CNS Module

Dr. Gamal Taha Abdelhady
Assistant Professor of Anatomy & Embryology

Embryology of the CNS

CNS Embryology

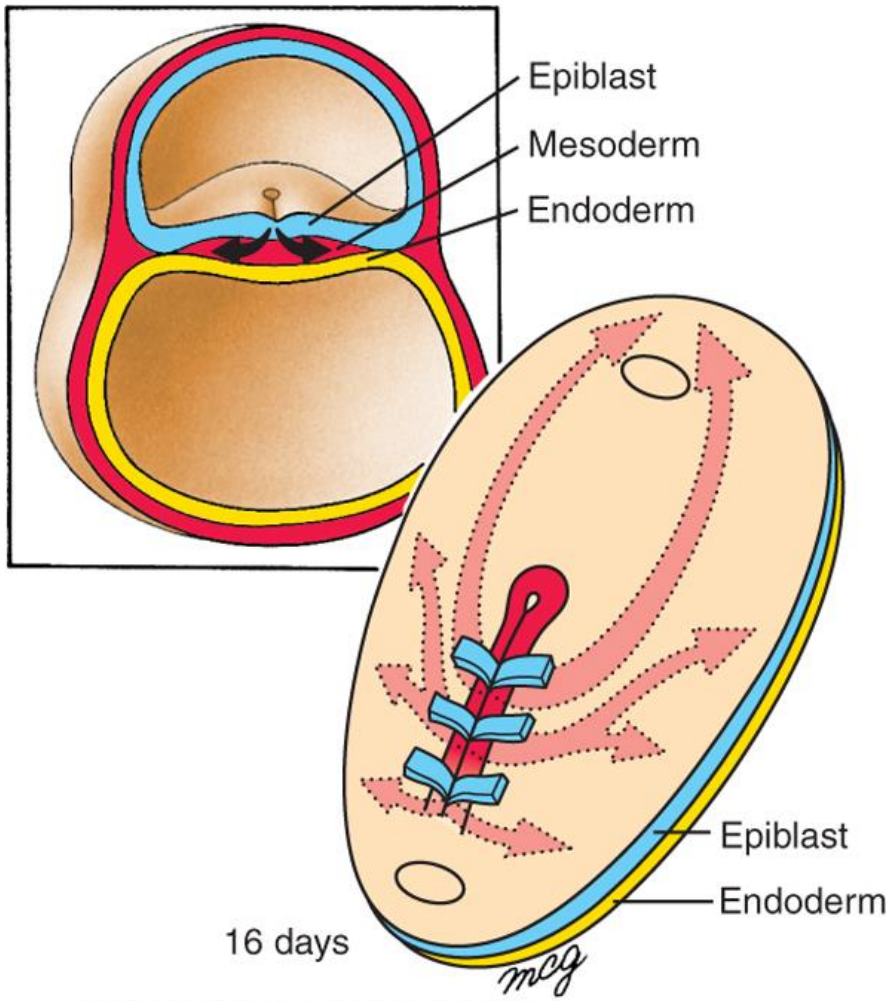
- ***By the end of this lecture, the student should be able to:***

1. Recognize the process of formation and development of the different parts of the CNS and get acquainted with its clinical relevance

The Three Germ Layers are Formed at Gastrulation

Ectoderm: outside, surrounds other layers later in development, generates **skin** and **nervous tissue.**

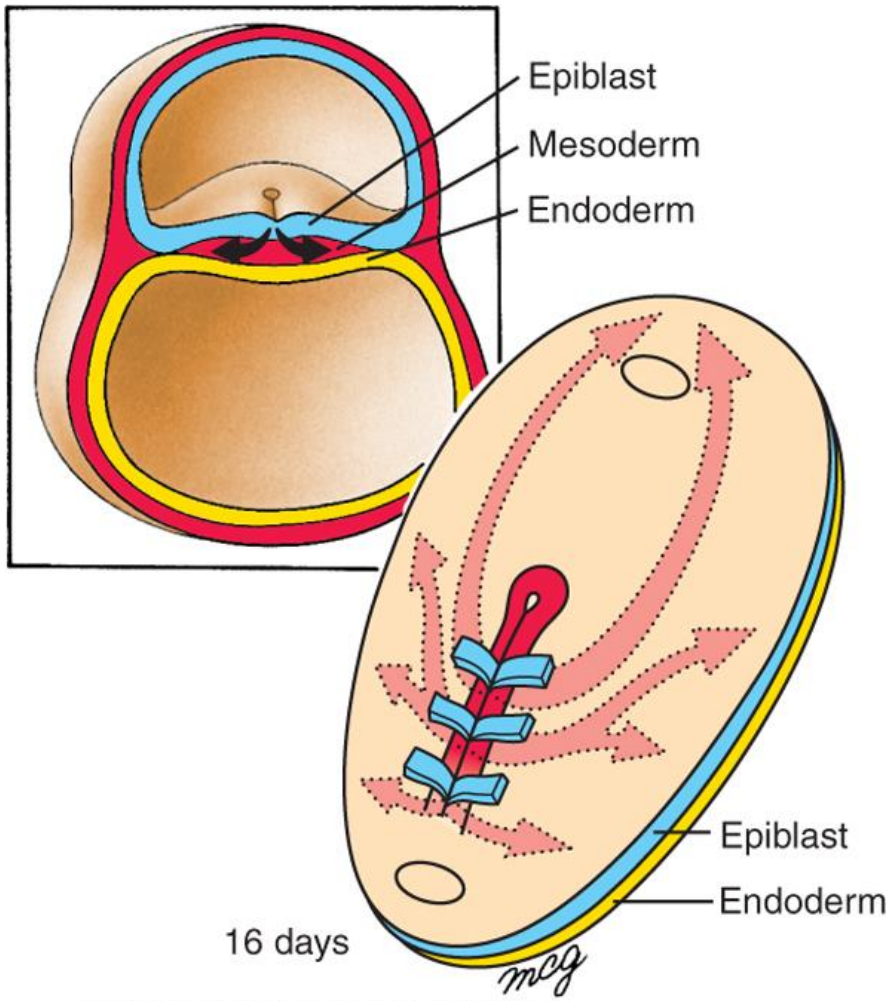
Mesoderm: middle layer, generates most of the **muscle, blood** and **connective tissues** of the body and placenta.



The Three Germ Layers are Formed at Gastrulation

Endoderm:

eventually most interior of embryo, generates the **epithelial lining** and associated **glands** of the **gut**, **lung**, and **urogenital tracts.**

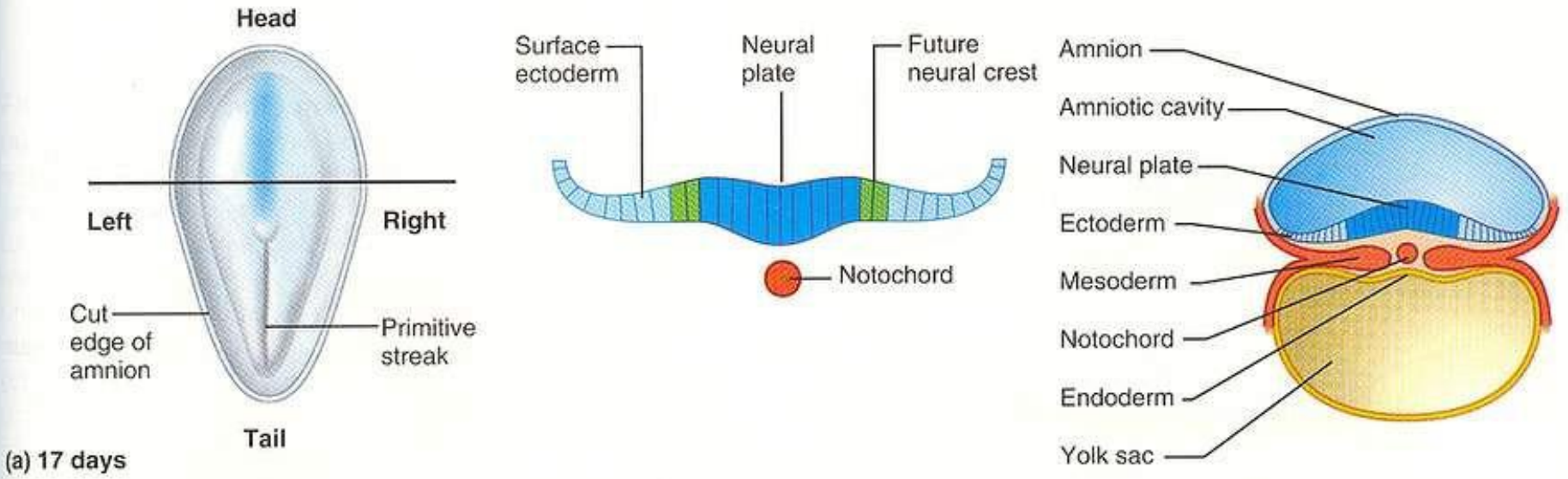


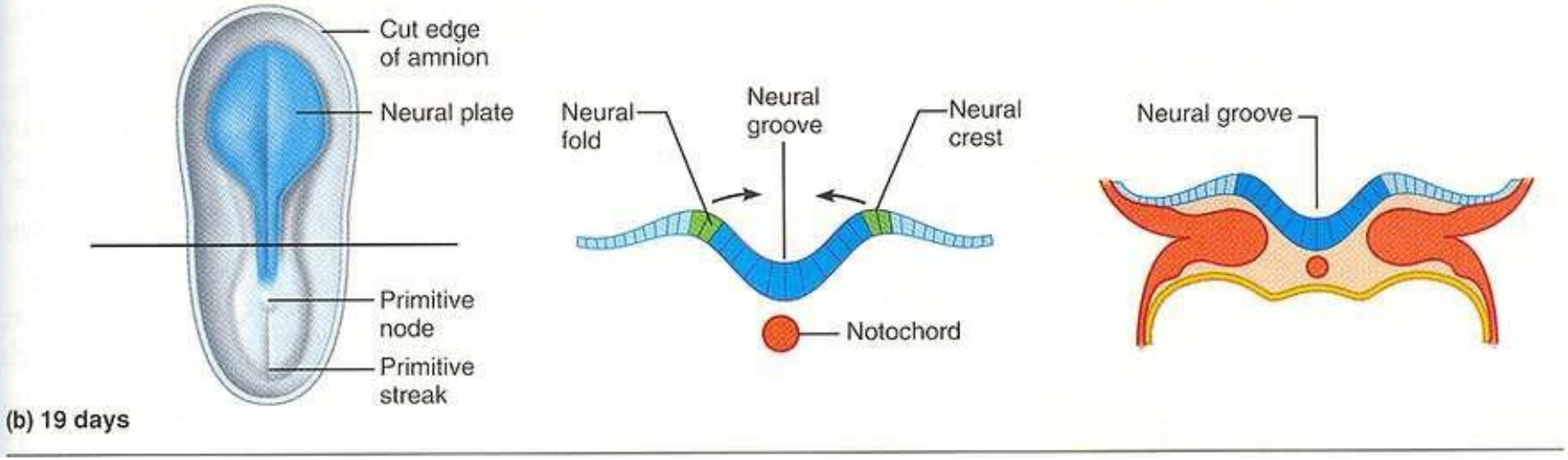
Development of the Nervous System

The neural tube

- At the beginning of the 3rd week, the ectoderm over the notochord is thickened forming a median band called neural plate (neuroectoderm) extending from the primitive node to buccopharyngeal membrane.

- ***Formation of neural groove:*** The edges of the neural plate become elevated forming Rt & Lt neural folds and as a result the neural plate is transformed into neural groove.


Head
Left
Right
Tail
Cut edge of amnion
Primitive streak
(a) 17 days
Surface ectoderm
Neural plate
Future neural crest
Notochord
Amnion
Amniotic cavity
Neural plate
Ectoderm
Mesoderm
Notochord
Endoderm
Yolk sac


Cut edge of amnion
Neural plate
Primitive node
Primitive streak
(b) 19 days
Neural fold
Neural groove
Neural crest
Notochord
Neural groove

Development of the Nervous System

- ***Formation of the neural tube:*** As the neural groove is deepened, the Rt and Lt neural folds approach each other in the middle line and start fusion at region of the 4th somite (***cervical region***) then spread to form a whole tube

- ***Closure of the anterior and posterior neuropores:*** At first the cranial and caudal ends of the canal are open (connected to the amniotic cavity), the openings are called the anterior and posterior neuropores.

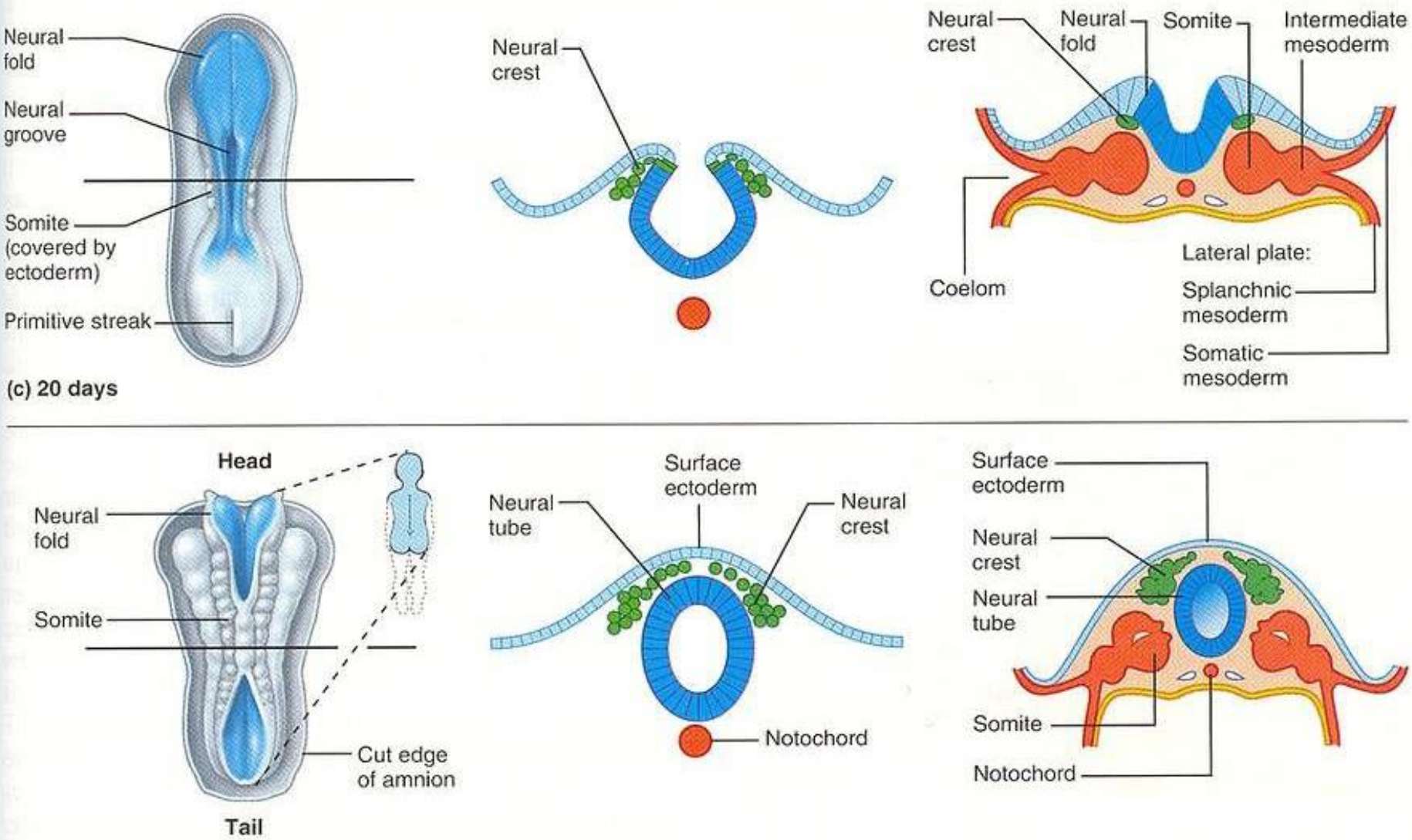
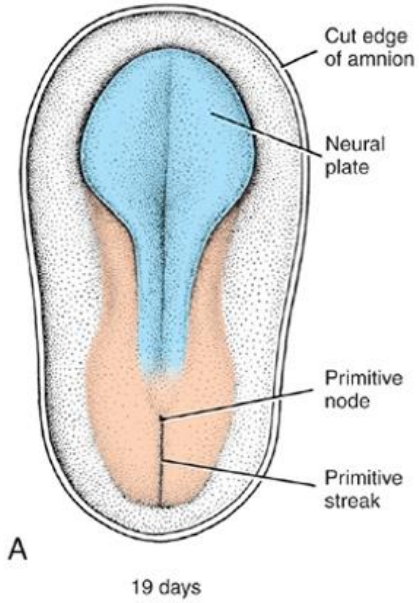


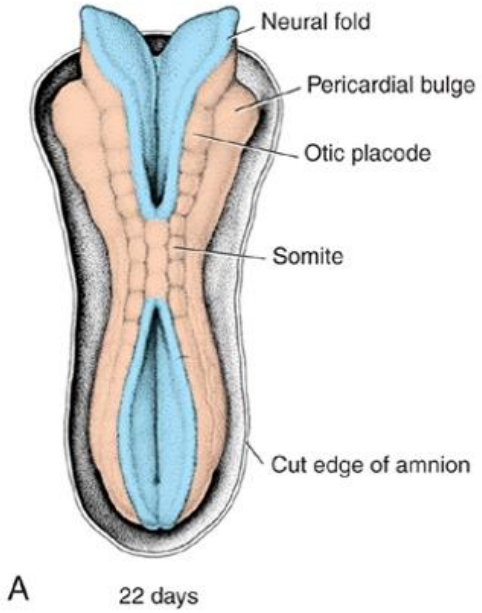
FIGURE 28.9 **Neurulation.** Dorsal surface views on the left; frontal sections on the right. **(a)** The flat three-layered embryo, which has accomplished gastrulation. The notochord and neural plate have formed. **(b)** The neural folds form by folding of the neural plate. **(c)** The neural folds begin to close. **(d)** The newly formed neural tube has detached from the surface ectoderm and lies between the surface ectoderm and the notochord; the neural crest is evident and the embryonic body is beginning to fold.

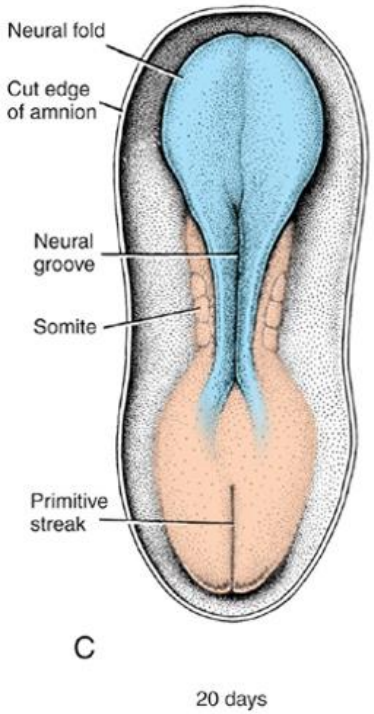
Neurulation: folding and closure of the neural plate

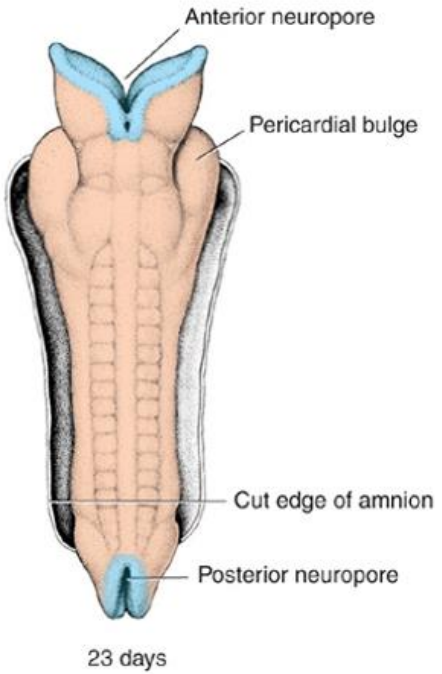
- The neural tube then "**zips**" up toward the head and toward the tail, leaving two openings which are the **anterior** and **posterior neuropores.**

- The anterior neuropore closes on the 25th day while the posterior neuropore closes on the 27th day.







