

HIGH-YIELD SYSTEMS

Neurology and Special Senses

“We are all now connected by the Internet, like neurons in a giant brain.”
—Stephen Hawking

“Exactly how [the brain] operates remains one of the biggest unsolved mysteries, and it seems the more we probe its secrets, the more surprises we find.”

—Neil deGrasse Tyson

“It’s not enough to be nice in life. You’ve got to have nerve.”
—Georgia O’Keeffe

“I not only use all the brains that I have, but all that I can borrow.”
—Woodrow Wilson

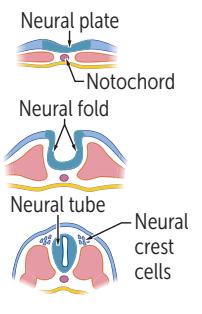
“The chief function of the body is to carry the brain around.”
—Thomas Edison

“I opened two gifts this morning. They were my eyes.”
—Zig Ziglar

Understand the difference between the findings and underlying anatomy of upper motor neuron and lower motor neuron lesions. Know the major motor, sensory, cerebellar, and visual pathways and their respective locations in the CNS. Connect key neurological associations with certain pathologies (eg, cerebellar lesions, stroke manifestations, Brown-Séquard syndrome). Recognize common findings on MRI/CT (eg, ischemic and hemorrhagic stroke) and on neuropathology (eg, neurofibrillary tangles and Lewy bodies). High-yield medications include those used to treat epilepsy, Parkinson disease, migraine, and pain (eg, opioids).

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▶ NEUROLOGY—EMBRYOLOGY

Neural development

Notochord (precursor to nucleus pulposus of intervertebral discs) induces ectoderm to form neuroectoderm → neural plate.

Neural plate gives rise to neural tube and neural crest cells.

Lateral walls of neural tube are divided into alar and basal plates.

Alar plate (dorsal): sensory; induced by bone morphogenetic proteins (BMPs)

Basal plate (ventral): motor; induced by sonic hedgehog (SHH)

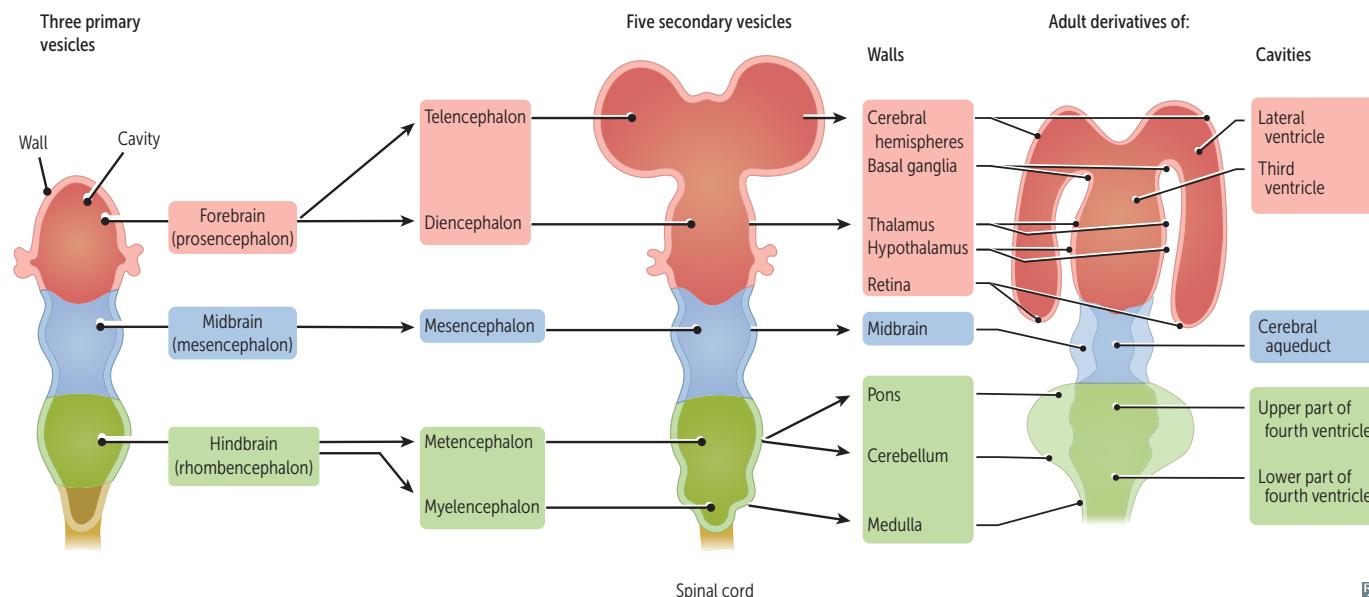
Homeobox (HOX) genes regulate neural tube segmentation, cranial-caudal differentiation.

Mutations → syndactyly (limbs), hypospadias (urogenital).

Same orientation as spinal cord

Regionalization of neural tube

Telencephalon is the 1st part. Diencephalon is the 2nd part. The rest are arranged alphabetically: mesencephalon, metencephalon, myelencephalon.

**Central and peripheral nervous systems origins**

Neuroepithelia in neural tube—CNS neurons, CNS glial cells (astrocytes, oligodendrocytes, ependymal cells).

Neural crest—PNS neurons (dorsal root ganglia, autonomic ganglia [sympathetic, parasympathetic, enteric]), PNS glial cells (Schwann cells, satellite cells), adrenal medulla.

Mesoderm—microglia (specialized macrophages).

Neural tube defects

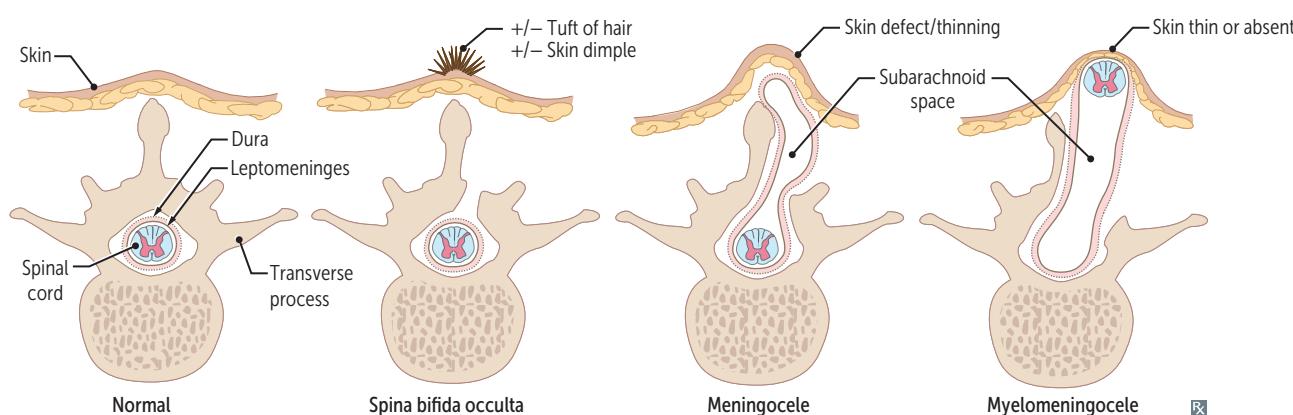
Failure of the neural tube to close completely by week 4 of development, associated with maternal folate deficiency or exposure to teratogens such as valproate and carbamazepine during pregnancy. Diagnosis: ultrasound, maternal serum AFP and/or amniotic fluid AChE (\uparrow in open NTDs).

Spinal dysraphism

Spina bifida occulta	Closed NTD. Failure of caudal neural tube to close, but no herniation. Dura is intact. Usually seen at lower vertebral levels. Associated with tuft of hair or skin dimple at level of bony defect.
Meningocele	Open NTD. Meninges (but no neural tissue) herniate through bony defect.
Myelomeningocele	Open NTD. Meninges and neural tissue (eg, cauda equina) herniate through bony defect.
Myeloschisis	Open NTD. Exposed, unfused neural tissue without skin/meningeal covering.

Cranial dysraphism

Anencephaly	Open NTD. Failure of rostral neuropore to close \rightarrow no forebrain, open calvarium. Often presents with polyhydramnios (\downarrow fetal swallowing due to lack of neural control).
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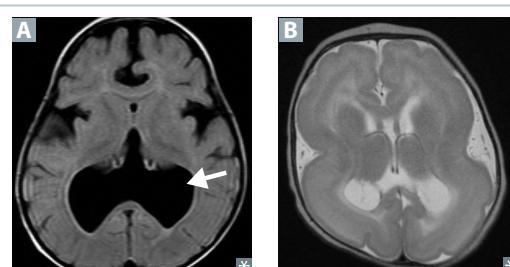
**Brain malformations**

Often incompatible with postnatal life. Survivors may be profoundly disabled.

Holoprosencephaly

Failure of forebrain (prosencephalon) to divide into 2 cerebral hemispheres; developmental field defect usually occurring at weeks 3–4 of development. Associated with SHH mutations. May be seen in Patau syndrome (trisomy 13), fetal alcohol syndrome.

Presents with midline defects: monoventricle **A**, fused basal ganglia, cleft lip/palate, hypotelorism, cyclopia, proboscis. \uparrow risk for pituitary dysfunction (eg, diabetes insipidus).

**Lissencephaly**

Failure of neuronal migration \rightarrow smooth brain surface that lacks sulci and gyri **B**.

Presents with dysphagia, seizures, microcephaly, facial anomalies.

Posterior fossa malformations**Chiari I malformation**

Downward displacement of cerebellar tonsils through foramen magnum (1 structure) **A**. Usually asymptomatic in childhood, manifests in adulthood with headaches and cerebellar symptoms. Associated with spinal cord cavitations (eg, syringomyelia).

Chiari II malformation

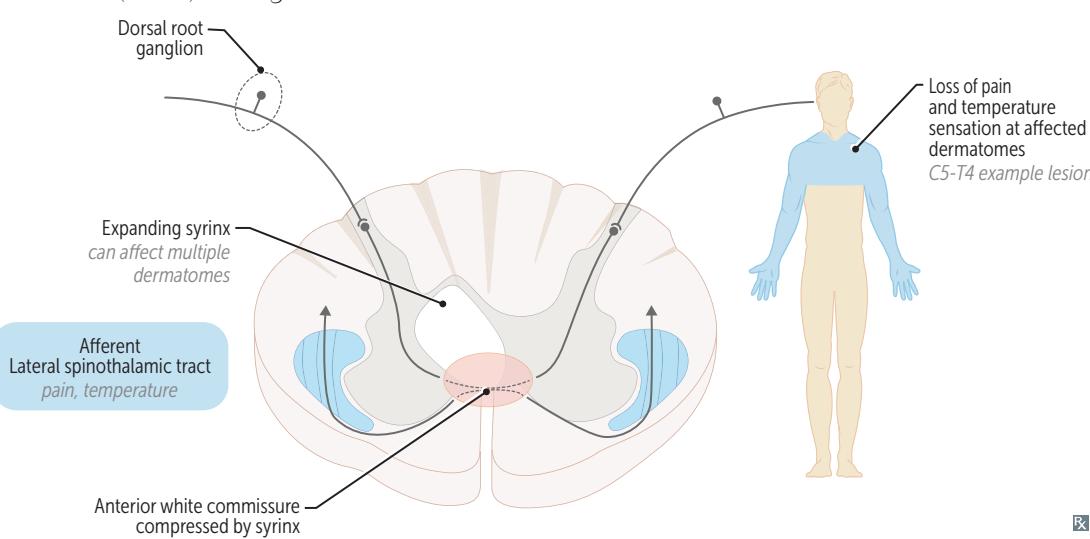
Downward displacement of cerebellum (vermis and tonsils) and medulla (2 structures) through foramen magnum → noncommunicating hydrocephalus. More severe than Chiari I, usually presents early in life with dysphagia, stridor, apnea, limb weakness. Associated with myelomeningocele (usually lumbosacral).

Dandy-Walker malformation

Agenesis of cerebellar vermis → cystic enlargement of 4th ventricle (arrow in **B**) that fills the enlarged posterior fossa. Associated with noncommunicating hydrocephalus, spina bifida.

**Syringomyelia**

Fluid-filled, gliosis-lined cavity within spinal cord (yellow arrows in **A**). Fibers crossing in anterior white commissure (spinothalamic tract) are typically damaged first → “cape-like” loss of pain and temperature sensation in bilateral upper extremities. As lesion expands it may damage anterior horns → lower motor neuron (LMN) findings.

**Syrinx** (Greek) = tube, as in “syringe.”

Most lesions occur between C2 and T9. Usually associated with Chiari I malformation (red arrow in **A**). Less commonly associated with other malformations, infections, tumors, trauma.

► NEUROLOGY—ANATOMY AND PHYSIOLOGY

Cells of the nervous system

Neurons and nonneuronal (glial) cells.
Neurons—permanent, signal-transmitting cells of the nervous system composed of dendrites (receive input), cell bodies, and axons (send output). Dendrites and cell bodies can be seen on Nissl staining (stains rough endoplasmic reticulum [RER]; not present in axons).
 Markers: neurofilament protein, synaptophysin.

CNS glial cells—neuroectoderm (except microglia, which derive from mesoderm).
 PNS glial cells—neural crest ectoderm.
 Myelin is a multilayer wrapping of electrical insulation formed around axons
 → ↑ conduction velocity of transmitted signals via saltatory conduction of action potentials at nodes of Ranvier ($\uparrow\uparrow$ Na^+ channel density).

CNS glial cells**Astrocytes**

Physical support, repair, removal of excess neurotransmitters, component of blood-brain barrier, glycogen fuel reserve buffer.
 GFAP \oplus .

Largest and most abundant glial cell in CNS.
 Reactive gliosis in response to neural injury.

Oligodendrocytes

Myelinate axons in CNS (including CN II). “Fried egg” appearance histologically (“oleggodendrocytes”).

Each myelinates many axons (~ 30).
 Predominant type of glial cell in white matter.
 Injured in multiple sclerosis, leukodystrophies, progressive multifocal leukoencephalopathy.
 Specialized ependymal cells (choroid plexus) produce CSF.

Ependymal cells

Ciliated simple columnar glial cells lining ventricles and central canal of spinal cord. Apical surfaces are covered with cilia (which circulate CSF) and microvilli (which help with CSF absorption).

Microglia

Activation in response to tissue damage
 → release of inflammatory mediators (eg, nitric oxide, glutamate). Not readily discernible by Nissl stain.

Phagocytic scavenger cells of CNS.
 HIV-infected microglia fuse to form multinucleated giant cells in CNS in HIV-associated dementia.

PNS glial cells**Satellite cells**

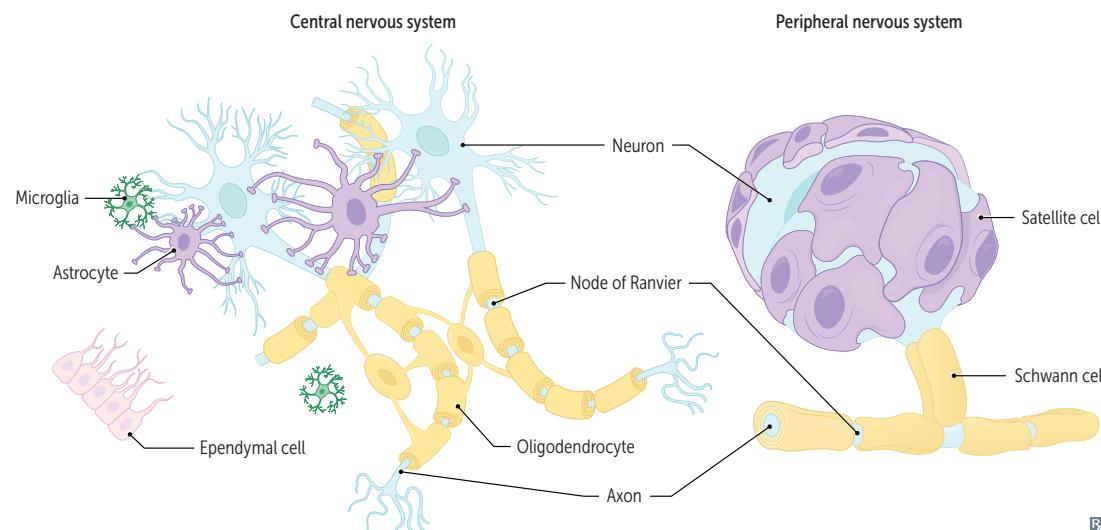
Surround neuronal cell bodies in ganglia.

Similar supportive role to astrocytes.

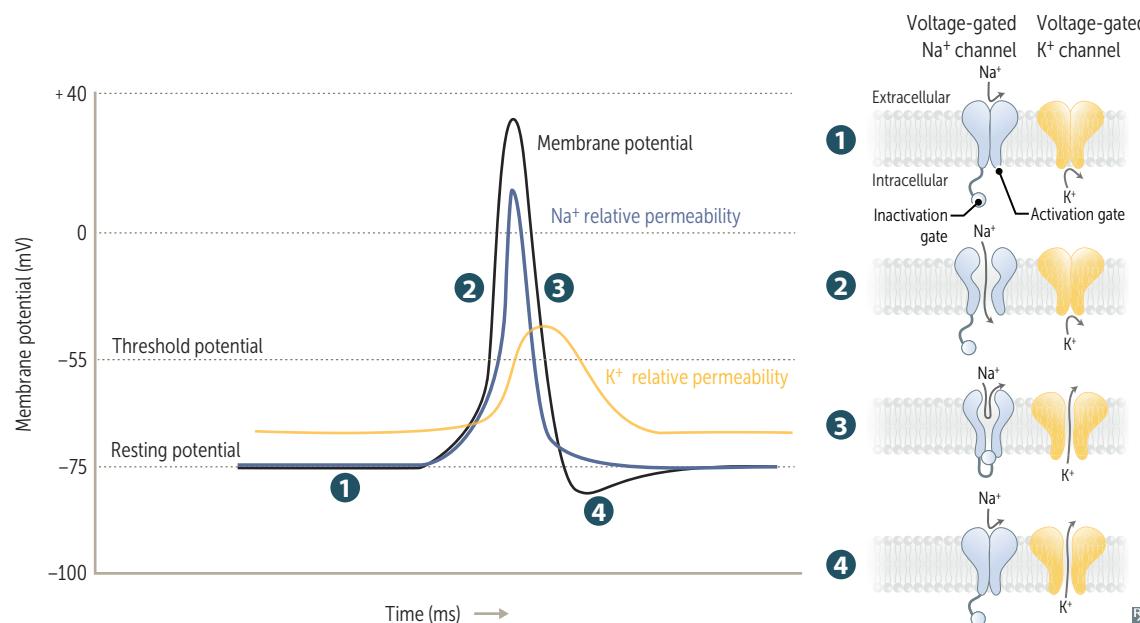
Schwann cells

Myelinate axons in PNS (including CN III-XII). S100 \oplus .

Each myelinates a single axon (“Schwone”).
 Injured in Guillain-Barré syndrome.

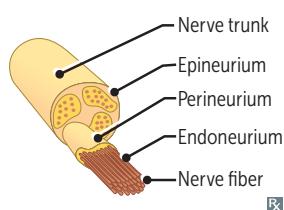


Neuron action potential



Sensory receptors

RECEPTOR TYPE	SENSORY NEURON FIBER TYPE	LOCATION	SENSES
Free nerve endings	Aδ—fast , myelinated fibers C—slow , unmyelinated A Delta plane is fast , but a tax C is slow	All tissues except cartilage and eye lens; numerous in skin	Pain, temperature
Meissner corpuscles	Large, myelinated fibers; adapt quickly	Glabrous (hairless) skin (eg, palms, soles, lips)	Dynamic, fine/light touch, low-frequency vibration, skin indentation
Pacinian corpuscles	Large, myelinated fibers; adapt quickly	Deep skin layers, ligaments, joints	High-frequency vibration, pressure (pressure cooker)
Merkel discs	Large, myelinated fibers; adapt slowly	Finger tips, superficial skin	Pressure, deep static touch (eg, shapes, edges)
Ruffini corpuscles	Large, myelinated fiber intertwined among collagen fiber bundles; adapt slowly	Finger tips, joints	Stretch, joint angle change

Peripheral nerve

Endoneurium—thin, supportive connective tissue that ensheathes and supports individual myelinated nerve fibers. May be affected in Guillain-Barré syndrome.

Perineurium (blood-nerve **permeability barrier**)—surrounds a fascicle of nerve fibers.

Epineurium—dense connective tissue that surrounds entire nerve (fascicles and blood vessels).

Endo = inner

Peri = around

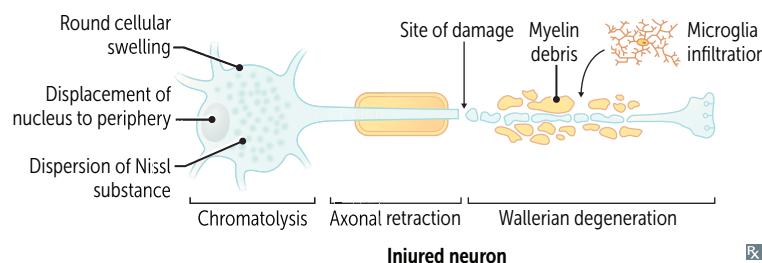
Epi = outer

Neuronal response to axonal injury

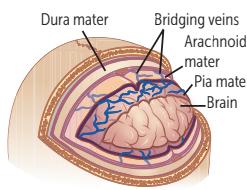
Chromatolysis—dispersion of Nissl substance throughout cytoplasm (RER no longer visible on staining). Neuronal cell body reaction reflecting ↑ protein synthesis in effort to repair damaged axon. Accompanied by round cellular swelling and displacement of nucleus to periphery.

Axonal retraction—proximal axon segment retracts and sprouts new protrusions that grow toward other neurons for potential reinnervation. In PNS, Schwann cells create a tract that guides axonal regeneration.

Wallerian degeneration—distal axon segment and associated myelin sheath disintegrates with macrophages removing debris. In CNS, persistence of myelin debris and reactive gliosis prevent axonal regeneration. Facilitate axonal regeneration in response to neural injury.

**Neurotransmitter changes with disease**

	LOCATION OF SYNTHESIS	ANXIETY	DEPRESSION	SCHIZOPHRENIA	ALZHEIMER DISEASE	HUNTINGTON DISEASE	PARKINSON DISEASE
Acetylcholine	Basal nucleus of Meynert (forebrain)				↓	↓	↑
Dopamine	Ventral tegmentum, SNc (midbrain)		↓	↑		↑	↓
GABA	Nucleus accumbens (basal ganglia)	↓				↓	
Norepinephrine	Locus ceruleus (pons)	↑	↓				
Serotonin	Raphe nuclei (brainstem)	↓	↓				↓

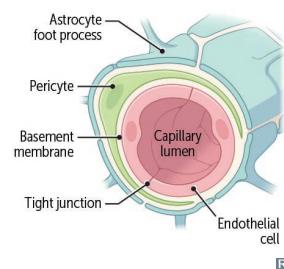
Meninges

Three membranes that surround and protect the brain and spinal cord. Derived from both neural crest and mesoderm:

- Dura mater—thick outer layer closest to skull.
- Arachnoid mater—middle layer, contains weblike connections.
- Pia mater—thin, fibrous inner layer that firmly adheres to brain and spinal cord.

CSF flows in the subarachnoid space, located between arachnoid and pia mater.

Epidural space—potential space between dura mater and skull/vertebral column containing fat and blood vessels. Site of blood collection associated with middle meningeal artery injury.

Blood-brain barrier

Prevents circulating blood substances (eg, bacteria, drugs) from reaching the CSF/CNS. Formed by 4 structures:

- Tight junctions between nonfenestrated capillary endothelial cells
- Basement membrane
- Pericytes
- Astrocyte foot processes

Glucose and amino acids cross slowly by carrier-mediated transport mechanisms.

Nonpolar/lipid-soluble substances cross rapidly via diffusion.

Circumventricular organs with fenestrated capillaries and no blood-brain barrier allow molecules in blood to affect brain function (eg, area postrema—vomiting after chemotherapy; OVLT [organum vasculosum lamina terminalis]—osmoreceptors) or neurosecretory products to enter circulation (eg, neurohypophysis—ADH release).

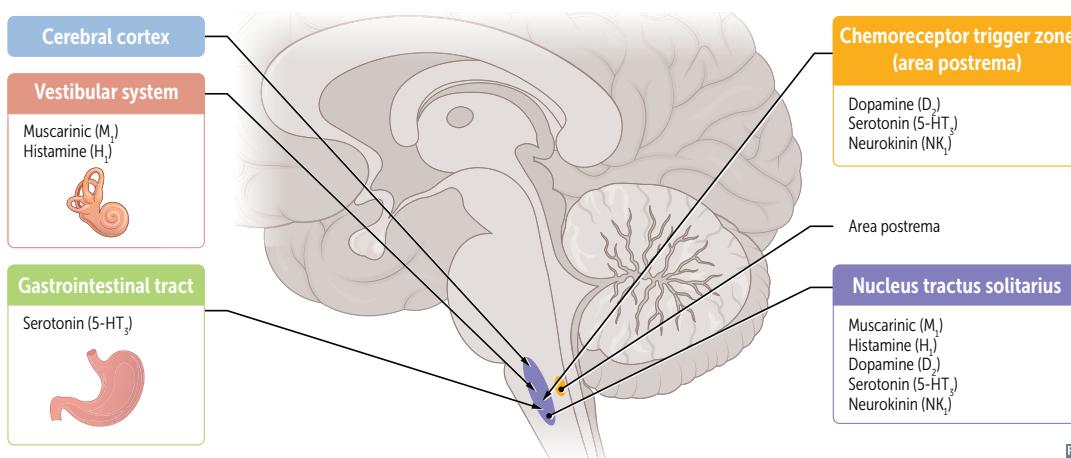
BBB disruption (eg, stroke) → vasogenic edema. Hyperosmolar agents (eg, mannitol) can disrupt the BBB → ↑ permeability of medications.

Vomiting center

Coordinated by NTS in the medulla, which receives information from the chemoreceptor trigger zone (CTZ, located within area postrema (pronounce “puke”-strema) at the base of the 4th ventricle), GI tract (via vagus nerve), vestibular system, and CNS.

CTZ and adjacent vomiting center nuclei receive input through 5 major receptors: histamine (H_1), muscarinic (M_1), neurokinin (NK-1), dopamine (D_2), and serotonin (5-HT₃).

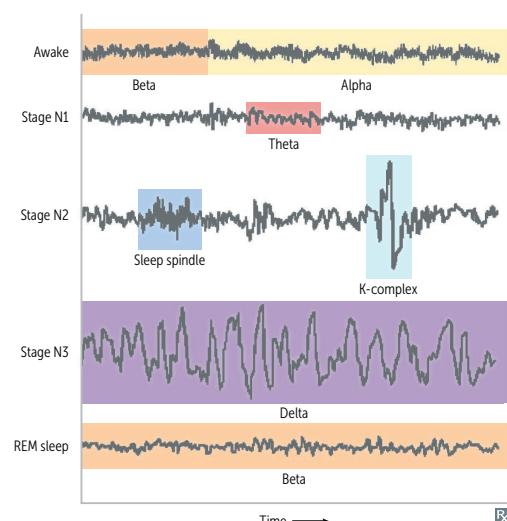
- 5-HT₃, D₂, and NK-1 antagonists treat chemotherapy-induced vomiting.
- H₁ and M₁ antagonists treat motion sickness; H₁ antagonists treat hyperemesis gravidarum.



Sleep physiology

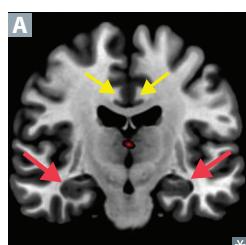
Sleep occurs in 4-6 cycles per night, each lasting ~90 mins and consisting of 2 main stages:

- Non-rapid eye movement (NREM) sleep
 - Rapid-eye movement (REM) sleep; duration of REM sleep ↑ through the night
- Sleep-wake cycle is regulated by circadian rhythm in the suprachiasmatic nucleus (SCN). ↓ light → ↓ SCN activity → ↑ NE from superior cervical ganglion → ↑ melatonin from pineal gland.
- EEG waveforms: **Beta**, **Alpha**, **Theta**, **Sleep spindle**, **Delta**, **Beta**. At night, **BATS DRink Blood**.

