



The Central Nervous System

◆ 1. Formation of Neural Tube

Timeline 

- Begins: Start of 3rd week

Origin

- From ectoderm (mid-dorsal thickening) → *Neural plate*
-



Neural Tube Formation Flowchart

Ectoderm → Neural plate formation → Lateral edges elevate → Neural folds → Neural folds fuse in midline → Formation of Neural tube

Fusion Pattern 

- Starts at cervical region
- Proceeds:

- Cranially (towards head)
 - Caudally (towards tail)
-

Neuropore Closure

Neural tube (open ends)

- Cranial neuropore closes → Day 25 (18-20 somites)
 - Caudal neuropore closes → Day 28
-

Clinical Correlation

Failure of closure

- Cranial end defect → Anencephaly
 - Caudal end defect → Spina bifida
-

◆ 2. Primary Brain Vesicles

Early dilatations at cephalic end

Vesicle	Derivative
Prosencephalon	Forebrain

Mesencephalon	Midbrain
Rhombencephalon	Hindbrain

Associated Flexures

Develop simultaneously:

- Cephalic flexure → midbrain region
- Cervical flexure → between hindbrain & spinal cord

◆ 3. Secondary Brain Vesicles (5th Week)

Subdivision Flowchart

Prosencephalon

→ Telencephalon → 2 lateral outgrowths → Cerebral hemispheres

→ Diencephalon → Formation of optic vesicles 

Mesencephalon

→ Remains undivided → Midbrain

Rhombencephalon

→ Metencephalon → Pons + Cerebellum

→ Myelencephalon → Medulla

 Pontine flexure marks boundary in hindbrain.

◆ 4. Brain Cavities (Neural Tube Lumen)

Region	Cavity Formed
Spinal cord	Central canal
Rhombencephalon	4th ventricle
Diencephalon	3rd ventricle
Telencephalon	Lateral ventricles
Mesencephalon	Aqueduct of Sylvius

Ventricular Connections

Lateral ventricles

- via Foramen of Monro → 3rd ventricle
- via Cerebral aqueduct → 4th ventricle



Development of the Spinal Cord

◆ 1. Layers of Neural Tube

Summary Table

Layer	Components	Final Structure
Neuroepithelial	Mitotic cells	Source of all CNS cells
Mantle	Neuroblasts	Gray matter
Marginal	Nerve fibers	White matter

Key Concept

- Mantle = Gray matter 
 - Marginal = White matter 
-

◆ 2. Functional Organization

Comparison Table

Structure	Location	Function
Basal plate	Ventral	Motor
Alar plate	Dorsal	Sensory

Organization Flowchart

Mantle layer thickening

- Ventral thickening → Basal plate → Motor neurons
 - Dorsal thickening → Alar plate → Sensory neurons
-

Sulcus Limitans

- Separates:
 - Motor (basal)
 - Sensory (alar)
-

Roof Plate & Floor Plate

- No neuroblasts
 - Function → crossing fiber pathways
-

◆ 3. Intermediate Horn

Formation

Neurons between basal & alar plates → Form

Intermediate horn → Contains Sympathetic neurons (ANS)

Present only at:

- T1-T12
 - L2-L3
-

◆ 4. Clinical Correlations


- Mantle/marginal defects → abnormal gray/white matter
 - Basal plate defect → motor deficits
 - Alar plate defect → sensory deficits
 - Intermediate horn defect → autonomic dysfunction
-




Histological Differentiation of Spinal Cord

◆ 1. Neuroblast → Neuron Differentiation

 Differentiation Flowchart

Neuroepithelial cell → Neuroblast → Early neuroblast (central process to lumen) → Apolar neuroblast (round cell) → Bipolar neuroblast (One process → Axon, Other process → Dendrites) → Multipolar neuron → Mature neuron 

 Important

- Neuroblasts lose mitotic ability after differentiation 
-

◆ Axonal Pathways

 Motor Pathway

Basal plate neuron → Axon exits spinal cord → Forms ventral root → Supplies muscles 💪

Sensory Pathway

Alar plate neuron → Axon ascends/descends → Forms interneurons

◆ 2. Glial Cell Differentiation

Types of Glial Cells

Cell Type	Function
Astrocytes	Support + metabolism
Oligodendrocytes	Myelination (CNS)
Microglia	Phagocytosis
Ependymal cells	Line central canal

Formation Flowchart

Neuroepithelial cells → Glioblasts → Differentiate into:

- Astrocytes (gray + white)
 - Oligodendrocytes (myelin)
 - Later: Microglia (from mesenchyme)
-

 High Yield

- Microglia ≠ neuroectoderm → mesenchymal origin
-

◆ 3. Neural Crest Cells

 Migration & Differentiation

Neural crest cells → Migrate laterally → Form multiple structures

 Derivatives Table

Category	Derivatives
Nervous	Sensory ganglia, sympathetic ganglia

Support	Schwann cells
Pigment	Melanocytes
Dental	Odontoblasts
Meninges	Pia + Arachnoid
Others	Pharyngeal arch mesenchyme

◆ Sensory Ganglia Formation

Flowchart

Neural crest cells → Neuroblasts → Bipolar neurons
- Central process → spinal cord
- Peripheral process → receptors
→ Form dorsal root ganglion

Key Concept

- Dorsal root ganglia = Neural crest origin
-


◆ 4. Clinical Correlations

! Neural Crest Defects

Failure of migration → Hirschsprung disease (aganglionic colon) → Neurocristopathies:

- Neuroblastoma
 - Pheochromocytoma
-

! Other Clinical Points

- Demyelination (e.g., MS) → oligodendrocyte damage
 - CNS infection/injury → microglial proliferation 
-

💡 Exam Pearls

- Neural tube closure:
 - Cranial → Day 25
 - Caudal → Day 28
- Mantle = Gray, Marginal = White
- Basal = Motor, Alar = Sensory

- Neural crest → PNS + multiple derivatives
 - Microglia → Mesenchymal origin (favorite MCQ)
-

Development of Spinal Nerves & Spinal Cord Changes

◆ 1. Formation of Spinal Nerves (Week 4)

Formation Flowchart

Basal plate (ventral horn neurons) → Motor fibers emerge → Form ventral roots

Neural crest cells → Form dorsal root ganglia (DRG) → Bipolar neurons develop

DRG neurons

- Central processes → enter spinal cord (dorsal horn)
- Peripheral processes → join ventral roots

→ Formation of mixed spinal nerve

Spinal Nerve Division

Mixed spinal nerve → Divides into:

Dorsal primary ramus → Supplies:

- Back muscles
- Vertebral joints
- Skin of back

Ventral primary ramus

→ Supplies:

- Limbs
- Ventral body wall

→ Forms plexuses:

- Brachial
 - Lumbosacral
-

◆ 2. Myelination



Peripheral vs Central Myelination

Feature	Peripheral Nervous System	Central Nervous System
Cell type	Schwann cells	Oligodendrocytes
Origin	Neural crest	Neuroepithelium
Axons per cell	1 axon	Up to 50 axons
Start time	4th fetal month	4th fetal month
Completion	Mostly before birth	Continues postnatally



Myelination Mechanism

PNS (Schwann cells)

Schwann cell → Wraps repeatedly around axon → Forms myelin sheath + neurilemma

CNS (Oligodendrocytes)

Oligodendrocyte → Sends processes to multiple axons →
Forms central myelin

 Golden Rule

Tract function begins → Myelination starts ⚡

 Clinical Insight

- Motor tracts → fully myelinated by 1st year of life



◆ 3. Positional Changes of Spinal Cord

 Developmental Change Flowchart

Early embryo (3rd month) → Spinal cord = full length of
vertebral column

Differential growth occurs → Vertebral column grows
faster than cord

→ Spinal cord "ascends" relative to vertebrae

Level of Termination

Stage	Level
3rd month	Entire length
Birth	L3
Adult	L2-L3 (sometimes L1)

Formation of Cauda Equina

Shortened cord → Nerve roots elongate downward →
Form Cauda equina 🐎

Filum Terminale


Tip of spinal cord → Pia mater extends downward →
Anchors to coccyx → Forms Filum terminale

 Function: Stabilizes spinal cord

 Important

- Dural sac extends to S2
-

◆ 4. Clinical Correlations (Spinal Cord)

 Lumbar Puncture

Performed at: L4-L5

Why safe?

Below spinal cord termination → Only cauda equina present → Nerve roots move away from needle

 Disorders

- Multiple sclerosis → CNS demyelination (oligodendrocytes)
- Peripheral neuropathy → Schwann cell dysfunction

- Tethered cord → abnormal fixation → limits ascent
-

Neural Tube Defects (NTDs)

◆ I. Overview


Pathogenesis Flowchart

Failure of neural tube closure (3rd-4th week) →

Defective development of:

- Vertebrae
- Meninges
- Muscles
- Skin ± neural tissue

→ Neural tube defects


 Common site: Spinal region → Spina bifida


Epidemiology

- Up to 1/200 births (high-risk populations)
 - Reduced to ~1/1500 with folic acid fortification
-

◆ 2. Types of Spina Bifida



● A. Spina Bifida Occulta (Mild)

Feature	Description
Defect	Failure of vertebral arch fusion
Skin	Intact
Site	S1-S2
Clue	Hair tuft 
Symptoms	Usually none

 Seen in ~10% of normal population

 B. Spina Bifida Cystica (Severe)

 Types

Type	Contents	Severity
Meningocele	Meninges + CSF	Moderate
Myelomeningocele	Neural tissue + meninges	Most common severe 
Myeloschisis	Open neural tissue	Most severe 

 Severe NTD Pathway


Defect in vertebral arches → Herniation of contents →
Neural tissue involvement → Motor + sensory deficits


Key Point

- Myelomeningocele = most common severe form

◆ 3. Associated Complications

Hydrocephalus Mechanism

Tethered cord / hindbrain displacement → Arnold-Chiari malformation → Cerebellar herniation ↓ → CSF flow obstruction → Hydrocephalus 

 Occurs in 80-90% cases

Treatment  → Ventriculoperitoneal (VP) shunt

◆ 4. Diagnosis



Prenatal Screening

Test	Finding
Maternal serum AFP	↑ Elevated
Amniotic fluid AFP	↑ Elevated
Ultrasound	Detects defect (by 12 weeks)



Fetal Surgery

- Done at ~22 weeks
- Defect repaired in utero
- Still experimental

◆ 5. Risk Factors (Teratogens)