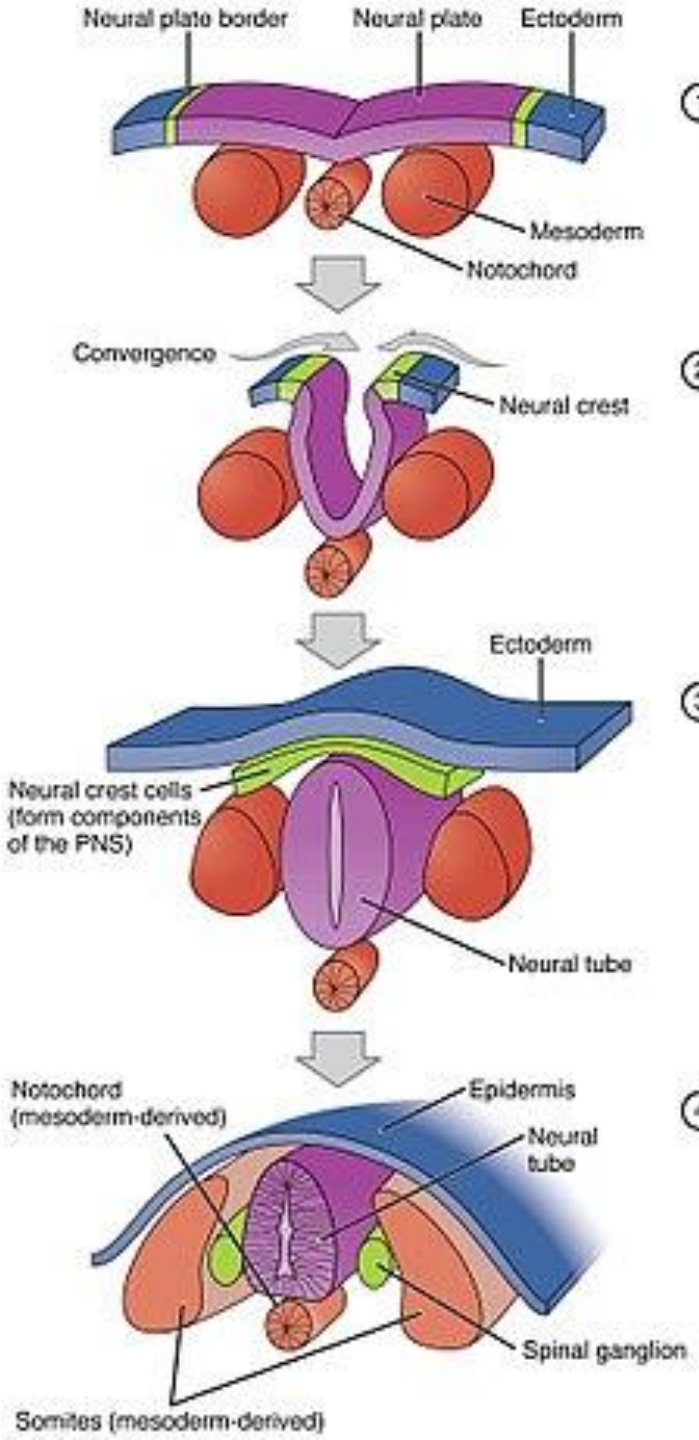


The Neural Crest

- As the neural folds elevate and fuse, cells at the lateral border or ***crest of the neuroectoderm*** begin to dissociate from their neighbors and form the neural crest,

- ***Derivatives of neural crest***

1. Cranial nerve ganglia
2. Spinal (dorsal root) ganglia
3. Sympathetic chain and preaortic ganglia
4. Parasympathetic ganglia of the gastrointestinal tract
5. Meninges
6. Schwann cells
7. Glial cells



1. Neuroectodermal tissues differentiate from the ectoderm and thicken into the neural plate. The neural plate border separates the ectoderm from the neural plate.

2. The neural plate bends dorsally, with the two ends eventually joining at the neural plate borders, which are now referred to as the neural crest.

3. The closure of the neural tube disconnects the neural crest from the epidermis. Neural crest cells differentiate to form most of the peripheral nervous system.

4. The notochord degenerates and only persists as the nucleus pulposus of the intervertebral discs. Other mesoderm cells differentiate into the somites, the precursors of the axial skeleton and skeletal muscle.

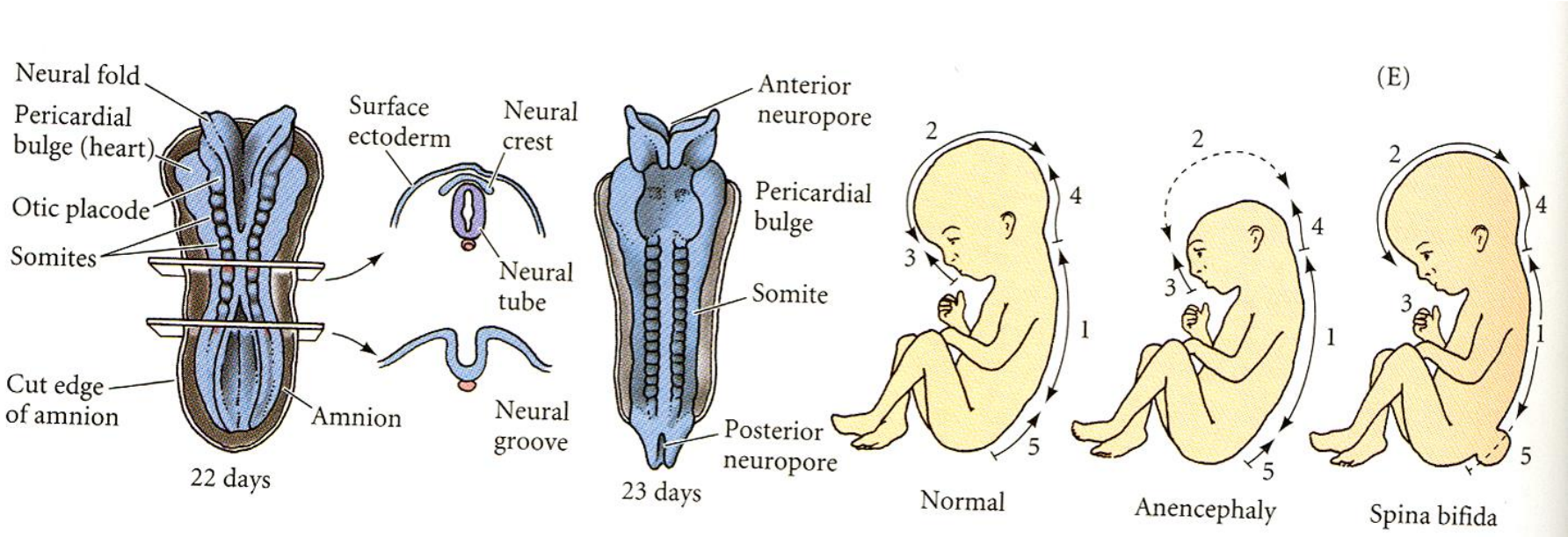
Failure of Neuropores to Close

- Most defects of the spinal cord result from abnormal closure of the neural folds in the ***third and fourth weeks*** of development.

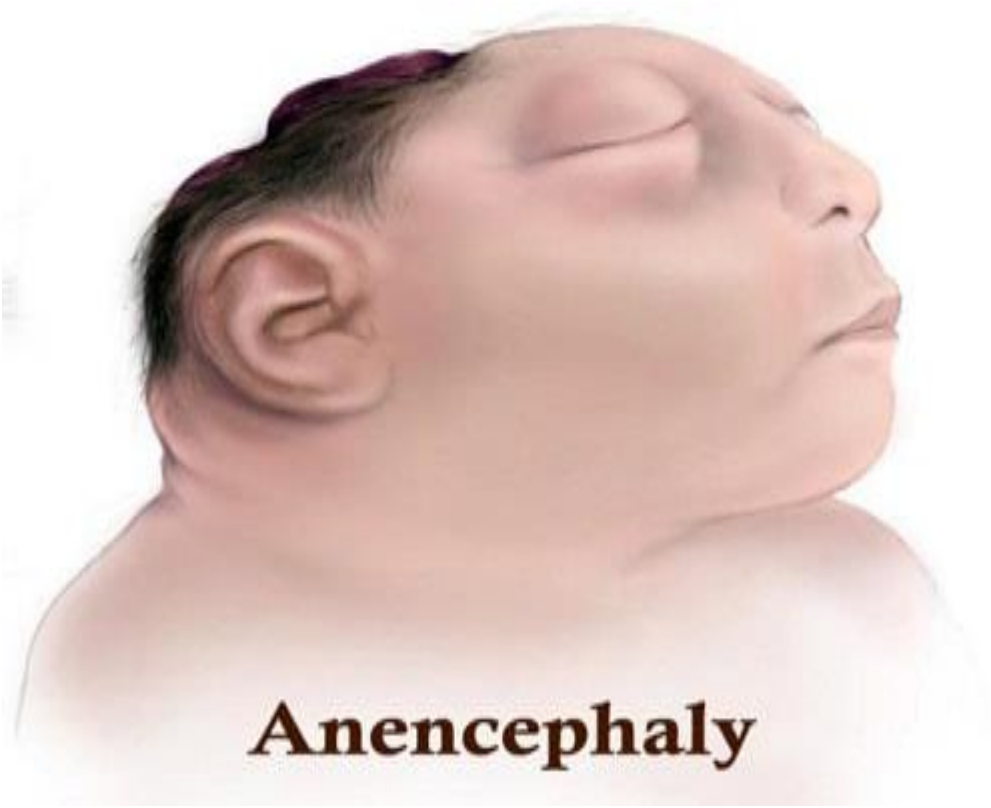
- The resulting abnormalities, neural tube defects (***NTDs***), may involve the meninges, vertebrae, muscles, and skin

Failure of Neuropores to Close

- **Can cause neural tube defects**
  Anterior neuropore: *Anencephaly*
  Posterior neuropore: *Spina bifida*



Anencephaly



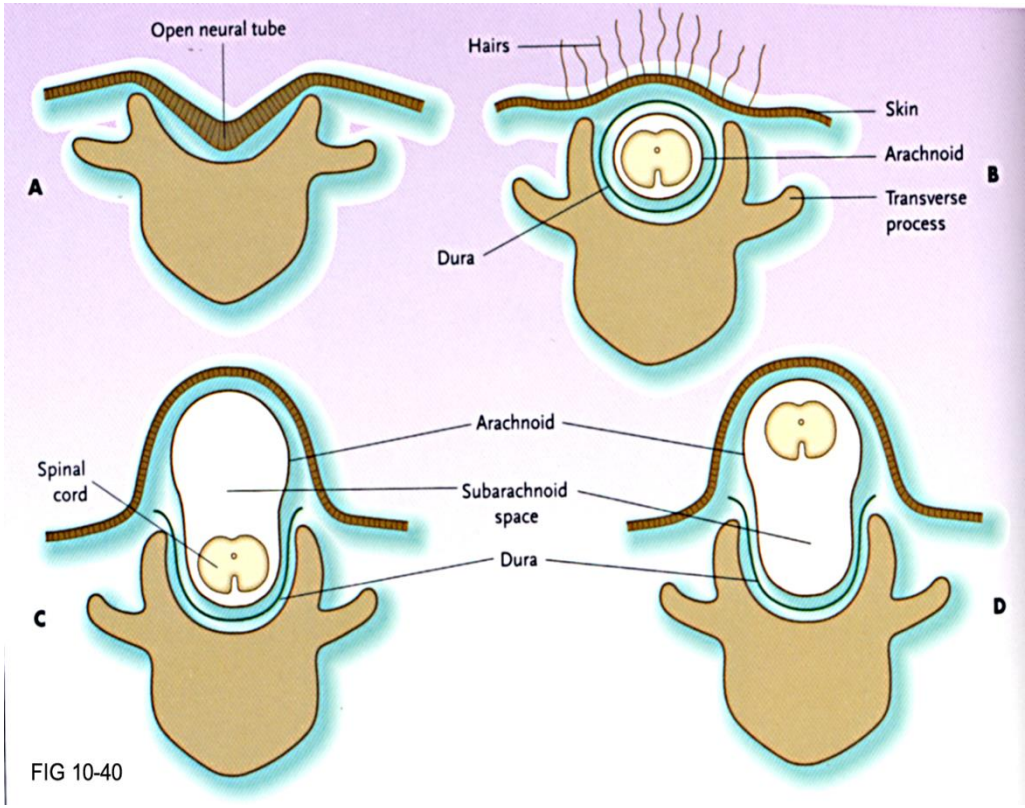
Neural Tube Closure Defects

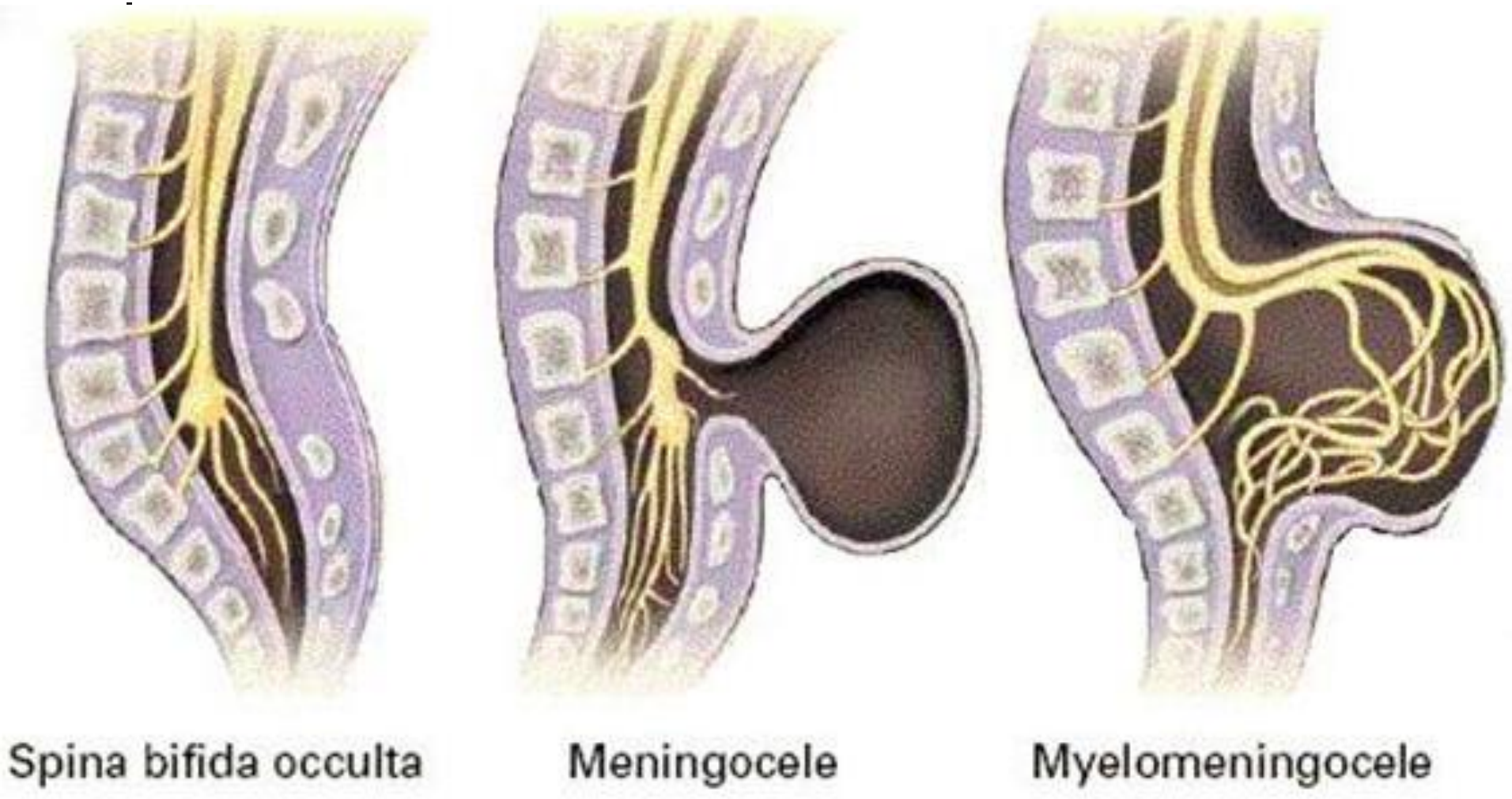
A. Rachischisis

B. Spina bifida occulta

C. Meningocele

D. Myelomeningocele




Spina bifida occulta
Meningocele
Myelomeningocele

Spina Bifida occulta

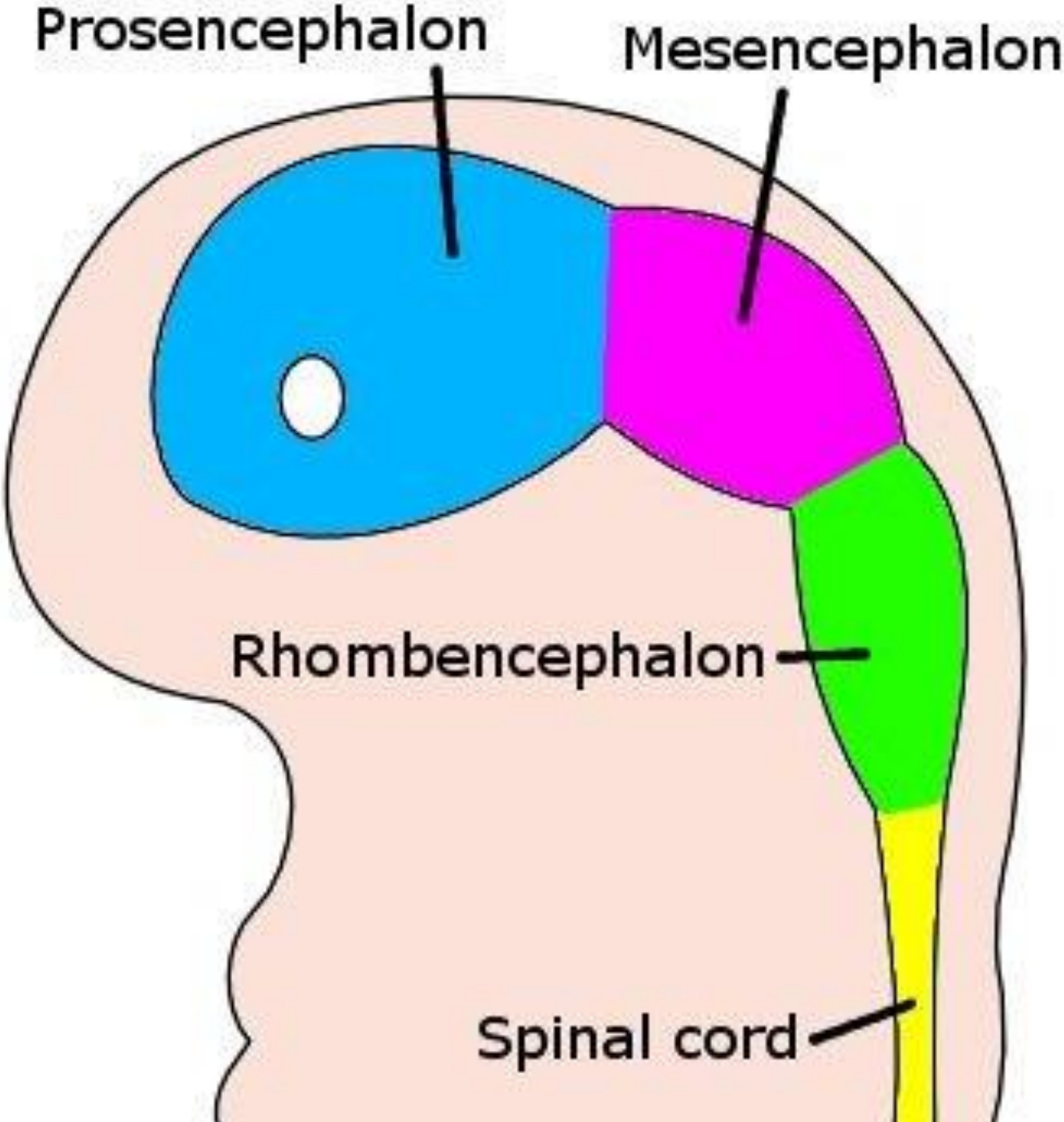
Spina Bifida manifesta

Rachischisis

Neural Tube Development

- Neurulation is then complete, and the central nervous system is represented by a closed tubular structure with a narrow ***caudal portion***, the ***spinal cord***

