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B.PHARM SEMESTER II | BP203T

HUMAN ANATOMY, PHYSIOLOGY AND PATHOPHYSIOLOGY II

(THEORY)

UNIT I

Nervous System: Structure, Function and Disorders

Short Notes as per PCI B.Pharm Syllabus

What is covered in this unit

UNIT I TOPICS

Part A – Organisation, neuron, neuroglia and nerve fibres: divisions of the nervous system, neuron, glial cells, classification and properties of nerve fibres.

Part B – Electrophysiology and communication: resting potential, action potential, nerve impulse, receptors, synapse and neurotransmitters.

Part C – Central nervous system: meninges, ventricles and CSF, brain (cerebrum, brainstem, cerebellum), spinal cord, tracts and reflex activity.

Part D – Pathophysiology: epilepsy, Parkinson's disease, stroke, migraine, depression, schizophrenia, Alzheimer's disease and meningitis.

Part E – Clinical correlation: cranial nerves and Glasgow Coma Scale.

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PART A: ORGANISATION OF THE NERVOUS SYSTEM, NEURON, NEUROGLIA AND NERVE FIBRES

1. Organisation of the Nervous System

The **nervous system** is the control and communication network of the body.

Functions of the nervous system

- **Sensory function:** detects changes (stimuli) such as touch, heat, light, sound and chemical change, through receptors.
- **Integrative function:** processes the incoming information, stores memory and takes decisions (mainly in the brain and spinal cord).
- **Motor function:** sends commands to effectors, which are muscles (contract) and glands (secrete).
- **Homeostasis:** controls heart rate, breathing, blood pressure, temperature, digestion and hormones.

Divisions of the nervous system

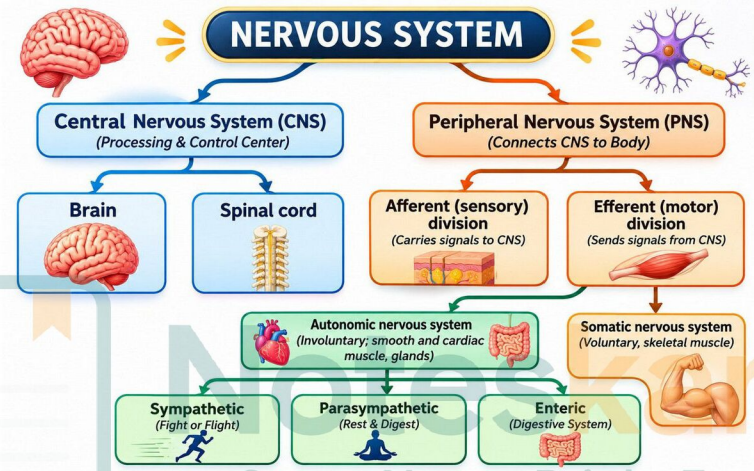

Figure 1: Organisation (divisions) of the nervous system

Division	Parts	Main role
Central nervous system (CNS)	Brain and spinal cord (protected by skull, vertebral column, meninges and CSF).	Integration, decision, memory, thought
Peripheral nervous system (PNS)	12 pairs of cranial nerves, 31 pairs of spinal nerves and ganglia	Carries messages between the CNS and the body
Somatic nervous system	Sensory nerves from skin, muscle, joints; motor nerves to skeletal muscle	Voluntary movement and body sensation
Autonomic nervous system (ANS)	Sympathetic, parasympathetic and enteric parts	Involuntary control of heart, glands, smooth muscle and gut

2. Neuron: The Structural and Functional Unit

A **neuron** (nerve cell) is the basic unit of the nervous system.

Structure of a neuron

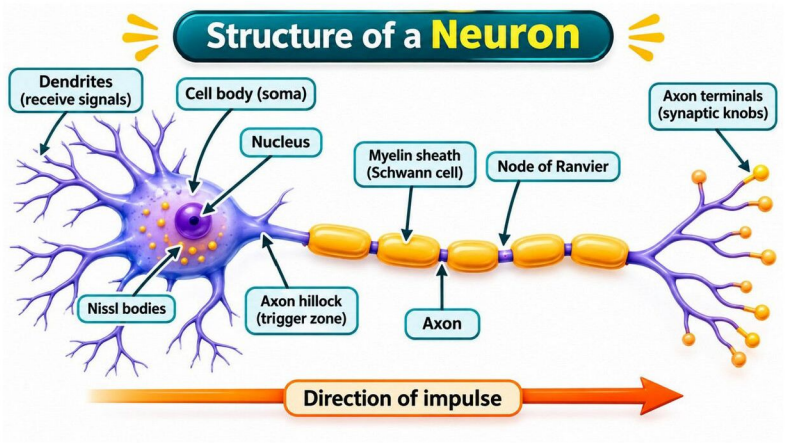

Figure 2: Structure of a typical (multipolar) motor neuron

Part	Structure	Function

Classification of neurons

A. According to structure (number of processes)

Type	Description	Examples
Unipolar (pseudounipolar)	One process that divides into two branches (peripheral and central)	Sensory neurons in dorsal root ganglia
Bipolar	Two processes: one dendrite and one axon	Retina, olfactory epithelium, inner ear
Multipolar	Many dendrites and one axon; the commonest type	Motor neurons, pyramidal cells of the cortex, Purkinje cells

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3. Neuroglia (Glial Cells)

Neuroglia (glia, meaning 'glue') are the supporting cells of the nervous system.

Glial cell	Location	Functions
Astrocytes	CNS	Largest and most numerous glia.
Oligodendrocytes	CNS	Form the myelin sheath of CNS axons; one cell myelinates many axons.
Microglia	CNS	Smallest glia; act as the **macrophages** of the CNS, remove debris and microbes.
Ependymal cells	Lining of ventricles and central canal	Ciliated cells that line the ventricles; help form and circulate CSF (choroid plexus).

Myelination

- **Myelin** is a layered wrapping of the glial cell membrane around the axon.
- It acts as an **electrical insulator**, so the current cannot leak and the impulse jumps between the nodes.
- In the PNS, the outer cytoplasm and nucleus of the Schwann cell form the **neurilemma** (sheath of Schwann), which helps regeneration.

Blood-brain barrier (BBB)

The **blood-brain barrier** is a selective barrier between blood and brain tissue.

4. Classification and Properties of Nerve Fibres

Nerve fibres differ in **diameter, myelination and conduction speed**. Larger and myelinated fibres conduct faster. Two classifications are in common use.

