[هذا العمل اجتهاد شخصي لا يغني عن المصدر الأساسي للمقرر]

Neurological disorders		
1	Stroke	
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MedEDnotes

Stroke:
1. Distinguish between hemorrhagic and ischemic stroke.
2. Implement clinical findings and diagnostic strategies to identify patients with stroke and outline key points in the management.
3. To understand the acute stroke therapy and when to use thrombolytics and endovascular intervention.

Myasthenia gravis:
1. Understand the **pathophysiology** of Myasthenia gravis.
2. Identify the **symptoms** and **signs** in patients with myasthenia gravis.
3. To be able to establish **diagnosis** based on clinical findings and investigations.
4. Understand the general key points in the **treatment** and management of myasthenia gravis.

Multiple sclerosis:
1. To be able to recognize the **clinical presentation** and symptoms of multiple sclerosis.
2. To recall the **diagnostic** criteria and testing.
3. To be able to specify the **treatment** for **acute** multiple sclerosis **relapse**.

Guillain-Barre syndrome:
1. To understand the pathophysiology behind the Guillain-Barre syndrome.
2. To be able to describe the key differences between multiple sclerosis and Guillain barre syndrome in clinical presentation and examination.
3. To understand the extreme complications of Guillain-Barre syndrome and be able to list the key points in the management.

Parkinson's disease:

1. To be able to recognize the **clinical features** of Parkinson's disease.
2. To be able to **differentiate** between **PD** and **drug induced parkinsonism.**
3. To list key **treatment** points for Parkinson's disease.

Headache:

1. To be able to outline the **approach** of headache.
2. List the causes of **primary** and **secondary** headache.
3. To evaluate patients with **thunderclap** headache and to understand the way to establish the **diagnosis.**
4. To be able to outline the **approach** a patient suspected to have **migraine** headache.
5. To be able to recognize patients with **tension** type headache and be able to initiate **management** plan.

Seizure disorder, epilepsy and status epilepticus:

1. To know the definition of **epilepsy.**
2. To differentiate between the **focal** and **generalized** seizures
3. To understand the **definition** of **status epilepticus.**
4. To be able to **approach** patients with **status epilepticus.**

Cranial nerves disorder:

1. To be able to identify cranial nerves injuries based on **eyes gaze and pupils.**
2. Understand **clinical findings** and causes of **bell palsy** and be able to differentiate it from stroke.
3. To be able to recall key points in the **treatment** of **bell palsy.**

Myasthenia gravis (MG)

- Autoimmune[1] neuromuscular disease → generalized muscle weakness.
- Associated with: Thymoma[2], females, other autoimmune diseases (hashimoto, RA, SLE, sarcoidosis).
- Main clinical forms: Ocular MG, generalized MG.[3]
- **Pathophysiology**:
  - Thymus involvement: It is hypothesized that the thymus is involved in the pathogenesis of MG.[4]
  - AChR antibodies: Sero (+ve/-ve) against AChR/MuSK.[5]

- Clinical course[6]: Sx worsen w/ muscle use and improves with rest. Sometimes associated w/ exacerbating factors.[7]
- **Clinical manifestations**:
  1. **Eye** muscle weakness (most common initial Sx) → **Ptosis**, Diplopia, Blurred vision.
  2. **Bulbar** muscle weakness → dysarthria, dysphagia, and fatigable chewing (**infant feeding difficulties**).
  3. **Proximal** limb weakness → Rising from chair, climbing stairs, brushing hair, **floppy infant w/ poor head control**.
  4. Weakness of **respiratory** muscles → respiratory insufficiency.

- **Dx**[8]:
  - **AChR antibody** test (most specific test).[9]
  - **Electrophysiology**: A decremental response following repetitive nerve stimulation & abnormal single fiber EMG.
  - Chest CT: always indicated in newly diagnosed MG patients to rule out thymoma.
  - Edrophonium test (Tensilon test): Rapid improvement after administration of a short-acting acetylcholinesterase inhibitor. High false positive rate.

- **Rx**[10]:
  - First line: **cholinesterase inhibitors** (pyridostigmine) provides symptomatic relief.
  - Supplemental immunosuppressants (Glucocorticoids)[11]: if Sx persists despite anticholinesterase treatment.
  - Rapid immunomodulating therapies (in cases of myasthenic crisis): Plasmapheresis, IVIG.
  - Thymectomy.[12]

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[1] Autoimmune: autoreactive ab directed against postsynaptic AChR or receptor-associated proteins (impairing neuromuscular transmission). In rare cases, can be caused by graft-versus-host reaction after allogeneic stem cell transplantation (especially in children).
[2] The most common primary tumor in the anterior mediastinum, 10-12% of pts. Thymic hyperplasia in 60-70% of patients.
[3] **1.** Ocular myasthenia (only the extraocular and/or eyelid muscles), **2.** Generalized myasthenia: all skeletal muscles may be involved; especially the ocular, bulbar, limb, and respiratory muscles.
[4] Muscle-like (myoid) cells in the thymus express AChR → thymic T cells target myoid cells → AChR Abs production → Abs target postsynaptic AChRs of normal muscle cells, competing with acetylcholine (ACh) → impaired signal transduction in the NMJ resulting in skeletal muscle weakness & fatigue, and AChR decay and reduced receptor density on the postsynaptic membrane.
[5] Seropositive MG (85% of cases): positive for Abs against AChR, or against muscle specific tyrosine kinase (MuSK). Seronegative MG (15% of cases): negative assays for both AChR-Ab and MuSK-Ab.
[6] The most common initial Sx are ptosis and/or diplopia due to ocular muscle weakness, with the disease usually progressing to generalized weakness within two years. At that point, patients have difficulties standing up, climbing stairs, and possibly even swallowing and/or chewing.
[7] Meds (muscle relaxants, BB, benzos, **aminoglycosides**, antipsychotics, TCAs, d-penicillamine), stress, infection, pregnancy. Smaller muscles responsible for fine movements (eye muscles) tend to be affected 1st, while larger muscles become affected later on.
[8] MG is diagnosed according to Hx, PEx, Abs testing, and EMG evaluation. All pts should be screened for thymomas via CT.
[9] 85% of pts with generalized MG have ab. 100% of pts with thymoma have ab. Other associated antibodies: anti-MuSK.
[10] The treatment of choice consists of acetylcholinesterase inhibitors, possibly in combination with immunosuppressive drugs if Sx persist. Acute exacerbations, as seen in myasthenic crisis, should be treated with either IV immunoglobulins or plasma exchange.
[11] Alternatives: azathioprine, cyclosporine, mycophenolate mofetil.
[12] Can be beneficial even if a thymoma is not present. Not for patients with MuSK antibody-associated MG without a thymoma.

Guillain-Barre syndrome (GBS)

- Acute postinfectious polyneuropathy characterized by symmetric and ascending flaccid paralysis (prototype “AIDP”).
- **Etiology**: majority of patients experience Sx of an URTI or GIT (diarrhea) infection 2-4 weeks prior to onset of GBS.[13]
- **Pathophysiology**: Postinfectious autoimmune reaction that generates cross-reactive antibodies attacks the host's own axonal antigens, resulting in inflammatory and demyelinating polyneuropathy.(molecular mimicry).[14]

- **Clinical features**:[15] [16]

  A. Initial symptoms: back and limb pain, esp. paresthesias affecting distal extremities (fingertips, toes).

  B. Advanced symptoms:
  - Ascending paralysis: Bilateral flaccid paralysis spreads from lower to upper limbs in a “stocking-glove” distribution.
    - Cranial nerve involvement: frequently bilateral facial nerve involvement (facial diplegia).
    - Landry paralysis: involvement of the respiratory muscles.
  - Reduced or absent muscle reflexes.
  - Peripheral, symmetric paresthesias in the hands and feet.
  - Autonomic dysfunction[17]: Cardiovascular (arrhythmia), voiding dysfunction, and/or intestinal dysfunction.

Subtype[18]	Details
AIDP (Acute inflammatory demyelinating polyneuropathy)	• Acute variant of Guillain-Barré syndrome. Predominant subtype. • Associated with **Campylobacter enteritis** and CMV. • Autoantibodies against various antigens. • Ascending paralysis, autonomic neuropathy, CN defects and pain, clinical nadir ~4 weeks.
Miller fisher syndrome	• **External ophthalmoplegia**, **ataxia**, and **muscle weakness** with **areflexia.** [19] • Serological detection of autoantibodies (against ganglioside GQ1b, GT1a) confirms Dx. • Brainstem auditory evoked potentials demonstrate peripheral & central conduction defects.

[13] Pathogens: bacteria (**Campylobacter jejuni**, Mycoplasma pneumoniae), viruses (**CMV**, Epstein-Barr virus, HIV, influenza). Campylobacter enteritis is the most common disease associated with GBS. Cytomegalovirus is the most common virus.

[14] Infection triggers humoral response → autoantibodies against gangliosides or other unknown antigens of peripheral Schwann cells → immune-mediated segmental demyelination → axonal degeneration.

[15] The classic presentation of GBS begins with **paresthesia** in the toes and fingertips followed by lower extremity **symmetric** or modestly asymmetric weakness that may **ascend** over hours to days to involve the arms and, in severe cases, the muscles of respiration. The predominant symptoms of GBS at presentation in children are **pain** and **gait difficulty**. In preschool-aged children, the most common symptoms are **refusal to walk** and pain in the legs.

[16] PEx typically reveals symmetric weakness w/ diminished/absent reflexes & gait abnormalities. Sensory Sx r usually "positive" (pain or paresthesia, reflecting nerve irritability) rather than "negative" (eg, loss of sensation). Early Sx may be atypical (difficult to Dx). Some cases present w/ initial proximal weakness, or less common findings such as sphincter disturbances, raising concerns about a possible spinal cord lesion.

[17] Orthostatic hypotension, transient or persistent hypertension, paralytic ileus, bladder dysfunction, abnormal sweating.