- Hyperthermia
- Valproic acid

- Hypervitaminosis A
 - Genetic + environmental factors
-

◆ 6. Prevention

Prevention Strategy

Folic acid intake → Proper neural tube closure → ↓ Risk of NTDs

Dosage

Group	Dose
All women	400 μ g/day
High risk (previous NTD)	4 mg/day

Timing

- From 1 month before conception → 3rd month of pregnancy
-

High-Yield

- Reduces NTD risk by 50-70% 100
-

Exam Pearls

- Ventral root = Motor, Dorsal root = Sensory
 - Schwann = PNS, Oligodendrocyte = CNS
 - Myelination begins 4th fetal month
 - Cord ends:
 - Birth → L3
 - Adult → L2-L3
 - LP done at L4-L5
 - Spina bifida occulta = asymptomatic + hair tuft
 - Myelomeningocele = most common severe NTD
 - AFP ↑ in NTDs
 - Folic acid = most important preventive factor
-

Brain Development - Hindbrain (Rhombencephalon)

◆ I. Overview

Structural Division

Brain

→ Brainstem


- Myelencephalon → Medulla
- Metencephalon → Pons
- Mesencephalon → Midbrain

→ Higher centers

- Cerebellum
 - Cerebral hemispheres
-

Developmental Pattern

Spinal cord-like organization → Basal plate (motor) +
Alar plate (sensory) → Separated by Sulcus limitans

Higher brain development → Alar plates expand massively
 → Basal plates relatively regress

◆ 2. Rhombencephalon (Hindbrain)

 Subdivisions

Division	Adult Structure
Myelencephalon	Medulla oblongata
Metencephalon	Pons + Cerebellum

◆ 3. Myelencephalon → Medulla Oblongata

 Structural Change

Spinal cord structure → Lateral walls evert (open out)
→ Gray matter spreads laterally

Basic Organization

Neural tube

- Basal plate → Motor nuclei (3 columns)
- Alar plate → Sensory nuclei (3 columns)
- Roof plate → Tela choroidea → Choroid plexus → CSF



Motor Nuclei (Basal Plate)


Column	Function	Cranial Nerves
Medial somatic efferent (GSE)	Tongue + eye muscles	XII, VI, IV, III
Intermediate special visceral efferent (SVE)	Pharyngeal arch muscles	XI, X, IX

Lateral general visceral efferent (GVE)	Autonomic (GIT, heart, respiration)	Mainly X
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Sensory Nuclei (Alar Plate)

Column	Function	Example
Lateral somatic afferent (GSA)	Pain, temp, touch	IX (pharynx)
Intermediate special afferent (SA)	Taste, hearing, balance	VIII
Medial general visceral afferent (GVA)	Interoception	Vagus

Exam Insight

- In brainstem → Motor = medial, Sensory = lateral (due to eversion) 
-

◆ 4. Metencephalon → Pons & Cerebellum

◆ Basal Plate (Motor Nuclei)

Type	Function	Cranial Nerves
GSE	Eye movement	VI
SVE	1st & 2nd arch muscles	V, VII
GVE	Parasympathetic	VII (salivary glands)

◆ Alar Plate (Sensory Nuclei)

Type	Function
GSA	Face sensation (Trigeminal)
SA	Hearing + balance (VIII)

GVA	Visceral sensation
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◆ Special Structures

 Pons Development

Marginal layer expansion → Formation of Pons →
Contains pontine nuclei (alar origin)


 Function

- Relay center:
 - Cortex ↔ Cerebellum ↔ Spinal cord
-

 Cerebellum Development

Alar plates of metencephalon → Proliferate & fuse →
Form Cerebellum

Function

- Coordination of movement
 - Posture & balance 
-

High-Yield Points

- Medulla:
 - Basal → 3 motor columns
 - Alar → 3 sensory columns
 - Pons:
 - Basal → VI, V, VII
 - Alar → V, VIII, visceral afferents
 - Cerebellum → Alar plate derivative
 - Choroid plexus → Roof plate + pia mater
-

Organization of Brainstem Nuclei


- ◆ I. General Somatic Efferent (GSE)
-

Key Features

- Motor to voluntary skeletal muscles
 - Not derived from branchial arches
-

Summary

Feature	Detail
Function	Eye + tongue movement
Cranial nerves	III, IV, VI, XII
Location	Medial (brainstem)

 Concept → "Simple motor system" controlling regular skeletal muscles

- ◆ 2. Special Visceral Efferent (SVE)

Key Features

- Motor to pharyngeal arch muscles
-

Summary

Feature	Detail
Function	Mastication, facial expression, swallowing
Cranial nerves	V, VII, IX, X
Origin	Branchial arches

 Concept → "Branchial motor system" 

- ◆ 3. General Visceral Efferent (GVE)
-

Key Features

- Parasympathetic output
-

Summary

Feature	Detail
Function	Smooth muscle + glands
Cranial nerves	III, IX, X
Examples	Pupil constriction, salivation

 Controls automatic body functions 

- ◆ 4. General Visceral Afferent (GVA)
-

Key Features

- Sensory from internal organs
-



Summary

Feature	Detail
Function	Interoception
Cranial nerves	X
Location	Medulla



Important for visceral reflexes (gag, cough)

- ◆ S. Special Afferent (SA)
-



Summary

Function	Cranial Nerves
Taste	VII, IX
Hearing & balance	VIII

 "Special senses"  

◆ 6. General Somatic Afferent (GSA)

 Summary

Function	Cranial Nerves
Pain, touch, temperature (face)	V, VII, IX

 Equivalent of body sensory system for head

FINAL INTEGRATION

Brainstem organization

- Basal plate (motor) → medial
 - Alar plate (sensory) → lateral
-

Motor columns (medial → lateral)

- GSE
 - SVE
 - GVE
-

Sensory columns (medial → lateral)