A. Erlanger and Gasser classification (according to diameter and velocity)

Type	Diameter (µm)	Velocity (m/s)	Myelin	Function
A alpha (Aα)	12 to 20	70 to 120	Yes	Motor to skeletal muscle; proprioception (muscle spindle and tendon organ)
A beta (Aβ)	5 to 12	30 to 70	Yes	Touch, pressure, vibration
A gamma (Aγ)	3 to 6	15 to 30	Yes	Motor to muscle spindle (intrafusal fibres)
A delta (Aδ)	2 to 5	12 to 30	Thin	Fast (sharp) pain, cold, some touch

B. Lloyd and Hunt classification (for sensory fibres of muscle and skin)

Group	Equivalent	Source / function
Ia	Aα	Primary endings of the muscle spindle (muscle length and speed of stretch).
Ib	Aα	Golgi tendon organ (muscle tension)
II	Aβ	Secondary endings of the muscle spindle; touch and pressure receptors
III	Aδ	Pain, cold and crude touch

Degeneration and regeneration of nerves

When an axon is cut, the part away from the cell body undergoes **Wallerian degeneration**: axon and myelin break down and are removed by macrophages.

PART B: ELECTROPHYSIOLOGY, RECEPTORS, SYNAPSE AND NEUROTRANSMITTERS

5. Electrophysiology of the Neuron: Resting Membrane Potential

Nerve cells communicate with **electrical signals**.

Resting membrane potential (RMP)

When a neuron is not sending a signal, the **inside is negative compared with the outside**.

6. Action Potential

The **action potential (AP)** is a rapid, temporary reversal of the membrane potential.

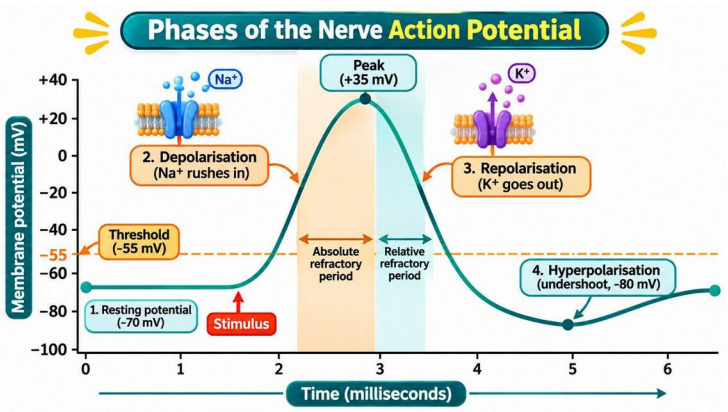

Figure 3: Phases of the nerve action potential

Phases of the action potential

Phase	What happens	Membrane potential
1. Resting state	All voltage-gated channels closed; K^+ leak keeps the potential negative	About −70 mV
2. Depolarisation	A stimulus opens some Na^+ channels. When the threshold is reached, many voltage-gated Na^+ channels open (positive feedback) and Na^+ rushes in	−55 mV rising to about +35 mV
3. Peak	Na^+ channels become inactivated and the Na^+ entry stops	About +35 mV
4. Repolarisation	Voltage-gated K^+ channels open (slowly); K^+ leaves the cell	+35 mV falling to −70 mV

Voltage-gated channels

- **Voltage-gated Na^+ channel** has two gates: a fast **activation gate** (opens on depolarisation) and a slower **inactivation gate** (closes after about 1 ms).
- **Voltage-gated K^+ channel** has one gate that opens slowly on depolarisation.
- After the AP, the Na^+/K^+ pump (not the AP itself) restores the ion balance.

Refractory periods

Period	Time	Reason	Meaning
Absolute refractory period	From threshold to about the end of repolarisation (about 1 ms).	Na^+ channels are open or inactivated	No second AP is possible, however strong the stimulus
Relative refractory period	During the undershoot	Some Na^+ channels have recovered but K^+ is still leaving	A second AP is possible only with a stronger stimulus

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7. Nerve Impulse and its Conduction

A **nerve impulse** is the action potential travelling along the axon.

Conduction in unmyelinated fibres (continuous conduction)

The AP is regenerated at **every point** of the membrane, one after the other, like a burning fuse.

Conduction in myelinated fibres (saltatory conduction)

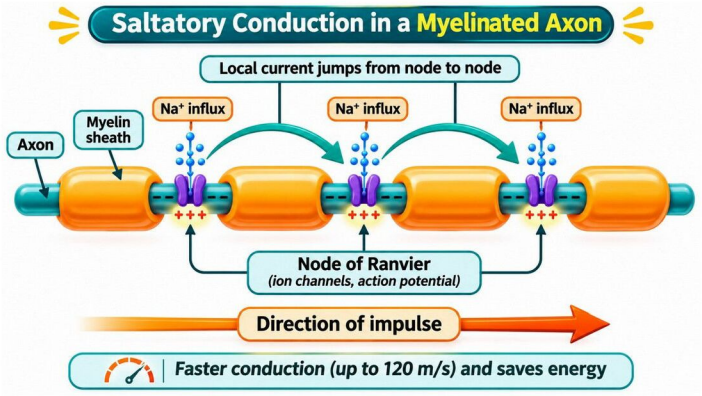

Figure 4: Saltatory conduction in a myelinated axon

- Myelin stops ion movement, so ion channels are crowded at the **nodes of Ranvier** only.
- The local current flows quickly through the cytoplasm under the myelin to the next node, where the AP is regenerated.

- Advantages: much **faster** (up to 120 m/s), uses **less energy** (fewer ions move).

8. Receptors (Sensory Receptors)

A **sensory receptor** is a specialised structure that detects a stimulus and converts it into a nerve signal.

Classification of receptors

Basis	Types	Examples
By type of stimulus	Mechanoreceptors	Touch, pressure, vibration, stretch, hearing, balance
	Thermoreceptors	Hot and cold receptors in skin and hypothalamus
	Nociceptors	Free nerve endings for pain (tissue damage)
	Chemoreceptors	Taste, smell, carotid and aortic bodies (O_2, CO_2, pH)

9. Synapse

A **synapse** is the junction where a neuron passes its signal to another neuron, a muscle cell or a gland cell.

Types of synapse

Type	Description	Features / examples
Chemical synapse	Transmission by a neurotransmitter across the cleft	Most synapses; one-way, slower, can be excitatory or inhibitory.
Electrical synapse	Ions pass directly through gap junctions (connexons)	Very fast, two-way, little modification; heart muscle, smooth muscle, some brain areas.