[18] Historically, GBS was considered a single disorder, but it is now known to be a heterogeneous syndrome with several variant forms. Most often, GBS presents as an acute monophasic paralyzing illness provoked by a preceding infection (AIDP). In addition to the demyelinating form, which is the most common type, axonal forms of GBS are also well-recognized (acute motor axonal neuropathy, acute sensorimotor axonal neuropathy, Miller Fisher syndrome).

[19] Incomplete forms include acute ophthalmoplegia without ataxia, and acute ataxic neuropathy without ophthalmoplegia.

Dx:

- **CSF**: Albuminocytologic dissociation: elevated protein levels and normal cell counts (WBCs is normal).[20]
- **Electroneurography**: reduced nerve conduction velocity (NCV) due to demyelination : increased F-wave latency.[21]
- **Serology**:
  - To identify potential pathogens (e.g., Campylobacter jejuni).
  - Detection of antibodies (IgG) directed against gangliosides (e.g., GQ1b, anti-GM1 antibodies).

Rx:

- Supportive management.[22]
- **IVIG** (High dose of intravenous immunoglobulins).
- Plasmapheresis (plasma exchange).[23]

PD (Parkinson's disease)

PD: is a neurodegenerative disease involving a progressive depletion of dopaminergic neurons in the basal ganglia, particularly the substantia nigra.

Definitions:

- Parkinsonism: a syndrome featuring bradykinesia and either resting tremor or rigidity (or both).
- Secondary parkinsonism: parkinsonism with 2ry causes such as medication[24], intoxication, or head trauma.
- Parkinson disease (PD): parkinsonism for which no cause can be determined (idiopathic).

Risk factors: FHx, environmental (exposure to Mg and other substances), diet/metabolism (low levels of VitD, high iron intake, obesity), structural damage (Hx of TBI).

Pathophysiology

- Progressive dopaminergic neuron degeneration in the **substantia nigra** (part of the basal ganglia) and the locus coeruleus → **dopamine deficiency** at the respective receptors of the striatum with **interrupted transmission** to the thalamus and motor cortex → **motor Sx** of PD.
- **Serotonin** and **noradrenaline** depletion (in the Raphe nuclei): likely cause of **depressive** Sx.
- **Ach surplus** (in the nucleus basalis of Meynert): likely cause of **dyskinesia.**
- A further pathological hallmark of PD is the appearance of **Lewy bodies.**

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[20] Breakdown of the blood-nerve barrier at the dural attachment allows transudation of plasma proteins into the cerebrospinal fluid.
[21] Electrodiagnostic studies are the most specific and sensitive tests for diagnosis of GBS, and establish the underlying pathophysiology as either **demyelinating** (prolonged latency and slow conduction velocity) or **axonal** (lower amplitudes).
[22] Monitor cardiac & resp function. ICU Tx and intubation may be indicated. Prevent decubitus and/or thrombosis (esp. PE).
[23] In children (only recommended in rapidly progressing or severe disease), In adults (equivalent outcome as IVIG).
[24] It is the most frequent cause of secondary parkinsonism: frequently used drugs with considerable anti-dopaminergic effects: typical antipsychotics (haloperidol), some antiemetics (metoclopramide), some CCB (amiodarone), valproate, and lithium.

Clinical features

- Clinical course > 10 years; **unilateral** onset with persistently asymmetrical course, but may progress to the contralateral side.
- **Parkinsonism**: Bradykinesia/akinesia[25], Resting tremor[26], Rigidity[27].
- Postural instability: Imbalance and tendency to fall, Pull test [28].
- Parkinsonian gait: **shuffling** gait with quickened and shortened steps.
- Unhabituated glabellar reflex[29], signs of dystonia[30], pyramidal signs (but normal tendon reflexes), good response to levodopa.

🧠 **TRAP – T**remor, **R**igidity, **A**kinesia, and **P**ostural instability

Diagnostics "PD is a clinical diagnosis!"[31]

General measures: physiotherapy, speech & language therapy, occupational therapy, support groups.

Medical therapy

A. Levodopa is the drug of choice for the symptomatic therapy of PD. Dopamine agonist in pts < 65 y/o.[32]

B. Patients <u>< 65 yo</u>, with no significant comorbidities:

a. First-line treatment: Non-ergot dopamine agonists (as monotherapy or in combination with levodopa/carbidopa), MAO-B inhibitors (may be used as a monotherapy or in combination with dopamine agonists or levodopa/carbidopa), COMT inhibitors (in combination with levodopa/carbidopa).

b. Alternatives: Levodopa[33], Ergot dopamine agonists (bromocriptine), NMDA antagonists (amantadine) → used to reduce levodopa-induced dyskinesias, Anticholinergics/muscarinic antagonists (useful in pts < 65 w/ tremor as the main complaint).

C. Pts <u>> 65 yo</u>, or <u>multimorbid</u> patients of any age: First-line → levodopa + decarboxylase inhibitor (carbidopa).

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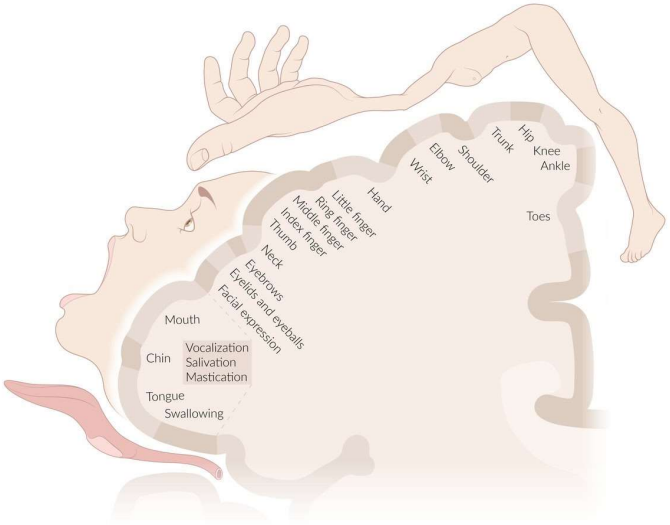
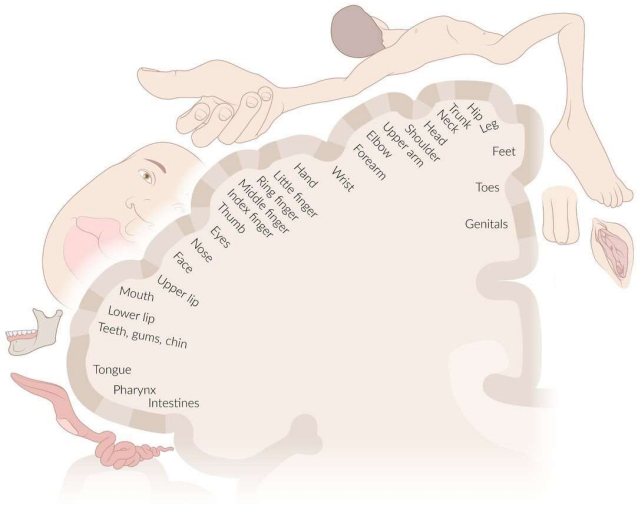
[25] Slowness of movement in combination with decreased amplitude or speed during a sequence of movement. Bradydiadochokinesia.
[26] Pill-rolling tremor that subsides w/ voluntary movements, but increases w/ stress. Typical in hands; may involve the legs, jaw, lips, & tongue.
[27] Increased and persistent resistance to passive joint movement that is independent of speed of movement. Froment maneuver → patient is asked to perform repetitive movements in the contralateral extremity (e.g., opening and closing of the left fist if the right side is examined) → Subclinical rigidity becomes more pronounced and may be detected. Special form: cogwheel rigidity.
[28] The examiner stands behind the patient and moderately pulls his or her shoulders. The patient's ability to maintain balance is evaluated.
[29] Primitive reflex elicited by tapping of the glabella, the area between the eyebrows, causing the subject to close his or her eyes.
[30] E.g., after raising the patient's head and suddenly releasing it, it sinks back down very slowly.
[31] **<u>Levodopa</u>** challenge test (alternatively apomorphine test): The result is positive if administration of levodopa/apomorphine relieves symptoms. **<u>Imaging</u>** is not routinely required for diagnosis, but should be considered in an atypical presentation or to r/o other underlying disorders → MRI (Conventional) r/o other possible causes of parkinsonism (strokes, tumors). **<u>Labs</u>** (r/o drugs, toxins, ...).
[32] In patients under the age of 65, it is generally recommended that treatment begin with a dopamine agonist to delay the onset of motor complications before moving on to levodopa, even though levodopa is more potent and has fewer side effects.
[33] Normally combined w/ a peripheral decarboxylase inhibitor. Most effective symptomatic Rx but carries high risk of dyskinesias than other meds.

Stroke overview

- **Stroke**: acute neurologic injury caused by ischemia or hemorrhage.
  - **Ischemic stroke**: hypoperfusion → cerebral infarction (ischemia & neuronal injury).
  - **TIA**: temporary, focal cerebral ischemia → neurologic deficits w/o acute infarction/permanent function loss.
  - **Hemorrhagic stroke**:
    - hemorrhage → cerebral infarction.
    - Intracerebral hemorrhage (bleeding within the brain parenchyma).
    - Subarachnoid hemorrhage (into the subarachnoid space).
    - Intraventricular hemorrhage (within the ventricles).

