raised intracranial tension**

1. Cushing's reflex → Bradycardia, bradypnea, hypotension.
2. Increased risk for arrhythmias.

• MRI Brain → to rule out intracranial space occupying lesions.

**Brain herniation**

1. Circumferential herniation (Subfalcine)
2. Central transtentorial herniation
3. Uncal herniation (m. c.)
4. Tonsilar herniation.

Cingulate herniation (subfalcine) 00:18:05

1. Cingulate gyrus
2. Anterior cerebellar artery (ACA)
3. Internal cerebral vein

Uncal Herniation:
- third nerve palsy
- PCA occlusion
- Kernohan's notch:
  - weakness on the side of herniation, called as ipsilateral hemiplegia.
  - hemiplegia. false localizing sign → Pressure ischaemia.
- third cranial nerve palsy
- PCA occlusion.
- as the herniating temporal lobe pushes the midbrain towards the opposite side of the insula.
- contralateral cerebral peduncle is forced against the hard edge of the tentorium.
- Abducen nerve palsy → false localizing sign (m. c.)
  - sign of raised ICP
- X-ray finding of increased ICP: silver beaten appearance.
a. subfascial (cingulate) herniation
b. uncal herniation
c. downward (central, transtentorial) herniation.
d. external herniation (not used now)
e. tonsillar herniation.

Cases

Dangerous headache ± blurring of vision in a healthy individual,
Fundus → papilledema.
MRI → normal (no intracranial space occupying lesion) → Sixth nerve palsy.

CASE I
1. Cerebral venous thrombosis (CVT)
   → headache + vomiting + signs of increased ICT, non specific weakness.
   → Infaracts with secondary hemorrhagic transformation.
   → MRI is required (specially in post partum) IUC.
   • CVT more common in post partum, females, underlying coagulopathies.
CT findings in CVT
• Cord sign → hyperdensity along the lines of transverse sinus.
• Dense triangle sign (Delta sign)
• Empty delta sign → in contrast enhanced CT.

• M2 venography is the investigation of choice.
   → empty delta sign

CASE II
2. Benign intracranial hypertension (Pseudotumor cerebri)
   → LP opening pressure more then 25 cm of H2O
   → 30-40 years, obese females.
   → Symptoms → headache, blurring of vision, tinnitus.
   → Fundus → papilledema.
MRI → No mass.
MRV → Normal
MRI shows → Empty sella → Primary empty sella syndrome.

Modified dandy criteria

1. Symptoms of raised ICP (headache, nausea, vomiting, transient visual obscuration, or papilledema.)
2. No localizing signs with the exception of 6th nerve palsy, patient is awake and alert.
3. Normal CT/MRI findings without evidence of thrombosis.
4. LP opening pressure of more than 25 cm H2O and normal biochemical and cytological composition of CSF.
5. No other explanation for the raised ICP

Approach:

Papilledema in a conscious alert patient with no neurologic signs except 6th nerve paresis

CT/Brain

SOL/hydrocephalus normal

LP

Abnormal Normal

CSF CSF

LP opening pressure high

MRV

Normal Abnormal

BIH CVT
secondary causes of benign intracranial hypertension
1. Electrolyte abnormality → Hypocalcemia.
2. Lead poisoning
3. Drugs: Growth hormone / Steroids / Danazol
   - Outdated tetrazyclines.
   - Nitrofurantoin
   - Vitamin A
   - Lithium

Treatment of BIH:
→ Weight loss
   → Acetazolamide
     or
     Topiramate
   +
   Furosemide
   → Repeated LP → Symptom relief
   → Refractory cases → CSF shunting
     or
     Optic nerve sheath fenestrations

Management of acute increased ICP:
1. Elevate head end.
2. Mannitol (15 to 30 mts for action)
3. Sedation
4. Hyperventilation
5. Pressor therapy to maintain CPP > 60 mmHg.
   → Thunderclap headache → most important cause subarachnoid hemorrhage
Other causes of thunderclap headache are
1. Apoplexy (Pituitary)
2. Acute hydrocephalus
3. CVT
4. Dissection (carotid or vertebral)
5. Hypertensive crisis (ICH, HTN encephalopathy)
   ∗ CT sign → star of death
NEUROCUTANEOUS SYNDROMES

- RIVA Neurooculocutaneous syndromes (embryonic ectoderm)
- RIVA Phakomatosis
  - NF-1 - Von Recklinghausen (Peripheral)
  - NF-2 - Central disease
  - Neurofibromatosis MC
  - Tuberous sclerosis
  - von Hippel Lindau disease
  - Sturge weber syndrome
  - Ataxia telangiectasia.

Tuberous sclerosis aka Bourneville disease
  - Pringle disease
  - Epilepsy
  - Low intelligence
  - Sebaceum

Sturge weber syndrome (RIVA Encephalotrigeminal angiomasis)

Neurofibromatosis

MC Phakomatosis
- NF-1: Neurofibromin, autosomal dominant chromosome 17
- Earliest manifestation: Cafe au lait spots
- Hyperpigmented: pre-pubertal > 5mm
- 2 or more spots
- post-pubertal > 15mm

Cafe au lait spots also seen in Mucune Albright syndrome

- Neurofibromas
  - MC: Peripheral - Requires 2 lesions to make diagnosis
  - Plexiform (even 1 single neurofibroma is sufficient)
Plexiform neurofibromas → premalignant
- Seen along the distribution of cranial nerves
  - Cutaneous & subcutaneous neurofibroma
  - Infratrochlear and facial branches of CN III - VI
  - Most commonly affects CN V
  - Diffuse plexiform neurofibroma of face
    and eyelid

Axillary freckles - Specific
- Small (0.5 cm) brown, well circumscribed
  macules
- Rarely in inguinal region
- Generally unnoticed

Optic nerve glioma: MC tumor seen in NF - I
- > 80% are asymptomatic
- B/L optic nerve gliomas - Diagnostic

Features on CT
- Abnormal enhancement
- Abnormal thickening
- Beading and elongation
  Optic nerve glioma, > astrocytoma, > brain stem glioma.

Other manifestations of NF - I

Lisch nodules - Iris
- A pigmented hamartomatous nevus
  affecting the iris
- Benign nodule (do not affect vision)
- No risk for malignancy
- Adult onset finding
- Only seen in slit lamp
  Diagnosis - 2 or more Lisch nodules

First degree relative in NF - I

Bone changes
- MC - Kyphoscoliosis > cortical thinning of long bones
- Classical - sphenoid dysplasia

Neurofibromas - peripheral nerve sheath tumors
Other Features
1. Astrocytoma.
2. Brainstem glioma.
4. Hypertension.
5. Mental impairment

Bony (less common)
1. Enlargement of intervertebral foramen
2. Ribbon ribs – Hypertrophied and twisted ribs
3. Posterior intervertebral scalloping

Neurofibromatosis - II

- Central neurofibromatosis
- B / L acoustic neuroma (Vestibular Schwannoma.)
- U / L acoustic neuroma
  + or + a / 5
  First degree relative
  1. Neurofibroma.
  3. Schwannoma.
  5. Posterior subcapsular cataract

Schwannomin / merlin gene - Chr. 22
Cutaneous manifestations are rare.
Other tumors – spinal cord ependymoma.

- Commonest presentation of vestibular schwannoma is progressive high frequency SNHL
- Meningiomas < 40yrs, benign
- Spinal cord tumors: Schwannoma > Ependymoma (MC)
- Schwannomas with NF-2 never undergo malignant change
- No cognitive impairment / mR
  No hypertension

Tuberous sclerosis

- AD with variable expression
- Spontaneous mutation
  TSC1 chr. 9 Hamartin
  TSC2 chr. 16 Tuberin
  (poor prognosis)
manifestations:

1. Ash leaf macule
   - Earliest manifestation - hypopigmented

2. Shagreen patch
   - 1 - 2 yrs age
   - Lumbosacral region / buttocks

3. Adenoma sebaceum
   - Cutaneous angiofibromas

IV. Fibrous plaques on forehead - specific

CNS manifestations
1. Earliest: Cortical tubers \( \to \) seizure
2. commonest: (cortical hamartomas)
3. \( 2^{nd} \text{ MC}: \) subependymal nodules
4. Subependymal giant cell astrocytoma (MC tumor) \( \downarrow \)
   (SEGA)
5. Obstructive Hydrocephalus
6. Infantile spasms
7. White matter lesions

Parieto occipital
e groove of lateral ventricle
Hoenen's tumor - Periungual fibroma (MC)
Subungual fibroma.

Systemic wise manifestation of tuberous sclerosis

1. Heart
   - Cardiac rhabdomyoma
   - Prenatal diagnosis of rhabdomyoma
     ↓
   - 80% risk for tuberous sclerosis
   - Apex of LV (MC site)
   - Benign tumor

2. Eyes
   - Retinal hamartomas - don't affect vision
   - Retinal achromatic patch
   - Retinal astrocytomas

3. Lung
   ↑ Risk for ILD
   - Pulmonary lymphangiomatosis
   - F > m
   - Cysts, pneumothorax
   - Rarely premalignant

4. Kidney
   - MC. Renal angiomyolipoma
     ↓
     - Bleeds into retroperitoneum
     - Bilateral large cyst
     - 1-2% risk for RCC

5. Other
   - Dental enamel pits - 100% patients
   - Confetti skin lesions - numerous hypopigmented macules over arms and legs
   - Bone cyst
   - Hamartomatous rectal polyps
   - Gingival fibroma
Von Hippel-Lindau Disease

- RD (chr. 3p)
- No cutaneous manifestations

Systemic manifestations:
- C - Clear cell Ca. of comma in between kidney and cysts in liver, kidney, and pancreas
- H - Hemangioblastoma of cerebellum and retina
- I - Islet cell tumor of pancreas
- P - Pheochromocytoma, papillary cystadenoma of uterus
- E - Endolymphatic sac tumor comma, b/w tumor and epididymal cyst
- S - Spinal cord tumors

Clear cell Ca.

<table>
<thead>
<tr>
<th>Non-VHL</th>
<th>VHL</th>
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<tbody>
<tr>
<td>Sporadic</td>
<td>RD</td>
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<tr>
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<td>Young</td>
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<td>M &gt; F</td>
<td>M = F</td>
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<td>Smoker</td>
<td>Non smoker</td>
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<tr>
<td>U/L</td>
<td>B/L</td>
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<tr>
<td>Blood spread</td>
<td>Lymphatic spread</td>
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VHL - Very few bilateral renal cysts
- RCC
- Cysts classically seen in pancreas

Pancreas

- Cyst
- Islet cell tumors

Hemangioblastoma - Cerebellar (MC)
- Retinal
- Spinal cord

Pheochromocytoma - Malignant
- Often bilateral

Hemangioblastoma:
- MC age: 20 - 50 years
- Multiple
- Seen in 2/3 patients of VHL
- Hallmark lesion of VHL
- MC cerebellar > medulla > pons > spinal cord (CNS)
- Epo secreting tumor - polycythemia
- Retinal - no visual loss

Medicina = v2.0 = Marrow 4.0 = 2020
Renal
- RCC
- Renal cysts - multiple, bilateral

Pancreas:
- Cyst
- Islet cell tumor

Sturge-Weber syndrome

- Sporadic
- No brain tumor
- Aka. encephalo-trigeminal angiomatosis
  i) Port wine stain at birth (U/L)
  a) Leptomeningeal capillary or venous
     malformation always ipsilateral
  b) Cerebral hemiatrophy
  C/F
  a. Seizures
  b. Congenital glaucoma / buphthalmos
  c. MR
  Calcification - Tram track / Rail track

Ataxia telangiectasia

- Autosomal recessive
- AT gene (Chr 11)
- Cerebellar ataxia (a - 4yrs)
- Oculomotor apraxia (a - 5yrs)
- Choreaathetosis
  Triad

Oculocutaneous telangiectasia

- Friedreich's ataxia - spinocerebellar tract problem
- Ataxia telangiectasia - cerebellar atrophy
1. Cutaneous granulomas
   a. Defective DNA repair and ↑ risk for malignancy
   b. Progeria (early onset aging)
   c. Hypertrichosis

MC malignancy - ALL (T cell > B cell)
- Dysgerminoma > HCC > Ca. stomach > Retinoblastoma.
- Increased risk of sino-pulmonary infection

Diagnosis
   α - Fetoprotein ↑
   Hypogammaglobulinemia (IgA ↓)
   Chromosomal breaks (X chr)
   Cerebellar atrophy.

Rare neurocutaneous syndromes

I. Hypomelanosis of Ito

   a) Sporadic
   b) 3rd MC neurocutaneous syndrome
      NF > TSC > Hypomelanosis of Ito
   c) Hypopigmented whorls, streaks
      and patches tend to follow Blaschko lines.

II. Incontinentia pigmenti A/V/A Bloch-Sulzberger syndrome

   a) X-linked dominant
   b) Functional mosaicism
      F > m
   c) Blistering and verrucous lesions

III. Phace syndrome

   P = post, Rosai, malformation
   H = Hemangioma
   A = Arterial anomalies
   C = Coarctation of aorta
   E = Eye anomalies
APPROACH TO PERIPHERAL NEUROPATHY

Lower motor neuron (LMN) Pathology:
- Lesion in M distal to the anterior horn cell (AHC)
- Lesion in P distal to the cranial nerve nuclei
Location:
- AHC: grey matter of spinal cord
- Cranial nerve nuclei: brain stem

Neuropathies
- Dorsal root ganglion - Sclerionopathy
- Spinal nerve root - Radiculopathy
  (dorsal + ventral root)
- Plexus - Plexopathy
- Nerves - Mononeuropathy
- Polyneuropathy
- Mononeuritis multiplex
  - Seen in medium vessel vasculitis
  - Typically polyarthritis nodosa
- Neuromuscular Junction
- Muscle

Neuropathy

peripheral polyneuropathy

Axonal Polyneuropathy

motor

Aδ fibers

Aβ fibers (Posterior column)

C (unmyelinated)

(A thick myelinated)

D, C (spinthalamic)

thin myelinated

Motor

Sensory

Autonomic

Nerve lesion

Demyelinating neuropathy

most common cause:
Guillain-Barré syndrome
usually acute
its usually polyradiculopathy

most common cause:
Diabetes mellitus(DM)
usually chronic
its usually peripheral
Polyneuropathy:
(Sensory >> motor)
Axonal Neuropathy

- Large fiber
  - Posterior column
  - Fine touch
  - Position, joint sense
  - Vibration sense

- Small fiber
  - Spinothalamic tract
  - Pain
  - Temperature
  - Crude touch, pressure
  - Tight band-like superficial pain

Axonal neuropathy

- Autonomic ±
  - Small fiber
  - Large fiber

- Autonomic -
  - Ganglionopathy
  - Radiculopathy

- Small fiber neuropathy

Causes:
- Most common cause: DM > Leprosy > Amyloidosis
  - Tangier's disease
  - Fabry's disease - Maximum pain
  - HIV
  - Vasculitis
  - SLE, CTD (Connective Tissue Disease)
  - Arsenic poisoning.

Clinical Presentation:
- Chronic axonal small fiber polyneuropathy
- Loss of key sensations such as: Pain, temperature, crude touch and pressure.
• Patients feel characteristic burning pain due to Regenerating nerves.
• Symmetrical involvement
• Evolution: distal to proximal - glove and stocking or dying back Neuropathy
• Minimal motor Symptoms
• Reflexes intact.
• Posterior column - intact.
• In early stages - nerve conduction - normal.
• In late stages - decrease in amplitude of motor / sensory action Potentials.
• Allodynia: non-noxious stimulus causes pain.
• Foot ulcers.

**Large fibre neuropathy**

**Causes:**

A. Vitamins
   - Vitamin B₁₂ ↓ - most common cause.
   - Pyridoxine Toxicity

B. Drugs:
   - Cisplatin, Taxanes
   - Friedreich's Ataxia.
   - Paraneoplastic Syndromes.

**Clinical Presentation:**

- Chronic axonal large fibre polyneuropathy
- Distal to proximal evolution
- Pins and needles, tingling, numbness and paresthesias
- Sensory ataxia.
- Diminished reflexes
- Motor findings - minimally present
- Nerve conduction studies - findings are more apparent.
  - Axonal - decrease in amplitude.

**Ganglionopathy and Radiculopathy**

**Ganglionopathy:**

- Causes: Sjogren Syndrome - most common cause.
  - Paraneoplastic Syndromes - Anti-Hu Antibodies
  - Small cell ca. of lung
- Rare causes: Cisplatin, Vitamin B₆ toxicity, HIV

**Clinical Presentation:**

- Only Posterior Column is involved - Truncal part
- Severe disproportionate sensory ataxia.
- Radiculopathy:
  - Asymmetrical
  - Root pain along the distribution.
  - Reflexes - lost
  - Muscles of that particular radicle is involved.
    
    \[ \text{Eg: if } L_4 \text{ root is involved ( } L_4 \text{ radiculopathy)} \]

    Supplies both Obturator and Femoral nerve

    Adduction of Hip and Extension of Knee - both are affected.

Combined small and large fibre neuropathy

Causes:
- Carcinomatous
- D.M
- Primary biliary cirrhosis
- Hereditary

Demyelinating neuropathies
Differences between Axonal and Demyelinating neuropathies:

**AXONAL**
- Mostly chronic
- Polyneuropathy
- Distal → proximal progression
- Reflexes - spared. (unless it's large fibre neuropathy)
- CSF: proteins - normal
- Sensory >> motor
- Wasting - minimal
- Nerve Conduction study CNCS] - Amplitude affected
- ANS ±

**DEMYELINATING**
- Mostly acute
- Polyradiculoneuropathy
- Diffuse proximal + distal
- Reflexes - lost
- CSF: Proteins - ↑
- Sensory - mild posterior column findings
- Motor >> Sensory
- Conduction velocity - ↓
- Distal latency affected
- ANS ±

Motor predominant neuropathies

**Causes**: ALD - GBS
- Acute intermittent porphyria.
- Diphtheria.
- Lead intoxication
- Hereditary motor sensory neuropathy
- Diabetic polyradiculoneuropathy / diabetic amyotrophy

**Predominant autonomic findings**:
- GBS - ALD
- DM
- Amyloidosis
- Porphyria.
- Paraneoplastic
- Drugs: Vincaistine, Cisplatin, Amiodarone.
- HIV.

Patterns of presentation

- Symmetrical proximal and distal weakness with sensory loss
  - Demyelinating disease. Eg ALD
- Symmetrical distal sensory loss with or without weakness
  - Axonal sensory motor neuropathy
- Asymmetrical distal weakness with sensory loss - mononeuritis multiplex or radiculopathies

Medicine v2.0, Marion 4.0, 2020
• Asymmetrical proximal and distal weakness with sensory loss - polymyelopathy or plexopathy.
• Asymmetrical distal weakness without sensory loss - amyotrophic lateral sclerosis (ALS) or multifocal motor neuropathy (MMN).
• Symmetrical sensory loss with distal areflexia and UMN features - Vit B6 / E / Copper ↓.
• Symmetrical weakness without sensory loss - muscle disorders or rarely anterior horn cell disorders like spinal muscular atrophy.
• Asymmetrical proprioceptive loss without weakness - ganglionopathy.

**Differences between demyelinating and Axonal disorders**

Based on nerve conduction study (NCS)

<table>
<thead>
<tr>
<th></th>
<th>Axonal</th>
<th>Demyelinating</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Amplitude - sensory / motor</td>
<td>Decreased</td>
<td>Normal</td>
</tr>
<tr>
<td>2. Distal latency</td>
<td>Normal</td>
<td>Prolonged</td>
</tr>
<tr>
<td>3. Conduction velocity</td>
<td>Normal</td>
<td>Slow</td>
</tr>
<tr>
<td>4. Conduction block</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>5. Temporal dispersion</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>6. F-wave</td>
<td>Normal</td>
<td>Prolonged</td>
</tr>
<tr>
<td>7. H-reflex</td>
<td>Normal</td>
<td>Prolonged</td>
</tr>
</tbody>
</table>

**F-Wave**:
- In Axonal pathology - No value for F-wave as the common motor action potential - [CMAP] is already reduced.
- In Early demyelinating pathology - CMAP - normal ↓
  - F wave latency prolonged.

**H-reflex**:
- It is equivalent to s, root / Ankle jerk.
- In Early demyelination - H-reflex prolonged.
PERIPHERAL NEUROPATHY: INHERITED AND ACQUIRED

Inherited peripheral neuropathies:
1. Charcot-Marie-Tooth disease
2. Familial Amyloid Polyneuropathy
3. Pernicious anemia
4. Fabry's disease
5. Refsum's disease
6. Tangier's disease

Charcot-Marie-Tooth Disease (CMTD)

Types 1, 2, 4 - Demyelinating
Types 1, 2, 3 - Autosomal Dominant
Type 2 - Axonal
MC - Type 1 CMTD
- Hereditary motor sensory neuropathy

Clinical features:
- Long, slow progressive history of weakness and muscle wasting
- Foot deformity: Pes cavus in an adult
- No definite sensory symptoms but definite large fiber sensory signs present.
- Distal muscles involved, proximal muscles spared.
- Uniformly slow motor conduction velocities - Demyelinating disease

(in acquired cause - patchy slowing)

On examination:
- Deep tendon reflexes: ankle jerks absent frequently associated with hypo/ areflexia.
- Upper limb involvement - in later 2/3rd of life.
- Distal muscles involved and proximal muscles spared.
- Inverted champagne legs.

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Inverted champagne legs  pes cavus

On Biopsy: Onion Bulb appearance – most classically in Type I

• Other deformities: Hammer toe, mild kyphosis in nearly 1/10th
• Enlarged palpable: Hypertrophic peripheral nerves – in 1/4 of
• Roussy–Levy syndrome: Hereditary motor sensory neuropathy +
upper limb postural tremors

CMTD – Type 2:
• Later in onset
• Axonal pathology
• Deformities – less prominent
• No nerve enlargement.
• No upper limb involvement.

CMTD – Type 3:
• Aka. Dejerine Sottas Disease – AD
• Childhood onset
• Severe disability
• Delayed motor development

Familial amyloid polyneuropathy and porphyrias

Familial Amyloid Polyneuropathy:
• Inherited Transthyretin gene mutation
• Small fiber sensory >> motor axonal neuropathy
• AMS Symptoms ++
• Numbness and painful paresthesias.

Porphyria:
• Only 3 forms of porphyria causes neuropathy
• Acute Intermittent Porphyria. No cutaneous manifestations
• Hereditary coproporphyria.
• Variegate porphyria. }
  Cutaneous manifestations ++
  ↓
  Blisters, hyperpigmentation.

• AD mode of inheritance
• First attack: 30 - 40 years of life.
• Female > male
• G.I. symptoms: abdominal pain, nausea, vomiting
• Severe AMS symptoms +++

Neuropathy in porphyria:
• Subacute in onset
• Proximal upper limb predominant motor neuropathy.
• (arm - affected first)
• Rapidly progressing muscle wasting
• Facial and bulbar involvement
• EDS like presentation
• Severe AMS Symptoms +++
• Sensory involvement - bathing suit pattern.

Fabry’s, Tangier’s and Refsum’s disease

Fabry’s disease:
• X.L- α- galactosidase deficiency
• Onset: childhood
• Painful small fiber axonal neuropathy
• Distal paresthesia and lancinating pain
• AMS symptoms ++
  Angiokeratoma + painful acral paresthesias.

Tangier’s disease:
• AR/ATP binding cassette protein defect
• Reduced HDL
• Asymmetrical mononeuropathy
• Orange tonsils
• Axonal degeneration
Peripheral neuropathy + retinitis pigmentosa + cerebellar ataxia...
Defect in α- oxidation of fatty acids due to deficiency of an enzyme called Rhodanese acid oxidase.

Acquired neuropathies

* Acquired demyelinating neuropathies:
  * AIDP
  * CIDP

Axonal acquired neuropathies:
* MCC of Acquired axonal neuropathy: Diabetes Mellitus

Diabetes mellitus:
* MC type of neuropathy in DM: Small fiber sensory >> motor neuropathy

Symmetrical, length dependant
* Distal to Proximal.
* Dying back/glove and stocking neuropathy
* ANS symptoms ++
  * Gustatory sweating
  * Nocturnal diarrhea

Other forms of Diabetic Neuropathy:
* Large fiber neuropathy
* Cranial Nerve Neuropathy: Pupil sparing 3rd Nerve Palsy > 6th Nerve palsy
* Diabetic Amyotrophy: Lumbo sacral radiculoplexopathy,
  * Unrelated to diabetic control
  * Asymmetrical
  * Pain along the distribution of radicle
  * Proximal lower limb pain and weakness.
  * If L4 involved -> knee jerk absent
  * Distal lower limb - not involved
  * Associated with weight loss.
* For radiculopathies -> SLR + ve (Straight Leg Raising Test)
  * Mononeuropathies can also occur in the form of carpal tunnel syndrome.

Primary light chain amyloidosis

* AL Amyloidosis
* Small fiber distal symmetric sensory polyneuropathy followed by large fiber involvement
• AUS Symptoms + + +
• \( \lambda \gg K \) chains
• MCC of death: cardiac failure
• MCC of restricted cardiomyopathy: Amyloidosis.

**HIV Neuropathy**

Different types of neuropathies in HIV:

- mc: diabetes like neuropathy
- GBS or CIDP like pattern
- Sensory ganglionopathy
- Polyneuropathy: most common in CMV infection.
- Mononeuritis multiplex: associated with medium vessel vasculitis
- In small fiber sensory neuropathy - pain and temperature are affected more.

**Critical illness polyneuropathy**

- Seen in sepsis/ MODS – in ICU patients (> 7 days)
- Suspected when there is difficulty in weaning off from ventilator
- Distal axonal sensorimotor neuropathy
- Severe flaccid weakness of both extremities.