SLEEP STAGE (% OF TOTAL SLEEP)	DESCRIPTION	EKG WAVEFORM
Awake	Alert, active mental concentration. Eyes open—beta waves (highest frequency, lowest amplitude). Eyes closed—alpha waves.	
NREM sleep		
Stage N1 (5%)	Light sleep; theta waves.	
Stage N2 (45%)	Deeper sleep; sleep spindles and K complexes. When bruxism occurs (“twoth” grinding in N2).	
Stage N3 (25%)	Deepest NREM sleep (slow-wave sleep); delta waves (lowest frequency, highest amplitude). When bedwetting , sleepwalking , and night terrors occur (wee and flee in N3).	
REM sleep (25%)	Loss of muscle tone (atonia) except in diaphragm and extraocular muscles, ↑ brain O ₂ use, variable pulse/BP. When dreaming , nightmares, and penile/clitoral tumescence occur (REMember dreams).	
REM sleep behavior disorder	Loss of atonia leading to dream enactment (often violent) and vocalization. Most commonly associated with Lewy body dementia and Parkinson disease.	
Factors affecting sleep architecture	Alcohol, benzodiazepines, barbiturates: ↓ N3 and REM sleep (benzodiazepines are useful for sleepwalking and night terrors). Aging: ↓ N3 and REM sleep, ↑ sleep-onset latency, early morning awakening. Depression: ↓ N3 sleep, ↑ REM sleep, ↓ REM latency, repeated nighttime awakenings, early morning awakening (terminal insomnia). Narcolepsy: ↓ REM latency.	

Hypothalamus	Maintains homeostasis by regulating Thirst and water balance, controlling Adenohypophysis (anterior pituitary) and Neurohypophysis (posterior pituitary) release of hormones produced in the hypothalamus, and regulating Hunger, Autonomic nervous system, Temperature, and Sexual urges (TAN HATS). Inputs (areas not protected by blood-brain barrier): OVLT (senses change in osmolarity), area postrema (found in dorsal medulla, responds to emetics).
Lateral nucleus	Hunger. Stimulated by ghrelin, inhibited by leptin.
Ventromedial nucleus	Satiety. Stimulated by leptin.
Anterior nucleus	Cooling, parasympathetic.
Posterior nucleus	Heating, sympathetic.
Suprachiasmatic nucleus	Circadian rhythm.
Supraoptic and paraventricular nuclei	Synthesize ADH and oxytocin.
Preoptic nucleus	Thermoregulation, sexual behavior. Releases GnRH.
Lateral injury makes you lean. Destruction → anorexia, failure to thrive (infants).	
Ventromedial injury makes you very massive. Destruction (eg, craniopharyngioma) → hyperphagia.	
A/C = Anterior Cooling.	
Heating controlled by posterior nucleus (“hot pot”).	
SCN is a Sun-Censing Nucleus.	
SAD POX: Supraoptic = ADH, Paraventricular = Oxytocin. ADH and oxytocin are carried by neurophysins down axons to posterior pituitary, where these hormones are stored and released. Destruction → central diabetes insipidus.	
Failure of GnRH-producing neurons to migrate from olfactory pit → Kallmann syndrome.	

Thalamus				
NUCLEI	INPUT	SENSES	DESTINATION	MNEMONIC
Ventral posterolateral nucleus	Spinothalamic and dorsal columns/medial lemniscus	Vibration, pain, pressure, proprioception (conscious), light touch, temperature	1° somatosensory cortex (parietal lobe)	
Ventral posteromedial nucleus	Trigeminal and gustatory pathway	Face sensation, taste	1° somatosensory cortex (parietal lobe)	Very pretty makeup goes on the face
Lateral geniculate nucleus	CN II, optic chiasm, optic tract	Vision	1° visual cortex (occipital lobe)	Lateral = light (vision)
Medial geniculate nucleus	Superior olive and inferior colliculus of tectum	Hearing	1° auditory cortex (temporal lobe)	Medial = music (hearing)
Ventral anterior and ventral lateral nuclei	Basal ganglia, cerebellum	Motor	Motor cortices (frontal lobe)	Venus astronauts vow to love moving

Limbic system

Collection of neural structures involved in emotion, long-term memory, olfaction, behavior modulation, ANS function.

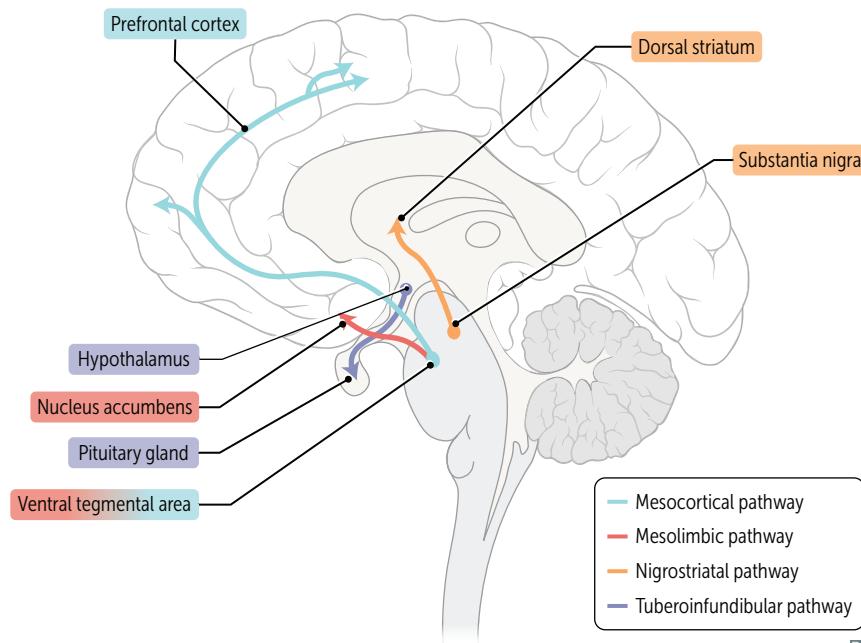
Consists of hippocampus (red arrows in A), amygdala, mammillary bodies, anterior thalamic nuclei, cingulate gyrus (yellow arrows in A), entorhinal cortex. Responsible for feeding, fleeing, fighting, feeling, and sex.

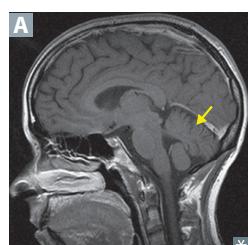
The famous **5 F's**.

Dopaminergic pathways

Commonly altered by drugs (eg, antipsychotics) and movement disorders (eg, Parkinson disease). The mesocortical and mesolimbic pathways are involved in addiction behaviors.

PATHWAY	PROJECTION	FUNCTION	SYMPTOMS OF ALTERED ACTIVITY	NOTES
Mesocortical	Ventral tegmental area → prefrontal cortex		↓ activity → negative symptoms	Antipsychotics have limited effect
Mesolimbic	Ventral tegmental area → nucleus accumbens	Motivation and reward	↑ activity → positive symptoms	1° therapeutic target of antipsychotics
Nigrostriatal	Substantia nigra → dorsal striatum	Motor control (pronounce "nigrostriatal")	↓ activity → extrapyramidal symptoms	Significantly affected by antipsychotics and in Parkinson disease
Tuberoinfundibular	Hypothalamus → pituitary	Regulation of prolactin secretion	↓ activity → ↑ prolactin	Significantly affected by antipsychotics



Cerebellum

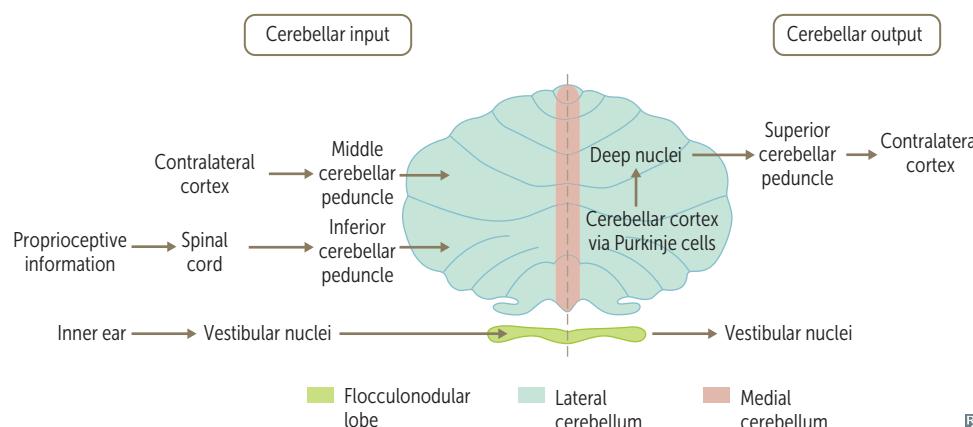
Modulates movement; aids in coordination and balance **A**.

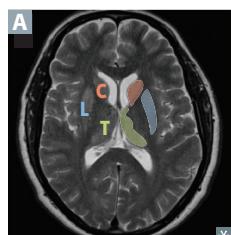
- Ipsilateral (unconscious) proprioceptive information via inferior cerebellar peduncle from spinal cord
- Deep nuclei (lateral → medial)—**d**entate, **e**mboliform, **g**lobose, **f**astigial (**d**on't eat **g**reasy foods)

Medial cerebellum (eg, vermis) controls axial and proximal limb musculature bilaterally (**medial** structures).

Lateral cerebellum (ie, hemisphere) controls distal limb musculature ipsilaterally (**lateral** structures).

Tests: rapid alternating movements (pronation/supination), finger-to-nose, heel-to-shin, gait, look for intention tremor.



Basal ganglia

Important in voluntary movements and adjusting posture **A**. Receives cortical input, provides negative feedback to cortex to modulate movement.

Striatum = putamen (motor) + Caudate nucleus (cognitive).

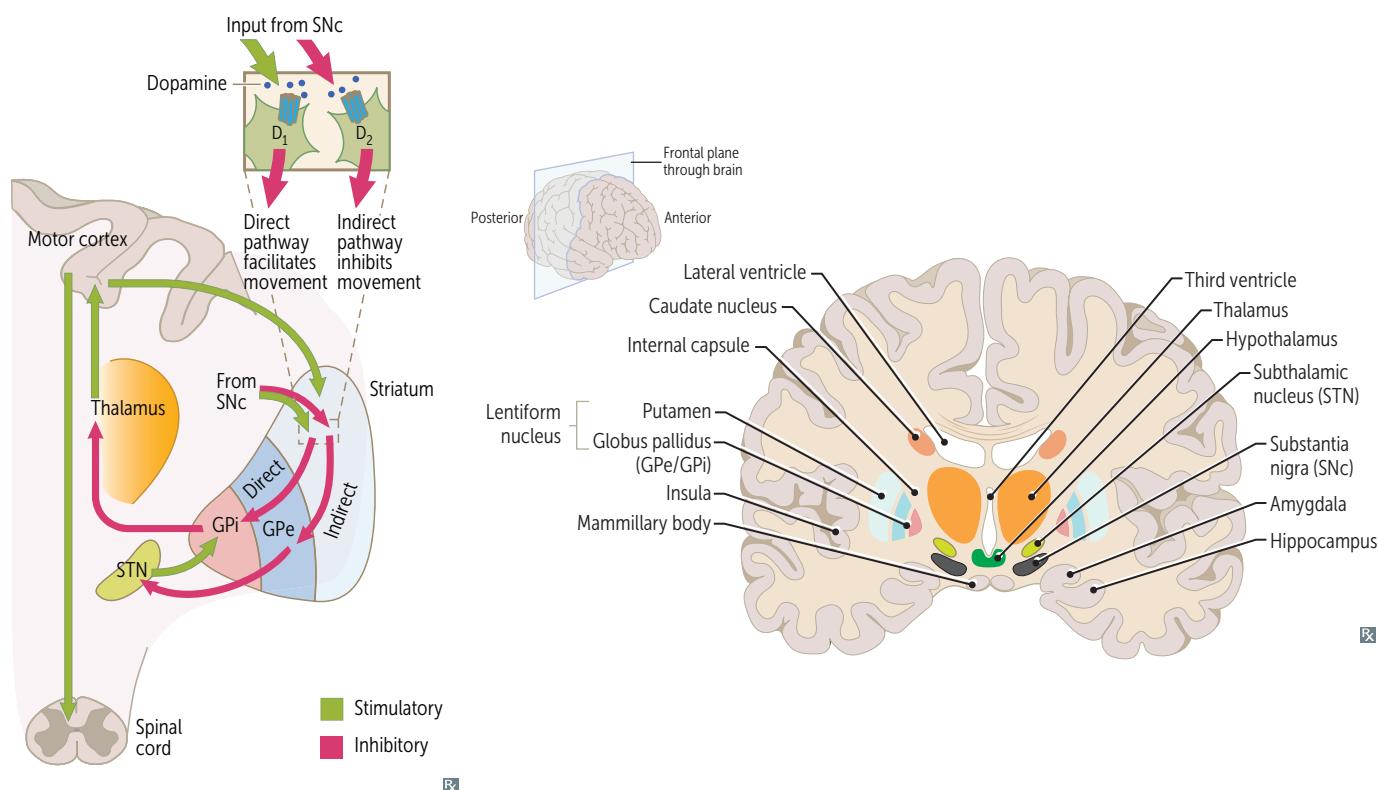
Lentiform nucleus = putamen + globus pallidus.

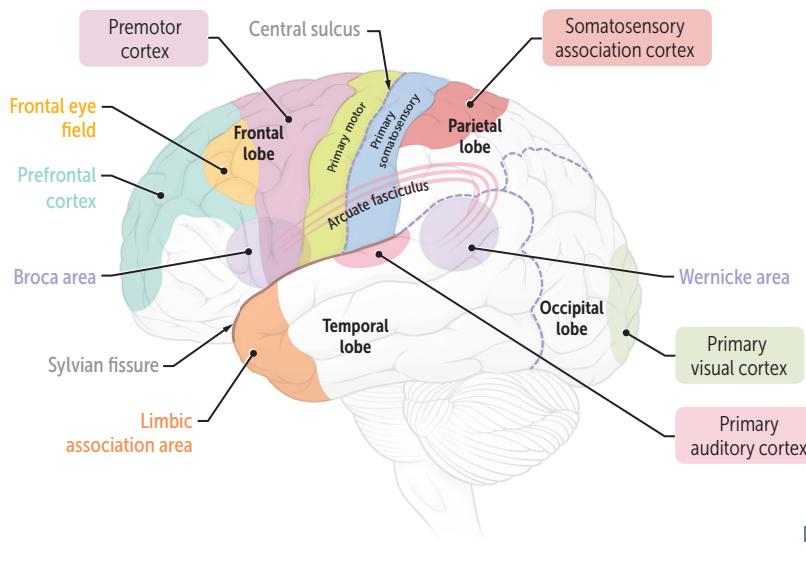
Direct (excitatory) pathway—cortical input (via glutamate) stimulates GABA release from the striatum, which inhibits GABA release from GPi, disinhibiting (activating) the Thalamus → ↑ motion.

Indirect (inhibitory) pathway—cortical input (via glutamate) stimulates GABA release from the striatum, which inhibits GABA release from GPe, disinhibiting (activating) the STN. STN input (via glutamate) stimulates GABA release from GPi, inhibiting the Thalamus → ↓ motion.

Dopamine from SNc (nigrostriatal pathway) stimulates the direct pathway (by binding to D₁ receptor) and inhibits the indirect pathway (by binding to D₂ receptor) → ↑ motion.

D₁ Receptor = **DIRect** pathway.
Indirect (D₂) = **Inhibitory**.



Cerebral cortex regions

Rx

Cerebral perfusion

Relies on tight autoregulation. Primarily driven by Pco_2 (Po_2 also modulates perfusion in severe hypoxia, eg, mountain sickness—hypoxia → ↑ cerebral vasodilation → ↑ cerebral blood flow → cerebral edema).

Also relies on a pressure gradient between mean arterial pressure (MAP) and intracranial pressure (ICP). ↓ blood pressure or ↑ ICP → ↓ cerebral perfusion pressure (CPP).

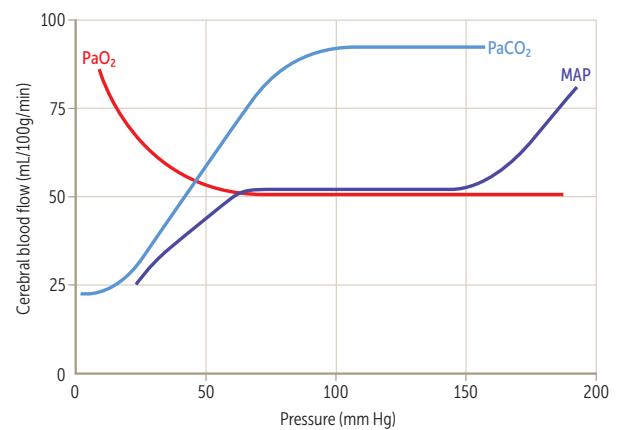
Cushing reflex—triad of hypertension, bradycardia, and respiratory depression in response to ↑ ICP.

Therapeutic hyperventilation → ↓ Pco_2 → vasoconstriction → ↓ cerebral blood flow → ↓ ICP. May be used to treat acute cerebral edema (eg, 2° to stroke) unresponsive to other interventions.

CPP = MAP – ICP. If CPP = 0, there is no cerebral perfusion → brain death (coma, absent brainstem reflexes, apnea).

Hypoxemia increases CPP only if $\text{Po}_2 < 50$ mm Hg.

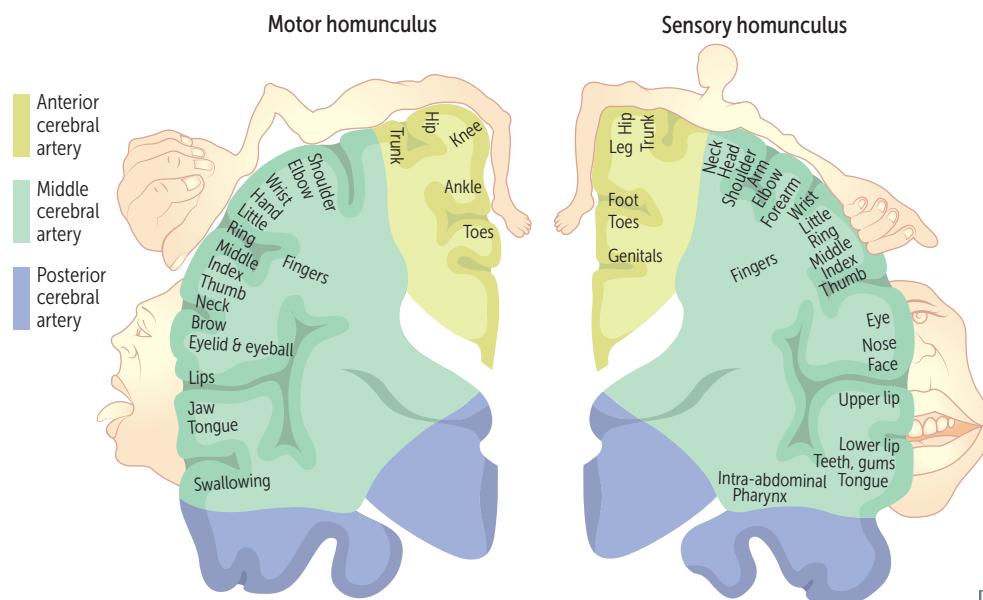
CPP is directly proportional to Pco_2 until $\text{Pco}_2 > 90$ mm Hg.



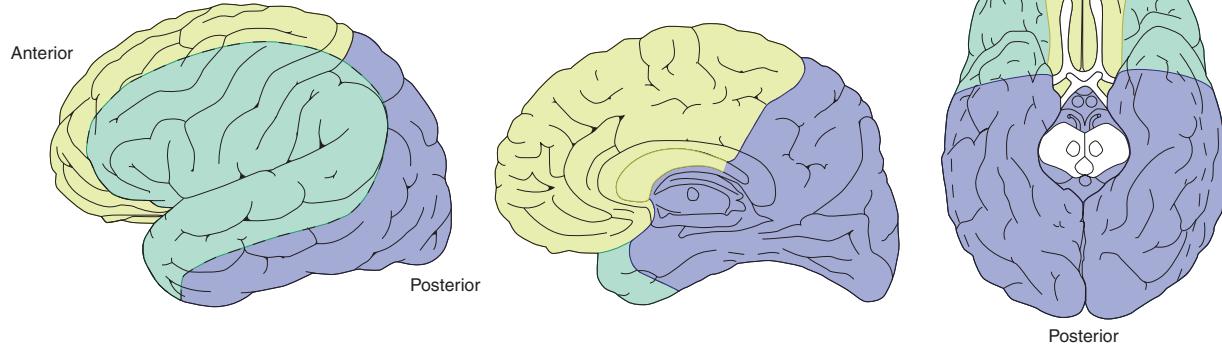
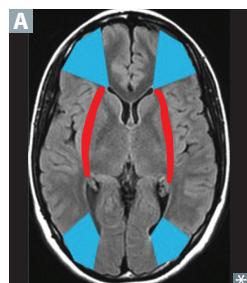
Rx

Homunculus

Topographic representation of motor and sensory areas in the cerebral cortex. Distorted appearance is due to certain body regions being more richly innervated and thus having ↑ cortical representation.

**Cerebral arteries—cortical distribution**

- [Yellow square] Anterior cerebral artery (supplies anteromedial surface)
- [Green square] Middle cerebral artery (supplies lateral surface)
- [Blue square] Posterior cerebral artery (supplies posterior and inferior surfaces)

**Watershed zones**

Cortical border zones occur between anterior and middle cerebral arteries and posterior and middle cerebral arteries (blue areas in A). Internal border zones occur between the superficial and deep vascular territories of the middle cerebral artery (red areas in A).

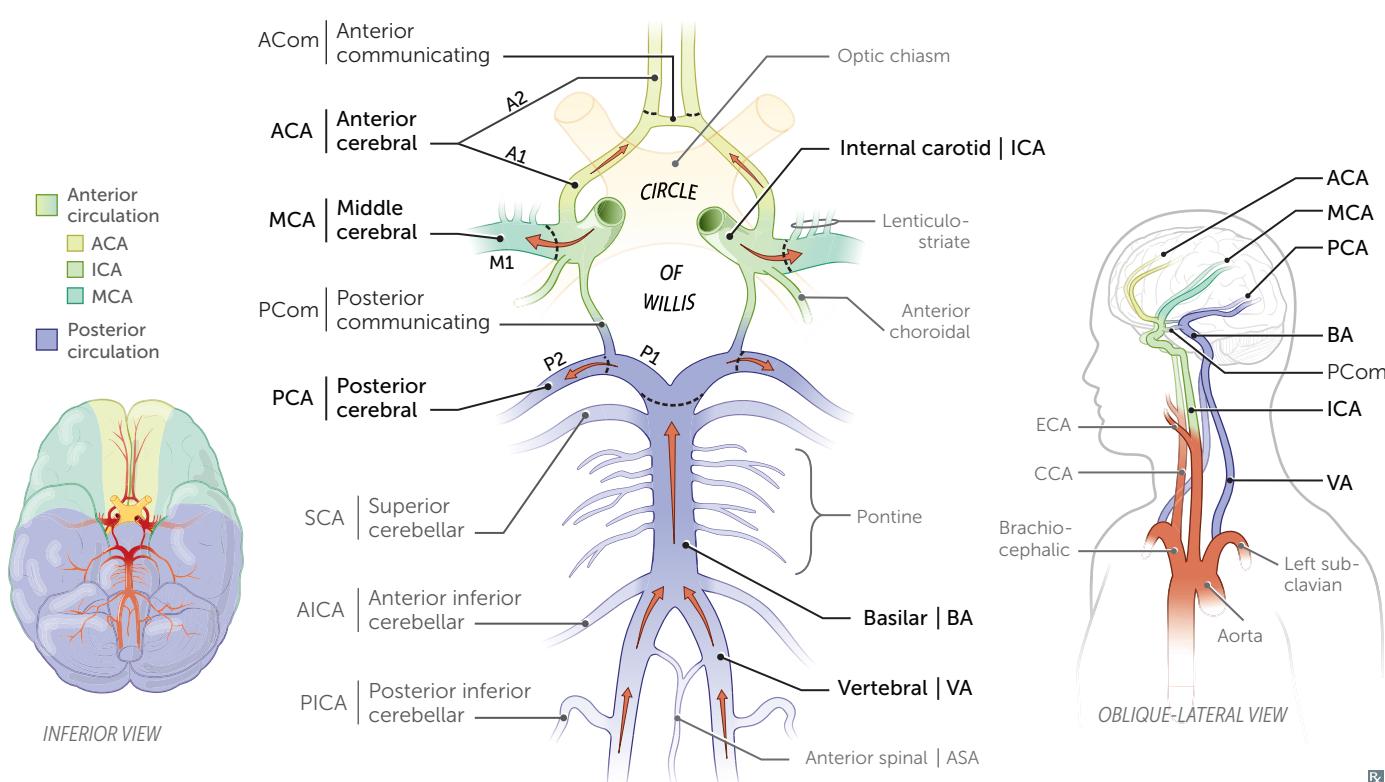
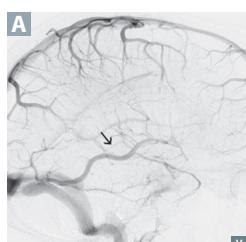
Common locations for brain metastases.

Infarct due to severe hypoperfusion:

- ACA-MCA watershed infarct—proximal upper extremity weakness sparing the lower extremities (“man-in-a-barrel syndrome”).
- PCA-MCA watershed infarct—higher-order visual dysfunction.

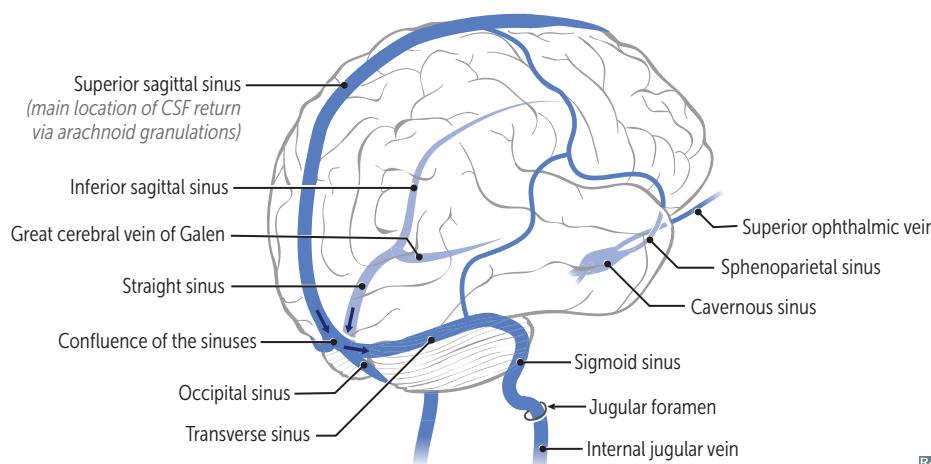
Circle of Willis

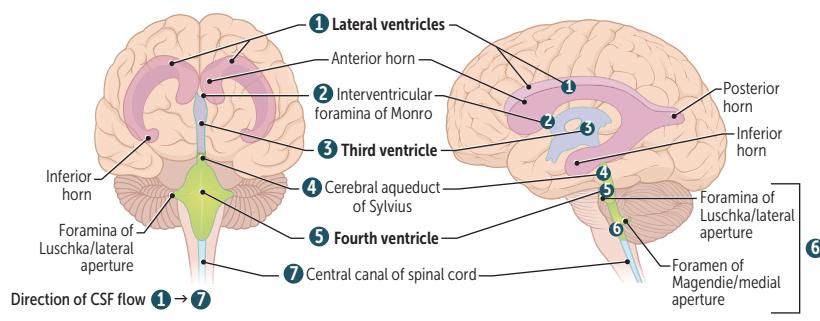
Anastomoses linking anterior and posterior circulations. Maintain cerebral perfusion in cases of occlusion/stenosis of major cranial arteries.

**Dural venous sinuses**

Large venous channels **A** that run through the periosteal and meningeal layers of the dura mater. Drain blood from cerebral veins (arrow) and receive CSF from arachnoid granulations. Empty into internal jugular vein.

Venous sinus thrombosis—presents with signs/symptoms of ↑ ICP (eg, headache, seizures, papilledema, focal neurologic deficits). May lead to venous hemorrhage. Associated with hypercoagulable states (eg, pregnancy, OCP use, factor V Leiden).



Ventricular system

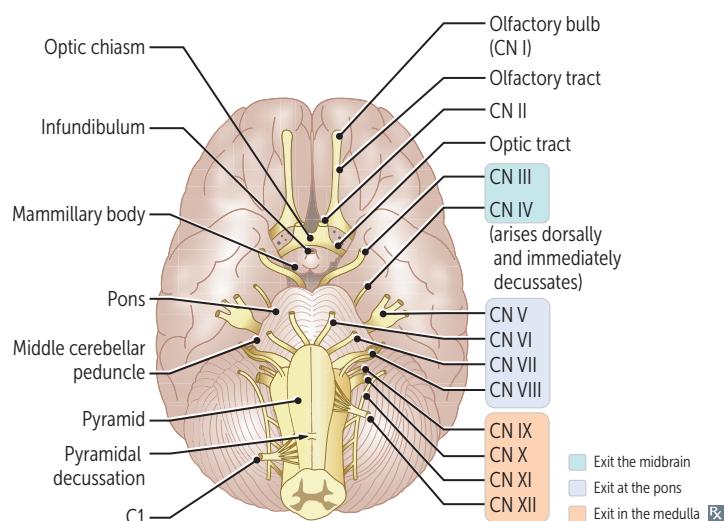
Lateral ventricles → 3rd ventricle via right and left interventricular foramina of Monro.