	Ischemic (85%)	**Hemorrhagic** (15%)	
		Intracerebral (10%)	**Subarachnoid** (5%)
Etiology	Embolism, thrombus, small vessel occlusion (lipohyalinosis)[34], Systemic hypoperfusion.	Ruptured cerebral artery or microaneurysm. Trauma. Reperfusion injury after ischemia.	Ruptured berry aneurysm. AV malformation. Trauma.
RF[35]	Age > 65, HTN, DM, Afib, carotid artery stenosis	Age > 65 years, HTN, Vasculitis, Malignancy, Ischemic stroke.	HTN, Tobacco, FHx.
SSx	Sudden onset of focal neurologic deficits	Headache, confusion, nausea. Sudden focal neurologic deficits	Rapid severe headache. Meningeal signs.[36] Sudden focal neurologic deficits.
Dx	Noncontrast head CT to r/o hemorrhage. MRI, CTA/MRA.[37]	Noncontrast head CT MRI, CTA/MRA.	Noncontrast head CT CTA. LP[38].
Rx	tPA (if within < 4.5 h of Sx onset). Intra-arterial thrombolysis. Thrombectomy. Aspirin or clopidogrel for 2ry prevention.	Reversal of coagulopathy. BP management. Surgical intervention if there are signs of herniation or ↑ ICP.	Reversal of coagulopathy. BP management. Prevention of vasospasm. Surgical clipping.

[34] A narrowing of an artery due to hypertrophy of the media of the vessel wall combined with lipofibrous deposition within the vessel wall. Lipohyalinosis of the vessel walls → focal damage → formation of microaneurysms → elevated risk of ruptures. Chronic HTN is a RF.
[35] For ischemic & hemorrhagic strokes, age is the most important nonmodifiable RF and arterial HTN is the most important modifiable RF!
[36] A collection of Sx associated with meningeal irritation (SAH, meningitis). Includes **nuchal rigidity, headache, and photophobia.**
[37] If the patient is a candidate for thrombectomy or to better identify the affected blood vessel
[38] If imaging is negative but suspicion for SAH remains high. CSF may show xanthochromia.

Homunculus	
Motor homunculus	Sensory homunculus
A map of the primary motor cortex (located in the precentral gyrus of the frontal lobes) that illustrates which areas of the brain process the motor output to which part of the body. The distorted representation of the body and the size of the correspondingly labeled cortical areas illustrate the proportional amount of motor output sent to the individual parts of the body. Accordingly, since areas like the tongue, face, and hands receive most motor innervation, these areas are represented as disproportionately large compared to other areas, like the trunk and lower limbs.	A map of the primary somatosensory cortex (located in the postcentral gyrus of the parietal lobes) that illustrates which areas of the brain process the sensory input from which part of the body. The distorted representation of the body and the size of the correspondingly labeled cortical areas illustrate the proportional amount of sensory input received from the parts of the body. Accordingly, since the sensory nerves arriving from, e.g., the face and hands, terminate over larger areas of the brain than, e.g., those of the arms & legs, these parts of the body are represented as disproportionately large.
	

Lacunar stroke type	Location[39] (most common)	Clinical features
Pure motor (> 50%)	Posterior limb of the internal capsule.[40]	Contralateral hemiparesis of the face, arm, and leg. No sensory impairment (circumduction gait). In some cases, dysarthria.
Pure sensory	Thalamus (most common).	Contralateral numbness and paresthesia of the face, arm, and leg
Sensorimotor	Post. limb of the intern. capsule.	Contralateral hemiparesis and sensory impairment
Ataxic hemiparesis	Post. limb of the intern. capsule.	Ipsilateral weakness w/ impaired coordination (ataxia, gait instability)

[39] **Motor** → may also involve the corona radiata, basal pons, medial medulla. Often caused by occlusion of the lenticulostriate artery. **Sensory** → may also involve the posterior limb of the internal capsule, pontine tegmentum, corona radiata. **Sensorimotor** → may also involve the thalamus, lateral medulla, putamen. **Ataxic hemiparesis** → may involve the corona radiata, thalamus, cerebral peduncle.

[40] Infarction of the posterior limb of the internal capsule is the most common type of lacunar stroke and may manifest clinically with pure motor stroke, pure sensory stroke (rare), sensorimotor stroke, dysarthria-clumsy hand syndrome, and/or ataxic hemiparesis.

ACA

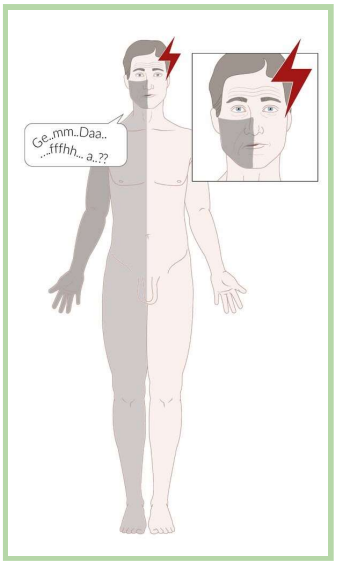
1. Contralateral **weakness** and **sensory** loss in the lower limbs > upper limbs. **Urinary incontinence.**
2. Abulia, dysarthria, transcortical motor aphasia, limb apraxia.

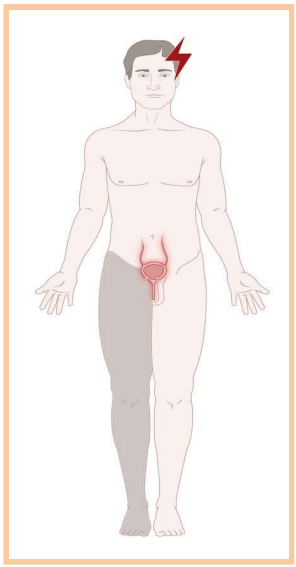
MCA (most common)

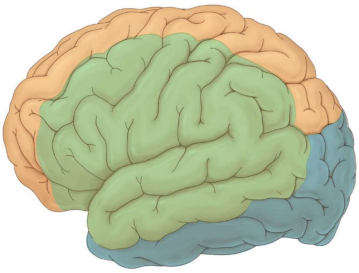
1. Contralateral **sensory** loss, gaze deviates **toward** the side of infarction.
2. Contralateral **weakness** in the arms, lower half of the face, and lower limbs.
3. Contralateral central (UMN) **facial nerve palsy** (patient can raise both eyebrows because the forehead receives bilateral facial nerve innervation.)
4. Contralateral homonymous **hemianopia** <u>without</u> macular sparing.[41]
5. **Aphasia** if in the dominant hemisphere (usually left MCA).[42] **Hemineglect** if in nondominant (usually right MCA).

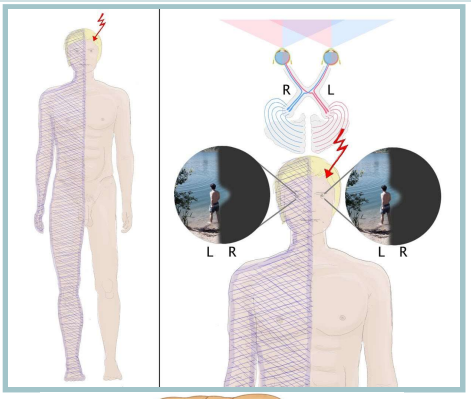
PCA

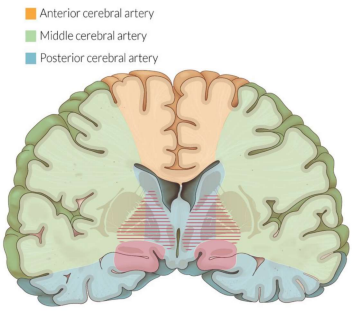
1. **General findings**: Contralateral homonymous **hemianopia** <u>with</u> macular sparing (because the macula receives collateral vascular supply from the middle cerebral artery). **Contralateral sensory** loss[43].
2. **Localized findings**: Lt PCA → alexia w/o agraphia, anomic aphasia, visual agnosia, Rt PCA → prosopagnosia.
3. **Midbrain syndromes**[44], **Thalamic syndromes**[45].

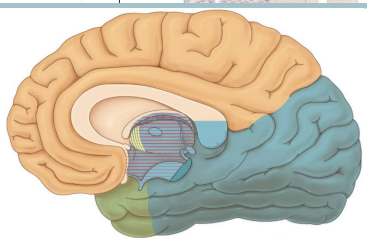


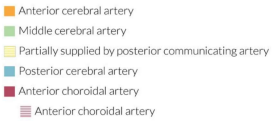


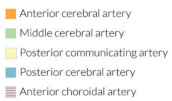












[41] Light from 1 side of the visual field falls onto the opposing ½ of each retina (the 2 right halves of the 2 retinae receive visual information from the two left halves of the two visual fields). The information is then sent through the optic nerve, optic chiasm, and optic tract and ultimately processed in the visual cortex that is ipsilateral to the retinal half (and, therefore, contralateral to the corresponding half of the visual field).
[42] Broca aphasia (lesion to inferior frontal gyrus, supplied by the superior division of MCA). Wernicke (lesion to superior temporal gyrus, supplied by the inferior division of MCA). Conduction (lesion to supramarginal gyrus, supplied by the inferior division of MCA).
[43] Due to lateral thalamic involvement: light touch, pinprick, and positional sense may be reduced. Memory deficits, vertigo, nausea.
[44] Medial midbrain syndrome (Weber syndrome), Lateral midbrain syndrome (Claude syndrome), Paramedian midbrain syndrome (Benedikt syndrome), Dorsal midbrain syndrome (Parinaud syndrome).
[45] Decreased arousal, Variable sensory loss, Aphasia, Visual field losses, Apathy, agitation, personality changes.

Diagnostics

A. Initial evaluation: Primary survey (ABC) → Clinical assessment and history:

a. Identify risk factors for ischemic or hemorrhagic stroke, including the presence of carotid bruits.
b. Identify signs that indicate the affected vessel and/or region of the brain.
c. Determine the time of onset of symptoms (e.g. "last known normal"): the time of stroke onset determines whether thrombolytic therapy is an option.

B. Imaging

★ Approach: noncontrast head CT to evaluate for acute hemorrhage → diffusion-weighted MRI to detect acute ischemia → consider further neurovascular imaging depending on the type of stroke.