**Subacute combined degeneration of spinal cord**

![Diagram showing the structure and symptoms associated with subacute combined degeneration of spinal cord]

- Vitamin B\(_2\) ↓
- Most important structures involved:
  - Lateral part of spinal cord
  - Lateral corticospinal tract (mc)
  - Posterior columns
  - Lateral spinothalamic tract (rarely)
  - Tingling, numbness, paresthesias
  - E/L Lower extremity weakness
  - Bilateral hypertonia.
  - Bilateral hyperreflexia (Early)
  - Large fiber Demyelinating
- Followed by peripheral neuropathies
  - Sensory ataxia.
  - Absent DTR (Final finding)
  - Ataxic paraplegia.
  - Gait ataxia.
Paraneoplastic, autoimmune and vasculitic causes of neuropathy

1. Paraneoplastic neuropathy:
   - Sensory → Ganglionopathy → Small cell Lung Cancer → anti Hu antibodies

2. Subacute motor Neuropathy → Asymmetric, proximal Upper limb predominant
   → Associated with Lymphoma.

3. Cerebellar findings → Gynecological malignancies → Antibodies.

Autoimmune and Vasculitic causes:

- SLE, Scleroderma, Rheumatoid arthritis, Vasculitis → DM like small fiber Neuropathy.

- Sjogren → ganglionopathy
- Medium vessel vasculitis → Mononeuritis multiplex
- Vasculitis: Severe neuropathy → Churg Strauss > Wegeners.
- Large vessel vasculitis do not produce neuropathy.

Charcot's disease, botulism

Charcot's disease:

- Severe form of neuropathy leading to progressive destructive arthritis
- Neuropathic joint disease
- Most common cause: DM > Amyloid > Leprosy > Tabes Dorsalis > Syringomyelia
- Most commonly affected joints: Medial tarsometatarsal joints
- Most common type: Atrophic type > Hypertrophic type

Botulism:

- Symmetrical cranial nerve palsy
- Facial descending symmetrical palsy
- Deep Tendon Reflexes → preserved
- Nausea, Vomiting, Abdominal pain with autonomic dysfunction
- Fever
- Sensory symptoms
- Mentation → Intact

AFL.france
NEUROMUSCULAR JUNCTION

Myasthenia Gravis

Pathophysiology:
1. Decrease in number of acetylcholine receptors in the postsynaptic membrane
2. Acetylcholine cannot bind to receptors
   - Blocking antibodies and destructive antibodies
   - Myasthenia gravis is T-Cell + B-cell mediated
   - TH1 mediated activation of T-cell → produces IL-4
     Stimulates B-cells
     Produces antibodies
     Produces disease

- Autoimmune disease with HLA association
- Majority population has thymus pathology
  - Produces T cells

Sero-positive myasthenia gravis
- Antibodies positive
- Anti acetylcholine receptor antibody (most specific)
Seronegative myasthenia gravis
1. Anti musk antibody (Muscle Specific Kinase)
2. Anti Lipoprotein receptor - 4
3. Anti striated muscle antibody

1. Ocular myasthenia. → 50% seropositive
   - Anti musk antibody

2. Generalized. → 80 - 90% seropositive
   → 75% → Thymus involvement
   → 65% → Thymic hyperplasia.
   → 10% → Thymoma.

Clinical features of myasthenia gravis

Age group: Bimodal
- Early onset → second to third decade
  - Females more common than males
  - Associated with other autoimmune disease → Hashimoto’s thyrroiditis, Addison’s, pernicious anemia, vitiligo, Type 1 DM

- Late onset → sixth to seventh decade
  → Incidence: Males > Females
  → Absence of thymus involvement
  → HLA DR2, LPRA
  → Antibodies → Antiacetylcholine receptor
    → antibody, Titin, Rygodine
  → Oropharyngeal and facial involvement
  → myasthenia gravis starts as ocular presentation then generalized
  → Fluctuating weakness and fatigueability
    → Weakness is more on repeated activity
  → Starts with ocular or pharyngeal then goes to generalized
    → weakness → proximal muscles of lower limb → Pharyngeal/Bulbar → Respiratory muscles
    → Late → respiratory involvement

- Early onset myasthenia.
  → F > M
  → Anti Acetylcholine receptor Antibodies +++
  → Thymic hyperplasia.
  → HLA - DR2, DR9, B8
Anti musk antibody

- Seen in ocular myasthenia.
- Seen in 40 to 50% cases of Seronegative myasthenia.
- Thymus not involved
- Females > males
- Characterized by severe oropharyngeal / buccal and facial involvement
- Tongue fasciculations are seen
- Proximal muscles and neck muscles are spared
- Refractory to standard therapy

Clinical presentation:

- Ocular
  - Ptosis with diplopia (Classical presentation)
  - Fluctuating with fatigue
  - Variable degree of ptosis
  - Ptosis can be unilateral or bilateral and asymmetrical
  - Binocular diplopia with sparing of pupils
  - Earliest ocular muscle affected - medial rectus
  - Cogan's lid twitch

- Pharyngeal
  - Dysphagia, dysarthria, nasal regurgitation, fatigue on chewing
  - Facial muscles (musk antibody)
    - Expressionless facies

- Proximal weakness of upper limb muscles (Lower limb weakness > upper limbs)
  - Neck weakness - drooped posture
  - Proximal muscle of lower limb
    - Typically hip muscles

- Respiratory muscle involvement

Differential diagnosis of myasthenia gravis

- Chronic progressive external ophthalmoplegia
  - Mitochondrial myopathy
  - Only ptosis present, no diplopia
  - No pharyngeal muscle involvement
  - No bulbar muscle involvement

Always examine:

- Severity of weakness
- Double vision on lateral gaze, ptosis, lid closure
- Swallowing
- Speech
- Hand grip for distal muscles
- Arm outstretched for proximal muscles
- Head lift for neck muscles
- Vital capacity for respiratory muscles

**Diagnosis**
- Ice pack → improves weakness
- Tensilon test (edrophonium) → dose of edrophonium for tension test = 2 mg
- Specific → Acetylcholine receptor antibody
- Sensitive → Repetitive nerve stimulation tests (decremental response in amplitude of compound motor action potential)
  - Single fibre electromyography
    → Increased jittering

**Lambert Eaton myasthenic syndrome**

- Paraneoplastic condition associated with small cell carcinoma of the lung
- Antibody against Presynaptic V/Q calcium channel receptors
- Proximal lower limb weakness with only mild diplopia and ptosis
- Reflexes absent
- NMS findings (+++)
- Nerve conduction study → incremental response on repetitive nerve stimulation
  → Diis sign

- 3, 4, Diamino pyridine useful

**Treatment of myasthenia gravis:**
- Pyridostigmine: 30-60 mg → 6th hourly, later taper off
- Relapse → Steroid ± Azathioprine
- Crisis → Respiratory crisis → IV Ig and PLEX (plasma exchange)

**Cholinergic crisis:**
- D → Diaphoresis
- U → Urination excess
- M → Miosis
- B → Bradycardia
- B → Bronchial secretions
- E → Emesis
- L → Lacrimation
- L → Loose stools
Role of IV Ig or PLEX:
- Myasthenia crisis → respiratory insufficiency, dysphagia.
- Refractory myasthenia.
- Surgery (bulbar dysfunction).
- Musk positive cases → refractory to cholinesterase inhibitors.

Thymectomy

Indications:
- Thymoma → associated with hypogammaglobulinemia.
- Good's syndrome
- Acetylcholine receptor antibody positive and generalized myasthenia. → 18-65 years.
- Musk positive, elderly, ocular myasthenia. → Thymectomy is not indicated.

Drugs that precipitate myasthenia:
- a- Pencillamine
- Procainamide
- B- blockers
- Amino glycosides
- Quinolones
- Macrolides
- Azathioprine

Congenital myasthenic syndromes
- Slow channel → most common
- Autosomal dominant
APPROACH TO MYOPATHY

LMN pathology / Lesion in the:
1. Anterior Horn cell:
   - No Sensory / ANS / cerebellum involvement
   - Asymmetrical involvement
   - Wasting
   - Fasciculations, atrophy + + +
   - Distal muscles > proximal muscles
   - Eg: Motor Neuron Disease
     - Spinal Muscular Atrophy
     - Hirayama’s Disease
     - Intramedullary - Syringomyelia.

2. Dorsal root ganglion:
   - Ganglionopathy
   - Only Posterior Column involved
   - Severe disproportionate Sensory Ataxia
   - Causes:
     - Sjogren Syndrome
     - Paraneoplastic - Small cell carcinoma of Lung
     - Anti-Hu Antibodies

3. Radiculopathy / Spinal Nerve Root
   - Asymmetrical
   - Root pain along the distribution of nerve
   - Sensory, motor and reflexes - Lost
   - Muscles of that particular nerve root is involved
   - Eg: If L5 radiculopathy → L5 supplies both obturator and femoral nerve → Both adduction of hip and extension of knee are lost

4. Plexus - Plexopathy

5. Peripheral Nerve - Sensory ± motor
   - Distal to proximal evolution
6. Neuromuscular junction:
   - Fatigability
   - Fluctuating weakness
   - Ocular problems
   - Pharyngeal muscle problems

7. Muscle:
   - Purely motor
   - Completely symmetrical
   - Almost always proximal, predominantly lower limb.
   - No wasting usually
   - Reflexes - normal

```
   muscle disorders
     ↓
   Intermittent weakness   Persistent weakness
     ↓
   myoglobinuria
     ↓
   Present     Not present
     ↓
   - Rhabdomyolysis     - Channelopathies
```

- Inherited
  1. Inherited
  2. Acquired
     - Infectious
     - Drugs
     - Endocrine
MYOPATHY

Myopathies

- LMN type of pure motor weakness.
- Proximal weakness >> distal weakness.
- No wasting / no atrophy / no fasciculations.
- Reflexes preserved.
- No involuntary movements.
- No sensory loss.
- AUS- normal.

Types of myopathy.

Intermittent weakness          Persistent weakness

Myoglobinuria.        No myoglobinuria.        Inherited        Acquired

Rhabdomyolysis        Channelopathies
                   myasthenia. gravis

Inflammatory

Endocrine
mitochondrial

Difference between Anterior horn cell and muscle.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Anterior horn cell</th>
<th>muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weakness and wasting</td>
<td>wasting &gt;&gt; weakness</td>
<td>weakness &gt;&gt; wasting</td>
</tr>
<tr>
<td>Symmetric</td>
<td>Asymmetric</td>
<td>Symmetric</td>
</tr>
<tr>
<td>Distribution</td>
<td>Distal &gt; proximal</td>
<td>proximal</td>
</tr>
<tr>
<td>Reflexes</td>
<td>Absent</td>
<td>Late hyporeflexia, proportionate</td>
</tr>
<tr>
<td>Involuntary movements</td>
<td>Fasciculations present</td>
<td>absent</td>
</tr>
</tbody>
</table>

Symptoms of a muscle disorder classification.

Positive symptoms          Negative symptoms

1. myalgia.               1. weakness
2. Cramps                 2. Fatigue
3. Contractions            3. Exercise intolerance
Symptoms of muscle disorder

1. Weakness:
   - Proximal lower extremities.
     * Difficulty in climbing stairs, rising from a low chair or toilet, or getting up from a squatting position.
   - Proximal upper extremities.
   - Trouble in lifting objects over the head and brushing the hair.
   - Distal upper extremities.
   - Difficulty in opening jars, inability to turn a key in the ignition.
   - Distal lower extremities.
     - Falling due to foot drop.

2. Fatigue and exercise intolerance
   - Non-specific symptom.
   - Abnormal fatigueability even after minimal exercise without involving sensory / autonomic nervous system.

   - Non-specific symptom.
   - Extremely uncommon for a myopathy to cause vague aches and muscle discomfort in presence of a normal neuromuscular examination and laboratory studies.
   - Fibromyalgia vs polymyalgia rheumatica.

<table>
<thead>
<tr>
<th>Fibromyalgia</th>
<th>Polymyalgia rheumatica</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Severe muscle pain</td>
<td>- Occurs in giant cell arteritis.</td>
</tr>
<tr>
<td>- Pain in trigger points.</td>
<td>- Associated with HLA-DRB1*04 - 04 gene.</td>
</tr>
<tr>
<td>- Easy fatigability</td>
<td>- Pain and stiffness in - Hip, shoulder, pelvic girdle</td>
</tr>
<tr>
<td>- Normal ESR</td>
<td>- ESR &gt; 50mm/hr</td>
</tr>
<tr>
<td>- Normal muscle enzymes</td>
<td>- 100% responsive to steroids.</td>
</tr>
<tr>
<td>- NSAIDS</td>
<td>- Normal muscle enzymes.</td>
</tr>
</tbody>
</table>

- Muscle cramps.
  - Not a feature of myopathy except Duchenne muscular dystrophy

Causes:
- Dehydration
  - Hypokalemia.
  - Azotemia.
- Mynedema.
- Disorders of the nerve or motor neuron.
  (especially amyotrophic lateral sclerosis)
- Renal failure.

5. Muscle contractures.

- Contractures differ from cramps → they last longer and are electrically silent with needle EMG.

- Fixed muscle contractures → Exercise provoked contractures

- Emery-Dreifuss muscular dystrophy (EMD)
- Glycolic pathway disorders
- Enzyme defects

- Contractures are uncommon.

6. Myotonia.

- The phenomenon of impaired relaxation of muscle after forceful voluntary contraction.
- Involves hands and eyelids.
- Occurs due to repetitive depolarization of the muscle membrane.
- Conditions showing myotonia:
  1) Myotonic dystrophy
  2) Myotonia congenita
  3) Hyperkalemic periodic paralysis
- Myotonia improves with exercise
- Exposure to cold worsens both myotonia & paramyotonia.
- Paramyotonia.
- Seen in paramyotonia, congenita.
- Worsens with exercise.
- In myotonia, patients complain of muscle stiffness resulting in difficulty to:
  1) Releasing handgrip after hand shake
  2) Opening eyelids if they forcefully shut their eyes.
- Myopathies present at birth.

Congenital myopathies
seen in 1) Central core myopathy
  a) Centronuclear myopathy
  2) Nemaline myopathy
  3) Congenital myotonic dystrophy.
Duchenne Muscular Dystrophy [DMD]

- X-linked recessive, progressive muscle degeneration.
- Dystrophin gene mutation
- Onset before 5 years (3-5 years)
- Proximal lower limb muscles affected (mc)
- Presentation:
  - Frequent falls
    - Lumbar Lordosis
    - Protruberant abdomen
    - Waddling gait
    - Mental retardation (IQ)
- Milestones:
  - 6 years → Toe walking
    - Heel cord contracture
  - 12 years → Wheel chair bound
  - 10-18 years → Recurrent pulmonary infection death (MC cause)
- Complications:
  - Pseudohypertrophy of calf muscles
  - Scoliosis → impairment of lung function
    - Recurrent pulmonary infections
  - Cardiomyopathy (Dilated cardiomyopathy)
    - Conduction abnormality
  - Management:
    - Steroids (limited use)
  - Limb-girdle weakness
    - Gower's sign
      - Observed when child arises from supine position

Becker’s muscular dystrophy & Limb girdle muscular dystrophy

Becker’s muscular dystrophy:
- X-linked recessive.
- Dystrophin gene mutation
- Enzymes, EMG, Biopsy → similar for both DMD and Beckers
- Variable disease onset (5-60 yrs)
- Survival up to 4th decade
- No mental retardation
- No contractures

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Scanned with CamScanner
- Mc cause of death -> Cardiomyopathy.
- Steroid work better in Becker's dystrophy

**Limb girdle muscle dystrophy**.
- Mc type of adult onset muscle dystrophy.

**Types**:

<table>
<thead>
<tr>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal dominant</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td>Protein: Caveolin</td>
<td>Protein: a A, Calpain</td>
</tr>
<tr>
<td>a B: Dystrophin</td>
<td></td>
</tr>
<tr>
<td>- Occurs in 2nd decade.</td>
<td></td>
</tr>
</tbody>
</table>

- Early onset limb girdle muscle dystrophy due to
  - Alpha, dystroglycan protein (within 10 years)
- Late onset limb girdle muscle dystrophy due to
  - Desmin protein

**Calpainopathy**
- Early finding: "Scapular winging"

**Causes**:
- Scoliosis
- Wrist, elbow, and finger contractures
- Achilles tendon contractures

- Causes toe walking
- Proximal lower limb muscles affected
  - Severely affected: Hip adductors

**Dysferlinopathy**
- Mutation in dysferlin gene located in chromosome 1p 13.
- Important in membrane repair
- Presents in adolescence or early adulthood
- Slow progression
- Diamond sign of thigh

- Occurs due to selective muscle wasting of vastus lateralis and rectus femoris in their upper and lower part with muscle sparing of the middle part portion.
Emery–Dreifuss syndrome and Fascio scapulo-humeral muscle dystrophy

Emery–Dreifuss muscle dystrophy.
- a modes of inheritance
  - X-linked recessive
  - Autosomal dominant
    - Emerin mutation
    - Laminin mutation

- Prominent contractures
- Muscles involved
  - Humeral
  - Peroneal
  - Cardiomyopathy
  - Colour blindness.

Fascioscapulohumeral muscle dystrophy.
- Autosomal dominant
- Severe in males
- Childhood onset
- Involves chromosome 4q
- Childhood facial weakness followed by weakness of shoulder girdle.
- Winging of scapula on abduction
- Biceps, triceps affected
- Deltoid spared.
- If lower limb involvement → Distal limb and ankle dorsiflexion affected.
- Associated with:
  - Nerve deafness
  - Coats disease
  - Colour blindness
  - Facial, shoulder and scapula girdle seen.
  - No cardiomyopathy.
Myotonic dystrophy

- Types.
  - DM1 - Type 1 → Distal muscle weakness (MC)
  - DM2 - Type 2 → Proximal muscle weakness, (rare)
  - Both Type 1 and Type 2

  Autosomal dominant, trinucleotide repeat disorders.
  - Facial involvement
    - Temporalis muscle
    - Masseter muscle
    - Buccal muscle.
  - Hatchet facies and frontal baldness seen.
  - Muscles of neck involved.
    - Sternocleidomastoid (MC)
    - Distal upper limb muscle involvement.
      (Upper limb involvement → lower limb involvement)
    - Bulbar dysarthria, (pharyngeal muscle weakness)
    - Myotonia → Percussion myotonia.
    - Respiratory involvement
  - Additional findings:
    1. Cardiac conduction abnormalities
    2. Intelect
    3. Posterior subcapsular cataract
    4. Gonadal atrophy
    5. Insulin resistance.
  - Management → phenytoin
  - For conduction abnormality → Pacemaker.
  - Type 1 fibres → Selective atrophy.

Congenital muscle dystrophy

- Fukutin
- Fukuyama
- Merosin deficiency

Distal myopathy

- Wastlander
- Nonaka
- Miyoshi
Mitochondrial myopathies

- Maternally inherited
- Types:
  1. Kearns-Sayre syndrome
  2. Chronic progressive external ophthalmoplegia (CPEO)
  3. Pure mitochondrial myopathies
  4. MERRF (myoclonic epilepsy with red ragged fibers)
  5. MELAS (mitochondrial encephalopathy, lactic acidosis and stroke-like episodes)
  6. Leber's hereditary optic neuropathy

Histopathological findings:
- Biopsy of muscle shows:
  'Red ragged fibers'
- Stain used: Gomori trichrome stain

Chronic progressive external ophthalmoplegia (CPEO)
- Presentation: 5th - 6th decade
- Autosomal dominant or sporadic
- Onset after puberty
- Symmetrical ptosis without diplopia
- Biopsy: Red ragged fibers
- Sensorineural hearing loss (deafness)

Kearns-Sayre syndrome:
- Onset: sporadic before 20 years
- Features:
  1. Findings of chronic progressive external ophthalmoplegia
  2. Retinitis pigmentosa
  3. Complete heart block
  4. Cerebellar ataxia
  5. Mental retardation
  6. Gonadal dysfunction
  7. Diabetes mellitus
- On biopsy: Red ragged fibers seen
MERRF syndrome and MELAS syndrome

MERRF SYNDROME:
• Myoclonic epilepsy with red ragged fibers.
• Features:
  1) Mitochondrial myopathy (proximal lower limb weakness)
  2) Myoclonic epilepsy.
  3) Cerebellar ataxia.
  4) Dementia.
  5) Optic atrophy.
• Onset: 10 - 30 years.
• Limb girdle distribution.

MELAS SYNDROME:
• Mitochondrial encephalopathy with lactic acidosis and stroke.
• Presentation < 40 years with partial seizures.
• Stroke-like without vascular distribution.
• Features:
  1) Weakness / hemiparesis
  2) Hemianopia. < 40 years.
  3) Lactic acidosis.
  4) Point mutation in mitochondrial + - RNA
  5) Red ragged fibers.
  6) Can be associated with:
      1) Hypothalamicpituitary gonadal dysfunction.
      2) Basal ganglion calcification

Rhabdomyolysis:
• Myoglobinuria with intermittent weakness.
• Causes:
  1) Muscle phosphorylase deficiency
     [ e.g. McArdle disease - G5D Type S ]
  2) Glycolytic pathway defect.
  3) Carnitine palmitoyl transferase deficiency.

Electrolyte abnormalities causing episodic weakness:
• Hyponatremia.
• Hypokalemia.
• Hyperkalemia.
• Hypercalcemia.
• Hypophosphatemia.
### Channelopathies

<table>
<thead>
<tr>
<th>Type</th>
<th>Disease</th>
</tr>
</thead>
</table>
| Calcium       | Episodic ataxia type 2  
                | Spinocerebellar ataxia type 6  
                | Hypokalemic periodic paralysis  
                | Familial hemiplegic migraine    |
| Sodium        | Hypokalemic periodic paralysis  
                | Paramyotonia congenita         
                | Normokalemic periodic paralysis|
| Chloride      | Episodic ataxia type 1  
                | Benign neonatal familial convulsions |
| Potassium     | Myotonia congenita                                                     |

1. **Calcium channelopathies**  
   - Episodic ataxia type 2
   - Spinocerebellar ataxia type 6
   - Hypokalemic periodic paralysis
   - Familial hemiplegic migraine

2. **Sodium channelopathies**
   - Hypokalemic periodic paralysis
   - Normokalemic periodic paralysis (Paramyotonia congenita)

3. **Chloride channelopathies**
   - Myotonia congenita

4. **Potassium channelopathies**
   - Episodic ataxia type 1
   - Andersen-Tawil syndrome
   - Benign neonatal familial convulsions

### Hypokalemic/Hyperkalemic periodic paralysis and Andersen-Tawil syndrome

**Presentation:** Acute onset, intermittent, bilateral weakness.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hypokalemic PP</th>
<th>Hyperkalemic PP</th>
<th>Paramyotonia Congenita</th>
<th>Andersen-Tawil Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of inheritance</td>
<td>4D</td>
<td>4D</td>
<td>4D</td>
<td></td>
</tr>
<tr>
<td>Age of onset</td>
<td>Adolescence</td>
<td>Early childhood</td>
<td>Early childhood</td>
<td>Early childhood</td>
</tr>
<tr>
<td>Myotonia</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Frequent attacks of weakness</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Presence of attacks of weakness</td>
<td>Early in youth</td>
<td>Early in youth</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Duration of attacks of weakness</td>
<td>2-12h</td>
<td>2-24h</td>
<td>2-24h</td>
<td></td>
</tr>
<tr>
<td>Seizures to level during attacks of weakness</td>
<td>Decreased</td>
<td>Increased or normal</td>
<td>Increased or normal</td>
<td>Transient</td>
</tr>
<tr>
<td>Effect of K+ loading</td>
<td>No change</td>
<td>Increased symptoms then weakness</td>
<td>Increased symptoms then weakness</td>
<td>No change</td>
</tr>
<tr>
<td>Effect of stimulus cooling</td>
<td>No change</td>
<td>Increased weakness</td>
<td>Increased weakness</td>
<td>No change</td>
</tr>
<tr>
<td>Final weakness</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Symptomatic features and cardiac abnormalities are distinguishing features (see text). Rarely paroxysmal in paramyotonia congenita. Abbreviations: 4D, late birth ashen; PP, periodic paralysis.*
Channelopathies

<table>
<thead>
<tr>
<th>Type</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>Epileptic ataxia type 2, spinocerebellar ataxia type 6, hypokalemic periodic paralysis, familial hemiplegic migraine</td>
</tr>
<tr>
<td>Sodium</td>
<td>Hyperkalemic periodic paralysis, paralympathony congenital, normokalemic periodic paralysis</td>
</tr>
<tr>
<td>Chloride</td>
<td>Myotonia congenita</td>
</tr>
<tr>
<td>Potassium</td>
<td>Epileptic ataxia type 1, benign neonatal familial convulsions</td>
</tr>
</tbody>
</table>

1) Calcium channelopathies (e.g. \( \delta, \delta^+, \delta^-, \delta^0 \))
- Epileptic ataxia type 2
- Spinocerebellar ataxia type 6
- Hypokalemic periodic paralysis
- Familial hemiplegic migraine

2) Sodium channelopathies
- Hyperkalemic periodic paralysis
- Normokalemic periodic paralysis, paralympathony congenital

3) Chloride channelopathies
- Myotonia congenita

4) Potassium channelopathies
- Epileptic ataxia type 1
- Andersen-Tawil syndrome
- Benign neonatal familial convulsions

Hypokalemic/Hyperkalemic periodic paralysis and Andersen-Tawil syndrome

Presentation: Acute onset, intermittent, bilateral weakness.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hypokalemic PP</th>
<th>Hyperkalemic PP</th>
<th>Paralympathony Congenital</th>
<th>Andersen-Tawil Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of inheritance</td>
<td>AD</td>
<td>AD</td>
<td>AD</td>
<td>AD</td>
</tr>
<tr>
<td>Age of onset</td>
<td>Childhood</td>
<td>Early childhood</td>
<td>Early childhood</td>
<td>Early childhood</td>
</tr>
<tr>
<td>Hypermotor</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Sensory weakness</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Frequency of attacks of weakness</td>
<td>Daily to weekly</td>
<td>May be 3-5</td>
<td>Rare to weekly</td>
<td>Daily to weekly</td>
</tr>
<tr>
<td>Duration of attacks of weakness</td>
<td>2-12 h</td>
<td>From 1-2 h to 24 h</td>
<td>2-24 h</td>
<td>2-24 h</td>
</tr>
<tr>
<td>Serum Ca level during attacks of weakness</td>
<td>Decreased</td>
<td>Increased or normal</td>
<td>Usually normal</td>
<td>Variable</td>
</tr>
<tr>
<td>Effect of ( \delta )-blocking</td>
<td>No change</td>
<td>Increased systolic, then diastolic</td>
<td>Increased systolic, then diastolic</td>
<td>No change</td>
</tr>
<tr>
<td>Effect of caffeine</td>
<td>No change</td>
<td>Increased systolic, then diastolic</td>
<td>Increased systolic, then diastolic</td>
<td>No change</td>
</tr>
<tr>
<td>Fluid resuscitation</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Diseases: Channelopathies and cardiac arrhythmias are distinguishing features (not tested). May be paraclinically in paralympathony congenital. Abbreviations: AD, autosomal dominant; PP, pseudo-periodic.
<table>
<thead>
<tr>
<th>Features</th>
<th>Hypokalemic periodic paralysis</th>
<th>Hyperkalemic periodic paralysis</th>
<th>Andersen-Tawil syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Channelopathy</td>
<td>Calcium</td>
<td>Sodium</td>
<td>potassium</td>
</tr>
<tr>
<td>Inheritance</td>
<td>RD</td>
<td>RD</td>
<td>RD</td>
</tr>
<tr>
<td>Onset</td>
<td>Early adulthood (&lt; 25 years)</td>
<td>Childhood</td>
<td>Childhood</td>
</tr>
<tr>
<td>Serum potassium</td>
<td>Low</td>
<td>Normal to high</td>
<td>Variable</td>
</tr>
<tr>
<td>Myotonia</td>
<td>absent</td>
<td>Present</td>
<td>absent</td>
</tr>
<tr>
<td>ECG changes</td>
<td>Changes of hypokalemia</td>
<td>Normal</td>
<td>Arrhythmia (↑ QT interval)</td>
</tr>
<tr>
<td>Facies</td>
<td>Normal</td>
<td>Normal</td>
<td>Dysmorphic</td>
</tr>
</tbody>
</table>

**Hypokalemic periodic paralysis**
- Autosomal dominant.
- Onset: adolescence < 25 years.
- Male > Female.
- Precipitated by: high carbohydrate meal.
- Pure proximal limb weakness, no myotonia.
- Hypokalemia during episodes.
- Propensity for arrhythmia.
- Management:
  - Never treat with IV potassium.
  - Oral potassium.
  - Acetazolamide.