- And a much ***broader cephalic portion*** characterized by a number of dilations, the ***brain vesicles***


Prosencephalon
Mesencephalon
Rhombencephalon
Spinal cord

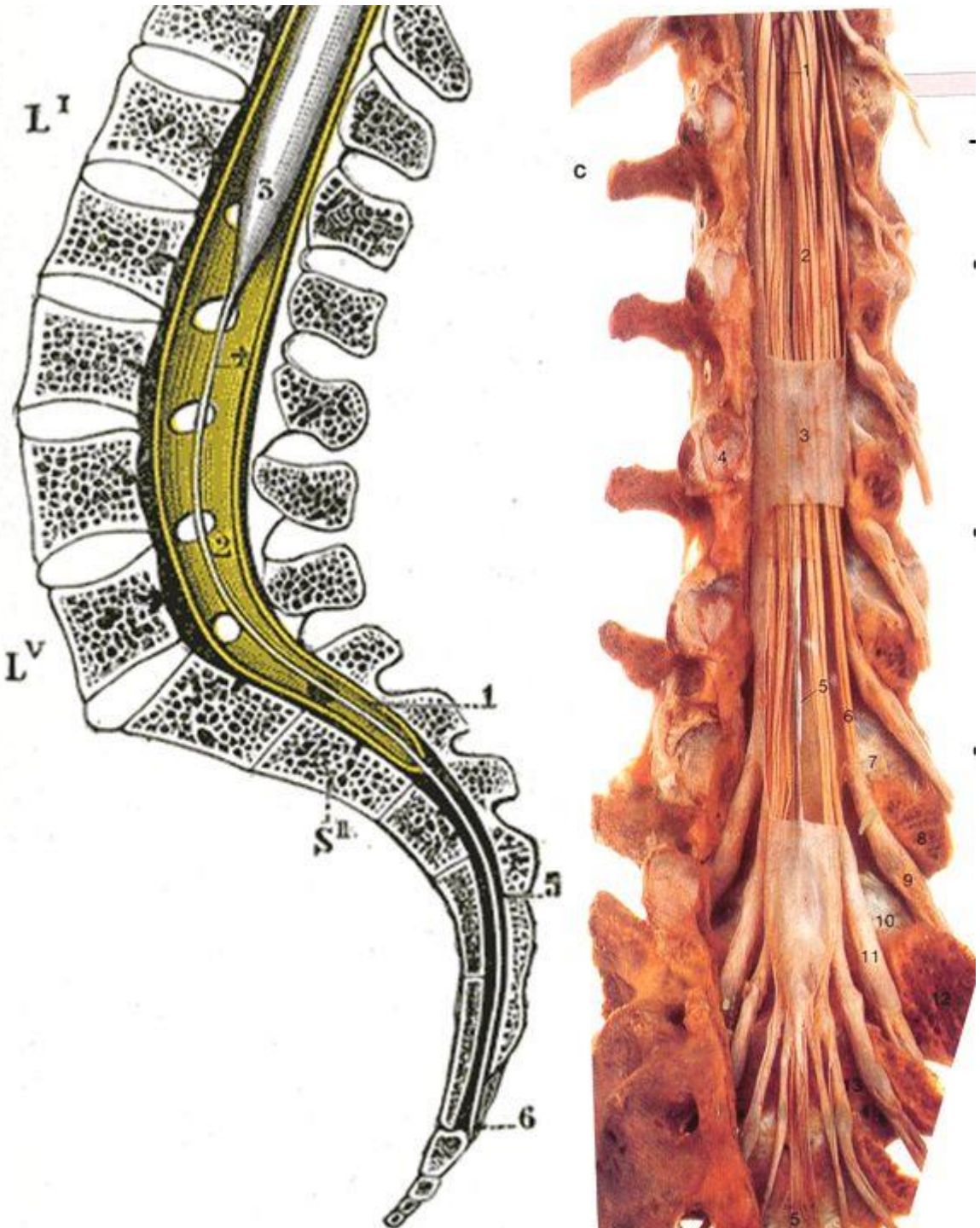
Regression of the Spinal Cord

The spinal cord and the vertebral column are the ***same length*** up until the ***3rd month IU.***

As each vertebral body grows thicker, the overall length of the vertebral column begins to exceed that of the spinal cord such that , in the ***adult*** the ***spinal cord terminates*** at ***L1-2*** and the dural sac ends at about S2.

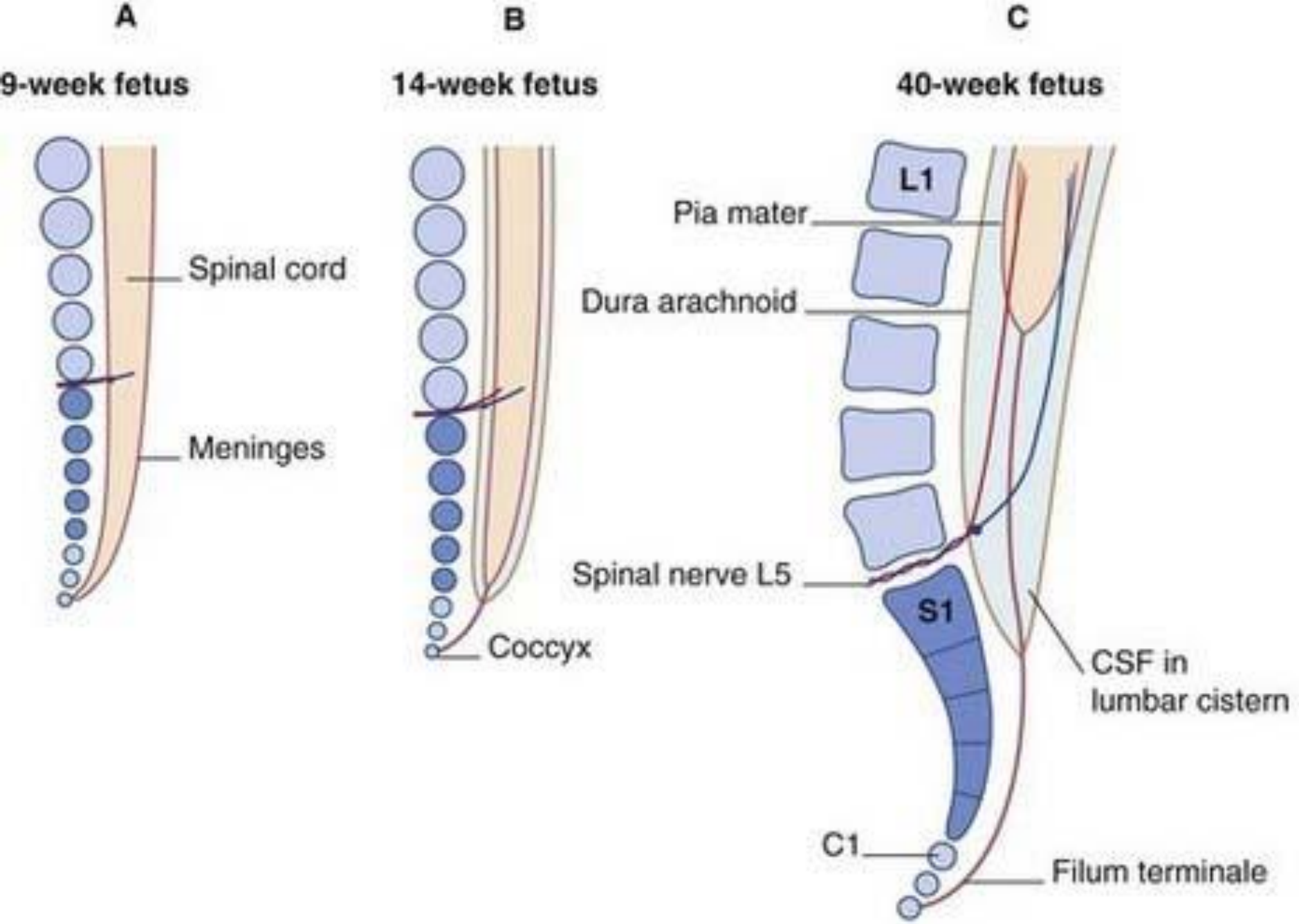
Regression of the Spinal Cord

The tail end of the dural sac covering the spinal cord and nerve roots remains attached at the coccyx and becomes a long, thin strand called the ***filum terminale***.


L I
L V
S II
1
2
3
4
5
6
C
1
2
3
4
5
6
7
8
9
10
11
12
5

Spinal Cord Summary

- At ***3rd month*** of ***intrauterine*** life the spinal cord ***fills*** the ***vertebral canal***
- At the ***5th month of intrauterine*** life the lower level of the cord at the level of ***L5*** or ***S1*** vertebra
- At ***birth*** the lower level of spinal cord at the level of ***3rd lumber*** vertebra


A
9-week fetus
Spinal cord
Meninges
B
14-week fetus
Coccyx
C
40-week fetus
L1
Pia mater
Dura arachnoid
Spinal nerve L5
S1
CSF in
lumbar cistern
C1
Filum terminale

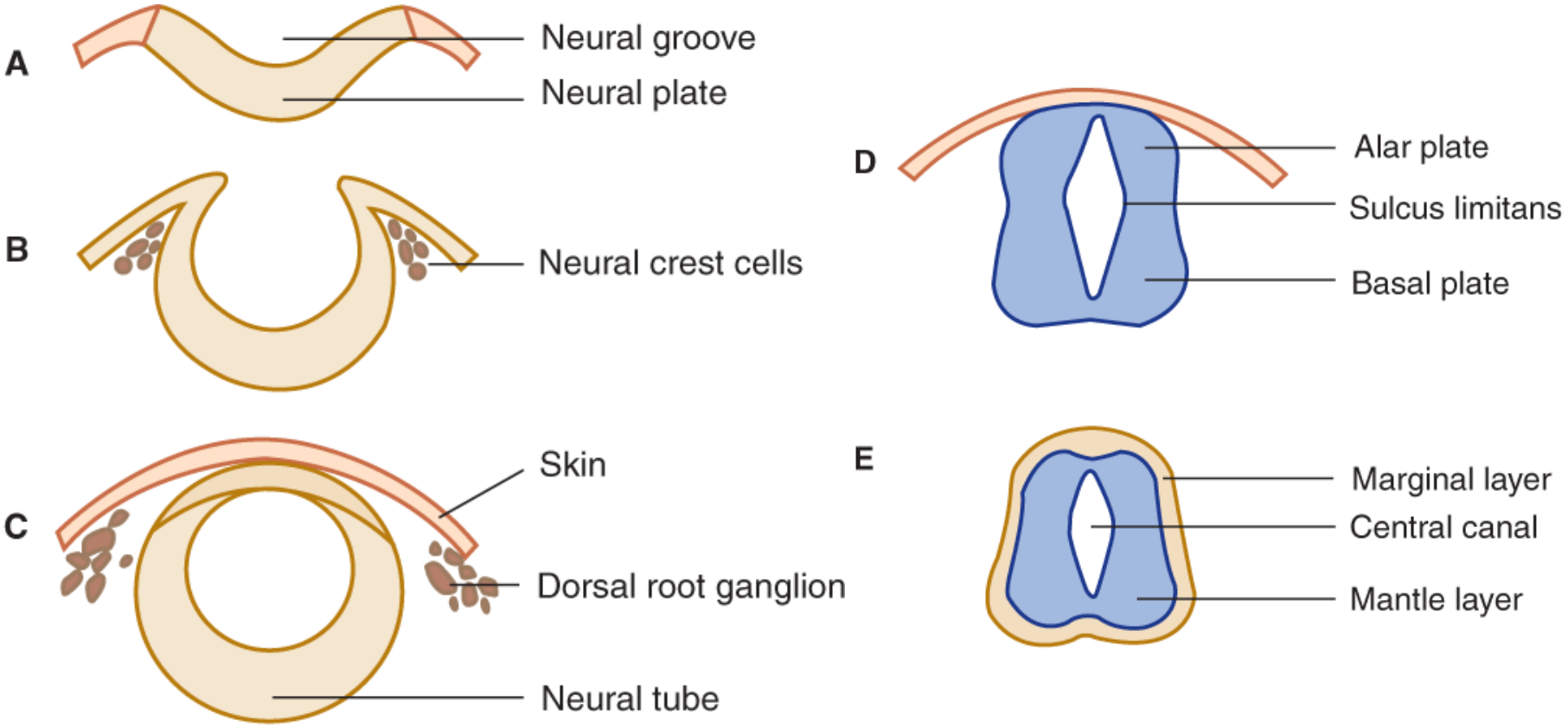
Neural Tube – Spinal Cord

- The wall of a ***recently closed neural tube*** consists of ***neuroepithelial*** cells, they ***divide rapidly***, producing more and more neuroepithelial cells which constitute the ***neuroepithelial layer***.

Neural Tube – Spinal Cord

- Once the neural tube closes, neuroepithelial cells begin to give rise to another cell type, the ***primitive nerve cells*** or ***neuroblasts*** which form the ***mantle layer***.

- The ***outermost layer*** of the neural tube is the ***Marginal layer*** which contains nerve fibers (***axons***) emerging from ***neuroblasts in the mantle layer (axons)***


A
Neural groove
Neural plate
B
Neural crest cells
C
Skin
Dorsal root ganglion
Neural tube
D
Alar plate
Sulcus limitans
Basal plate
E
Marginal layer
Central canal
Mantle layer

Spinal Cord

- ***As the histogenesis of the neural tube is already described in spinal cord lecture.***

- ***The following changes occur in the wall of the neural tube:***

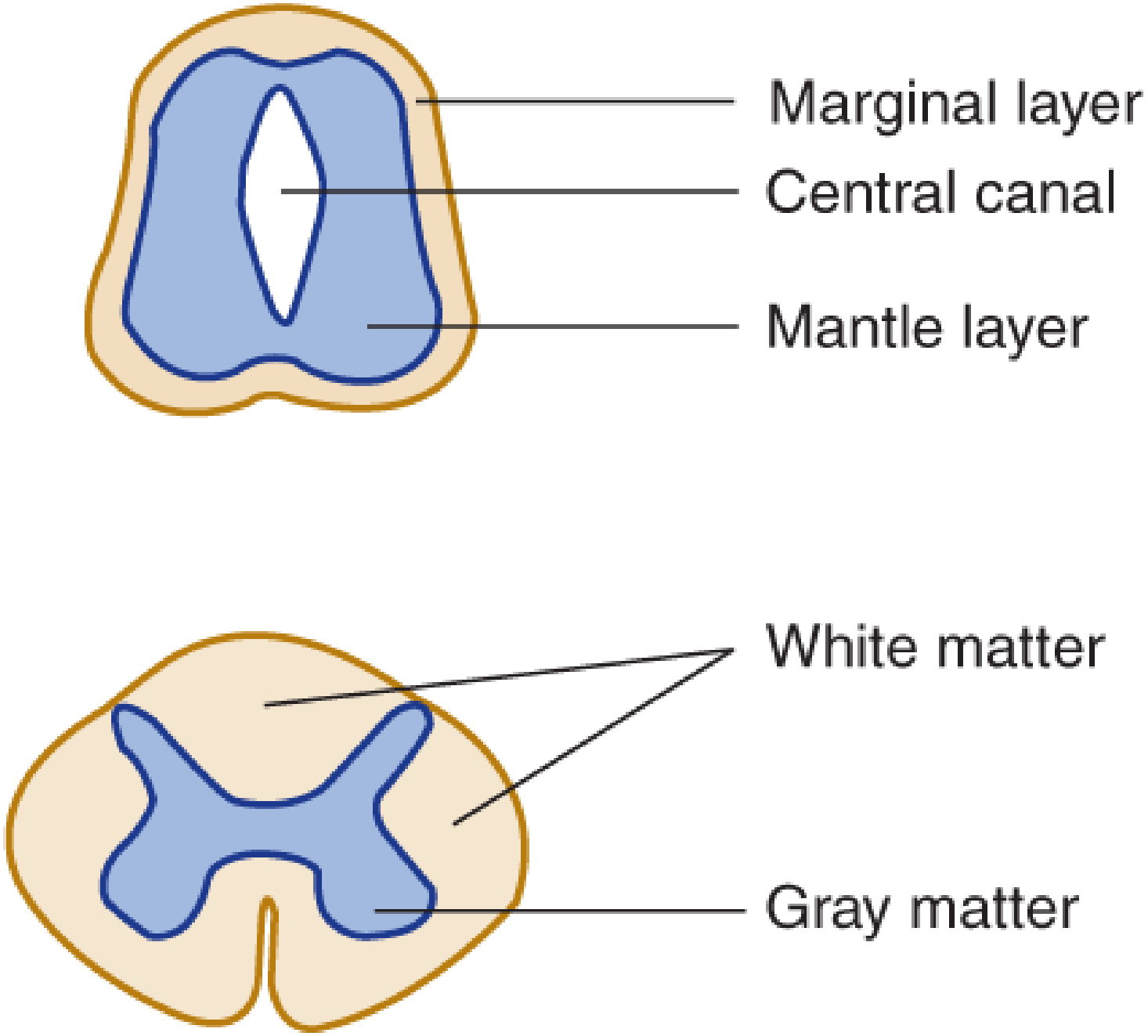
1. ***The diamond-shaped lumen*** becomes circular: the central canal

Spinal Cord

2. ***The ependymal layer:*** the ciliated columnar lining of the central canal.