1. Noncontrast head **CT** (first-line imaging):
   a. Allows for detection of acute hemorrhage but cannot be used to reliably identify early ischemia.
   b. Indicated in all patients suspected of having an acute stroke to rule out intracranial hemorrhage before administering thrombolytic therapy.
2. Diffusion-weighted **MRI**:
   a. Allows identification of ischemia earlier than a CT (within 3–30 minutes after onset).
   b. Allows detection of hyperacute hemorrhage.
   c. Evaluates reversibility of ischemic injury:
      - Perfusion-weighted imaging (PWI): visualizes areas of decreased perfusion and allows quantification of perfusion parameters, e.g., mean transit time (MTT), cerebral blood flow (CBF) and volume (CBV).
      - Perfusion-diffusion mismatch MRI: allows identification of the penumbra [46] (or "tissue-at-risk").

C. Laboratory evaluation: Initial (serum glucose) [47] → Additional evaluation: CBC, electrolytes, Coagulation parameters (INR, PTT), Urine drug screen (cocaine), blood alcohol level, Serum troponin.

Management

A. Stabilization and monitoring

1. Maintain euvolemia (fluid replacement), electrolyte repletion as needed, and analgesia as needed.
2. Maintain a sufficient oxygen supply and consider intubation if the patient shows signs of increased intracranial pressure (e.g., altered mental state). Monitor for signs of elevated ICP.
3. Maintain euglycemia (within 140–180 mg/dL), Normothermia (antipyretics) and normal acid-base status.
4. Cardiac monitoring (for at least 24 h), seizures should be treated pharmacologically. Evaluate for dysphagia.

B. Blood pressure management

1. Always treat hypotension (e.g., with fluid replacement, vasopressors).
2. Ischemic stroke: permissive HTN [48] → Only treat severe HTN (> 220 systolic and/or 120 mm Hg diastolic).
3. Hemorrhagic stroke: Reduce systolic blood pressure to approx. 140–160 mm Hg.

★ Nitrates should be avoided because they can increase ICP.

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[46] Area of relative ischemia w/ brain tissue that isn't yet irreversibly damaged and can be salvaged. The ischemic core, as measured by DWI, is usually smaller than the area of insufficient perfusion as measured by PWI. The difference between the 2 areas represents the penumbra.
[47] For most patients with acute ischemic stroke, only serum glucose is required prior to administration of tPA. Symptoms of hyper- and hypoglycemia can resemble a stroke. Laboratory studies should not delay imaging for patients with acute stroke.
[48] HTN is treated less aggressively in ischemic stroke than in hemorrhagic; in ischemic, the perfusion of the penumbra depends on the MAP.

Complications

- Medical complications: Cardiac dysfunction (arrhythmias, MI/due to catecholamines surge), Aspiration pneumonia (dysphagia → aspiration), DVT & PE, UTI, Bleeding (GI), Delirium, Depression.
- Neurologic complications
  - **A.** All strokes
    - Elevated intracranial pressure and brain herniation (Cushing triad 'HTN, resp depression, bradycardia')
    - Seizures, Neuropathic pain, SIADH.
    - Persistent neurologic deficits (hemiparesis, aphasia) and disability.
    - Central poststroke pain:
      - Affects < 10% of all stroke patients.
      - Unilateral facial pain and/or extremity pain associated with previous stroke.
      - Initial paresthesia → neuropathic pain (allodynia, dysesthesia).
      - Can occur with thalamic lesions.
  - **B.** Ischemic stroke: Hemorrhagic transformation, Vascular dementia.
  - **C.** Hemorrhagic stroke: Recurrent hemorrhage, Intraventricular hemorrhage, Hydrocephalus, Vasospasm (typically occurs 5–7 days after SAH) → may result in ischemic stroke.

ISCHEMIC

Nonmodifiable risk factors: Age (≥ 65), gender (♂ > ♀), FHx (CVS/cerebrovascular disease), genetic (sickle cell disease), Hx of TIA, migraine with aura.
Modifiable risk factors: HTN, DM, CVS (Carotid stenosis, Afib), atherosclerosis, obesity, coagulopathy (protein C/S def), hyperhomocysteinemia, alcohol, tobacco, recreational drug (cocaine can cause cerebral vasospasm), OCPs, HRT.

Etiology

1. Embolic (~ 20%) "MCA most affected"[49]
2. Thrombotic strokes (40%): Large vessel atherosclerosis[50] (20%), Small vessel occlusion (e.g. lacunar infarct) (20%).
3. Global cerebral ischemia
   - Systemic hypoperfusion: Shock or bilateral large artery atherosclerosis (e.g., of carotid arteries) → decreased effective oxygen delivery to the whole brain. Can result in watershed infarct.
   - Hypoglycemia: repeated episodes of hypoglycemia (e.g., due to insulinoma) increase the risk of cerebral ischemia.
   - Severe and/or chronic hypoxia: hypoxemia (e.g., due to respiratory arrest) → global tissue hypoxia in the brain.
4. Other causes.[51]

Clinical features

- Sudden onset of focal neurologic deficits (weakness/paralysis, paresthesias, aphasia, dysarthria).
- Nonspecific symptoms (impaired consciousness, N/V, headache, seizures). Sx depend on the location of the stroke.

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[49] **Cardiac emboli** → Afib, Atrial/ventricular thrombi, rheumatic heart disease, ventricular aneurysms, **Atheroemboli** → Internal carotid artery, aortic arch (less common), **Infectious emboli** → bacterial endocarditis, **Paradoxical embolism** → in patients with right-to-left cardiac shunt (e.g., persistent foramen ovale or atrial septal defect).
[50] Rupture of an atherosclerotic plaque and exposure of subendothelial collagen → formation of a thrombus. Thrombus formation most commonly occurs at branch points in arteries (internal carotid artery bifurcation or where the MCA branches from the circle of Willis).
[51] **Hypercoagulable states**: Inherited thrombophilia (e.g., factor V Leiden mutation, protein C deficiency), polycythemia, OCP, HRT, Sickle cell disease. **Vasculitis** (e.g., giant cell arteritis). **Arterial dissection** (e.g., due to trauma or fibromuscular dysplasia).

Diagnostics

A. Initial evaluation

1. Determine the time of onset of symptoms: The time of stroke onset is used to determine treatment options.
2. Stabilize the patient if needed → check serum glucose → emergency imaging.

B. Imaging

- Immediate noncontrast head CT to evaluate for acute hemorrhage prior to thrombolytic therapy.
- Further choice of imaging depends on head CT findings:
  - Diffusion-weighted MRI is a more sensitive test for acute ischemia (if head CT is negative but clinical suspicion for acute stroke is still high).
  - Neurovascular studies (CTA or MRA) for more specific identification of the occluded vessel.

1. Noncontrast CT -Ischemic changes can be detected ~ 6 hours after stroke onset- Findings:
   - Acute (within 12 h of Sx onset): Hyperdense occluded vessels, hypodense parenchyma, effacement of the sulci and loss of corticomedullary differentiation. 12–24 h → hypodense, > 24 h of onset → hyperdense.
2. Diffusion-weighted MRI "Ischemic changes can be detected ~ 3 m after onset, but takes longer to perform"
   - Findings: T1 (hypointense signal), T2 (hyperintense signal).
3. Neurovascular studies
   a. CTA -Allows identification of the exact location of the defect (in most cases)- Indications:
      i. When there is a high index of suspicion for stroke but no ischemia found on noncontrast CT or MRI.
      ii. If cannot give tPA (outside of the time window) but may be a candidate for mechanical thrombectomy.
   b. MRI angiography (MRA): indications similar to CTA.

C. Laboratory evaluation

- Initial evaluation (serum glucose) → Subsequent laboratory tests to consider (after emergent imaging is complete): CBC, electrolytes, coagulation parameters (INR, APTT), serum troponin, Urine drug screen (e.g., cocaine), blood alcohol level, serum lipids.
- Hypercoagulable workup: consider if patient is < 50 years old and/or has Hx of thrombosis: Protein C and S (deficient ?), antiphospholipid antibodies, VDRL/RPR, Lyme serology (ANA, IgM), factor V Leiden mutations, ANA, ESR, rheumatoid factor.

★ Immediate imaging or administration of tPA for ischemic stroke should not be delayed to obtain laboratory studies!

D. Additional diagnostic workup: ECG to r/o Afib and myocardial ischemia, Continuous cardiac rhythm monitoring for paroxysmal Afib, TTE and/or TEE to evaluate for intracardiac thrombus and patent foramen ovale (PFO), Carotid US to evaluate for carotid artery stenosis.

Treatment

Reperfusion therapy

- Goal is to prevent further tissue ischemia and irreversible infarction.
- Should be administered as soon as possible in eligible candidates (see below for specific indications).

A. IV thrombolytic therapy: administration of IV recombinant tPA (alteplase, tenecteplase) to break down blood clots.[52]

- Indications: Acute ischemic stroke after r/o intracranial **hemorrhage**, Initial onset of Sx ≤ **4.5** hours, Age ≥ **18** yo.
- Complications: Bleeding, Intracranial and extracranial hemorrhage, Angioedema.
- Exclusion criteria
  - Current conditions: Intracranial bleeding, Active internal bleeding or bleeding diathesis, HTN> 185/110 mm Hg, Anticoagulation (prolonged PTT or INR > 1.7), Low platelet count, Hypoglycemia < 50 mg/dL or hyperglycemia > 400 mg/dL, Minor stroke or TIA.
  - Preexisting conditions: Previous intracranial hemorrhage, Head trauma or ischemic stroke (within the past 3 m), Recent intracranial or intraspinal surgery, Arterial puncture at a noncompressible site (within the past 7 d), Intracranial neoplasm, AV malformation, or aneurysm.

B. Intra-arterial thrombolysis: intra-arterial (not IV) administration of a thrombolytic agent (prourokinase)[53] - Indication: MCA stroke pts with onset of Sx < 6 h who are not eligible for IV thrombolytic therapy.