**Hyperkalemic periodic paralysis**
- Autosomal dominant.
- Presentation: first decade (< 10 years).
- Sodium channelopathy.
- Normal potassium during attacks.
- Proximal muscle weakness.
- Precipitated by: rest.
- Myotonia.

**Andersen-Tawil syndrome**
- Potassium channel disorder.
- Due to inward rectifying potassium channel.
- Dysmorphic features.
- Cardiac arrhythmias.
- Prolonged QT interval.
Drug induced myopathies

Drugs causing:
(1) Acute onset Rhabdomyolysis:
  → Heroin
  → Alcohol
  → amphetamine
  → cocaine.

(a) statins can cause:
  → asymptomatic rise in CKM
  → myalgia.

(b) Glucocorticoids can cause:
  → Acute quadriplegia (acute presentation)
  → Proximal muscle weakness (chronic presentation)
  → d-Penicillamine → produce autoimmune myopathy (resemble polymyositis)
  → Zidovudine → produce mitochondrial myopathy (red ragged fibers)
  → Amiodarone, Hydroxychloroquine → produce painless weakness with autophagic vacuoles on biopsy.

Endocrine myopathies

- Both hypothyroidism and hyperthyroidism induced myopathies are:
  → Proximal myopathies
  → Normal EMG.

- Hypothyroidism induced myopathy:
  → Muscle cramps, pain and stiffness
  → Pure proximal myopathy
  → Creatine kinase ↑↑
  → No fasciculations

- Hyperthyroidism induced myopathy:
  → Asymptomatic
  → Proximal + bulbar + esophageal
  → Normal creatine kinase
  → Fasciculations ++
GUILLAIN - BARRE SYNDROME

Guillain - Barre syndrome

Types:
1. Acute inflammatory demyelinating polyneuropathy (AIDP) → most common
2. Acute motor axonal neuropathy (AMAN)
3. Acute motor sensory axonal neuropathy (AMSAN)
4. Miller - Fischer syndrome

- Mean age → 40 years (no particular age)
- Males are more commonly affected
- 4 weeks duration (monophasic)
  - More than 8 weeks → Chronic
- Molecular mimicry → cross reacting antigens → myelin (MC)
  → Antecedent infections → 70% cases

Triggers:
- Campylobacter jejuni (MC)
  - CMV → diarrhoea
  - EBV
  - Mycoplasma
  - Hep A, B, HIV
  - Zika virus

- Acute inflammatory polyradiculoneuropathy
  → Radicular pain (back pain) with tingling, numbness etc.
  → 2 - 3 days prior to weakness
- Proximal and distal weakness which starts in lower limb
  → then upper limb → Brain stem
- Respiratory muscle involvement in 50%
- Areflexia, Flaccidity, paraparesis going into quadriplegia
- Sensory signs minimal → posterior column
- Autonomic nervous system (ANS) involvement
- Bowel bladder symptoms may be seen
- No cerebellar findings
- No higher mental functions involvement
- Cranial nerve palsy as disease progresses
  → Starts with IV, V, VI, then VII, then III, IV, VI

Diagnostic criteria for Guillain-Barre syndrome

- Features required for diagnosis
  - Progressive weakness in both arms and legs
  - Areflexia

- Features strongly supporting diagnosis
  → Progression of symptoms over days, up to four weeks
  → Relative symmetry of symptoms
  → Mild sensory symptoms or signs
  → Cranial nerve involvement III, VII
  → Recovery beginning two to four weeks after progression ceases
  → Autonomic dysfunction
  → Absence of fever at onset
  → High concentration of protein in cerebrospinal fluid, with fewer than 10 cells per cubic millimeter

  → Typical electrodiagnostic features
    - Prolonged or absent F/A, temporal dispersion, distal latency, decreased conduction velocity, blocks

  → LP → albuminocytologic dissociation
    → Increased CSF protein
    → Less than 10 cells/mm³

Pain due to nerve root inflammation

Features excluding diagnosis:
- Diagnosis of botulism, myasthenia, polymyelitis or toxic neuropathy
- Abnormal porphyria metabolism
- Recent diphtheria
- Purely sensory syndrome, without weakness
Electro diagnosis:
Most sensitive test in evaluating GBSS

Patterns:
1. Motor conduction block
2. Prolonged distal latencies
3. Temporal dispersion
4. Slowing of nerve conduction
5. Increased F-wave latency

- Electro diagnostic parameters are the most reliable indicators of prognosis

AIDP → most common
AMAN → Prognosis same
ANNAN → Poor prognosis
Miller → Ophthalmoplegia, Ataxia
Fisher syndrome → Areflexia
- Axonal
- Demyelinating

Antibody
Anti GM1 antibodies
Anti GQ1a antibodies

Bickerstaff’s encephalitis

- Brainstem encephalitis → altered sensorium
- Hyperreflexia
- Ophthalmoplegia
- Ataxia
- Anti GQ1b
- Response to PLEX (Plasma exchange)

Management of Guillain Barre Syndrome
- No role of steroids
- IV Immunoglobulin → 0.4 g/kg for 5 days
- Plasma exchange

Clinical course
- Disease progresses for days to 4 weeks
- Typical course is steady progression to nadir within 2 weeks in most cases and 4 weeks in all cases from onset of paresthesia
- Variable plateau phase
- 10 - 15% mortality
- 80 - 85% recovery
60 - 65% complete recovery
10 - 20% residual disability

**Chronic inflammatory demyelinating polyneuropathy**

- More than 8 weeks
- Relapsing, remitting pattern
- Steroid responsive
- No antecedent events
- No major autonomic
- Bulbar involvement rare → less than 20%
- Generally idiopathic

Secondary causes:
- HIV
- Hodgkin's disease
- Plasma cell disorders (most important)

Pattern: Motor + Sensory → large fibre predominant
- More distal to proximal
- Areflexia

- Tremor is more common in CIDP

Treatment:
- Steroids → no response → IVIG
- If no response to IV, Ig
  - PLEX

**Differential diagnosis**

- POEMS
  - P - Polyneuropathy → CIDP
  - O - Organomegaly
  - E - Endocrinopathy
  - M - Skin changes
  - S - Multiple myeloma (monoclonal gammopathy)
    - Sclerotic lesions
    - Refractory to therapy → \( \lambda \) (Lamba) chain
MOTOR NEURON DISEASE

Classification of motor neuron disease

- Upper motor neuron (UMN)
  - UMN features
- Lower motor neuron (LMN)
  - LMN features
  - Amyotrophic lateral Sclerosis
  - Primary lateral Sclerosis
  - Multi focal motor neuropathy associated with paraproteinemia.

Amyotrophic Lateral Sclerosis (ALS)

- M. C. type.
  - 90% sporadic
    - Seen in 60-70 yrs
    - Males > Females (1.5:1)
  - 10% familial
    - Mutation in Cu-Zn Superoxide dismutase
    - Seen in young population

- ALS is the degeneration of neurons in

  - Anterior horn cells in spinal cord
  - Nuclei in brainstem
  - Cranial nerve fibres / corticobulbar

- LMN features
  - UMN features
    - Bulbar palsy
  - UMN features
    - Pseudobulbar palsy

- Average survival from onset of symptoms: 2.5 - 3.5 years
Amyotrophic lateral sclerosis – symptoms

- In ALS – sensory
  - Higher mental function
  - Extracocular muscle
  - Autonomic nervous system (bowel/ bladder)
  - Cerebellum
  \( \rightarrow \) Not affected/ normal

- Asymmetrical onset of symptoms

  \[ \downarrow \]

  - Local muscle weakness –

    \[ \begin{align*}
    & \text{Distal upper limb weakness} \\
    \downarrow & \quad \text{Muscle cramps} \\
    & \text{Progressive weakness} \\
    \downarrow & \quad \text{Wasting of muscle} \\
    & \text{Fasciculations} \\
    \downarrow & \quad \text{Frequent & multiple} \\
    & \text{Localised or} \\
    & \text{Generalised}
    \end{align*} \]

Upper motor findings – In amyotrophic lateral sclerosis

- MNC finding – Exaggerated or positive reflexes
- ALS – suspected only if LMN + UMN findings are present
- If only asymmetrical:

  \[ \downarrow \]

  - Suspect – multifocal motor neuropathy
  - Hirayama disease (dural buckling) (or)
  - Monomelic amyotrophy
• Rarely facial weakness
• Neck extension affected – Drooped head Syndrome
• Respiratory muscle involvement

Amyotrophic lateral sclerosis - Diagnosis, management

• Definitive diagnosis - Electromyography
  Long duration polyphasic action potential is seen

Cranial nerve palsy in amyotrophic lateral sclerosis

- Cranial nerve palsy
  Lmnw cranial nerve palsy
  due to cranial nerve nuclei involvement at brainstem
  Symptoms -
  • Bulbar dysarthria.
  • Dysphagia.
  • Nasal regurgitation

  Umnw cranial nerve palsy
  due to involvement of corticobulbar fibres
  Symptoms -
  • Spastic dysarthria.
  (Pseudobulbar)
• Flaccid tongue
• Palatal reflex
• Pharyngeal reflex → ++
• Jaw jerk
• Emotional incontinence
• Small, spastic tongue
• Painful yawning

<table>
<thead>
<tr>
<th>CLINICAL FEATURE</th>
<th>PSEUDOBULBAR PALSY</th>
<th>BULBAR PALSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>PALATAL REFLEX</td>
<td>++++</td>
<td>—</td>
</tr>
<tr>
<td>PHARYNGEAL REFLEX</td>
<td>++++</td>
<td>—</td>
</tr>
<tr>
<td>JAW JERK</td>
<td>++++</td>
<td>—</td>
</tr>
<tr>
<td>EMOTIONAL</td>
<td>++++</td>
<td>—</td>
</tr>
<tr>
<td>PARALYSIS</td>
<td>SPASTIC</td>
<td>FLACCID</td>
</tr>
<tr>
<td>DYSARTHRIA</td>
<td>SPASTIC</td>
<td>FLACCID</td>
</tr>
<tr>
<td>TONGUE</td>
<td>SMALL,SPASTIC</td>
<td>WRENGLING/ATROPHY,FASCICULATIONS</td>
</tr>
</tbody>
</table>

Split hand Syndrome
Thenar eminence affected > Hypothenar

management
• Riluzole - reduces excitotoxicity by inhibiting glutamate release
• Edaravone - free radical scavenger

X-linked spinobulbar muscle atrophy

• X/k/A Kennedy's disease
• Pure LMN type
• X - linked trinucleotide disease
• Associated with Androgen insensitivity
• Progressive weakness of limb and bulbar muscles
SEIZURES AND EPILEPSY- 1

Seizure - Paroxysmal, abnormal/excessive or hypersynchronous neuronal activity in the brain

Epilepsy - a or more unprovoked seizure without any identifiable cause leads to clinical syndrome called as epilepsy

Classification of seizure

New definition suggests that one epileptic seizure is sufficient to term it as epilepsy if there is additional enduring alteration in brain that increases likelihood of seizures. Old classification -

Generalised - Tonic clonic, absence, atonic, myoclonic

Partial - simple + intact awareness (focal without dyscognition)

(focal) > complex + loss of awareness (focal with dyscognition)

Focal Generalised Unknown
onset onset onset

Focal without Focal with
dyscognitive dyscognitive
features features

(Simple partial seizures) (Complex partial seizures)

Never a part of a part of epileptic syndrome
epileptic syndrome
(always secondary part of epileptic syndrome
to cause)

inter-ictal EEG normal

MC - mesial temporal lobe sclerosis
Aura - mc- abdominal > visual > sensory
Majonless stare (LOC)

Automatism (movement) smacking
Simple partial seizure

1. Jacksonian march - distal → proximal, upper limb
2. Todd's palsy - post ictal transient weakness of upper limb → lower limb (12-24 hours)
3. Epilepsy Partialis continua - Continuous SPS which are lasting for > 24 hours
   - Refractory to drugs (Rare)
   - May be part of SPS
   - Aura can include paresthesias / Rashning light / autonomic

Complex partial seizure

Mesial temporal sclerosis
- $T_2$ MRI - Abnormal Hyperintensity + small sized asymmetrical hippocampus
  - Medically refractory seizures
  - Surgically treatable with hippocampectomy
  - H/O febrile seizure in childhood
  - Post ictal disorientation

EEG in complex partial seizure

- Spike
- Sharp
- Spike & wave
- Sharp & wave
EEG - Focal (temporal) spikes/sharps

Complex partial seizures

Generalised seizures:
- Absence
- Tonic clonic
- Atonic

Generalised - absence seizure

- Part of epileptic syndrome
- Age of onset 6 years
- M > F
- Sudden brief LOC without loss of postural control

  Regains consciousness quickly

  No post ictal confusion

- Hyperventilation can precipitate the seizure
- Presentation - Day dreaming with normal IQ
  MRI - □

\[\text{EEG = Slomo Spike and wave}\]

\[\text{EEG Generalised 3Hz slow spike and wave}\]

Atypical absence seizure

1. LOC for longer duration
2. Motor signs
3. Asymmetrical 3Hz spike and wave

  Abnormal inter-ictal background

Myoclonic seizure

- Sudden brief electric shock like contraction

  myoclonus
It can be subtle → dramatic
- LOC → impossible to determine
- Epileptic syndrome → juvenile myoclonic epilepsy
- Can be component of GTCS/absence
  juvenile myoclonic epilepsy → upper limb > lower limb
- Adolescent
- IQ normal
- F > m
- Upon awakening
- Triggered by sleep deprivation
- Associated with GTCS/absence
- Respond to drugs → lifetime valproate therapy
- Carbamazepine / phenytoin
  ↓ Trigger
  myoclonic epilepsy/seizures
Levetiracetam
Lamotrigine
Topiramate
Rx

EEG → Generalised slow poly spike and wave

Atonic seizure

- Part of epileptic syndromes
- Associated with myoclonic seizure
- Lennox-Gastaut syndrome
- Characterised by sudden loss of tone

ILAE classification

Focal onset → Generalised onset → Unknown onset
↓
Aware / impaired awareness
motor tonic / clonic
Atonic
Myoclonic

motor / non-motor
Tonic
Sensory
Clonic
Autonomic
Myoclonic
Behavioural
Hyperkinetic arrest
Automatism

Non motor - Absence seizures
- Tonic (atypical absence)
  Clonic
  Myoclonic
Seizures V/S Syncope

→ mc differential diagnosis of seizures is syncope.

Types of syncope:
(1) Vasovagal syncope (mc)
(2) Cardiac syncope.
(3) Orthostatic hypotension

Vasovagal syncope
* unpleasant to patients, → prefers to lie flat.

Features:
(1) Precipitating factor → emotional
(2) Premonitory symptoms → Nausea, Sweating, Thirsty,
    feeling of warmth, tunneling of vision
    Appears pale
(3) Position → erect
(4) Gradual LOC with few myoclonic jerks.
(5) Transition to LOC → gradual over seconds.
(6) Regaining consciousness → rapid within seconds.
(7) Post ictal period → no confusion / disorientation.
    (maximum ≤ 5 mins)
(8) Tonic clonic movements → may be present
    (<15 seconds)
(9) Other features → biting of tongue
    (rare) bladder / bowel incontinence.

<table>
<thead>
<tr>
<th>TABLE 41-2 Features That Distinguish Generalized Tonic-Clonic</th>
<th>SEIZURE</th>
<th>SYNODE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate precipitating factor</td>
<td>Usually none</td>
<td>Emotional stress, Vasovagal, orthostatic hypotension, cardiac</td>
</tr>
<tr>
<td>Premonitory symptoms</td>
<td>None or unrecognizable</td>
<td>Tingling, numbness, diaphoresis, tunneling of vision</td>
</tr>
<tr>
<td>Duration of syncope</td>
<td>Minutes</td>
<td>Usually acute</td>
</tr>
<tr>
<td>Duration of ictal period</td>
<td>30-60 s</td>
<td>Usually acute</td>
</tr>
<tr>
<td>Facial appearance during ictal period</td>
<td>Cyanosis, frothing at mouth</td>
<td>Pharyngeal</td>
</tr>
<tr>
<td>Duration of post-ictal period</td>
<td>Many minutes to hours</td>
<td>&lt;5 min</td>
</tr>
<tr>
<td>Asking of muscles after event</td>
<td>Often</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Biting of tongue</td>
<td>Sometimes</td>
<td>Rarely</td>
</tr>
<tr>
<td>Impairment</td>
<td>Sometimes</td>
<td>Sometimes</td>
</tr>
<tr>
<td>Headache</td>
<td>Sometimes</td>
<td>Rarely</td>
</tr>
</tbody>
</table>
Pseudo seizures.

Common seen in adolescent age.

<table>
<thead>
<tr>
<th>Features</th>
<th>Pseudo seizures</th>
<th>True seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axial thrusting movements</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Pupils</td>
<td>Normal</td>
<td>Dilated (Sympathetic Activity)</td>
</tr>
</tbody>
</table>

**Generalized Tonic Clonic Seizures [GTCS]**

- In generalised seizures
  - MC type: Tonic clonic seizures
    - Called as GTCS.

**Causes:**

- Epilepsy
- Medical cause.
- Non-compliance with drugs → MC cause in India.

**Status Epilepticus (SE)**

**Definition**

- 5 minutes or more of continuous seizures
  - Operational definition
    - 5 minutes or more of continuous clinical and/or electrographic seizure activity or
    - Recurrent seizure activity without recovery (impending to baseline) between seizures.

**Phases**

**Initial compensatory phase.**

1. ↑ Sympathetic activity collapse.
2. ↑ Cardiac output.
4. ↑ RBS (sugar levels).

**Decompensation phase.**

1. Cardiorespiratory collapse.
2. Electrolyte imbalance.
3. Rhabdomyolysis and delayed tubular necrosis.
4. Hyperthermia.
Diagnosis:
Continuous EEG monitoring.
- Initiated within 1 hour of seizure.
- Done for at least 48 hours.
- Evaluate for non-convulsive seizures.

Causes Of Seizures

1. Drug associated (MC)
   - Non-adherence to drugs (MC in India).
2. Alcohol (MC)
4. Traumatic
5. Stroke/tumor (most focal seizures)
6. Chronic structural injury to brain
7. Metabolic causes:
   - Hypoglycemia.
   - Hypo/Hypernatremia.
   - Hyperkalemia.
   - Hypermagnesemia.
   - Hypo/Hyperkalemia not related to seizures.
   - Hyper phosphatemia → seizures when associated with hypocalcemia.
8. Hepatic encephalopathy.
10. Sepsis.
Drugs precipitating seizures
- Theophylline
- Imipenem
- Cefepime
- Quinolones
- Lithium
- TCA
Other causes:
- Viral encephalitis
  - MC cause for new onset refractory status epilepticus (NORSE)
- Autoimmune encephalitis
  - anti NMDA ab (N-methyl D-aspartate Ab)
- Paraneoplastic encephalitis - anti Yo Ab.

Management Of Status Epilepticus

Initial stabilization (2 IV lines)
- 1st IV line: Lorazepam (DOC) 0.1 mg/kg (IV)
  - or
- Midazolam 0.2 mg/kg (IV/IM)
  - 0.5 mg/kg (buccal/intranasal)
  - or
- Clonazepam 0.015 mg/kg IV

2nd line
- Phenytoin / Phosphoryl 30 mg/kg
  - or
- Levetiracetam 50-50 mg/kg
  - or
- Valproate 20-30 mg/kg

No response
- IV Propofol ± midazolam
  - No response
  - Refractory status epilepticus
  - DOC: Phenobarbital
  - No response
  - Anesthetic drugs
EEG pattern

- In status epilepticus → generalised, poly spikes.
- In focal
  - Simple partial seizures → normal EEG pattern.
  - Complex partial seizures → regional spikes (temporal lobe)
- GTCS → poly spikes.
- Atonic seizures CME → polyspikes and wave pattern.
- Absent seizures → 3 Hz, slow sp., and wave pattern.

Management Of Generalised Seizures

Indication:
1. 1st attack of seizure with high risk →
   - Post seizure EEG abnormality.
   - Family history of epilepsy.

2. 2nd attack of epilepsy.

Drugs: 1st line

- Valproate (D)C
  - 50-125 μg/ml
  - Dose related toxicity:
    - Ataxia
    - Sedation
    - Tremors
  - Inhibits metabolism of other drugs.
  - Side effects:
    - Vomiting

- Lamotrigine
  - 5.25-80 μg/ml
  - Dose dependent toxicity:
    - Ataxia
    - Diplopia
    - Sedation
    - Steven Johnson syndrome
- ↑ Ammonia levels
- Alopecia.
- Liver toxicity.
- Pancreatitis.
- Renal side effects
- Weight gain
- Thrombocytopenia.
- Teratogenic

2^nd line drugs:
(1) Carbamazepine
(2) Topiramate → Renal stones
   Weight loss
   Glaucoma.
(3) Felbamate → Aplastic Anemia.
(4) Zonisamide → Renal stones
(5) Phenytoin
   → Indications to stop drugs:
   a year seizure free interval
   with:
   (a) No family history
   (b) Normal EEG
   (c) Normal MRI

Management Of Absence Seizures And Partial Seizures 00:35:58

* Absence seizures

1^st line drugs

- Valproate (DOC)
- Ethosuximide SE: Optic nerve damage

↓

* Drugs in management of partial seizures:
(1) Carbamazepine (DOC)
   → 4-12 µg/ml
   → Dose dependent toxicity
   - Ataxia
   - Diplopia
   - Vertigo
   → Side effects:
   - SADH
   - Liver toxicity
   - Aplastic anemia

2^nd line drugs

- Lamotrigine
- Clonazepam
(a) Levetiracetam
(b) Phenytoin
(c) Lamotrigine

→ management of seizures in pregnancy

* Drugs with →
  1) Maximum risk for fetal malformation
      ↓ valproate (4.7-10%)
  2) Least risk for fetal malformation
      → Lamotrigine (3-3.4%)
      → Levetiracetam (0-2.4%)
* Preferred drugs for seizures in pregnancy:
  → Lamotrigine (500mg)
  → Levetiracetam
* Folic acid given along with these drugs.

* 50-30-20 Rule.
  50% → no change in status of seizures.
  30% → seizure worsen/increase
  20% → improvement of seizure

**Laforas Disease And Rolandic Seizures**

Laforas disease
→ autosomal recessive myoclonic epilepsy
→ 10-18 years
→ poor prognosis
→ clinical features:
  (1) myoclonus
  (2) Dementia
  (3) Hallucination
  (4) Low IQ

Microscopy: PAS positive

→ Intracellular polyglucosan inclusion bodies
  ↓ "Lafora bodies"

Rolandic seizures:
→ 5-10 years of age
→ completely resolves by puberty.
→ good prognosis
→ aka: Benign epilepsy with centrotemporal high voltage spikes

→ infrequent partial seizures.

West Syndrome

- aka. infantile spasms
- age 3-7 months.
- boys > girls.
- in 2/3rd cases

↓

Structural brain lesion
↓

Due to brain hypoxia, during delivery.
- Associated with tuberous sclerosis
- Clinical features:
  - Triad of (1) infantile spasm / jack knife / flexor spasms / salaam spasms (40%)
    (a) severe mental retardation
    (b) EEG - Hypsarrhythmia
    (large mountain waves)
  - Psychomotor deterioration
  - Permanent motor and mental disability
  Salaam spasm
  abrupt flexion of neck and trunk
  ↓
  arms raise forwards
  ↓
  flexion at elbow
  ↓
  legs elevated with flexion at hips and knees.