3rd ventricle → 4th ventricle via cerebral aqueduct of Sylvius.

4th ventricle → subarachnoid space via:

- Foramina of **Luschka** = lateral.
- Foramen of **Magendie** = medial.

CSF made by choroid plexuses located in the lateral, 3rd, and 4th ventricles. Travels to subarachnoid space via foramina of Luschka and Magendie, is reabsorbed by arachnoid granulations, and then drains into dural venous sinuses.

Brainstem—ventral view

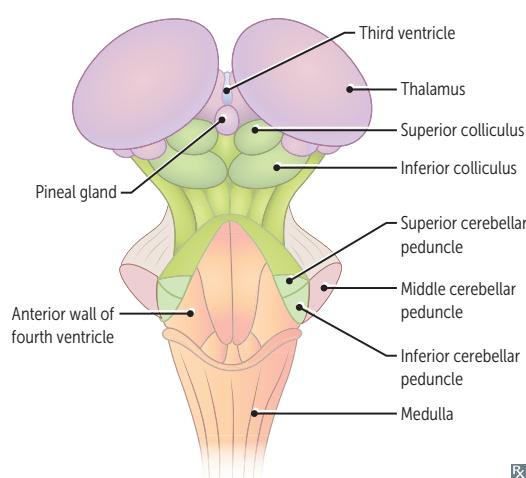
4 CN exit above pons (I, II, III, IV).

4 CN exit the pons (V, VI, VII, VIII).

4 CN exit in medulla (IX, X, XI, XII).

4 CN nuclei are medial (III, IV, VI, XII).

“Factors of 12, except 1 and 2.”

Brainstem—dorsal view (cerebellum removed)

Pineal gland—melatonin secretion, circadian rhythm.

Superior colliculi—process visual stimuli; direct eye and head movements primarily to visual stimuli.

Inferior colliculi—auditory processing; direct eye movements to auditory stimuli.

Eyes **above** ears → superior colliculus (visual) **above** inferior colliculus (auditory).

Cranial nerve nuclei

Located in tegmentum portion of brainstem (between dorsal and ventral portions):

- Midbrain—nuclei of CN III, IV
- Pons—nuclei of CN V, VI, VII, VIII
- Medulla—nuclei of CN IX, X, XII
- Spinal cord—nucleus of CN XI

Lateral nuclei = sensory (alar plate).

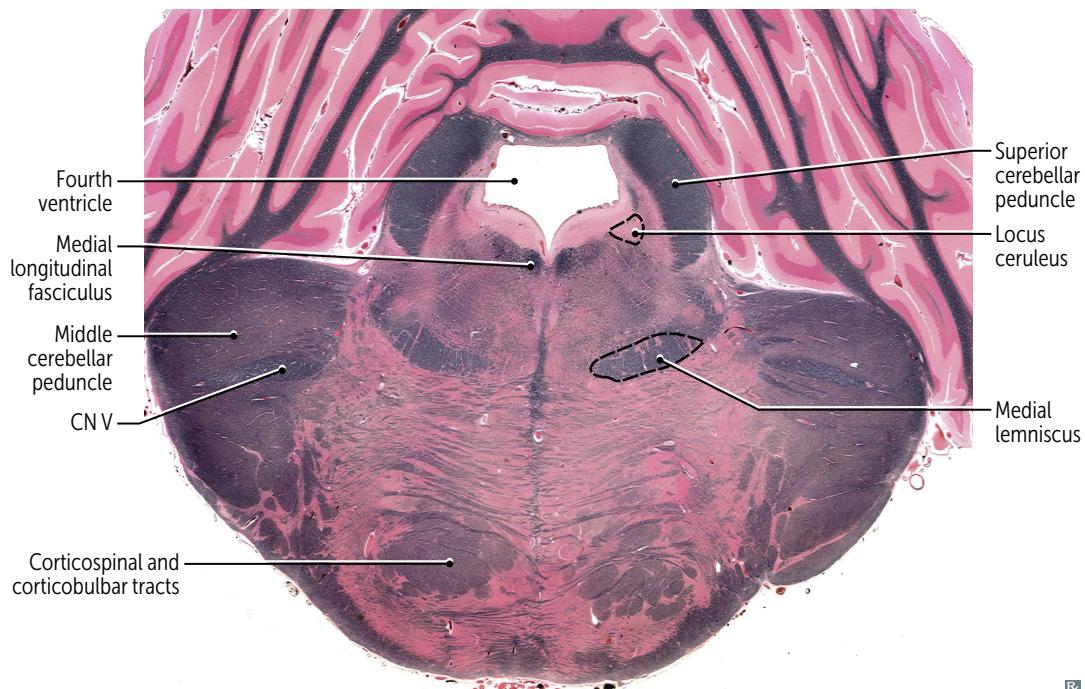
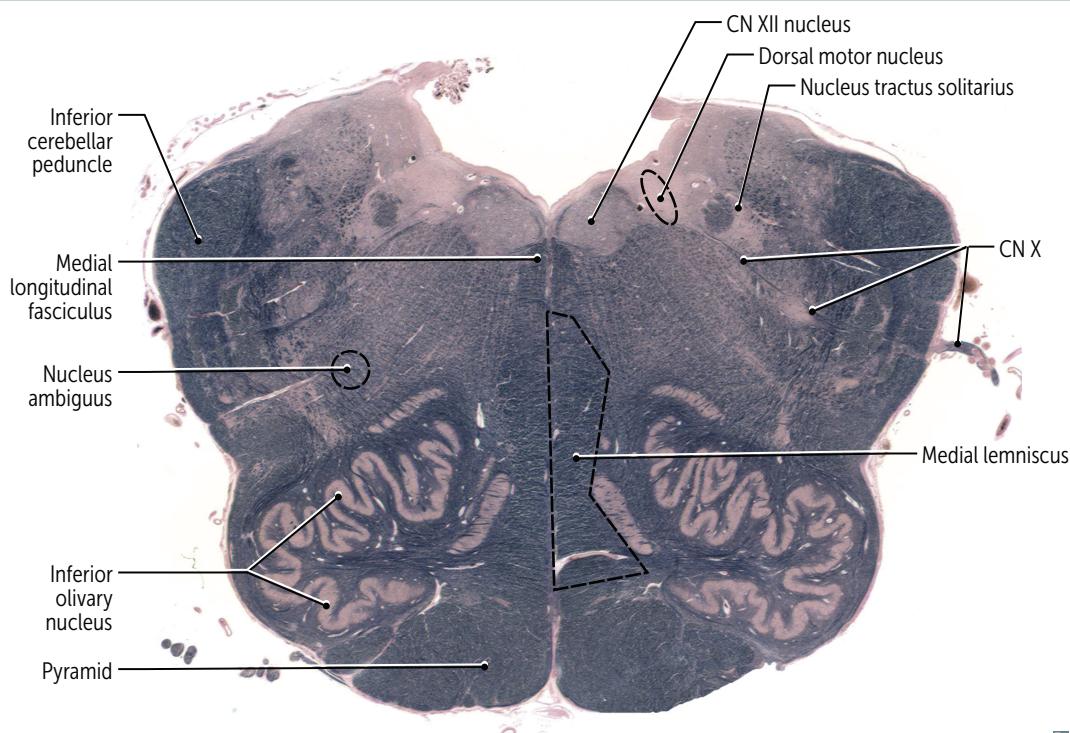
—Sulcus limitans—

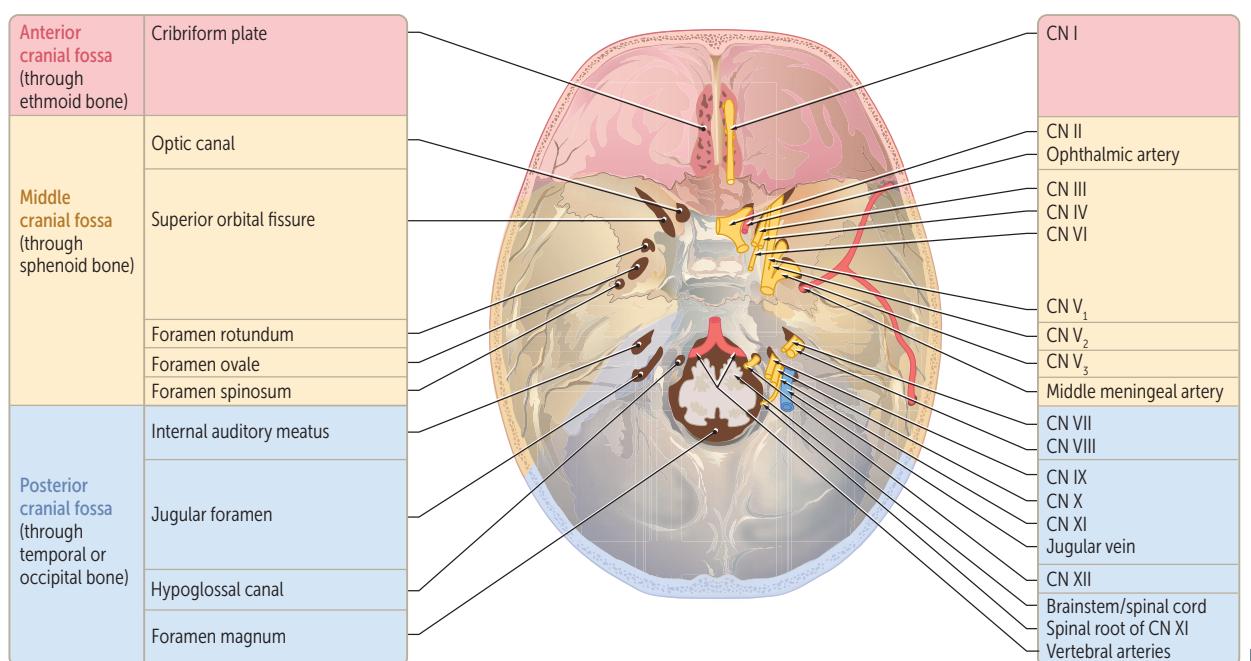
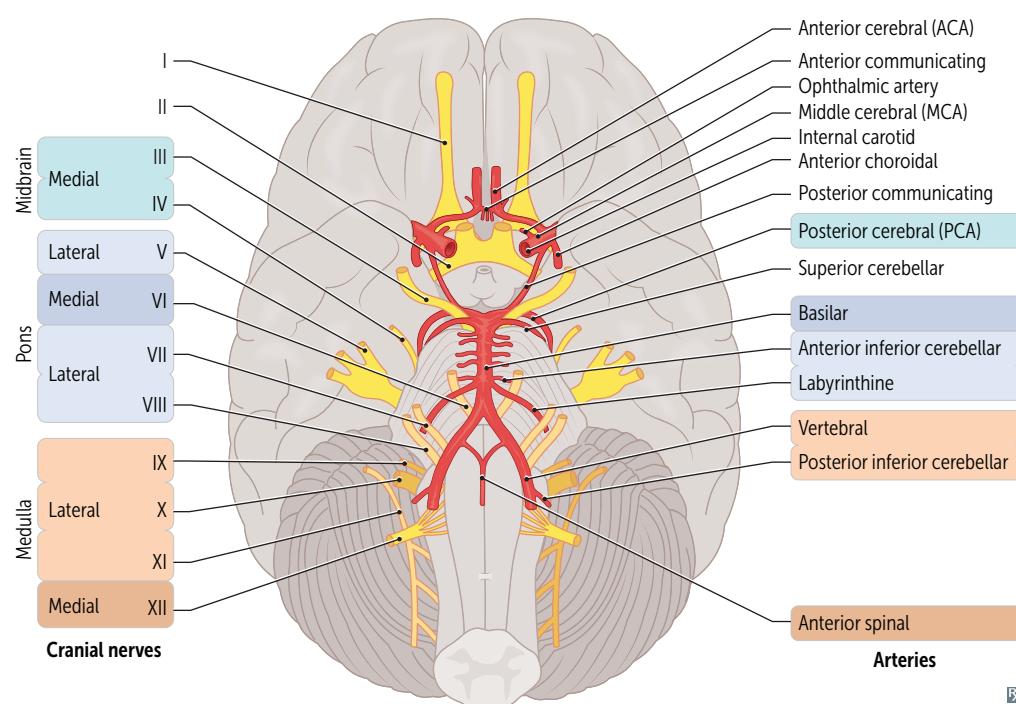
Medial nuclei = **motor** (basal plate).

Vagal nuclei

NUCLEUS	FUNCTION	CRANIAL NERVES
Nucleus tractus solitarius	Visceral sensory information (eg, taste, baroreceptors, gut distention) May play a role in vomiting	VII, IX, X
Nucleus ambiguus	Motor innervation of pharynx, larynx, upper esophagus (eg, swallowing, palate elevation)	IX, X
Dorsal motor nucleus	Sends autonomic (parasympathetic) fibers to heart, lungs, upper GI	X

Brainstem cross sections**Midbrain**

Brainstem cross sections (continued)**Pons****Medulla**

Cranial nerves and vessel pathways**Cranial nerves and arteries**

Cranial nerves

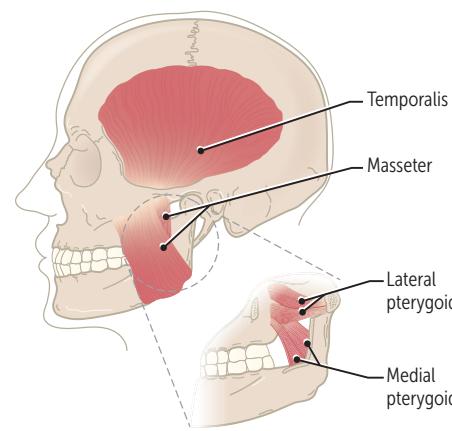
NERVE	CN	FUNCTION	TYPE	MNEMONIC
Olfactory	I	Smell (only CN without thalamic relay to cortex)	Sensory	Some
Optic	II	Sight	Sensory	Say
Oculomotor	III	Eye movement (SR, IR, MR, IO), pupillary constriction (sphincter pupillae), accommodation (ciliary muscle), eyelid opening (levator palpebrae)	Motor	Marry
Trochlear	IV	Eye movement (SO). Crosses midline → only CN with contralateral function	Motor	Money
Trigeminal	V	Mastication, facial sensation (ophthalmic, maxillary, mandibular divisions), somatosensation from anterior 2/3 of tongue, dampening of loud noises (tensor tympani)	Both	But
Abducens	VI	Eye movement (LR)	Motor	My
Facial	VII	Facial movement, eye closing (orbicularis oculi), auditory volume modulation (stapedius), taste from anterior 2/3 of tongue (chorda tympani), lacrimation, salivation (submandibular and sublingual glands are innervated by CN seven)	Both	Brother
Vestibulocochlear	VIII	Hearing, balance	Sensory	Says
Glossopharyngeal	IX	Taste and sensation from posterior 1/3 of tongue, swallowing, salivation (parotid gland), monitoring carotid body and sinus chemo- and baroreceptors, and elevation of pharynx/larynx (stylopharyngeus)	Both	Big
Vagus	X	Taste from supraglottic region, swallowing, soft palate elevation, midline uvula, talking, cough reflex, parasympathetics to thoracoabdominal viscera, monitoring aortic arch chemo- and baroreceptors	Both	Brains
Accessory	XI	Head turning, shoulder shrugging (SCM, trapezius)	Motor	Matter
Hypoglossal	XII	Tongue movement	Motor	Most

Cranial nerve reflexes

REFLEX	AFFERENT	EFFECTIVE
Accommodation	II	III
Corneal	V ₁ ophthalmic (nasociliary branch)	Bilateral VII (temporal and zygomatic branches—orbicularis oculi)
Cough	X	X (also phrenic and spinal nerves)
Gag	IX	X
Jaw jerk	V ₃ (sensory—muscle spindle from masseter)	V ₃ (motor—masseter)
Lacrimation	V ₁ (loss of reflex does not preclude emotional tears)	VII
Pupillary	II	III

Mastication muscles

3 muscles close jaw: **masseter**, **temporalis**, **medial pterygoid** (**my teeth munch**).
Lateral pterygoids lower (open) and **protrude** jaw.
All are innervated by mandibular branch of trigeminal nerve (CN V₃).



Rx

Spinal nerves

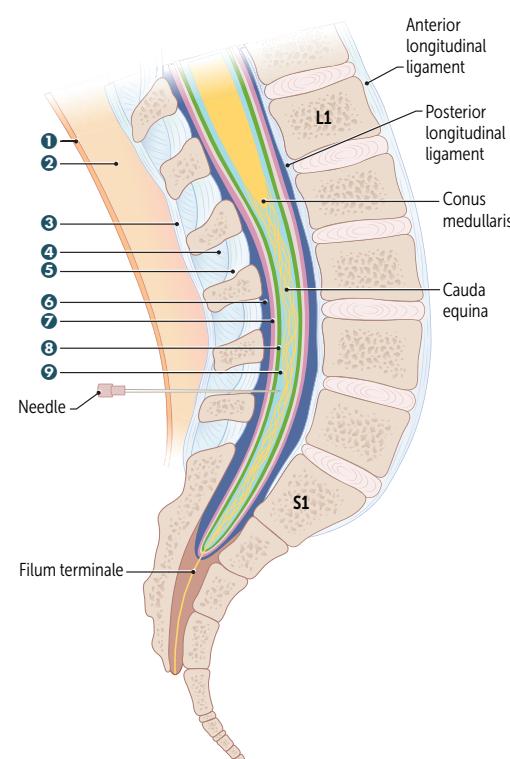
There are 31 pairs of spinal nerves: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, 1 coccygeal. Nerves C1–C7 exit above the corresponding vertebrae (eg, C3 exits above the 3rd cervical vertebra). C8 spinal nerve exits below C7 and above T1. All other nerves exit below (eg, L2 exits below the 2nd lumbar vertebra).

Spinal cord—lower extent

In adults, spinal cord ends at lower border of L1–L2 vertebrae. **Subarachnoid space** (which contains the CSF) extends to lower border of **S2** vertebra. Lumbar puncture (LP) is usually performed between L3–L4 or L4–L5 (level of cauda equina) to obtain sample of CSF while avoiding spinal cord. To **keep** the cord **alive**, keep the spinal needle between **L3** and **L5**.

Needle passes through:

- ① Skin
- ② Fascia and fat
- ③ Supraspinous ligament
- ④ Interspinous ligament
- ⑤ Ligamentum flavum
- ⑥ Epidural space
(epidural anesthesia needle stops here)
- ⑦ Dura mater
- ⑧ Arachnoid mater
- ⑨ Subarachnoid space
(CSF collection occurs here)



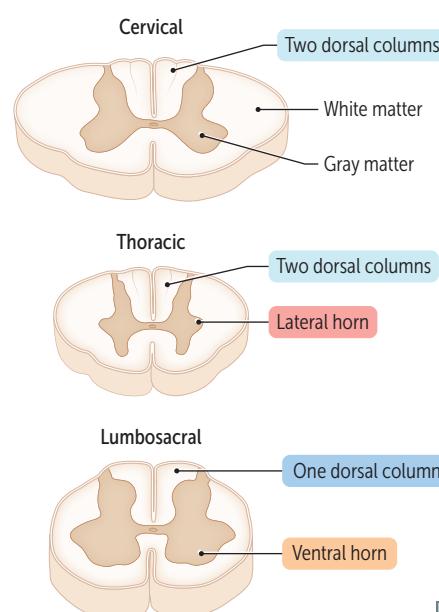
Rx

Conus medullaris and cauda equina syndrome

Rare neurosurgical emergencies caused by compression (eg, disc herniation, tumors, trauma) of terminal end of spinal cord (conus medullaris) or lumbosacral spinal nerve roots (cauda equina). Present with radicular low back pain, saddle/perianal anesthesia, bladder and bowel dysfunction, lower limb weakness → symmetric with upper motor neuron (UMN) signs (eg, spastic) in conus medullaris syndrome, asymmetric with LMN signs (eg, flaccid) in cauda equina syndrome.

Spinal cord levels and associated tracts

Legs (lumbosacral) are lateral in lateral corticospinal, spinothalamic tracts.
Dorsal columns are organized as you are, with hands at sides. “Arms outside, legs inside.”

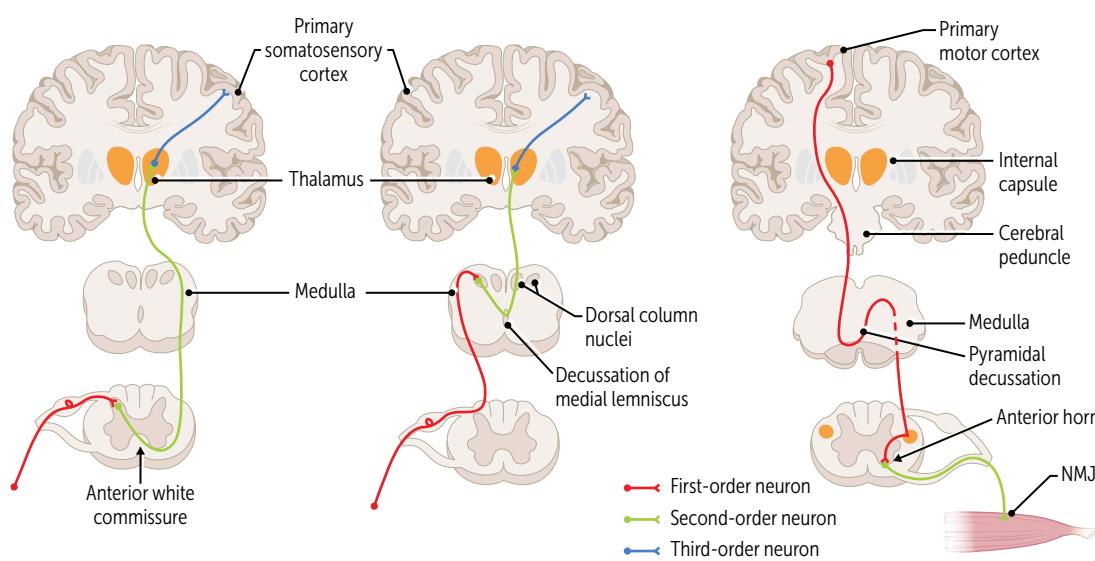


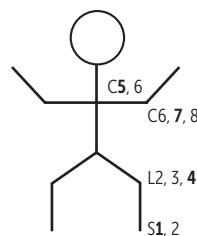
Rx

Spinal tract anatomy and functions

Spinothalamic tract and dorsal column (ascending tracts) synapse then cross.
Corticospinal tract (descending tract) crosses then synapses.

	Spinothalamic tract	Dorsal column	Corticospinal tract
FUNCTION	Pain, temperature	Pressure, vibration, fine touch, proprioception (conscious)	Voluntary movement
1ST-ORDER NEURON	Sensory nerve ending (A δ and C fibers) of pseudounipolar neuron in dorsal root ganglion → enters spinal cord	Sensory nerve ending of pseudounipolar neuron in dorsal root ganglion → enters spinal cord → ascends ipsilaterally in dorsal columns	UMN: 1 $^{\circ}$ motor cortex → descends ipsilaterally (through posterior limb of internal capsule and cerebral peduncle), decussates at caudal medulla (pyramidal decapsulation) → descends contralaterally
1ST SYNAPSE	Posterior horn (spinal cord)	Nucleus gracilis (medial, lower limbs, below T6) and nucleus cuneatus (lateral, upper limbs, above T6) in the ipsilateral medulla (grass on the ground, clouds in the sky)	Anterior horn (spinal cord)
2ND-ORDER NEURON	Decussates in spinal cord as the anterior white commissure → ascends contralaterally	Decussates in medulla → ascends contralaterally as the medial lemniscus	LMN: leaves spinal cord
2ND SYNAPSE	VPL (thalamus)	VPL (thalamus)	NMJ (skeletal muscle)
3RD-ORDER NEURON	Projects to 1 $^{\circ}$ somatosensory cortex	Projects to 1 $^{\circ}$ somatosensory cortex	



Clinical reflexes

Reflexes count up in order (main nerve root in **bold**):

Achilles reflex = S₁, S₂ (“buckle my shoe”)

Patellar reflex = L₂-L₄ (“kick the door”)

Biceps and brachioradialis reflexes = C₅, C₆ (“pick up sticks”)

Triceps reflex = C₆, C₇, C₈ (“lay them straight”)

Additional reflexes:

Cremasteric reflex = L₁, L₂ (“testicles move”)

Anal wink reflex = S₃, S₄ (“winks galore”)

Reflex grading:

0: absent

1+: hypoactive

2+: normal

3+: hyperactive

4+: clonus

Primitive reflexes

Primitive CNS reflexes present in healthy infants which disappear within 1st year of life due to inhibition from developing frontal lobe. Absent in neurologically intact adult. May reemerge in adults with frontal lobe lesions → loss of inhibition.

Moro reflex

“Hang on for life” reflex—abduct/extend arms when startled, and then draw together.

Rooting reflex

Movement of head toward one side if cheek or mouth is stroked (nipple seeking).

Sucking reflex

Sucking response when roof of mouth is touched.

Palmar reflex

Curling of fingers if palm is stroked.

Plantar reflex

Dorsiflexion of large toe and fanning of other toes with plantar stimulation.

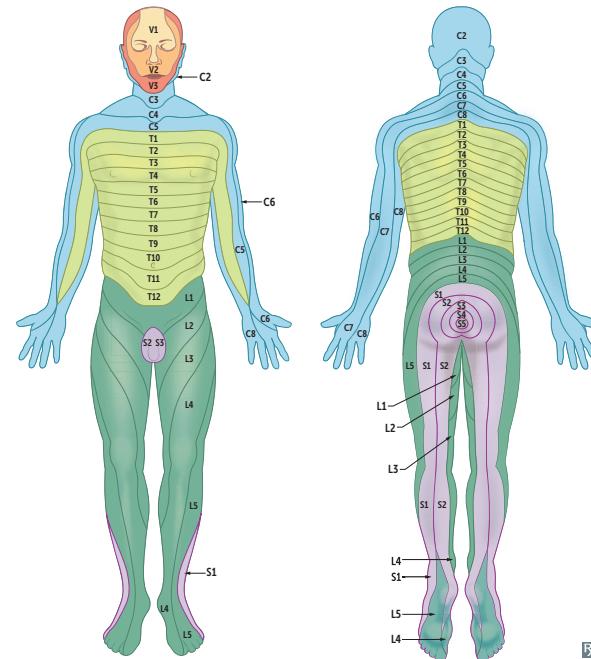
Babinski sign—presence of this reflex in an adult, which may signify a UMN lesion.

Galant reflex

Stroking along one side of the spine while newborn is in ventral suspension (face down) causes lateral flexion of lower body toward stimulated side.

Landmark dermatomes

DERMATOME	CHARACTERISTICS
C ₂	Posterior half of skull
C ₃	High turtleneck shirt Diaphragm and gallbladder pain referred to the right shoulder via phrenic nerve C₃, 4, 5 keeps the diaphragm alive
C ₄	Low-collar shirt
C ₆	Includes thumbs Thumbs up sign on left hand looks like a 6
T ₄	At the nipple T ₄ at the teat pore
T ₇	At the xiphoid process 7 letters in xiphoid
T ₁₀	At the umbilicus (belly button) Point of referred pain in early appendicitis
L ₁	At the Inguinal Ligament
L ₄	Includes the kneecaps Down on ALL 4's
S ₂ , S ₃ , S ₄	Sensation of penile and anal zones S₂, 3, 4 keep the penis off the floor



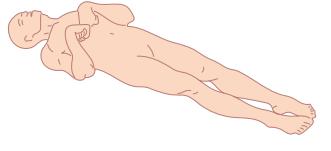
▶ NEUROLOGY—PATHOLOGY

Common brain lesions

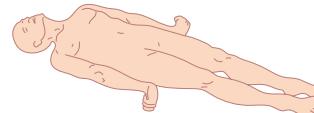
AREA OF LESION	COMPLICATIONS
Prefrontal cortex	Frontal lobe syndrome —disinhibition, hyperphagia, impulsivity, loss of empathy, impaired executive function, akinetic mutism. Seen in frontotemporal dementia.
Frontal eye fields	Eyes look toward brain lesion (ie, away from side of hemiplegia). Seen in MCA stroke.
Paramedian pontine reticular formation	Eyes look away from brain lesion (ie, toward side of hemiplegia).
Dominant parietal cortex	Gerstmann syndrome —agraphia, acalculia, finger agnosia, left-right disorientation.
Nondominant parietal cortex	Hemispatial neglect syndrome —agnosia of the contralateral side of the world.
Basal ganglia	Tremor at rest, chorea, athetosis. Seen in Parkinson disease, Huntington disease.
Subthalamic nucleus	Contralateral hemiballismus.
Mammillary bodies	Bilateral lesions → Wernicke-Korsakoff syndrome (due to thiamine deficiency).
Amygdala	Bilateral lesions → Klüver-Bucy syndrome —disinhibition (eg, hyperphagia, hypersexuality, hyperorality). Seen in HSV-1 encephalitis.
Hippocampus	Bilateral lesions → anterograde amnesia (no new memory formation). Seen in Alzheimer disease.
Dorsal midbrain	Parinaud syndrome (often due to pineal gland tumors).
Reticular activating system	Reduced levels of arousal and wakefulness, coma.
Medial longitudinal fasciculus	Internuclear ophthalmoplegia (impaired adduction of ipsilateral eye; nystagmus of contralateral eye with abduction). Seen in multiple sclerosis.
Cerebellar hemisphere	Intention tremor, limb ataxia, loss of balance; damage to cerebellum → ipsilateral deficits; fall toward side of lesion. Cerebellar hemispheres are laterally located—affect lateral limbs.
Cerebellar vermis	Truncal ataxia (wide-based, “drunken sailor” gait), nystagmus, dysarthria. Degeneration associated with chronic alcohol overuse. Vermis is centrally located—affects central body.