3. ***The mantle layer:*** the **grey matter**

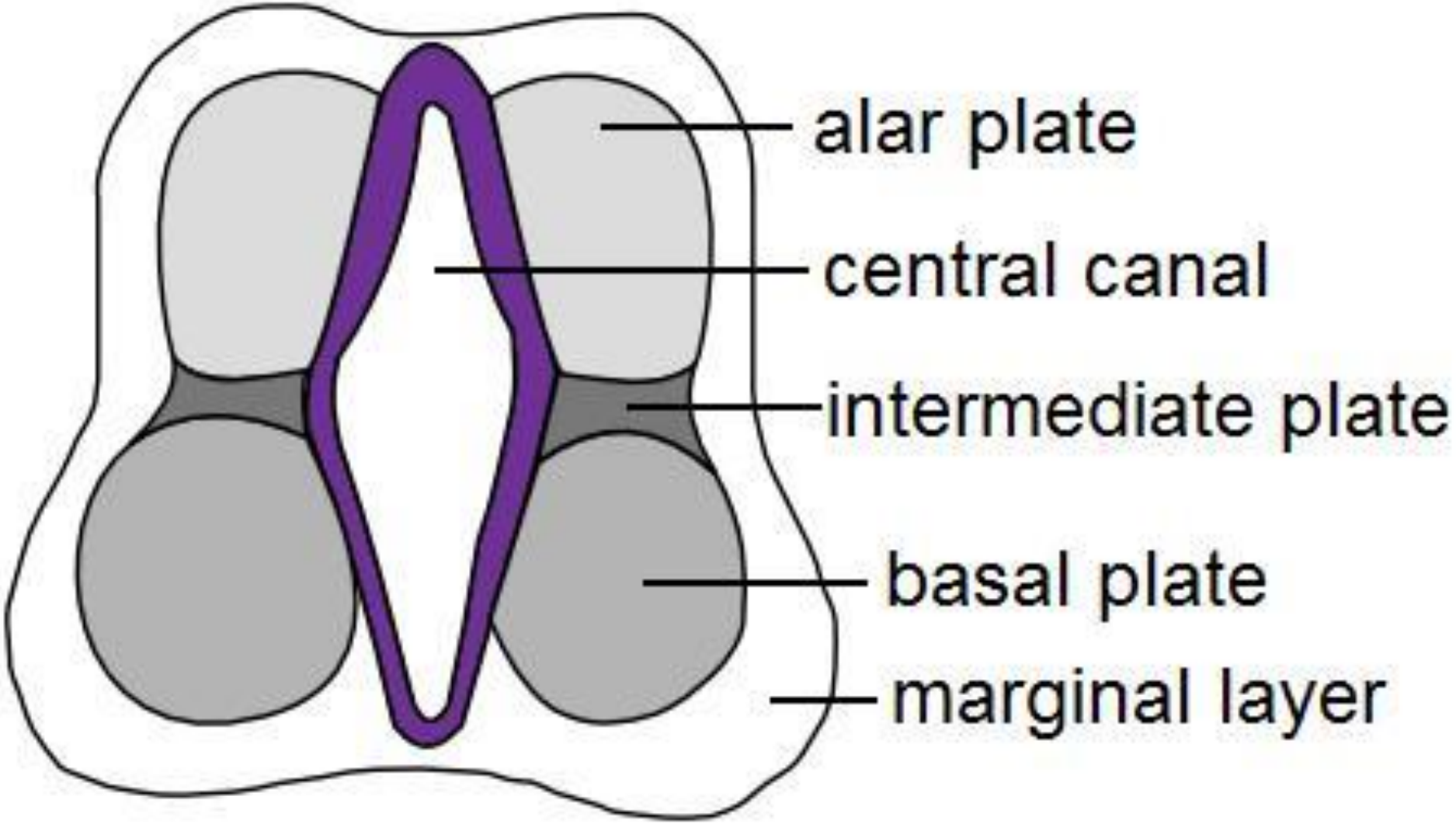
4. ***The marginal layer*** is invaded by ingrowing axons of the **white matter**

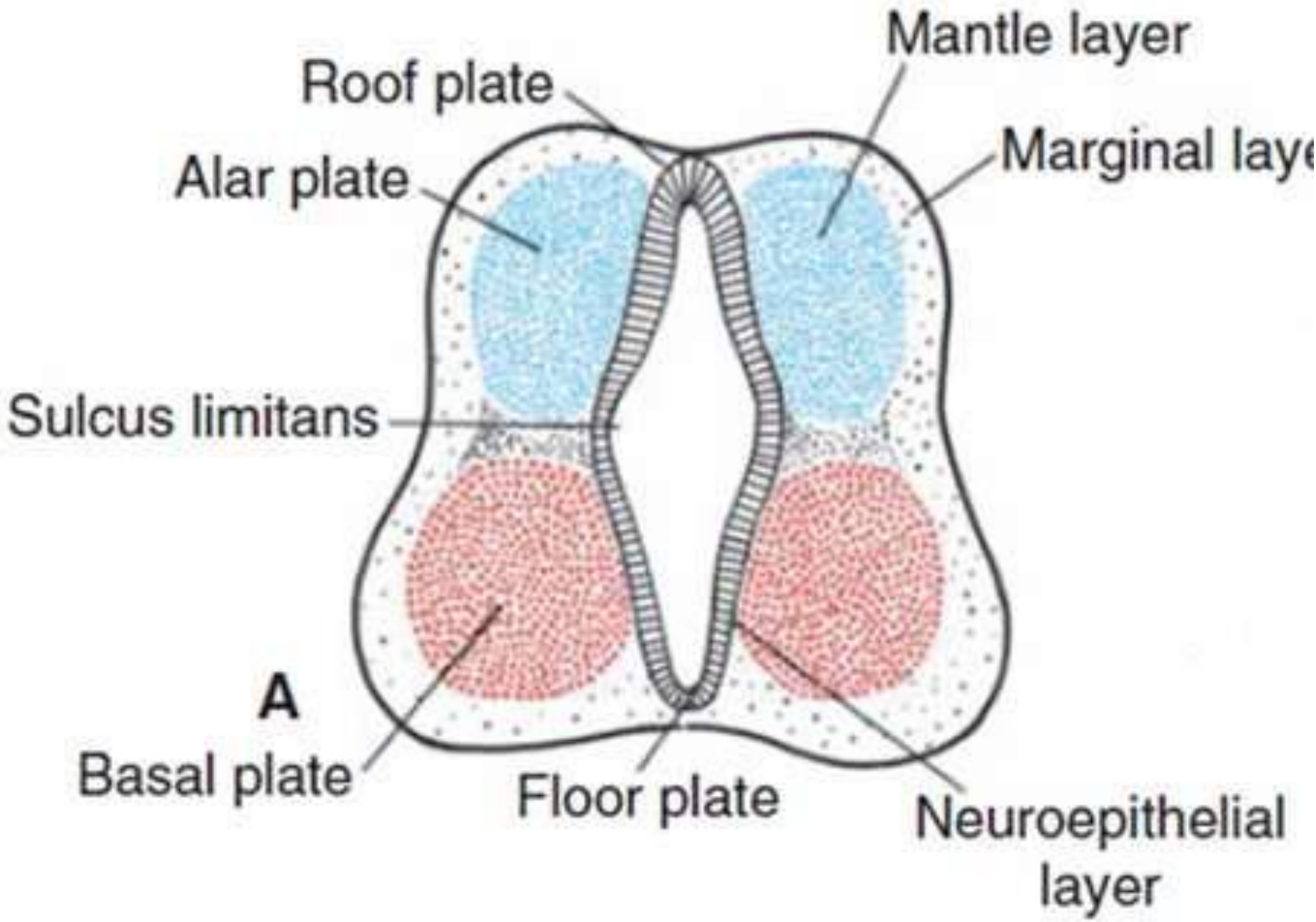

Marginal layer
Central canal
Mantle layer
White matter
Gray matter

Basal, Alar, Roof, and Floor Plates

- As a result of continuous addition of neuroblasts to the mantle layer, each side of the neural tube shows a ventral and a dorsal thickening.

- The ventral thickenings, ***The Basal plates***, which form the ***motor*** areas in the neural tube

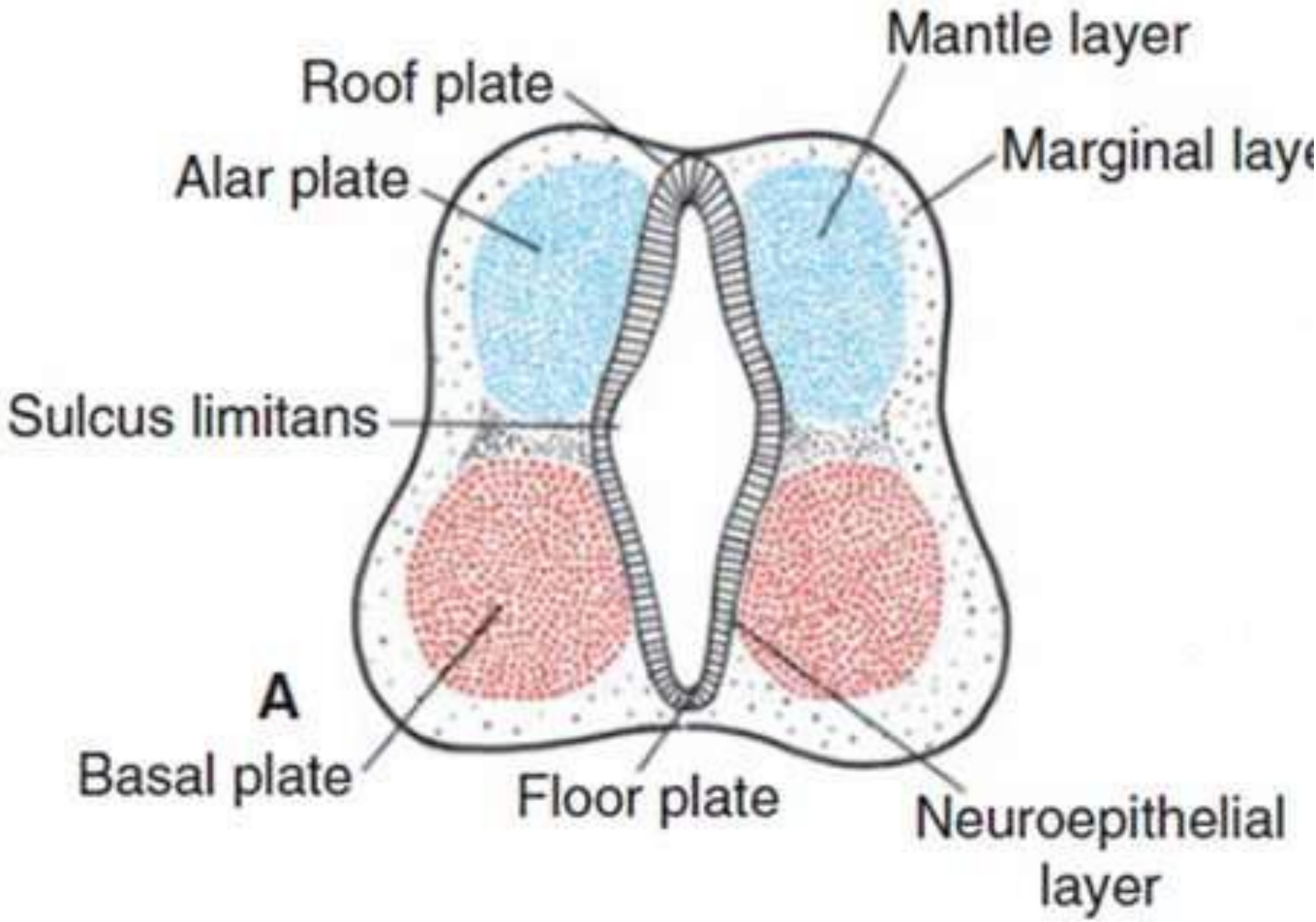

alar plate
central canal
intermediate plate
basal plate
marginal layer


Mantle layer
Roof plate
Marginal laye
Alar plate
Sulcus limitans
A
Basal plate
Floor plate
Neuroepithelial
layer

Basal, Alar, Roof, and Floor Plates

- The dorsal thickenings, ***The Alar plates***, form the ***sensory*** areas.

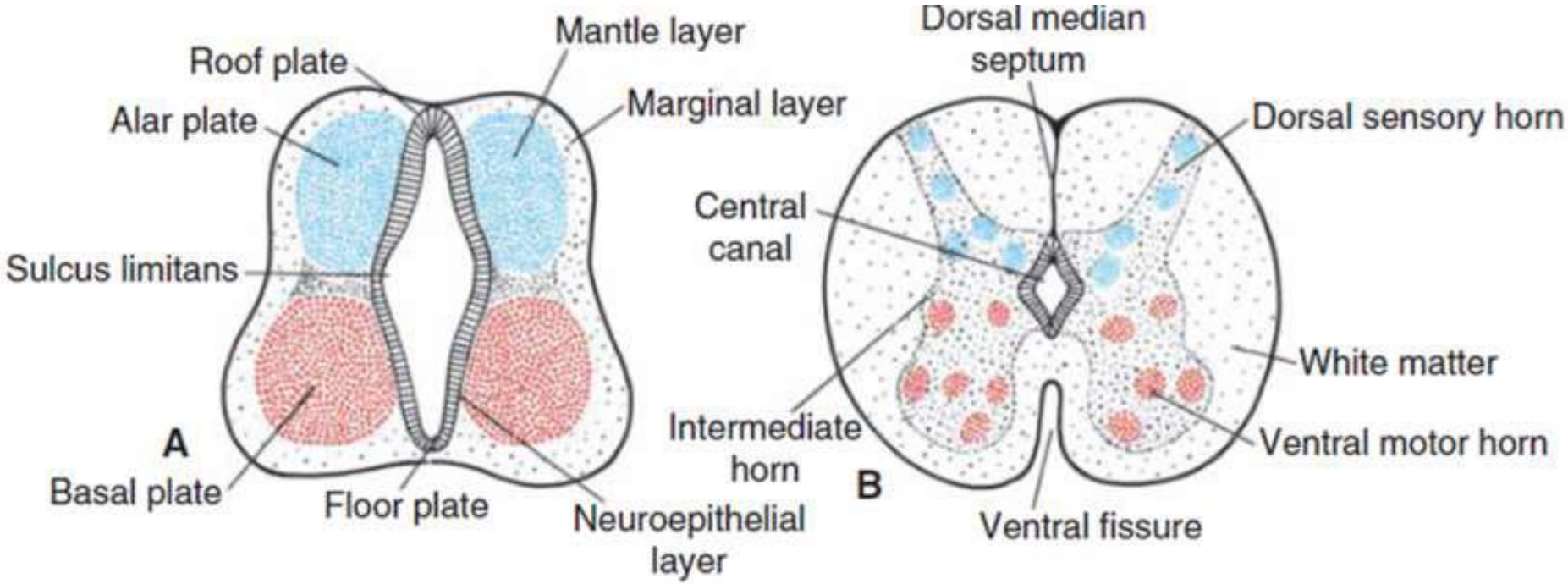
- The dorsal and ventral midline portions of the neural tube, known as the ***roof*** and ***floor plates***, respectively, ***do not contain neuroblasts (only mantle layer)***

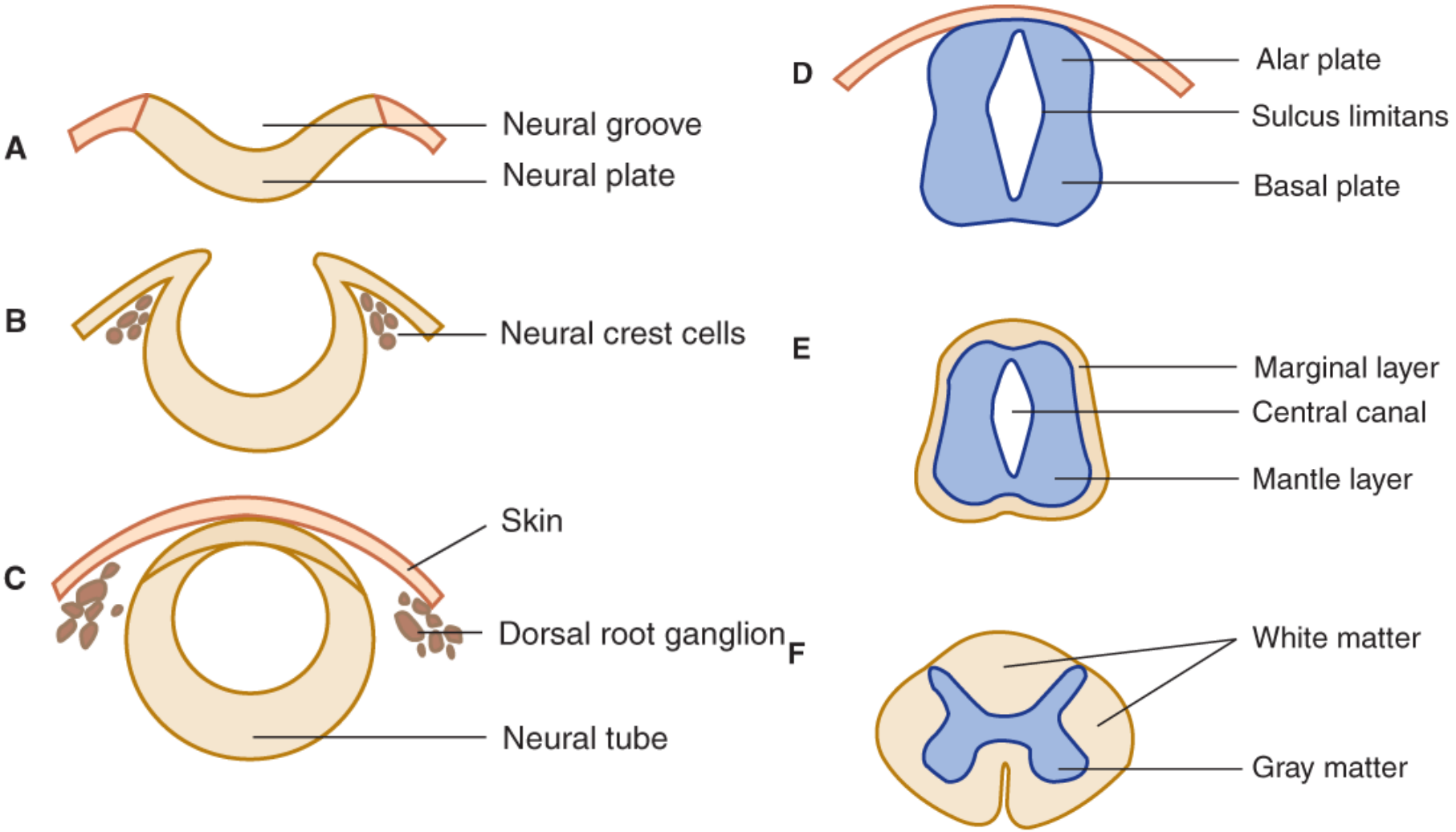

Mantle layer
Roof plate
Marginal laye
Alar plate
Sulcus limitans
A
Basal plate
Floor plate
Neuroepithelial
layer

Spinal Cord Development

- In addition to the ventral motor horn and the dorsal sensory horn, **a group of neurons** accumulates between the two areas and forms a small ***intermediate horn***.