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Steps of chemical synaptic transmission

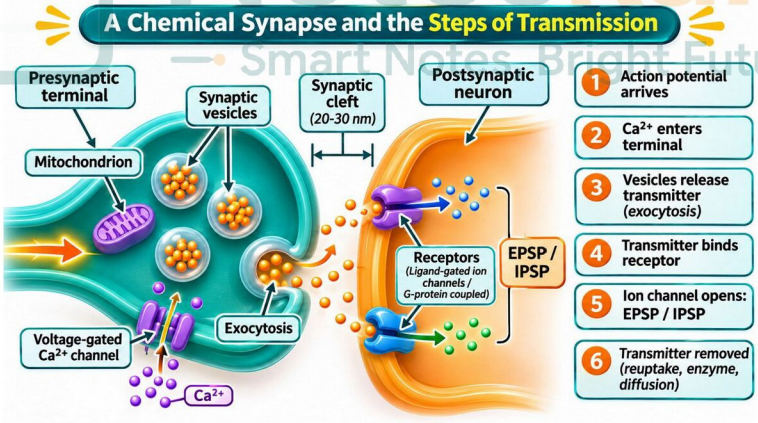

Figure 5: A chemical synapse and the steps of transmission

- The AP reaches the axon terminal and opens **voltage-gated Ca^{2+} channels**.
- Ca^{2+} enters and makes **synaptic vesicles** fuse with the membrane (**exocytosis**, using SNARE proteins).
- Neurotransmitter diffuses across the cleft and binds to **receptors** on the postsynaptic membrane.
- Receptors open ion channels (**ionotropic**) or start second messenger pathways (**metabotropic**, G-protein coupled).

Postsynaptic potentials

Feature	EPSP (excitatory)	IPSP (inhibitory)
Full name	Excitatory postsynaptic potential	Inhibitory postsynaptic potential
Channel opened	Na^+ (or Na^+/K^+ cation) channels	Cl^- channels or K^+ channels
Effect on membrane	Depolarisation	Hyperpolarisation

Feature	EPSP (excitatory)	IPSP (inhibitory)
Effect on neuron	Moves towards threshold	Moves away from threshold

10. Neurotransmitters

A **neurotransmitter** is a chemical released by a neuron at a synapse that carries the signal to the next cell.

Classification of neurotransmitters

Group	Members
Cholinergic	Acetylcholine (ACh)
Biogenic amines (monoamines)	Dopamine, noradrenaline (norepinephrine), adrenaline (epinephrine), serotonin (5-HT), histamine
Amino acids	Excitatory: glutamate, aspartate. Inhibitory: GABA, glycine
Neuropeptides	Substance P, enkephalins, endorphins, neuropeptide Y, CGRP, orexin

PART C: CENTRAL NERVOUS SYSTEM

11. Meninges

The **meninges** are three connective tissue membranes that cover and protect the brain and the spinal cord, between the bone and the nervous tissue.

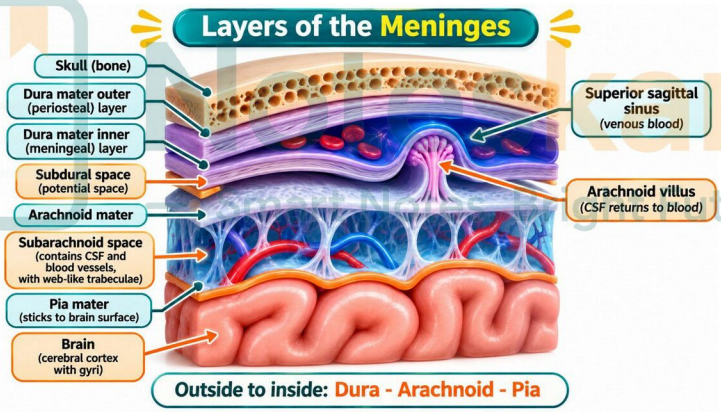

Figure 6: Layers of the meninges (cranial), with arachnoid villus and venous sinus

Layer	Structure	Special features
Dura mater ('tough mother')	Thick, strong, fibrous.	Layers separate to form the **dural venous sinuses**.
Arachnoid mater ('spider-like')	Thin, delicate, avascular membrane with web-like trabeculae	Subarachnoid space lies beneath it and contains **CSF** and blood vessels.
Pia mater ('tender mother')	Very thin, vascular layer closely stuck to the surface of brain and cord, following every fold	Carries blood vessels into the brain.

12. Ventricles of the Brain and Cerebrospinal Fluid (CSF)

Ventricles of the brain

The **ventricles** are four connected, fluid-filled cavities inside the brain, lined by **ependymal cells**.

Cerebrospinal fluid (CSF)

CSF is a clear, colourless fluid that fills the ventricles, the central canal and the subarachnoid space.

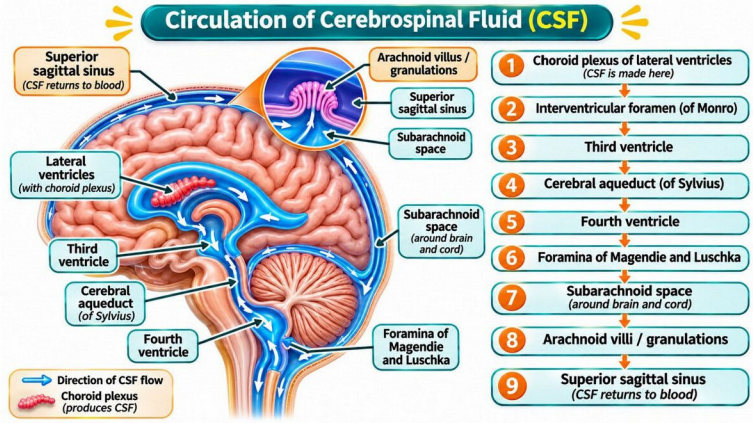

Figure 7: Pathway (circulation) of cerebrospinal fluid

13. Structure and Functions of the Brain

The adult brain weighs about **1.3 to 1.4 kg** and uses about **20% of the body's oxygen and glucose** although it is only 2% of body weight.

A. Cerebrum

The **cerebrum** is the largest part (about 80% of brain weight).

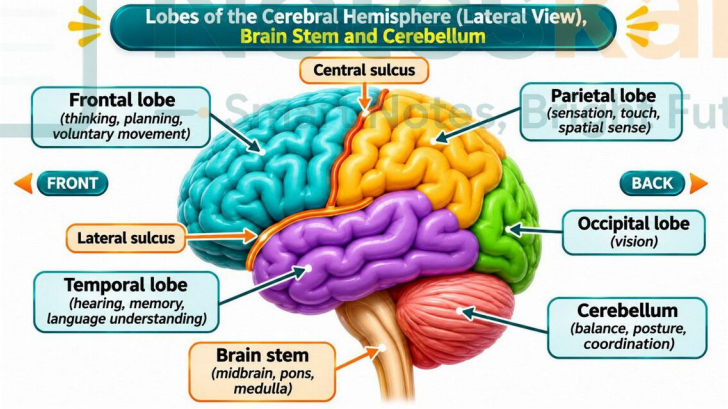

Figure 8: Lobes of the cerebral hemisphere (lateral view), brain stem and cerebellum

B. Brainstem

The brainstem connects the cerebrum with the spinal cord.