Abnormal motor posturing

	Decorticate (flexor) posturing	Decerebrate (extensor) posturing
SITE OF LESION	Above red nucleus (often cerebral cortex)	Between red and vestibular nuclei (brainstem)
OVERACTIVE TRACTS	Rubrospinal and vestibulospinal tracts	Vestibulospinal tract
PRESENTATION	Upper limb flexion, lower limb extension	Upper and lower limb extension
NOTES	“Your hands are near the cor (heart)”	Worse prognosis



Rx



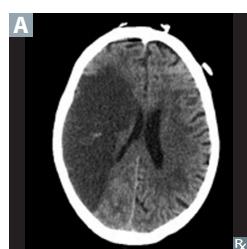
Rx

Ischemic brain disease/stroke

Irreversible neuronal injury begins after 5 minutes of hypoxia. Most **vulnerable**: hippocampus (CA1 region), neocortex, cerebellum (Purkinje cells), watershed areas (“**vulnerable hippos need pure water**”).

Stroke imaging: noncontrast CT to exclude hemorrhage (before tPA can be given). CT detects ischemic changes in 6–24 hr. Diffusion-weighted MRI can detect ischemia within 3–30 min.

TIME SINCE ISCHEMIC EVENT					
	12–24 HOURS	24–72 HOURS	3–5 DAYS	1–2 WEEKS	> 2 WEEKS
Histologic features	Eosinophilic cytoplasm + pyknotic nuclei (red neurons)	Necrosis + neutrophils	Macrophages (microglia)	Reactive gliosis (astrocytes) + vascular proliferation	Glial scar

Ischemic stroke

Ischemia → infarction → liquefactive necrosis.

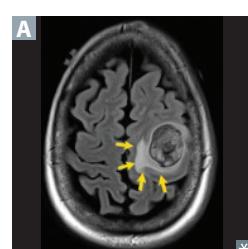
3 types:

- Thrombotic—due to a clot forming directly at site of infarction (commonly the MCA **A**), usually over a ruptured atherosclerotic plaque.
- Embolic—due to an embolus from another part of the body. Can affect multiple vascular territories. Examples: atrial fibrillation, carotid artery stenosis, DVT with patent foramen ovale (paradoxical embolism), infective endocarditis.
- Hypoxic—due to systemic hypoperfusion or hypoxemia. Common during cardiovascular surgeries, tends to affect watershed areas.

Treatment: tPA (if within 3–4.5 hr of onset and no hemorrhage/risk of hemorrhage) and/or thrombectomy (if large artery occlusion). Reduce risk with medical therapy (eg, aspirin, clopidogrel); optimum control of blood pressure, blood sugars, lipids; smoking cessation; and treat conditions that ↑ risk (eg, atrial fibrillation, carotid artery stenosis).

Transient ischemic attack

Brief, reversible episode of focal neurologic dysfunction without acute infarction (⊖ MRI), with the majority resolving in < 15 minutes; ischemia (eg, embolus, small vessel stenosis). May present with amaurosis fugax (transient visual loss) due to retinal artery emboli from carotid artery disease.

Cerebral edema

Fluid accumulation in brain parenchyma → ↑ ICP. Types:

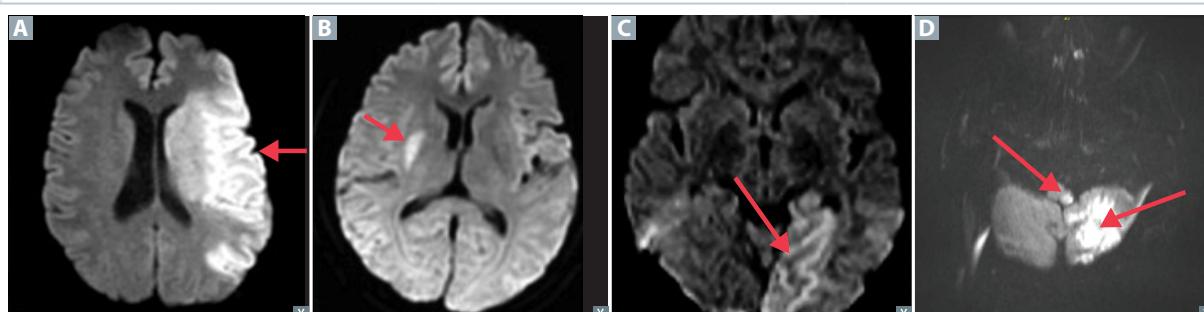
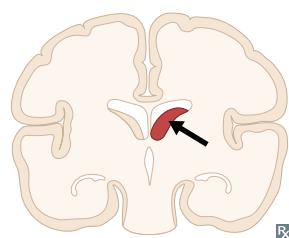
- Cytotoxic edema—intracellular fluid accumulation due to osmotic shift (eg, Na⁺/K⁺-ATPase dysfunction → ↑ intracellular Na⁺). Caused by ischemia (early), hyperammonemia, SIADH.
- Vasogenic edema—extracellular fluid accumulation due to disruption of BBB (↑ permeability). Caused by ischemia (late), trauma, hemorrhage, inflammation, tumors (arrows in **A** show surrounding vasogenic edema).

Effects of strokes

ARTERY	AREA OF LESION	SYMPOTMS	NOTES
Anterior circulation			
Anterior cerebral artery	Motor and sensory cortices—lower limb.	Contralateral paralysis and sensory loss—lower limb, urinary incontinence.	
Middle cerebral artery	Motor and sensory cortices A —upper limb and face. Temporal lobe (Wernicke area); frontal lobe (Broca area).	Contralateral paralysis and sensory loss—lower face and upper limb. Aphasia if in dominant (usually left) hemisphere. Hemineglect if lesion affects nondominant (usually right) hemisphere.	Wernicke aphasia is associated with right superior quadrant visual field defect due to temporal lobe involvement.
Lenticulo-striate artery	Striatum, internal capsule.	Contralateral paralysis. Absence of cortical signs (eg, neglect, aphasia, visual field loss).	Pure motor stroke (most common). Common location of lacunar infarcts B , due to microatheroma and hyaline arteriosclerosis (lipohyalinosis) 2° to unmanaged hypertension.
Posterior circulation			
Posterior cerebral artery	Occipital lobe C .	Contralateral hemianopia with macular sparing; alexia without agraphia (dominant hemisphere, extending to splenium of corpus callosum); prosopagnosia (inability to recognize familiar faces; nondominant hemisphere).	Weber syndrome —midbrain stroke due to occlusion of paramedian branches of PCA → ipsilateral CN III palsy and contralateral hemiplegia (damage to ipsilateral cerebral peduncle).
Basilar artery	Pons, medulla, lower midbrain. Corticospinal and corticobulbar tracts. Ocular cranial nerve nuclei, paramedian pontine reticular formation.	If RAS spared, consciousness is preserved. Quadriplegia; loss of voluntary facial (except blinking), mouth, and tongue movements. Loss of horizontal, but not vertical, eye movements.	Locked-in syndrome (locked in the basement).
Anterior inferior cerebellar artery	Facial nerve nuclei. Vestibular nuclei. Spinothalamic tract, spinal trigeminal nucleus. Sympathetic fibers. Middle and inferior cerebellar peduncles. Inner ear.	Paralysis of face (LMN lesion vs UMN lesion in cortical stroke), ↓ lacrimation, ↓ salivation, ↓ taste from anterior 2/3 of tongue. Vomiting, vertigo, nystagmus ↓ pain and temperature sensation from contralateral body, ipsilateral face. Ipsilateral Horner syndrome. Ipsilateral ataxia, dysmetria. Ipsilateral sensorineural deafness, vertigo.	Lateral pontine syndrome. Facial nerve nuclei effects are specific to AICA lesions. Supplied by labyrinthine artery, a branch of AICA.

Effects of strokes (continued)

ARTERY	AREA OF LESION	SYMPTOMS	NOTES
Posterior inferior cerebellar artery	Nucleus ambiguus (CN IX, X). Vestibular nuclei. Lateral spinothalamic tract, spinal trigeminal nucleus. Sympathetic fibers. Inferior cerebellar peduncle.	Dysphagia, hoarseness, ↓ gag reflex, hiccups. Vomiting, vertigo, nystagmus ↓ pain and temperature sensation from contralateral body, ipsilateral face. Ipsilateral Horner syndrome. Ipsilateral ataxia, dysmetria.	Lateral medullary (Wallenberg) syndrome. Nucleus ambiguus effects are specific to PICA lesions D . “Don’t pick a (PICA) lame horse (hoarseness) that can’t eat (dysphagia).”
Anterior spinal artery	Corticospinal tract. Medial lemniscus. Caudal medulla—hypoglossal nerve.	Contralateral paralysis—upper and lower limbs. ↓ contralateral proprioception. Ipsilateral hypoglossal dysfunction (tongue deviates ipsilaterally).	Medial Medullary syndrome —caused by infarct of paramedian branches of ASA and/or vertebral arteries. Ants love M&M’s.

**Neonatal intraventricular hemorrhage**

Bleeding into ventricles (arrow in illustration shows blood in intraventricular space). ↑ risk in premature and low-birth-weight infants. Originates in germinal matrix, a highly vascularized layer within the subventricular zone. Due to reduced glial fiber support and impaired autoregulation of BP in premature infants. Can present with altered level of consciousness, bulging fontanelle, hypotension, seizures, coma.

Extracranial injuries

Occur during birth leading to blood accumulation within the scalp and skull. Commonly seen in vacuum-assisted delivery.

DISORDER	PRESENTATION
Caput succedaneum	Self-limited, benign, edematous swelling above periosteum; crosses suture lines. May be caused by prolonged fetal–birth canal engagement. Resolves spontaneously.
Subgaleal hemorrhage	Serious, life-threatening damage of fetal emissary veins → blood accumulation between periosteum and galea aponeurosis. Presents as diffuse, fluctuant scalp swelling extending posteriorly and laterally. May lead to anemia and hypovolemic shock.
Cephalohematoma	Blood accumulation between skull and periosteum; does not cross suture lines. May be caused by forcep delivery. Presents with firm, localized swelling over parietal or occipital lobe. May lead to indirect hyperbilirubinemia.

Intracranial hemorrhage**Epidural hematoma**

Rupture of middle meningeal artery (branch of maxillary artery), often 2° to skull fracture (circle in **A**) involving the pterion (thinnest area of the lateral skull). Might present with transient loss of consciousness → recovery (“lucid interval”) → rapid deterioration due to hematoma expansion. Scalp hematoma (arrows in **A**) and rapid intracranial expansion (arrows in **B**) under systemic arterial pressure → transtentorial herniation, CN III palsy. CT shows biconvex (lentiform), hyperdense blood collection **B** **not crossing suture lines**.

Subdural hematoma

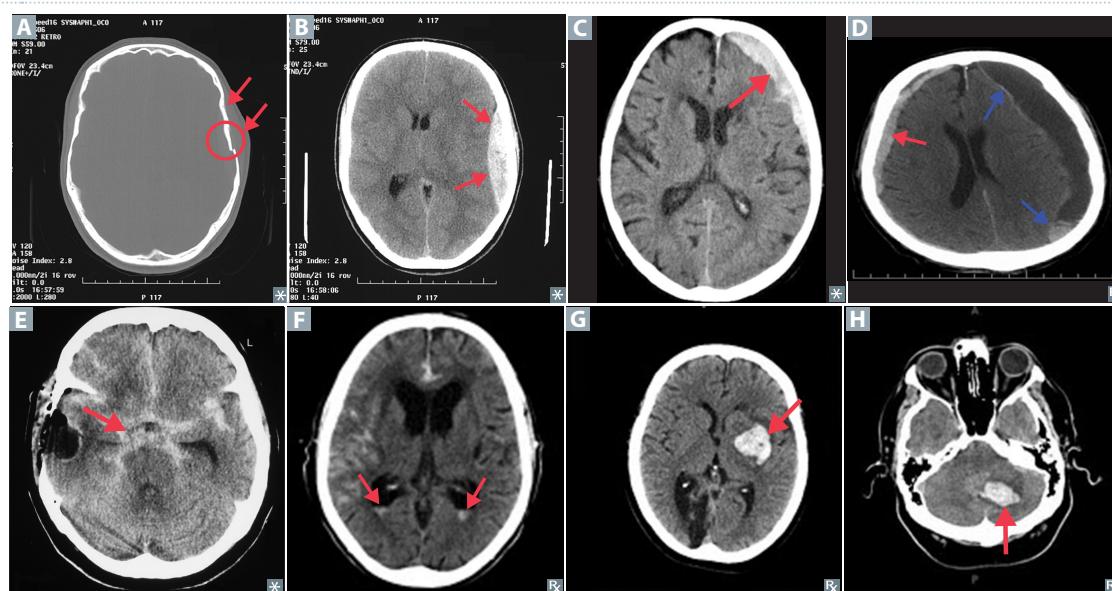
Rupture of bridging veins. Can be acute (traumatic, high-energy impact → brighter, or hyperdense, on CT) or chronic (associated with mild trauma, cerebral atrophy, ↑ age, chronic alcohol overuse → darker, or hypodense, on CT). Also seen in shaken babies. Crescent-shaped hemorrhage (red arrows in **C** and **D**) that **crosses suture lines**. Can cause midline shift, findings of acute (hyperdense border) on chronic (hypodense crescent) hemorrhage (blue arrows in **D**).

Subarachnoid hemorrhage

Bleeding **E F** due to trauma, or rupture of an aneurysm (such as a saccular aneurysm) or arteriovenous malformation. Rapid time course. Patients complain of “worst headache of my life.” Bloody or yellow (xanthochromic) LP. Vasospasm can occur due to blood breakdown or rebleed 3–10 days after hemorrhage → ischemic infarct; nimodipine used to prevent/reduce vasospasm. ↑ risk of developing communicating and/or noncommunicating hydrocephalus.

Intraparenchymal hemorrhage

Most commonly caused by systemic hypertension. Also seen with amyloid angiopathy (recurrent lobar hemorrhagic stroke in older adults), arteriovenous malformations, vasculitis, neoplasm. May be 2° to reperfusion injury in ischemic stroke. Hypertensive hemorrhages (Charcot-Bouchard microaneurysm) most often occur in putamen/globus pallidus of basal ganglia (lenticulostriate vessels **G**), followed by internal capsule, thalamus, pons, and cerebellum **H**.



Thalamic pain syndrome

Severe, treatment-resistant neuropathic pain following thalamic lesions; may be due to occlusion of a lenticulostriate artery. Initial paresthesias followed in weeks to months by allodynia (ordinarily painless stimuli cause pain), hyperalgesia (hypersensitivity to pain), and dysesthesia (altered sensation) on the contralateral side.

Phantom limb pain

Sensation of burning, aching, or electric shock–like pain in a limb that is no longer present. Common after amputation. Associated with reorganization of the 1° somatosensory cortex.

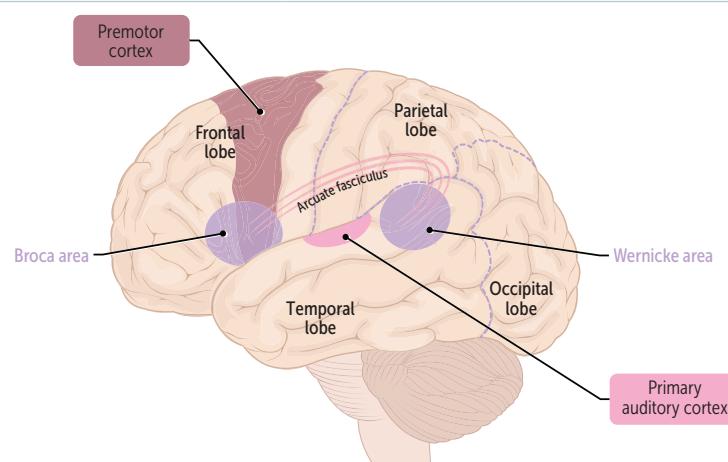
Diffuse axonal injury

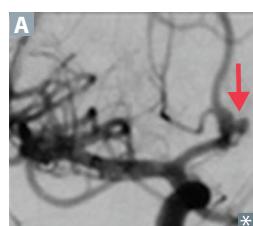
Traumatic shearing of white matter tracts during rapid acceleration and/or deceleration of the brain (eg, motor vehicle accident). Usually results in devastating neurologic injury, often causing coma or persistent vegetative state. MRI shows multiple lesions (punctate hemorrhages) involving white matter tracts **A**.

Aphasia

Higher-order language deficit (inability to understand/produce/use language appropriately); caused by pathology in dominant cerebral hemisphere (usually left). Distinguish from **dysarthria**—motor inability to produce speech (movement deficit).

TYPE	COMMENTS
Broca (expressive)	Broca area in inferior frontal gyrus of frontal lobe. Nonfluent speech with intact language comprehension. Patients appear frustrated, insight intact. Broca = b roken b oca (<i>boca</i> = mouth in Spanish).
Wernicke (receptive)	Wernicke area in superior temporal gyrus of temporal lobe. Fluent speech with impaired language comprehension. Patients do not have insight. Wernicke is a w ord s alad and makes no sense.
Conduction	Can be caused by damage to arcuate fasciculus. Impaired speech repetition.
Global	Broca and Wernicke areas affected. Nonfluent speech with impaired language comprehension.



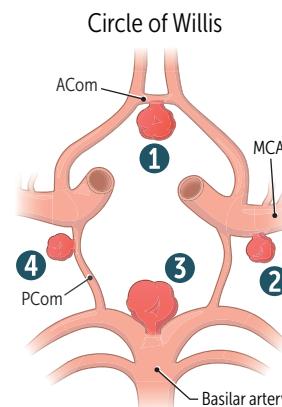
Aneurysms**Saccular aneurysm**

Abnormal dilation of an artery due to weakening of vessel wall.

Also called berry aneurysm **A**. Occurs at bifurcations in the circle of Willis. Most common site is junction of ACom and ACA. Associated with ADPKD, Ehlers-Danlos syndrome. Other risk factors: advanced age, hypertension, tobacco smoking.

Usually clinically silent until rupture (most common complication) → subarachnoid hemorrhage (“worst headache of my life” or “thunderclap headache”) → focal neurologic deficits. Can also cause symptoms via direct compression of surrounding structures by growing aneurysm.

- ACom—compression → bitemporal hemianopia (compression of optic chiasm); visual acuity deficits; rupture → ischemia in ACA distribution → contralateral lower extremity hemiparesis, sensory deficits.
- MCA—rupture → ischemia in MCA distribution → contralateral upper extremity and lower facial hemiparesis, sensory deficits.
- PCom—compression → ipsilateral CN III palsy → mydriasis (“blown pupil”); may also see ptosis, “down and out” eye.



1 Anterior communicating artery (ACom) aneurysm

2 Middle cerebral artery (MCA) aneurysm

3 Basilar tip aneurysm

4 Posterior communicating artery (PCom) aneurysm

Charcot-Bouchard microaneurysm

Common, associated with chronic hypertension; affects small vessels (eg, lenticulostriate arteries in basal ganglia, thalamus) and can cause hemorrhagic intraparenchymal strokes. Not visible on angiography.

Fever vs heat stroke

	Fever	Heat stroke
PATHOPHYSIOLOGY	Cytokine activation during inflammation (eg, infection)	Inability of body to dissipate heat (eg, exertion)
TEMPERATURE	Usually < 40°C (104°F)	Usually > 40°C (104°F)
COMPLICATIONS	Febrile seizure (benign, usually self-limiting)	CNS dysfunction (eg, confusion), rhabdomyolysis, acute kidney injury, ARDS, DIC
MANAGEMENT	Acetaminophen or ibuprofen for comfort (does not prevent future febrile seizures), antibiotic therapy if indicated	Rapid external cooling, rehydration and electrolyte correction

Seizures

Characterized by synchronized, high-frequency neuronal firing. Consist of 3 phases:

- Aura—early part of a seizure, may include odd smells or tastes.
- Ictal—time from first symptom to end of seizure activity.
- Postictal—period of gradual recovery back to preseizure baseline level of function/awareness.

Focal seizures

Originate in a single area of the brain, most commonly the medial temporal lobe. Types:

- **Focal aware** (formerly called simple partial)—consciousness intact; motor, sensory, autonomic, psychic symptoms
- **Focal impaired awareness** (formerly called complex partial)—impaired consciousness, automatisms

Generalized seizures

Diffuse. Types:

- **Absence (petit mal)**—3 Hz spike-and-wave discharges on EEG; short (usually 10 seconds), frequent episodes of blank stare, possible automatisms; no postictal confusion. Can be triggered by hyperventilation
- **Myoclonic**—quick, repetitive jerks; no loss of consciousness or postictal confusion
- **Tonic-clonic (grand mal)**—alternating stiffening and movement, postictal confusion, urinary incontinence, tongue biting
- **Tonic**—stiffening
- **Atonic**—“drop” seizures (falls to floor); commonly mistaken for fainting

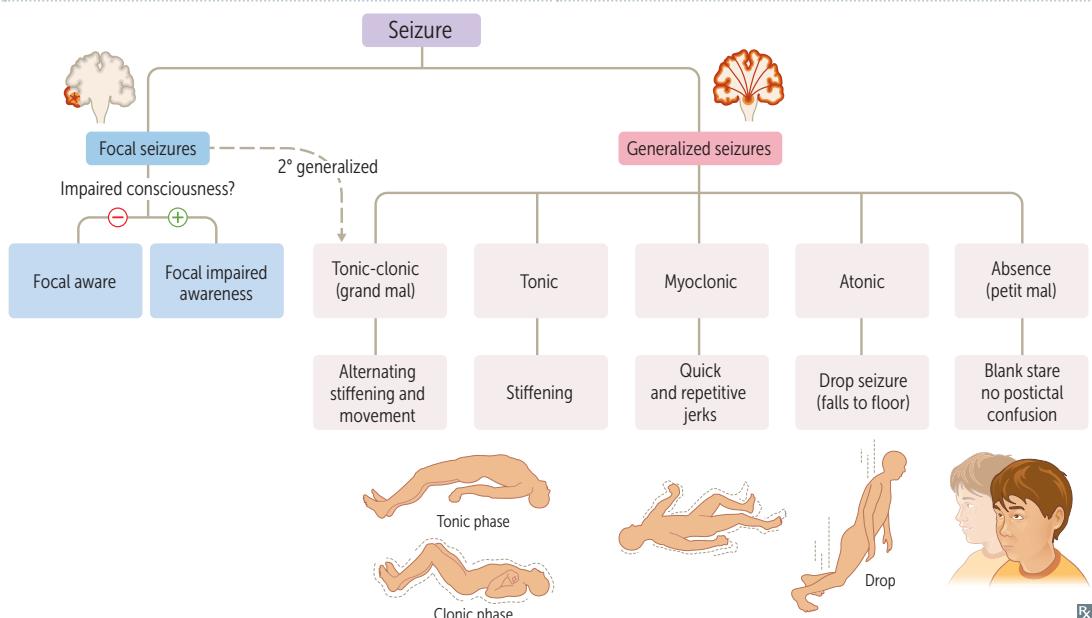
Epilepsy—disorder of recurrent, unprovoked seizures (febrile seizures are not epilepsy).

Convulsive status epilepticus—continuous (≥ 5 min) or recurring seizures without interictal return to baseline consciousness that may result in brain injury.

Causes of seizures by age:

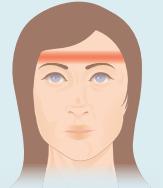
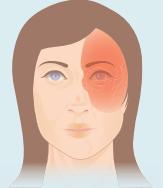
- Children < 18—genetic, infection (febrile), trauma, congenital, metabolic
- Adults 18–65—tumor, trauma, stroke, infection
- Adults > 65—stroke, tumor, trauma, metabolic, infection

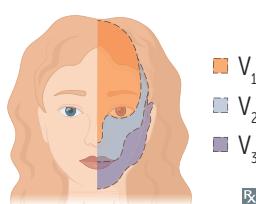
Psychogenic nonepileptic events—resemble prolonged (> 1 minute) syncopal or tonic-clonic episodes without postictal phase, autonomic disturbances, or tongue biting. Often witnessed with vocalizations and preceding aura. Female sex predominance. Risk factors: history of psychiatric disorders, substance use. Normal video EEG.



Headaches

Pain due to irritation of intra- or extracranial structures (eg, meninges, blood vessels). Primary headaches include tension-type, migraine, and cluster. Secondary headaches include medication overuse, meningitis, subarachnoid hemorrhage, hydrocephalus, neoplasia, giant cell arteritis.

CLASSIFICATION	LOCALIZATION	DURATION	DESCRIPTION	TREATMENT
Tension-type  Rx	Bilateral	> 30 min (typically 4–6 hr); constant	Steady, “bandlike” pain. No nausea or vomiting. No more than one of photophobia or phonophobia. No aura. Most common primary headache; more common in females.	Acute: analgesics, NSAIDs, acetaminophen. Prophylaxis: TCAs (eg, amitriptyline), behavioral therapy.
Migraine  Rx	Unilateral	4–72 hr	Pulsating pain with nausea, photophobia, and/or phonophobia. May have “aura.” Due to irritation of CN V, meninges, or blood vessels (release of vasoactive neuropeptides [eg, substance P, calcitonin gene-related peptide]). More common in females. POUND —Pulsatile, One-day duration, U nilateral, N ausea, D isabling.	Acute: NSAIDs, triptans, dihydroergotamine, antiemetics (eg, prochlorperazine, metoclopramide). Prophylaxis: lifestyle changes (eg, sleep, exercise, diet), β -blockers, amitriptyline, topiramate, valproate, botulinum toxin, anti-CGRP monoclonal antibodies.
Cluster  Rx	Unilateral	15 min–3 hr; repetitive	Excruciating periorbital pain with autonomic symptoms (eg, lacrimation, rhinorrhea, conjunctival injection). May present with Horner syndrome. More common in males.	Acute: sumatriptan, 100% O ₂ . Prophylaxis: verapamil.

Trigeminal neuralgia

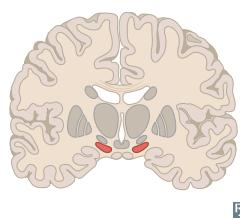
Recurrent brief episodes of intense unilateral pain in CN V distribution (usually V₂ and/or V₃). Most cases are due to compression of CN V root by an aberrant vascular loop. Pain is described as electric shock-like or stabbing and usually lasts seconds. Typically triggered by light facial touch or facial movements (eg, chewing, talking). Treatment: carbamazepine, oxcarbazepine.