- EEG
  Large mountain waves
  (Himalayan waves)

Management

- 
- Vigabatrin

↓

- in case of tuberous sclerosis
- visual field defects.
Lennox Gastaut Syndrome

- most severe childhood epilepsy
- bad prognosis
- progressive cognitive disturbance.
  • Clinical features (triad)
  1) multiple types of seizure - mostly atomic
  2) severe mental retardation.
  3) Characteristic EEG.

EEG
- Slow spikes (1.5 – 2.5 Hz)
- Spike and wave pattern.
- Bilaterally synchronous
- Dominant over frontocentral region
- Symmetric.

Management.
Lamotrigine + Valporate
- Drug with:
  - Effect on cognitive function → Felbamate
  - Effect against drop attacks → Topiramate.
- Surgery: Callosotomy
- New drug: Cannabidiol

syndrome...
- Refractory unremitting focal seizure in children
- Cerebral hemiatrophy
- Contralateral hemiparesis

EEG:
- Periodic lateralised epileptiform discharges.

Landau persylvian seizure
- Abrupt loss of previously acquired language at 5-7 years
- Epileptiform activity in persylvian zone

Benign neonatal familial convulsions.
- 5th day seizures
- Due to potassium channel defect.
Demyelinating Disorders of CNS

- Myelin in CNS - By oligodendrocytes
- Myelin in PNS - By Schwann cells
- Biochemical abnormality in myelin - Leukodystrophy

Multiple sclerosis (MS)

Antibodies + T-cells

Target antigens: Myelin oligodendrocyte glycoprotein (MOG)
Myelin basic protein (MBP)

Loss of myelin sheath (Demyelination)

Loss of saltatory conduction

Continuous propagation of nerve impulse instead of saltatory conduction → less effective

- T-cell + Antibody mediated → Autoimmune demyelination
demyelination

F > 30 y. (20-40 years)

- Chronic inflammation + demyelination → Gliosis / scarring

2nd Axonal injury

Cerebral atrophy

- MS is purely a CNS disease. No demyelination occurs in PNS.
- Perivascular cuffing - by T-cell infiltrate

Affect white matter, disruption of BBB, demyelination and loss or saltatory conduction.
Classification Of M.S

Classification of Multiple Sclerosis

1. Benign Multiple Sclerosis
2. Relapsing Remitting Multiple Sclerosis
3. Secondary Chronic Progressive
4. Primary Progressive

Types:
- Relapsing remitting type - 85% - most common, good prognosis
- Primary progressive - 15% - Bad prognosis, rare
- Secondary chronic progressive - Bad prognosis, rare

Benign MS - Best prognosis
Clinical Features:
- F >> M - 30-40 years
- Associated with other autoimmune illnesses
- 33% risk of if identical twin has MS
- Vitamin D deficiency - Recurrent relapses
- High socioeconomic status
- Associated with HLA DRB1*1501
- HLA DRB1*2
- Cumulative axonal loss is the cause for progressive neuronal damage MS

Clinical Presentations:
- Most common: Long tract symptoms - Sensory
- 2nd MC: Optic neuritis
- Motor presentation - 3rd MC
- Autonomic presentation - 4th MC
- Spinal cord syndrome: Presents as Acute Transverse Myelitis
- Rarely - ON in PPRMS (Primary Progressive MS)
- Brain stem syndrome

Long Tract Symptoms:
- Sensory > Motor
- Hypesthesia / Hyperesthesia
- Unpleasant sensations are also common
- Spasticity causing movement induced muscle spasms
- UMN type of weakness with loss of strength, speed & exercise induced fatigue
Optic Neuritis:
- Painful monocular loss of vision.
- Optic Atrophy
- Fundus - Normal
- Diplopia - Binocular due to B/L INO (Internuclear Ophthalmoplegia).

Brain stem:
- Ataxia
- Tinnitus
- Vertigo
- Rare:
- Bell's palsy with preserved taste.
- B/L Trigeminal neuralgia.
- Cognition is preserved till the end.
- Detrusor sphincter dyssynergia / detrusor hyperreflexia.
- Cognitive loss towards the late stage

Positive Symptoms Of M.S:
1. Uhthoff's phenomenon: Abnormal Heat Sensitivity
   - Unilateral visual blurring in hot showers.
2. Lhermitte's sign: Not specific
   - Flexion of neck → Shock-like sensation in back.
3. Facial Myokymia: Abnormal facial flickering
4. Glossopharyngeal Neuralgia

Diagnosis Of M.S

- Mainstay: MRI

- Common sites for T₂ hyperintensities on T₂ W MRI:
  - Juxtacortical
  - Periventricular - most common
  - Internal capsule
  - Deep white matter
- Brain stem - especially adjacent to CSF space.
- Cerebellum
- Spinal cord
- Corpus callosum - Dawson's fingers - very typical

**McDonald criteria for MS**

<table>
<thead>
<tr>
<th>ATTACKS</th>
<th>LESIONS</th>
<th>ADDITIONAL CRITERIA FOR DIAGNOSIS MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 or more</td>
<td>3 or more</td>
<td>None. Clinical evidence alone will suffice</td>
</tr>
<tr>
<td>2 or more</td>
<td>1 lesion</td>
<td>Dissemination in space on MR (or extent further clinical attack implicating ≥2 different CNS sites)</td>
</tr>
<tr>
<td>1 attack</td>
<td>2 lesions</td>
<td>Dissemination in time on MR (or extent further clinical attack implicating ≥2 different CNS sites)</td>
</tr>
<tr>
<td>1 attack</td>
<td>1 lesion</td>
<td>Dissemination in space and time (or extent further clinical attack implicating ≥2 different CNS sites)</td>
</tr>
</tbody>
</table>
| 0 attack progression from onset | | AND at least 2 out of 3 criteria:  
- Dissemination in space in the brain  
- Dissemination in space in the spinal cord based on ≥2 or more T2 lesions  
- Positive CSF |

- Kurtzke's disability score - For MS.
- In CSF: Oligoclonal bands - Detected by Immunofixation Electrophoresis

Intrathecal IgG
(Present in CSF, Absent in Serum)
- CSF pressure - normal
- Cell - increased in 1/3 patients
- Proteins - ↑ IgG

Treatment of MS:

<table>
<thead>
<tr>
<th>Disease course/stage</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monosymptomatic-Acute attack</td>
<td>IV methylprednisolone 1000 mg for 3 days, without oral taper</td>
</tr>
<tr>
<td>Relapsing-remitting, no disease activity and/or no activity on MRI</td>
<td>IV corticosteroids if acute attack occurs</td>
</tr>
<tr>
<td>Relapsing-remitting, current disease activity and/or activity on MRI</td>
<td>IV corticosteroids for acute attacks, plus for prevention</td>
</tr>
<tr>
<td></td>
<td>(1) INF β-1b, 30 μg IM weekly;</td>
</tr>
<tr>
<td></td>
<td>(2) Glatiramer, 20 μg SC daily</td>
</tr>
</tbody>
</table>

- Acute attack - IV methylprednisolone
- Disease modifying therapies:
  - IFN β
  - Glatiramer acetate
  - Natalizumab
  - Fingolimod
  - Mitoxantrone

Neuromyelitis optica / Devic's disease

- Acquired disease
- Auto-antibodies against Aquaporin 4
- Autoimmune, MC in females - 40%
- Severe transverse myelitis + B/L acute optic neuritis
- Disabling disease, non progressive
- Treatment: Responsive to steroids
  -↑ fails
  - Plasma exchange (PLEX)
  - Normal MRI
**Acute Disseminated Encephalomyelitis (ADEM)**

**Definition:** Acute inflammatory demyelinating disorder of CNS, characterised by multifocal white matter involvement which is typically monophasic and usually follows an infection or vaccination.

- Post infectious - 95%
- 5% follow immunisation
- Children > Adults
- Most common cause: Rubella, > measles > chicken pox
- Reason: Molecular mimicry
- Clinical Presentation:
  - Prodromal symptoms - 20%
  - Meningismus
  - Encephalopathy
  - Coma
  - B/L extensor plantar
  - Very Rapid progression.
- In CSF: Oligoclonal bands; Pleocytosis.
- On MRI: Asymmetrical large hyperintensities on T2 MRI.
- Treatment: Steroids +/- PE.

**Difference between MS and ADEM**

<table>
<thead>
<tr>
<th>ADEM</th>
<th>MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: before 12 yrs</td>
<td>Age: After 12 yrs.</td>
</tr>
<tr>
<td>Male preponderance in children; reversed in adults</td>
<td>Twice common in women</td>
</tr>
<tr>
<td>Preceding triggers.</td>
<td>No preceding triggers.</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>No constitutional symptoms</td>
</tr>
<tr>
<td><strong>ADEM</strong></td>
<td><strong>MS</strong></td>
</tr>
<tr>
<td>ON - Bilateral</td>
<td>ON-unilateral</td>
</tr>
<tr>
<td>Complete myelopathy - unusual</td>
<td>Myelopathy - complete</td>
</tr>
<tr>
<td>Encephalopathy - common</td>
<td>Encephalopathy - less common</td>
</tr>
<tr>
<td>Monophasic</td>
<td>Relapsing remitting</td>
</tr>
</tbody>
</table>
CORTEX - LOBAR ORGANISATION - I

Neurological examination:
I. Higher mental functions
II. Cranial nerves
III. Motor system examination
IV. Sensory system examination
V. Cerebellum
VI. Miscellaneous - Autonomic nervous system
   Meningeal signs
   Skull and spine

Frontal lobe - Motor area

Organization of cortex:
  Lobes - Frontal, Parietal, Temporal, Occipital

Superalateral surface:
  Frontal lobe: lies above sylvian fissure and to the left of central
1. Motor cortex (Area 4)
   - Precentral gyrus (location)
   - Origin of 80% of corticospinal tract
   - Lowest threshold to initiate movements
   - Fine distal movements

Lesion of motor cortex:
   - Involves middle cerebral artery
   - Causes contralateral UMN weakness - predominantly face & arms
   - CL simple partial seizures - marching / Jacksonian type
   - Also called adverse seizures

Somatotropic representation
   - Face & arms: represented on suprolateral surface
   - Lower limbs: medial surface
     (Supplied by anterior cerebral artery)

Note:
   - Motor cortex matures by age of 4 years
   - Betz cells: giant pyramidal cells in layer 5 of motor cortex

Frontal lobe - Premotor cortex

- Also called supplementary motor cortex.
- Pre-motor cortex: Area 6, 8
- Origin of 30% of cortico-spinal tract
- Function: Planning and organizing sequence of movements.

Lesion of pre-motor cortex:
- Spasticity more than weakness.
- Primitive reflexes (①)

Frontal eye field

- Anterior to pre-motor cortex
- Part of pre-frontal cortex (Area 9, 10, 11)

Function:
   - Helps to look to opposite side
   - Ex. ① Frontal eye field → Activate ② VI nerve nucleus
   - ② Lateral rectus
   - Look to right side

Medicine v2.0 - Marrow 4.0 - 2020
Lesion of frontal eye field:
- Gaze towards site of lesion and away from side of weakness.

Eg: (1) Unilateral weakness \(\rightarrow\) (2) Frontal cortex lesion
(= hemiplegia.)
(\(\rightarrow\))  (2) Frontal eye field affected.

Patient looks to (\(\rightarrow\)) side
- Cannot look to (\(\rightarrow\)) side.

Gaze towards site of lesion
- Gaze away from side of weakness.

Broca's area
Location: Inferior fronto-gyrus
Area: 44, 45

Lesion: Broca's aphasia.
- Motor non-fluent aphasia.
- Word output ↓
- Talks with difficulty
- Dysarthric / Telegraphic speech
- Prosody of speech → Lost
- Pronunciation wrong
- Comprehension intact
- Repetition lost.

Pre-frontal cortex
Area: 9, 10, 11
Functions → Personality
- Problem solving ability and creativity
- Intelligence
- Executive function
- Motivation
- Abstract thinking
Attention
Retrieval of memory
Appropriate social behaviour
Language.

Pick's disease: Atrophy of pre-frontal cortex.

Pre-frontal cortex connected to sub-cortex (striatum) by fronto-striatal fibres.

Pick's disease → motor manifestations like akinesia, rigidity

**Frontal lobe - Medial surface**

Predominant blood supply

↓

Anterior cerebral artery (ACA)

Lesion in medial surface
weakness in lower limbs
urinary incontinence (Paracentral lobule involvement)

Cingulate gyrus: Emotional and conditional response.

↑

ACA

Causes: a. Anterior Cingulate gyrus syndrome
aka. Akinesic mutism of A11. A11
no movement (even to pain)
no speech
B/L frontal lobe lesions:
- Akinetic mutism
- Urinary incontinence
- Hemianopia, sensory changes
- Gait apraxia, a.k.a. ignition foot phenomenon.

Parietal lobe

lies posterior to the central sulcus.

Boundaries:
- Central sulcus
- Sylvian fissure
- Parieto-temporal sulcus
- Parieto-occipital sulcus

Parts of parietal cortex

1. Sensory cortex - Area 3, 1, 2
   a) origin of 40% of corticospinal tract
   b) Sensations relayed to area 3, 1, 2.
      - Cortical sensations
         ↓
         Tactile localization
         Tactile / two-point discrimination
         Stereognosis
         Graphesthesia.
Lesion of sensory cortex: C / L weakness
loss of cortical sensations.

2. Supramarginal gyrus
   Function: Praxis.

   Lesion:
   Apraxia - Inability to carry out a voluntary motor act in the presence of normal motor / sensory system / cerebellum.

   Types → ideational apraxia,
            ideomotor apraxia.

3. Angular gyrus
   Function: Gnosis → Ability to recognize an object by touch or vision or sound.

   Lesion of dominant lobe:
   a) Tactile agnosia (astereognosis)
   b) Acalculia
dominant:
   c) Finger agnosia.
   lobe
d) Right left disorientation
e) Agraphia with alexia.

   Note:
   Lesion of parietal lobe → Inferior homonymous quadrantanopia.

Non-dominant parietal lobe lesion

Features:
1. Visuo- Spatial disorientation
2. Constructional apraxia.
3. Dressing apraxia.
4. Anosognosia. (Left sided hemispatial neglect)
   right hemisphere → right & left extrapersonal space
   left hemisphere → right extrapersonal space.

   * when left hemisphere affected, right hemisphere compensates for right extrapersonal space
   * when right hemisphere affected

   No compensation.

   Left sided hemispatial neglect.
Temporal cortex

No Corticospinal tracts, \( \therefore \) no weakness
Non-dominant hemisphere features\( \Theta \)
No sensory symptoms

Important areas:
1. Auditory cortex (area 41, 12)
   \( \rightarrow \) e/\' lesion \( \rightarrow \) deafness
   Secondary auditory cortex
   Lesion \( \rightarrow \) auditory agnosia.

2. Visual association cortex (area 30, 18)
   Lesion \( \rightarrow \) Visual agnosia.

Other features of temporal lobe lesions:
- Superior homonymous quadrantanopia.
- Olfactory and gustatory hallucinations

Wernicke's area:
Area 22 - in superior temporal gyrus
Lesion \( \rightarrow \) Wernicke's aphasia [without weakness]
   Fluent (sensory) aphasia.
   Word output \( \uparrow \uparrow \)
   Jargon, neologism.
   Comprehension and repetition - lost

Hippocampus:
Storage of short-term memory
Transfer of memory to neo cortex [for long-term memory]
Lesion \( \rightarrow \) Episodic amnesia/lost.
**Amygdala**

Amygdala (Limbic cortex)

B/L Lesion → Klüver Bucy syndrome
- ↑ Aggression
- Loss of fear
- Loss of satiety
- ↑ Sexual drive

Goal directed behavior - lost

- Rage, aggression → Amygdala and hypothalamus
- Fear → Amygdala and hypothalamus
- Feeding → Hypothalamus (satiety centers)
- Sexual drive and behavior → Hypothalamus and limbic system
- Goal directed behavior (reward and punishment) → Hypothalamus and frontal cortex

B/L Temporal lobe lesion
1) Klüver Bucy syndrome
2) Deafness
3) Korsakoff's amnesic state

**Occipital lobe**

Primary visual cortex (area 17)
Secondary visual cortex
- Peristriate and parastriate cortex (area 18/19)
  - Function: visual memory
  - Ocular fixation
  - Identify size / shape / color
Visual pathway

Optic nerve → Chiasma → Optic tract → Lateral geniculate body → Optic radiations

Magnocellular Pathway

Parvocellular Pathway

Layers of LGN: 1, 2, 3, 4, 5, 6 → Visual cortex (occipital lobe)

− Parvocellular pathway:
  Smaller receptive field
  Colour vision
  No response to moving stimuli
  Stereopsis / depth of vision

Lesions in visual pathway:

Optic nerve → Monocular vision loss
Optic chiasma → Bi temporal (heteronymous) hemianopia
Optic tract → Homonymous hemianopia (incongruous)
Lateral geniculate body → Homonymous hemianopia.
Visual Cortex Lesions

W/L lesion in visual cortex
- Contralateral homonymous hemianopia.
  - Macular sparing +
  - Congruous hemianopia.

L/R Visual cortex lesion:
- Anton's syndrome
  - Cortical blindness
  - Patient denies of blindness
  - Light reflex preserved

Balint's syndrome
- Optic ataxia
- Oculomotor apraxia
- Simultagnosia

Agnosia in occipital lobe lesions:
1) Colour agnosia.
2) Prosopagnosia (inability to identify person by face)
LOBAR DYSFUNCTION - APHASIA

Aphasia

- Disorder of language
- Dominant hemisphere lesion (cause)

Speech apparatus

Wernicke's area (area 22 in superior temporal gyrus)
  Identifies word as a language symbol
  ↓
  Language symbols to be recognised
  ↓
  Sent to the angular gyrus
  ↓
  Sent back to Wernicke's area.
  ↓
  Sent to Broca's area by arcuate fasciculus
  (area 44/45 - in inferior frontal gyrus)
  ↓
  Converts language symbol to motor activity
Aphasia - classification

- Sensory aphasia
  - Fluent aphasia
  - Types of sensory aphasia
    - Comprehension - good
    - Comprehension - poor
      - Good understanding of written and spoken language
      - Reading and writing - normal
      - Ability to repeat
      - Intact
      - Nominal aphasia
      - mild
    - Conduction aphasia
      - Poor understanding of written and spoken language
      - Reading and writing - impaired
      - Ability to repeat
      - Lost
      - Transcortical sensory aphasia
      - Severe

Sensory aphasia - nominal and conduction aphasia

- Nominal aphasia
  - Site of lesion - angular gyrus
  - C/F: Difficulty in word finding or naming
    - Comprehension (+)
    - Repetition (+)
    - Good reading and writing skills
    - Good speech output

- Conduction aphasia
  1) Site of lesion - arcuate fasciculus
  2) Repetition lost
  3) Paraphasia (unintended words in between speech)
Sensory aphasia - Transcortical sensory, Wernicke's aphasia

Transcortical sensory aphasia.
- Due to watershed territory infarct
- Causes of infarct - Hypotension, Hyboalbuminemia.
  Repetition intact

Wernicke's aphasia.
- Due to inferior division of MCA infarct (middle cerebral artery)
- C/F - no dysarthria, logorrhea, irrelevant speech
  Neologism (new words), Paraphasia.
  Jargon aphasia.
  Repetition - lost

Note:
Common C/F (in both):
- Loss of ability to understand written/spoken language
- Impaired reading/writing

Motor aphasia

Good understanding of written and spoken language
- Transcortical motor aphasia.
  Repetition intact
  Repetition lost
  Mild

Poor understanding of written and spoken language
- Broca's aphasia.
  Repetition intact
  Repetition lost

Isolation aphasia
- Global aphasia.
  Repetition intact
  Repetition lost
  Severe
# Broca Aphasia

<table>
<thead>
<tr>
<th>Feature</th>
<th>Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous speech</td>
<td>Nonfluent, mute or telegraphic, usually dysarthric</td>
</tr>
<tr>
<td>Naming</td>
<td>Impaired</td>
</tr>
<tr>
<td>Comprehension</td>
<td>Intact (mild difficulty with complex grammatical phrases)</td>
</tr>
<tr>
<td>Repetition</td>
<td>Impaired</td>
</tr>
<tr>
<td>Reading</td>
<td>Often impaired (&quot;third alesia&quot;)</td>
</tr>
<tr>
<td>Writing</td>
<td>Impaired (dysmorphia, dysgrammatical)</td>
</tr>
<tr>
<td>Associated signs</td>
<td>Right hemiparesis</td>
</tr>
<tr>
<td></td>
<td>Right hemisensory loss</td>
</tr>
<tr>
<td></td>
<td>Aprasia of left limbs</td>
</tr>
</tbody>
</table>
LOBAR DYSFUNCTION - DEMENTIA

Dementia.

Development of multiple cognitive defects

including memory & at least one of the following cognitive
disturbances:
  1) Aphasia. (language)
  2) Agnosia.
  3) Apraxia. (supramarginal gyrus)
  4) Executive dysfunction (prefrontal cortex)

Memory

Immediate

↓

Recent

↓

Remote

↓

Reticular

activating system

Retrieval of memory: Prefrontal cortex

Storage of memory: Hippocampus

Discarded

Transferred to neocortex

for long term memory

Long term memory

00:16:09

Declarative

(Explicit)

↓

Non declarative

(implicit)

↓

Semantic

Factual

Cortical association areas

↓

Episodic

Medial temporal

↓

Neocortex

Medicine v2.0 - Marrow 4.0 - 2020
Non declarative (Implicit)

Procedural Skills
priming
conditionary Amygdala.

Basal ganglia (-seen usually in adults
Corpus striatum -modification of one's behaviour
based on previous experience)

Dementia

Alzheimer's disease
• Biggest risk factor: Age
• < 65 years, Genetic factors

↑ Apo E4
Ch. 19
Presentin 1
(PSRN 1)
chr. 14
Chr. 1

Critical molecule - Aβ amyloid,
{derived from APP gene
amyloid precursor protein on chr 21}
1) Forms β pleated sheets that aggregates
2) Resistant to degradation
3) Neurotoxic response from astrocytes and microglia.

Facts:

- Most important genetic risk factor for sporadic - early Alzheimer's disease
- Single most important biological marker for AD risk
1. Presentin-1 (chr 14)
- Most common defect in early onset familial AD
- Involved in cleavage of APP
3. Presentin-2 (chr 1)

Medicine v2.0 + Marrow 4.0 + 2020
Histopathology in Alzheimer’s

- Neurofibrillary
- Hyperphosphorylated Tau Protein
- Hence known as Tauopathy
- Neuritic plaques
- Aβ amyloid

Risk Factors
1. Old age
2. Positive family history
3. Pm
4. Aluminium / mercury
5. Apo E4 → risk
6. History of head trauma / concussions
7. Past history of stroke

Alzheimer’s disease = TDP
Due to manifestation of insulin resistance in the brain
- Apo E2 / NSAIDS / HRT - protective factors

Pathology of Alzheimer’s Disease

1) Hippocampus → Diffuse atrophy
   a) Degeneration of cholinergic neurons of nucleus basalis of Meynert.
2) Hyperphosphorylated tau protein - Neurofibrillary tangles
3) Senile / neurtic plaques - Aβ amyloid
4) Extravascular degeneration

Clinical manifestations
- Characteristic pattern of Alzheimer’s - memory impairment → language → visuospatial defects → executive dysfunction

Stage of Alzheimer’s disease
i) Nonspecific amnestic state
   1) Hippocampal atrophy
   a) Gradual onset of memory loss
   b) Declerative episodic memory.

ii) Dysnomia → affects language
    - Nominal aphasia
    - Comprehension
    - Fluency
    1) Halting in speech / writing
2) Acalculia.
ii) Visuospatial defects

Parietal

1) Praxia → Supramarginal gyrus
2) Gnosia → Angular gyrus
3) Non-dominant → Visuospatial disorientation
   • Constructional apraxia.
   • Anosognosia.

iv) Prefrontal cortex – Personality affected

Alzheimer’s – diagnosis

A PET Scan – IOC (earlier MRI was considered IOC)

↓

• Hypometabolism
• Fibrillar Aβ amyloid
• Hyperphosphorylated tau protein

B. EEG – normal or non-specific slowing
C. CSF analysis
   1) Low Aβ 42 amyloid levels
   2) High phosphorylated tau levels

Differential diagnosis of alzheimer’s

Differential diagnosis
- Pick’s disease
- Vascular dementia
- Normal pressure hydrocephalus
- Diffuse Lewy body dementia

Reversible causes – Vitamin B12
- Thiamine

Treatment of Alzheimer’s
Cholinesterase inhibitors are Doc
- Tacrine (hepatotoxic)
- Rivastigmine
- Donepezil (mCi)
- Galantamine

Medicine + v2.0 + Marrow 4.0 + 2020
moderate to severe \( \text{NMDA antagonist: memantine} \)

**Pick's disease (Fronto-temporal dementia)**
1. Age 50 - 70 yrs
2. Gene MAPT (Chr. 17)
3. 50% have family history
4. Hypophosphorylated tau protein
5. Pick's bodies
   ↓
6. Contain hypophosphorylated tau
7. Selective atrophy of frontal and temporal

Disease starts in frontal (prefrontal cortex)
↓
Behavourial personality affected
mc variant - behavioural variant of Fronto temporal dementia.
(bvFTD)
7. +/- subcortical symptoms (reason- prefronal cortex connected to corpus striatum)
8. Impaired planning, judgement & language

- memory relatively preserved (in early stage)
- Transcortical motor aphasia
- Progresses rapidly.

**DLB Dementia**

<table>
<thead>
<tr>
<th>Cortical dementia</th>
<th>Subcortical dementia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Alzheimer's disease</td>
<td>1. Huntington's disease</td>
</tr>
<tr>
<td>Pick's disease</td>
<td>DLB dementia</td>
</tr>
<tr>
<td>2. Memory affected</td>
<td>a. Memory - spared/less severe</td>
</tr>
<tr>
<td>3. more - severe</td>
<td>3. Less severe</td>
</tr>
<tr>
<td>5. Extra pyramidal (-)</td>
<td>(Apathy, depression)</td>
</tr>
<tr>
<td>6. Aphasia</td>
<td>5. +</td>
</tr>
<tr>
<td>Apraxia</td>
<td>6. -</td>
</tr>
<tr>
<td>Agnosia</td>
<td>affects thalamus/corpus striatum/midbrain</td>
</tr>
</tbody>
</table>
Parkinson's Dementia

Parkinson's Dementia v/s DLB dementia.