C. Cerebellum

The **cerebellum** ('little brain') lies behind the pons and medulla, under the occipital lobes, separated from them by the tentorium cerebelli.

14. Spinal Cord

Gross structure

- The spinal cord is a long, cylindrical structure about **42 to 45 cm** long.
- It ends in adults at the lower border of **L1 (or L1-L2)** as the cone-shaped **conus medullaris**.
- Below the conus, the lumbar and sacral nerve roots hang like a horse's tail.
- It has **31 pairs of spinal nerves**: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral and 1 coccygeal.

Internal structure (cross-section)

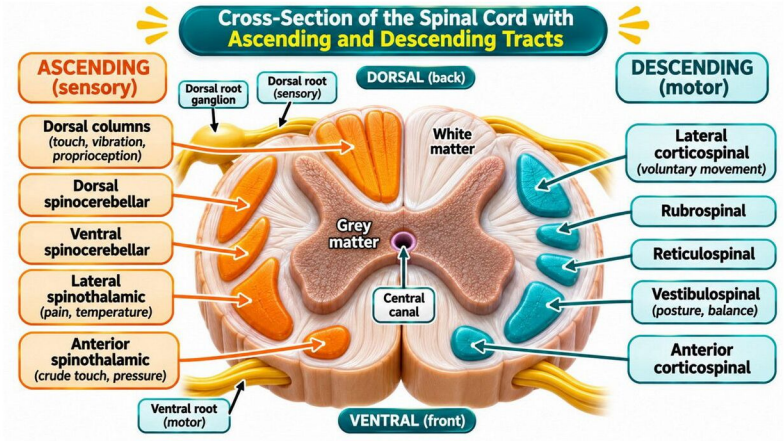

Figure 9: Cross-section of the spinal cord with ascending (left) and descending (right) tracts

- **Grey matter** (butterfly or H shaped, inside): **dorsal (posterior) horn** receives sensory fibres.
- **White matter** (outside): bundles of myelinated axons arranged in three **columns (funiculi)**: dorsal.
- **Dorsal root** carries sensory fibres and has the **dorsal root ganglion**; **ventral root** carries motor fibres.

Functions of the spinal cord

- Conducts sensory impulses up to the brain and motor impulses down to the body.
- Acts as the centre for **spinal reflexes** (knee jerk, withdrawal), without involving the brain.
- Controls bladder and bowel emptying, and sexual reflexes (sacral cord).
- Contains the autonomic outflow (thoracolumbar and sacral).

Afferent (ascending) tracts

Tract	Carries	Course	Crossing
Dorsal column - medial lemniscus (fasciculus gracilis and cuneatus)	Fine (discriminative) touch, vibration, proprioception (position sense)	Dorsal column up to the medulla.	Crosses in the **medulla**
Lateral spinothalamic	Pain and temperature	Dorsal horn, crosses, ascends in the lateral column to the thalamus then cortex	Crosses at the **same spinal level** (within 1 to 2 segments).
Anterior spinothalamic	Crude touch and pressure	As above in the anterior column	Crosses at the spinal level
Dorsal (posterior) spinocerebellar	Unconscious proprioception from the lower limb and trunk	To the cerebellum through the inferior peduncle	Uncrossed (ipsilateral)

Efferent (descending) tracts

Tract	Origin to end	Function	Crossing
Lateral corticospinal (pyramidal)	Motor cortex to anterior horn cells	Voluntary, fine, skilled movements of limbs, especially the hand	About 85 to 90% cross at the **medullary pyramids**
Anterior corticospinal	Motor cortex to anterior horn	Voluntary movement of the trunk and proximal muscles	Crosses at the spinal level
Rubrospinal	Red nucleus (midbrain) to the cord	Tone of flexor muscles; assists the corticospinal tract	Crosses in the midbrain
Reticulospinal	Reticular formation to the cord	Posture, muscle tone, autonomic functions; pontine part facilitates extensors	Mostly uncrossed

15. Reflex Activity

A **reflex** is a rapid, automatic, involuntary and stereotyped response to a stimulus.

Reflex arc

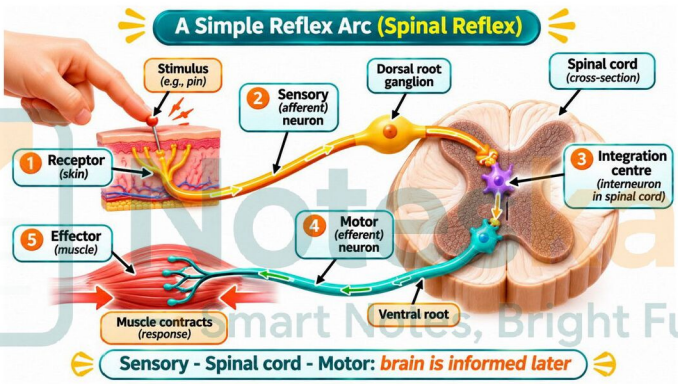

Figure 10: A simple reflex arc (spinal reflex)

Component	Role
1. Receptor	Detects the stimulus (for example muscle spindle, pain receptor)
2. Afferent (sensory) neuron	Carries the signal through the dorsal root to the spinal cord.
3. Integrating centre	Synapse(s) in the grey matter of the cord or brainstem (one synapse in monosynaptic arcs; interneurons in polysynaptic arcs).
4. Efferent (motor) neuron	Carries the response through the ventral root

Classification of reflexes

Basis	Types
Number of synapses	**Monosynaptic** (one synapse; stretch reflex such as knee jerk) and **polysynaptic** (more than one synapse; withdrawal reflex).
Inborn or learned	**Unconditioned (inborn)** reflexes (withdrawal, sucking) and **conditioned (learned)** reflexes (Pavlov's salivation to a bell).
Effector	**Somatic reflex** (skeletal muscle) and **visceral (autonomic) reflex** (smooth muscle, gland, heart).
Site of the centre	Spinal, brainstem (pupillary, corneal) or cortical reflex

Important spinal reflexes

1. Stretch (myotatic) reflex

- Stimulus: sudden stretch of a muscle (for example tapping the patellar tendon).
- The Ia fibre synapses **directly** with the alpha motor neuron of the same muscle (**monosynaptic**) and the muscle contracts.
- At the same time an inhibitory interneuron relaxes the opposing (antagonist) muscle: **reciprocal inhibition**.
- Function: keeps muscle length and posture.

PART D: PATHOPHYSIOLOGY OF NEUROLOGICAL AND PSYCHIATRIC DISORDERS

Pathophysiology explains how normal function is changed in disease.