Dyskinesias

DISORDER	PRESENTATION	NOTES
Akathisia	Restlessness and intense urge to move	Can be seen with neuroleptic use or as an adverse effect of Parkinson disease treatment
Asterixis	“Flapping” motion upon extension of wrists	Associated with hepatic encephalopathy, Wilson disease, and other metabolic derangements
Athetosis	Slow, snakelike, writhing movements; especially seen in the fingers	Caused by lesion to basal ganglia Seen in Huntington disease
Chorea	Sudden, jerky, purposeless movements	<i>Chorea</i> (Greek) = dancing Caused by lesion to basal ganglia Seen in Huntington disease and acute rheumatic fever (Sydenham chorea).
Dystonia	Sustained, involuntary muscle contractions	Writers cramp, blepharospasm, torticollis Treatment: botulinum toxin injection
Essential tremor	High-frequency tremor with sustained posture (eg, outstretched arms); worsened with movement or anxiety	Often familial Patients often self-medicate with alcohol, which ↓ tremor amplitude Treatment: nonselective β-blockers (eg, propranolol), barbiturates (primidone)
Intention tremor	Slow, zigzag motion when pointing/extending toward a target	Caused by cerebellar dysfunction
Resting tremor	Uncontrolled movement of distal appendages (most noticeable in hands); tremor alleviated by intentional movement	Caused by lesion to substantia nigra Occurs at rest ; “pill-rolling tremor” of Parkinson disease; when you park your car, it is at rest
Hemiballismus	Sudden, wild flailing of one side of the body	Caused by lesion to contralateral subthalamic nucleus (eg, due to lacunar stroke) In hemiballismus , half -of-body is going ballistic
Myoclonus	Sudden, brief, uncontrolled muscle contraction	Jerks; hiccups; common in metabolic abnormalities (eg, renal and liver failure), Creutzfeldt-Jakob disease

Restless legs syndrome

Uncomfortable sensations in legs causing irresistible urge to move them. Emerge during periods of inactivity; most prominent in the evening or at night. Transiently relieved by movement (eg, walking). Usually idiopathic (often with genetic predisposition), but may be associated with iron deficiency, CKD, diabetes mellitus (especially with neuropathy). Treatment: gabapentinoids, dopamine agonists.

Neurodegenerative movement disorders**Parkinson disease**

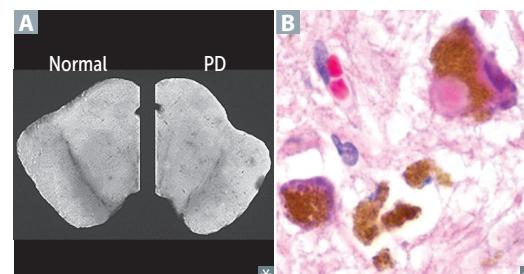
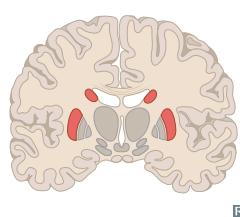
Loss of dopaminergic neurons in substantia nigra pars compacta (depigmentation in **A**). Symptoms typically manifest after age 60 (“body TRAP”):

- Tremor (pill-rolling tremor at rest)
- Rigidity (cogwheel or leadpipe)
- Akinesia/bradykinesia → shuffling gait, small handwriting (micrographia)
- Postural instability (tendency to fall)

Dementia is usually a late finding.

Affected neurons contain Lewy bodies: intracellular eosinophilic inclusions composed of α -synuclein **B**. Think “Parkin**synuclein**.”

Progressive supranuclear palsy—a Parkinson-plus syndrome. Clinical presentation: TRAP features, vertical gaze palsy, and cognitive dysfunction. Associated with “hummingbird sign” on midbrain MRI.

**Huntington disease**

Loss of GABAergic neurons in striatum. Autosomal dominant trinucleotide (CAG)_n repeat expansion in **huntingtin (HTT)** gene on chromosome **4** (**4 letters**) → toxic gain of function.

Symptoms typically manifest between age 30 and 50: chorea, athetosis, aggression, depression, dementia (sometimes initially mistaken for substance use).

Atrophy of caudate and putamen with ex vacuo ventriculomegaly.

↑ dopamine, ↓ GABA, ↓ ACh in brain. Neuronal death via NMDA receptor binding and glutamate excitotoxicity.

Anticipation results from expansion of **CAG** repeats. Caudate loses ACh and GABA.

Dementia

Decline in cognitive ability (eg, memory, executive function) with intact consciousness. Reversible causes of dementia include depression (pseudodementia), hypothyroidism, vitamin B₁₂ deficiency, neurosyphilis, normal pressure hydrocephalus.

Neurodegenerative**Alzheimer disease**

Most common cause of dementia in older adults. Advanced age is the strongest risk factor. Down syndrome patients have ↑ risk of developing early-onset Alzheimer disease, as amyloid precursor protein (APP) is located on chromosome 21. ↓ ACh in brain.

Associated with the following altered proteins:

- ApoE-2: ↓ risk of sporadic form
- ApoE-4: ↑ risk of sporadic form
- APP, presenilin-1, presenilin-2: familial forms (10%) with earlier onset

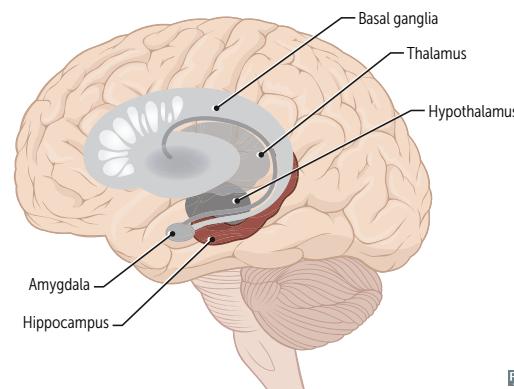
ApoE-2 is “protwoctive,” ApoE-4 is “four” Alzheimer disease.

Widespread cortical atrophy, especially in hippocampi. Narrowing of gyri and widening of sulci.

Senile plaques **A** in gray matter: extracellular amyloid- β (A β) core; may cause amyloid angiopathy → intraparenchymal hemorrhage; A β is derived from cleavage of APP.

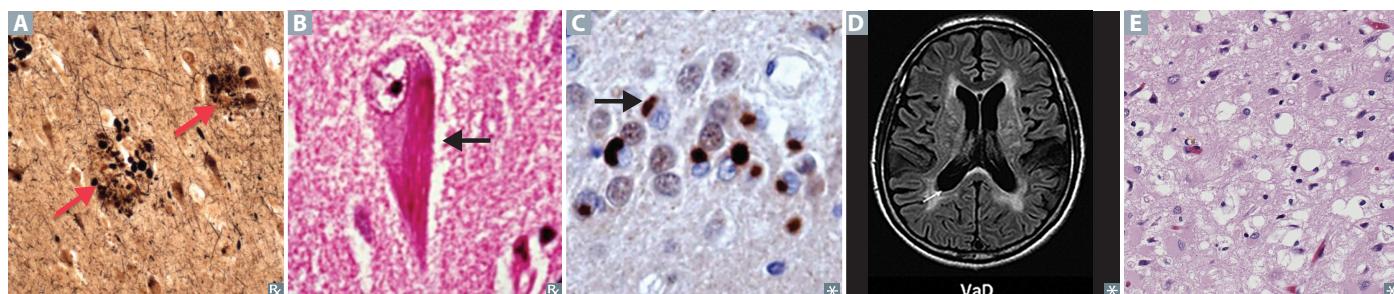
Neurofibrillary tangles **B**: intracellular, hyperphosphorylated tau protein = insoluble cytoskeletal elements; number of tangles correlates with degree of dementia.

Hirano bodies: intracellular eosinophilic proteinaceous rods in hippocampus.



Dementia (continued)

Frontotemporal dementia	Formerly called Pick disease. Early changes in personality and behavior (behavioral variant), or aphasia (primary progressive aphasia). May have associated movement disorders.	Frontal and/or temporal lobe atrophy. Inclusions of hyperphosphorylated tau (round Pick bodies C) or ubiquitinated TDP-43.
Lewy body dementia	Visual hallucinations (“haLewycinations”), dementia with fluctuating cognition/alertness, REM sleep behavior disorder, and parkinsonism.	Intracellular Lewy bodies primarily in cortex. Called Lewy body dementia if cognitive and motor symptom onset < 1 year apart, otherwise considered dementia 2° to Parkinson disease.
Vascular		
Vascular dementia	2nd most common cause of dementia in older adults. Result of multiple arterial infarcts and/or chronic ischemia. Step-wise decline in cognitive ability with late-onset memory impairment.	MRI or CT shows multiple cortical and/or subcortical infarcts D .
Infective		
Creutzfeldt-Jakob disease	Rapidly progressive (weeks to months) dementia with myoclonus (“startle myoclonus”) and ataxia. Fatal. Caused by prions: PrP ^c → PrP ^{sc} (β -pleated sheet resistant to proteases). Typically sporadic, but may be transmitted by contaminated materials (eg, corneal transplant, neurosurgical equipment).	Spongiform cortex E (vacuolation without inflammation). Associated with periodic sharp wave complexes on EEG and ↑ 14-3-3 protein in CSF.
HIV-associated dementia	Subcortical dysfunction associated with advanced HIV infection. Characterized by cognitive deficits, gait disturbance, irritability, depressed mood.	Diffuse gray matter and subcortical atrophy. Microglial nodules with multinucleated giant cells.



Idiopathic intracranial hypertension

Also called pseudotumor cerebri. ↑ ICP with no obvious structural findings on imaging. Risk factors include **female** sex, **Tetracyclines**, **Obesity**, vitamin **A** excess, **Danazol** (**female TOAD**). Associated with dural venous sinus stenosis. Findings: headache (exacerbated when lying down), tinnitus, diplopia (usually from CN VI palsy), no change in mental status. Impaired optic nerve axoplasmic flow → papilledema. Visual field testing shows enlarged blind spot and peripheral constriction. LP reveals ↑ opening pressure and provides temporary headache relief.

Treatment: weight loss, acetazolamide, invasive procedures for refractory cases (eg, CSF shunt placement, optic nerve sheath fenestration surgery for visual loss).

Hydrocephalus

↑ CSF volume → ventricular dilation +/- ↑ ICP.

Communicating**Communicating hydrocephalus**

↓ CSF absorption by arachnoid granulations (eg, arachnoid scarring post-meningitis) → ↑ ICP, papilledema, herniation. All ventricles are dilated.

Normal pressure hydrocephalus

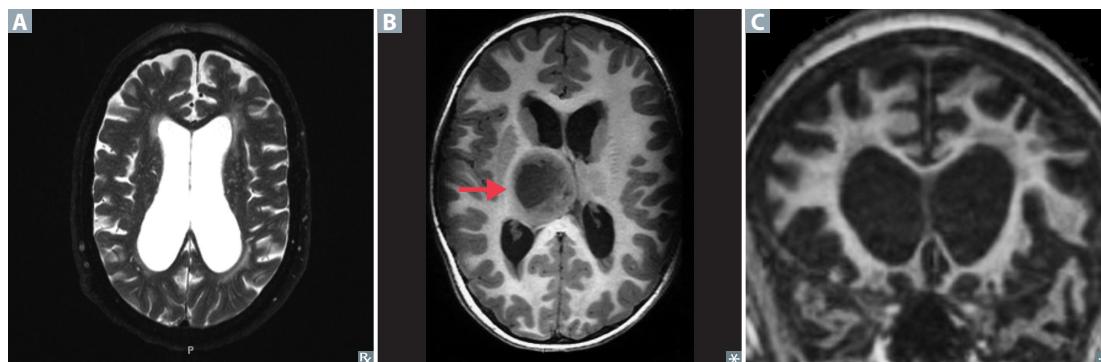
Affects older adults; idiopathic; CSF pressure elevated only episodically; does not result in increased subarachnoid space volume. Expansion of ventricles **A** distorts the fibers of the corona radiata → triad of **gait apraxia** (magnetic gait), **cognitive dysfunction**, and **urinary incontinence**. “**Wobbly, wacky, and wet.**” Treatment: CSF drainage via LP or shunt placement.

Noncommunicating (obstructive)**Noncommunicating hydrocephalus**

Caused by structural blockage of CSF circulation within ventricular system (eg, stenosis of aqueduct of Sylvius, colloid cyst blocking foramen of Monro, tumor **B**). Ventricles “upstream” of the obstruction are dilated.

Hydrocephalus mimics**Ex vacuo ventriculomegaly**

Appearance of ↑ CSF on imaging **C**, but is actually due to ↓ brain tissue and neuronal atrophy (eg, Alzheimer disease, HIV, frontotemporal dementia, Huntington disease). ICP is normal; NPH triad is not seen.



Multiple sclerosis

Autoimmune inflammation and demyelination of CNS (brain and spinal cord) with subsequent axonal damage. Most often affects females aged 20–40; higher prevalence in individuals who grew up farther from equator and have ↓ serum vitamin D levels. Can present with

- Optic neuritis (acute painful monocular visual loss, associated with relative afferent pupillary defect)
- Brainstem/cerebellar syndromes (eg, diplopia, ataxia, vertigo, scanning speech, dysarthria, intention tremor, nystagmus/intranuclear ophthalmoplegia [INO] [bilateral > unilateral])
- Pyramidal tract demyelination (eg, weakness, spasticity)
- Spinal cord syndromes (eg, electric shock–like sensation originating from cervical flexion, transmitted along the spinal cord [Lhermitte sign], neurogenic bladder, paraparesis, sensory manifestations affecting the trunk or one or more extremities)

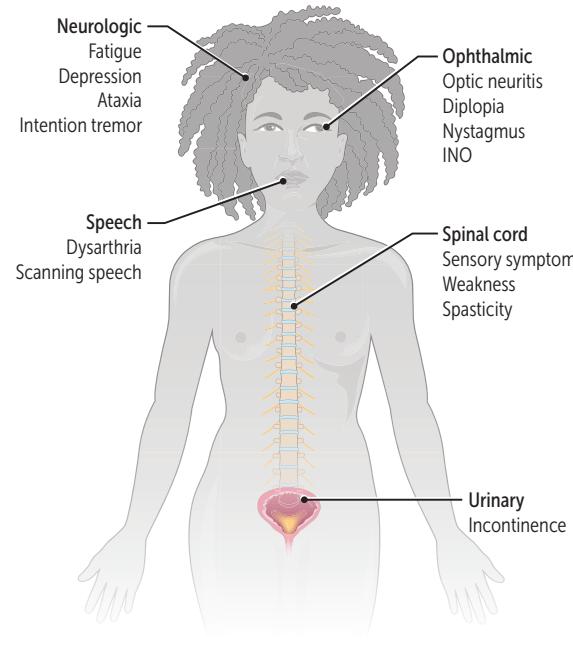
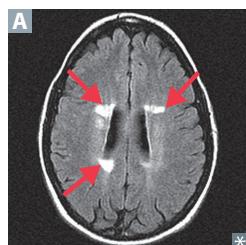
Symptoms may be exacerbated by stressors (eg, heat [Uhthoff phenomenon], exercise, or infection). Relapsing and remitting is most common clinical course.

FINDINGS

↑ IgG level and myelin basic protein in CSF. Oligoclonal bands in CSF aid in diagnosis. MRI is gold standard. Periventricular plaques A (areas of oligodendrocyte loss and reactive gliosis). Multiple white matter lesions disseminated in space and time.

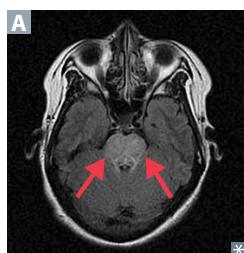
TREATMENT

Stop relapses and halt/slow progression with disease-modifying therapies (eg, β-interferon, glatiramer, natalizumab). Treat acute flares with IV steroids. Symptomatic treatment for neurogenic bladder (muscarinic antagonists, botulinum toxin injection), spasticity (baclofen, GABA_B receptor agonists), pain (TCAs, anticonvulsants).



Other demyelinating and dysmyelinating disorders

Osmotic demyelination syndrome



Also called central pontine myelinolysis. Massive axonal demyelination in pontine white matter

A 2° to rapid osmotic changes, most commonly iatrogenic correction of hyponatremia but also rapid shifts of other osmolytes (eg, glucose). Acute paralysis, dysarthria, dysphagia, diplopia, loss of consciousness. Can cause altered level of consciousness.

Correcting serum Na^+ too fast:

- “From low to high, your pons will die” (osmotic demyelination syndrome)
- “From high to low, your brains will blow” (cerebral edema/herniation)

Acute inflammatory demyelinating polyneuropathy

Most common subtype of **Guillain-Barré syndrome**.

Autoimmune condition that destroys Schwann cells via inflammation and demyelination of motor fibers, sensory fibers, peripheral nerves (including CN III-XII). Likely facilitated by molecular mimicry and triggered by inoculations or stress. Despite association with infections (eg, *Campylobacter jejuni*, viruses [eg, Zika]), no definitive causal link to any pathogen.

Results in symmetric ascending muscle weakness/paralysis and depressed/absent DTRs beginning in lower extremities. Facial paralysis (usually bilateral) and respiratory failure are common. May see autonomic dysregulation (eg, cardiac irregularities, hypertension, hypotension) or sensory abnormalities. Most patients survive with good functional recovery.

↑ CSF protein with normal cell count (albuminocytologic dissociation).

Respiratory support is critical until recovery. Disease-modifying treatment: plasma exchange or IV immunoglobulins. No role for steroids.

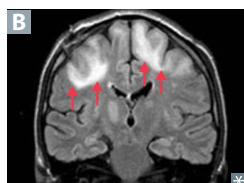
Acute disseminated (postinfectious) encephalomyelitis

Multifocal inflammation and demyelination after infection or vaccination. Presents with rapidly progressive multifocal neurologic symptoms, altered mental status.

Charcot-Marie-Tooth disease

Also called hereditary motor and sensory neuropathy. Group of progressive hereditary nerve disorders related to the defective production of proteins involved in the structure and function of peripheral nerves or the myelin sheath. Typically autosomal dominant and associated with foot deformities (eg, pes cavus, hammer toe), lower extremity weakness (eg, foot drop), and sensory deficits (eg, decreased vibration, proprioception). Most common type, **CMT1A**, is caused by PMP22 gene duplication (**Can't Move Toes**).

Progressive multifocal leukoencephalopathy



Demyelination of CNS **B** due to destruction of oligodendrocytes (2° to reactivation of latent JC virus infection). Associated with severe immunosuppression (eg, lymphomas and leukemias, AIDS, organ transplantation). Rapidly progressive, usually fatal. Predominantly involves parietal and occipital areas; visual symptoms are common. ↑ risk associated with organ transplantation, medications (eg, natalizumab).

Critical illness polyneuropathy

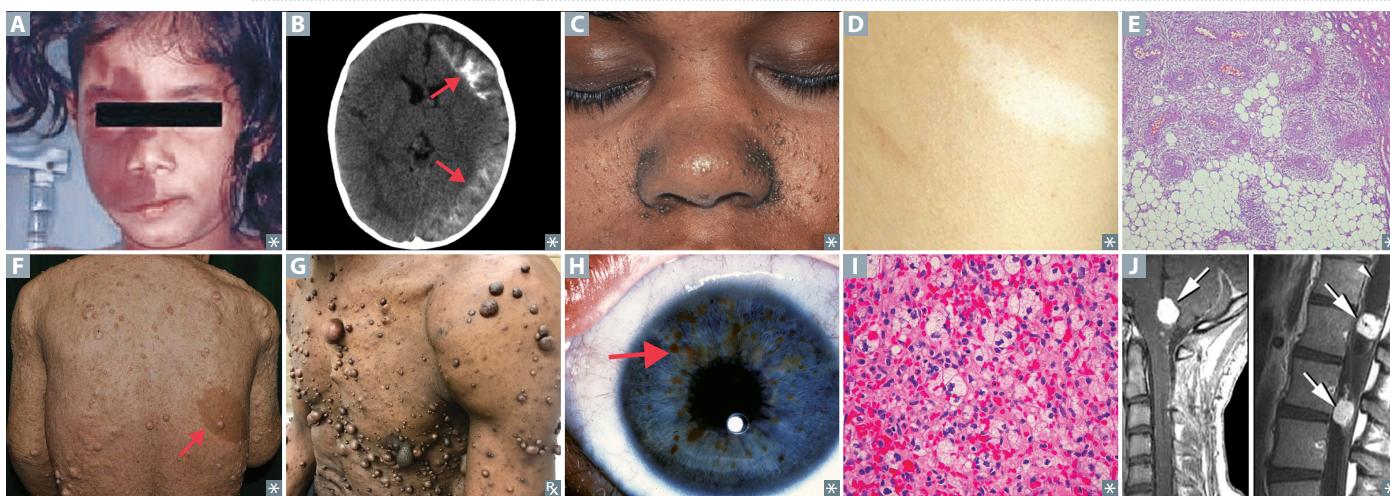
Axonal degeneration (likely from inflammatory mediators and microcirculation injury), ↓ nerve excitability 2° to Na^+ channel inactivation → symmetric weakness (proximal > distal), ↓ deep tendon reflexes; diaphragmatic weakness may lead to difficulty weaning from mechanical ventilation.

Other disorders

Krabbe disease, metachromatic leukodystrophy, adrenoleukodystrophy.

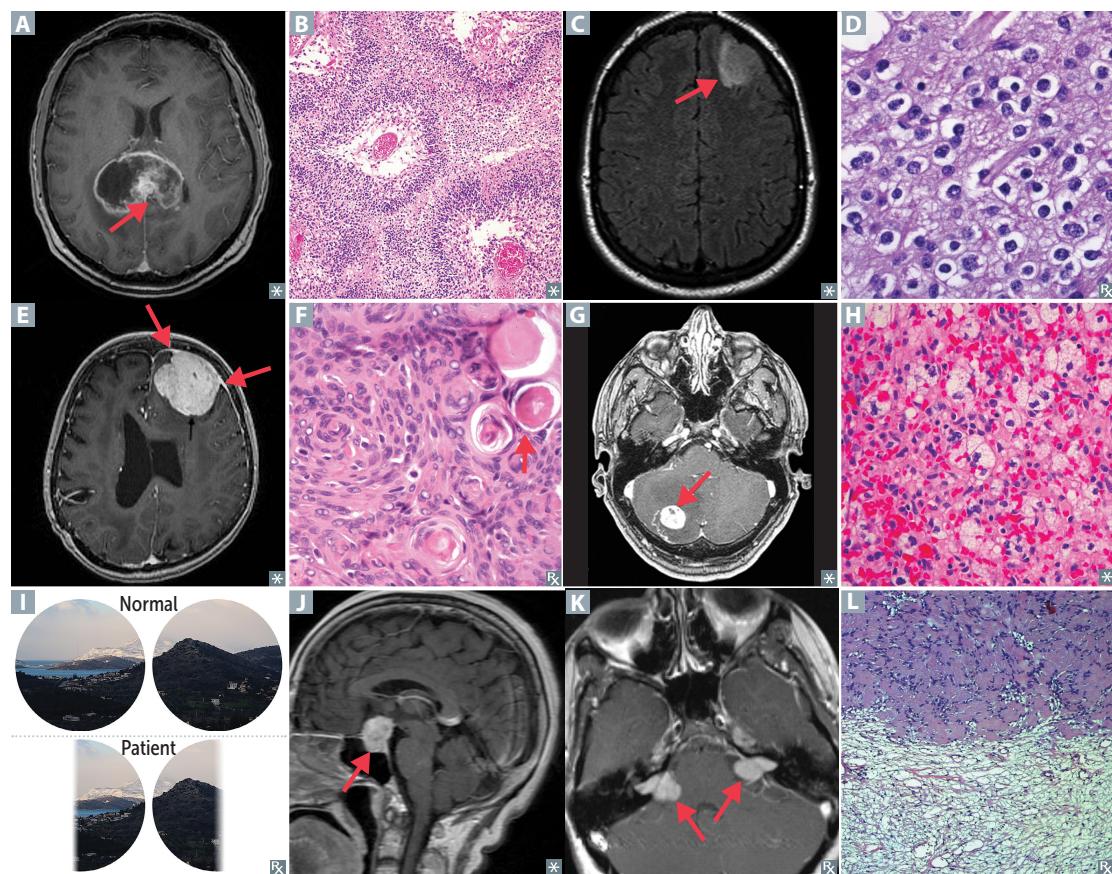
Neurocutaneous disorders

DISORDER	GENETICS	PRESENTATION	NOTES
Sturge-Weber syndrome	Congenital nonhereditary anomaly of neural crest derivatives. Somatic mosaicism of an activating mutation in one copy of the GNAQ gene.	Capillary vascular malformation → port-wine stain A (nevus flammeus or non-neoplastic birthmark) in CN V ₁ /V ₂ distribution; ipsilateral leptomeningeal angioma with calcifications B → seizures/epilepsy; intellectual disability; episcleral hemangioma → ↑ IOP → early-onset glaucoma.	Also called encephalotrigeminal angiomatosis.
Tuberous sclerosis complex	AD, variable expression. Mutation in tumor suppressor genes TSC1 on chromosome 9 (hamartin), TSC2 on chromosome 16 (tuberin; pronounce “twoberin”).	Hamartomas in CNS and skin, angiofibromas C , mitral regurgitation, ash-leaf spots D , cardiac rhabdomyoma, intellectual disability, renal angiomyolipoma E , seizures, shagreen patches.	↑ incidence of subependymal giant cell astrocytomas and ungual fibromas.
Neurofibromatosis type I	AD, 100% penetrance. Mutation in NFI tumor suppressor gene on chromosome 17 (encodes neurofibromin, a negative RAS regulator).	Café-au-lait spots F , Intellectual disability, Cutaneous neurofibromas G , Lisch nodules (pigmented iris hamartomas H), Optic gliomas, Pheochromocytomas, Seizures/focal neurologic Signs (often from meningioma), bone lesions (eg, sphenoid dysplasia).	Also called von Recklinghausen disease. 17 letters in “von Recklinghausen.” CICLOPSS .
Neurofibromatosis type II	AD. Mutation in NF2 tumor suppressor gene (merlin) on chromosome 22.	Bilateral vestibular schwannomas, juvenile cataracts, meningiomas, ependymomas.	NF2 affects 2 ears, 2 eyes.
von Hippel-Lindau disease	AD. Deletion of VHL gene on chromosome 3p. pVHL ubiquitinates hypoxia-inducible factor 1α.	Hemangioblastomas (high vascularity with hyperchromatic nuclei I) in retina, brainstem, cerebellum, spine J ; Angiomatosis; bilateral Renal cell carcinomas; Pheochromocytoma. HARP .	Numerous tumors, benign and malignant. VHL = 3 letters = chromosome 3 ; associated with RCC (also 3 letters).



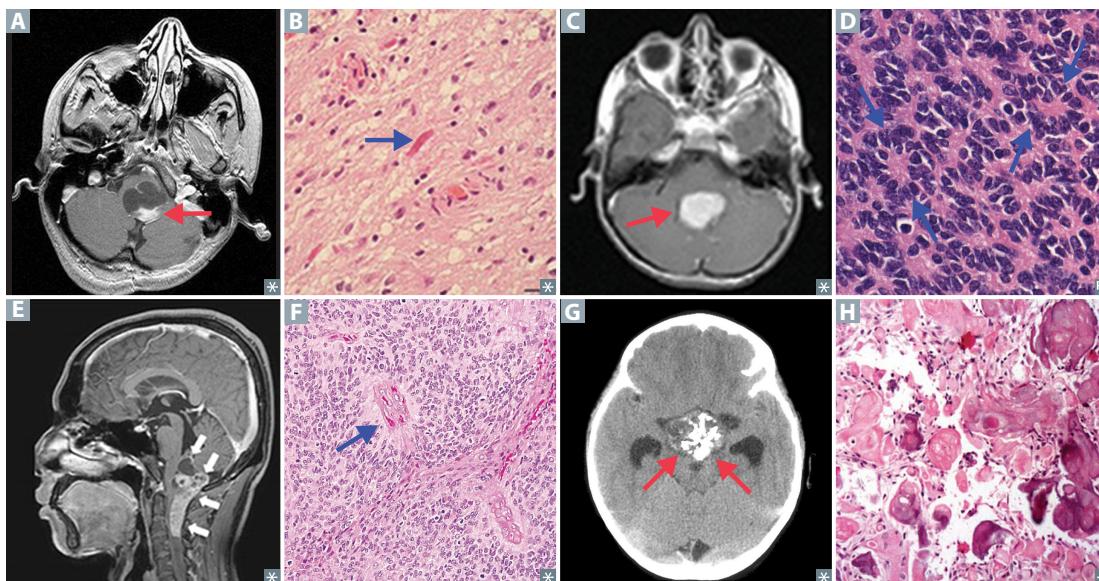
Adult primary brain tumors

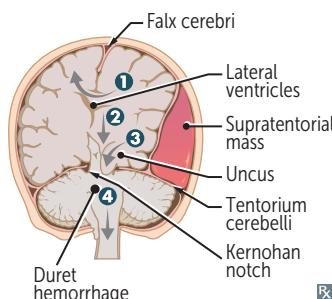
TUMOR	DESCRIPTION	HISTOLOGY
Glioblastoma	Common, highly malignant 1° brain tumor with ~ 1-year median survival. Found in cerebral hemispheres. Can cross corpus callosum (“butterfly glioma” A). Associated with EGFR amplification.	Astrocyte origin, GFAP +. “Pseudopalisading” pleomorphic tumor cells B border central areas of necrosis, hemorrhage, and/or microvascular proliferation.
Oligodendrogloma	Relatively rare, slow growing. Most often in frontal lobes C . Often calcified.	Oligodendrocyte origin. “Fried egg” cells—round nuclei with clear cytoplasm D . “Chicken-wire” capillary pattern.
Meningioma	Common, typically benign. Females > males. Occurs along surface of brain or spinal cord. Extra-axial (external to brain parenchyma) and may have a dural attachment (“tail” E). Well circumscribed, spherical or lobular shape. Often asymptomatic; may present with seizures or focal neurologic signs. Treatment: resection and/or radiosurgery.	Arachnoid cell origin. Spindle cells concentrically arranged in a whorled pattern; psammoma bodies (laminated calcifications, arrow in F).
Hemangioblastoma	Most often cerebellar G . Associated with von Hippel-Lindau syndrome when found with retinal angiomas. Can produce erythropoietin → 2° polycythemia.	Blood vessel origin. Closely arranged, thin-walled capillaries with minimal intervening parenchyma H .
Pituitary adenoma	May be nonfunctioning (silent) or hyperfunctioning (hormone-producing). Nonfunctional tumors present with mass effect (eg, bitemporal hemianopia [due to pressure on optic chiasm I]). Pituitary apoplexy → hypopituitarism. Prolactinoma classically presents as galactorrhea, amenorrhea, ↓ bone density due to suppression of estrogen in females and as ↓ libido, infertility in males. Treatment: dopamine agonists (eg, bromocriptine, cabergoline), transsphenoidal resection.	Hyperplasia of only one type of endocrine cells found in pituitary. Most commonly from lactotrophs (prolactin) J → hyperprolactinemia. Less commonly, from somatotrophs (GH) → acromegaly, gigantism; corticotrophs (ACTH) → Cushing disease. Rarely, from thyrotrophs (TSH), gonadotrophs (FSH, LH).
Schwannoma	Classically at the cerebellopontine angle K , benign, involving CNs V, VII, and VIII, but can be along any peripheral nerve. Often localized to CN VIII in internal acoustic meatus → vestibular schwannoma (can present as hearing loss, tinnitus, and unsteady gait). Bilateral vestibular schwannomas found in NF-2. Treatment: resection or stereotactic radiosurgery.	Schwann cell origin, S-100 +. Biphasic, dense, hypercellular areas containing spindle cells alternating with hypocellular, myxoid areas L .