1) PD - unresponsive to L-dopa.
   - Tremor uncommon
   - Cognitive impairment within 2 years of onset
2) Hallucination
3) E/L motor symptoms common
4) Axial symptoms / gait dysfunction - Early

NOTE
- and MC cause of dementia - vascular dementia.
- Dementia can precede or occur along with Parkinson's.

- Never give antipsychotics

↓

↑ dopamine

- Dopaminergic deficit
- α-synucleinopathies
- DLB dementia is an α-synucleinopathy
- Intraneuronal cytoplasmic inclusions (ie Lewy bodies) are seen in Substantia nigra, brainstem, limbic cortex

Prion disease

- Infectious proteins which lacks nucleic acid.
  - Abnormal folding of prion protein [PrP]
    - Normal - PrP
    - Abnormal - PrP → PrPSc
      - (alpha) (beta pleated)

- May manifest as: infectious/genetic/sporadic
- No immune response
- Spongiform changes in cortex → neuronal loss

Example
- Creutzfeldt - Jakob disease
- Gerstmann- Straussler Scheinker syndrome
- Kuru
- Familial fatal insomnia.
Diagnosis:

1) Long incubation period
   a) Dementia + myoclonus
   b) Ribon shaped hyperintensities on MRI
   c) EEG - high voltage slow & sharp waves in a low voltage background

10C - Brain biopsy

Drug - Flupirtine maleate
   (Centrally acting non opioid analgesic)

Vascular Dementia

- 2nd mc type of dementia.
- Dementia - cerebro-vascular accident (CVA)
  - Onset within 3 months of CVA
  - Deterioration of cognitive function
    1. Step wise deterioration
    2. Prefrontal cortex
       - Executive Function
       - Frontal
       - Parietal
    3. 6/6 corticospinal & corticobulbar involvement
       - Appear like pseudobulbar palsy (emotional incontinence)
    4. Memory - involved later
    5. Urinary abnormalities
       - due to paracentral lobule involvement
       - Gait abnormality
       - Gait apraxia, (ignition foot abnormality)
1. multiple lacunar infarcts (white matter disease)
   ↓
  Binswanger disease
   ↓
   Confusion + Psychosis + motor disability
   MRI - normal pressure hydrocephalus

D/D of dementia:
- normal pressure hydrocephalus
- ventricles are filled with CSF & therefore expands the ventricle
- CSF pressure: normal
- cortical
- prominent subcortical gyri

Triad

Dementia (subcortical)

Ataxia
Urinary incontinence

"Gait apraxia," Ignition foot phenomenon
EPS: ANATOMY AND PHYSIOLOGY

Subcortex

Grey matter
- Corona radiata
- Thalamus
- Basal ganglia
- Amygdaloid nucleus

White matter
- Tracts: Corticospinal & Corticobulbar
- Pass through white matter

Basal ganglia

- Functionally related nuclei in the Subcortex:
  - Caudate nucleus
  - Putamen
  - Globus pallidus
  - Subthalamus nucleus
  - Substantia nigra

- All these nuclei form the largest component of EPS (Extra Pyramidal System)
EPS - components & basic functions

Components of EPS:
1. Basal ganglia, with its connections
2. Rubrospinal tract (mid brain-red nucleus)
3. Reticulo spinal tract
4. Tectospinal (tectal nuclei) tract
5. Vestibulo spinal tract

- These tracts do not cross through Pyramids of Thalamus. Hence called as EPS.
- Initiation & partly integration of fine, skilled distal voluntary movements controlled by Pyramidal tracts.
- Prepares for movement, thought process, regulation of posture, modulation by EPS.
- Finess to the movement - Cerebellum

Basic functions of EPS:
- Cognitive control of motor activity - Caudate nucleus
- Complex patterns of motor activity
- Timing and scaling the intensity of movements }

Basal ganglia circuits

- Basal ganglia - Receives inputs from and projects back to motor cortex via thalamus
- It is a closed loop
- Majority of the inputs to Basal ganglia - Corpus Striatum via Cortical Association areas
- Main output of Basal ganglia - Via Globus Pallidus Interna, > Substantia nigra
- Excitatory pathways - Glutamatergic
- Inhibitory pathways - GABA
- Dopaminergic pathways can be excitatory or inhibitory
Circuit:

Association cortex → Premotor cortex

Superior colliculus of mid brain (vertical gaze movements)

 Corpus striatum → Dopamine → Substantia nigra → Glutamate

GABA ↑

Subthalamic nucleus → Globus Pallidus interna. → GABA → Thalamus

Dopamine release onto D1 = Increased excitation of motor cortex.

Direct and indirect pathways

Nigrostriatal pathway

D1 - Direct Pathway

Excitation of Premotor cortex

Loss of Direct pathway: Hypokinetic movements

Paucity of movement unrelated to weakness or spasticity

Eg: Parkinson's Disease

D2 - Indirect Pathway

Inhibition of Premotor cortex

Loss of Indirect pathway: Hyperkinetic movements

Excessive movements

Eg: Involuntary movements
Movement Disorders

- Hypokinetic
- Hyperkinetic
- Combination

Basal ganglia summary:
- Planning, Programming and initiation of motor activity.
- Lesion: leads to alteration in the sum of impulses channelled to basal ganglia, resulting in movement disorders.
- Crude movements also affected.
PARKINSON’S DISEASE

Hypokinetic movements: Paucity unrelated to weakness or spasticity

Hypokinetic movements

Parkinson’s disease

Non Parkinson etiologies:
- Hypothyroidism
- Catatonia

- Most common Neurodegenerative disease: Alzheimer’s disease
- 2nd most common Neurodegenerative Disease: Parkinson’s disease
- Most common Subcortical Neurodegenerative disease: Parkinson’s disease

Pathology:

Subcortex → Grey matter → Basal ganglia

Nigrostriatal Dopaminergic Neurons gets degenerated.

[Direct pathway]

Loss of excitatory signals to Premotor cortex

Hypokinesia / Bradykinesia

- Age group of Parkinson’s disease - 65 years and above.
- Less than 60 years: Familial Parkinson’s disease

- Familial Parkinson’s Disease
  - PARK 1: A-D - α-Synuclein - α-syn
  - PARK 2 - A2 - Parkin - chr6
- Intracytoplasmic proteinaceous inclusions called Lewy bodies
- On MRI: Loss of Pigmentation
  - in Substantia nigra.
  - MRI at the upper mid brain shows
  - Right/L. Hyperintense
  - Grey matter (Substantia nigra)
- Absent Swallow tail Sign-
  - > 90% Diagnostic accuracy

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Apart from substantia nigra, Lewy bodies are also seen in:
- Other pigmented brain stem nuclei
- Dorsal nucleus of vagus
- Nucleus basalis
- Other cortical association areas

Parkinson's Disease

- Idiopathic (80%) or
- Primary
  - Sporadic
  - Familial
- Secondary
  - Drugs, neuroleptic
  - Metabolic: Wilson's
  - Infection: Whipple's
  - Nutritional toxicity: manganese
  - Endocrine: hypothyroidism
  - Toxins: MPTP (methylphenyltetrahydro pyridine)

Symptomatology of Parkinson's disease

- Asymmetrical
- Rigidity
- Tremor
- Bradykinesia
- Postural instability

Clinical phenotypes of Parkinson's disease:

- Tremor predominant (most common)
  - In younger patients (60-70 years)
  - Slower disease progression
  - Better prognosis
- Akinesis-Rigidity Syndrome
  - In older patients (> 70 years)
  - Faster disease progression
  - Poor prognosis

Tremor:
- The presenting symptom
- 2/3 of the patients present with tremor
- Asymmetrical
- Resting distal upper limb tremor
• Frequency: 4-6 Hz
• Brought on by concentration
• Pulirolling tremor
• Pattern: Ipsilateral arm → Ipsilateral leg → Contralateral leg → Contralateral arm.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Parkinson's Disease tremor</th>
<th>Essential tremor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tremor</td>
<td>At rest &amp; oromotor</td>
<td>Postural tremor</td>
</tr>
<tr>
<td>Frequency</td>
<td>4-6 Hz</td>
<td>5-12 Hz</td>
</tr>
<tr>
<td>Distribution</td>
<td>Asymmetric</td>
<td>Mostly symmetric</td>
</tr>
<tr>
<td>Body parts affected</td>
<td>Hands &amp; legs</td>
<td>Hands, head, voice</td>
</tr>
<tr>
<td>Writing</td>
<td>Small (micrographia)</td>
<td>Large and tremulous</td>
</tr>
<tr>
<td>Course</td>
<td>Progressive</td>
<td>Stable or slowly progressive</td>
</tr>
<tr>
<td>Family history</td>
<td>Uncommon (1%)</td>
<td>Common (5-10%)</td>
</tr>
<tr>
<td>Extra pyramidal signs</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>(Bradykinesia, rigidity, and loss of postural reflex)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Releasing factors</td>
<td>Levodopa, dopamine</td>
<td>Alcohol, propranolol,</td>
</tr>
<tr>
<td></td>
<td>agonists, anticholinerges</td>
<td>pramidone, hyperalgetic,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>guanethidine, clonazepam</td>
</tr>
<tr>
<td>Usual site for surgical treatment with deep brain stimulation</td>
<td>Subthalamic nucleus or globus pallidus interna</td>
<td>Ventral intermediate thalami</td>
</tr>
</tbody>
</table>

Bradykinesia:
• Facial Hypomimia.
• Reduced Arm swing
• Small Hand writing - micrographia.
• Difficulty in fine limb movements - cutting, using zipper, putting buttons.
• Wheel chair Sign: Rising from wheel chair
• Difficulty in turning in bed.
• Hypophonic voice
• Stooped Posture
• Bradykinesia + Posture instability → Poor balance
  • Unsteadiness and falls
  • Abnormal pull test - falls backwards
  • Freezing phenomenon.

Rigidity or hypertonia

• Involuntary increase in the muscle tone
• Cog wheel or lead pipe
• By slow passive movements across the joints
• Rigidity is associated with pain and stiffness of muscle
• Froment's Sign: Activity induced increase in contralateral rigidity
Hypertonia:

- Rigidity
  - Pathology: Extrapyramidal System
  - Velocity independent
  - Uniform throughout the range of motion
  - Equal in any direction
  - Lead pipe - at wrist
  - Log wheel - at elbow

- Spasticity
  - Pathology in Pyramidal System
  - Velocity dependent
  - More at the time of initiation
  - Clasp knife spasticity
  - More in one direction

Gait dysfunction:
- Short shuffling gait, Festinant gait
- Festination: Tendency to increase the velocity but with shorter steps
- Narrow based gait in Parkinson's disease, Broad based in Parkinson disease like in MSA-C, PSP
- Stooped posture with flexion of neck, trunk, knees

Head to foot features:
- Rest tremor
- Rigidity - lead pipe / cog wheel
- Posture instability
- Bradykinesia
- Elabellar tap sign
- Reduced blinking
- Speech - Hypophonia
- Festinant gait
- Micrographia
- Autonomic disturbances

Parkinson's disease - Other features:

- Sensory
  - Muscle pain
  - Radicular pain

- ANS
  - Constipation
  - Urinary urgency
  - Erectile dysfunction
  - Orthostatic hypotension

- Cognition
  - Dementia, with Hallucinations
  - Depression
  - Apathy
  - Anxiety

- Sleep
  - Rem sleep is affected
  - Excessive daytime sleepiness
Sequence of Symptoms:
Tremor → Bradykinesia → Axial skeleton → Cognitive symptoms.

↓
Gait & Postural abnormalities

<table>
<thead>
<tr>
<th>Sensory</th>
<th>Autonomic Dysfunction</th>
<th>Neuropsychiatric</th>
<th>Sleep Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Orthostatic hypotension</td>
<td>Anxiety</td>
<td>Excessive daytime sleepiness</td>
</tr>
<tr>
<td>Hyposmia (loss of smell)</td>
<td>Erectile dysfunction</td>
<td>Apathy</td>
<td>Reduced sleep efficiency</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>Bradyphrenia (slowed thinking)</td>
<td>Reduced slow wave sleep</td>
</tr>
<tr>
<td>Urinary urgency</td>
<td>Depression</td>
<td>REM sleep behavioral disorder (RBD)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dementia</td>
<td>Restless legs syndrome</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hallucinations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Differences between Parkinson's disease and diffuse Lewy body dementia

Lewy bodies - are also seen in diffuse Lewy body dementia.

Comparison of Clinical Presentations of Parkinson's Disease Dementia and Dementia With Lewy Bodies

<table>
<thead>
<tr>
<th>Parkinson's Disease Dementia</th>
<th>Dementia With Lewy bodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive impairment occurs at least 12 months after motor manifestations of the disease (usually 4 to 5 years at least).</td>
<td>Cognitive impairment usually occurs within 12 months of motor manifestations of disease.</td>
</tr>
<tr>
<td>Hallucinations occur later and after Parkinson's disease medication use.</td>
<td>Hallucinations occur earlier and sometimes prior to Parkinson's disease medication use.</td>
</tr>
<tr>
<td>Tremor is common.</td>
<td>Bilateral motor symptoms are more common.</td>
</tr>
<tr>
<td>Predominantly unilateral motor symptoms are common.</td>
<td>Axial symptoms and gait difficulty are less common.</td>
</tr>
<tr>
<td>Axial symptoms and gait difficulty are more common.</td>
<td>Axial symptoms and gait difficulty are more common.</td>
</tr>
</tbody>
</table>
Atypical Parkinson’s (or) Parkinson plus syndromes

1. Progressive Supranuclear Palsy (or) Steele Richardson Syndrome
2. Diffuse Lewy body Dementia.
3. Multisystem Atrophy
   - Parkinson plus syndromes are suspected when:
     • There is no response to L-dopa.
     • Absence of Rest tremor at presentation.
     • Severe early onset ANS Symptoms
     • Early dementia / hallucinations
     • Cortical abnormalities → Apraxia
     • Supranuclear Gaze Palsies
     • Predominant cerebellar or pyramidal findings
     • Early onset repeated falls
     • Symmetrical bradykinesia.
PARKINSON PLUS SYNDROME

Pathophysiology

- α-synuclein
  - Aggregates in neurons
    - Known as Lewy bodies
    - Seen in PD (Parkinson's Disease)
      - DLBD (Diffuse Lewy Body Dementia)
    - Aggregates in glial cells
    - Seen in MSA (Multi-system Atrophy)
  - Tau proteins
    - Aggregates in
      - PSP (Progressive Supranuclear Palsy)
  - CJD (Cortico-Basal Degeneration)
  - Alzheimer's → Hyperphosphorylated Tau proteins
  - Pick's Disease → Hyperphosphorylated Tau proteins

Multi-system Atrophy (MSA)

i) Parkinson Plus Syndrome

ii) Types

- MSA-P
  - Parkinson-like presentation
  - 80% cases

- MSA-C
  - Cerebellar-like presentation
  - 5% cases

- MSA-A
  - Autonomic-like
  - 15% cases
  - Also known as Shy-Drager syndrome

iii) Characteristic features

  a) Tremors at presentation → Absent (But may present later)
  b) Cerebellar / Autonomic dysfunction (Shy Drager syndrome)
  - Present
  c) Pyramidal involvement → present
  d) Cervical dystonia → present
  e) Glial cytoplasmic inclusion which stains for α-synuclein
  f) 90% → unresponsive to L-dopa

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vi) Falls → less frequent
vii) Jerky postural / rest tremor / loss of postural stability ⇒ occurs late
viii) Cranio - cervical dystonia - present
ix) High pitched dysarthria - present
x) Radiological findings in MSA

![MRI images showing Cruciform hyperintensity (Hot cross bun sign), Putamen rim hyperintensity, and Hot cross bun sign.]

T₁W - mR1
- Putamen rim hyperintensity
- Cruciform Hyperintensity ⇒ Hot cross bun sign

**Progressive Supranuclear Palsy [PSP]**

1) Also known as Steele - Richardson Olszewski syndrome
2) Characteristic features
   - Extension hypotonia. (In contrary, Parkinson - Flexion Hypertonia)
   - Frequent falls
   - Eyelid apraxia ⇒ Down gaze palsy
   - Broad based gait
   - Retrocollis
   - Facial dystonia ⇒ Procerus / Surprise sign

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ii) A type of Tau proteinopathy

iv) Tremors - uncommon

v) Pseudo bulbar involvement (Bilateral corticobulbar +/- Corticospinal involvement)
   - Spastic dysarthria
   - Emotional incontinence

vi) Applause sign - present

vii) Humming bird sign on MRI (Atrophy of mid brain)

retrocolis
Facial dystonia

viii) Frontal Release sign

ix) Humming Bird sign / Penguin sign

*labels of image above*

- Mid Brain - Atrophy of tegmentum

- Cerebellum ) Normal
  - Pons
Corticobasal Ganglionic Degeneration (CBD)

1) A type of Tauopathy
2) Histopathological difference between PSP & CBD

- PSP - tufted astrocyte
- CBD - astrocytic plaques

3) CBD - Parkinson's motor onset with predominant Cortical findings +

- MRI - Cortical atrophy

4) Features in CBD
   - Apraxia, Agnosia
   - Rien limb phenomenon
   - Asymmetrical dystonic contractions
   - Dementia

A
CBD - Cortical atrophy

B
MSA - Putamen Hyperintensity

C
MSA - Hot cross Buns
TREATMENT OF PARKINSON’S DISEASE & HYPERKINETIC DISORDERS

Treatment of Parkinson’s disease (PD)

- Neuroprotective Drugs
  - MAO - B [Mono Amine Oxidase -B] inhibitor
    - Selegiline
  - Glutamate Antagonist
    - Riluzole

- Symptomatic Therapy
  - L-Dopa (Levodopa)

  - Advantage
    - Most symptomatically efficacious drug
    - Virtually all PD patients → improve

  - Disadvantages
    - Dose - dependent adverse effects
      1) Dyskinesia. [Peak dose dyskinesia.] Choreaform, Athetotic, Ballismus
      2) Neuro - psychiatric adverse effects
      3) Acute - Vomiting, nausea
      4) Does not stop disease progression

    - Symptoms that do not improve with L-dopa.
      1) ANS (Automatic Nervous System) symptoms
      2) Postural instability
      3) Falls
      4) Cognitive Impairment

- Wearing off phenomenon
  - Response ↓ at the end of the dose

- On - Off phenomenon
  - Unpredictable fluctuation ⇒ Hyperkinetic movements
    - Dyskinesia - most common [Peak Dose effect] ⇒ "On" phenomenon
- Dystonia (patients not responding to L-dopa) → "Off" phenomenon
- Diphasic dyskinesia (dyskinesia, immobility, dyskinesia)

Pisa syndrome

- [Off period]

a. Dopaminergic Agonists
   - L-dopa sparing effect
   - ↓ motor complications

   **Dopaminergic agonists**

   - Ergot derivatives
     - Pergolide, Bromocriptine
     - Quinagolide
   - Non-ergot derivatives
     - Pramipexole
     - Ropinirole, Rotigotine

**Advantages**
- Efficacious when used as monotherapy / adjunct to L-dopa

**Disadvantages**
- Neuropsychiatric features
  - Hallucination, psychosis
- Efficacy - less (compared to L-dopa)
- Does not completely prevent development of levodopa-related motor complications
- Does not treat all features of PD
- Does not stop disease progression

b. COMT inhibitors
   - Catechol-O-methyl Transferase Inhibitors
   - Inhibits metabolism of dopamine
   - Drugs: 1) Tolcapone → inhibits both central & peripheral COMT
     2) Entacapone → inhibits only peripheral COMT
   - ↓ Levodopa dose requirement by 25%
4. Centrally acting anticholinergics
   - Drug: Trihexyphenidyl
   - Used in drug induced parkinsonism [ parkinsonism tremor ]
   - No effect on rigidity / postural instability
   - Has cognitive side effects

Other drugs used in parkinson's disease

5. Amantadine
   - Advantages
   - Mild anti parkinsonism action
   - Antidyskinetic effects [ Rescue agent ]
   - Disadvantages
   - May develop tolerance
   - Cognitive side effects

Treatment of early parkinson's disease

Patient < 60 yrs
   - Mild symptoms  → Amantadine

Patient > 60 yrs or < 60 years with functional disability
   - Start with dopamine agonist (DA)
   - Add L-Dopa when response is inadequate

Advantages of starting dopamine agonist (DA)
   - DA are associated with 1/3 risk for inducing MFD (motor related
     fluctuations) compared to L-dopa.
   - Comparable anti-parkinsonian effect for initial 2-3 yrs
   - Levodopa added to enhance clinical benefit (when response
     is inadequate)

Abnormal movements & related disorder

1. Chorea.

  Conditions in which chorea is evident:

i) Acute rheumatic fever → Sydenham's chorea
ii) Huntington's chorea
iii) Chorea gravidarum
iv) Metabolic disorders
v) Autoimmune disorders
vi) Behçet's disease
vii) Encephalitis → anti NMDA
viii) Nig-

- An involuntary, irregular, non-rhythmic quasi-purposive hyperkinesia
- Abrupt, brief, rapid, jerky & unsustained movement
- Distal > proximal
- Cause: lesion of caudate nucleus

a. Huntington's Disease
   - Autosomal Dominant
   - Chromosome 4 defect
   - Trinucleotide repeat [CAG repeats]
   - Age ~ 25 - 45 yrs
   - Typically characterised by anticipation of disease
   - High penetration
   - Components: mental + motor: [basal ganglia component]
     ↓
     Behaviour & cognitive impairment: choreiform movement
     ↓
     Dementia, myoclonus, dystonia, bradykinesia.
   - Cause: atrophy of striatum, predominantly caudate nucleus
   - Westphal variant
     * Seen in young patients with Huntington's disease
     * Known as akinetic rigid syndrome
   - Intrastriatal GABAergic & cholinergic neuron → degenerates
   - No cure
   - Tetraabenazine (may have some effect)

![Box-car ventricle sign](image)

Caudate nucleus → partially atrophied
Frontal horns → enlarged

Medicine v2.0 Marrow 4.0 2020
Dystonia, athetosis, hemiballismus

3. Dystonia
   Types of neck dystonia
   - Torticollis
   - Laterocollis
   - Retrocollis
   - Antecollis

   A type of hyperkinesia.
   - Spontaneous, involuntary & sustained muscle contraction that forces the affected part of the body into abnormal movements / posture

   - Types of dystonia: Cervical
     - Orofacial
     - Somatoform
     - Spasmodic
     - Epileptic

4. Athetosis
   - Unilateral, slow, involuntary, rhythmic writhing movements
   - More sustained & larger amplitude than chorea
   - Cause: Lesion in putamen

   Pseudoathetosis
   - Sensory ataxia
   - Posterior column involvement

5. Hemiballismus
   - Wild, writhing movements
   - Cause: Lesion in the contralateral subthalamic nucleus

   Note:
   - Brain pacemaker
     - Hemiballismus
     - Transcranial deep brain stimulation
     - Stimulation of subthalamic (or) Globus pallidus interna
     - Very good impact on PD
SPINAL CORD - ANATOMY

Spinal Cord - Introduction

- Elongated cylindrical structure
- Extends from upper border of atlas to lower border of L1 (or)
  - Junction between L1-L2 - adults
  - Junction between L3-L4 - Children
- Continues above with medulla oblongata
- Foramen magnum to lower border of L1
- 31 Segmental vertebrae
- Vertebral canal - 70 cm long
- Spinal cord - 45 cm long
- Conus medullaris - S5, S4, S3, Coccygeal
- Filum terminale - Extends from tip of conus medullaris to dorsum of 1st coccygeal vertebrae

Vertebrae - Cervical - 7
  Thoracic - 12
  Lumbar - 5
  Sacral - 5
  Coccygeal - 4

Spinal nerves / spinal segments - Cervical - 8
  Thoracic - 12
  Lumbar - 5
  Sacral - 5
  Coccygeal - 1

Spinal Cord - Cross Sectional Anatomy

1. White matter of spinal cord
   - Fibres are called funiculus / tracts
   - Dorsal, ventral, lateral funiculi

2. Grey matter of spinal cord
   - Motor neurons

3. Spinal nerve root
- Sensory nerve enters spinal cord
- Motor nerve leaves the spinal cord
- Spinal nerve root is formed by sensory nerve & motor nerve

Relation of spinal nerve roots to vertebrae

- Spinal cord ends at lower border of L
- Spinal nerve roots do not emerge in correspondence to vertebrae
  - T1-vertebrae → L1, Spinal nerve root emerges
  - T2-vertebrae → L2, L3 nerve root
  - T1-vertebrae → L4, L5 nerve root

L1 vertebra.

- Epiconus → s1, s2 nerve roots
- Conus medullaris → s3, s4, s5, c1 nerve roots.

<table>
<thead>
<tr>
<th>Spinal Cord Level</th>
<th>Corresponding Vertebra Body</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper cervical</td>
<td>Same as cord level</td>
</tr>
<tr>
<td>Lower cervical</td>
<td>1 level higher</td>
</tr>
<tr>
<td>Upper thoracic</td>
<td>2 levels higher</td>
</tr>
<tr>
<td>Lower thoracic</td>
<td>2 to 3 levels higher</td>
</tr>
<tr>
<td>Lumbar</td>
<td>T1-T12</td>
</tr>
<tr>
<td>Sacral</td>
<td>T2-L1</td>
</tr>
</tbody>
</table>
Conus medullaris, cauda equina, filum terminale

- **Conus medullaris**
  - Conical structure, continuous with filum terminale

- **Cauda Equina**
  - Sheath of nerve root from lumbar & caudal segments in subarachnoid space enlargement
  - Horse tail appearance

- **Filum terminale**
  - 20 cm long
  - Below the level of conus medullaris only pia mater is continued as a fibrous cord, extending to dorsum of C7 (coccygeal) segment.