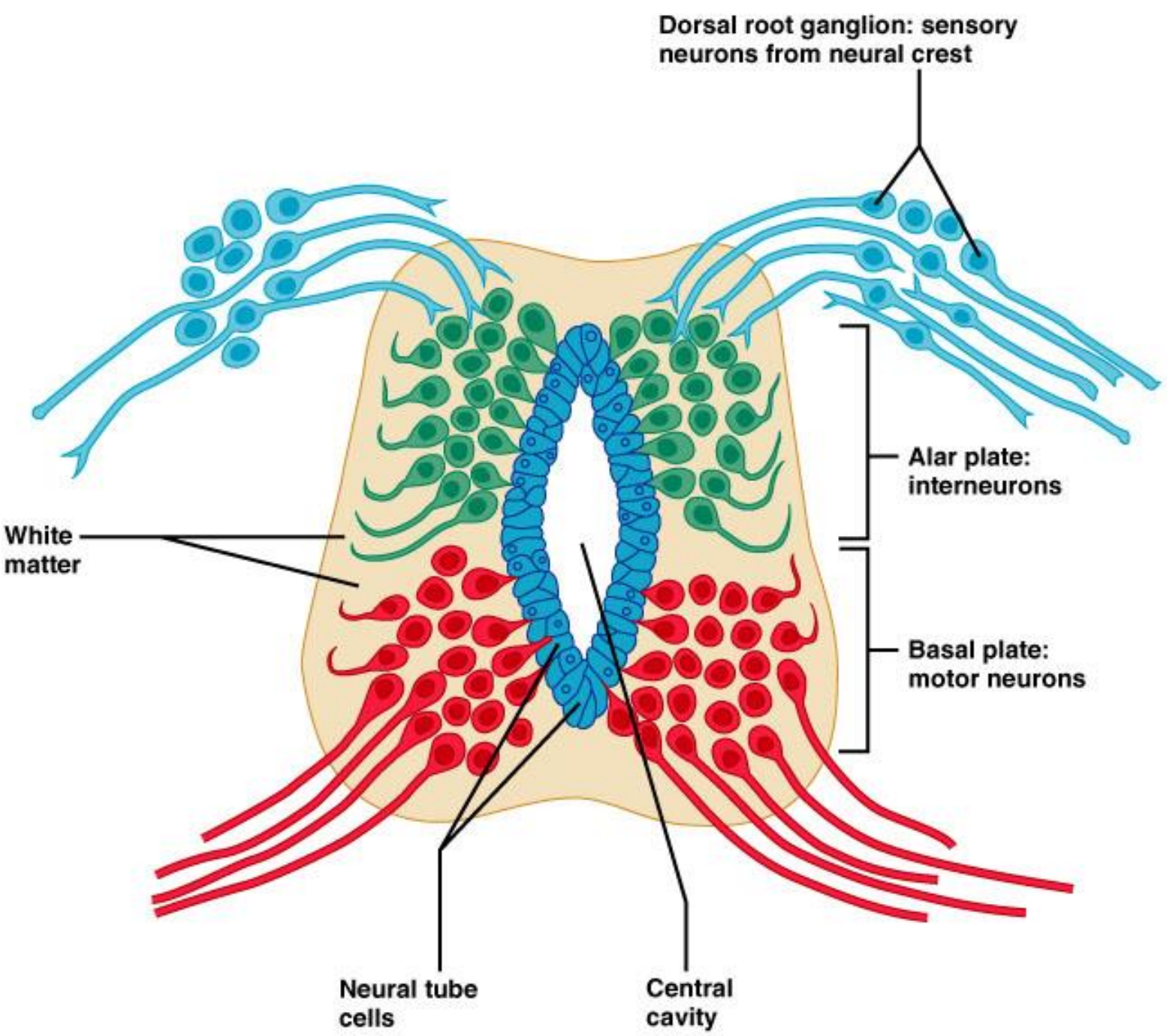
- This horn, containing neurons of the ***sympathetic portion of the autonomic nervous system (ANS)***, is present only at thoracic (***T1–T12***) and upper lumbar levels (***L1 or L2***) of the spinal cord.

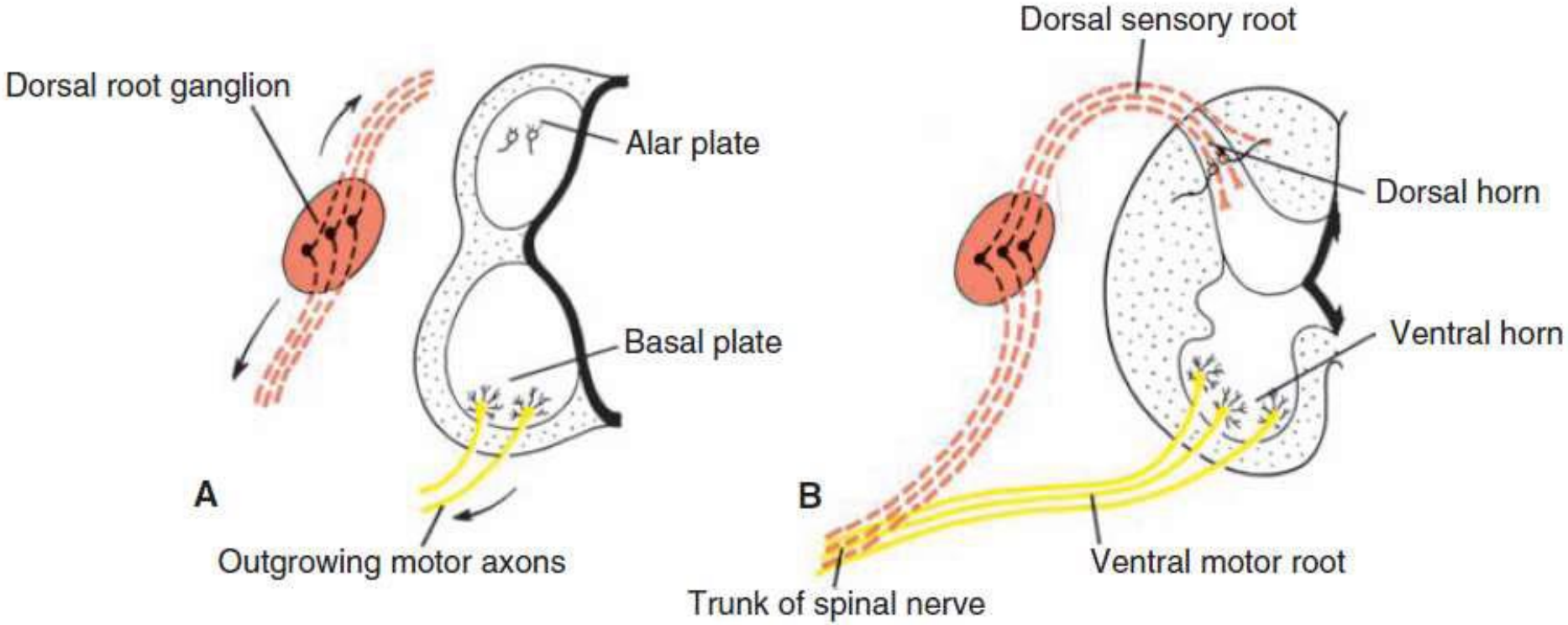

Roof plate
Alar plate
Mantle layer
Marginal layer
Sulcus limitans
A
Basal plate
Floor plate
Neuroepithelial layer
Dorsal median septum
Dorsal sensory horn
Central canal
White matter
Intermediate horn
Ventral motor horn
B
Ventral fissure



Development of Spinal Nerves

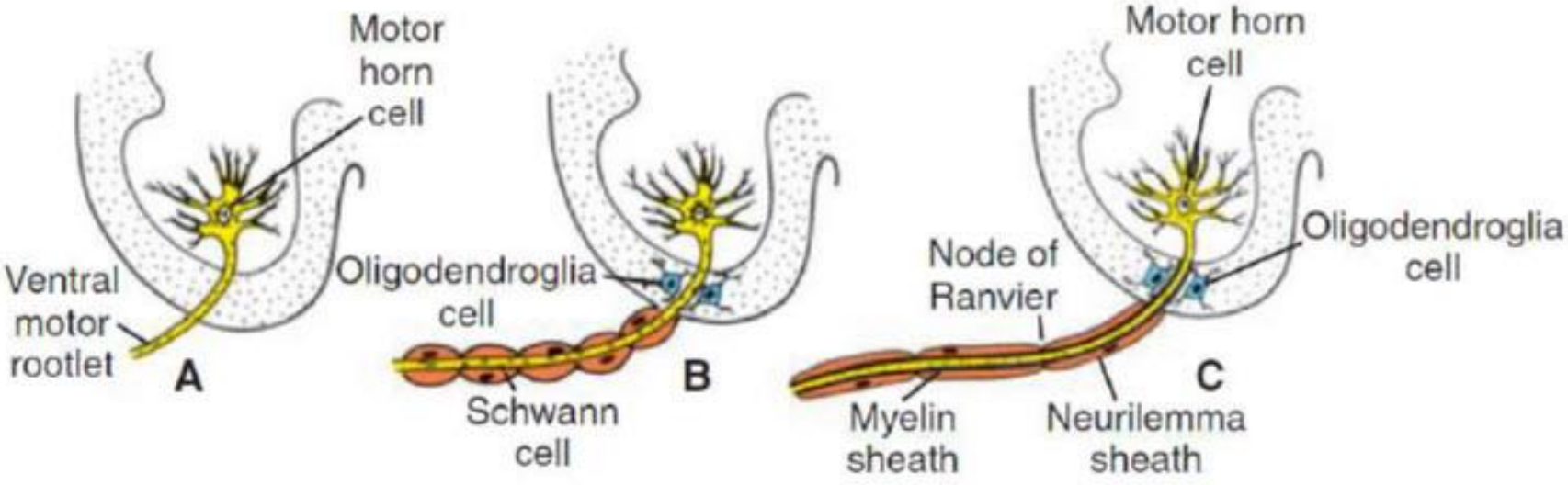
- Motor axons growing out from neurons in the basal plate
- Components arise centrally and peripherally from growing fibers of nerve cells in the dorsal root ganglion.
- Nerve fibers of the ventral motor and dorsal sensory roots join to form the trunk of the ***spinal nerve***




Dorsal root ganglion
Alar plate
Basal plate
A
Outgrowing motor axons
Dorsal sensory root
Dorsal horn
Ventral horn
B
Ventral motor root
Trunk of spinal nerve

Myelination of Spinal Nerve

- In the spinal cord, the myelin sheath is formed by oligodendroglia cells; outside the spinal cord, the sheath is formed by Schwann cells.



Development of the Brain

- The cephalic end of the neural tube shows three dilations, the ***primary brain vesicles:***

1. **Prosencephalon,** or **Forebrain**

2. **Mesencephalon,** or **Midbrain**

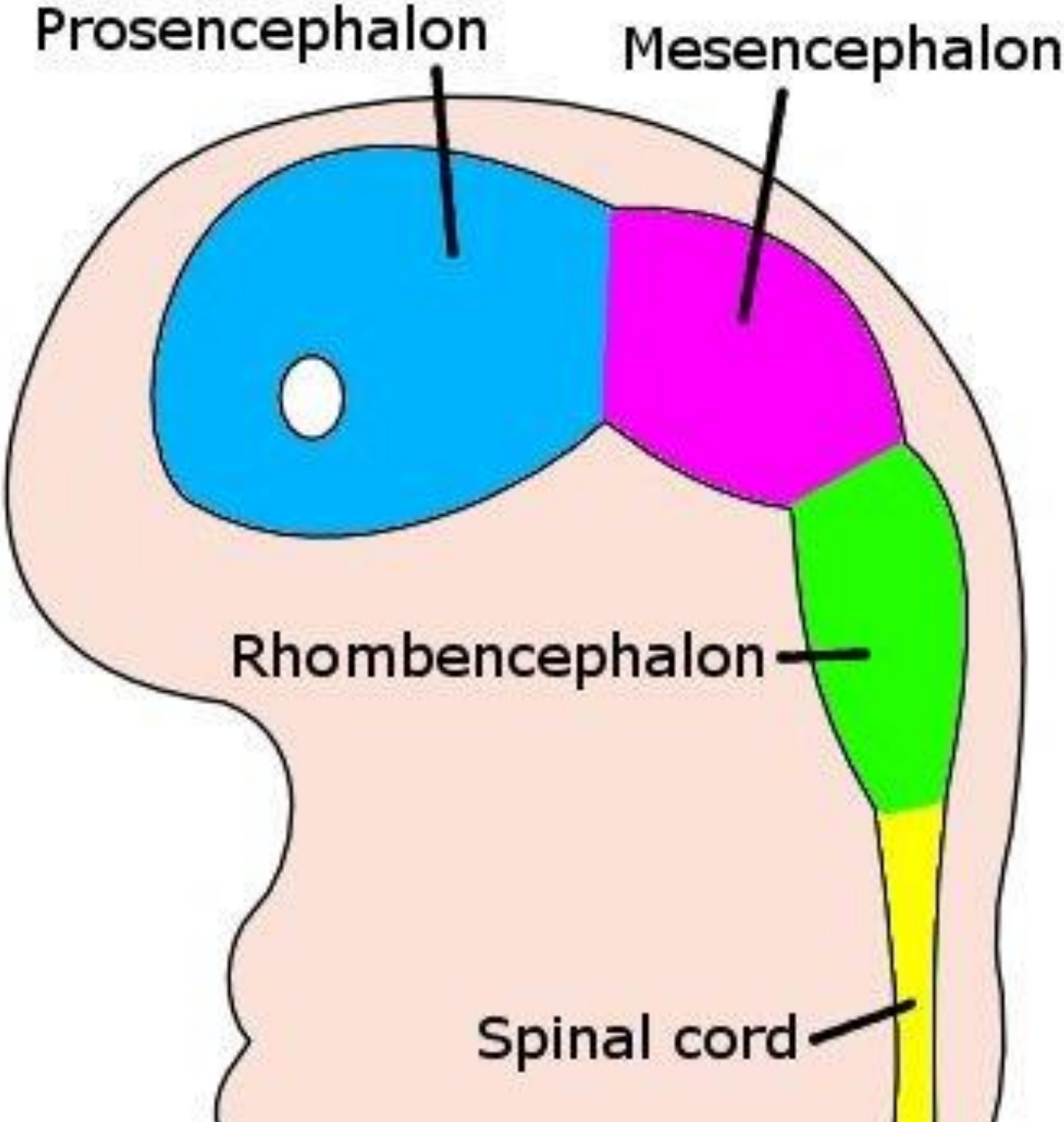
Development of the Brain

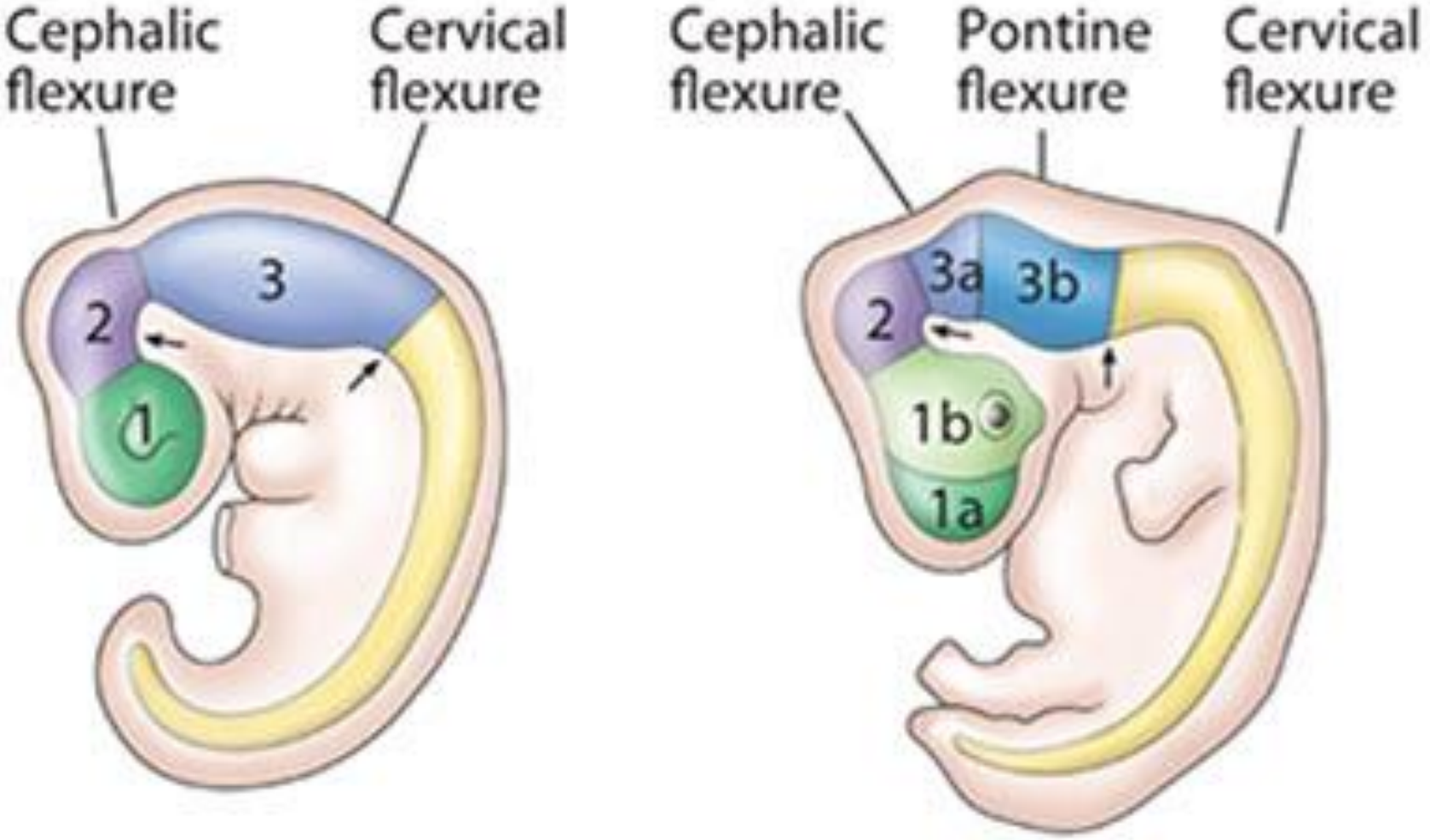
3. **Rhombencephalon,** or **Hindbrain**.