16. Epilepsy

Definition

Epilepsy is a chronic brain disorder with a lasting tendency to produce **unprovoked, recurrent seizures**.

Causes and risk factors

Group	Examples
Genetic	Mutations of Na^+, K^+, Ca^{2+} channels and GABA-A receptor genes (channelopathies).
Structural	Head injury, stroke, brain tumour, scar after meningitis, cortical malformations
Infectious	Meningitis, encephalitis, neurocysticercosis (very common cause in India)
Metabolic	Low blood glucose, low sodium or calcium, kidney or liver failure.

Pathophysiology

Normal brain activity is a balance between **excitation (glutamate)** and **inhibition (GABA)**.

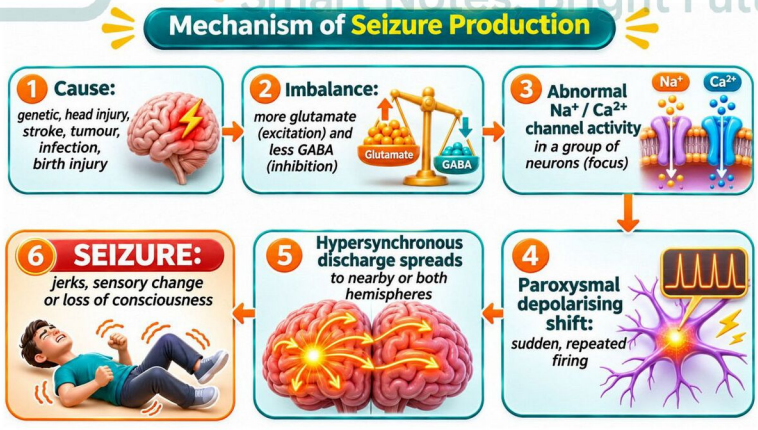

Figure 11: Mechanism of seizure production

Classification of seizures (ILAE)

Type	Features
Focal onset seizure	Starts in one area of one hemisphere.
Focal to bilateral tonic-clonic	Focal seizure that spreads to both sides (secondary generalisation)
Generalised tonic-clonic (grand mal)	Sudden loss of consciousness, **tonic phase** (stiffening.
Absence (petit mal)	Brief (5 to 15 s) staring spells without falling, in children; no post-ictal state; EEG shows 3 Hz spike and wave

Diagnosis and basis of treatment

- **EEG** (electroencephalogram) shows spikes and sharp waves; **CT/MRI** looks for structural causes; blood tests exclude metabolic causes.
- **Treatment aims** to reduce excitation or increase inhibition: **Na^+ channel blockers** (phenytoin, carbamazepine, lamotrigine).
- A few patients with drug-resistant epilepsy benefit from surgery, vagus nerve stimulation or ketogenic diet.

17. Parkinson's Disease

Definition

Parkinson's disease (PD) is a slowly progressive **neurodegenerative movement disorder** caused by the loss of **dopamine-producing neurons in the substantia nigra pars compacta**.

Causes and risk factors

- Mostly **idiopathic** (unknown cause); ageing is the main risk; more common in men.
- **Genetic factors** (about 10%): mutations in SNCA (α-synuclein), LRRK2, PARK2 (parkin), PINK1 and DJ-1.
- **Environmental toxins:** pesticides (paraquat, rotenone), MPTP (a contaminant of illicit opioids that selectively destroys nigral neurons), heavy metals.
- **Drug-induced parkinsonism:** antipsychotics (haloperidol), metoclopramide and reserpine block or deplete dopamine.

Pathophysiology

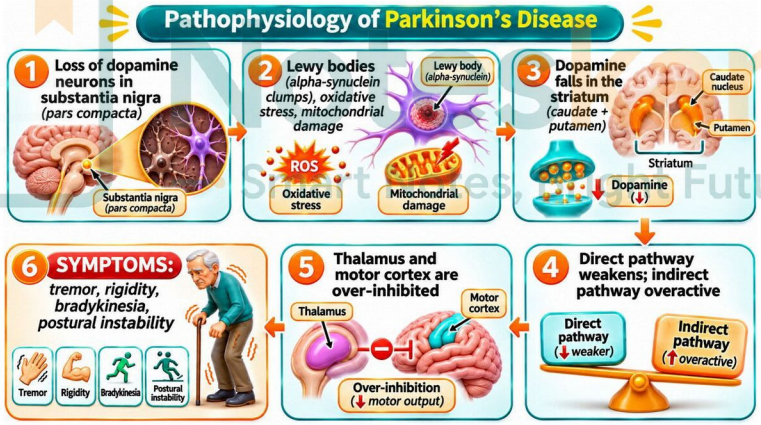

Figure 12: Pathophysiology of Parkinson's disease

- **Loss of neurons:** symptoms appear when about **50 to 60% of nigral neurons** are lost and **striatal dopamine falls by 70 to 80%**.
- **Lewy bodies:** round inclusions inside neurons made of misfolded **α-synuclein.**
- **Causes of cell death:** oxidative stress, mitochondrial complex I dysfunction, impaired protein clearance (ubiquitin-proteasome), neuroinflammation.
- **Basal ganglia circuits:** dopamine normally **excites the direct pathway** (D1 receptors.

Clinical features

Motor feature (TRAP)	Description
Tremor	Resting 'pill-rolling' tremor, 4 to 6 Hz, decreases on movement
Rigidity	Increased tone in both flexors and extensors: 'lead-pipe'; with tremor, 'cogwheel' rigidity.
Akinesia / bradykinesia	Slowness and poverty of movement; mask-like face, small handwriting (micrographia).

Motor feature (TRAP)	Description
Postural instability	Stooped posture, shuffling small-step gait, festination, falls (late)

Basis of treatment

Drug group	How it works
Levodopa + carbidopa	Levodopa crosses the BBB and is changed to dopamine.
Dopamine agonists (pramipexole, ropinirole)	Stimulate D2/D3 receptors directly
MAO-B inhibitors (selegiline, rasagiline)	Reduce the breakdown of dopamine
COMT inhibitors (entacapone)	Prolong the action of levodopa

18. Stroke (Cerebrovascular Accident)

Definition

A **stroke** is the sudden loss of brain function due to a **disturbance of blood supply** to part of the brain.

Types

Type	Share	Cause
Ischemic stroke	About 85%	Blockage of an artery.
Haemorrhagic stroke	About 15%	Rupture of a vessel.

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Risk factors

- **Non-modifiable:** age, male sex, family history, previous stroke or TIA.
- **Modifiable: hypertension (most important)**, diabetes, atrial fibrillation, high cholesterol, smoking, obesity, lack of exercise.