- **Cauda Equina [L1 - C, nerve roots]**
  - Lumbar enlargement
  - Epiconus
  - Conus
  - Pia mater continues till tip of coccyx (Filum terminale)

- **Cervical enlargement [C3 - T1 vertebrae]**
- **Lumbar enlargement [L1 - S3 vertebrae]**

- **Spinal enlargements**

- **Active space**
  - Conus medullaris
  - Dura mater and arachnoid mater
  - Filum terminale
  - Root prominence
  - Lower level of subarachnoid space
  - Conus medullaris
  - Sclera

- **Medicine v2.0 * Marrow 4.0 * 2020**
Spinal cord - general internal organisation

a. Spinal Cord - Embryology
   • Spinal cord arises from
     - Caudal part of neural tube in the 4th week of embryonic life
   • Spinal cord wall forms
     - 3 layers: ependymal mantie marginal

b. Grey matter & white matter of spinal cord
   i) Grey matter of spinal cord
      • Fibres ➔ Columns / tracts
      • Has AHC (anterior horn cell)
        ↓
        - Medial group ➔ Supplies axial muscles
        - Lateral group ➔ Supplies limb muscles
   ii) Lesions
      - lesions up to AHC ➔ UMN (upper motor neuron)
      - lesions from AHC ➔ LMN (lower motor neuron)

   • Extra-Pyramidal ➔ AHC ➔ Pyramidal
     - Tecto spinal
     - Rubrospinal
     - Reticulospinal
     - Vestibulo Spinal tract

   • (CBT) Cortico Bulbar Tract ➔ Bulbar nuclei in brain stem

   Lesion of the above tracts ➔ UMN lesion

   • Lesion at 1 below AHC ➔ LMN lesion
   • Grey matter
     - Central column
     - H-Shaped lateral mass connected by grey commissure
     - Anterior, posterior 1 lateral columns
1) White matter of spinal cord

Tracts

- Dorsal
- Lateral column
- Ventral column

Dorsal
- Dorsal / Posterior Column pathway
- Lateral (CST)
- Rubro spinal
- Reticulo spinal
- Lateral spino thalamic
- Spinocerebellar
- Ventral
- Spinothalamic

Sensory
- Motor
- Extra-pyramidal system (EPS)
- Cerebellar

- Posterior column (Lateral CST)
- Spinothalamic

Posterior column
- Lateral column
- Rubrospinal
- Reticulospinal

Lateral
- Ventral column
- Tectospinal
- Vestibulospinal

Distal limb movements
- Axial and proximal limb movements

Medicine v2.0 - Marrow 4.0 - 2020
- **EPS**
  - Tectospinal
  - Vestibulospinal

**Tracts**

- **Anterior**
  - Ascending
    - Anterior corticospinal
    - Spinothalamic
  - Descending
    - Vestibulospinal
    - Tectospinal

- **Posterior**
  - Ascending
    - Lateral CST
    - Spinocerebellar
  - Descending
    - Rubrospinal (Anterior)
    - (Anterior)

- **Lateral**
  - Ascending
    - Olivospinal (lateral reticulospinal)
    - Reticulospinal (ventral)
    - Ascending Tracts
      - Fasciculus gracilis
      - Fasciculus cuneatus
  - Descending
    - Lateral
    - Spinthalamic
    - Spinothalamic
    - Spinoreticular
    - Spino-olivary
Ascending tracts in posterior column pathway

- Dorsal / Posterior column / medial lemniscal pathway
- Sensory
- Responsible for:
  - Fine touch
  - Vibration
  - Proprioception
- Tracts:
  - Fasciculus gracilis (medial)
  - Fasciculus cuneatus (lateral)

Sensory cortex

Hemicorpectomy = Loss of posterior column sensations of the same side
Spino Thalamic Tract

- Spinothalamic Tract
  - Ventral
  - Lateral
  - Crude touch
  - Pain
  - Pressure
  - Temperature
  - Spinothalamic Tract goes Lateral > Ventral

Lateral spinothalamic Tract

Crosses over at the level of spinal cord

Representation of fibres

- Cervical (medial)
- Sacral (Lateral)

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Cortico Spinal Tract

Pathway:
- Pyramidal system (EPS)
- Extrapyramidal system
- Lateral corticospinal
- Initiation of voluntary movements
- Lesions produce weakness

Hemiconduction:
- Loss of lateral CST sensation of same side
- Loss of lateral spinothalamic tract sensation of opposite side

EPS Tracts:
- Vestibulospinal: Posture
- Tectospinal: Head and neck movements (vision, auditory sense)
- Reticulospinal: Proximal upper limb movements
- Rubrospinal: Rudimentary in humans

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Spinal Cord - Blood Supply

1. Anterior spinal artery
   - Supplies ventral 2/3 of spinal cord. (Anterior & Lateral columns)
   - 1 in number

2. Posterior spinal artery
   - Supplies dorsal 1/3 of spinal cord. (Posterior Column)
   - 2 in number

3. Radicular arteries
   - Upper half of cervical cord → no radicular arteries
   - Lower cervical & first 3 thoracic → 4 radicular arteries
   - Mid thoracic → 1 radicular artery
   - Arterial radicularis magna → major blood supply to the lower 2/3 (Lower thoracic to Coccygeal)
   - Known as artery of Adamkiewicz
Syndromes of spinal cord

1. Anterior spinal artery syndrome

Area of cord damage

Loss of motor power, pain, and temperature, with preservation of position, vibration, and touch sense

Anterior cord syndrome

- Also known as anterior cord syndrome
- Most common cause: Trauma.
- Loss → anterior 2/3" of spinal cord
- Preserved → posterior 1/3"
- Preserved sensations → Fine touch, Proprioception, Vibration
- Loss of CST, Spinthalamic tract below the level of lesion
- Loss of autonomic nervous system

2. Posterior spinal artery syndrome

Area of cord damage

Loss of position, vibration and touch sense. Preservation of motor power, pain and temperature

Posterior cord syndrome

Cord damage and associated motor and sensory loss.

- Most common cause: Trauma (Hyper-extension force)
- Loss → Posterior column fibres
- All the other fibres are preserved

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3. Brown - Sequard Syndrome

Hemisection of the cord
- Same side as lesion
  - UMN weakness
  - Loss of position & vibration
- Opposite side of lesion
  - Loss of pain & temperature

4. Central cord syndrome

- Intramedullary lesion
- Dissociative sensory loss → involvement of spinothalamic with posterior column sparing
  - Of corticospinal tract → very late, sacral sparing
MYELOPATHY APPROACH: COMPRESSIVE

- Paraplegia → lesion below the level of T10
- Quadriplegia → lesion above the level of T10

Level of lesion

- with respect to spinal nerve root
- Level: sensory, motor, spinal level, reflex
- Clinical manifestations based on level of lesion
  i) Below the level of lesion
     a) UMN (upper motor neuron) weakness, exaggerated reflex (hyperreflexia)
     b) Complete sensory loss
  ii) Above the level of lesion
     Complete sparing
  iii) At the level of lesion
     a) Sensory component – Root pain/ dyesthesia/ paresthesia.
     b) Motor component – LMM (lower motor neuron) weakness
     c) Reflex component – lost

- Anatomical marking for spinal Nerves
  T1 → Nipple
  T5 → Xiphisternum
  T10 → Umbilicus

- Foramen magnum → Around the clock weakness (or) Esberg phenomenon (left upper limb → left lower limb → Right lower limb → Right upper limb weakness)

- Paraplegia → Below T10
- Beevor's sign
  - To evaluate if paraplegia is below T10 or above T10
  - Abdominal reflex
    - Preserved → lesion below T10
    - Absent → lesion above T10
  - on flexion of neck + contraction of abdominal muscles
    - If umbilicus moves 2-3cm upward → T10 pathology
    - [Reason: loss of tone lower than T10]
      i.e., Upper abdominal reflex + preserved
      Lower abdominal reflex → lost → Beevor's positive
- Superficial reflexes
  - Abdominal reflex (T12-T10)
  - Cremasteric (L1)
  - Plantar (L5-S1)

i) All the above reflexes present → lesion is above T12 (or) (T11-T10)

ii) Upper Abdominal reflex - present → lesion is below T11
    Lower Abdominal reflex - absent → lesion is around T11
    Cremasteric reflex - lost
    Plantar - extensor

iii) Abdominal reflex (Upper or Lower) - present
     Cremasteric Reflex - Lost
     Lesion is between T11-T12

Spinal Nerve Root
- C5, C6 → biceps, supinator
- C7 → triceps
- C8, T1 → finger flexion
- L1 → hip flexion
- L2-L4 → knee extension
- L5, S1 → ankle dorsiflexion, hip extension
- S2 → plantar flexion

Reflexes
- L4 → knee jerk
- S1 → ankle jerk

Myelopathies - classification

```
myelopathy
    Non - compressive
      Cause - Infection
        Inflammation
          Nutritional
        Extramedullary
        Intramedullary
          Tumors
          i) Acute transverse myelitis
          ii) Medulloblastoma
          iii) Ependymoma
          iv) Oligodendroglioma
          Disease
          i) Vitamin B12 deficiency
          Disease
          Syringomyelia

Extradural

Intradural
```

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### Difference between extra medullary & intra medullary

<table>
<thead>
<tr>
<th>Extra - Medullary lesions</th>
<th>Intra - Medullary lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Manifestations</strong></td>
<td></td>
</tr>
<tr>
<td>Stages 1 - Root Pain / Girdle pain</td>
<td></td>
</tr>
<tr>
<td>- along the distribution of the root.</td>
<td></td>
</tr>
<tr>
<td>- pain aggravates by coughing.</td>
<td></td>
</tr>
<tr>
<td>Stages 2 - Brown sequard syndrome</td>
<td></td>
</tr>
<tr>
<td>Stages 3 - Complete cord transection</td>
<td></td>
</tr>
<tr>
<td>Extramedullary</td>
<td>Intramedullary</td>
</tr>
<tr>
<td>2. Motor involvement → early</td>
<td>a. Motor involvement → late, sacral sparing</td>
</tr>
<tr>
<td>3. Dissociative sensory loss</td>
<td></td>
</tr>
<tr>
<td>- Spinothalamic → lost</td>
<td></td>
</tr>
<tr>
<td>- Posterior column → spared</td>
<td></td>
</tr>
<tr>
<td>- ie pain, temperature, touch, pressure, foot</td>
<td></td>
</tr>
<tr>
<td>4. ANS [Autonomic Nervous system]</td>
<td></td>
</tr>
<tr>
<td>- Early onset</td>
<td></td>
</tr>
<tr>
<td>- Predominantly bowel &amp; bladder affected</td>
<td></td>
</tr>
<tr>
<td>5. AHC [Anterior horn cell]</td>
<td></td>
</tr>
<tr>
<td>- Wasting, Fasciculations, atrophy</td>
<td></td>
</tr>
<tr>
<td>LMN - due to cord involvement</td>
<td></td>
</tr>
<tr>
<td>LMN - due to AHC involvement</td>
<td></td>
</tr>
<tr>
<td>6. Trophic changes</td>
<td></td>
</tr>
<tr>
<td>- Very common</td>
<td></td>
</tr>
<tr>
<td>- Due to loss of pain</td>
<td></td>
</tr>
<tr>
<td>5. Trophic Changes</td>
<td></td>
</tr>
<tr>
<td>- May occur</td>
<td></td>
</tr>
<tr>
<td>CLINICAL FEATURE</td>
<td>INTRAMEDULLARY</td>
</tr>
<tr>
<td>-----------------------</td>
<td>----------------</td>
</tr>
<tr>
<td>ROOT PAIN</td>
<td></td>
</tr>
<tr>
<td>DISASSOCIATED</td>
<td></td>
</tr>
<tr>
<td>SENSORY LOSS</td>
<td>* * * *</td>
</tr>
<tr>
<td>BACRAL SPARING</td>
<td>* * * * * *</td>
</tr>
<tr>
<td>TROPHIC CHANGES</td>
<td>* * * * * *</td>
</tr>
<tr>
<td>PYRAMIDAL SIGNS</td>
<td>LATE</td>
</tr>
<tr>
<td>LUM SIGNS</td>
<td>++</td>
</tr>
<tr>
<td>BOWEL/BLADDER</td>
<td>++</td>
</tr>
<tr>
<td>SPINAL DEFORMITY</td>
<td></td>
</tr>
<tr>
<td>SPINAL TENDERNES</td>
<td></td>
</tr>
<tr>
<td>CSF PROTIENS</td>
<td></td>
</tr>
</tbody>
</table>

Conus Medullaris Vs Cauda Equina syndrome

<table>
<thead>
<tr>
<th>Corneus Medullaris</th>
<th>Cauda equina</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Lesion → S₃, S₄, S₅, C₆</td>
<td>* Lesion → L₁, → C₆ (root fibres)</td>
</tr>
<tr>
<td>* Bilateral (B/L)</td>
<td>* Unilateral (U/L)</td>
</tr>
<tr>
<td>* Acute onset</td>
<td>* Gradual process</td>
</tr>
<tr>
<td>* Bowel &amp; Bladder → Affected</td>
<td>* Asymmetrical</td>
</tr>
<tr>
<td>* Root pain☑</td>
<td>* Bowel &amp; Bladder → Not affected</td>
</tr>
<tr>
<td>* Weakness☑</td>
<td>* Root pain ☑</td>
</tr>
<tr>
<td>* Dissociative sensory loss☑</td>
<td>* U/L motor weakness</td>
</tr>
<tr>
<td>* Reflex</td>
<td>* Dissociative sensory loss☑</td>
</tr>
<tr>
<td>- Bulbocavernous</td>
<td>* Reflex</td>
</tr>
<tr>
<td>- Anal</td>
<td>- Any Reflex can be lost</td>
</tr>
<tr>
<td>* B/L saddle anaesthesia</td>
<td>* U/L - any pattern of anaesthesia can occur</td>
</tr>
</tbody>
</table>
Syringomyelia

- Caudal expansion of central canal of spinal cord (especially lower cervical)
- Congenital > Acquired
- Associated with Arnold-Chiari type I [75% cases]
- Like intramedullary lesion [dissociative sensory loss]
- Involves spinothalamic tract [initially L/T, later B/L]
- Syringomyelia > reaching medulla is syringobulbia
- Seen in males > females
- Half - cage distribution of sensory loss
  [Loss of pain / sensory loss along chest, upper arm, shoulder]
- Onion peel pattern on face [loss of sensation of face]
- Compression of ventral horn cells → wasting of Thenar eminence
  - Forearm
  - Arm

- Spastic weakness
- Horner's syndrome
  [due to C8, T1 involvement]
- Kyphoscoliosis, Pes Cavus, Spina Bifida
MYELOPATHY APPROACH - NON-COMPRESSIVE

Acute transverse myelitis

- Inflammation of full thickness of spinal cord
  - MRI changes & CSF changes

- Causes
  1. Post infectious (Post - viral)
  2. Post vaccination
  3. Demyelination
    - Multiple sclerosis
    - Neuromyelitis optica

- Components - 3

  - Sensory
    1. Definite sensory level
    2. Loss of sensation below the definite level
    3. Band-like sensation
    4. Predominant sensory ataxia

  - Motor
    1. Weakness
    2. Evolve from (4 hours - 4 days)
    3. Usually bilateral
    4. May be asymmetrical
    5. UMN spastic weakness
    6. ↑ tone
    7. Legs > Arms
    8. Reflex - brisk
    9. Babinski sign - (+)

  - Autonomic Nervous System (ANS)
    1. Bladder symptoms
      - Severe
      - Incontinence / retention

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### Transverse Myelitis vs Guillain–Barre Syndrome (GBS)

<table>
<thead>
<tr>
<th>Acute Transverse Myelitis</th>
<th>GBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Lower limb &gt; upper limb</td>
<td>1. Progressive lower limb weakness [proximal &gt; distal]</td>
</tr>
<tr>
<td>2. Symmetrical weakness</td>
<td>2. Ascends to upper limbs &amp; facial weakness</td>
</tr>
<tr>
<td>3. Hyper-reflexia (below the lesion)</td>
<td>3. Areflexia</td>
</tr>
<tr>
<td>4. Sensory ataxia</td>
<td>4. Normal sensory examination</td>
</tr>
<tr>
<td>5. Bladder symptoms</td>
<td>5. No bladder symptoms</td>
</tr>
<tr>
<td>7. Definite sensory level</td>
<td>7. No level for sensory loss</td>
</tr>
</tbody>
</table>

MRI in Acute Transverse Myelitis

![MRI - Gadolinium enhancement](image)

Diagnostic criteria for Transverse Myelitis

**DIAGNOSTIC CRITERIA FOR TRANSVERSE MYELITIS**

1. Bilateral (not necessarily symmetric) sensorimotor and autonomic spinal cord dysfunction
2. Clearly defined sensory level
3. Progression to nadir of clinical deficits between 4 hours and 21 days after symptom onset
4. Demonstration of spinal cord inflammation:
   1. Cerebrospinal fluid pleocytosis or
   2. Elevated IgG index, or
   3. MRI revealing a gadolinium-enhancing cord lesion
5. Exclusion of compressive, postradiation, neoplastic, and vascular causes

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Treatment
1. Steroids → high dose
   Good Response
2. Plasmapheresis
   In patients unresponsive to steroids

Friedreich Ataxia (FA)

- Autosomal recessive (more common)
  - early onset
- Autosomal dominant
  - late onset
- Males > Females
- Frataxin gene on chromosome 9
- Structures involved
  1. DRA (Dorsal Root Ganglia) → sensory ataxia, loss of reflex
  2. Spinal cord → CST (Corticospinal Track) → spinocerebellar involvement
     - Posterior column
  3. Peripheral nerves → demyelination
- Associated with myocardial fibrosis (90% cases)
- Cerebellar findings
  - Dysarthric speech
  - Horizontal nystagmus
  - Sphincters unaffected
  - Lower limb reflexes with extensor → absent
  - Plantar response → present
  - Ataxic gait
  - Romberg's sign → positive

- Non-neurological findings
  - Myocardial fibrosis
  - Optic atrophy
  - Pes cavus
  - Kyphoscoliosis
  - Hammer toe
  - Diabetes mellitus
  - Cardiomyopathy
Friedreich’s Ataxia - Cerebellar anatomy - normal but;
- Spinocerebellar tracts involved
Ataxia, Telangiectasia - Cerebellar atrophy seen

### Sub Acute Combined Degeneration [ SACD ]

<table>
<thead>
<tr>
<th>FA</th>
<th>SACD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Tracts</td>
<td>DRG $\rightarrow$ Spinal cord $\rightarrow$ Spinal cord&lt;br&gt;Peripheral nerves $\rightarrow$&lt;br&gt;Posterior column $\rightarrow$ CST $\rightarrow$&lt;br&gt;Peripheral nerve</td>
</tr>
<tr>
<td>2. Reflex</td>
<td>Areflexia in lower limb $\rightarrow$ lost late due to peripheral neuropathy</td>
</tr>
<tr>
<td>3.</td>
<td>Sensory Ataxia $\rightarrow$ loss of vibration sense, tingling &amp; numbness</td>
</tr>
<tr>
<td>4. Weakness</td>
<td>UMN weakness $\rightarrow$ UMN weakness</td>
</tr>
<tr>
<td>5. Associated</td>
<td>Cardiomyopathy / skeletal / optic atrophy $\rightarrow$ Vitamin B$_6$ deficiency</td>
</tr>
</tbody>
</table>

**Note**

SACD
- UMN lesion cannot cause brisk reflex as they are already damaged by peripheral nerve lesion

**Associated Findings**
- B/L optic neuropathy
- CNS changes: dementia
- Urinary retention
Tabes dorsalis

i) Structures involved -
   DRG followed by spinal root

ii) Features:
   DRG → Areflexia, Sensory ataxia
   Spinal root → Severe root pain [due to posterior root lesion],
   Loss of sensation, muscle

iii) Only LMM weakness

iv) Seen 15-20 yrs after syphilis infection

v) Bladder involvement

vi) Argyll Robertson pupil

vii) Posterior column - lost (due to DRG involvement)

viii) Extensor plantar - Absent
ACUTE BACTERIAL MENINGITIS

Definition: Acute purulent infection in the subarachnoid space
Bacterial meningitis - Only acute
- Pt. presents within 24 hours of onset of symptoms
- 80% cases: CSF Culture positive and organism can be isolated.
- CSF acts as a culture medium for the organism to grow.

Organisms causing acute bacterial meningitis:
- Most common organism in adults
  - Streptococcus Pneumoniae
- Neisseria meningitidis
- Group B Streptococci
- Listeria monocytogenes
- H. influenzae type B

<table>
<thead>
<tr>
<th>PATIENT GROUP</th>
<th>BACTERIAL PATHOGEN</th>
<th>RECOMMENDED EMPirical therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE &lt; 1 MONTH</td>
<td>ENTEROBACTERIACEAS, TREP AGALACTIAE AND LISTERIA</td>
<td>AMPICILLIN + 3rd GEN CEPHALOSPORIN</td>
</tr>
<tr>
<td>1-23 MONTHS</td>
<td>S. AGALACTIAE, E. COLI, H. INFLUENZA, STREP, PNEUMONIA, N. MENINGITIS DIS</td>
<td>AS ABOVE PLUS VANCOMYCIN IF PRSP SUSPECTED</td>
</tr>
<tr>
<td>2-50 YRS</td>
<td>STREP, PNEUMONIA, N. M. MENINGITIS DIS</td>
<td>3rd GEN CEPHALOSPORIN PLUS VANCOMYCIN</td>
</tr>
<tr>
<td>&gt; 50 YRS</td>
<td>S. PNEUMONIA, N. MENINGITIS DIS, L. MONOCYTONEGENES, N. MENINGITIS DIS, P. AERUGINOSA</td>
<td>ABOVE PLUS AMPLICILLIN</td>
</tr>
<tr>
<td>IMMUNOCOMPROMISED</td>
<td>S. PNEUMONIA, L. MONOCYTONEGENES, N. MENINGITIS DIS</td>
<td>CEFTAZIDIME + AMP + VANCO</td>
</tr>
<tr>
<td>Post cranio/orbital trauma, CSF rhinorhea</td>
<td>GNB</td>
<td>CEFTAZIDIME + VANCO</td>
</tr>
<tr>
<td>POST shunting or cmmay reflux</td>
<td>S. AUREUS, CONS</td>
<td>SAME AS ABOVE</td>
</tr>
</tbody>
</table>

- 2 - 50 years - Streptococcus pneumoniae - most common
  - Neisseria meningitidis
  - Group B Streptococci
  - H. influenzae
  - Listeria monocytogenes
    - in immunocompromised (↓ in cell mediated immunity)
    - pregnancy

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> 50 years - Listeria is more common than H.influenza, but Strep. pneumoniae is most common.
> In post shunting or Ommaya Reservoir (Intrathecal chemotherapy)
> - meningitis is caused by - Staph aureus > CONS.
> Post craniotomy meningitis
> (or)
> CSF rhinorrhea meningitis
> (or)
> Head injury associated meningitis
> In < 1 month - E.coli > Strep. agalactiae
> 1 month - 2 years - Strep. agalactiae

Pathophysiology of acute bacterial meningitis

nasopharyngeal colonisation and intravascular extension of meningococci and pneumococci
↓
not phagocytosed due to polysaccharide capsule
↓
Reach choroid plexus epithelial cells
↓
Gain access to CSF
↓
Organism multiplies and release its Products
↓
severe inflammatory response against bacterial products
↓
mediated by IL-1β, TNF-α
↓
It is combination of interstitial, Cytotoxic and vasogenic edema.
↓
- Cerebral edema ⇒ ↑ intra Cranial Pressure and herniation
- Alteration in Cerebral blood flow
- Ischaemia

Cerebral edema
↓
Vasogenic edema
↓
Cytotoxic edema
↓
Interstitial edema
↓
Due to altered BBB
permeability

Cytokines by leukocytes due to Edudate in the subarachnoid space
↓
Reactive Oxygen species
↓
Cell injury
↓
Hydrocephalus

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Meningococcus

- Gram negative cocccus
- Catalase +ve
- Oxidase +ve
- Diplococci - half moon shaped
  - it has capsular polysaccharide
- Ferments Glucose and maltose - used to differentiate it from gonococci
- Strict aerobic organisms
- Culture medium: Modified Thayer Martin medium
- Group A - Epidemics
  - B - Epidemics and outbreaks
  - C - Outbreaks
  - W- 135 / Y - Sporadic cases
- Most common - Group B - in India.
- No plasmid, no drug resistance

In media - polyethanol sulfatate - can augment the growth of the organism
- It colonises with the help of Pili (Fimbriae), Opacity associated protein
- LPS = Lipopolysaccharide endotoxin → Endothelial injury
  \[ \text{massive capillary leak} \]
  \[ \text{Severe Hypotension} \]
- In blood - oponosised by C5b - C9
  - C5 - C9 deficiency → increased risk of meningococcal infection
- Uniformly susceptible to Penicillin
- Drug of choice: Cephalosporins
- If Penicillin allergy → Drug of choice: Chloramphenicol
- Carrier State: Cephalosporins, Rifampicin, Ciprofloxacin - in 20%
- Most common mode of spread - Nasopharynx - across the epithelial cells in membrane bound vacuole
- Classical clinical finding: Purpuric rash
  - Capillary leak → shock
  - Adrenal Hemorrhage - Waterhouse Friderichsen Syndrome
- Increased risk of infection in C5 - C9 deficiency
  - Hypogammaglobulinemia, hypoponplasmia

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Pneumococci

- Gram positive, α - hemolytic
- Catalase Negative, Pasteurian
- Flame or lanceolate shaped
- Greenish coloured on Blood agar due to partial Hemolysis - draughtsman colony
- Bile soluble, Optochin susceptible, Inulin fermentors - used to differentiate it from strep pneumonia and viridans.
- Antigens: Capsular polysaccharide, Penumolysin, IgA I protease.
- Abnormal protein which precipitates with somatic 'C' antigen of Pneumococci - C - Reactive Protein.
- Rapid identification: Quelungs reaction.
- Adherence to Nasopharynx, Invasion is seen Only with Serotype 3.
- Penumolysin - is a Cytolytic toxin which forms pores in the cell membrane.
- Risk Factors: >65 yrs. Age
  - Sickle cell Anemia.
  - Celiac disease
  - HIV
  - DM
  - Cochlear implant
  - CSF leak - E-ve organisms

Non infectious causes of meningitis:
1. Drug Induced
2. Autoimmune: SLE
3. Chemical meningitis: Due to tumor cells infiltrating into Subarachnoid Space
   - Seen with Craniopharyngioma, Dermoid cyst.
4. Post traumatic meningitis

Causes of aseptic meningitis:
- Most common cause: Virus - Enterovirus Type 71
- HIV
- Listeria
- Drugs
- Partially treated meningitis.