Adult primary brain tumors (continued)

Childhood primary brain tumors

TUMOR	DESCRIPTION	HISTOLOGY
Pilocytic astrocytoma	Most common 1° brain tumor in childhood. Usually well circumscribed. In children, most often found in posterior fossa (eg, cerebellum). May be supratentorial. Cystic appearance with mural nodule A . Benign; good prognosis.	Astrocyte origin, GFAP \oplus . Bipolar neoplastic cells with hairlike projections. Associated with microcysts and Rosenthal fibers (eosinophilic, corkscrew fibers B).
Medulloblastoma	Most common malignant brain tumor in childhood. Commonly involves cerebellum C . Can involve the cerebellar vermis → truncal ataxia. Can compress 4th ventricle → noncommunicating hydrocephalus → headaches, papilledema. Can send “drop metastases” to spinal cord.	Form of primitive neuroectodermal tumor (PNET). Homer-Wright rosettes (small, round, blue cells surrounding central area of neuropil D). Synaptophysin \oplus .
Ependymoma	Most commonly found in 4th ventricle E → noncommunicating hydrocephalus. Poor prognosis.	Ependymal cell origin. Characteristic perivascular pseudorosettes F . Rod-shaped blepharoplasts (basal ciliary bodies) found near the nucleus.
Craniopharyngioma	Most common childhood supratentorial tumor. G . Calcification is common. Commonly arises along pituitary stalk → compression of optic chiasm → bitemporal hemianopia (may be confused with pituitary adenoma). Associated with a high recurrence rate.	Derived from remnants of Rathke pouch (ectoderm). Anucleate squamous cells (“ghost cells”) forming keratinous nodules with dystrophic calcifications H . Cholesterol crystals found in “motor oil”-like fluid within tumor.
Pineal gland tumors	Most commonly extragonadal germ cell tumors. ↑ incidence in males. Present with noncommunicating hydrocephalus (compression of cerebral aqueduct), Parinaud syndrome (compression of dorsal midbrain)—triad of upward gaze palsy, convergence-retraction nystagmus, and light-near dissociation.	Similar to testicular seminomas.



Herniation syndromes

1 Cingulate (subfalcine) herniation under falk cerebri

Can cause anterior cerebral artery compression
→ contralateral lower extremity weakness. If affecting the dominant hemisphere, can cause arcuate fasciculus compression → aphasia.

2 Central/downward transtentorial herniation

Caudal displacement of brainstem → rupture of paramedian basilar artery branches → Duret hemorrhages. Usually fatal.

3 Uncal transtentorial herniation

Uncus = medial temporal lobe. Early herniation → ipsilateral blown pupil (unilateral CN III compression), contralateral hemiparesis. Late herniation → coma, Kernohan phenomenon (misleading ipsilateral hemiparesis +/- contralateral blown pupil due to contralateral cerebral peduncle +/- CN III compression against Kernohan notch).

4 Cerebellar tonsillar herniation into the foramen magnum

Coma and death result when these herniations compress the brainstem.

Motor neuron signs

SIGN	UMN LESION	LMN LESION	COMMENTS
Weakness	+	+	Lower motor neuron = everything lowered (\downarrow muscle mass, tone, reflexes, toes)
Atrophy	-	+	Upper motor neuron = everything up (\uparrow tone, reflexes, toes)
Fasciculations	-	+	
Reflexes	\uparrow	\downarrow	
Tone	\uparrow	\downarrow	Fasciculations = muscle twitching Positive Babinski is normal in infants
Babinski	+	-	
Spastic paresis	+	-	
Flaccid paralysis	-	+	
Clasp knife spasticity	+	-	

Spinal cord lesions**Poliomyelitis**

Destruction of anterior horns by poliovirus. Fecal-oral transmission → replication in lymphoid tissue of oropharynx and small intestine → spread to CNS via bloodstream.

Acute LMN signs (**asymmetric** weakness) and symptoms of viral meningitis (eg, fever, headache, neck stiffness). Respiratory muscle involvement leads to respiratory failure.

CSF shows ↑ WBCs (lymphocytic pleocytosis) and slight ↑ of protein (with no change in CSF glucose). Poliovirus can be isolated from stool or throat secretions.

Spinal muscular atrophy

Congenital degeneration of anterior horns. Autosomal recessive **SMN1** mutation (encodes survival motor neuron protein) → defective snRNP assembly → LMN apoptosis. Spinal muscular atrophy type 1 (most common) is also called **Werdnig-Hoffmann disease**.

LMN signs only (**symmetric** weakness). “Floppy baby” with marked hypotonia (flaccid paralysis) and tongue fasciculations.

Amyotrophic lateral sclerosis

Combined UMN (corticospinal/corticobulbar) and LMN (brainstem/spinal cord) degeneration. Usually idiopathic. Familial form (less common) may be linked to **SOD1** mutations (encodes superoxide dismutase 1). ALS is also called **Lou Gehrig disease**.

LMN signs: flaccid limb weakness, fasciculations, atrophy, bulbar palsy (dysarthria, dysphagia, tongue atrophy). UMN signs: spastic limb weakness, hyperreflexia, clonus, pseudobulbar palsy (dysarthria, dysphagia, emotional lability). No sensory or bowel/bladder deficits.

Fatal (most often from respiratory failure). Treatment: riluzole (“riLouzole”), edaravone (free radical scavenger) → slow functional decline.

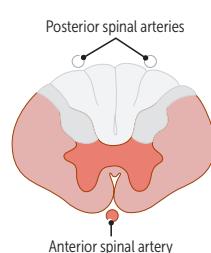
Tabes dorsalis

Degeneration/demyelination of dorsal columns and roots by *T pallidum* (3° syphilis). Causes progressive sensory ataxia (impaired proprioception → poor coordination). ⊕ Romberg sign and absent DTRs. Associated with shooting pain, Argyll Robertson pupils, Charcot joints.

Subacute combined degeneration

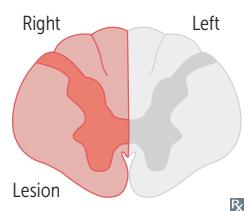
Demyelination of **Spinocerebellar tracts**, **lateral Corticospinal tracts**, and **Dorsal columns (SCD)** due to vitamin B₁₂ deficiency.

Ataxic gait, paresthesias, impaired position/vibration sense (⊕ Romberg sign), UMN signs.

Anterior spinal artery occlusion

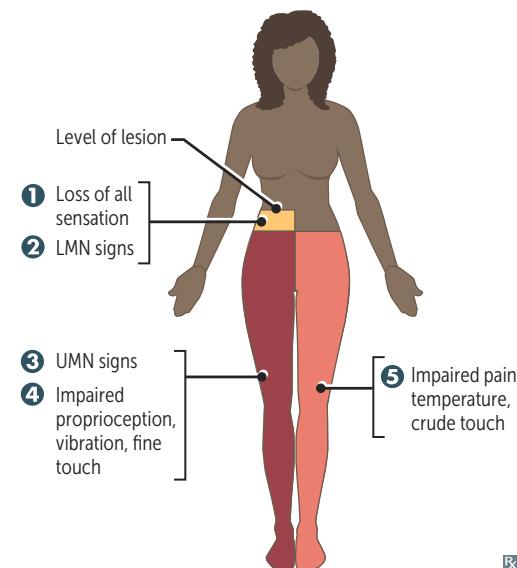
Spinal cord infarction sparing dorsal horns and dorsal columns. Watershed area is mid-thoracic ASA territory, as the artery of Adamkiewicz supplies ASA below T8. Can be caused by aortic aneurysm repair.

Presents with UMN signs below the lesion (corticospinal tract), LMN signs at the level of the lesion (anterior horn), and loss of pain and temperature sensation below the lesion (spinothalamic tract).

Brown-Séquard syndrome

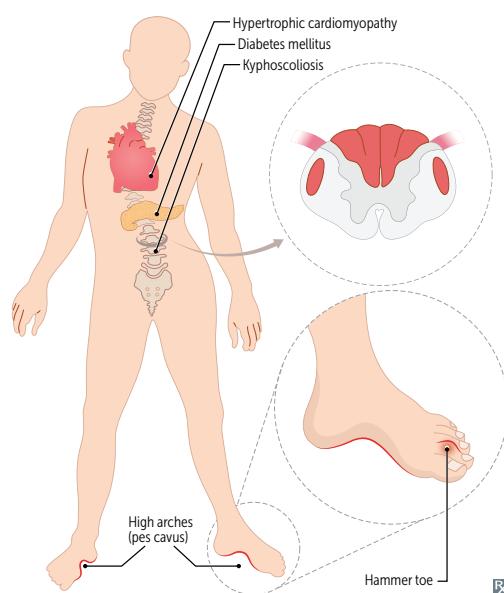
Hemisection of spinal cord. Findings due to deficits in

- ① All sensory pathways—ipsilateral loss of all sensation **at** the lesion level.
 - ② Corticospinal tract—ipsilateral LMN signs (eg, flaccid paralysis) **at** lesion level.
 - ③ Corticospinal tract—ipsilateral UMN signs **below** lesion level.
 - ④ Dorsal columns—ipsilateral loss of proprioception, vibration, and fine (2-point discrimination) touch **below** lesion level.
 - ⑤ Spinothalamic tract—contralateral loss of pain, temperature, and crude (nondiscriminative) touch **below** lesion level.
- Oculosympathetic pathway (if lesion occurs above T1)—ipsilateral Horner syndrome.

**Friedreich ataxia**

Autosomal recessive trinucleotide repeat disorder (**GAA**)_n on chromosome 9 in gene that encodes frataxin (iron-binding protein). Leads to impairment in mitochondrial functioning. Degeneration of lateral corticospinal tract (spastic paralysis), spinocerebellar tract (ataxia), dorsal columns (↓ vibratory sense, proprioception), and dorsal root ganglia (loss of DTRs). **Staggering** gait, frequent **falling**, nystagmus, dysarthria, pes cavus, hammer toes, **diabetes mellitus**, **hypertrophic cardiomyopathy** (cause of death). Presents in childhood with kyphoscoliosis **A**.

Friedreich is **frataxic** (**frataxin**): he's your favorite **frat** brother, always **staggering** and **falling** but has a **sweet, big heart**. Ataxic **GAAit**.

**Cerebral palsy**

Permanent motor dysfunction resulting from nonprogressive injury to developing fetal/infant brain. Most common movement disorder in children.

Multifactorial etiology; prematurity and low birth weight are the strongest risk factors. Associated with development of periventricular leukomalacia (focal necrosis of white matter tracts).

Presents with UMN signs (eg, spasticity, hyperreflexia) affecting ≥ 1 limbs, persistence of primitive reflexes, abnormal posture, developmental delay in motor skills, neurobehavioral abnormalities (excessive docility, irritability).

Treatment: muscle relaxants (eg, baclofen), botulinum toxin injections, selective dorsal rhizotomy. Prevention: prenatal magnesium sulfate for high-risk pregnancies ↓ incidence and severity.

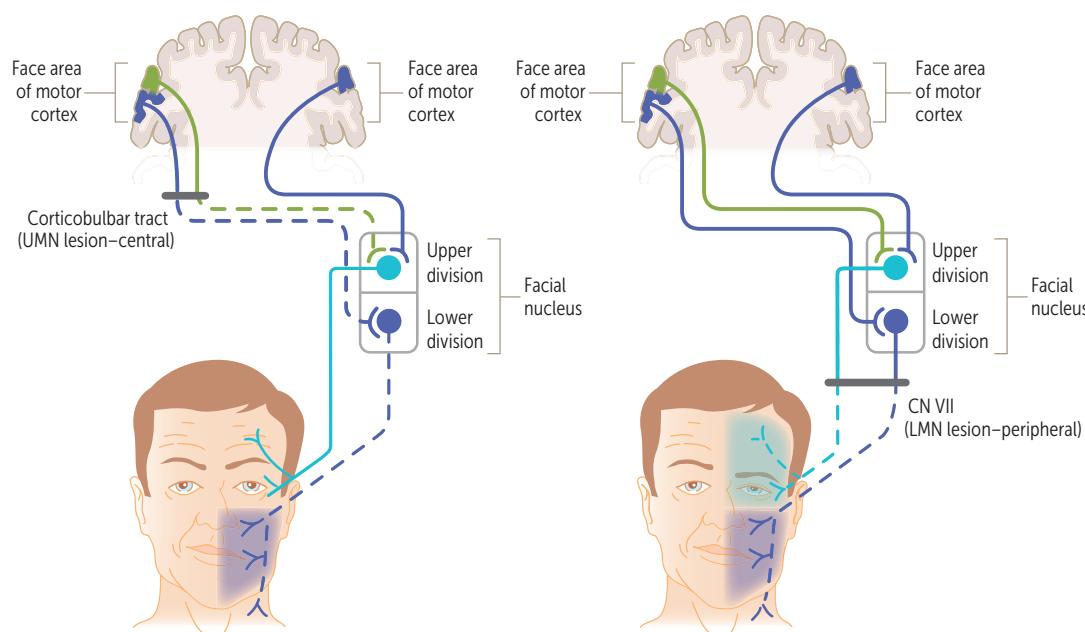
Common cranial nerve lesions

CN V motor lesion	Jaw deviates toward side of lesion due to unopposed force from the opposite pterygoid muscle.
CN X lesion	Uvula deviates away from side of lesion. Weak side collapses and uvula points away.
CN XI lesion	Weakness turning head away from side of lesion (SCM). Shoulder droop on side of lesion (trapezius).
CN XII lesion	LMN lesion. Tongue deviates toward side of lesion (“lick your wounds”) due to weakened tongue muscles on affected side.

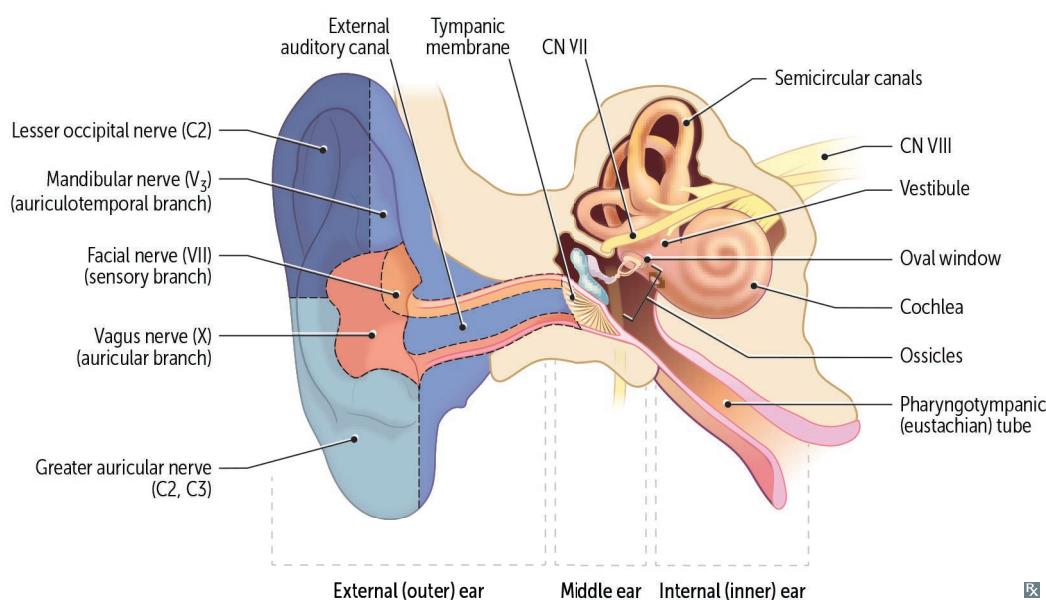
Facial nerve lesions

Bell palsy is the most common cause of peripheral facial palsy **A**. Usually develops after HSV reactivation. Treatment: glucocorticoids +/- acyclovir. Most patients gradually recover function, but aberrant regeneration can occur. Other causes of peripheral facial palsy include Lyme disease, herpes zoster (**Ramsay Hunt syndrome**)—triad of ipsilateral facial paralysis, otalgia, and vesicles near the auditory canal), sarcoidosis, tumors (eg, parotid gland), diabetes mellitus.

	Upper motor neuron lesion	Lower motor neuron lesion
LESION LOCATION	Motor cortex, connection from motor cortex to facial nucleus in pons	Facial nucleus, anywhere along CN VII
AFFECTED SIDE	Contralateral	Ipsilateral
MUSCLES INVOLVED	Lower muscles of facial expression	Upper and lower muscles of facial expression
FOREHEAD INVOLVEMENT	Spared, due to bilateral UMN innervation	Affected
OTHER SYMPTOMS	Variable; depends on size of lesion	Incomplete eye closure (dry eyes, corneal ulceration), hyperacusis, loss of taste sensation to anterior tongue



► NEUROLOGY—OTOTOLOGY

Auditory anatomy and physiology**Outer ear**

Visible portion of ear (pinna), includes auditory canal and tympanic membrane. Transfers sound waves via vibration of tympanic membrane.

Middle ear

Air-filled space with three bones called the ossicles (malleus, incus, stapes). Ossicles conduct and amplify sound from tympanic membrane to inner ear.

Inner ear

Snail-shaped, fluid-filled cochlea. Contains basilar membrane that vibrates 2° to sound waves.

Vibration transduced via specialized hair cells → auditory nerve signaling → brainstem.

Each frequency leads to vibration at specific location on basilar membrane (tonotopy):

- Low frequency heard at apex near helicotrema (wide and flexible).
- High frequency heard best at base of cochlea (thin and rigid).

Otitis externa

Inflammation of external auditory canal. Most commonly due to *Pseudomonas*. Associated with water exposure (swimmer's ear), ear canal trauma/occlusion (eg, hearing aids).

Presents with otalgia that worsens with ear manipulation, pruritus, hearing loss, discharge **A**.

Malignant (necrotizing) otitis externa—invasive infection causing osteomyelitis. Complication of otitis externa mostly seen in older patients with diabetes. Presents with severe otalgia and otorrhea. May lead to cranial nerve palsies. Physical exam shows granulation tissue in ear canal.

Otitis media

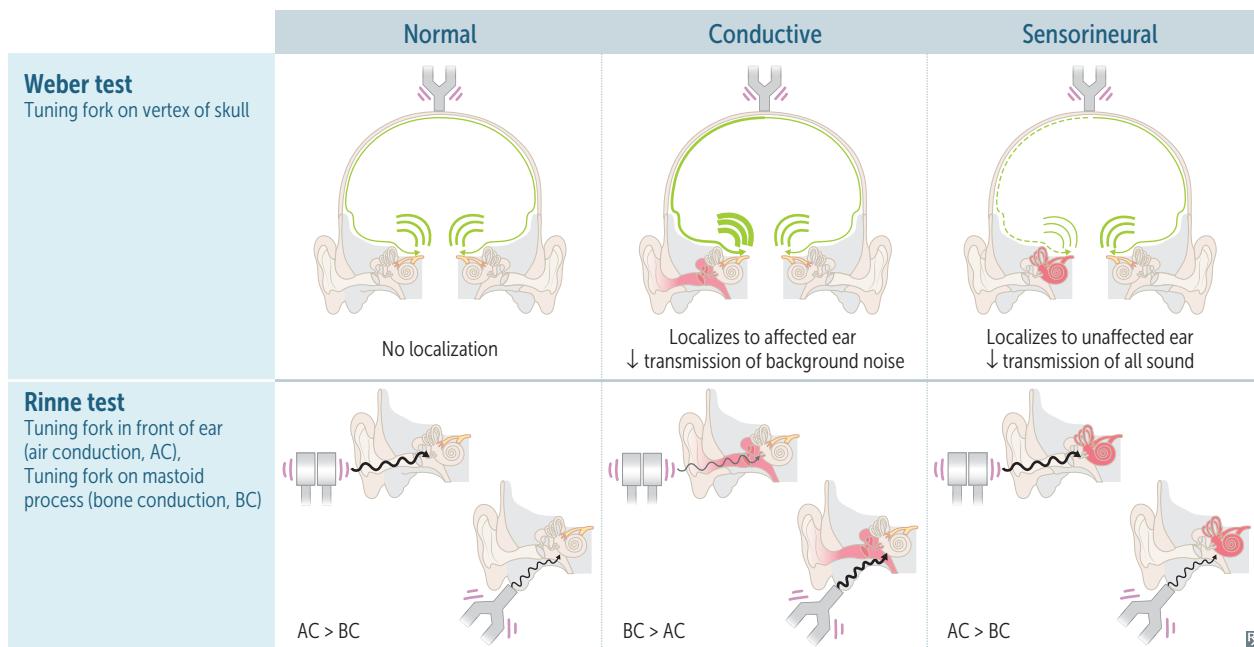
Inflammation of middle ear. Most commonly due to nontypeable *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*. Associated with eustachian tube dysfunction, which promotes overgrowth of bacterial colonizers of upper respiratory tract.

Usually seen in children < 2 years old. Presents with fever, otalgia, hearing loss. Physical exam shows bulging, erythematous tympanic membrane **A** that may rupture.

Mastoiditis—infection of mastoid process of temporal bone. Complication of acute otitis media due to continuity of middle ear cavity with mastoid air cells. Presents with postauricular pain, erythema, swelling. May lead to brain abscess.

Common causes of hearing loss

Noise-induced hearing loss	Damage to stereociliated cells in organ of Corti. Loss of high-frequency hearing first. Sudden extremely loud noises can produce hearing loss due to tympanic membrane rupture.
Presbycusis	Aging-related progressive bilateral/symmetric sensorineural hearing loss (often of higher frequencies) due to destruction of hair cells at the cochlear base (preserved low-frequency hearing at apex).

Diagnosing hearing loss**Cholesteatoma**

Abnormal growth of keratinized squamous epithelium in middle ear **A** (“skin in wrong place”). Usually acquired, but can be congenital. 1° acquired results from tympanic membrane retraction pockets that form due to eustachian tube dysfunction. 2° acquired results from tympanic membrane perforation (eg, due to otitis media) that permits migration of squamous epithelium to middle ear. Classically presents with painless otorrhea. May erode ossicles → conductive hearing loss.

Vertigo

Sensation of spinning while actually stationary. Subtype of “dizziness,” but distinct from “lightheadedness.” Peripheral vertigo is more common than central vertigo.

Peripheral vertigo

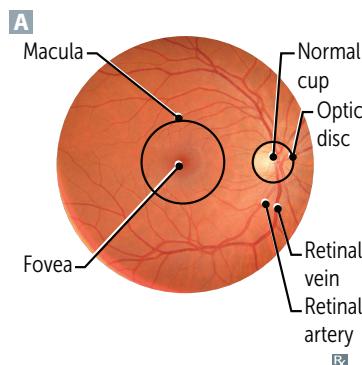
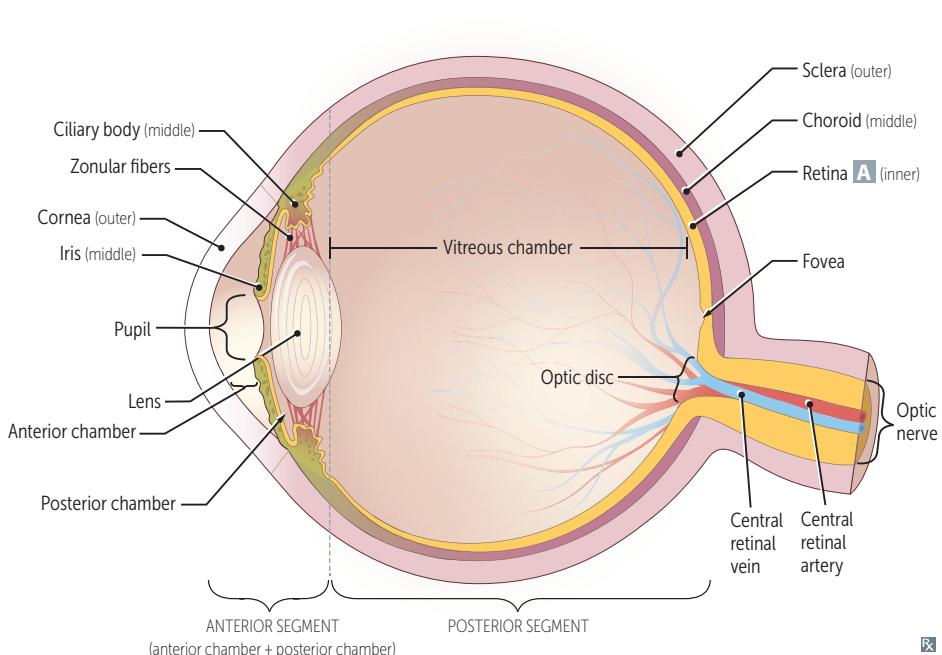
Due to inner ear pathologies such as vestibular neuritis; **benign paroxysmal positional vertigo**—semicircular canal debris → episodic vertigo lasting ≤ 1 minute provoked by certain head movements (diagnosed via Dix-Hallpike maneuver, treated via Epley maneuver); and **Ménière disease**—endolymphatic hydrops (↑ endolymph in inner ear) → triad of **vertigo**, **sensorineural hearing loss**, **tinnitus** (“men wear vests”). Findings: mixed horizontal-torsional nystagmus (never purely torsional or vertical) that does not change direction and is suppressible with visual fixation.

Central vertigo

Due to brainstem or cerebellar lesions (eg, stroke affecting vestibular nuclei, demyelinating disease, or posterior fossa tumor). Findings: nystagmus of any direction that is not suppressible with visual fixation, neurologic findings (eg, diplopia, ataxia, dysmetria).

▶ NEUROLOGY—OPHTHALMOLOGY

Normal eye anatomy



Conjunctivitis



Inflammation of the conjunctiva → red eye **A**.

Allergic—itchy eyes, bilateral.

Bacterial—purulent discharge; treat with antibiotics.

Viral—most common, often adenovirus; sparse mucous discharge, swollen preauricular node, ↑ lacrimation; self-resolving.

Neonatal—eyelid swelling, exudative discharge after vaginal birth. Detect bacterial etiologies with NAAT. Maternal prenatal screening and treatment ↓ incidence.

- *C trachomatis* serotypes D-K (most common)—onset 5–14 days after birth; treat with erythromycin or azithromycin.
- *N gonorrhoeae*—onset 2–5 days after birth; prophylaxis: erythromycin eyedrops; treat with ceftriaxone to prevent blindness.
- Other pathogens—HSV, adenovirus.

Refractive errors

Common cause of impaired vision, correctable with glasses. **My cave “hy”-des (hides) vexed cylinders.**

Myopia

Most common. Also called “nearsightedness.” Eye too long for refractive power of cornea and lens → light focused in front of retina. Correct with **concave** (diverging) lens.

Hyperopia

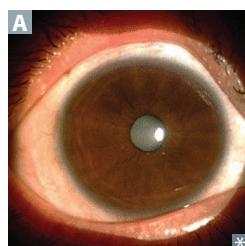
Also called “farsightedness.” Eye too short for refractive power of cornea and lens → light focused behind retina. Correct with **convex** (converging) lens.