Pathophysiology of ischemic stroke (ischemic cascade)

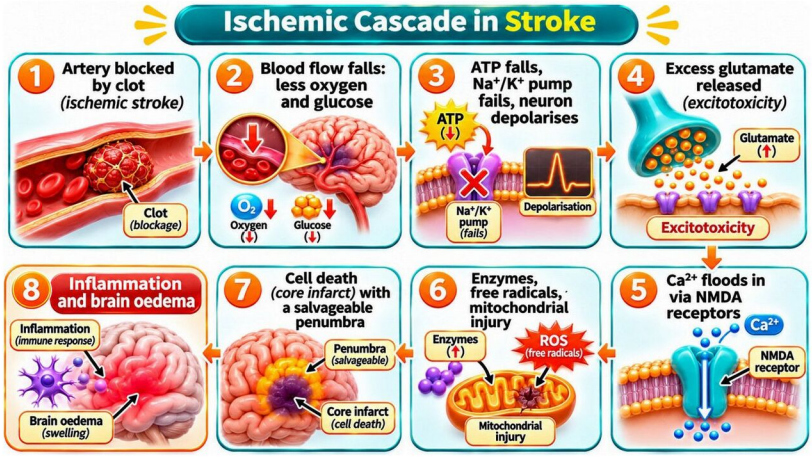

Figure 13: Ischemic cascade in stroke

- Brain tissue has almost no store of oxygen and glucose.
- **Core (infarct) zone:** where flow is very low (below about 10 mL/100 g/min); cells die quickly by necrosis.
- **Ischemic penumbra:** the area around the core with reduced flow (10 to 20 mL/100 g/min); cells are alive but not working.
- **Energy failure:** fall of ATP stops the Na^+/K^+ pump, so cells depolarise and swell (cytotoxic oedema).

Clinical features (depend on the artery involved)

Artery	Area supplied	Main features
Middle cerebral artery (MCA)	Lateral surface of the frontal, parietal and temporal lobes	Weakness and sensory loss of the opposite face and arm more than the leg; aphasia if the left (dominant) side is involved; neglect if the right side.
Anterior cerebral artery (ACA)	Medial frontal and parietal lobes	Weakness of the opposite **leg** more than the arm; behavioural change; urinary incontinence.
Posterior cerebral artery (PCA)	Occipital lobe, medial temporal lobe	Opposite visual field loss (homonymous hemianopia)
Vertebrobasilar system	Brainstem, cerebellum	Vertigo, double vision, ataxia, difficulty in swallowing, crossed signs, coma

Diagnosis and basis of treatment

- **CT scan** is done first to exclude haemorrhage; MRI is more sensitive for early ischemia.
- **Ischemic stroke:** intravenous **thrombolysis (alteplase/tenecteplase)** within about **4.5 hours** of onset.
- **Haemorrhagic stroke:** no thrombolytics; control blood pressure, reduce raised ICP, surgery or clipping/coiling of an aneurysm.
- **Prevention:** control hypertension, diabetes and lipids, stop smoking, exercise.

19. Migraine

Definition

Migraine is a common, recurrent **headache disorder** with attacks of moderate to severe, usually **one-sided, pulsating headache** lasting **4 to 72 hours.**

Types

Type	Features
Migraine without aura (common migraine)	About 70 to 80% of cases; headache with associated symptoms but no aura.
Migraine with aura (classic migraine)	In about 20 to 30%; **aura** (visual zigzag lights.
Chronic migraine	Headache on 15 or more days per month for over 3 months.

Pathophysiology

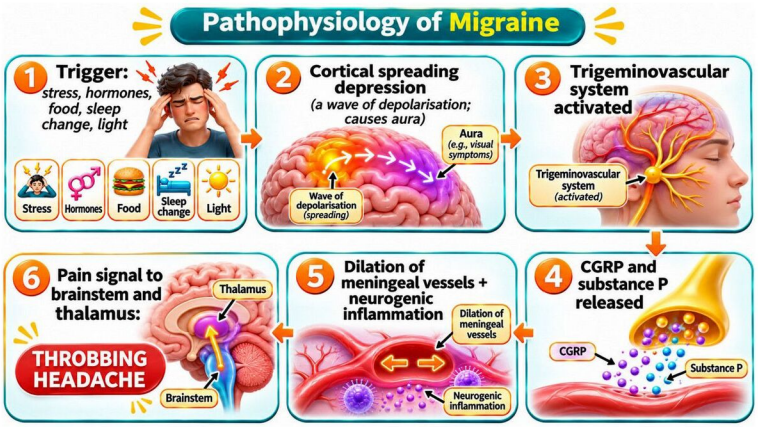

Figure 14: Pathophysiology of migraine

- Migraine is mainly a **neurovascular disorder** of an over-excitable brain rather than only a vascular one (the old 'vasodilation' theory is incomplete).

- **Cortical spreading depression (CSD):** a slow wave (2 to 5 mm/min) of neuronal and glial depolarisation moves across the cortex, followed by suppression of activity.
- **Trigeminovascular system:** sensory fibres of the **trigeminal nerve** that supply the meningeal and cerebral vessels are activated and release **CGRP (calcitonin gene-related peptide), substance P and neurokinin A**.
- **Neurogenic inflammation:** these peptides cause vasodilation, plasma leakage and mast cell activation around the meningeal vessels, and sensitise the pain fibres (peripheral and central sensitisation), giving **throbbing pain and allodynia**.

Basis of treatment

Aim	Drugs and explanation
Acute attack	NSAIDs, paracetamol with antiemetics (metoclopramide, domperidone); **triptans** (sumatriptan, rizatriptan.
Prevention (if attacks are frequent)	Propranolol, amitriptyline, topiramate, valproate, flunarizine; **CGRP monoclonal antibodies** (erenumab, fremanezumab)
Non-drug	Avoid triggers, regular sleep and meals, rest in a dark, quiet room.

20. Depression

Definition

Depression (major depressive disorder) is a mood disorder with **persistent low mood or loss of interest and pleasure (anhedonia)** lasting at least **2 weeks**, along with other symptoms, that interferes with daily life.

Diagnosis (DSM-5 criteria)

Five or more of the following nine symptoms during the same 2-week period, including at least one of the first two: depressed mood; loss of interest or pleasure; weight or appetite change; sleep disturbance (insomnia or hypersomnia); psychomotor agitation or slowing; tiredness or loss of energy; feelings of worthlessness or guilt; poor concentration or indecision; recurrent thoughts of death or suicide.