- GVA
 - SA
 - GSA
-

 Mnemonic Tip 

- Motor = "Go Out" (Efferent)
 - Sensory = "Arrives" (Afferent)
-

Exam Pearls (Rapid Revision)

- Brainstem = spinal cord pattern modified
 - Eversion → motor medial, sensory lateral
 - Cerebellum = alar plate derivative
 - Pontine nuclei = alar origin (VERY COMMON MCQ)
 - GSE = III, IV, VI, XII
 - SVE = V, VII, IX, X
 - GVE = III, IX, X
 - GVA mainly = X
 - SA = VII, IX, VIII
 - GSA = V (main)
-

Development of Higher Brain Centers

- ◆ I. Cerebellum (Metencephalon – Alar Plate)

Development Flowchart

Dorsolateral alar plates → Form Rhombic lips → Caudal parts remain separate → Cranial parts fuse → Form Cerebellar plate

Structural Organization

Region	Structure
Midline	Vermis
Lateral	Hemispheres

Primitive Part

- Flocculonodular lobe → oldest part ⚡
-

Histogenesis

Layer Formation

Neuroepithelial layer → Mantle layer → Marginal layer

→ External granular layer forms → Migrates to surface

→ Acts as proliferative zone

Cell Differentiation

External granular layer → Granule cells

White matter cells

- Basket cells
- Stellate cells

Mantle layer

- Purkinje cells
 - Golgi II neurons
-

Key Points

- Purkinje cells → main output neurons

- Deep cerebellar nuclei (e.g., dentate) → form before birth
- Cortex completes after birth 🧒

👉 Function: Coordination of posture & movement ⚖️

◆ 2. Mesencephalon (Midbrain)

◆ Basal Plate (Motor)

Type	Nuclei	Function
GSE	III, IV	Eye movement 👁️
GVE	Edinger-Westphal	Pupillary constriction

◆ Marginal Layer → Forms Crus cerebri → Contains descending cortical fibers

Pathway



Cerebral cortex → Descending fibers → Crus cerebri → Pons + spinal cord

- ◆ Alar Plate (Sensory → Colliculi)
-

Development Flowchart


Alar plate → Two elevations → Divided by transverse groove → Form colliculi

Colliculi Functions

Structure	Function
Superior colliculus	Visual reflex 
Inferior colliculus	Auditory reflex 

 Neuroblasts arrange → layered structure

◆ 3. Diencephalon

 Basic Structure

- Roof plate
 - Two alar plates
 - Floor plate (uncertain but suggested by SHH)
-

◆ Roof Plate Derivatives

 Development

Roof plate → Choroid plexus → CSF 

→ Pineal gland develops

Pineal Gland

- Appears Week 7
- Midline evagination
- Function → regulates circadian rhythm 🌙

Clinical

- Frequently calcified → radiological landmark 🔥
-

◆ Alar Plate Derivatives

Division

Alar plate → Divided by Hypothalamic sulcus

→ Dorsal → Thalamus

→ Ventral → Hypothalamus

Thalamus vs Hypothalamus

Feature	Thalamus	Hypothalamus
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Position	Dorsal	Ventral
Function	Sensory relay	Autonomic + endocrine
Special feature	Massa intermedia	Mammillary bodies

Thalamus Development

Thalamus → Enlarges → Projects into 3rd ventricle →
Right & left may fuse → Massa intermedia

Hypothalamus Development

Hypothalamus → Differentiates into nuclei → Controls:

- Sleep 🤪
- Temperature 🌡️
- Emotions ❤️
- Digestion

◆ 4. High-Yield Exam Points

- 💡 Cerebellum = Alar plate derivative
 - 💡 Flocculonodular lobe = oldest part
 - 💡 Superior colliculus = visual reflex
 - 💡 Inferior colliculus = auditory reflex
 - 💡 Thalamus vs hypothalamus → separated by hypothalamic sulcus
 - 💡 Pineal calcification = radiological landmark
-

🧬 Development of Pituitary (Hypophysis)

◆ 1. Dual Origin

🔄 Development Flowchart

Oral ectoderm (stomodeum) → Rathke's pouch

Neuroectoderm (diencephalon) → Infundibulum

→ Both grow toward each other → Fuse → Form
Pituitary gland

Golden MCQ

- Anterior = Ectodermal
 - Posterior = Neuroectodermal
-

◆ 2. Developmental Process

Timeline

3rd week → Rathke's pouch forms → Grows dorsally

End of 2nd month → Loses oral connection → Contacts
infundibulum

◆ 3. Derivatives



Adenohypophysis (Rathke's Pouch)

Part	Origin
Pars distalis	Anterior wall
Pars tuberalis	Extension along stalk
Pars intermedia	Posterior wall




Note

- Pars intermedia = rudimentary in humans



Neurohypophysis (Infundibulum)

Part	Feature
Pars nervosa	Posterior lobe
Stalk	Infundibular connection

 Contains:

- Pituicytes (glial cells)
 - Axons from hypothalamus
-

◆ 4. Final Structure


Part	Function
Adenohypophysis	Hormone secretion
Neurohypophysis	Storage & release

◆ 5. Clinical Correlations

 Pathology Flowchart

Rathke's pouch remnants → Abnormal proliferation → Craniopharyngioma


Features

- Location → Above sella turcica
 - Effects:
 - ↑ ICP → Hydrocephalus 
 - Hormonal issues:
 - Diabetes insipidus
 - Growth retardation
 - Hypopituitarism
-