C. Mechanical thrombectomy: physical retrieval of the thrombus via a catheter (usually femoral A.) - Indications: proximal large artery occlusion in anterior cerebral circulation (usually in addition to intravenous thrombolytic therapy)

BP management

- High BP is generally tolerated in acute ischemia (permissive HTN; To maintain cerebral perfusion, which depends on the MAP).
- For pts with severe HTN (> 220 mm Hg / > 120 mm Hg)
  - Pts who do not undergo thrombolytic therapy: Reduce BP by ~ 15% within the first 24 h of stroke onset.
  - Pts who undergo thrombolytic therapy: Reduce BP to ≤ 185 mm Hg / ≤ 100 mm Hg prior to administering tPA.

Supportive care "Mentioned above"

Other: prevent post-stroke complications, secondary prevention, early rehabilitation (physiotherapy, occupational and speech therapy) and mobilization.

Prevention

- **Primary**: management of modifiable RF to decrease the likelihood of having a first stroke: healthy diet, physical activity, weight loss, smoking cessation, medical management of RF (HTN, DM, Afib, dyslipidemia)
- **Secondary**:
  - Antiplatelet therapy (aspirin/clopidogrel): Start 24-48 h after Sx onset of ischemic stroke. CI for 24 h after thrombolytics.
  - Medical management of RF: **HTN** (lifestyle modifications, antihypertensives), Afib (anticoagulation "e.g., warfarin"), DM (lifestyle, glycemic control), Hyperlipidemia (lifestyle, statin therapy), Thrombophilia (anticoagulation).
  - Medical management and/or carotid endarterectomy for carotid artery stenosis.

[52] tPA binds to fibrin in the clot and converts plasminogen to plasmin, which initiates local thrombolysis.
[53] Urokinase converts plasminogen to plasmin, resulting in thrombolysis. However, it works via a slightly different biochemical mechanism than tPA. Localized thrombolysis reduces the risk of bleeding that is associated with systemic IV thrombolysis.

Subtypes and variants (EXTRA)

★ **Transient ischemic attack** (TIA): temporary, focal cerebral ischemia that results in neurologic deficits without acute infarction or permanent loss of function (previously defined as lasting < 24 hours).[54]

- **Clinical features**: Acute transient focal neurologic symptoms (depend on the affected territory). Typically, symptoms last < 1 hour.
- **Dx**: diffusion-weighted MRI to identify areas of ischemia and r/o infarction.
- **Rx**: treatment of underlying etiology (e.g., management of HTN, DM, carotid artery disease, Afib)

★ **Lacunar infarct:** noncortical infarcts characterized by the absence of cortical signs (e.g., no aphasia, hemianopsia, agnosia, apraxia).

- **Etiology:** Most common - chronic hypertensive vasculopathy → lipohyalinosis of the small vessels → occlusion of small, penetrating arteries (e.g., lenticulostriate artery)[55] → lacunar stroke resulting in specific lacunar syndromes.[56]
- **Clinical features:** Acute transient focal neurologic symptoms that often have a stuttering course (Sx depend on the affected territory).[57]
- **Dx**: diffusion-weighted MRI.
- **Rx**: same as other ischemic strokes.

★ **Watershed infarct:** border-zone infarct in the region b/w the territory of 2 major arteries that supply the brain.

- **Etiology**: sudden decrease in BP or cessation of blood flow through both vessels → ischemia in the susceptible region between two vascular territories:
  - Cortical border zones: territories b/w the ACA and MCA and b/w MCA and PCA.
  - Internal border zones: territories b/w the superficial and deep branches of the MCA.
- **Clinical features**:
  - Signs of systemic hypoperfusion (e.g., tachycardia, low blood pressure, pallor, sweating).
  - Diffuse neurologic deterioration.
  - Bilateral visual loss (cortical blindness).
  - Proximal limb weakness with sparing of the face, hands, and feet.

[54] Definition has changed recently and the duration of Sx has been de-emphasized. The most important defining factor is the absence of infarction.
[55] The penetrating arteries supply the subcortical regions of the brain (internal capsule, pons, thalamus, putamen, and caudate).
[56] Less common: Cardioembolic event, Microatheroma formation, Microbleed (rare). - RF: DM, HTN (The abrupt change in caliber from the large arteries to the small penetrating arteries makes the latter particularly sensitive to arterial hypertension.).
[57] Commonly affected areas: Internal capsule, corona radiata, Pons, Basal ganglia (striatum, putamen, globus pallidus, thalamus, caudate).

ICH (Intracerebral hemorrhage)

Etiology: Spontaneous[58], traumatic (TBI).

Clinical features

- Headache: absent in small hemorrhages, most common in cerebellar and lobar hemorrhages.
- Focal neurologic SSx may occur, depending on the location and size of the hemorrhage.
- Course:
  - Progress gradually over minutes to a few hours.
  - Focal deficits worsen with expansion of the hematoma.
  - Late: Sx of increased ICP → N/V, confusion and LOC, bradycardia, fixed pupils.

Diagnostics

A. Initial evaluation

- Immediate **noncontrast head CT** : Best initial test
  - Expected findings: Acute → **hyperdense lesion** with **hypodense perifocal edema**. Hyperacute (hypodense lesion) - Chronic (may appear as hypodense). Midline shift and/or mass effect → suggest impending herniation.
- Diffusion-weighted MRI: More sensitive than head CT
  - Expected findings: Hyperacute → T1 (hypointense), T2 (hyperintense). Acute → hypointense.

B. Subsequent evaluation

- Laboratory: CBC (platelet), coagulation parameters, blood glucose. troponin, toxicology screen.
- Angiography (CTA and/or MRA) to identify the source of the bleeding if the patient does not have any risk factors.

Treatment

A. Medical therapy:

a. Reverse anticoagulation.

b. BP management

- SBP > 220 mm Hg → rapidly lower to 140–160 mm Hg, SBP 150-220 mm Hg → rapidly lower to 140 mm Hg.
- Recommended agents: IV labetalol, nicardipine, enalapril, and/or hydralazine

c. Maintain euvolemia, normoglycemia, avoid/treat hyponatremia.

d. If there are signs of elevated ICP (e.g., Cushing triad): consider intubation with hyperventilation, head elevation (30°), IV mannitol, removal of CSF (LP).

B. Surgical therapy

a. Craniotomy and clot evacuation (Indications)[59].

b. If hydrocephalus is present: ventricular drain, serial LPs, or permanent VP shunt may be indicated.

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[58] HTN (most common), AVM (most common in children), Cerebral amyloid angiopathy (most common in > 60 yo). Vasculitis (giant cell arteritis), Neoplasms (meningioma), Ischemic stroke (due to reperfusion injury), CNS infections (HSV), Septic emboli, Coagulopathy (hemophilia, anticoagulant use), Stimulant use (cocaine and amphetamines).

[59] Signs of brain herniation (e.g. cushing triad), brainstem compression, obstructive hydrocephalus, cerebellar hemorrhage w/ progressive neurological deterioration, cerebellar hemorrhage extension > 3 cm. Pts w/ hemorrhage in the basal ganglia or internal capsule should not undergo surgical clot removal.

SAH (subarachnoid hemorrhage)

Etiology: traumatic, non-traumatic (ruptured aneurysm in circle of willis, ruptured AVM).

RF: alcohol, smoking, HTN, FHx.

Clinical features

1. Thunderclap headache: Sudden, severely painful, holocephalic, radiates to the neck and back and may present with opisthotonus.
2. Meningeal signs : Neck stiffness, photophobia, N/V, Kernig & Brudzinski signs.
3. Nonspecific signs: Impaired consciousness (somnolent to comatose) , fever, sweating, hemodynamic instability.
4. Signs due to mass effect: CNs disorders, altered mental status (e.g., delirium), focal neurologic deficits (affected vessel or region), seizures.
5. Prodromal symptoms due to sentinel leak (a "warning leak")[60]: Sudden, severe headache, transient diplopia.

Diagnostics

A. Initial evaluation
   a. Immediate **noncontrast head CT** → blood in subarachnoid space (**hyperdensity**).
   b. **LP** → if CT inconclusive nut suspicion is still high → ↑↑ RBC count (red discoloration), ↑ Protein (gamma globulin), ↑ Or normal opening pressure, Xanthochromia[61], ↑ WBCs, normal glucose.

B. Subsequent evaluation:
Angiography → if CT and lumbar puncture are negative but clinical suspicion for SAH is still high and/or to identify the source of ongoing bleeding (prior to intervention) → Digital subtraction angiography (DSA), CTA.

C. Additional testing to consider: CXR (r/o pulmonary complications), Serum troponin in all patients (predicts neurological complications and outcome), coagulation parameters (to evaluate for coagulopathy), ECG (r/o MI).

Treatment

A. Medical therapy:
   a. Reverse anticoagulation.
   b. BP management: Target SBP < 160 mm Hg is reasonable to prevent rebleeding. Recommended agents (BB, CCB).
   c. Prevent vasospasm in all patients → CCB (oral nimodipine).
   d. Maintain euvolemia & normoglycemia, avoid/treat hyponatremia. Seizure prophylaxis.[62]
   e. If a patient has elevated ICP: consider intubation with hyperventilation, head elevation (30°), IV mannitol.

B. Surgical therapy: Should be performed as early as possible to prevent rebleeding !
   a. Definitive treatment options for aneurysmal SAH: Surgical clipping, endovascular coiling.[63]
   b. If the patient has hydrocephalus: ventricular drain, serial LPs, or permanent VP shunt may become necessary.

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[60] Likely due to low-grade leak of blood into the subarachnoid space → thrombus formation → fibrinolysis → hemorrhage.
[61] The yellowish discoloration of CSF is due to the presence of xanthematin, a yellow pigment derived from hematin that is released when RBCs break down. remember that LP results can be falsely -ve in the first few Hs when xanthochromia has not yet developed.
[62] Consider seizure prophylaxis in the immediate posthemorrhagic period. Consider long-term anticonvulsants in patients with a high risk for seizures (e.g., with a history of prior seizures).
[63] **Clipping** → Following a craniotomy, the neck of an aneurysm is surgically occluded with the help of metal clips. Treatment of choice but more invasive than coiling. **Coiling** → Platinum coils are placed into the aneurysm to induce thrombotic occlusion of the aneurysm. Less invasive than clipping but higher risk of recurrent bleeding. Consider for poor surgical candidates.