Types

Type	Features
Major depressive disorder	Single or recurrent episodes meeting the criteria
Persistent depressive disorder (dysthymia)	Milder depression lasting 2 years or more
Bipolar disorder	Depressive episodes alternating with mania or hypomania; antidepressants alone can trigger mania.
Seasonal affective disorder	Recurs in winter

Pathophysiology

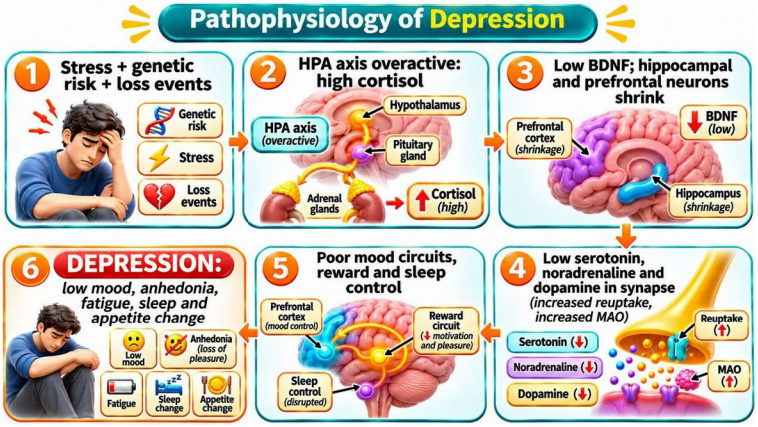

Figure 15: Pathophysiology of depression

- **Monoamine hypothesis:** depression is linked to a **functional deficiency of serotonin, noradrenaline and dopamine** at brain synapses.
- **Neurotrophic hypothesis:** stress and high cortisol **reduce BDNF** (brain-derived neurotrophic factor).
- **HPA axis hyperactivity:** chronic stress overactivates the hypothalamic-pituitary-adrenal axis.
- **Inflammation:** raised cytokines (IL-6, TNF-α, CRP) in some patients; cytokine therapy (interferon) can produce depression.

Clinical features

Area	Features
Emotional	Sadness, emptiness, irritability, hopelessness, guilt, anhedonia
Cognitive	Poor concentration, slow thinking, indecision, negative thoughts, suicidal thoughts
Physical (somatic)	Fatigue, sleep and appetite changes, weight change, aches and pains, low libido, constipation.
Behavioural	Withdrawal, slowed or agitated movements, neglect of work and self-care

Basis of treatment

Group	Mechanism	Examples
SSRIs	Block serotonin reuptake (SERT)	Fluoxetine, sertraline, escitalopram
SNRIs	Block serotonin and noradrenaline reuptake	Venlafaxine, duloxetine
TCAs	Block reuptake of NA and 5-HT (also block muscarinic, H1 and alpha receptors, which gives side effects)	Amitriptyline, imipramine
MAO inhibitors	Block the breakdown of monoamines	Phenelzine, moclobemide (cheese reaction risk)

21. Schizophrenia

Definition

Schizophrenia is a chronic, severe **psychotic disorder** with disturbed thinking, perception, emotion and behaviour, and loss of contact with reality.

Causes

- **Genetic:** the strongest risk factor; heritability about 80%.
- **Neurodevelopmental:** prenatal infection or malnutrition, obstetric complications, abnormal brain development, with onset in adolescence when synapses are 'pruned'.

- **Environmental:** cannabis use, urban living, migration, childhood trauma, and stress.
- **Structural brain changes:** enlarged ventricles, reduced grey matter in the prefrontal cortex and temporal lobe, reduced hippocampal volume.

Symptoms

Group	Features	Related to
Positive (added to normal behaviour)	Hallucinations (mostly auditory voices), delusions (persecution, reference, control), disorganised speech and behaviour, catatonia.	Excess dopamine in the **mesolimbic** pathway
Negative (loss of normal function)	Flat or blunted affect, poverty of speech (alogia), loss of motivation (avolition), social withdrawal, anhedonia	Low dopamine in the **mesocortical** pathway; NMDA hypofunction
Cognitive	Poor attention, working memory, planning and learning	Prefrontal dysfunction
Mood	Depression, anxiety, suicide risk	

Pathophysiology

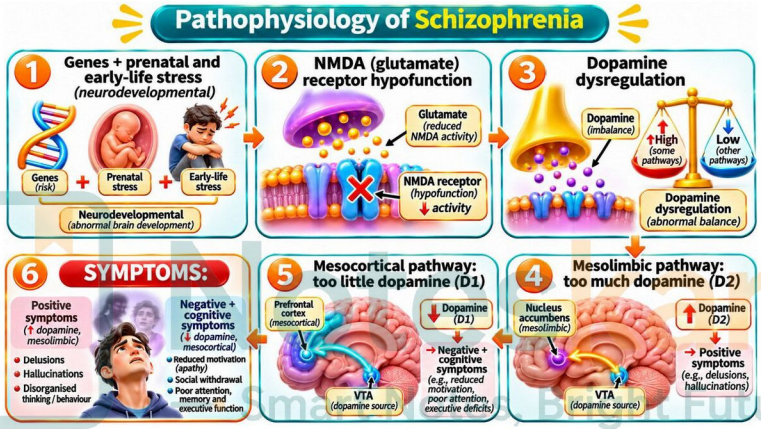

Figure 16: Pathophysiology of schizophrenia

- **Dopamine hypothesis:** the classic theory says the positive symptoms are due to **overactivity of dopamine in the mesolimbic pathway (D2 receptors)**.
- **Revised dopamine hypothesis:** at the same time there is **too little dopamine in the mesocortical pathway (D1 receptors) of the prefrontal cortex**, causing negative and cognitive symptoms.
- **Glutamate (NMDA receptor hypofunction) hypothesis:** NMDA blockers such as **phencyclidine (PCP) and ketamine** produce positive, negative and cognitive symptoms in healthy people.
- **Serotonin:** LSD-like hallucinogens act on 5-HT2A receptors; atypical antipsychotics block 5-HT2A as well as D2.

Basis of treatment

- **Typical (first-generation) antipsychotics:** haloperidol, chlorpromazine, fluphenazine; strong **D2 blockers.**
- **Atypical (second-generation) antipsychotics:** clozapine, olanzapine, risperidone, quetiapine, aripiprazole; block **5-HT2A and D2.**
- Psychosocial treatment, family education and rehabilitation are important.

22. Alzheimer's Disease

Definition

Alzheimer's disease (AD) is a progressive **neurodegenerative disorder** and the commonest cause of **dementia** (60 to 70% of cases).

Risk factors

- **Age** is the greatest risk factor; the risk doubles about every 5 years after 65.
- **Genes: APOE ε4** allele (chromosome 19) increases the risk for late-onset AD. Rare **early-onset familial AD** is due to mutations in **APP (chromosome 21), PSEN1 (chromosome 14) or PSEN2 (chromosome 1)**.
- **Others:** head injury, hypertension, diabetes, obesity, smoking, low education, depression, female sex.