Other

- Pharyngeal hypophysis → ectopic remnant
-

Exam Pearls

- Dual origin = favorite MCQ 
- Craniopharyngioma = Rathke's pouch remnant

- Posterior pituitary = neural tissue (not glandular)
-

Development of Telencephalon

Formation Flowchart

Prosencephalon → Telencephalon → Two lateral outgrowths → Cerebral hemispheres

Key Structures

Structure	Description
Hemispheres	Major brain mass
Lamina terminalis	Median portion
Lateral ventricles	Cavities

Ventricular Connection

Lateral ventricles → Via Foramen of Monro → 3rd ventricle

Key Concept

- Telencephalon = most rostral brain part
-

FINAL INTEGRATION FLOWCHART

Forebrain (prosencephalon)

→ Telencephalon → Cerebral hemispheres

→ Diencephalon → Thalamus + Hypothalamus

Hindbrain (rhombencephalon)

→ Metencephalon → Pons + Cerebellum

→ Myelencephalon → Medulla

Ultra High-Yield Exam Pearls

- Cerebellum → Alar plate
 - Pineal gland → calcifies (landmark)
 - Pituitary → dual origin (VERY IMPORTANT)
 - Pars intermedia → rudimentary
 - Colliculi:
 - Superior = visual
 - Inferior = auditory
 - Thalamus = sensory relay
 - Hypothalamus = homeostasis control
-

Development of Cerebral Hemispheres

◆ I. Early Stages

Formation Flowchart

Prosencephalon (forebrain) → Week 5: Bilateral evaginations → Formation of cerebral hemispheres

Corpus Striatum Formation

Basal part of hemispheres enlarges → Bulges into lateral ventricle → Forms floor of Foramen of Monro

→ Develops striated appearance → Forms Corpus striatum

◆ 2. Choroid Plexus Formation

Development

Area where hemisphere attaches to diencephalon → No neuroblast formation → Thin wall persists

→ Ependymal cells + vascular mesenchyme → Form Choroid plexus

Location:

- Projects into ventricle via choroidal fissure

High-Yield

- Origin = Ependyma + mesenchyme (NOT neuroblasts)
-

◆ 3. Hippocampus

Formation

Region above choroidal fissure → Wall thickens →
Forms Hippocampus → Bulges into lateral ventricle

Function (early) → Olfaction

◆ 4. Expansion & Differentiation

Growth Pattern

Cerebral hemispheres enlarge rapidly → Cover:

- Diencephalon
 - Mesencephalon
 - Upper metencephalon
-

Corpus Striatum Division

Corpus striatum enlarges → Cortical axons pass through → Split structure → Forms:

- Caudate nucleus (dorsomedial)
 - Lentiform nucleus (ventrolateral)
-

 Structure formed between them: → Internal capsule

◆ S. Fusion & Relations

Relationship Formation

Medial hemisphere wall → Fuses with lateral diencephalon
→ Caudate nucleus lies adjacent to Thalamus

◆ 6. Lobes Formation

Directional Growth

Continuous expansion → Forms lobes:

- Anterior → Frontal lobe
 - Dorsal → Parietal lobe
 - Inferior → Temporal lobe
 - Posterior → Occipital lobe
-

Insula Formation

Region between frontal & temporal lobes → Forms Insula → Initially exposed → Later overgrown by surrounding lobes → Becomes hidden at birth

Exam Favorite

- Insula = buried cortex 🔥


◆ 7. Final Fetal Stage

Cortical Folding

Rapid brain growth → Surface folds → Forms:

- Gyri (convolutions)
 - Sulci (grooves)
-

Purpose

- ↑ Surface area → ↑ neurons 
-

Exam Pearls (Hemispheres)

- Corpus striatum → caudate + lentiform
- Internal capsule splits them (VERY COMMON MCQ)
- Choroid plexus ≠ neuroblasts
- Insula = hidden cortex
- Gyri/sulci = late fetal development



Development of Cerebral Cortex

◆ 1. Origin



Pallium Division

Part	Description
Paleopallium (Archipallium)	Primitive cortex
Neopallium	Major functional cortex



Neopallium = main cerebral cortex

◆ 2. Neuroblast Migration

Inside-Out Pattern

Neuroblasts form in ventricular zone → Migrate outward

Early neurons → Stay deep

Later neurons → Pass through earlier ones → Settle superficially

Golden Concept

- Old = deep, New = superficial
-

◆ 3. Final Cortex

Layer Specialization

Area	Cells
Motor cortex	Large pyramidal cells

Sensory cortex	Granular cells
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◆ 4. Olfactory System Development

Formation Flowchart

Ectoderm (frontonasal prominence) + neural crest →
Form Olfactory placodes

Telencephalon floor → Forms Olfactory bulbs

Placodal cells → Become primary sensory neurons →
Axons grow → Synapse in olfactory bulbs (by week 7) →
Form Olfactory nerve (CN I)

Development of Commissures

◆ 1. Overview


- Connect right & left hemispheres
 - Develop in Lamina terminalis
-

◆ 2. Sequence of Development

Commissure Formation Flowchart

1. Anterior commissure (first)
 - Connects olfactory regions
 2. Hippocampal commissure (fornix)
 - From hippocampus → mammillary bodies
 3. Corpus callosum (most important)
 - Appears ~10th week
 - Connects non-olfactory cortex
-


Later additions:

- Posterior commissure
- Habenular commissure
- Optic chiasma 

Cerebrospinal Fluid (CSF)

◆ 1. Production

- By Choroid plexus
- Composition:
 - Modified ependymal cells
 - Vascular tissue