Astigmatism

Irregular or asymmetric curvature of the cornea or lens → different refractive power at different axes. Correct with **cylindrical** lens.

Lens disorders**Presbyopia**

Aging-related impairment in accommodation (focusing on near objects). Pathophysiology not fully understood but likely includes ↓ lens elasticity. Patients often need reading glasses or magnifiers.

Cataract

Painless, often bilateral, opacification of lens **A**. Can result in glare, loss of red reflex, and ↓ vision, especially at night.

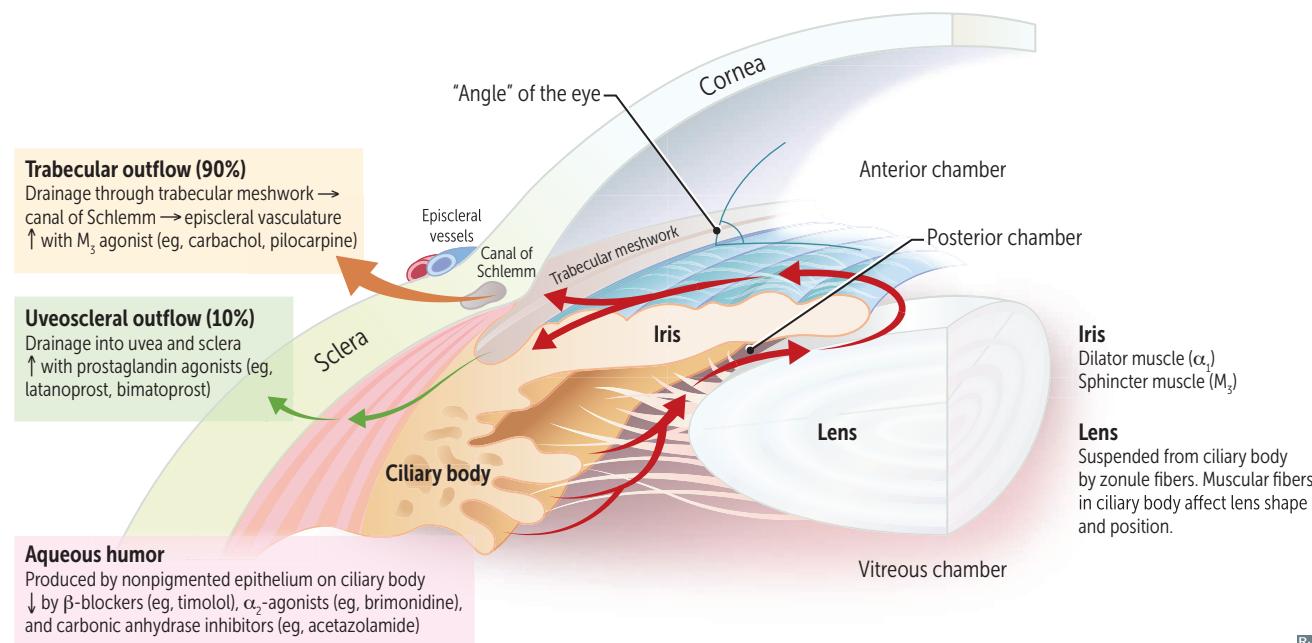
Acquired risk factors: ↑ age, tobacco smoking, alcohol overuse, excessive sunlight, prolonged glucocorticoid use, diabetes mellitus, trauma, infection.

Congenital risk factors: classic galactosemia, galactokinase deficiency, trisomies (13, 18, 21), TORCH infections (eg, rubella), Marfan syndrome, Alport syndrome, myotonic dystrophy, NF-2.

Treatment: surgical replacement with an artificial lens.

Lens dislocation

Also called ectopia lentis. Displacement or malposition of lens. Usually due to trauma, but may occur in association with systemic diseases (eg, Marfan syndrome, homocystinuria).

Aqueous humor pathway

Glaucoma

Optic neuropathy causing progressive vision loss (peripheral → central). Usually, but not always, accompanied by ↑ intraocular pressure (IOP). Etiology is most often 1°, but can be 2° to an identifiable cause (eg, uveitis, glucocorticoids). Funduscopy: optic disc cupping (normal **A** vs thinning of outer rim of optic disc **B**). Treatment: pharmacologic or surgical lowering of IOP.

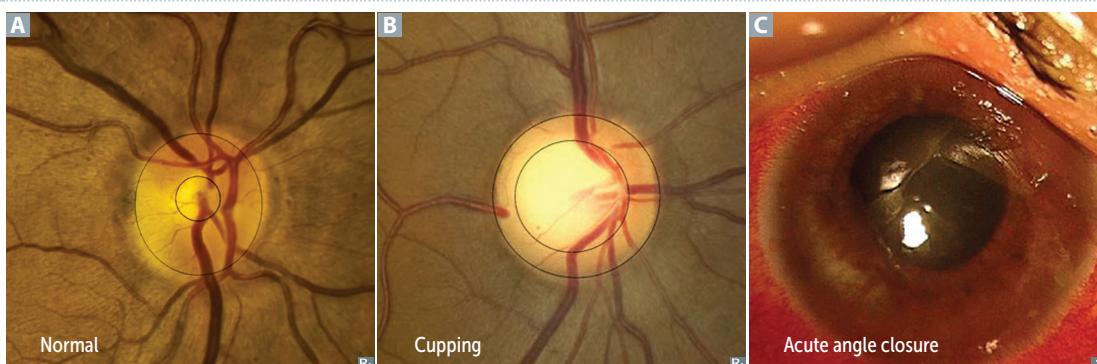
Open-angle glaucoma

Anterior chamber angle is open (normal). Most common type in US. Associated with ↑ resistance to aqueous humor drainage through trabecular meshwork. Risk factors: ↑ age, race (↑ incidence in Black population), family history, diabetes mellitus. Typically asymptomatic and discovered incidentally. Treat with prostaglandins or β-blockers.

Angle-closure glaucoma

Anterior chamber angle is narrowed or closed. Associated with anatomic abnormalities (eg, anteriorly displaced lens resting against central iris) → ↓ aqueous flow through pupil (pupillary block) → pressure buildup in posterior chamber → peripheral iris pushed against cornea → obstruction of drainage pathways by the iris. Usually chronic and asymptomatic, but may develop acutely.

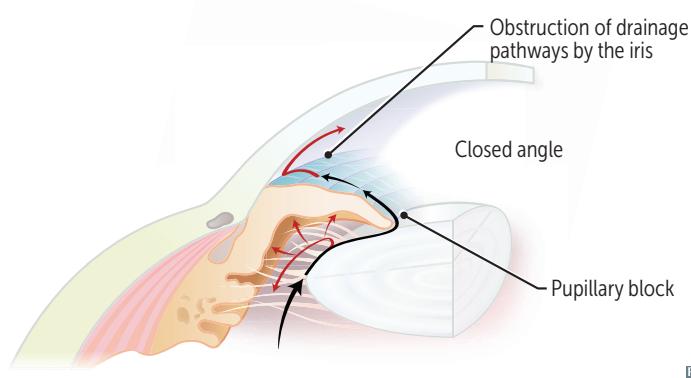
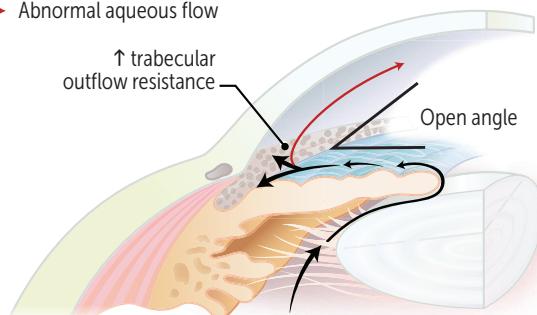
Acute angle-closure glaucoma—complete pupillary block causing abrupt angle closure and rapid ↑ IOP. Presents with severe eye pain, conjunctival erythema **C**, sudden vision loss, halos around lights, headache, fixed and mid-dilated pupil, nausea and vomiting. Hurts in a hurry with halos, a headache, and a “half-dilated” pupil. True ophthalmic emergency that requires immediate management to prevent blindness. Mydriatic agents are contraindicated. Treat with β-blocker, α₂-agonist, pilocarpine, acetazolamide, mannitol.



Open-angle glaucoma

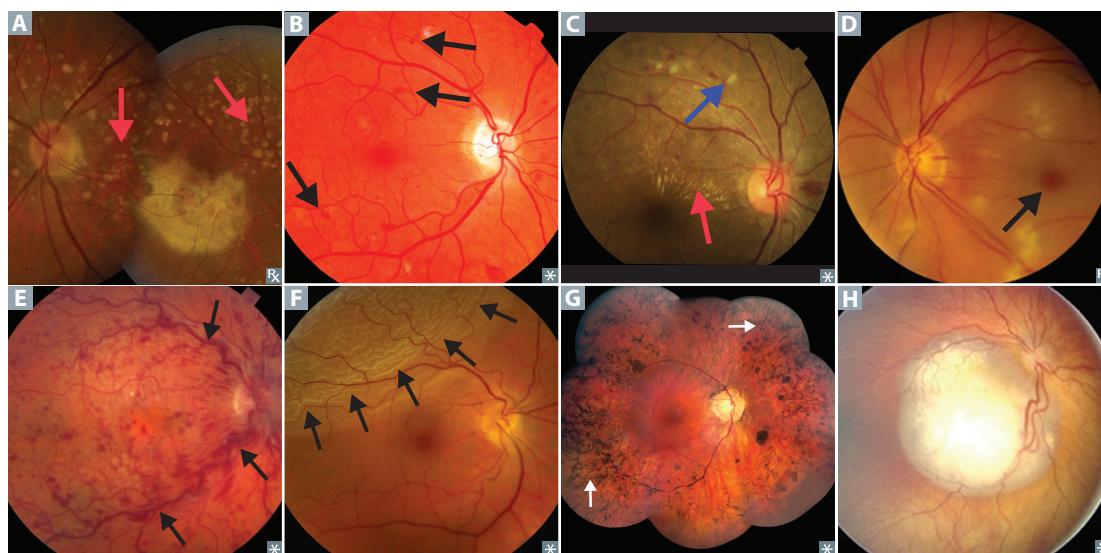
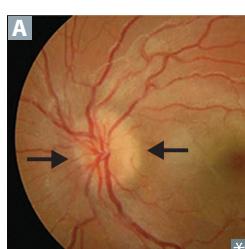
Angle-closure glaucoma

- Normal aqueous flow
- Abnormal aqueous flow



Retinal disorders

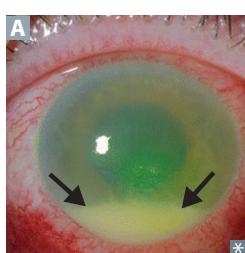
Age-related macular degeneration	Degeneration of macula (central area of retina) → loss of central vision (scotomas). Two types: <ul style="list-style-type: none"> ▪ Dry (most common)—gradual ↓ in vision with subretinal deposits (drusen, arrows in A). ▪ Wet—rapid ↓ in vision due to bleeding 2° to choroidal neovascularization. Distortion of straight lines (metamorphopsia) is an early symptom.
Diabetic retinopathy	Chronic hyperglycemia → ↑ permeability and occlusion of retinal vessels. Two types: <ul style="list-style-type: none"> ▪ Nonproliferative (most common)—microaneurysms, hemorrhages (arrows in B), cotton-wool spots, hard exudates. Vision loss mainly due to macular edema. ▪ Proliferative—retinal neovascularization due to chronic hypoxia. Abnormal new vessels may cause vitreous hemorrhage and tractional retinal detachment.
Hypertensive retinopathy	Chronic hypertension → spasm, sclerosis, and fibrinoid necrosis of retinal vessels. Funduscopy: arteriovenous nicking, microaneurysms, hemorrhages, cotton-wool spots (blue arrow in C), hard exudates (may form macular “star,” red arrow in C). Presence of papilledema is indicative of hypertensive emergency and warrants immediate lowering of blood pressure.
Retinal artery occlusion	Blockage of central or branch retinal artery usually due to embolism (carotid artery atherosclerosis > cardiogenic); less commonly due to giant cell arteritis. Presents with acute, painless monocular vision loss. Funduscopy: cloudy retina with “cherry-red” spot at fovea D , identifiable retinal emboli (eg, cholesterol crystals appear as small, yellow, refractile deposits in arterioles).
Retinal vein occlusion	Central retinal vein occlusion is due to 1° thrombosis; branch retinal vein occlusion is due to 2° thrombosis at arteriovenous crossings (sclerotic arteriole compresses adjacent venule causing turbulent blood flow). Funduscopy: retinal hemorrhage and venous engorgement (“blood and thunder” appearance; arrows in E), retinal edema in affected areas.
Retinal detachment	Separation of neurosensory retina from underlying retinal pigment epithelium → loss of choroidal blood supply → hypoxia and degeneration of photoreceptors. Two types: <ul style="list-style-type: none"> ▪ Rhegmatogenous (most common)—due to retinal tears; often associated with posterior vitreous detachment (↑ risk with advanced age, high myopia), less frequently traumatic. ▪ Nonrhegmatogenous—tractional or exudative (fluid accumulation). Commonly presents with symptoms of posterior vitreous detachment (eg, floaters, light flashes) followed by painless monocular vision loss (“dark curtain”). Funduscopy: opacification and wrinkling of detached retina F , change in vessel direction. Surgical emergency.
Retinitis pigmentosa	Group of inherited dystrophies causing progressive degeneration of photoreceptors and retinal pigment epithelium. May be associated with abetalipoproteinemia. Early symptoms: night blindness (nyctalopia) and peripheral vision loss. Funduscopy: triad of optic disc pallor, retinal vessel attenuation, and retinal pigmentation with bone spicule-shaped deposits G .
Retinopathy of prematurity	Preterm birth → loss of normal hypoxic environment in utero → relative hyperoxia (↑ with supplemental O ₂ for NRDS) → ↓ VEGF → arrest of normal retinal vascularization. As the eyes grow → hypoxia of avascular retina → ↑ VEGF → retinal neovascularization (may cause tractional retinal detachment). Common cause of childhood blindness.
Retinoblastoma	Most common intraocular malignancy in children. Arises from immature retinal cells H . Caused by mutations to both <i>RBL</i> tumor suppressor genes on chromosome 13, which normally impede G ₁ → S phase progression. Can be sporadic or familial (loss of heterozygosity). Presents with leukocoria, strabismus, nystagmus, eye redness.

Retinal disorders (continued)**Papilledema**

Optic disc swelling (usually bilateral) due to ↑ ICP (eg, 2° to mass effect). Results from impaired axoplasmic flow in optic nerve. Funduscopic findings: elevated optic disc with blurred margins **A**.

Leukocoria

Loss (whitening) of the red reflex. Important causes in children include retinoblastoma **A**, congenital cataract.

Uveitis

Inflammation of uvea; specific name based on location within affected eye. Anterior uveitis: iritis; posterior uveitis: choroiditis and/or retinitis. May have hypopyon (accumulation of pus in anterior chamber **A**) or conjunctival redness. Associated with systemic inflammatory disorders (eg, sarcoidosis, Behçet syndrome, juvenile idiopathic arthritis, HLA-B27-associated conditions).

Pupillary control**Miosis**

Constriction, parasympathetic:

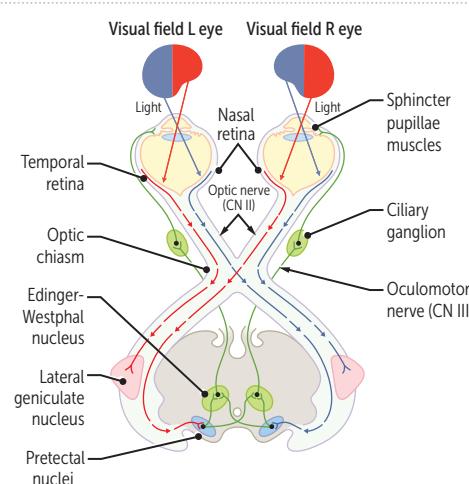
- 1st neuron: Edinger-Westphal nucleus to ciliary ganglion via CN III
- 2nd neuron: short ciliary nerves to sphincter pupillae muscles

Short ciliary nerves **shorten** the pupil diameter.

Pupillary light reflex

Light in either retina sends a signal via CN II to pretectal nuclei in midbrain that activates bilateral Edinger-Westphal nuclei; pupils constrict bilaterally (direct and consensual reflex).

Result: illumination of 1 eye results in bilateral pupillary constriction.

**Mydriasis**

Dilation, sympathetic:

- 1st neuron: hypothalamus to ciliospinal center of Budge (C8–T2)
- 2nd neuron: exit at T1 to superior cervical ganglion (travels along cervical sympathetic chain near lung apex, subclavian vessels)
- 3rd neuron: plexus along internal carotid, through cavernous sinus; enters orbit as long ciliary nerve to pupillary dilator muscles. Sympathetic fibers also innervate smooth muscle of eyelids (minor retractors) and sweat glands of forehead and face.

Long ciliary nerves make the pupil diameter **longer**.

Relative afferent pupillary defect

Also called Marcus Gunn pupil. Extent of pupillary constriction differs when light is shone in one eye at a time due to unilateral or asymmetric lesions of afferent limb of pupillary reflex (eg, retina, optic nerve). When light shines into a normal eye, constriction of the ipsilateral eye (direct reflex) and contralateral eye (consensual reflex) is observed. When light is swung from a normal eye to an affected eye, both pupils dilate instead of constricting.

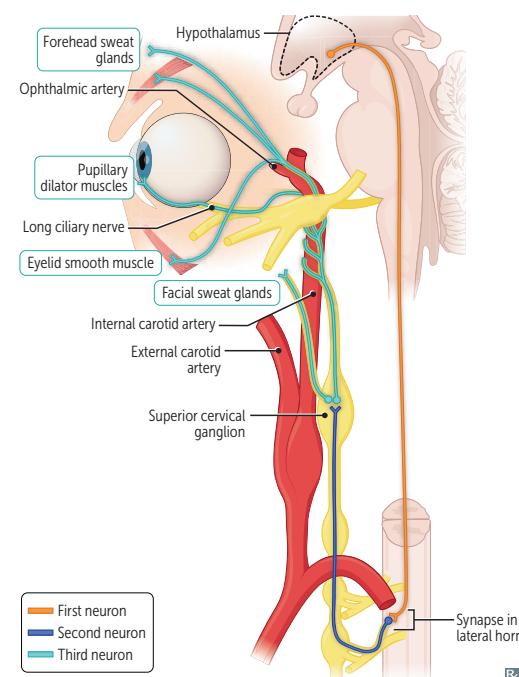
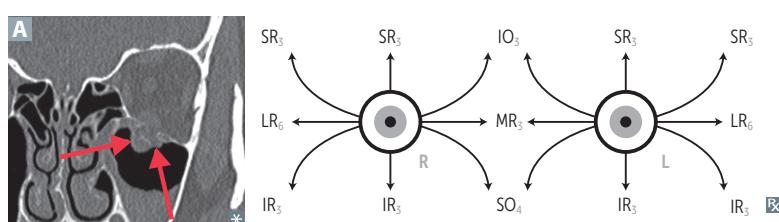
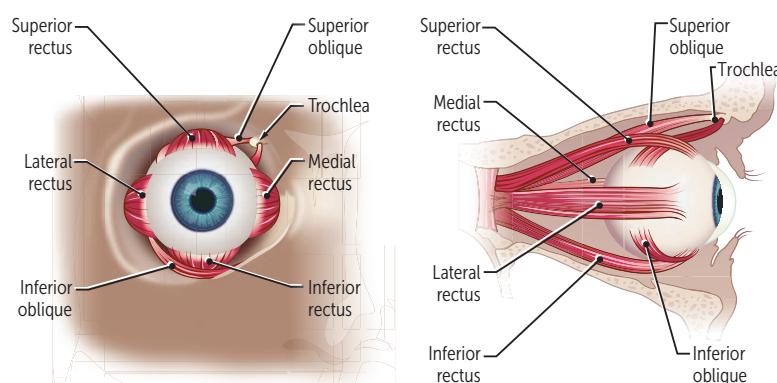
Horner syndrome

Sympathetic denervation of face:

- Ptosis (slight drooping of eyelid: superior tarsal muscle)
- Miosis (pupil constriction)
- Anhidrosis (absence of sweating) and absence of flushing of affected side of face

Associated with lesions along the sympathetic chain:

- 1st neuron: pontine hemorrhage, lateral medullary syndrome, spinal cord lesion above T1 (eg, Brown-Séquard syndrome, late-stage syringomyelia)
- 2nd neuron: stellate ganglion compression by Pancoast tumor
- 3rd neuron: carotid dissection (painful); anhidrosis is usually absent

**Ocular motility****Strabismus**

Eye misalignment (“crossed eyes”). Deviation of eye toward the nose (esotropia) is the most common type of strabismus in children. Complications include amblyopia, diplopia, adverse psychosocial impact.

CN VI innervates the **Lateral Rectus**.
CN IV innervates the **Superior Oblique**.
CN III innervates the **Rest**.
The “chemical formula” **LR₆SO₄R₃**.

Arrows in illustration depict direction of gaze with which to test each muscle.
Obliques go Opposite (left SO and IO tested with patient looking right)
IOU: IO tested looking Up

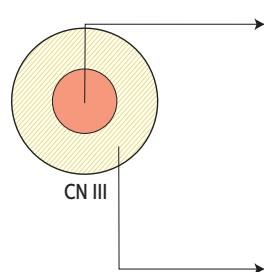
Blowout fracture—orbital floor fracture; usually due to trauma to eyeball or infraorbital rim. ↑ risk of IR muscle **A** and/or orbital fat entrapment. May lead to infraorbital nerve injury.

Amblyopia (“lazy eye”)—↓ visual acuity due to maldevelopment of visual cortex. Caused by abnormal visual experience early in life (eg, due to strabismus). Typically unilateral.

Cranial nerve III, IV, VI palsies**CN III damage**

CN III has both motor (central) and parasympathetic (peripheral) components. Common causes include:

- Ischemia → pupil sparing (motor fibers affected more than parasympathetic fibers)
- Uncal herniation → coma
- PCom aneurysm → sudden-onset headache
- Cavernous sinus thrombosis → proptosis, involvement of CNs IV, V₁/V₂, VI
- Midbrain stroke → contralateral hemiplegia

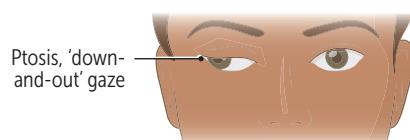


Motor output to extraocular muscles—affected primarily by vascular disease (eg, diabetes mellitus: glucose → sorbitol) due to ↓ diffusion of oxygen and nutrients to the interior (**middle**) fibers from compromised vasculature that resides on outside of nerve. Signs: ptosis, “down-and-out” gaze.

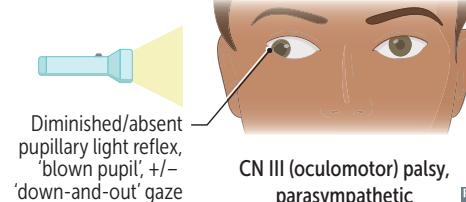
Parasympathetic output—fibers on the **periphery** are first affected by compression (eg, PCom aneurysm, uncal herniation). Signs: diminished or absent pupillary light reflex, “blown pupil” often with “down-and-out” gaze.

Motor = middle (central)

Parasympathetic = peripheral



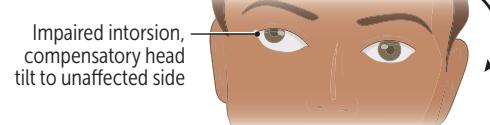
CN III (oculomotor) palsy, motor



CN III (oculomotor) palsy, parasympathetic

CN IV damage

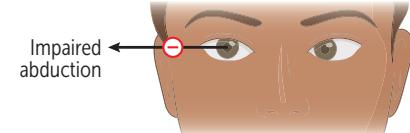
Pupil is higher in the affected eye. Characteristic head tilt to contralateral/unaffected side to compensate for lack of intorsion in affected eye. Can't see the **floor** with CN **IV** damage (eg, difficulty going down stairs, reading).



CN IV (trochlear) palsy

CN VI damage

Affected eye unable to abduct and is displaced medially in primary position of gaze.



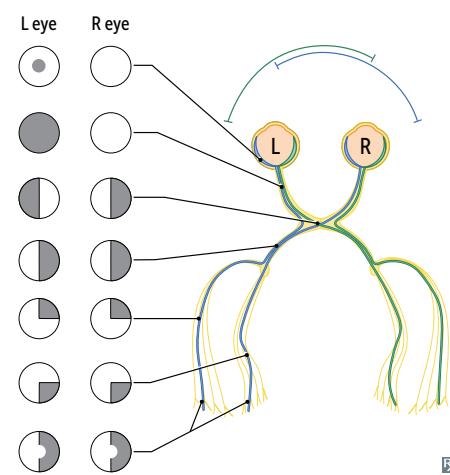
CN VI (abducens) palsy

Visual field defects

Ventral optic radiation (Meyer loop)—lower retina; travels through temporal lobe; loops around inferior horn of lateral ventricle.
 Dorsal optic radiation—superior retina; travels through parietal lobe.

Defect in visual field of:

- ① Macula
Central scotoma
(macular degeneration)
- ② Optic nerve
Left anopia
- ③ Optic chiasm
Bitemporal hemianopia
- ④ Optic tract
Right homonymous hemianopia
- ⑤ Meyer loop
Right upper quadrantanopia
(left temporal lesion)
- ⑥ Dorsal optic radiation
Right lower quadrantanopia
(left parietal lesion)
- ⑦ Visual cortex
Right homonymous hemianopia
with macular sparing
(PCA infarct)



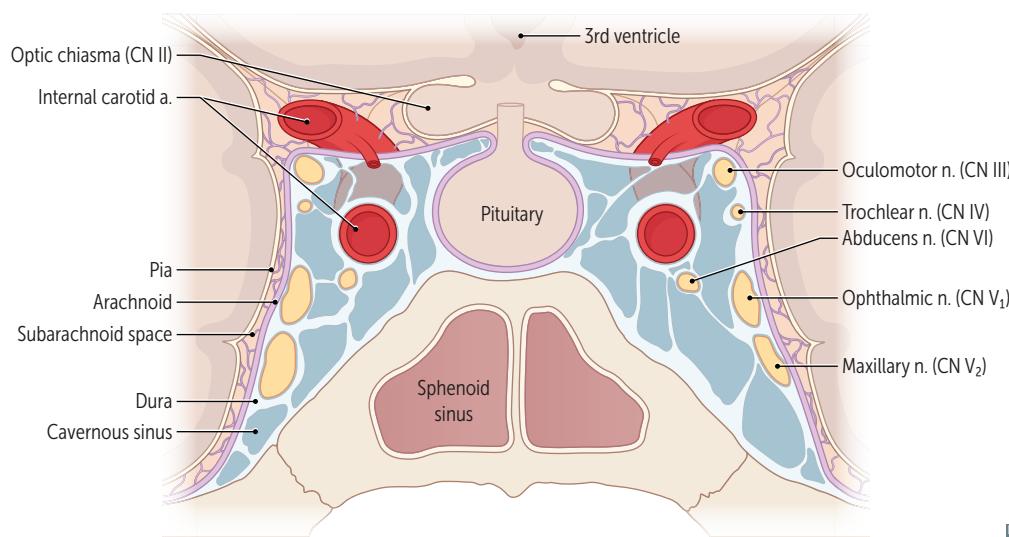
Note: When an image hits 1° visual cortex, it is upside down and left-right reversed.

Cavernous sinus

Collection of venous sinuses on either side of pituitary. Blood from eye and superficial cortex → cavernous sinus → internal jugular vein.

CNs III, IV, V₁, V₂, and VI plus postganglionic sympathetic pupillary fibers en route to orbit all pass through cavernous sinus. Cavernous portion of internal carotid artery is also here. Internal carotid artery, Trigeminal nerve (Ophthalmic and Maxillary divisions), Abducens nerve, Trochlear nerve, Oculomotor nerve (**I, TOMATO**).