MS (Multiple Sclerosis)

- A chronic, degenerative disease of the CNS that is caused by an immune-mediated inflammatory process.
- This process results in the demyelination of white matter in the brain and spinal cord. Impaired vision (due to retrobulbar neuritis) is usually the first manifestation of the disease.

Clinical features

1. **Optic neuritis** (most often the earliest manifestation): impaired vision and color blindness.
2. Internuclear ophthalmoplegia (INO) as a result of a lesion in the medial longitudinal fasciculus (MLF[64]).[65]
3. **Demyelination of spinal cord tracts:**
   a. Lhermitte's sign: a shooting electric sensation that travels down the spine when flexing the neck.
   b. Absent abdominal reflex.
   c. Pyramidal tract lesion: UMN weakness → spasticity, hyperreflexia, and a positive Babinski's sign.
   d. Involvement of the dorsal spinal column: loss of vibration and fine touch sensations, numbness, paresthesias, sensory ataxia.
4. **Cerebellar involvement** → Charcot's neurological triad (Scanning speech, Nystagmus, Intention tremors).
5. **Other**: CNs palsies, autonomic dysfunction (bowel and bladder disorders, impaired sexual activity), change in mental state (memory deficits, impaired concentration, and/or depression),

★ Uhthoff's phenomenon: reversible exacerbation of neurological Sx after physical exertion, warm bath or fever.[66]

Diagnostics

1. Plain **MRI** (brain and spine): investigation of choice
   - Multiple sclerotic plaques (most commonly seen in periventricular white matter) with finger-like radial extensions (Dawson's fingers).
   - Contrast MRI (w/ gadolinium): enhancement of active lesion during and up to 6 weeks after the exacerbation.

2. Electrophysiology: slowed nerve **conduction** → increased **latency** of visually evoked potentials (VEP).

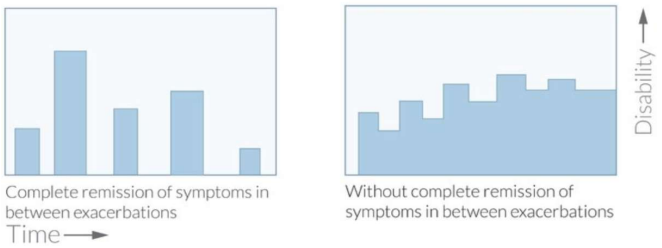
3. LP for CSF examination → if MRI is inconclusive → Findings: Lymphocytic pleocytosis. Oligoclonal bands (↑ production of IgG subfractions).

[64] MLF, which is located in the midbrain, enables conjugate eye movements by connecting the abducens nucleus (responsible for eye abduction) on contralateral side with the oculomotor nucleus (responsible for eye adduction, among other movements) on the ipsilateral side.
[65] Ipsilateral medial rectus weakness but an intact convergence reflex. Disconjugate, lateral gaze nystagmus in the contralateral eye.
[66] Impulse conduction is dependent on temperature. ↑ in body temperature presumably worsens impulse conduction in demyelinated nerves.

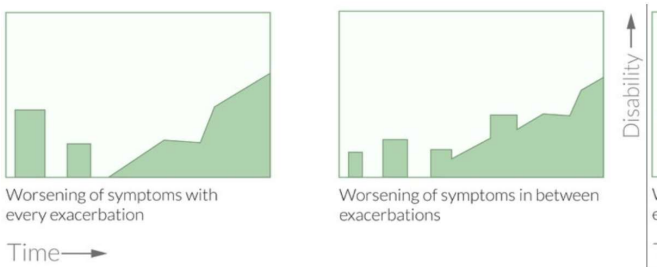
Mc Donald criteria		
ATTACKS	**LESIONS**	**ADDITIONAL CRITERIA FOR DIAGNOSIS MS**
≥ 2	**≥ 2**	**None**. Clinical evidence alone will suffice
≥ 2	**1**	Dissemination in **space** on MR (or await further clinical attack implicating a different CNS site).
1	**2**	Dissemination in **time** on MR (or await further clinical attack implicating a different CNS site).
1	**1**	Dissemination in **space** and **time** (or await further clinical attack implicating a different CNS site).
0 attack Progression from onset		1 year of disease progression (retro- or prospective) **AND** at least 2 out of 3 criteria: 1. Dissemination in **space** in the **brain.** 2. Dissemination in **space** in the **spinal cord** based on 2 or more T2 lesions. 3. Positive **CSF**.

Clinical course

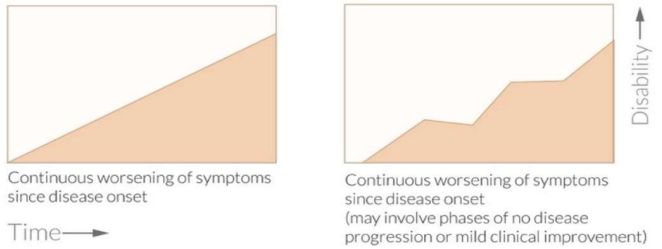
Relapsing-remitting MS (RR-MS): Exacerbations occur. Symptoms remit almost completely between exacerbations. **90%**



Secondary progressive MS (SP-MS): Exacerbations occur. Continuous worsening of Sx in between exacerbations.



Primary progressive MS (PP-M): No exacerbations. Continuous worsening of Sx from the very onset of the disease.



★ Definition of relapse/exacerbation: **new** symptoms or **significant worsening** of existing symptoms, both of which last at least 24 hours and are preceded by at least 30 days of relative clinical stability.

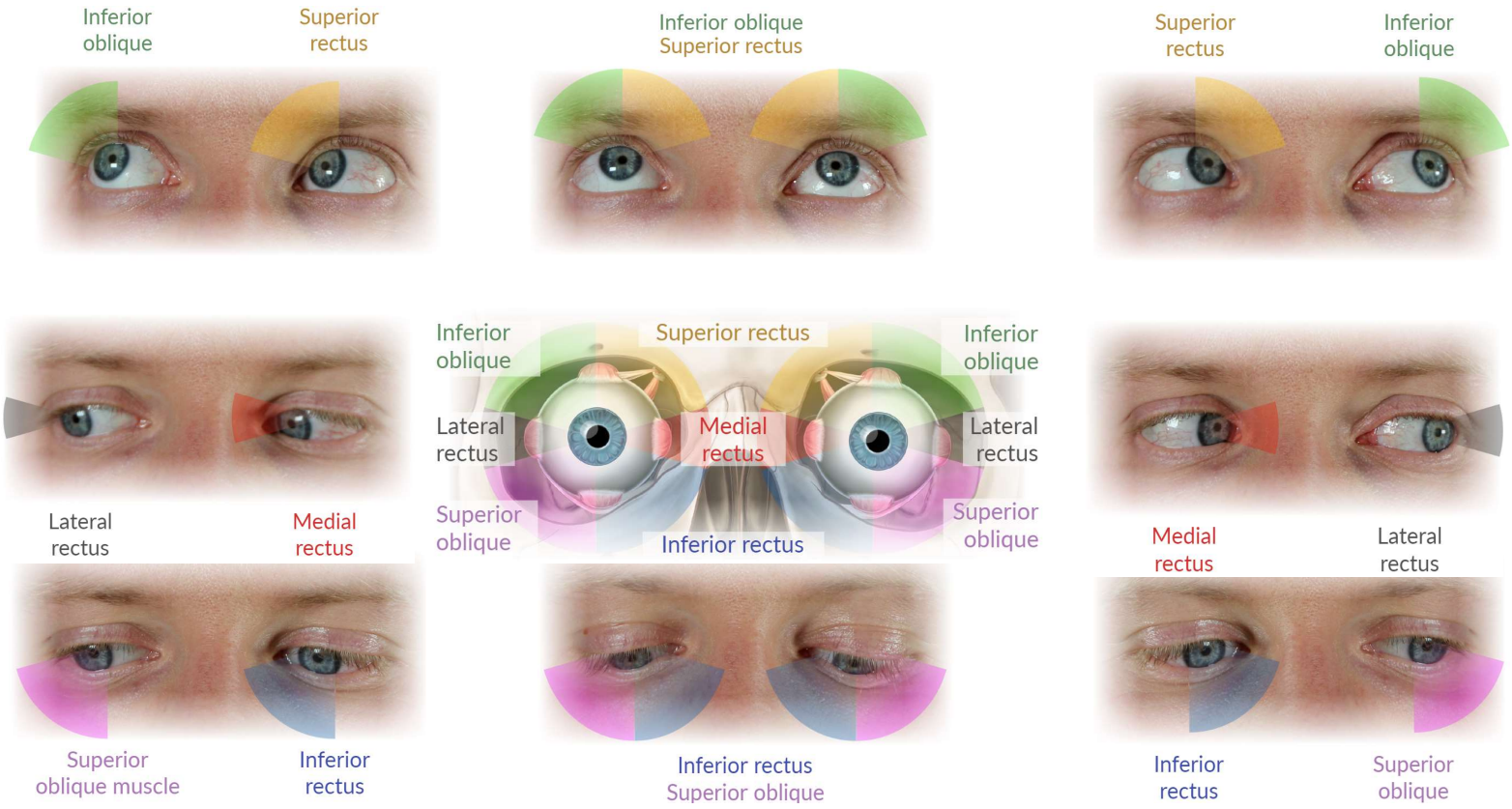
★ If two episodes appear within 30 days of each other, they are considered as parts of one exacerbation.

Treatment

- The goal is to begin treatment as early as possible to treat the primary exacerbation, prevent further exacerbations, and slow down the disease process.
- Therapeutic strategies include
  - Escalation therapy: Patients who do not respond to first-line therapy with disease-modifying drugs (DMDs), are switched to second-line DMDs.
  - Induction therapy: Patients with severe disease activity at onset, first receive strong immunosuppressant drugs , followed by long-term maintenance therapy with DMDs.