 Volume: 400–500 mL/day

◆ 2. Flow Pathway

CSF Circulation


Lateral ventricles → Foramen of Monro → 3rd ventricle
→ Cerebral aqueduct → 4th ventricle → Spinal canal →
Exits via apertures → Subarachnoid space

◆ 3. Absorption

Pathway

Subarachnoid space → Arachnoid granulations → Venous sinuses → Especially Superior sagittal sinus

◆ 4. Functions

- Provides buoyancy 
 - Protects brain (shock absorber)
 - Prevents compression of vessels/nerves
-

FINAL INTEGRATION FLOWCHART

Telencephalon → Cerebral hemispheres → Cortex develops (inside-out) → Commissures connect hemispheres

Choroid plexus → Produces CSF → Circulates through ventricles → Absorbed via arachnoid granulations



Exam Pearls

- Inside-out migration = classic MCQ
 - Corpus callosum appears at 10 weeks
 - Anterior commissure = first
 - Choroid plexus = ependymal + mesenchymal
 - Internal capsule splits corpus striatum
 - Insula = hidden cortex
 - CSF absorbed via arachnoid granulations → superior sagittal sinus
 - Olfactory system = placodes + telencephalon
-



Clinical Correlates of Cranial Defects

● I. Holoprosencephaly (HPE)

Definition

- Failure of midline division of forebrain
-

Spectrum Flowchart

Normal forebrain division

→ Partial failure → Mild HPE

→ Complete failure → Alobar HPE (severe)

Severe (Alobar)

Single telencephalic vesicle → Fusion of lateral ventricles

→ Cyclopia → Single nasal chamber

Mild Forms

Incomplete hemisphere separation → Hypoplastic/absent corpus callosum → Absent olfactory tracts → Single central incisor (classic clue)

! Causes Flowchart

SHH mutation → Defective ventral midline induction



Defective cholesterol synthesis → Smith-Lemli-Opitz syndrome (AR) → ↓ SHH signaling



Other genes → SIX3, TGIF, ZIC2

📌 Exam Pearls

- HPE = SHH problem
 - Single central incisor = 🔥 classic MCQ
-

● 2. Schizencephaly

🔄 Pathology

EMX2 mutation → Defective cortical development →
Clefts in cerebral hemispheres → Loss of brain tissue

 Rare but very characteristic defect


3. Cranial Ossification Defects

 Mechanism

Failure of skull bone closure → Intracranial contents herniate

 Types

Type	Contents
Meningocele	Meninges
Meningoencephalocele	Meninges + brain
Meningoencephalocele	Meninges + brain + ventricle

 Most common site → Squamous occipital bone

4. Exencephaly → Anencephaly

 Progression Flowchart (VERY IMPORTANT)

Failure of cranial neuropore closure → Exencephaly
(brain exposed) → Degeneration of exposed brain →
Anencephaly

 Severe Extension

Anencephaly → Extends caudally → Craniorachischisis
(with spina bifida)

 Features

- Absent cranial vault
- No forebrain

- Brainstem present
 - Polyhydramnios (no swallowing reflex)
-


Prevention

Folic acid deficiency → Neural tube defect



Give 400 μ g/day folic acid

Exam Pearls

- Polyhydramnios = anencephaly clue
 - Exencephaly → anencephaly sequence 
-

5. Hydrocephalus

Definition

- Excess CSF in ventricles

Pathogenesis Flowchart

Aqueductal stenosis (MCC in neonates) → Obstruction of CSF flow → CSF accumulates → Lateral + 3rd ventricles enlarge → Skull expands (open sutures) → Thin cortex

 Appearance → "Watermelon head"

6. Microcephaly

 Definition

- Small brain → small skull
-

 Causes

Genetic (AR)



Infections (TORCH) → Toxoplasmosis / CMV / Rubella



Teratogens → Alcohol (most common) / Radiation / Drugs



Hyperthermia → Fever / hot tubs

Associations

- Intellectual disability (>50%)
 - Cerebral calcifications
-

7. Intellectual Disability & Subtle Defects

Causes

Chromosomal → e.g., Down syndrome



Infections → Rubella, CMV, toxoplasmosis



Teratogens → Alcohol (MCC overall)

Important Concepts

- Absent corpus callosum → may be asymptomatic
 - Severe ID can occur without structural defect
-

HIGH-YIELD SUMMARY

- HPE → SHH defect
 - Smith-Lemli-Opitz → cholesterol defect → ↓ SHH
 - Hydrocephalus → aqueduct stenosis (MCC)
 - Microcephaly → alcohol (MCC)
 - Anencephaly → polyhydramnios
 - NTD prevention → folic acid
-

Development of Cranial Nerves


◆ 1. General Overview

Timeline

Week 4 → All cranial nerve nuclei present

Exceptions

- CN I (Olfactory) → forebrain origin
- CN II (Optic) → diencephalon

 Not true cranial nerves

◆ 2. Brainstem Origin

Origin Flowchart

Midbrain → CN III (Oculomotor)

Hindbrain → CN IV → XII

◆ 3. Rhombomeres

Definition

- Segmented hindbrain (8 parts)
-

Function

Rhombomeres → Give rise to motor nuclei of:

CN IV, V, VI, VII, IX, X, XI, XII


Clinical Link

- Defects → cranial nerve abnormalities + facial defects
-

◆ 4. Spinal Nerve Homology

Comparison

Feature	Cranial	Spinal
Motor	Brainstem	Ventral horn
Sensory	Outside brain	Dorsal root ganglion