Simultaneously, it forms two flexures:

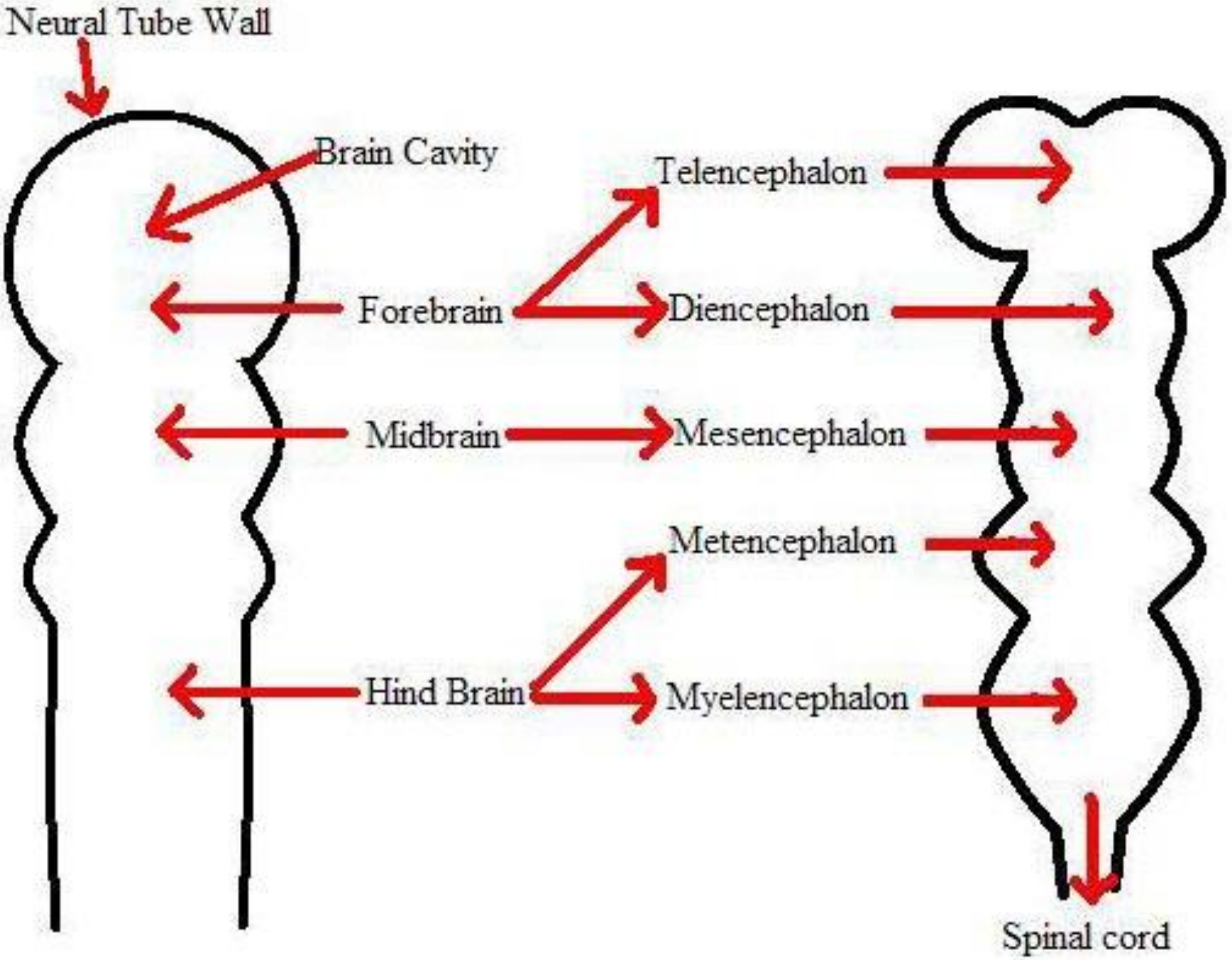
1. ***Cervical flexure*** at the junction of the hindbrain and the spinal cord

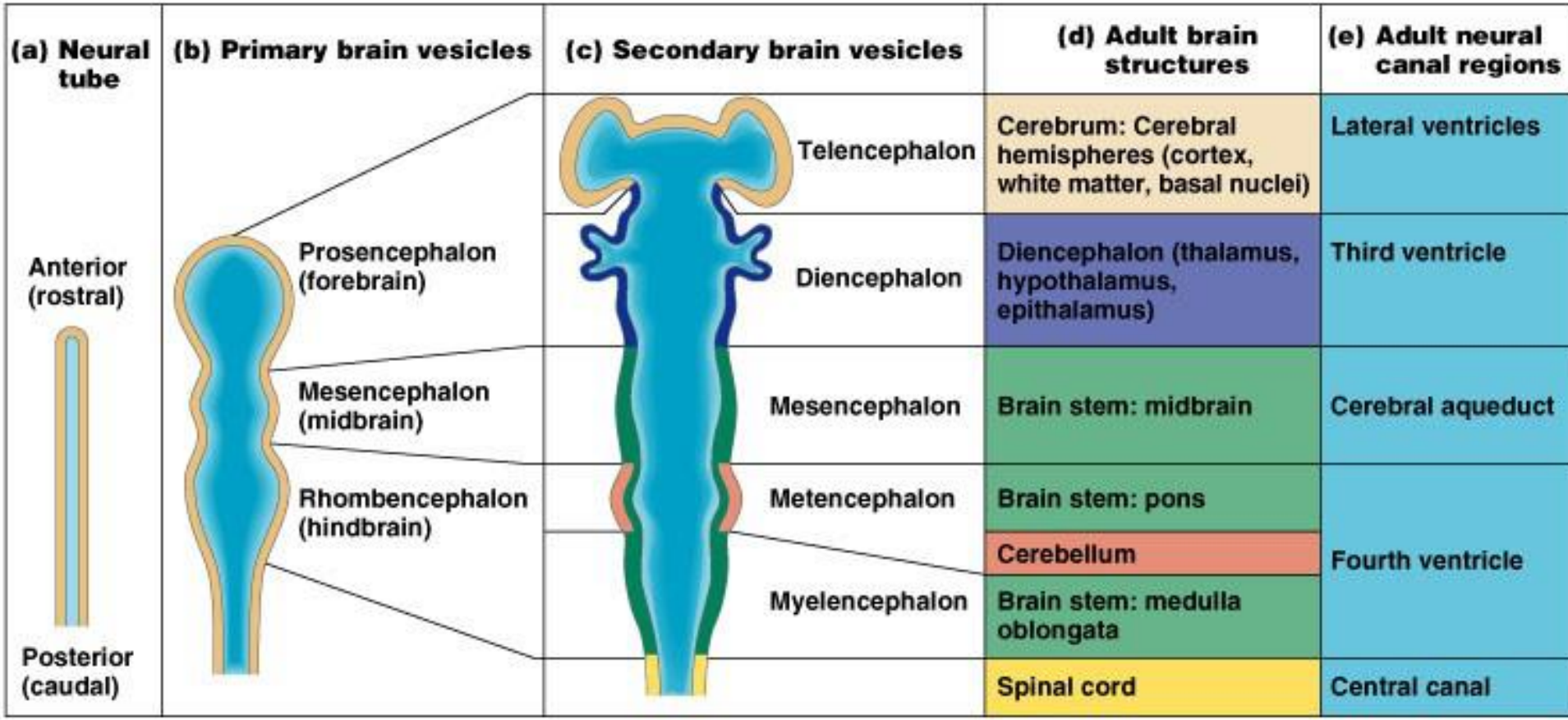
2. ***Cephalic flexure*** in the midbrain region.

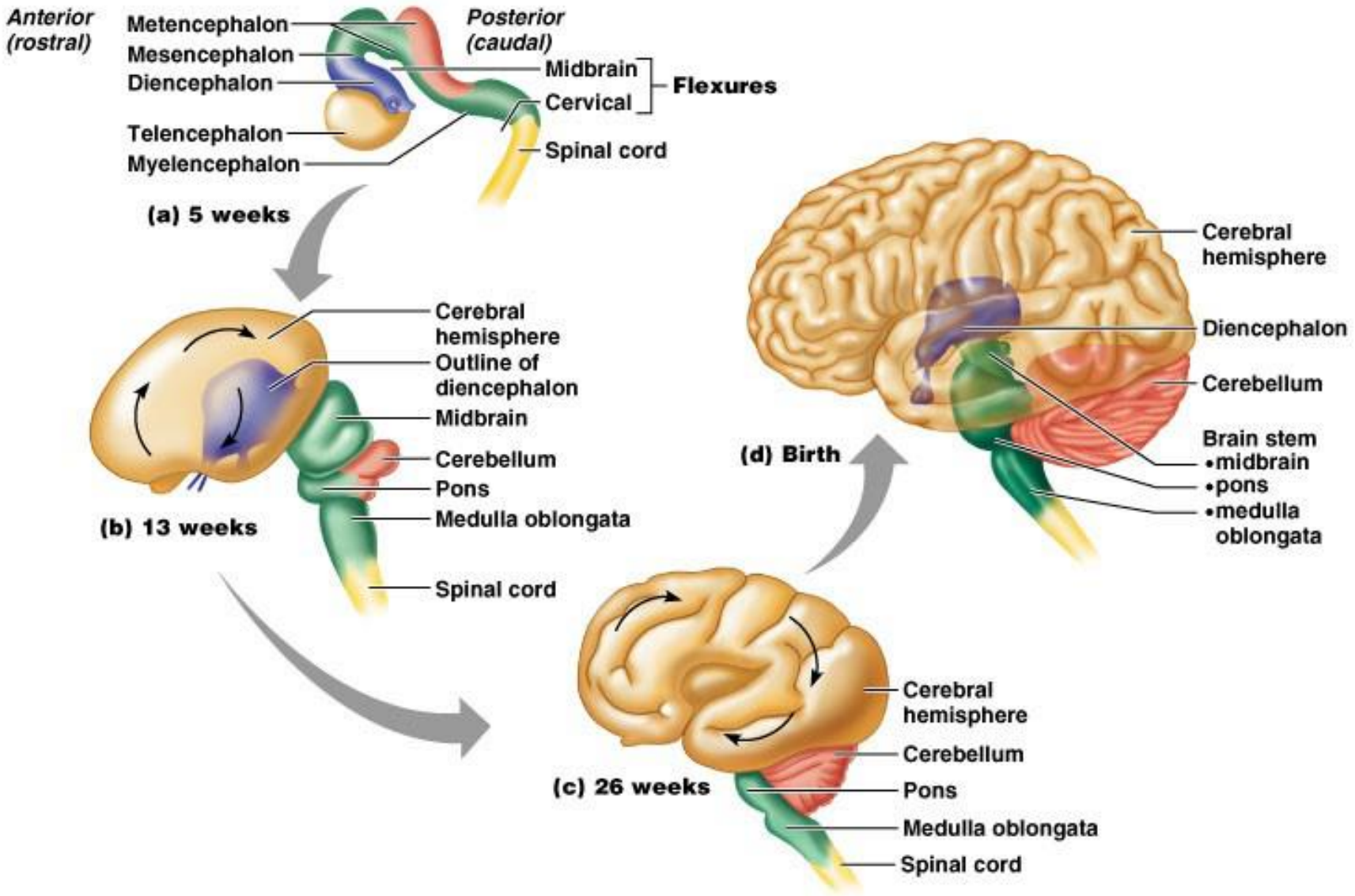

Prosencephalon
Mesencephalon
Rhombencephalon
Spinal cord



Source: Tony Mosconi, Victoria Graham:
Neuroscience for Rehabilitation


Neural Tube Wall
Brain Cavity
Telencephalon
Forebrain
Diencephalon
Midbrain
Mesencephalon
Metencephalon
Hind Brain
Myelencephalon
Spinal cord


(a) Neural tube
(b) Primary brain vesicles
(c) Secondary brain vesicles
(d) Adult brain structures
(e) Adult neural canal regions
Anterior (rostral)
Posterior (caudal)
Prosencephalon (forebrain)
Mesencephalon (midbrain)
Rhombencephalon (hindbrain)
Telencephalon
Diencephalon
Mesencephalon
Metencephalon
Myelencephalon
Cerebrum: Cerebral hemispheres (cortex, white matter, basal nuclei)
Diencephalon (thalamus, hypothalamus, epithalamus)
Brain stem: midbrain
Brain stem: pons
Cerebellum
Brain stem: medulla oblongata
Spinal cord
Lateral ventricles
Third ventricle
Cerebral aqueduct
Fourth ventricle
Central canal



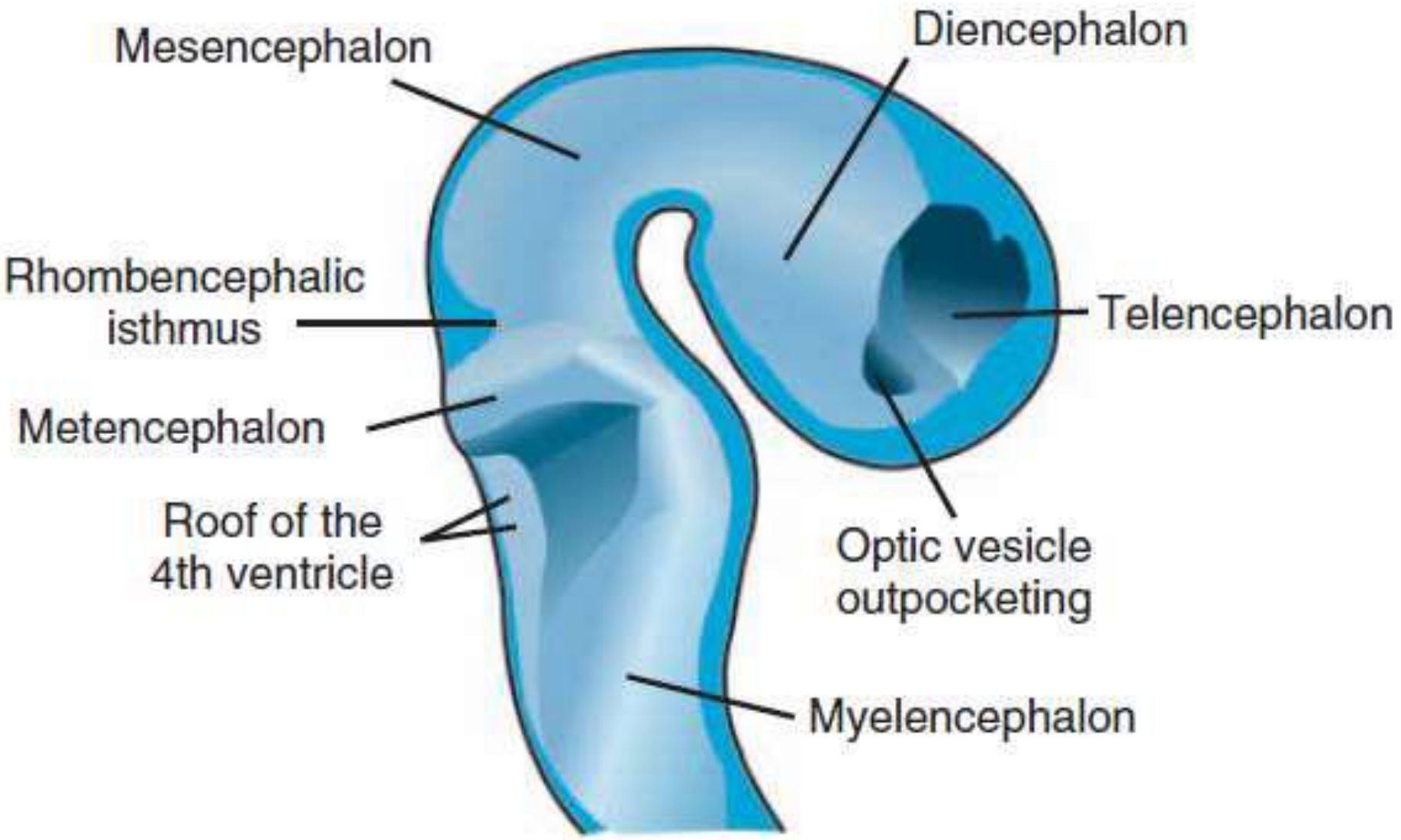
Development of the Hind Brain

- ***Rhombencephalon***

- The boundary between these two portions and the mesencephalon is marked by the pontine flexure (***Rhombencephalic isthmus***)

1. ***Metencephalon***, which later forms the pons and cerebellum

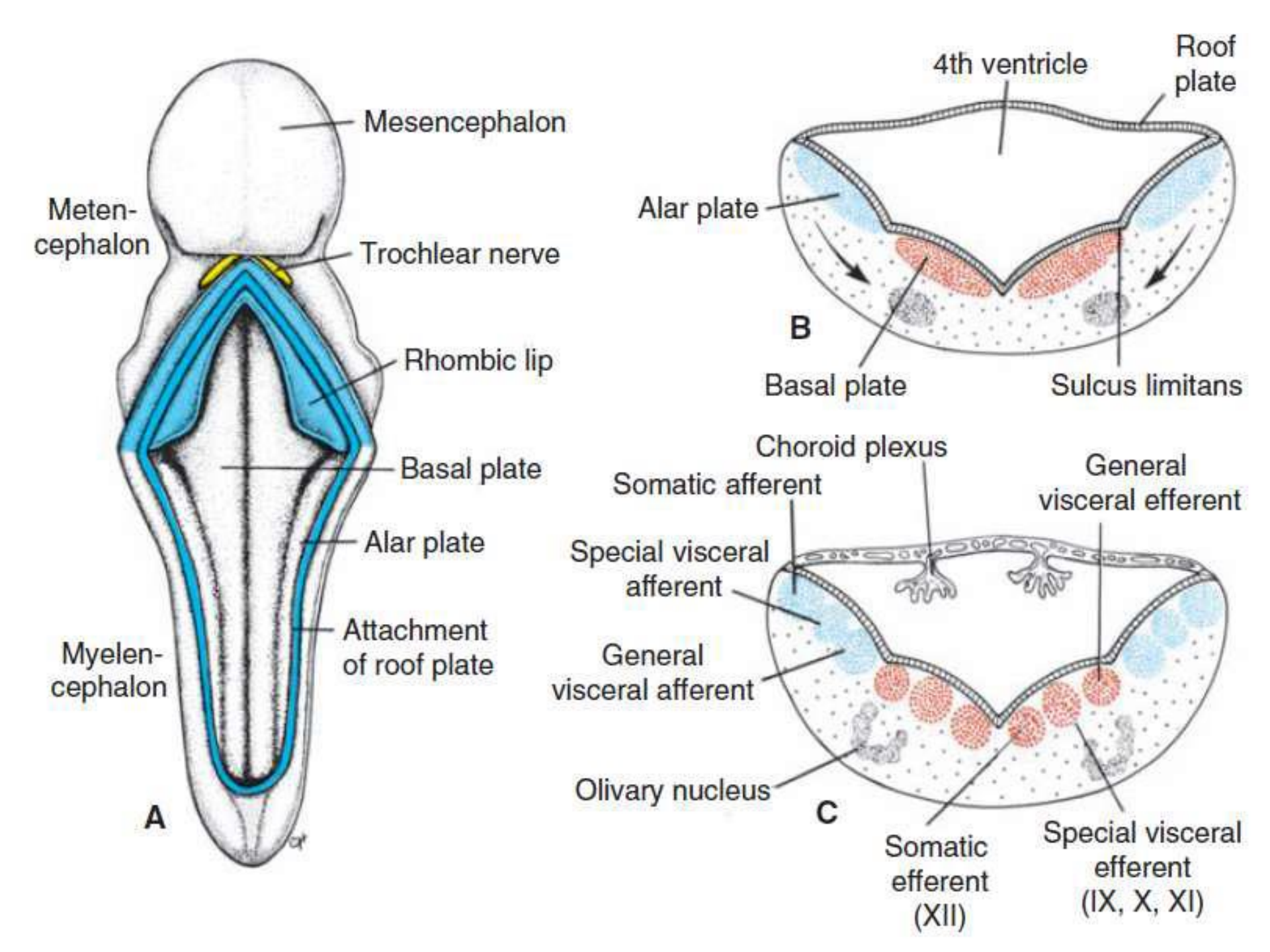
2. ***Myelencephalon***, Gives rise to the medulla oblongata.


Mesencephalon
Diencephalon
Rhombencephalic isthmus
Telencephalon
Metencephalon
Roof of the 4th ventricle
Optic vesicle outpocketing
Myelencephalon

Myelencephalon - Medulla

- It differs from the spinal cord in that the cavity dilates forming the 4th ventricle and the lateral walls rotate around the axis of the floor plate like opening a book.