Summary of **MS** therapy			
Indication	**RR-MS**	**SP-MS**	**PP-MS**
Acute exacerbation	First line: high-dose glucocorticoids for 3–5 days (methylprednisolone 500–1000 mg/d IV or PO).[67] Second line: plasmapheresis.		No exacerbations present
Prevention of exacerbations	First line: Glatiramer acetate, Interferon therapy (IFN-β). Second line: natalizumab	- Interferon therapy (IFN-β). - IV glucocorticoid and/or cyclophosphamide pulses. - IV methotrexate.	- There is no established therapy for PP-MS. -Supportive therapy is essential.

[67] If Sx decreases: End glucocorticoid by slowly tapering the dose. Prophylaxis against SE → PPIs to prevent gastritis and LMWH (thromboprophylaxis).

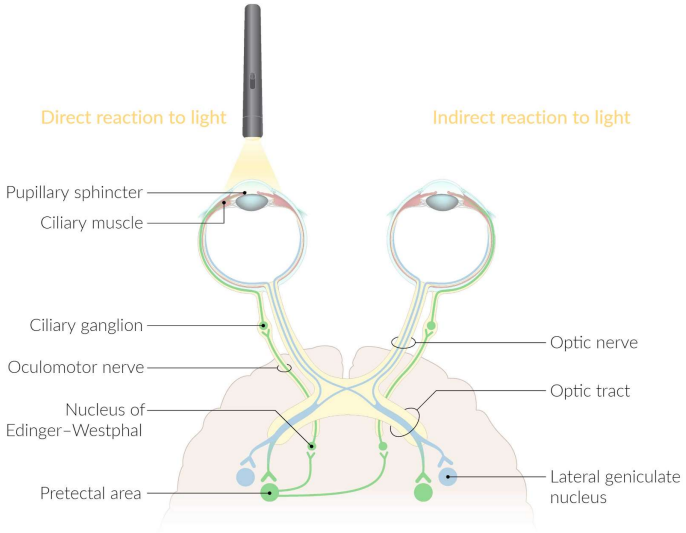


Pupillary light reflex

A. The **afferent** pathway (blue tract) is initiated when light hits the retina: Retinal photoreceptors → ipsilateral optic nerve → nuclei of bilateral pretectal areas (nasal fibers of the optic nerve cross to the contralateral side at the optic chiasma)

B. The efferent pathway (green tract) transmits neural impulses to the iris sphincter muscles: Nuclei of pretectal area → bilateral Edinger Westphal nuclei (parasympathetic preganglionic nucleus of the oculomotor nerve) → bilateral oculomotor nerves (synapse at the ciliary ganglion) → bilateral iris sphincter muscles → bilateral pupillary constriction.

C. Shining a light into one eye causes constriction of the ipsilateral pupil (direct pupillary reflex) as well as that of the contralateral pupil (indirect or consensual pupillary reflex).



INO (Internuclear ophthalmoplegia)

- Damage to the medial longitudinal fasciculus (the connection between the abducens nucleus, CN VI, on one side and the oculomotor nucleus, CN III, on the other), which leads to impaired lateral gaze.
- Manifests primarily with impaired adduction of the eye ipsilateral to the lesion (ipsilateral to the MLF lesion).
- Depending on which eye is affected, INO is classified as left, right, or bilateral.

Pathophysiology

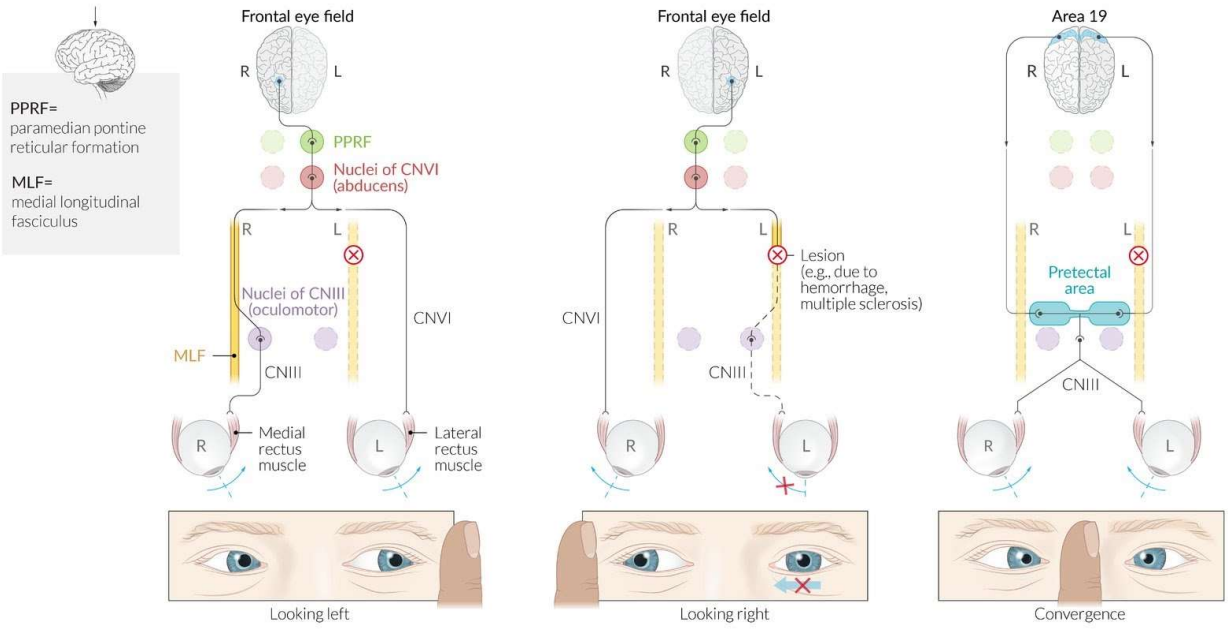
- Normally, CN VI receives a signal from the ipsilateral paramedian pontine reticular formation and sends a signal to the contralateral CN III via the MLF.
  - Activation of the CN VI ipsilateral to the lesion → activation of the ipsilateral lateral rectus → abduction of the ipsilateral eye.
  - Activation of the CN III contralateral to the lesion → activation of the contralateral medial rectus → adduction of the contralateral eye
- Disruption of the MLF fibers linking the CN VI ipsilateral and the CN III contralateral to the lesion → failure of signal transmission from CN VI to CN III → the ipsilateral lateral rectus is activated while the contralateral medial rectus is not → abduction of the ipsilateral eye, no adduction of contralateral eye
- Firing from CN VI which fails to be transmitted to CN III is instead partially transmitted to the lateral rectus ipsilateral to the lesion → nystagmus of the ipsilateral abducting eye

Clinical findings

- Adduction limited in horizontal eye movements and retained in convergence reaction.
- Dissociated nystagmus: gaze to the opposite side → nystagmus of the abducted contralateral eye

INO is characterized by **I**mpaired adduction of the eye ipsilateral to the lesion and **N**ystagmus on the **O**pposite side!

A horizontal gaze palsy, due to a lesion in the left MLF. The left gaze remains unaffected, while the right gaze shows an inability to adduct the ipsilateral eye (horizontal gaze palsy). Convergence may be preserved in pts, due to the innate and primitive ability to converge on near-targets. This pathway is thought to originate from the pretectal nuclei; it is part of the subcortical visual system involved in mediating nonconscious behavioral responses to acute changes in light.



Isolated **oculomotor** nerve palsy

Clinical features:

1. **Paralytic squint**: Adduction weakness. Affected eye looks outwards (exotropia) and downwards (hypotropia).[68]
2. **Ptosis**.[69]
3. **Horizontal diplopia** that is worse when the head is turned away from the side of the nerve palsy
4. **Pupillary** involvement: Compressive lesions → a non-reactive, dilated pupil, Ischemic microangiopathy → typically sparing of the pupil.[70]

> 🧠 With an isolated ocuLOVEmotor nerve palsy, nobody loves you when you are down and out (the pupil points outwards and downwards)!

Trochlear nerve palsy (CN.IV)

Clinical features:

1. **Extorsion**: inability to depress and adduct simultaneously (pupil shoots upward during attempt to adduct).
2. **Diplopia** (Vertical or oblique diplopia):
   a. Exacerbated on downgaze (e.g., reading) away from side of affected muscle.
   b. Worsens when patient turns the head towards the paralyzed muscle → head tilt to opposite side of lesion.
3. **Mild esotropia**.[71]

Abducens nerve palsy (CN.VI)

1. **Horizontal diplopia** that worsens when looking at distant objects.
2. **Esotropia**: medial deviation of the affected eye at primary gaze.
3. Inability to **abduct** the eye (affected individuals will rotate the head to look to the side).

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[68] This type of squint is only seen in isolated CN.III palsy and occurs because of the action of the LR muscle and the SO muscle.
[69] occurs because the levator palpebrae superioris, which elevates the eyelid, is innervated by the superior division of the oculomotor nerve.
[70] The pial vessels, which supply the parasympathetic fibers, are located superficially and are the first to be affected. Microangiopathy typically involves the vasa nervorum within CN.III, while the pial blood vessels which supply the superficial parasympathetic fibers are spared.
[71] Paralysis of the superior oblique leads to mildly impaired abduction of the eyeball, causing transient inappropriate adduction of the affected eye.

Facial palsy

Def: A neurological in which function of CN.VII is partially or completely lost.

Etiology: Idiopathic (50%, AKA Bell's palsy) or secondary → stroke, trauma (edema). Infection (Herpes zoster, HSV, HIV), tumors, DM, GBS.

Types: Central[72] or peripheral[73].

★ Facial nerve has UMN in the cortex, and LMN in the brainstem (Pons). Upper face has ipsilateral and contralateral supply (dual), while lower face has only contralateral supply (single) → UMNL will cause lower face palsy, while LMNL will cause facial paralysis.[74]

Facial nerve:

A. Motor: orbicularis oculi and frontalis (eyelid closure, frown, forehead wrinkles), orbicularis oris (smile).
B. Sensory: stapedius muscle (control voice vibration), taste of anterior ⅔ of the tongue.
C. Autonomic: lacrimation (great petrosal N), salivation (chorda tympani).