 Not all cranial nerves are mixed

◆ S. Sensory Ganglia Development

 Flowchart

Ectodermal placodes + neural crest → Sensory ganglia

 Placode Contributions

Nasal placode → CN I

Otic placode → CN VIII

Epibranchial placodes → CN V, VII, IX, X

◆ 6. Parasympathetic Ganglia

 Origin

Neural crest cells → Parasympathetic ganglia

 Distribution (COPS)

Ganglion	Nerve
Ciliary	CN III
Otic	CN IX
Pterygopalatine	CN VII
Submandibular	CN VII

FINAL INTEGRATION FLOWCHART

Placodes + Neural crest → Sensory ganglia

Neural crest → Parasympathetic ganglia

Rhombomeres → Motor nuclei



Cranial nerves form → Closely linked to pharyngeal arches

→ Defects → craniofacial anomalies

CLINICAL PEARLS

- Placode defect → anosmia / deafness
- Neural crest defect → DiGeorge, Treacher Collins
- CN defects → always think pharyngeal arches
- CN I & II ≠ true cranial nerves
- Rhombomeres = motor patterning centers

Origins of Cranial Nerves & Their Composition

◆ OVERVIEW

Forebrain (Telencephalon + Diencephalon) → CN I, CN II



Midbrain (Mesencephalon) → CN III, CN IV



Hindbrain

- Metencephalon → CN V, VI, VII, VIII
 - Myelencephalon → CN IX, X, XI, XII
-

◆ CRANIAL NERVES (I-XII)

● CN I - Olfactory

Telencephalon → Nasal epithelium → Smell perception

📌 Type: SA (Special Afferent)

👉 Pure sensory

● CN II - Optic

Diencephalon → Retina → Vision

📌 Type: SA

👉 Pure sensory

● CN III - Oculomotor

Mesencephalon


→ Somatic motor

- Extraocular muscles
- Levator palpebrae

→ Parasympathetic (via ciliary ganglion)

- Sphincter pupillae
 - Ciliary muscle
-

 Types: GSE + GVE

 Eye movement + pupil constriction

CN IV - Trochlear

Mesencephalon → Superior oblique muscle

 Type: GSE

 Eye moves down & in

Special Feature

- Only nerve exiting dorsally 
-

CN V - Trigeminal

Metencephalon

- Sensory (face, teeth, anterior 2/3 tongue)
 - Motor (mastication muscles)
-

 Types: GSA + SVE

 Main sensory nerve of face

CN VI - Abducens

Metencephalon → Lateral rectus muscle

 Type: GSE

 Eye abduction

CN VII - Facial

Metencephalon

- Taste (anterior 2/3 tongue)
 - Facial expression muscles
 - Parasympathetic to glands
-

 Types Flowchart

Facial nerve

- SA → Taste
 - GSA → Ear sensation
 - SVE → Facial muscles
 - GVE → Salivary + lacrimal glands
-

 Mixed nerve

● CN VIII - Vestibulocochlear

Metencephalon

- Vestibular apparatus → Balance
 - Cochlea → Hearing
-

 Type: SA

 Pure sensory

● CN IX - Glossopharyngeal

Myelencephalon


- Taste (posterior 1/3 tongue)
- Stylopharyngeus (motor)
- Parotid gland (parasympathetic)
- Carotid body & sinus

Types Flowchart

CN IX

- SA → Taste
- GVA → Visceral sensation
- GSA → Ear
- SVE → Stylopharyngeus
- GVE → Parotid gland

 Key for gag reflex + swallowing

 CN X - Vagus

Myelencephalon → Extensive visceral supply

 Functional Flowchart

Vagus nerve

- SA → Taste (epiglottis)
 - GVA → Thoracic + abdominal viscera
 - GSA → External ear
 - SVE → Pharynx + larynx
 - GVE → Parasympathetic to organs
-

👉 "Wanderer nerve" 🔥

● CN XI - Accessory

Myelencephalon

- Sternocleidomastoid
 - Trapezius
-

📌 Types: SVE ± GSE (with X)

👉 Shoulder elevation + head rotation

● CN XII - Hypoglossal

Myelencephalon → Tongue muscles (except palatoglossus)

 Type: GSE

 Pure motor

FINAL INTEGRATION FLOWCHART

Cranial nerves classification

- Pure sensory → CN I, II, VIII
 - Pure motor → CN III, IV, VI, XI, XII
 - Mixed → CN V, VII, IX, X
-

FUNCTIONAL COMPONENT LOGIC

Somatic motor (GSE) → Eye + tongue muscles



Branchial motor (SVE) → Pharyngeal arch muscles



Parasympathetic (GVE) → Smooth muscle + glands



Sensory

- GSA → Skin
- GVA → Viscera
- SA → Special senses



EXAM PEARLS

-
- CN I & II → not true cranial nerves
 - CN III, VII, IX, X → parasympathetic carriers
 - CN V → main sensory of face
 - CN X → widest distribution (thorax + abdomen)

- CN XII lesion → tongue deviates towards side of lesion
 - CN IV → dorsal exit (unique)
 - CN VI → most vulnerable in ↑ ICP
-



MNEMONIC BOOST

◆ Sensory Only

“Some Say Money Matters” → I, II, VIII

◆ Motor Only

“Money Matters Most But My Brother Says Big Brains Matter More” → III, IV, VI, XI, XII

◆ Parasympathetic (COPS)