Clinical features & diagnosis of meningitis

- Classical triad: Fever + Neck stiffness + Altered Sensorium
  [Lethargy, Drowsiness]
- Most common symptom: Head ache
Bacterial Meningitis

Bedside tests:
1. Kernig's sign: Pain when the leg is extended from flexed position.

- Involuntary flexion of Hip and Knee.
- Done in supine position.
- No lymphadenopathy.
- Cerebral infarction at presentation - Pneumococci.
- Petechiae, Purpura, concurrent arthritis - N. meningitidis.
- Seizure with Ataxia.

Cranial nerve palsy

Meningitis

↑ Intracranial tension [ICT]

Surest sign: Papilledema - Fundus examination.

- If no papilledema.
- No neurological deficit.
- Maintained consciousness.
- No signs of increased ICT.

Definitive diagnosis: Lumbar Puncture

Start Antibiotics

Imaging needed before lumbar puncture:
- Focal neurological signs.
- Immuno-compromised adults.
- Papilledema.
- Recent onset seizures.
- Impaired consciousness.
- Hypertension and bradycardia.

Normal values of CSF in adults:

- Colourless.
- Specific gravity: 1.006 - 1.008.
- Opening pressure: 50 - 180 mm H₂O.
- Proteins: 20 - 45 mg/dL.
- Sugar: 2/3 of blood sugar = 40 - 70 mg/dl
  - CSF
  - S. glucose = 0.4
- Cellularity: < 5 wBCs
- pH: 7.28 - 7.3a
- Chloride: 115 - 120 mg/dL
- LDH: 10% of Serum levels.

**Normal**

<table>
<thead>
<tr>
<th>Pressure</th>
<th>50-150 mm H₂O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>Colourless</td>
</tr>
<tr>
<td>Proteins</td>
<td>20 - 45 mg/dl</td>
</tr>
<tr>
<td>Sugars</td>
<td>CSF = 0.4 s. glucose = 0.4</td>
</tr>
<tr>
<td>Cellularity</td>
<td>Normal (upto 5 wBC's)</td>
</tr>
</tbody>
</table>

**Acute bacterial meningitis**

<table>
<thead>
<tr>
<th>Pressure</th>
<th>↑ ↑ ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>In severe cases</td>
<td>&gt;400mm of H₂O</td>
</tr>
<tr>
<td>Colour</td>
<td>Cloudy</td>
</tr>
<tr>
<td>Proteins</td>
<td>&gt; 100 mg/dl</td>
</tr>
<tr>
<td>Sugars</td>
<td>S. glucose &lt; 0.4</td>
</tr>
<tr>
<td>Cellularity</td>
<td>High</td>
</tr>
<tr>
<td>Predominant cells</td>
<td>Neutrophils</td>
</tr>
</tbody>
</table>

**Investigation to detect the organism:**
- Previously: Latex agglutination test
- Now: CSF - PCR
- CSF - lactate: ↑ ↑ in bacterial meningitis.
- CSF - Procalcitonin: ↑ ↑ in bacterial meningitis.
- Limulus lysate test: Gram -Ve Organisms

**Treatment of Acute bacterial meningitis**

- Immunocompetent Adult (<50y):
  - meningococci
  - Pneumococci
- Empirical therapy: Inj. Ceftriaxone 2gm IV BD + Vancomycin, 1gm IV BD
- Adult (>50y):
  - Listeria is also common - Intrinsically resistant to Cephalosporin.
  - Empirical therapy: Inj. Ceftriaxone 2gm IV BD + Vancomycin 1gm IV BD + Ampicillin (for Listeria)

**Monitoring:**
- Check for ↑ IOT and impending on herniation; check for pupillary reaction ↓
- Hutchinson's pupil
- Monitor S, Na - for SIDH
- Severe listeriosis: Ampicillin + Gentamicin
- DOC: Ceftriaxone + Vancomycin
Pneumococcal meningitis:
- Follows nasopharyngeal colonisation.
- Focus of infection elsewhere.
- Most severe form of meningitis can cause ischaemia.
- Complications: Aphasia and Cranial neuropathy.
- High CSF opening pressure.
- Steroids in Pneumococcus:
  - Steroids are added in bacterial meningitis.
  - Steroid of choice: Dexamethasone, 3-5 days, 0.15 mg/kg Q6H.
    (15-20 mins before the Antibiotics).

Meningococcal Meningitis:
- Septicemia, DIC, shock, Adrenal Hemorrhage, Arthritis.
- Rash - Non blanching.
- Classical triad: less common.
- Gram negative diplococci.
- Better Prognosis.

Listeria monocytogenes:
- Gram positive bacillus.
- Slow tumbling motility at 25°C.
- Growth at 4°C.
- Food poisoning: Soft cheese, Hot dogs, Milk and Salads.
- Defect in CMI is mandatory.
- Organism cannot be cultured.
- Rhombencephalitis: Ataxia.
  - Myoclonic seizures.
  - Cranial nerve palsy.
- Intrinsically resistant to Cephalosporin.
- Ampicillin + Gentamycin - Treatment.
- Penicillin Allergy: Cotrimoxazole.
- Lymphocytic pleocytosis.
TUBERCULAR MENINGITIS

Classification of CNS - tuberculosis:

- Classification of CNS TB
  - Intracranial
    - Tuberculous meningitis
    - Tuberculous encephalopathy
    - Tuberculous vasculopathy
    - Space Occupying Lesions
      - Tuberculoma
      - Tuberculous abscess
  - Spinal
    - Pott's spine and Pott's paraplegia
    - Tuberculous arachnoiditis
    - Non-osseous spinal tuberculoma
    - Spinal meningitis

CNS TB - Secondary tuberculosis

Pathogenesis of tubercular meningitis:

- In secondary tuberculosis - 5% have
- In 1% rupture of Subependymal tubercles into Subarachnoid space
- Inflammatory changes at the base of brain
- Proliferative basal arachnoiditis
  - Exudate → Fibrous mass
  - Enbrace cranial nerves blocks CSF → Penetrate vessels
  - Vessels involved: Small perforating vessels
    - Necrotising arteritis
    - Ischaemic infarcts
    - Cranial nerve involvement

Diagnostic triad of tubercular meningitis:

1) Presence of basal exudates
2) Infarcts
3) Hydrocephalus
   - Specificity: 100%
   - Lower Sensitivity
* Most common manifestation of CNS TB in all age groups.

* Meningeal enhancement has been found in up to 90% of cases and is considered to be the most sensitive feature of tubercular meningitis.

Axial T1C - florid meningeal enhancement, most pronounced within the basal cisterns

CECT - acute hydrocephalus and meningeal enhancement.

* Meningeal enhancement - On non-contrast imaging

* Differential diagnosis:
  - Mass lesion
  - CNS tuberculoma
  - Neurocysticercosis

Clinical features of T.B. Meningitis:

* Subacute presentation → 2-8 weeks
* It has 3 phases:
  i. Prodromal phase:
  - Low grade fever for 2-3 weeks
  - General malaise, headache
  - Altered behaviour pattern, ↑ ISE

  ii. Meningitis phase:
  - Severe headache and signs of meningeal irritation
  - Vomiting

  iii. Paralytic phase:
  - Altered consciousness/Stupor/Coma.
### Cerebrospinal Fluid (CSF) Findings in TB Meningitis

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Bacterial</th>
<th>T.B</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF pressure</td>
<td>150-450 mm H₂O</td>
<td>&gt; 400 mm H₂O</td>
<td>↑↑</td>
</tr>
<tr>
<td>(in severe cases)</td>
<td></td>
<td>&gt; 400 mm H₂O</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td>20-45 mg/dl</td>
<td>&gt; 100 mg/dl</td>
<td>100-500 mg/dl</td>
</tr>
<tr>
<td>CSF/glucose</td>
<td>0.6</td>
<td>&lt; 0.4</td>
<td>0.4-0.6</td>
</tr>
<tr>
<td>Lacquer</td>
<td>up to 5 w/a/c</td>
<td>↑↑</td>
<td>100-500 cells</td>
</tr>
<tr>
<td>(lymphocytes mostly)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Early paradox:**
- In early phase → in CSF examination → PMNs predominate
- (0-10 days)
- (Poly morpho nuclear cells)

**Therapeutic paradox:**
- After starting ATT → in CSF examination → Again PMNs are seen

- AOA levels → 10 u/litre → suggestive of T.B
- Subacute onset of nerve root and cord compression signs
- Slowly progressive dementia → Suggestive of T.B
- CSF lactate
  - Procalcitonin favours Bacterial meningitis
- CSF chloride ↓↓ favours T.B meningitis
- In elderly → CSF is a cellular sometimes
  - (75 years)

**Treatment:** 3HR2E + 7-9 months RPE

**Diagnosis:** CSF Geneexpert - by MTB/RIF
- Nucleic acid amplification method

### Tuberculoma

- Presents as a ring enhancing lesion on imaging
- Differential diagnosis:
  - Tuberculoma
  - Neurocysticercosis

<table>
<thead>
<tr>
<th>Tuberculoma</th>
<th>Neurocysticercosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Larger (&gt;30 mm)</td>
<td>Smaller</td>
</tr>
<tr>
<td>Irregular</td>
<td>Regular</td>
</tr>
<tr>
<td>Midline shift +/-</td>
<td>Not seen</td>
</tr>
<tr>
<td>Variable intensity</td>
<td>T. - Hypointense</td>
</tr>
</tbody>
</table>
Eosinophilic meningitis

- >10 eosinophils/μl of CSF
- Major Parasites:
  - Angiostrongylus cantonensis
  - Erathostoma
- Rarely:
  - Schistosoma
  - Cysticercosis
  - Toxoplasma

Treatment: 2HRZE + 7-9 months HRE
Diagnosis: CSF GeneXpert - bu m.tuberculosis
- nucleic acid amplification method.
VIRAL MENINGOEENCEPHALITIS

Viral meningitis
- Most common organism: Enterovirus (type II)
  HSV - a
  VZV

Viral encephalitis:
- Most common organism: HSV - I
- Most common cause for epidemics of viral encephalitis
  (in Asians) → Arbovirus → Japanese encephalitis

Viral meningitis

- Benign
- Rare
- Clinical Features:

Non-specific prodrome with fever
(2-3 days)

Remission

Fever returns + meningeal symptoms

Headache, nausea, vomiting, photophobia,
Terminal neck stiffness, no altered sensorium

Good recovery
### CSF Findings

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Bacterial</th>
<th>TB</th>
<th>Viral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure</td>
<td>5-150 mm H₂O</td>
<td>↑↑↑</td>
<td>↑↑</td>
<td>Normal to ↑ (≤200 mm H₂O)</td>
</tr>
<tr>
<td>Cells</td>
<td>&lt; 5 cells</td>
<td>↑↑↑</td>
<td>100-500</td>
<td>100-300 (&lt;300 cells)</td>
</tr>
<tr>
<td>Protein</td>
<td>20-45 mg/dl</td>
<td>↑↑↑</td>
<td>↑↑, 100-500</td>
<td>50-100 mg/dl</td>
</tr>
<tr>
<td>Sugars, CSF/S. glucose</td>
<td>0.4</td>
<td>&lt; 0.4</td>
<td>0.4-0.8</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.4 (very severe)</td>
<td></td>
</tr>
</tbody>
</table>

### Viral encephalitis

- Arboviruses and HSV-1
- Hemorrhagic necrosis of infero-medial temporal lobe and frontal lobe
- Clinically more severe than meningitis
  - Acute onset brain parenchymal disease
  - Seizures (status epilepticus)
  - Fever + Personality changes
  - Behavioural changes
- CSF shows lymphocytic pleocytosis
- MRI: Bilateral temporal lobe hyperintensities (T₁)

JE show bilateral thalamic hyperintensities

- Diagnosis: antigen detection in CSF by PCR
  - anti JE, anti HSV
- EEG: APLED
  - Periodic lateralized epileptiform discharges

*Images of MRI scans are shown.*
• Treatment: IV Acyclovir 10 mg/kg tds
• D/V: Autoimmune encephalitis (anti NMDA)
  Paraneoplastic (anti Hu, anti Yo)

Cryptococcal (fungal) meningitis

• Causative agent: Cryptococcus neoformans
  through inhalation of spores
• Seen in immunocompromised (HIV)
• Subacute presentation - 1-3 weeks
• High predilection for CNS: can cross blood brain barrier

In CSF:
  pressure ↑↑ 400-500 mm H₂O
  cells < 50/ml
  protein ↑
  sugar ↓, < 100 mg/dl

• Angioinvasion: invasion of blood vessels
• Investigations:
  - Gram staining of CSF: yeast like forms
  - Confirmed by India ink staining
    clear zone around each yeast cell
- Cryptococcal antigen detection in CSF (fastest) by PCR or Latex agglutination

* Treatment: Liposomal Amphotericin B + S-Fluorocytosine

Algorithm to diagnose meningitis from CSF findings:

- Meningitis
  - CSF pressure
    - Normal to high
    - Very high
      - Cells in CSF
        - Very low < 50/mL
        - Fungal meningitis
          - ↑ protein
            - Bacterial meningitis
              - PMN predominant
                - (polymorphonuclear leukocytes)
            - ↑ protein
              - TB meningitis
                - Lymphocyte predominant

**APPROACH TO UMN PATHOLOGY**

**Introduction**

- **Hemiplegia:**
  - Weakness: Corticospinal tract or Pyramidal tract involved (major motor pathology)
  - Spasticity: increased tone
  - Hyperreflexia.

- **Pyramidal tract:** initiation of fine, skilled, voluntary (distal) movements.

- **EPS (Extra-pyramidal system):** modulating and regulating movement planning, sequence and organisation (basal ganglia)

- **Cerebellum:** finesse to the movement

**Upper motor neurons**

1. Corticospinal tract
2. EPS
3. Corticobulbar tract

- **Lower Motor Neurons (LMN) to muscle**
  - Anterior horn cells of spinal cord
  - Cranial nerve nuclei on brainstem

- **Upper motor neurons**
  - Pyramidal tract fibres
  - Extra-pyramidal fibres
  - Corticobulbar fibres
descending motor systems which merge on the anterior horn cells of spinal cord or Cranial nerve nuclei on brainstem
Origin of corticospinal tract

- Origin of Corticospinal Tract (CST)

- Pyramidal cells or giant pyramidal cells of Betz are seen in layer 5 of motor cortex

- Pyramidal tract
  - Cortex
    - Medial
      - Lower limbs
        - Anterior cerebral artery
    - Surface
      - Superior lateral face and upper limbs
        - Cerebral artery
  - Lower limbs
    - Anterior

Anatomy of internal capsule

- Internal capsule
  - Anterior limb
    - Frontopontine fibres, anterior thalamic radiations
  - Genu
    - Corticobulbar fibres
  - Posterior limb
    - CST (anterior 2/3rd), superior thalamic radiations
  - Optic radiation
    - Lateral geniculate body
  - Auditory radiation
    - Medial geniculate body
Lesions of internal capsule

- Characterised by C/L:
  - Hemiplegia
  - Dense
  - Hemisensory loss
  - Homonymous hemianopia
  - Half (lower) of face affected
Every cranial nerve —— bilateral representation nuclei
- Exception: Facial nerve nucleus
  - upper part —— bilateral innervation
  - lower part —— unilateral innervation
- In L MN lesion, lower half of face is affected while upper part of face is spared.
  Angle of mouth deviated to opposite side

Lesions of brainstem

- Middle 3/5th of cerebral peduncle —— Corticospinal tracts (lateral)
  Corticobulbar tracts (medial)
- They are characterised by
  - Crossed hemiplegia —— Ipsilateral L MN cranial nerve palsy
  - Contralateral weakness
- Corticospinal tract is present as disjoined fascicles at basilar part of pons.
- Corticospinal tract decussates at the pyramidal level in the caudal medulla.
- 50% cervical
  - 20% thoracic
  - 30% lumbosacral portion
Clinical features of pyramidal lesions

Example: Acute onset weakness of left upper and lower limb spasticity & hyperreflexia.

Left-sided UMN hemiplegia involving either

- Right cortex
- Right corona radiata
- Right internal capsule
- Right brainstem
+ Cortical finding
  - Pure weakness
  - HHH with UMN 7th nerve palsy
  - Crossed hemiplegia

- When CST is involved, look for pyramidal pattern of weakness. It is as follows:
  - Lower facial involvement
  - Voluntary > emotional
  - Deglutition / articulation not affected
  - Voluntary skilled learned action most affected
  - Wrist / fingers / elbow extensors / supinators / abduction and external rotation of shoulders are affected
  - Hip flexion and internal rotation of knee flexion / dorsiflexion / eversion at ankle is also lost

Clinical manifestations of CST:
- Loss of skilled voluntary movement
- Impairment of integration of movement
- Over activity of lower segmental centres due to loss of inhibition
- Disrupted movement in contrast to specific muscles
- Others: Spasticity
  - Clasp-knife phenomenon
  - Reflexes ++
  - Power loss
  - Sensory (more at level of internal capsule)
Cranial nerve III : Oculomotor

Origin: Mid brain - Superior colliculus (ventral to cerebellar aquaduct).

- Parasympathetic → Via ciliary ganglion → Sphincter pupillae, Ciliaris
  (Pupil constriction)
- Motor nerve: Extraocular muscles (IO, SR, IR, MR, LPS)
  (no sensory)
- Single unpaired nucleus for LPS;
- Edinger westphal nucleus (EW) → Light reflex
  paired nucleus for MR, IR, IO, SR
- Superior Rectus → Contralateral supply by 3rd nerve nucleus.
- Rest of the muscle → Ipsilateral supply
- Nuclear lesion: Bilateral palsy + contralateral superior rectus palsy
- For convergence → Single unpaired nucleus.
- At level of interpeduncular fossa: Subarachnoid course
- Passes between the Posterior-cerebral Artery and Superior cerebellar Artery

**Post-Communicating Artery aneurysm**

- Laterally to Post-Communicating Artery, coursing anteriorly and piercing the dura.
- In aneurysm of Post-Communicating artery (PCOM), Compression of CN III

**Nerve Fibers**

- Superficial: Peripheral parasympathetic fibers → Pial vessels
- Deep: Motor fibers → Vasa nervorum

**Compression**

- PCOM Aneurysm: Pupil involvement (or)
- ICH or Herniation through the brainstem

**At the level of cavernous sinus**: Lateral wall → III

**At the level of sup. orbital fissure**: divides into 2 parts

**Sup. division**

- LPS, SR

**Inf. division**

- MR, IO, Pupil supplying fibers

**Ocular movements**

- Yoke muscle (SR ↔ IO, RR ↔ SO, MR ↔ LR)
- Recti: Origin: Annulus of Zinn
  - Insertion: Sclera (angle = Anatomical axis)
  - Recti act best in abducted position
- Obliques: Insertion: 30° to anatomical axis
  - Best act in adducted position
  - Additional action: Torsion
Eyemovements - horizontal gaze

- **Horizontal Gaze**
  - Rapid saccades → Supra nuclear control of gaze
  - Arises from left frontal lobe → Connected to right PREC (para pontine reticular formation) → Connected to right sixth nerve nucleus in pons
    → Connected to right lateral rectus

- **Slow pursuit movements** → Peritontorosteal (PTO) cortex → Dorsolateral pontine nucleus

- **Oculovestibular Reflex** → Vestibular nucleus → Ipsilateral 3rd nerve when head is rotated—eyeball movements in the opposite direction with eye in place.
Disorders of FMP circuit

- Inter nuclear ophthalmoplegia: [INO]
  - Upward gaze & downward gaze → Rostral interstitial nucleus in midbrain
  - Lesion involving left MLF
  - Detect left adduction & strabismus right eye
  - Normal left gaze
  - Convergent drift if lesion discrete
  - Important causes:
    - Demyelination: usually bilateral
    - Vascular disease
    - Tumours of brainstem

- PTO cortex connected to rostral interstitial nucleus.
  - Left MLF lesion: Left III CN cannot act
    - Left MR non-functional
    - Right LR Abduction → Nystagmus
    - Left side adduction weakness, contralateral abduction nystagmus → INO

- One and a half syndrome: MLF + PPRF lesion
  - Eg: lesion in right PPRF + right MLF lesion → Right 6th CN - Non functional
  - Left 3rd CN - Non functional
  - Right 3rd CN - Non functional
  - Ipsilateral 6th CN, contralateral 3rd CN, Ipsilateral 3rd CN
Not functional | Only contralateral 6th CN functional
↓
Abduction
(opposite eye)

Combined lesion of left MLF and PPK

* Ipsilateral (left) gaze palsy
* Deviation left abduction
* Normal right abduction with tonic nystagmus

Localisation:
- Frontal eye field - eyes deviate towards the site of lesion
- Thalamus - wrong-way eyes
- Basal ganglia / PSP - downward gaze palsy
- Pretectal area (Parinaud's Syndrome) - upgaze palsy
  - Bilateral IMA = multiple sclerosis
  - Unilateral IMA = Wernicke's encephalopathy, DM
  - 8 1/2 syndrome = 1 1/2 syndrome + Unilateral Facial nerve palsy
  - 15 1/2 syndrome = 1 1/2 syndrome + Bilateral Facial nerve Palsy

Horners syndrome

- Sympathetic fibres involved

Horners syndrome = partial ptosis + miosis + anhidrosis + apparent enophthalmus + loss of cilia - spinal reflex

Hypothalamus

(1st order)

Neuron

Neurons

Spinal cord

(T1, T2)

2nd order

Superior cervical ganglion

(Stellate ganglion (C8-T1))

Neuron

(via thorax)

Sweating/vasomotor 

Fibres following

Muscles

Internal carotid A.

3rd - order fibres

Neurons

Pupil - Course with Nasociliary
Lesion
1st order → Brain stem lesion
2nd order → Lung tumor (Pancoast)
3rd order → ICA aneurysm

Cocaine Test
- To confirm Horner's syndrome.
- Cocaine → sympathomimetic → dilatation of pupil
Failure of dilatation after cocaine → Horner's confirmed

Hydroxyamphetamine Test
- Amphetamine → epinephrine (sup. cervical ganglion)
  Preganglionic → pupils dilate
  Post ganglionic → no dilatation
- Differentiate between pre & post ganglionic lesion.