If CN.VII is injured:

1. Facial muscles → upper (lagophthalmos[75], forehead is not wrinkled, can't raise eyebrow and eyelid drooping), lower (lower lip drooping and loss of nasolabial fold).
2. Painful sensation around or behind ear or numbness of one side of the face, taste disorders, hyperacusis.
3. Lacrimal, submandibular, sublingual and nasal mucosa glands (dryness).

★ Sequence of branches (proximo-distal): Greater petrosal (dry eye "lacrimation") > nerve of stapedius (hyperacusis) > chorda tympani[76] (dry mouth "salivary glands", taste disorder "A ⅔ of tounge").
★ Lesion proximal to chorda tympani → dry mouth, taste disorder, hyperacusis and dry eye.
★ Lesion proximal stapedius nerve → hyperacusis and dry eye.
★ Lesion proximal to greater petrosal → dry eye.

Dx: Hx (Sx onset and duration, recent infections, and outdoor trips) → PEx (perform facial movements "frown, whistle, inflated cheeks, smile, show teeth/grimace, close eyes tightly, blink").

Rx: Prednisone, Valacyclovir for 1 week and eye care by artificial tears (in severe cases), surgical decompression or nerve repair (if traumatic).

[72] Unilateral lesion b/w cortex and brainstem nuclei → muscles of the eyelids and forehead are still supplied by input from the other other side → function is preserved.
[73] Unilateral lesion between nuclei and muscles → no input to the ipsilatera;l eyelid and forehead muscles → paralysis.
[74] The muscles responsible for eyelid and forehead movements are innervated by fibers from both sides. The lower facial muscles are only innervated by fibers from the contralateral hemisphere (via ipsilateral nuclei and the ipsilateral peripheral nerve) → paralyzed in both central and peripheral facial palsy.
[75] The patient cannot properly and fully close the eyes (due to paralysis of the orbicularis oculi muscle). Therefore, there is a risk of ocular dehydration and subsequent keratitis.
[76] A nerve arises from the mastoid segment of the facial nerve, carrying afferent special sensation from the anterior ⅔ of the tongue via the lingual nerve, as well as efferent parasympathetic secretomotor innervation to the submandibular and sublingual glands.

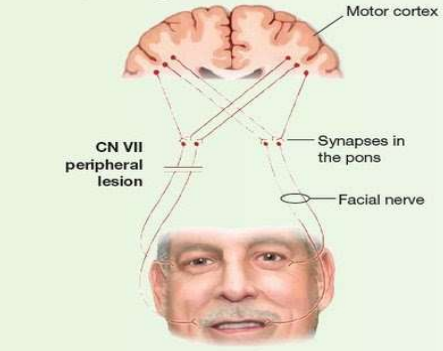
Types of Facial Paralysis

Facial weakness or paralysis may result either from (1) a peripheral lesion of CN VII, the facial nerve, anywhere from its origin in the pons to its periphery in the face, or (2) a central lesion involving the upper motor neuron system between the cortex and the pons. A peripheral lesion of CN VII, exemplified here by a Bell's palsy, is compared with a central lesion, exemplified by a left hemispheric cerebrovascular accident. These can be distinguished by their different effects on the upper part of the face.

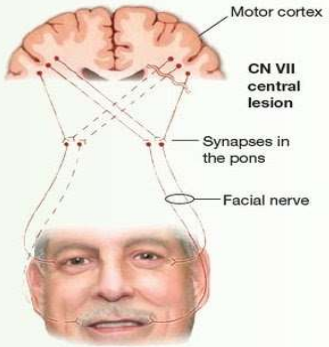
The lower part of the face normally is controlled by upper motor neurons located on only one side of the cortex—the opposite side. *Left hemispheric damage to these pathways, as in a stroke, paralyzes the right lower face.* The upper face, however, is controlled by pathways from both sides of the cortex. Even though the upper motor neurons on the left are destroyed, others on the right remain, and the right upper face continues to function fairly well.

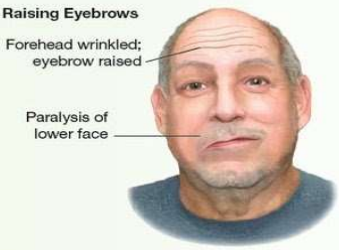
CN VII—Peripheral Lesion

Peripheral nerve damage to CN VII paralyzes the entire right side of the face, including the forehead.



CN VII—Central Lesion





Headache

Approach to management

1. Check vital signs → Perform focused history and examination.
2. If red flags[77] are present: Obtain brain imaging (either CT or MRI brain with and/or without contrast) based on the red flag symptoms. Perform further targeted diagnostics.
3. If no red flags are present and suspicion for life-threatening causes is low: Perform a detailed history and clinical exam. Consider whether further diagnostic testing is necessary.
4. Provide supportive care → Identify and treat the underlying cause.

Life-threatening conditions:

- Intracranial hemorrhage: SAH, epidural hemorrhage, intracerebral hemorrhage.
- CNS infection: meningitis, encephalitis, brain abscess, subdural empyema. Conditions causing increased ICP.
- Hypertensive emergency, internal carotid artery dissection, vertebral artery dissection, Ischemic stroke. CO poisoning, Hypoglycemia, Cerebral venous sinus thrombosis. Pre-eclampsia or eclampsia, pituitary apoplexy.
- Non-life-threatening conditions requiring urgent attention: Acute angle-closure glaucoma, giant cell arteritis.

Primary headache: a headache that is not caused by another underlying condition: Includes migraine headache, tension headache, trigeminal autonomic cephalalgias (e.g., cluster headache).

Secondary headache: caused by another underlying condition (e.g., trauma, space-occupying lesion).

DDx

A. Primary headache: Migraine, Tension-type headache, Cluster headaches.

B. Secondary headache:

- Bleeding: Epidural, subdural, subarachnoid or Intracerebral hemorrhage
- Vascular: Cerebral venous thrombosis, pituitary apoplexy, stroke, TIA, aneurysms, carotid artery dissection, vertebral artery dissection.
- Autoimmune: Temporal arteritis.
- Drug/toxin-related: Alcohol use, alcohol/caffeine/opioid withdrawal, sympathomimetics (e.g., nicotine), medication overuse headache, nitroglycerin, carbon monoxide poisoning
- Infectious: Intracranial infections (meningitis, encephalitis, brain abscess, subdural empyema, aseptic meningitis, toxoplasmosis), Systemic infections (e.g., influenza).
- Other: Increased ICP, decreased ICP(e.g., post-LP headache), Glaucoma, Brain tumors, Trigeminal neuralgia, Hypoxia and/or hypercapnia (e.g., high-altitude headache), HTN, Hypoglycemia, Hypothyroidism, Iridocyclitis, Refractive errors, Rhinosinusitis, Post-ictal headache, Cervicogenic headache (e.g., cervical disc disease), TMJ disorders, Post-herpetic neuralgia, Optic neuritis. Psychiatric (Somatization disorder, Psychotic disorder).

[77] Sudden-onset severe headache ("thunderclap headache", can be SAH or intracranial hemorrhage), Fever, Focal neurological deficits (SAH, ischemic stroke, neoplasm, ICH), New headache at age > 50 (neoplasm, giant cell arteritis), Progressively worsening headache (neoplasm, meningoencephalopathy), Immunodeficiency (especially HIV → RF for meningoencephalitis, neoplasm, cerebral abscess, toxoplasmosis, and cerebral lymphoma), Seizures, Meningeal signs (SAH, infection), Psychiatric symptoms, Failure to respond to analgesics, "Worst headache of my life" (vertebral artery dissection, acute angle closure glaucoma, hypertensive emergency, SAH), Visual deficits (acute angle-closure glaucoma, giant cell arteritis), Pregnancy or postpartum period (pituitary apoplexy, pre-eclampsia, eclampsia), Signs of increased ICP (e.g., papilledema → cerebral abscess, meningitis, neoplasm, hemorrhage), Confusion or impaired LOC (infection, ischemic stroke).

	Tension	Migraine [78]	Cluster
Duration	30 minutes to a couple of days	4–72 hours	30–180 m. Short, recurring attacks
Frequency	Occasionally to daily. Episodic or chronic	Occasionally to several times a month.	1–3 episodes every 24 hours. Usually occur in a cyclical pattern (clusters).
Localization	Holocephalic or bifrontal	60% are unilateral.	Mostly unilateral
Character	Dull, non-pulsating, band-like or vise-like pain	Pulsating, boring/hammering pain	Localized to the periorbital and/or temporal region
Intensity	Mild to moderate	Moderate to severe	Severe, agonizing pain
Additional symptoms	No autonomic Sx (N/V, phonophobia, or photophobia). Tightness in the posterior neck muscles. Pericranial tenderness.	N/V, Hyperacusis, Photophobia, Phonophobia, Preceding aura, Prodrome.	Ipsilateral autonomic symptoms: conjunctival injection and/or lacrimation, rhinorrhea and nasal congestion. Partial Horner syndrome: ptosis and miosis, but no anhidrosis.
Triggers/ exacerbating factors	**Tension**: Stress, Lack of sleep, fatigue. Routine activities (climbing stairs) do not exacerbate Sx. **Migraine**: Stress. Fluctuation in hormone levels: OCP, menstruation. Certain types of food (e.g., those containing tyramines or nitrates such as processed meat, chocolate, cheese). Exacerbated by exertion. Improved with sleeping/darkness. **Cluster**: Alcohol		

Note: Headache and seizures are not included in this file.
Best wishes 💪😎
Adel Al Shihri ^-^

[78] The typical migraine headache is "**POUND**": **p**ulsatile, **o**ne-day duration, **u**nilateral, **n**ausea, **d**isabling intensity.