Pathophysiology

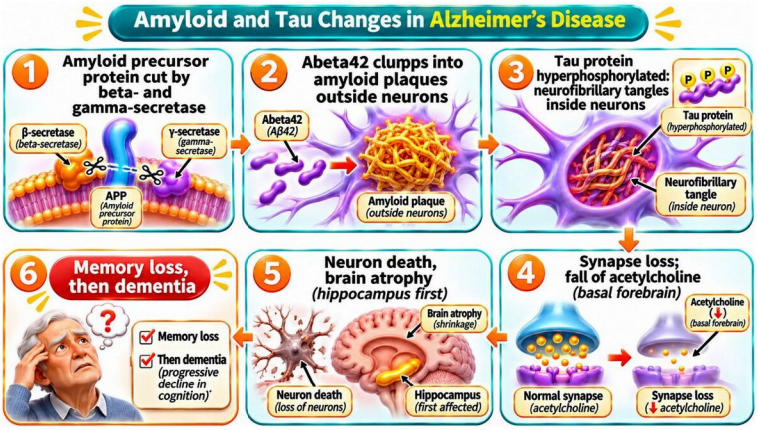

Figure 17: Amyloid and tau changes in Alzheimer's disease

Hypothesis / change	Explanation
Amyloid cascade	Amyloid precursor protein (APP) is normally cut by α-secretase.
Tau pathology	**Tau** normally stabilises microtubules.
Cholinergic hypothesis	Loss of cholinergic neurons of the **nucleus basalis of Meynert** reduces ACh (and choline acetyltransferase) in the cortex and hippocampus, causing memory and attention problems.
Glutamate excitotoxicity	Chronic over-activation of NMDA receptors damages neurons; memantine blocks this

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Diagnosis and basis of treatment

- Clinical assessment and cognitive tests (MMSE, MoCA); exclude other causes (B12 or thyroid deficiency.
- **Cholinesterase inhibitors** (donepezil, rivastigmine, galantamine) increase ACh in the synapse: mild to moderate AD.
- **Memantine** (NMDA receptor antagonist): moderate to severe AD.
- **Anti-amyloid antibodies** (lecanemab, donanemab) remove plaques and may slow early disease.

23. Meningitis

Definition

Meningitis is **inflammation of the meninges** (arachnoid and pia mater) and the CSF in the subarachnoid space, usually due to infection.

Types and causes

Type	Common causes	Course
Bacterial (acute pyogenic)	Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae type b.	Severe, rapid (hours to days)
Viral (aseptic)	Enteroviruses (commonest), mumps, herpes simplex, varicella-zoster, HIV	Milder, usually self-limiting
Tuberculous	Mycobacterium tuberculosis	Subacute, over weeks
Fungal	Cryptococcus neoformans (in HIV), Candida	Chronic; in immunosuppressed

Pathophysiology of bacterial meningitis

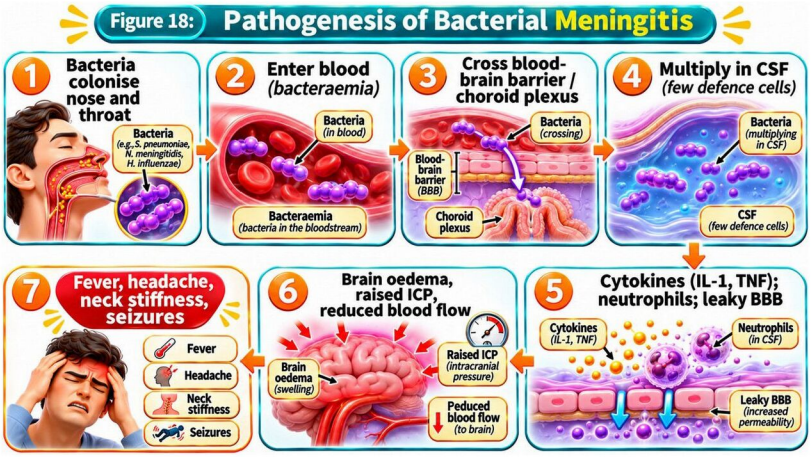

Figure 18: Pathogenesis of bacterial meningitis

- **Entry:** bacteria colonise the nasopharynx, invade the mucosa and enter the blood.
- **Crossing into CSF:** bacteria with a **polysaccharide capsule** escape the immune system and cross the BBB or choroid plexus.
- **Multiplication in CSF:** CSF has very little complement and few antibodies and white cells, so bacteria multiply freely.
- **Inflammation:** bacterial cell wall fragments and toxins stimulate microglia.

Clinical features

- **Classical triad: fever, severe headache and neck stiffness (nuchal rigidity)**; also photophobia, vomiting, confusion and drowsiness, and seizures.
- **Kernig's sign:** with the hip and knee flexed to 90 degrees.
- **Brudzinski's sign:** flexion of the neck makes the hips and knees flex involuntarily.
- **Meningococcal meningitis:** a **non-blanching purpuric (petechial) rash** with shock (meningococcaemia, Waterhouse-Friderichsen syndrome).

Basis of treatment and prevention

- **Bacterial meningitis:** start empirical **intravenous antibiotics immediately** (ceftriaxone or cefotaxime.
- **Viral:** supportive; **acyclovir** for herpes simplex.
- **Tuberculous:** long course of anti-tuberculosis drugs (isoniazid, rifampicin, pyrazinamide, ethambutol) with steroids.
- **Fungal:** amphotericin B with flucytosine, then fluconazole.

PART E: CLINICAL CORRELATION AND REFERENCE TABLES

24. Cranial Nerves and Clinical Assessment

The twelve cranial nerves

No.	Name	Type	Main function
I	Olfactory	Sensory	Smell
II	Optic	Sensory	Vision
III	Oculomotor	Motor	Eye movement, eyelid, pupil constriction, lens accommodation
IV	Trochlear	Motor	Superior oblique muscle of the eye
V	Trigeminal	Mixed	Facial sensation, chewing (muscles of mastication)

No.	Name	Type	Main function
VI	Abducens	Motor	Lateral rectus (moves the eye outward)
VII	Facial	Mixed	Facial expression, taste (anterior two-thirds of the tongue), tears and saliva
VIII	Vestibulocochlear	Sensory	Hearing and balance
IX	Glossopharyngeal	Mixed	Taste (posterior third), swallowing, parotid gland, carotid sinus
X	Vagus	Mixed	Parasympathetic supply of heart, lungs and gut; swallowing, voice
XI	Accessory	Motor	Trapezius and sternocleidomastoid
XII	Hypoglossal	Motor	Movement of the tongue

Glasgow Coma Scale (GCS)

The GCS measures the level of consciousness.

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NOTE FOR STUDENTS

These notes are prepared for study and revision. Reference values (for example CSF and drug details) vary slightly between textbooks; always follow your prescribed textbook and current clinical guidelines.