Light reflex
- Pretectal nucleus → EW nucleus → ciliary ganglion
  ↓
  Short Ciliary Nerves

- Lesion of optic nerve
  (Optic neuritis) → Relative afferent pupillary defect
  ↓
  Marcus Gunn pupil
- Swinging flashlight test: to diagnose Marcus Gunn pupil
- Wernicke's hemianopic pupil → distal optic tract
  ↓
  Homonymous hemianopia

- Argyll Robertson's pupil → Light - near dissociation
  ↓
  Light reflex - absent
  Accommodation Reflex - present
  - Seen in Tabes dorsalis, DM, Alcoholism
- Holmes Adie pupil → due to ciliary ganglion lesion
  ↓
  Young girl with dilated circular regular pupil reacting slowly
to light and accommodation
  "Vermiform movements"
  Loss of distal tendon reflexes
Dermotion hypersensitivity: Pilocarpine of 0.25%

Ocular motor cranial nerves

SO → 1st CN → Longest intracranial/Sub arachnoid
course → Exit dorsally
  • Dorsal decussation
  • Thinnest CN

LR → 6th CN
  • Fist affected in ↑ICT
  • Longest intradural course
CRANIAL NERVES – 2

Trigeminal nerve

- Cranial nerve (CN) V
  - Largest CN
  - Mixed nerve
  - Large sensory nucleus - laterally
  - Middle 1/3rd of pons
  - Small motor nucleus - medially
  - Muscles of mastication, anterior belly of digastric

- Sensory root:
  - Has 3 parts (Nucleus):
    - Mesencephalic - midbrain: Proprioception, main centre for jaw jerk
    - Gasserian - Main sensory - pons: Touch & temperature
    - Ganglion - Spinal nucleus - medulla: Pain

[Diagram of the trigeminal nerve and its components]
- Main sensory nucleus → Cross over to opposite side
  (Giant thalamic tract)
  ↓
  Joins medial lemniscus
- Spinal nucleus → Descend up to c2 level → Cross over
  ↓
  Join spinthalamic tract

**Facial nerve**

- Motor nucleus
  - Wind around 6th CN nucleus (Facial colliculus)
- Muscles of facial expression: posterior belly of
  Digastric, Styloglossus, Stapedius
- Sensory nucleus: Nucleus Tractus → Taste to anterior 2/3rd of
  solitarius
  - Tongue
  - General sensations from
    External ear
- Parasympathetic nucleus: Superior Salivary & Lacrimal nucleus

![Diagram of facial nerve pathways](image)

Nervus intermedius of → Motor nucleus + Sensory nucleus

Wrisberg

Spinal nucleus + Tract of Trigeminal nerve → General sensation

- On leaving pons:
  - Motor root
  - Sensory root
  - Parasympathetic Root

Wrisberg

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Sensory nucleus:  • Nucleus Tractus → Taste to anterior 2/3 tongue
  • Spinal nucleus of V nerve
  • At ponto medullary junction:
    - Motor fibers of VII CN
    - Nervus intermedius
    - VII Nerve
    - Labyrinthine artery

• Internal auditory meatus: Intrapetrous course
  1st part: Internal Auditory Meatus till Meatus to Metal Foramen
  → Meatal segment

  and segment: Labyrinthine part (narrowest part)
  3rd segment: Horizontal part (Tympanic segment) Inside Facial Canal
  4th segment: Mastoid part

  Meatal Foramen to Geniculate Ganglion - Labyrinthine part
  (Inner ear)

  Medial wall of middle ear - Horizontal part
  Vertical segment - Mastoid part
Facial nerve: branches

Branches of Distribution

Facial canal
A. Nerve to stapedius
B. Greater petrosal nerve
C. Chorda tympana

Stylomastoid foramen
A. Posterior auricular
B. Nerve to stylohyoid
C. Nerve to digastric (posterior belly)

In face
A. Temporal
B. Zygomatic
C. Buccal
D. Marginal mandibular
E. Cervical

- Meatal segment → No branch
- Labyrinthine segment → At the level of geniculate ganglion
  greater superficial petrosal nerve
  Join with deep petrosal nerve

Pterygo palatine ← "Nerve of pterygoid canal" aka vidian nerve

Ganglion
- Lacrimal
- Nasal
- Palatine glands

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Facial nerve palsy

UMN

- Corticobulbar fibers
  seen at the level of
gen of internal
Capsule

- Facial nerve nucleus
  Infarct (vascular ischemia)
Stroke affect corticobulbar fibers

- Upper part of face has bilateral
  representation
- Lower part of the face -
  unilateral representation
- UMN 7th nerve palsy → lower 1/2 of face is involved
- Emotional fibers → enter separately

↓

in UMN facial palsy, involuntary emotional expression

- UMN facial palsy presentation - eg: right UMN hemiplegia
  ↓ site of lesion
  Right UMN 7th nerve palsy
  Left internal capsule

LMN Facial nerve palsy:
- Pons: Facial nerve nucleus

  Unilateral LMN Nuclear palsy
  Stroke
  - Contralateral UMN hemiplegia
  - Ipsilateral UMN 7th nerve palsy

  Bilateral LMN Nuclear palsy
  At the level of brainstem:
  - GBS
  - Syringobulbia
  - Polyneuritis cranialis (SLE, vasculitis)

- Intrapetrous part:
  * Mental
  * Labyrinthine (inner ear)
  * Horizontal (middle ear)
  * Mastoid (mastoid process)

mec → Bell's palsy [Idiopathic LMN]
mec Association with Bell's palsy → HSV, HZV, CMV
mec site → labyrinthine segment (Narrowest part)

LMN 7th nerve palsy → Tests for Bell's Palsy
  * Forehead wrinkle (Frontalis muscle) → Absent
  * Eye closure (Orbicularis oculi) → Absent

  * Bell's phenomenon → On forceful closure of eye → eye moves upward → seen in LMN lesion

  * Wide smile → Angle of mouth deviated to opposite side
  CO → 10 ° 7 → deviation to opposite side.
  CO → 12 ° 5 → deviation to same side.
• Whistling → Θ
• Blowing → Θ
• Feeding → drooling from angle of mouth on the same side, dripping of saliva.
• Hearing → • Hyperacusis
    • Pain behind ear
• Loss of taste sensation.

Bells palsy

- Maximum weakness - 48 hrs
- Recovery seen in 3 weeks
- Partial palsy → very good prognosis
- Any sign of recovery within 1 week → good prognosis

V/L LMN 7th nerve → brain stem causes
palsy
- GBS
- Syringobulbia
- Vasculitis
- SLE
- Lymphoma
- Sarcoidosis

Management:
- Corneal care
- Short course steroids: Oral prednisolone mg/kg/day for 3–5 weeks later taper the dose
- ± Acyclovir
- General prognosis - good
STROKE: INTRODUCTION, CLASSIFICATION AND RISK FACTORS

Introduction

Stroke Definition: [WHO]
- A neurological deficit of
  - Sudden onset.
  - With focal rather than global dysfunction.
  - In which after adequate investigations, Symptoms are presumed to
    be of non-traumatic vascular origin.
  - Which lasts for > 24 hours.

Definition of Transient Ischemic Attack [TIA]:
- A brief episode of neurological dysfunction caused by focal brain or
  retinal ischaemia, with clinical symptoms lasting for <1 hr without
  any evidence of infarction.
- No permanent changes of brain occurs in TIA.
- Risk factor for stroke: MI.

Investigations In Stroke

- CT - Angiography:

Stroke is due to sudden vascular occlusion

Multimodal Diffusion - Perfusion MRI:
Multimodal Diffusion-Perfusion MRI

- Diffusion weighted MRI: Tissue level compromise.
- Perfusion weighted MRI: Hemodynamic compromise - Ischemia vs Infarction
- MRA Angiogram: Site of Occlusion or Stenosis

Diffusion weighted MRI:

- Very subtle hypodensity and swelling in the left frontal region with effacement of sulci compared with the contralateral side.
- DWI shows marked superiority in detecting infarct.
• Stroke - On CT:

![CT images showing progression of infarct](image)

- CT - normal - can only exclude bleed, but not the infarct in the first 6 hours.
- Earliest CT findings in stroke - Hyperdense MCA Sign (Middle Cerebral Artery)
  - Seen in 1-6 hours.

![Axial unenhanced CT image](image)

Axial unenhanced CT images in a proximal segment of the left MCA in a 53-year-old man obtained 2 hours after the onset of right hemiparesis and aphasia, show areas of hyperattenuation (arrow) suggestive of intravascular thrombi.

• Insular Ribbon Sign - Seen in > 6 hours.

![Axial unenhanced CT image](image)

Axial unenhanced CT image, obtained in a 73-year-old woman 2½ hours after the onset of left hemiparesis, shows hyperattenuation and obscuration of the posterior part of the right lentiform nucleus (white arrow) and a loss of gray matter - white matter definition in the lateral margins of the right insula (black arrows). The latter feature is known as the insular ribbon sign.
• In insula - there is loss of grey white differentiation.
  - Obscuration and hypodensity at the level of lentiform nucleus.

**Obscuration lentiform nucleus**

Axial unenhanced CT image shows hypo attenuation and obscuration of the left lentiform nucleus (arrows), which, because of acute ischemia in the lenticulostriate distribution, appears abnormal in comparison with the right lentiform nucleus.

**Subacute Infarcts**

Pathophysiology of stroke

• Stroke is due to loss of Cerebral auto regulation.

  • Cerebral blood flow = \( > 25 \text{ ml} / 100 \text{ gm} / \text{min} \) - Normal

    \[ \text{CBF} \]

    \( \text{Cerebrovascular Resistance} = \frac{\text{Mean Arterial Pressure}}{\text{CBF}} \)

    \[ \text{MAP} \]

• MAP and cerebrovascular resistance adjusts themselves to maintain a constant cerebral blood flow.
* MAP from 60 - 180 mm Hg

Cerebral blood flow remains constant (cerebral autoregulation)

In stroke : Loss of cerebral autoregulation.
* Blood flow of > 25 ml / 100 gm of brain tissue → Normal
* Blood flow of < 10 ml / 100gm → Infarction.
* Blood flow of 10 - 25 ml / 100gm → Ischemic penumbra.

Salvageable / Management is done.
* Ischemic penumbra can be identified in perfusion weighted MRI.

Pathology of stroke:
Loss of cerebral autoregulation

Hypoperfusion mediated ↓ in ATP

Failure of Na⁺ - K⁺ ATPase

Glutamate release and Ca²⁺ entry

Liquefactive necrosis.

Classification of stroke

---

<table>
<thead>
<tr>
<th>Stroke Type</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial</td>
<td>99%</td>
</tr>
<tr>
<td>Venous</td>
<td>1%</td>
</tr>
<tr>
<td>Ischemic</td>
<td>85%</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>15%</td>
</tr>
<tr>
<td>Thrombotic</td>
<td>25%</td>
</tr>
<tr>
<td>Embolic</td>
<td>60%</td>
</tr>
</tbody>
</table>

MC: Intraparenchymal bleed
Subarachnoid haemorrhage
MC site: At the origin of Posterior Communicating Artery, mostly Aneurysmal.

Embolic Stroke (60%)
Artery to Artery Embolic stroke
Cardioembolic stroke
Lacunar Stroke:
- Seen in 30 - 300 µm vessel.
- Infarct Size: 3mm - 2cm
- Lipohyalinosis > Atherosclerosis.

Ischaemic Stroke
- Infarct
- Large vessel
  - Thrombotic
  - Embolic
    - Artery to artery
    - Cardiac embolic

Circulation of brain

- Branches of vertebral artery:
  - PICA (Posterior Inferior Cerebellar Artery)
  - Anterior Spinal Artery

Basilar Artery
- AICA (Anterior Inferior Cerebellar Artery)
- Pontine branches
- Labyrinthine branches
- Superior Cerebellar Artery
- Posterior Cerebral Artery

Cerebral Arteries
- Anterior Cerebral Artery
- Middle Cerebral Artery
- Posterior Artery

Proximal to Anterior Communicating Artery (ACOM)
- Distal to Posterior Communicating Artery (PCom)

A₁ Segment A₂ Segment P₁ Segment P₂ Segment
Causes Of Stroke

![Stoke Diagram](image)

**Thrombotic**
- Most Common Cause: Atherosclerosis
- Vasculitis: Takayasu
- Fibromuscular dysplasia
- Hypercoagulable states: APLA
- Homocysteinemia
- Myeloproliferative disorders
- CADASIL: Cerebral Autosomal Dominant Arteriopathy with Stroke and Ischaemia. Leukoencephalopathy NOTCH III gene mutation.
- Moya moya disease.

**Embolic**
- Artery to Artery - Carotid atherosclerosis
- Cardioembolic - Most common - Atrial fibrillation
  (Non - Rheumatic)
- Other: MS
- Sick sinus syndrome
- Infective endocarditis
- Recent MI
- Prosthetic valve.

**Risk Factors**

| TABLE 407-21 COMMON STROKE RISK FACTORS |
|-------------------------------|-----------------|-----------------|
| FACTOR                      | POPULATION-ATTRIBUTABLE RISK | RISK REDUCTION WITH TREATMENT |
| LIFESTYLE                   |                              |                              |
| Cigarette smoking           | 12-14%                       | 50% within 1 year of quitting |
| Physical inactivity         | 30%                          | ?                            |
| Excess alcohol consumption  | 7%                           | ?                            |
| MEDICAL                     |                              |                              |
| Hypertension                | >90%                         | 32%                          |
| Diabetes                    | 5-27%                        | 2-14%                        |
| Atrial fibrillation         | 2-24%                        | 64%                          |
| Carotid stenosis            | 2.7%                         | 50%                          |
| Sickle cell disease         | —                            | 91% with transfusion therapy in children |

- Non modifiable risk factors: Age (most important), male gender
- Modifiable risk factors: HTN > DM

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Scanned with CamScanner
STROKE: VASCULAR LOCALIZATION

Middle Cerebral Artery (MCA)

- Almost entire superficial lateral surface of brain → MCA
- Medial surface, major supply → Ant. Cerebral Artery (ACA)
- Stem of MCA
  - m1 segment
  - m2 segment
- m3 segment
  - K/A
  - Lenticulo striate branch (lazunar vessel)
    - Supply
      - Caudate nucleus
      - Putamen
      - Globus pallidus
      - Posterior limb of internal capsule
- m4 segment
  - Superior division
  - Inferior division

Occlusion
- Stem of MCA

Effect
- C/L hemiplegia
- C/L hemisensory loss
- C/L homonymous hemianopia
  - Global aphasia (dominant lobe)
  - Non-dominant lobe involvement
    - Apraxia - constructional and dressing
    - Visual space disorientation
    - Hemispatial neglect
    - Anosognosia
- **m₁ segment** → Lacunar stroke
- **m₂ segment**
  - Superior division → C/L hemiplegia + Broca's aphasia
  - Frontal lobe features
  - Inferior division → No weakness + Wernicke's aphasia.

Lacunar stroke: Risk factor → Hypertension, elderly

- Pure motor stroke → m₁ segment
- Pure sensory stroke → Thalamus lesion
- Dysarthria, with clumsy hand → genu lesion [Corticobulbar pathway]
  - Thalamus → dysarthria.

- Ataxic hemiparesis

**Pure motor**
- Contralateral hemiparesis
  - Internal capsule
    - posterior limb
  - Corona radiata
  - Basis pontis

**Pure sensory**
- Contralateral hemisensory loss
  - VPL, nucleus of thalamus

**Dysarthria-clumsy hand**
- Skewed speech and weakness of contralateral hand (fine motor)
  - Basis pontis (between rostral 1/3rd and caudal 2/3rd)

**Ataxia-hemiparesis**
- Contralateral hemiparesis and ataxia out of proportion to weakness
  - Internal capsule-posterior limb

**Anterior Cerebellar Artery (ACA)**

- a segments
  - A₁ - proximal to Anterior Communicating Artery (ACOM)
    - Occlusion
      - No clinical presentation (due to collaterals)
  - A₂ - distal to ACOM

  - A₁ supplies - Anterior hypothalamus
  - Anterior perforating substance
  - Anterior limb of internal capsule
  - Anterioinferior of caudate nucleus
  - Amygdala (partly)
**Lesion**

$P_3$ supplies $\rightarrow$
- C/L weakness (foot/LL weakness)
- Paracentral
- Bilateral ACA syndrome (if both branches are from a single ACA stem)
  - Gait apraxia
  - Primate reflex
  - Akinetic mutism

**Posterior Cerebral Artery (PCA)**

- PCA $P_1$: Proximal to PCOM $\rightarrow$ medial brain $\rightarrow$ mid brain syndrome
- $P_2$: Distal to PCOM $\rightarrow$ Sub thalamus, thalamus
  ($\text{Thalamo-Geniculate artery}$)

*PCOM = Posterior Communicating Artery*

- Dejerine Roussy Syndrome $\{C/L$ hemisensory loss with burning pain

Artery of Percheron (5-10%)
- Rare Condition (variation)
  - From PCA $\rightarrow$ 1 branch $\rightarrow$ supply midbrain, thalamus, sub thalamus
  - If occlusion here: Drowsiness, loss of consciousness, gaze palsy
  - Affects alertness / wakefulness

$P_3$ supplies medial temporal lobe $\&$ occipital lobe
  - On Occlusion: $\bullet$ Acute disturbance in memory
  - $\bullet$ Visual Agnosia
  - Splenium if involved $\rightarrow$ Alexia without Agraphia.
Gerstmann syndrome - Parietal lobe lesion → Alexia with Agraphia.
Occipital lobe lesion - C/L congruous homonymous hemianopia, sparing macula.

If bilateral PA Occlusion → b/L Occipital lobe infarction

- Anton syndrome
- Balint's syndrome
  • Oculomotor apraxia.
  • Simultaneous agnosia.
  • Paraphasia.

Anterior choroidal Artery

- Arises from internal carotid artery
- Supplies lower part of posterior limb of internal capsule
- Occlusion → Hemiplegia.
  • Hemisensory loss
  • Homonymous hemianopia.
Ataxic hemiparesis due to Basal Pontine Infarction

C/L Ataxia + C/L Hemiparesis

Course of corticospinal tract and position at various levels of brainstem

Cerebellum
Regulate Movement
Dentato Rubro Thalamo Cortical Fibers

Periphery
Cortex ponto Cerebellar Fibers

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STROKE: BRAIN STEM SYNDROME

Brain stem- introduction

1) Crossed Hemiplegia:
   - Corticospinal track decussates at the level of medulla.
   - Lesion at level of brain stem
     → Contralateral (ULN) weakness.
   - Lesion on nuclei
     → Ipsilateral (ULN) cranial nerve palsy.
2) Mid brain: Posterior view:
   - Tectum:
     1) Corpora quadrigemina.
     2) 4th cranial nerve.
   - Tegmental part:
     - Forms upper parts of 4th ventricle
     - Median sulcus
     - Median eminence (Fetal colliculus)
     - Sulcus limitans

Transverse section at the level of superior colliculus.
Ventral midbrain syndromes

Transverse Section at the level of the superior colliculus

1) Weber's syndrome
   • Cause: Lesion at base of midbrain (crus cerebri)
   • Structures involved:
     1. III nerve fascicles
     2. Corticospinal tract
   • Deficits:
     1. Ipsilateral III nerve palsy
     2. Contralateral hemiparesis

2) Claude syndrome
   • Cause: Lesion at tegmentum
   • Structures involved:
     1. Ipsilateral III nerve
     2. Superior cerebellar peduncle
     3. Red nucleus
   • Deficits:
     1. Ipsilateral III nerve palsy
     2. Contralateral ataxia
     (dentatorubrothalamic tract cerebrum→red nucleus)
     3. Contralateral tremors

3) Benedikt's syndrome
   • Site:
     - Tegmentum & peduncle
     - Red nucleus
     - Nigrostriatal pathway
   • Deficits:
     - Ipsilateral oculomotor paresis
     - Contralateral (C/L) hemiparesis
     - Contralateral tremor & ataxia
     - C/L hemiballismus (hemichorea, hemidystonia)

(Acl 2000)

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Dorsal midbrain syndrome

Parinaud's syndrome.
- Site: midbrain dorsum.
  - Pretectal nucleus involved
  - Periaqueductal grey matter lesion
  - Me cause: pineoloma.
- Deficits:
  - Impaired upgaze (pretectal nucleus is connected to rostral interstitial nucleus in the mid brain—upgaze)
  - Convergence retraction nystagmus
  - Light near dissociation.
  - Sun setting sign.
  - Colliers sign—lid retraction due to loss of supranuclear inhibitory control.
  - Skew deviation of eyes.
  - Argyll Robertson pupil—light near dissociation (accommodation reflex—present, light reflex—absent)
- Parinaud's oculoglandular syndrome—associated with Tuleremia infection.

Nothnagel syndrome:
- Site: lesion in the roof of tectum and quadrigeminal plate.
- Features:
  - Ipsilateral LMN 3rd nerve palsy
  - Ipsilateral ataxia—superior cerebellar peduncle.
- Due to dorsal extension—features of parinaud's seen.

Pontine vascular syndromes

Vascular supply:
- Anterior—Basilar artery.
- Dorsal pontine—Superior cerebellar artery.
- Lateral—Basilar and anterior inferior cerebellar artery.
Transverse section through lower part of pons.

Lateral pontine syndrome:
- also, Marie - Foix syndrome.
- Blood vessel involved - anterior inferior cerebellar artery basilar artery (AICA) or basilar artery.

Involves 3 structures:
- Spinothalamic tract → contralateral pain & temperature loss.
- Corticospinal tract → contralateral hemiparesis.
- Middle cerebellar peduncle → ipsilateral ataxia.

Ventral pontine syndrome:

- Millard-Gubler syndrome
  - Facial nerve, sixth nerve, contralateral hemiplegia syndrome
    - Involves basilar artery
    - Contralateral hemiplegia
    - 7th - 6th cranial nerve palsy.

- Raymond syndrome
  - SH syndrome
  - Involves basilar artery
  - Contralateral hemiplegia
  - 8th cranial nerve palsy.

Dorsal pontine syndrome, Locked in syndrome,
Top of basilar occlusion

1. Dorsal pontine syndrome: Foville syndrome.
   - Superior cerebellar artery involved.
   - Site → dorsal pontine tegmentum in caudal 3/4 of the pons.
   - Structures involved →
     - Ipsilateral corticospinal tract.
Brain Stem Syndrome

- Nucleus / fascicle of Facial nerve.
- Parapontine reticular Formation.
- Deafness
  1. Contralateral hemiplegia.
  2. Ipsilateral peripheral (Linn) facial nerve palsy.
  3. Ipsilateral conjugate gaze palsy.

2) Locked in syndrome
- Site: Ventral tegmentum / pontine infarction.
- Bilateral corticospinal / corticobulbar tract involved.
- Quadriplegia.
- Consciousness (intact RAS) and vertical gaze preserved.

3) Top of basilar occlusion
- Topmost part of basilar artery involved.
- Bilateral PA occlusion (occipital & medial temporal lobe) + occlusion of pre-tectal nucleus
- Features:
  - Ataxia.
  - Amnesia.
  - Altered behaviour.
  - Vertical gaze palsy.

Medullary syndrome

Lateral medullary syndrome.
- Involves:
  1) Ventral artery (V1 segment) > Posterior inferior cerebellar artery
- Structures involved:
  1. Cranial nerves
     - Nerves not involved: 1, 2, 3, 4, 6, 7, 8
     - Nerves involved: 5th cranial nerve (spinal nucleus of trigeminal nerve): Ipsilateral loss of pain & temperature
     - 7th cranial nerve (nucleus tractus solitarius): Ipsilateral loss of taste in anterior 2/3rd of tongue.
     - 8th cranial nerve (vestibulocerebellar fibers)
     - 9th & 10th cranial nerve + nucleus ambiguous: dysphagia, hoarseness
     - Dorsal nucleus of vagus & symptoms
     - 13th cranial nerve: Horner’s syndrome
  2. Sensory fibers
     - Dorsal column: Ipsilateral loss of fine touch, proprioception
     - Spinocerebellar tract: Contralateral loss of pain & temperature.
Features: on side of lesion
1. Numbness, pain & impaired sensation on one side of face.
2. Loss of taste (anterior 2/3 of tongue).
3. Ataxia, giddiness, vertigo.
4. Dysphagia, nasal regurgitation, hoarseness of voice.
5. Horner's syndrome.
6. Nystagmus, diplopia, nausea, vomiting.

On opposite side of lesion:
- Impaired pain and thermal sensation over half of face.

Medial medullary syndrome

- Occlusion of vertebral artery or branch of vertebral / lower basilar.

On side of lesion:
- Ipsilateral 12th nerve involvement (hypoglossal nucleus).
- Paralysis with atrophy of one half of the tongue.

On opposite side of lesion:
- Involves contralateral pyramidal tract & medial lemniscus.
- Paralysis of arm and leg, sparing face, impaired tactile and proprioceptive sense over one half of the body.

Cruciate paralysis:
- Brachial diplegia - weakness of both arms with relative sparing of legs.
- Due to lesion involving rostral portion of the pyramidal decussation.
- Or
- Paralysis of one arm and opposite leg.
Avelis syndrome:
- Site: tegmentum of medulla.
- Involves: (mnemonic: TSH syndrome)
  1. Ipsilateral tenth cranial nerve
     ↓
     Ipsilateral LMN 10th nerve palsy.
  2. Ipsilateral spinocerebellar tract
     ↓
     Ipsilateral pain & temperature loss.
  3. Ipsilateral corticospinal tract
     ↓
     Ipsilateral hemiplegia.

Jackson syndrome:
- Site: tegmentum of medulla (Avelis + ipsilateral LMN 10th nerve involvement)
- Structures involved:
  1. Vagus nerve
  2. Spinothalamic tract
  3. Hypoglossal nucleus
- Defect:
  1. Features of Avelis syndrome
  2. Ipsilateral tongue paralysis.
MANAGEMENT OF STROKE

Stroke Investigations

1) Plain CT
   - Done on admission
   - Rule out bleeding.
   - Initial 6 hours → Hyperdense middle cerebral artery (MCA) sign.
   - 6 - 48 hrs → Insular ribbon sign
   - Lentiform nuclear obstruction.
   - Infarct formation requires > 48 hours.

2) T2 MRI
   - May be negative up to
   - 2 - 4 hours post ictal period.
   - MRI Hyper intensity = CT Hypodensity.

Thrombolysis:
   - Golden hour: within 4.5 hours.
   - Previously → 3 hours.
   - Endovascular intervention (bedside) → up to 6 hours (12-24 hours)

Indications for IV Thrombolysis:
1) If CT brain shows no bleed, no edema, > 1/3rd of MCA.
2) Patient has significant sensorimotor weakness.
3) No facilities for MRI.
4) > 18 years age.
5) No history of surgery in last 31 days.
6) BP < 185/110 mmHg
7) Platelets > 100k.
8) No history of bleeding disorders.

- IV Thrombolysis → Alteplase (Recombinant tissue plasminogen activator)
- Dose: Alteplase - 0.9 mg/Kg.
  - 10% - LV stat (bolus)
  - 90% - Infusion over 1 hour.

Note: Success rate - high.
Rate of post lysis bleed - high.
3) Diffusion weighted MRI (DW MRI)
   - Normal → No infarction.
   - Hyperdense → Infarction.

**Penumbra**

- 10 ml - 25 ml / 100g / min.
- Core of irreversibly infarcted tissue surrounded by a perinuclear region of ischemia but salvageable tissue.
- Infarct gradually expands to include penumbra.

10C: perfusion weighted MRI (Pu-MRI)

- In T2w MRI or DW MRI infarct will.

- Diffusion weighted MRI in brain infarction will be positive → for approximately 3 weeks after onset.

- ADC (Apparent diffusion coefficient) → Hypointensity up to 24 hours.
d) CT brain \( \rightarrow \) Rule out bleeding

\[ \text{normal} \quad \text{Hyperintense} \]

\[ \text{no further} \quad \text{Perfusion} \quad \text{RDC sequence} \]

\[ \text{investigations} \quad \text{mRI} \rightarrow \text{Penumbra} \quad \text{hypointense (acute case)} \]

\[ \text{site: mRI angiography} \]

\[ \text{accessible} \quad \text{Not accessible} \]

\[ \text{Endovascular stenting} \quad \text{IV Thrombolysis} \]

**NOTE:**
- Aspirin: 150 mg loading dose.
  - In patients not eligible for thrombolysis.
- Statins \( \rightarrow \) Along with aspirin for prophylaxis.
- Double antiplatelet \( \rightarrow \) Transient Ischemic Attack (TIA), mild stroke, stroke while on aspirin.
- Routine anticoagulants \( \rightarrow \) not recommended.
- Mannitol
  - 100 ml IV infusion/ecessary - risk of intracranial tension is high for 3 - 5 days.
- Hyperglycemia, Hyperthermia at presentation \( \rightarrow \) bad prognosis.
- Carotid endarterectomy
  - done post stroke
  - unFix \( \rightarrow \) carotid stenting.