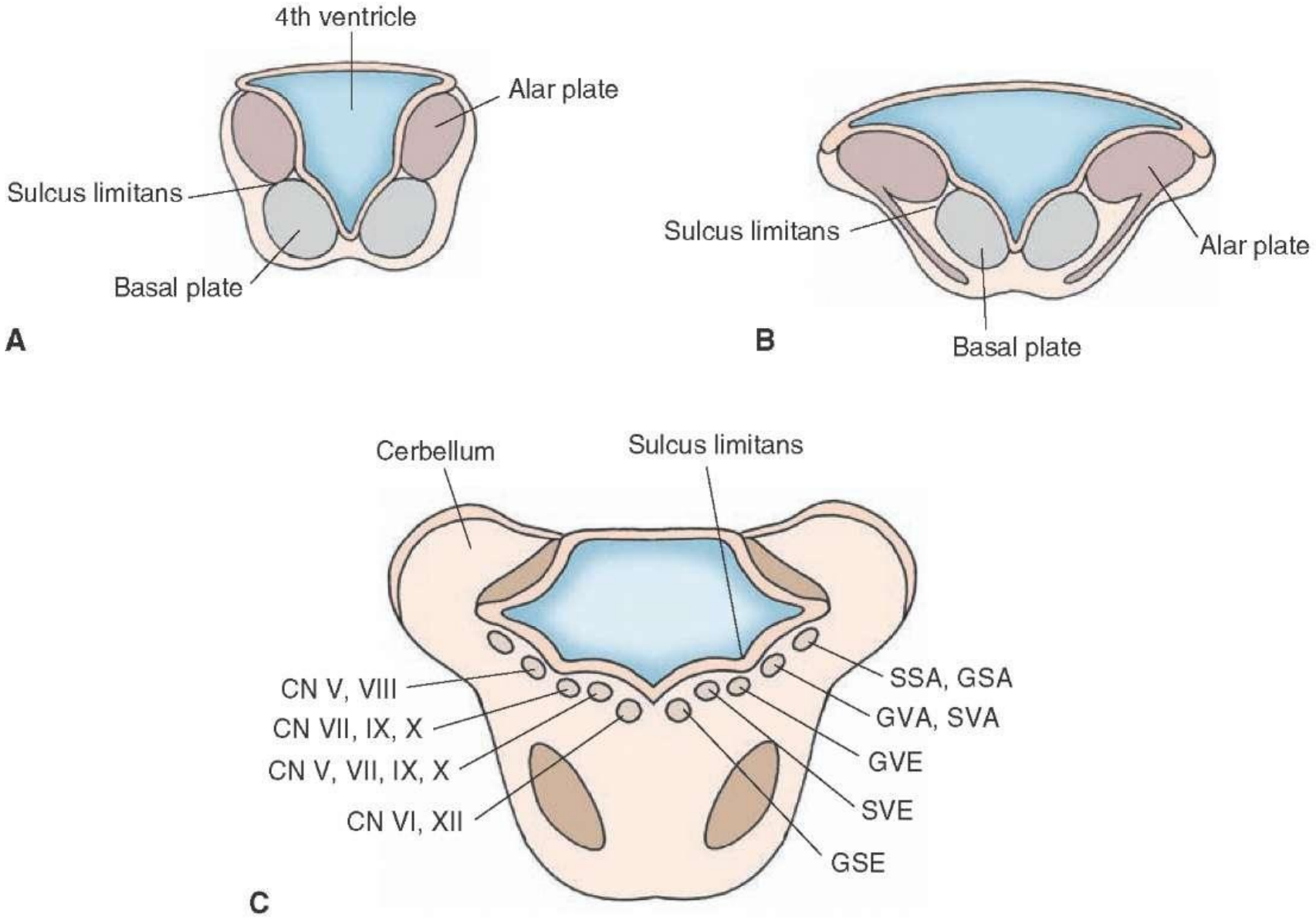
- In this way, the ***basal lamina becomes medial*** & the ***alar lamina becomes lateral.***


Mesencephalon
Meten-
cephalon
Trochlear nerve
Rhombic lip
Basal plate
Alar plate
Attachment
of roof plate
Myelen-
cephalon
A
4th ventricle
Roof
plate
Alar plate
B
Basal plate
Sulcus limitans
Choroid plexus
Somatic afferent
General
visceral efferent
Special visceral
afferent
General
visceral afferent
Olivary nucleus
C
Somatic
efferent
(XII)
Special visceral
efferent
(IX, X, XI)

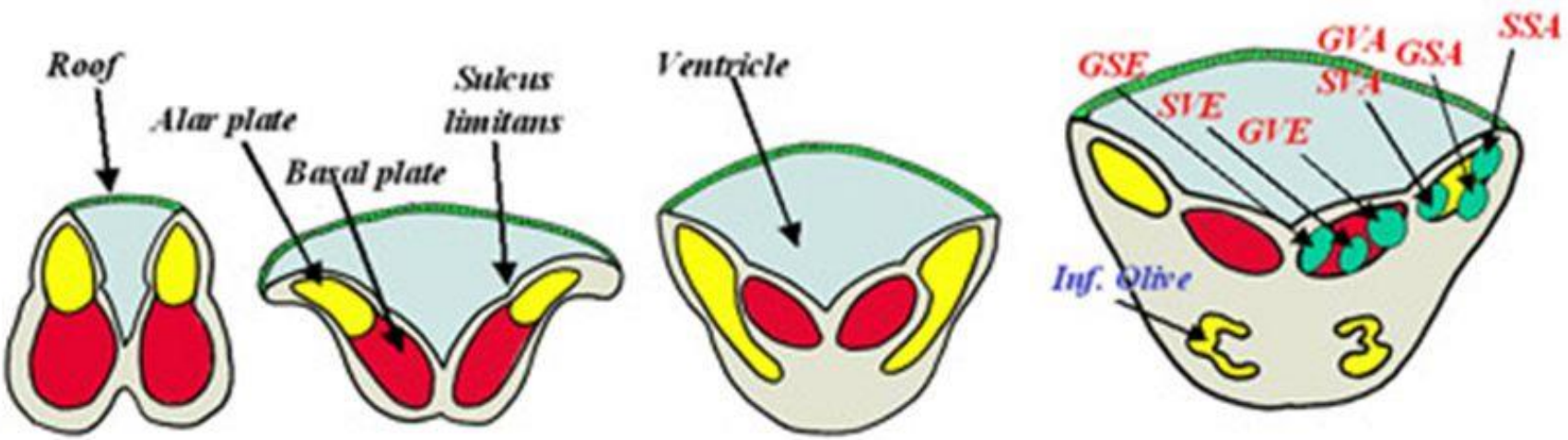
Myelencephalon - Medulla

- Alar and basal plates separated by the sulcus limitans.

- The roof plat of the myelencephalon consists of a single layer of ependymal cells covered by vascular mesenchyme (Choroid plexus) covered by the pia mater (***roof of 4th ventricle***)


4th ventricle
Alar plate
Sulcus limitans
Basal plate
A
Sulcus limitans
Alar plate
Basal plate
B
Cerbellum
Sulcus limitans
CN V, VIII
CN VII, IX, X
CN V, VII, IX, X
CN VI, XII
SSA, GSA
GVA, SVA
GVE
SVE
GSE
C

MYELENCEPHALON DEVELOPMENT



Metencephalon

- ***Metencephalon differentiate into:***

- ***Pons:*** (The pathway for nerve fibers between the spinal cord and the cerebral and the cerebellar cortices)

- ***Cerebellum:*** (coordination center for posture and movement)

Motor and Sensory Nuclii

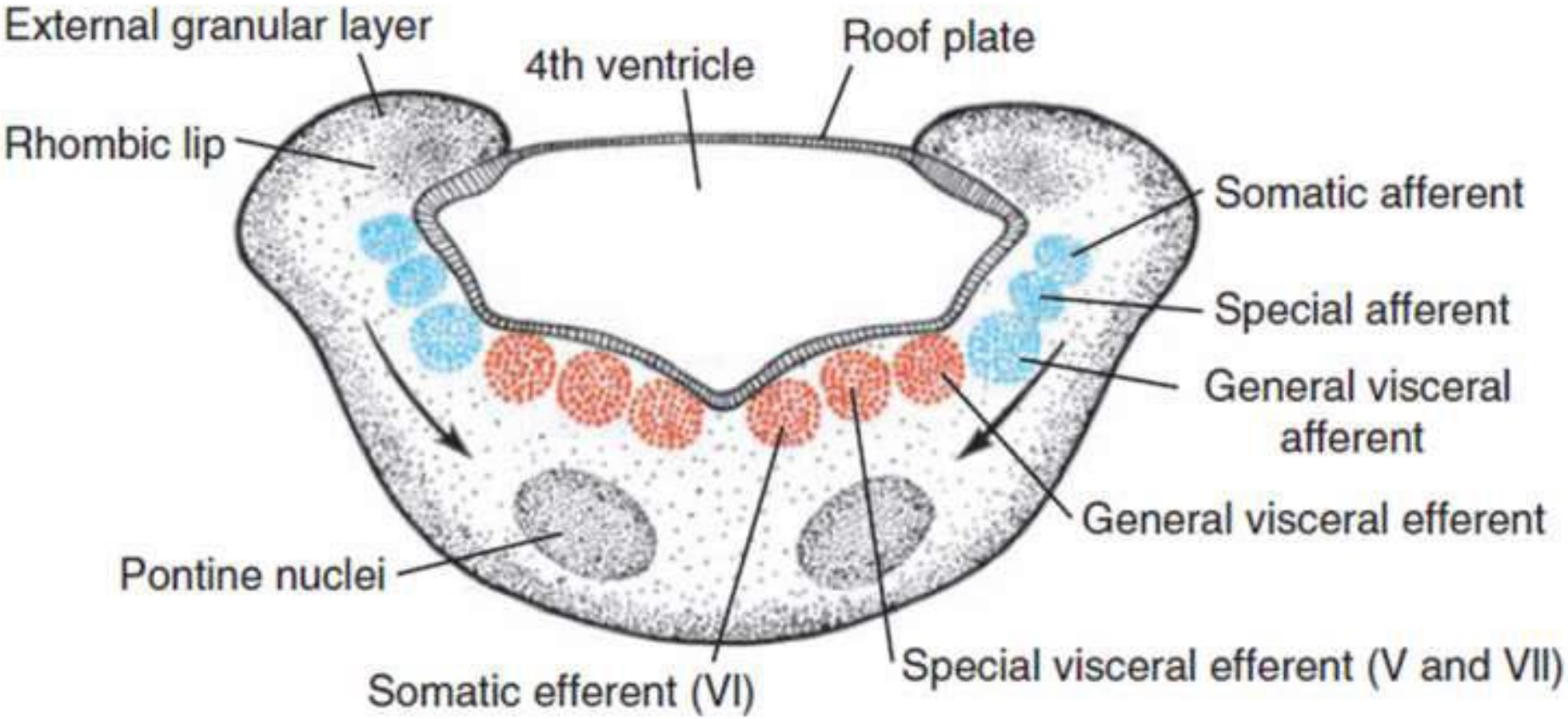
- ***The basal plate contains motor nuclei which divided into 3 groups:***

1. General Somatic Efferent group (medial in position) ***supplying voluntary muscles***
2. Special Visceral Efferent group (intermediate) ***supplying muscles of the pharyngeal arches***
3. General Visceral Efferent group (lateral in position) , ***autonomic nervous system that provide motor innervation to smooth muscle, cardiac muscle, and glands***

Motor and Sensory Nuclii

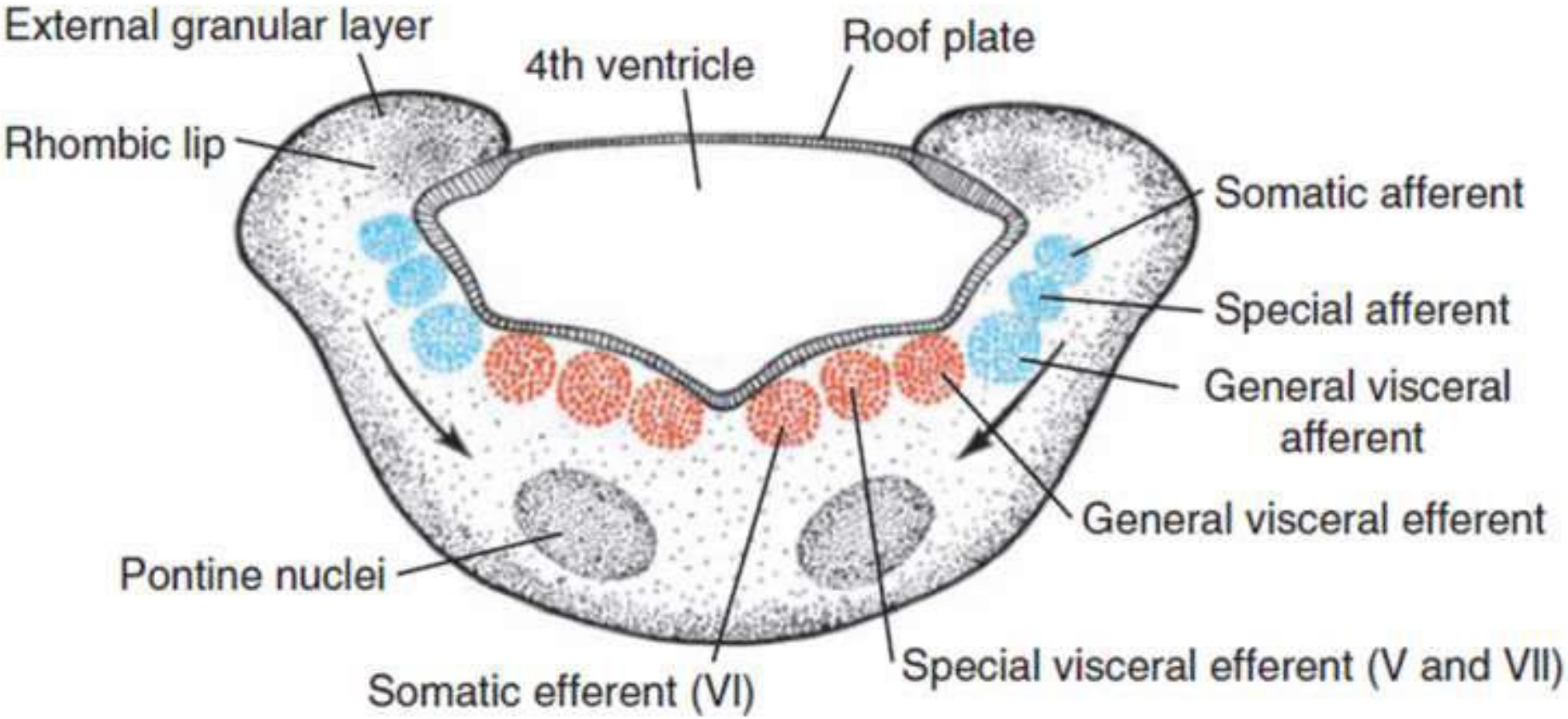
- ***The alar plate contains 4 groups of sensory relay nuclei***

1. Special Somatic Afferent group (lateral in position), receives ***impulses from the ear by way of the vestibulocochlear nerve***.
2. General Somatic Afferent *receives impulses from the head and face*
3. Special Visceral Afferent group receives impulses from ***taste buds of the tongue and from the palate, oropharynx, and epiglottis.***
4. General Visceral Afferent, group (medial in position) receives ***interoceptive information from the gastrointestinal tract and heart***


External granular layer
4th ventricle
Roof plate
Rhombic lip
Somatic afferent
Special afferent
General visceral afferent
General visceral efferent
Pontine nuclei
Somatic efferent (VI)
Special visceral efferent (V and VII)

Development of Cerebellum

1. Moving the alar plates laterally then bending medially.
2. Stretching and thinning of the roof plate
3. Widening of the cavity to form the 4th ventricle

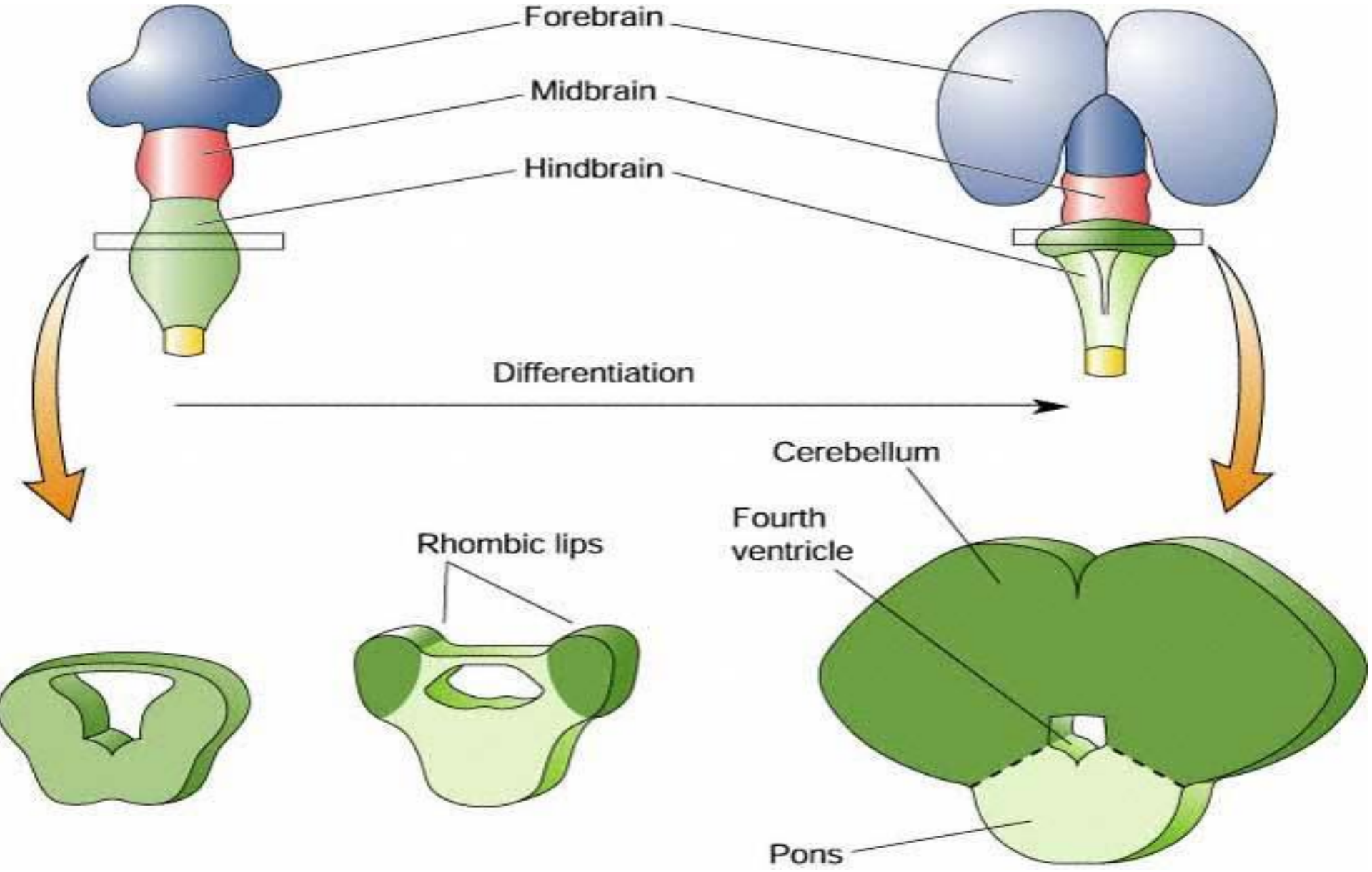

External granular layer
4th ventricle
Roof plate
Rhombic lip
Somatic afferent
Special afferent
General visceral afferent
General visceral efferent
Pontine nuclei
Somatic efferent (VI)
Special visceral efferent (V and VII)

Development of Cerebellum

5. Some neuroblasts ***migrate*** from the mantel layer to the marginal layer and form the ***cerebellar cortex***.

6. Others ***remains*** in the mantel layer and give rise to the ***cerebellar nuclei***.

7. The ***cerebellar peduncles*** develop later as the ***axons*** of the ***neurons*** of the ***cerebellar nuclei*** grows out to ***reach*** the ***brain stem***.