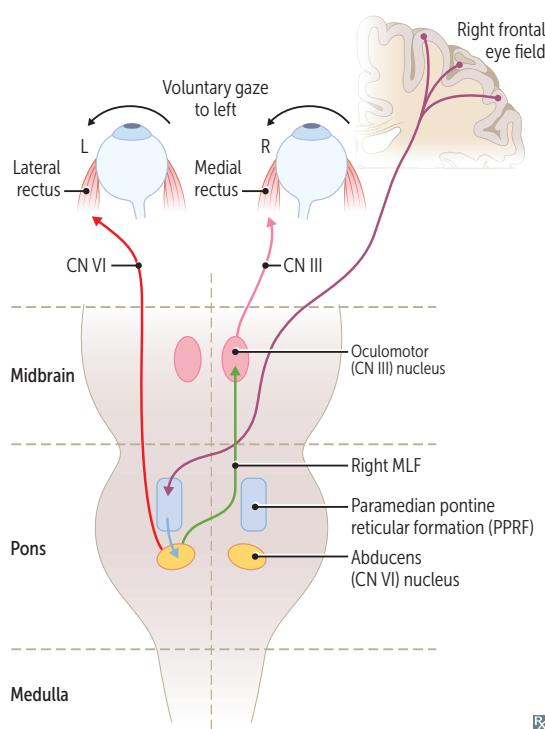
Cavernous sinus syndrome—presents with variable ophthalmoplegia (eg, CN III and CN VI), ↓ corneal sensation, Horner syndrome and occasional ↓ maxillary sensation. 2° to pituitary tumor mass effect, carotid-cavernous fistula, or cavernous sinus thrombosis related to infection (spread due to lack of valves in dural venous sinuses).



Internuclear ophthalmoplegia

Medial longitudinal fasciculus (MLF): pair of tracts that interconnect CN VI and CN III nuclei. Coordinates both eyes to move in same horizontal direction. Highly myelinated (must communicate quickly so eyes move at same time). Lesions may be unilateral or bilateral (latter classically seen in multiple sclerosis, stroke).

Lesion in MLF = internuclear ophthalmoplegia (INO), a conjugate horizontal gaze palsy. Lack of communication such that when CN VI nucleus activates ipsilateral lateral rectus, contralateral CN III nucleus does not stimulate medial rectus to contract. Abducting eye displays nystagmus (CN VI overfires to stimulate CN III). Convergence normal.

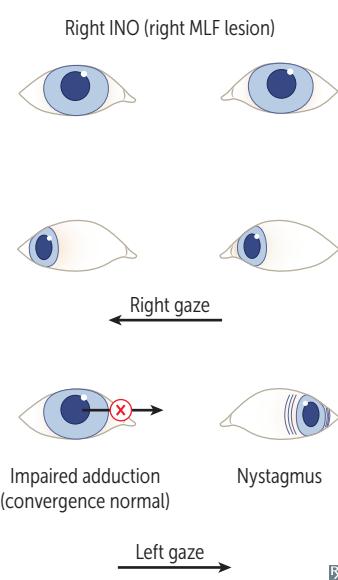


MLF in MS.

When looking left, the left nucleus of CN VI fires, which contracts the left lateral rectus and stimulates the contralateral (right) nucleus of CN III via the right MLF to contract the right medial rectus.

Directional term (eg, right INO, left INO) refers to the eye that is unable to adduct.

INO = Ipsilateral adduction failure, Nystagmus Opposite.



Eyelid disorders

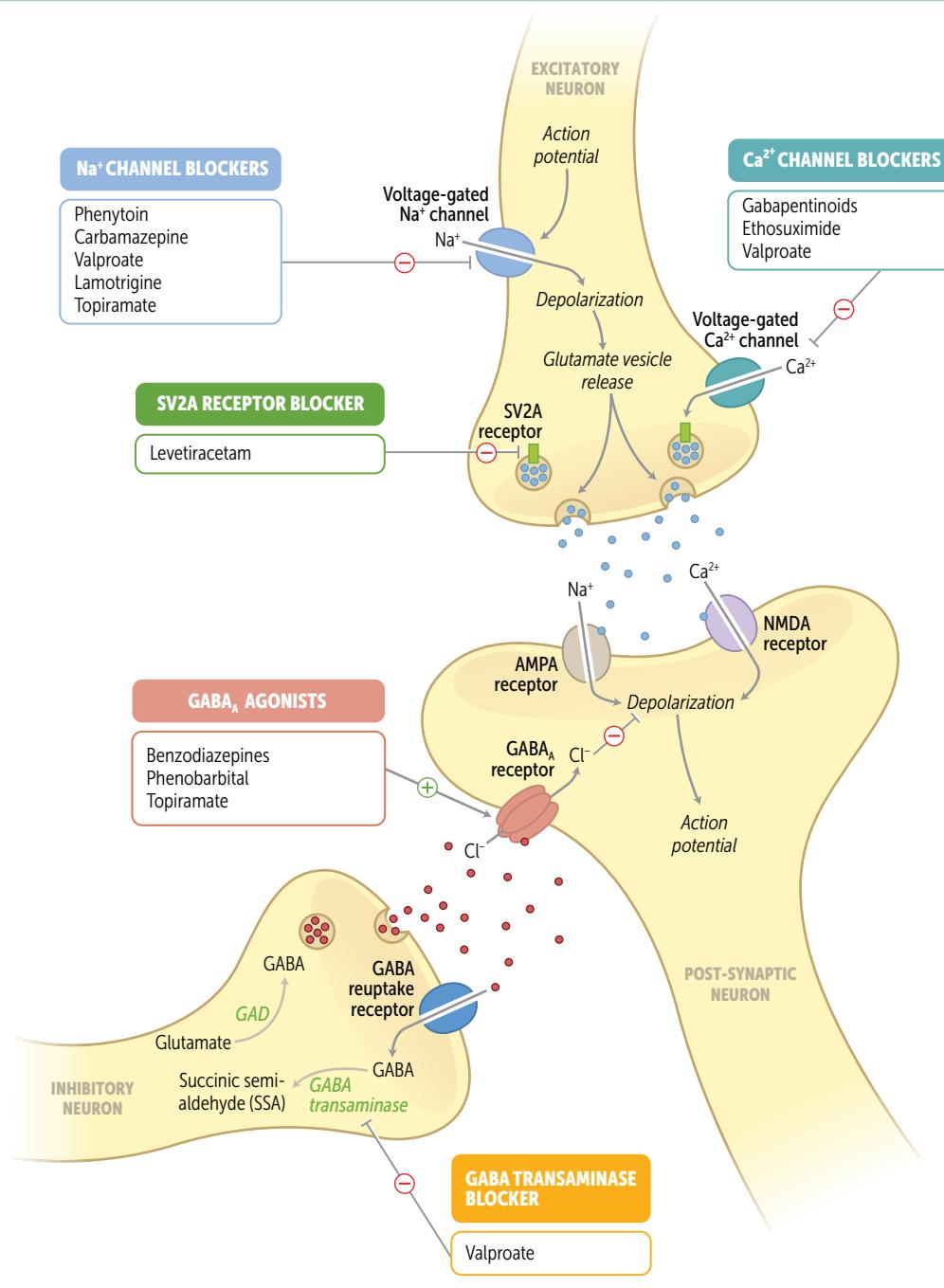
DISORDER	PRESENTATION
Preseptal cellulitis	Anterior soft tissue eyelid infection. Mild presentation with unilateral ocular pain, swelling, and erythema present at rest.
Orbital cellulitis	Posterior eyelid infection affecting orbit contents (fat and muscles). Pain with ocular movement. Infection affecting the orbital contents (fat and muscles), usually secondary to bacterial sinusitis. Pain and double vision (diplopia) with ocular movement. Risk of vision loss, cavernous sinus thrombosis, and intracranial spread. Most commonly caused by <i>S aureus</i> and streptococci.
Blepharitis	Eyelid margin and lid inflammation, irritation, and crusting.
Hordeolum (stye)	Acute infection of the sebaceous or sweat glands of the eyelid. Tender, erythematous nodule.
Chalazion	Noninfectious granulomatous inflammation caused by obstruction of a meibomian (modified sebaceous) or Zeis (sebaceous) gland.
Xanthelasma	Yellowish patch on medial eyelid. May be associated with genetic and lifestyle factors, eg, high cholesterol.

▶ NEUROLOGY—PHARMACOLOGY

Anticonvulsants

	MECHANISM	COMMON ADVERSE EFFECTS	RARE BUT SERIOUS ADVERSE EFFECTS
Narrow spectrum (focal seizures)			
Phenytoin	Block Na ⁺ channel	Sedation, dizziness, diplopia, gingival hypertrophy (preventable with folate supplementation), rash, hirsutism, drug interactions (CYP450 induction)	SJS, DRESS, hepatotoxicity, neuropathy, osteoporosis, folate depletion, teratogenicity
Carbamazepine		Sedation, dizziness, diplopia, vomiting, diarrhea, SIADH, rash, drug interactions (CYP450 induction)	SJS, DRESS, hepatotoxicity, agranulocytosis, aplastic anemia, folate depletion, teratogenicity
Gabapentinoids Gabapentin, pregabalin	Block Ca ²⁺ channel	Sedation, dizziness, ataxia, weight gain	
Narrow spectrum (absence seizures only)			
Ethosuximide	Blocks Ca ²⁺ channel	Sedation, dizziness, vomiting	
Broad spectrum (focal and generalized seizures)			
Valproate	Blocks Na ⁺ channel Blocks Ca ²⁺ channel Blocks GABA transaminase	Sedation, dizziness, vomiting, weight gain, hair loss, easy bruising, drug interactions (CYP450 inhibition)	Hepatotoxicity, pancreatitis, teratogenicity (highest risk of all anticonvulsants)
Lamotrigine	Blocks Na ⁺ channel	Sedation, dizziness, rash	SJS, DRESS
Levetiracetam	Blocks Synaptic Vesicle protein 2A (SV2A)	Sedation, dizziness, fatigue	Neuropsychiatric (eg, psychosis)
Topiramate	Blocks Na ⁺ channel Potentiates GABA _A receptor	Sedation, dizziness, mood disturbance (eg, depression), weight loss, paresthesia	Kidney stones, angle-closure glaucoma

Anticonvulsants (continued)



Barbiturates

Phenobarbital, pentobarbital.

MECHANISM Facilitate GABA_A action by ↑ duration of Cl⁻ channel opening, thus ↓ neuron firing (barbiturates ↑ duration).

CLINICAL USE Sedative for anxiety, seizures, insomnia; alcohol or sedative withdrawal.

ADVERSE EFFECTS Respiratory and cardiovascular depression (can be fatal); CNS depression (exacerbated by alcohol use); dependence; drug interactions (induces CYP-450). Contraindicated in porphyria. Overdose treatment is supportive (assist respiration and maintain BP).

Benzodiazepines	Diazepam, lorazepam, triazolam, temazepam, oxazepam, midazolam, chlordiazepoxide, alprazolam.
MECHANISM	Facilitate GABA _A action by ↑ frequency of Cl ⁻ channel opening (“frenzodiazepines” ↑ frequency). ↓ REM sleep. Most have long half-lives and active metabolites (exceptions [ATOM]: Alprazolam, Triazolam, Oxazepam, and Midazolam are short acting → higher addictive potential).
CLINICAL USE	Anxiety, panic disorder, spasticity, status epilepticus (lorazepam, diazepam, midazolam), eclampsia, medically supervised withdrawal (eg, alcohol/DTs; long-acting chlordiazepoxide and diazepam are preferred), night terrors/sleepwalking (↓ N3 and REM sleep), general anesthetic (amnesia, muscle relaxation), hypnotic (insomnia). Lorazepam, Oxazepam, and Temazepam can be used for those with liver disease who drink a LOT due to minimal first-pass metabolism.
ADVERSE EFFECTS	Dependence, additive CNS depression effects with alcohol and barbiturates (all bind the GABA _A receptor). Less risk of respiratory depression and coma than with barbiturates. Treat overdose with flumazenil (competitive antagonist at GABA benzodiazepine receptor). Can precipitate seizures by causing acute benzodiazepine withdrawal.

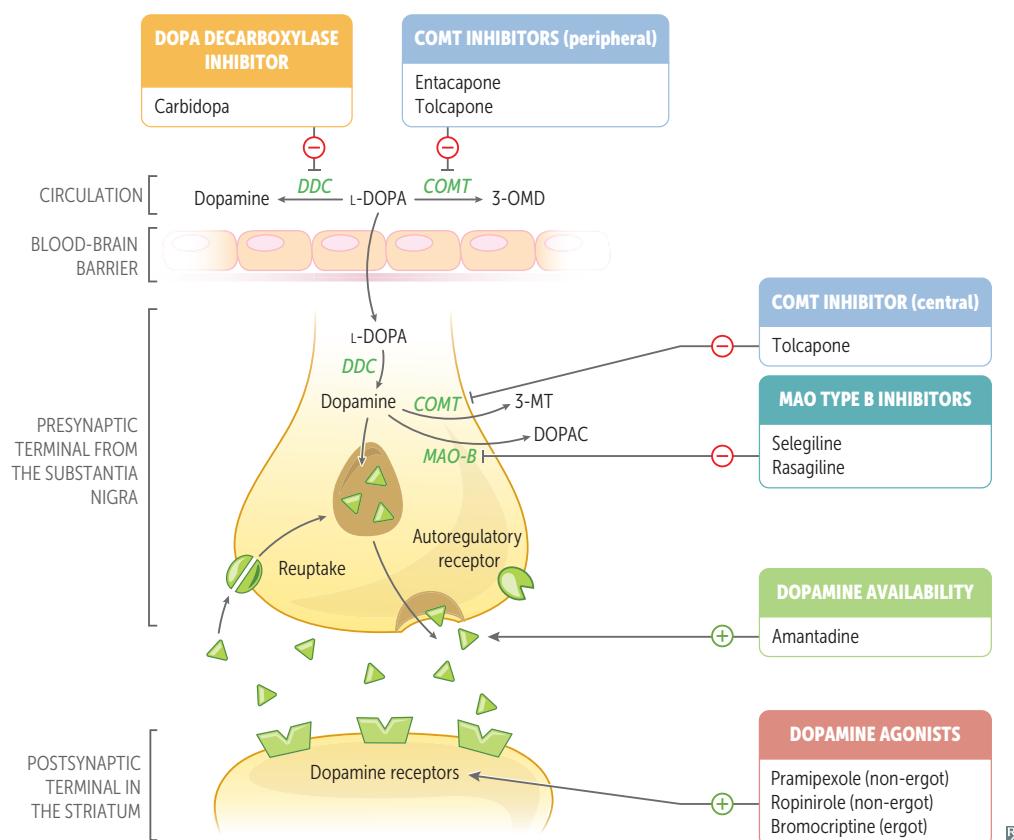
Insomnia therapy

AGENT	MECHANISM	ADVERSE EFFECTS	NOTES
Nonbenzodiazepine hypnotics	Examples: Zolpidem, Zaleplon, esZopiclone Act via the BZ ₁ subtype of GABA receptor	Ataxia, headaches, confusion Cause only modest day-after psychomotor depression and few amnestic effects (vs older sedative-hypnotics)	These ZZZs put you to sleep Short duration due to rapid metabolism by liver enzymes; effects reversed by flumazenil ↓ dependency risk and ↓ sleep cycle disturbance (vs benzodiazepine hypnotics)
Suvorexant	Orexin (hypocretin) receptor antagonist	CNS depression (somnolence), headache, abnormal sleep-related activities	Contraindications: narcolepsy, combination with strong CYP3A4 inhibitors Not recommended in patients with liver disease Limited risk of dependency
Ramelteon	Melatonin receptor agonist: binds MT1 and MT2 in suprachiasmatic nucleus	Dizziness, nausea, fatigue, headache	No known risk of dependency

Triptans**Sumatriptan**

MECHANISM	5-HT _{1B/1D} agonists. Inhibit trigeminal nerve activation, prevent vasoactive peptide release, induce vasoconstriction.
CLINICAL USE	Acute migraine, cluster headache attacks. A sumo wrestler trips and falls on their head.
ADVERSE EFFECTS	Coronary vasospasm (contraindicated in patients with CAD or vasospastic angina), mild paresthesia, serotonin syndrome (in combination with other 5-HT agonists).

Parkinson disease therapy	Most effective treatments are non-ergot dopamine agonists (younger patients) and levodopa/carbidopa (older patients). Deep brain stimulation of the STN or GPi aids in advanced disease.
STRATEGY	AGENTS
Dopamine agonists	Non-ergot (preferred)—pramipexole, ropinirole; toxicity includes nausea, impulse control disorder (eg, gambling), postural hypotension, hallucinations, confusion, sleepiness, edema. Ergot—bromocriptine; rarely used due to toxicity.
↑ dopamine availability	Amantadine (\uparrow dopamine release and \downarrow dopamine reuptake); mainly used to reduce levodopa-induced dyskinesias; toxicity = peripheral edema, livedo reticularis, ataxia.
↑ L-DOPA availability	Agents prevent peripheral (pre-BBB) L-DOPA degradation \rightarrow \uparrow L-DOPA entering CNS \rightarrow \uparrow central L-DOPA available for conversion to dopamine. <ul style="list-style-type: none"> ■ Levodopa (L-DOPA)/carbidopa—carbidopa blocks peripheral conversion of L-DOPA to dopamine by inhibiting DOPA decarboxylase. Also reduces adverse effects of peripheral L-DOPA conversion into dopamine (eg, nausea, vomiting). ■ Entacapone and tolcapone prevent peripheral L-DOPA degradation to 3-O-methyldopa (3-OMD) by inhibiting COMT. Used in conjunction with levodopa.
Prevent dopamine breakdown	Agents act centrally (post-BBB) to inhibit breakdown of dopamine. <ul style="list-style-type: none"> ■ Selegiline, rasagiline—block dopamine \rightarrow 3,4-dihydroxyphenylacetic acid (DOPAC) conversion via selective inhibition of MAO-B, which is more commonly found in the Brain than periphery. Improve symptoms for patients with cyclic fluctuations in levodopa efficacy (on/off phenomenon). ■ Tolcapone—crosses BBB and blocks conversion of dopamine to 3-methoxytyramine (3-MT) in the brain by inhibiting central COMT. Tolcapone pays the toll and can cross the BBB.
Curb excess cholinergic activity	Benztropine, trihexyphenidyl (Antimuscarinic; improves tremor and rigidity but has little effect on bradykinesia in Parkinson disease). Tri Parking my Mercedes-Benz.



Carbidopa/levodopa

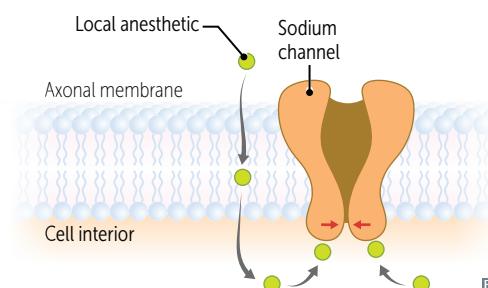
MECHANISM	↑ dopamine in brain. Unlike dopamine, L-DOPA can cross BBB and is converted by DOPA decarboxylase in the CNS to dopamine. Carbidopa, a peripheral DOPA decarboxylase inhibitor that cannot cross BBB, is given with L-DOPA to ↑ bioavailability of L-DOPA in the brain and to limit peripheral adverse effects.
CLINICAL USE	Parkinson disease.
ADVERSE EFFECTS	Nausea, hallucinations, postural hypotension. With progressive disease, L-DOPA can lead to “on-off” phenomenon with improved mobility during “on” periods, then impaired motor function during “off” periods when patient responds poorly to L-DOPA or medication wears off.

Neurodegenerative disease therapy

DISEASE	AGENT	MECHANISM	NOTES
Alzheimer disease	Donepezil, rivastigmine, galantamine	AChE inhibitor	1st-line treatment Adverse effects: nausea, dizziness, insomnia; contraindicated in patients with cardiac conduction abnormalities Dona Riva forgot the gala
	Memantine	NMDA receptor antagonist; helps prevent excitotoxicity (mediated by Ca ²⁺)	Used for moderate to advanced dementia Adverse effects: dizziness, confusion, hallucinations
Amyotrophic lateral sclerosis	Riluzole	↓ neuron glutamate excitotoxicity	↑ survival Treat Lou Gehrig disease with riLouzole
Huntington disease	Deutetrabenazine, tetrabenazine	Inhibit vesicular monoamine transporter (VMAT) → ↓ dopamine vesicle packaging and release	May be used for Huntington chorea and tardive dyskinesia

Local anesthetics

Esters—benzocaine, chloroprocaine, cocaine, tetracaine.
 Amides—**bupivacaine**, **lidocaine**, **mepivacaine**, **prilocaine**, **ropivacaine** (amides have **2 i's** in name).

**MECHANISM**

Block neurotransmission via binding to voltage-gated Na^+ channels on inner portion of the channel along nerve fibers. Most effective in rapidly firing neurons. 3° amine local anesthetics penetrate membrane in uncharged form, then bind to ion channels as charged form.
 Can be given with vasoconstrictors (usually epinephrine) to enhance block duration of action by ↓ systemic absorption.
 In infected (acidic) tissue, alkaline anesthetics are charged and cannot penetrate membrane effectively → need more anesthetic.
 Order of loss: (1) pain, (2) temperature, (3) touch, (4) pressure.

CLINICAL USE

Minor surgical procedures, spinal anesthesia. If allergic to esters, give amides.

ADVERSE EFFECTS

CNS excitation, severe cardiovascular toxicity (bupivacaine), hypertension, hypotension, arrhythmias (cocaine), methemoglobinemia (benzocaine, prilocaine).

General anesthetics

CNS drugs must be lipid soluble (cross the BBB) or be actively transported.
 Drugs with ↓ solubility in blood (eg, nitrous oxide [N_2O]) = rapid induction and recovery times.
 Drugs with ↑ solubility in lipids (eg, isoflurane) = ↑ potency.
MAC = **M**inimum **A**lveolar **C**oncentration (of inhaled anesthetic) required to prevent 50% of subjects from moving in response to noxious stimulus (eg, skin incision). Potency = 1/MAC.

MECHANISM	ADVERSE EFFECTS/NOTES	
Inhaled anesthetics		
Sevoflurane	Respiratory depression, ↓ cough reflex	
Desflurane	Myocardial depression, ↓ BP	
Isoflurane	↑ cerebral blood flow (↑ ICP), ↓ metabolic rate ↓ skeletal and smooth muscle tone Postoperative nausea and vomiting Malignant hyperthermia	
N_2O	Diffusion into and expansion (N_2O) of gas-filled cavities (eg, pneumothorax); very low potency	
Intravenous anesthetics		
Propofol	Potentiates GABA_A receptor Inhibits NMDA receptor	Respiratory depression, ↓ BP; most commonly used IV agent for induction of anesthesia
Etomide	Potentiates GABA_A receptor	Acute adrenal insufficiency, postoperative nausea and vomiting; hemodynamically neutral
Ketamine	Inhibits NMDA receptor	Sympathomimetic: ↑ BP, ↑ HR, ↑ cerebral blood flow (↑ ICP), bronchodilation Psychotomimetic: hallucinations, vivid dreams

Neuromuscular blocking drugs

Muscle paralysis in surgery or mechanical ventilation. Selective for N_m nicotinic receptors at neuromuscular junction but not autonomic N_n receptors.

Depolarizing neuromuscular blocking drugs

Succinylcholine—strong N_m nicotinic receptor agonist; produces sustained depolarization and prevents muscle contraction.

Reversal of blockade:

- Phase I (prolonged depolarization)—no antidote. Block potentiated by cholinesterase inhibitors.
- Phase II (repolarized but blocked; N_m nicotinic receptors are available, but desensitized)—may be reversed with cholinesterase inhibitors.

Complications include hypercalcemia, hyperkalemia, malignant hyperthermia. ↑ risk of prolonged muscle paralysis in patients with pseudocholinesterase deficiency.

Nondepolarizing neuromuscular blocking drugs

Atracurium, cisatracurium, pancuronium, rocuronium, vecuronium—competitive N_m nicotinic receptor antagonist.

Reversal of blockade—sugammadex or cholinesterase inhibitors (eg, neostigmine). Anticholinergics (eg, atropine, glycopyrrolate) are given with cholinesterase inhibitors to prevent muscarinic effects (eg, bradycardia).

Malignant hyperthermia

Rare, life-threatening, hypermetabolic condition caused by the administration of potent inhaled anesthetics (sevoflurane, desflurane, isoflurane) or succinylcholine in susceptible individuals.

Susceptibility to malignant hyperthermia is caused by de novo or inherited (autosomal dominant) mutations to ryanodine (*RYR1*) or dihydropyridine receptors (*DHPR*).

↑↑ Ca^{2+} release from sarcoplasmic reticulum → sustained muscle contraction → hypercapnia, tachycardia, masseter/generalized muscle rigidity, rhabdomyolysis, hyperthermia.

Treatment: dantrolene (ryanodine receptor antagonist).

Skeletal muscle relaxants

DRUG	MECHANISM	CLINICAL USE	NOTES
Baclofen	GABA _B receptor agonist in spinal cord	Muscle spasticity, dystonia, multiple sclerosis	Acts on the back (spinal cord) May cause sedation
Cyclobenzaprine	Acts within CNS, mainly at the brainstem	Muscle spasms	Centrally acting Structurally related to TCAs May cause anticholinergic adverse effects, sedation
Dantrolene	Prevents release of Ca ²⁺ from sarcoplasmic reticulum of skeletal muscle by inhibiting the ryanodine receptor	Malignant hyperthermia (toxicity of inhaled anesthetics and succinylcholine) and neuroleptic malignant syndrome (toxicity of antipsychotics)	Acts directly on muscle
Tizanidine	α ₂ agonist, acts centrally	Muscle spasticity, multiple sclerosis, ALS, cerebral palsy	

Opioid analgesics

MECHANISM	Act as agonists at opioid receptors ($\mu = \beta$ -endorphin, $\delta = \text{enkephalin}$, $\kappa = \text{dynorphin}$) to modulate synaptic transmission—close presynaptic Ca ²⁺ channels, open postsynaptic K ⁺ channels → ↓ synaptic transmission. Inhibit release of ACh, norepinephrine, 5-HT, glutamate, substance P.
EFFICACY	Full agonist: morphine, meperidine (long acting), methadone, codeine (prodrug; activated by CYP2D6), fentanyl. Partial agonist: buprenorphine. Mixed agonist/antagonist: butorphanol, nalbuphine. Antagonist: naloxone, naltrexone, methylnaltrexone.
CLINICAL USE	Moderate to severe or refractory pain, diarrhea (loperamide, diphenoxylate), acute pulmonary edema, maintenance programs for opiate use disorder (methadone, buprenorphine + naloxone), neonatal abstinence syndrome (methadone, morphine).
ADVERSE EFFECTS	Nausea, vomiting, pruritus (histamine release), opiate use disorder, respiratory depression, constipation, sphincter of Oddi spasm, miosis (except meperidine → mydriasis), additive CNS depression with other drugs. Tolerance does not develop to miosis and constipation. Treat toxicity with naloxone and prevent relapse with naltrexone once detoxified.

Tramadol

MECHANISM	Very weak opioid agonist; also inhibits the reuptake of norepinephrine and serotonin.
CLINICAL USE	Chronic pain.
ADVERSE EFFECTS	Similar to opioids; decreases seizure threshold; serotonin syndrome.

Butorphanol, nalbuphine

MECHANISM	μ -opioid receptor partial agonists and κ -opioid receptor full agonists.
CLINICAL USE	Analgesia for severe pain (eg, labor).
NOTES	Mixed opioid agonists/antagonists cause less respiratory depression than full opioid agonists. Can cause opioid withdrawal symptoms if patient is also taking full opioid agonist (due to competition for opioid receptors). Not easily reversed with naloxone.

Capsaicin

Naturally found in hot peppers.
MECHANISM
Excessive stimulation and desensitization of nociceptive fibers \rightarrow ↓ substance P release \rightarrow ↓ pain.
CLINICAL USE
Musculoskeletal and neuropathic pain.

Glaucoma therapy

↓ IOP via ↓ amount of aqueous humor (inhibit synthesis/secretion or ↑ drainage).

“ $\beta\alpha D$ ” humor may not be politically correct.”

DRUG CLASS	EXAMPLES	MECHANISM	ADVERSE EFFECTS
β -blockers	Timolol, betaxolol, carteolol	↓ aqueous humor synthesis	No pupillary or vision changes
α -agonists	Epinephrine (α_1), apraclonidine, brimonidine (α_2)	↓ aqueous humor synthesis via vasoconstriction (epinephrine) ↓ aqueous humor synthesis (apraclonidine, brimonidine) ↑ outflow of aqueous humor via uveoscleral pathway	Mydriasis (α_1); do not use in closed-angle glaucoma Blurry vision, ocular hyperemia, foreign body sensation, ocular allergic reactions, ocular pruritus
Diuretics	Acetazolamide	↓ aqueous humor synthesis via inhibition of carbonic anhydrase	No pupillary or vision changes
Prostaglandins	Bimatoprost, latanoprost (PGF _{2α})	↑ outflow of aqueous humor via ↓ resistance of flow through uveoscleral pathway	Darkens color of iris (browning), eyelash growth
Cholinomimetics (M ₃)	Direct: pilocarpine, carbachol Indirect: physostigmine, echothiophate	↑ outflow of aqueous humor via contraction of ciliary muscle and opening of trabecular meshwork Use pilocarpine in acute angle closure glaucoma—very effective at opening meshwork into canal of Schlemm	Miosis (contraction of pupillary sphincter muscles) and cyclospasm (contraction of ciliary muscle)