Ciliary → CN III

Otic → CN IX

Pterygopalatine → CN VII

Submandibular → CN VII

● AUTONOMIC NERVOUS SYSTEM (ANS) - DEVELOPMENT

◆ Overview

Division	Outflow	Segmental Origin
Sympathetic	Thoracolumbar	T1-L2/3
Parasympathetic	Craniosacral	CN III, VII, IX, X + S2-S4

◆ Sympathetic Nervous System

- ◆ Formation of Sympathetic Trunks
 - 5th week: Neural crest cells migrate bilaterally (behind dorsal aorta)
 - form segmental sympathetic ganglia
 - Ganglia interconnect → sympathetic trunks (chains)
 - Neuroblasts migrate:
 - Cranially → cervical ganglia
 - Caudally → lumbosacral ganglia
 - Segmental pattern → partial fusion (especially cervical region)
-

- ◆ Preaortic (Collateral) Ganglia
 - Neuroblasts migrate anterior to aorta → form:
 - Celiac ganglion
 - Superior mesenteric ganglion
 - Inferior mesenteric ganglion
-

- ◆ Sympathetic Plexuses

- Neural crest cells migrate to organs → form organ-specific plexuses:
 - Cardiac
 - Pulmonary
 - Enteric
-

- ◆ Preganglionic Fibers

- Origin: Lateral horn (T1-L2/3)
- Myelinated

- ◆ Pathways

1. Synapse at same level
 2. Ascend/descend → synapse at different level
 3. Pass through chain → synapse in preaortic ganglia
- Exit via white rami communicantes
 - 👉 Present only from T1-L2/3
-

- ◆ Postganglionic Fibers

- Origin: Sympathetic ganglia
- Unmyelinated

◆ Pathways

- Via gray rami communicantes → all spinal levels
→ supply:
 - Blood vessels
 - Sweat glands
 - Arrector pili
 - Direct fibers → visceral organs (via plexuses)
-

🔑 High-Yield Points

- White rami → T1-L2/3 only
 - Gray rami → all spinal levels
 - Sympathetic chain → extends entire vertebral column
-

◆ Clinical Correlates (Sympathetic)

- Horner's syndrome
 - Cause → cervical sympathetic trunk lesion
 - Features → ptosis, miosis, anhidrosis
- Neuroblastoma

- Tumor of neural crest-derived sympathetic cells
-

- ◆ Cranial Nerve Ganglia (Neural Crest + Placodes)

- ◆ Rule of Thumb

- Neural crest → general sensory + autonomic ganglia
 - Placodes → special sensory ganglia
-

- ◆ Key Cranial Nerve Ganglia

CN	Ganglia	Origin	Function
III (Oculomotor)	Ciliary	Neural crest	Pupil constriction, accommodation
V (Trigeminal)	Trigeminal	Neural crest + placode	Facial sensation, mastication

VII (Facial)	Geniculate + parasympathetic ganglia	Neural crest + 1st placode	Taste (ant. 2/3), lacrimal & salivary glands
VIII (Vestibulo cochlear)	Cochlear, Vestibular	Otic placode (+ crest)	Hearing & balance
IX (Glossopharyngeal)	Superior, Inferior (petrosal), Otic	Crest + 2nd placode	Taste (post. 1/3), parotid gland
X (Vagus)	Superior, Inferior (nodose)	Crest + 3rd/4th placodes	Thoracoabdominal viscera

◆ Adrenal Gland Development

◆ Dual Origin

Component	Origin
Cortex	Mesoderm

Medulla	Neural crest
---------	--------------

◆ Cortex Development

- 5th week: Mesothelial cells → primitive cortex
- Second wave → definitive cortex

◆ Postnatal Changes

- Outer layer → zona reticularis develops later
 - Adult zones fully organized by puberty
-

◆ Medulla Development

- Neural crest cells → migrate into cortex → form chromaffin cells
-

🔑 High-Yield:

- Cortex = mesoderm
- Medulla = neural crest

◆ Parasympathetic Nervous System

◆ Preganglionic Neurons

- Brainstem nuclei:
 - CN III, VII, IX, X
 - Sacral outflow:
 - S2-S4
-

◆ Postganglionic Neurons

- Derived from neural crest cells
 - Located near or within target organs
-

◆ Target Organs

Nerve	Function
-------	----------

CN III	Pupil constriction
CN VII	Lacrimal & salivary glands
CN IX	Parotid gland
CN X	Thoracic & abdominal viscera
S2-S4	Pelvic organs

◆ Clinical Correlate

-
- ◆ Hirschsprung Disease (Congenital Megacolon)
 - ◆ Cause
 - Failure of neural crest cell migration
 - absence of enteric parasympathetic ganglia
 - ◆ Genetics

- RET mutation
-

- ◆ Pathology

- Distal bowel → aganglionic → narrow
 - Proximal bowel → dilated → megacolon
-

- ◆ Key Features

- Always involves rectum
 - Involves sigmoid colon (~80%)
-

- 🔑 High Yield Summary

- Sympathetic = T1-L2/3 (thoracolumbar)
 - Parasympathetic = craniosacral
 - Neural crest → ANS ganglia + adrenal medulla
 - White rami → limited | Gray rami → everywhere
 - Hirschsprung → neural crest migration failure
-

Takeaways

- Sympathetic trunk = neural crest, T1-L2/3 outflow.
- Gray rami → all spinal levels; white rami → only T1-L2/3.
- Cranial parasympathetic ganglia = neural crest; sensory ganglia = neural crest + placodes.
- Adrenal cortex = mesoderm; medulla = neural crest.
- Hirschsprung disease = failure of neural crest migration → RET gene defect.

-> The End <-