Forebrain
Midbrain
Hindbrain
Differentiation
Cerebellum
Fourth ventricle
Rhombic lips
Pons

Development of Cerebellum

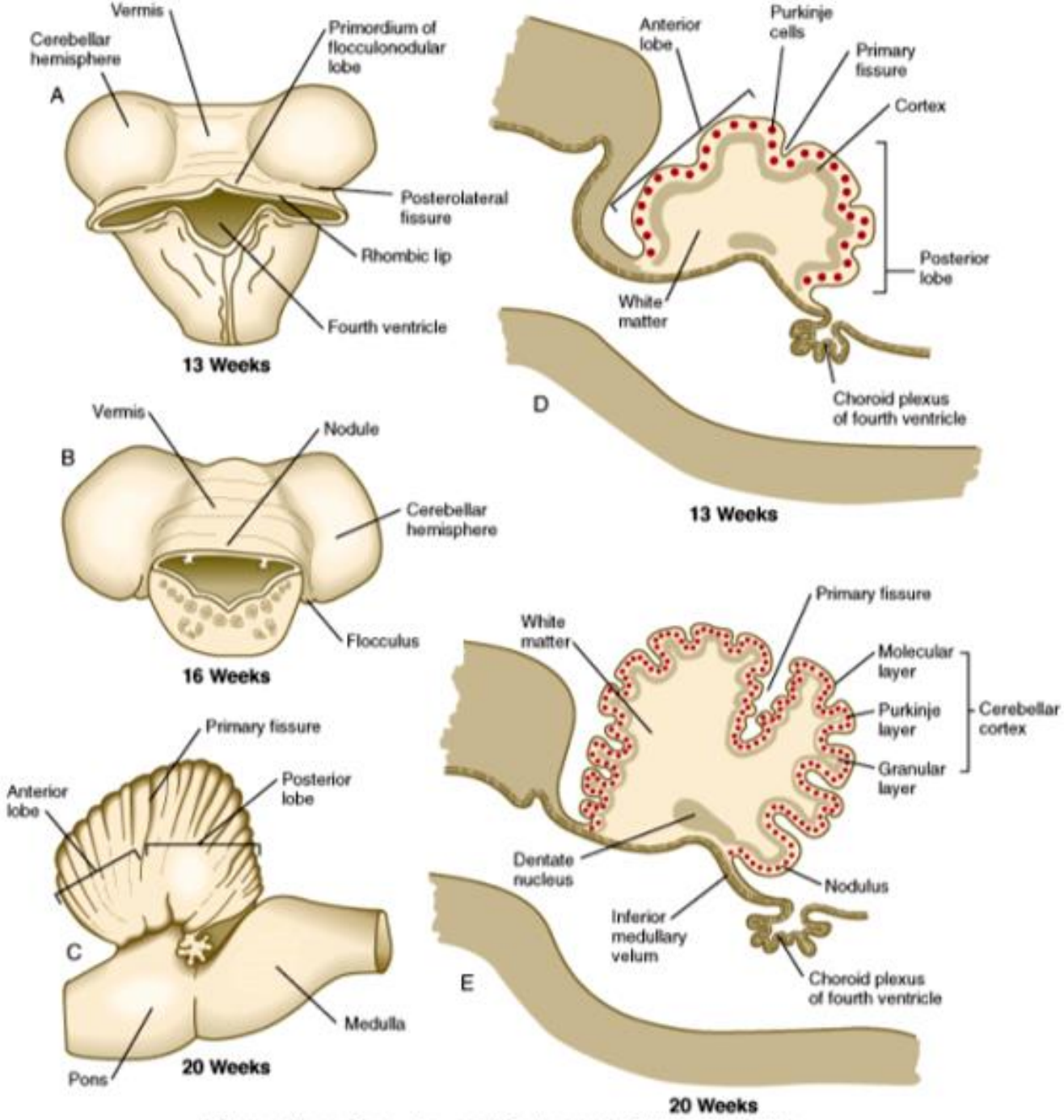
- In a ***12-week embryo***, this plate shows a small midline portion, the ***vermis***, and two lateral portions, the ***hemispheres***.

- A transverse fissure soon separates the nodule from the vermis and the lateral flocculus from the hemispheres.

Development of Cerebellum

- As the cerebellar hemispheres develops they undergo a complicated process of transverse folding and form closely packed, leaf-like transverse gyri called ***folia***.

- These processes of fissure formation and foliation continue throughout embryonic, fetal, and postnatal life, and they vastly ***increase the surface area of the cerebellar cortex***.

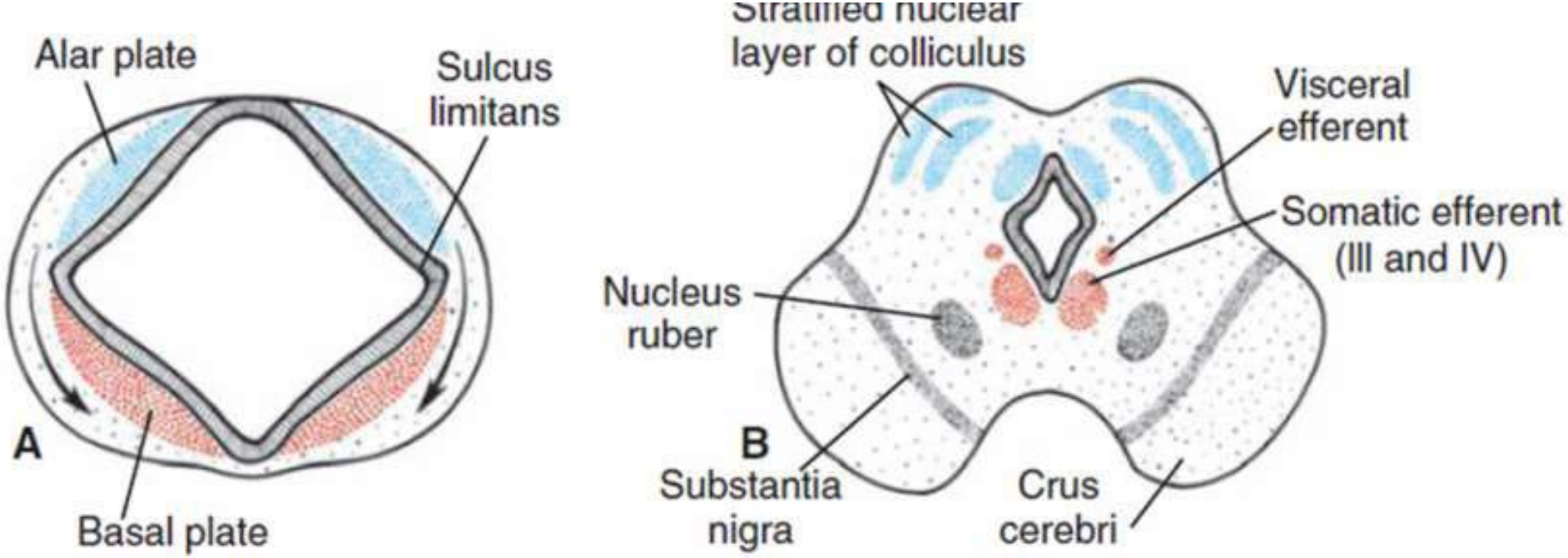


Development of the Midbrain

- The mesencephalon, or midbrain has ***basal efferent*** and ***alar afferent*** plates.

- The marginal layer of each basal plate enlarges and forms the ***crus cerebri***. These crura serve as pathways for nerve fibers descending from the cerebral cortex to lower centers in the pons and spinal cord.

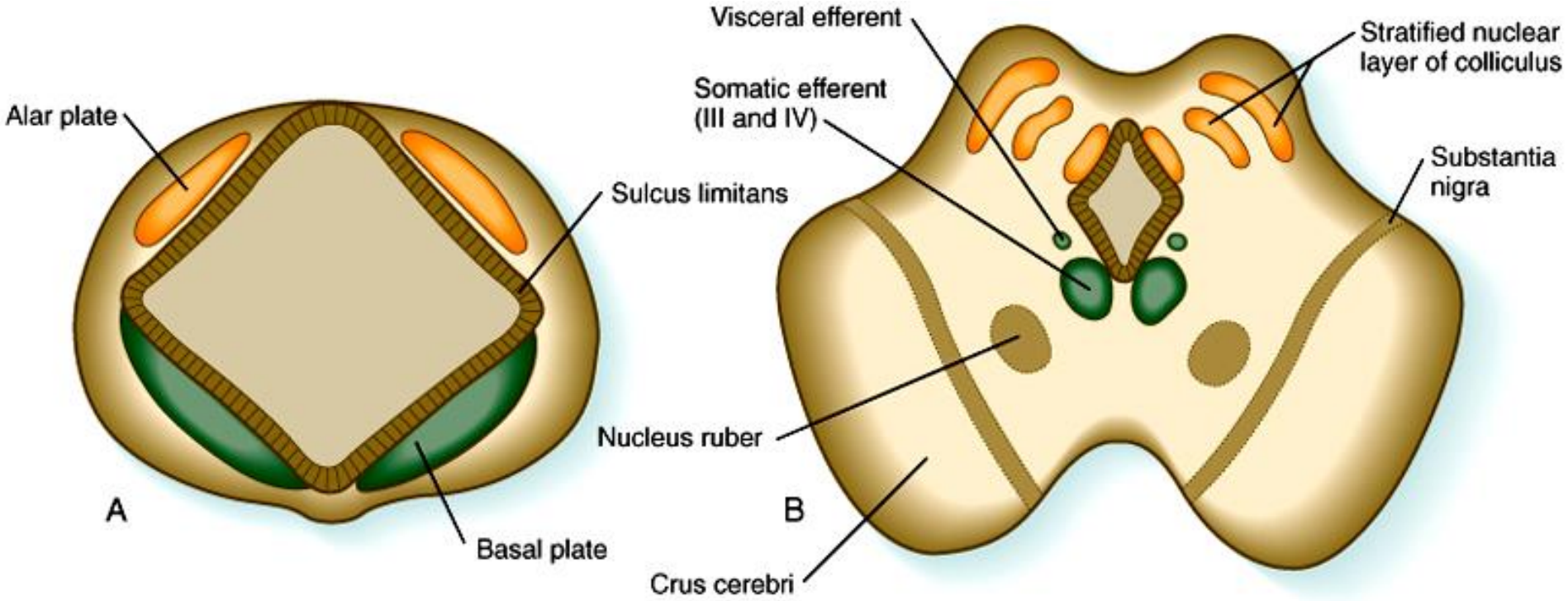
- The mesencephalon's ***alar plates*** form ***the superior and posterior colliculi*** as ***relay stations*** for ***visual*** and ***auditory reflex*** centers, respectively.


Alar plate
Sulcus limitans
A
Basal plate
Stratified nuclear layer of colliculus
Visceral efferent
Somatic efferent (III and IV)
Nucleus ruber
B
Substantia nigra
Crus cerebri

Development of the Midbrain

- ***Basal plate generates 4 motor tracts:***

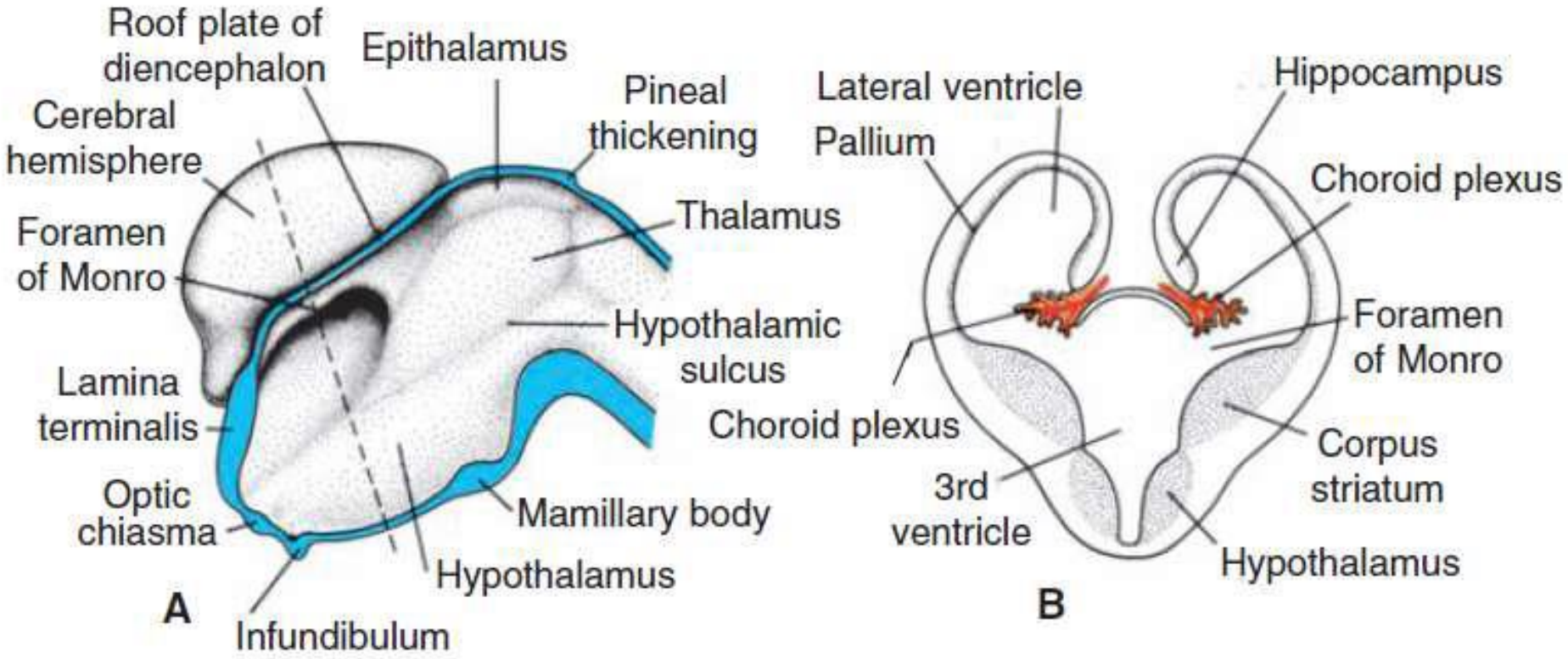
1. **Somatic efferent (*motor output to extraocular muscles, CN III, IV*)**
2. **Visceral efferent (*motor output to ciliary ganglion of the eye, CN III*)**
3. **Red nucleus (*motor relay to flexor muscles of the upper limb*)**
4. **Substantia nigra (*dopaminergic output to the basal ganglia of the telencephalon*)**



Development of Forebrain

- In the 7th week: The ***prosencephalon*** subdivides into the ***diencephalon posteriorly (thalamus)*** and the ***telencephalon anteriorly (primitive cerebral cortex)***.

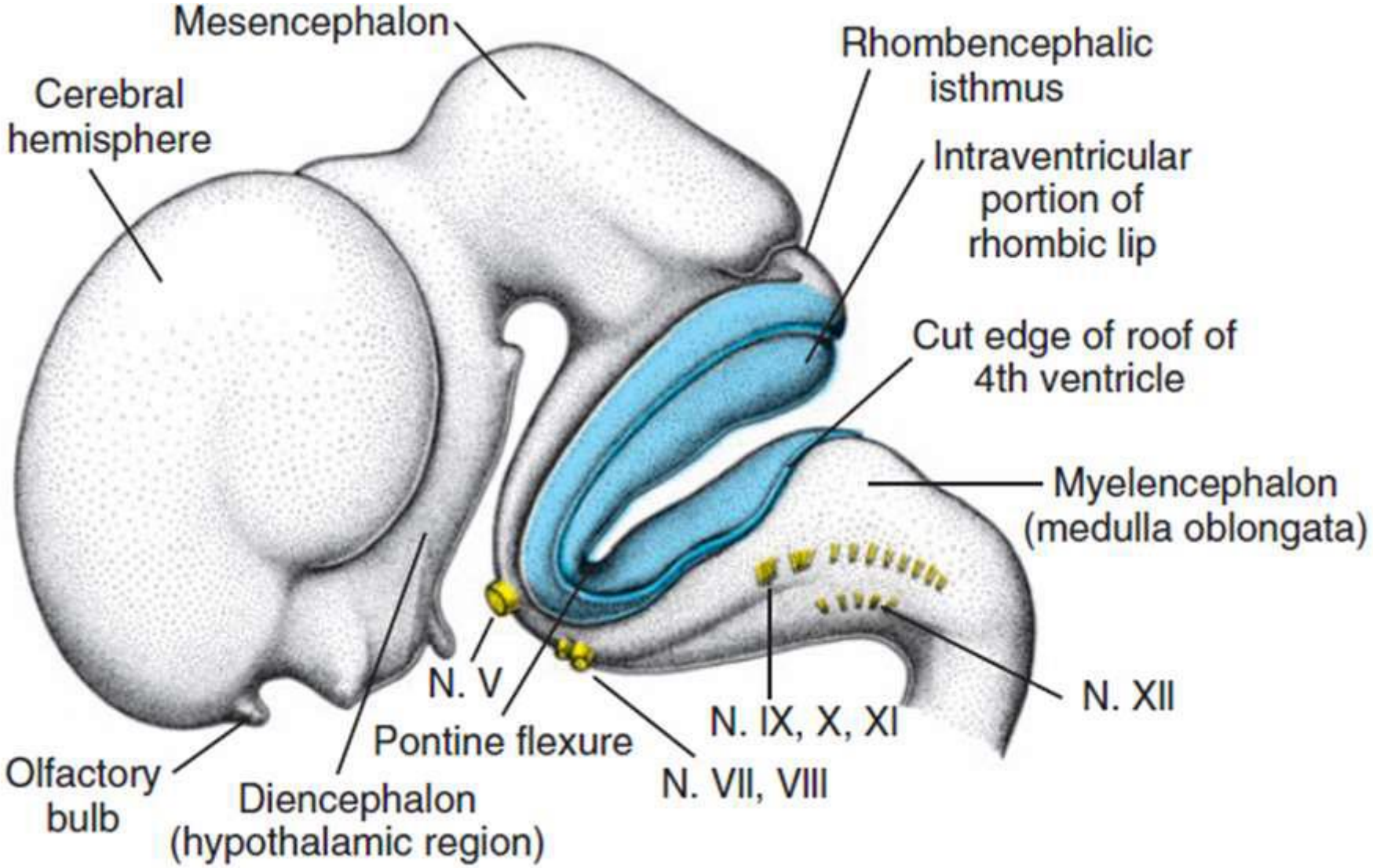
7 Weeks Embryo



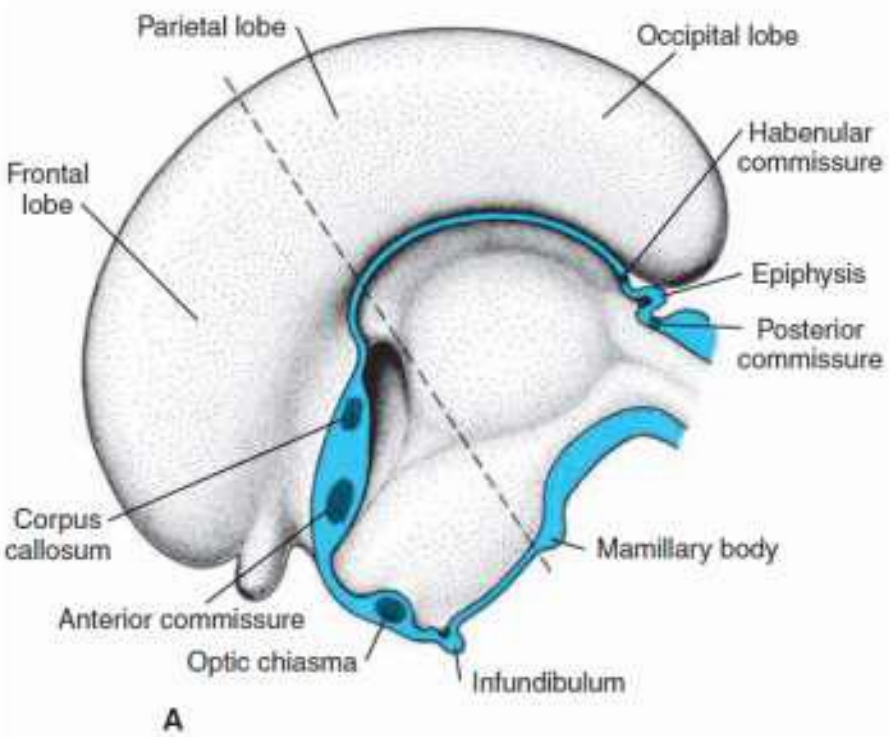
Development of Forebrain

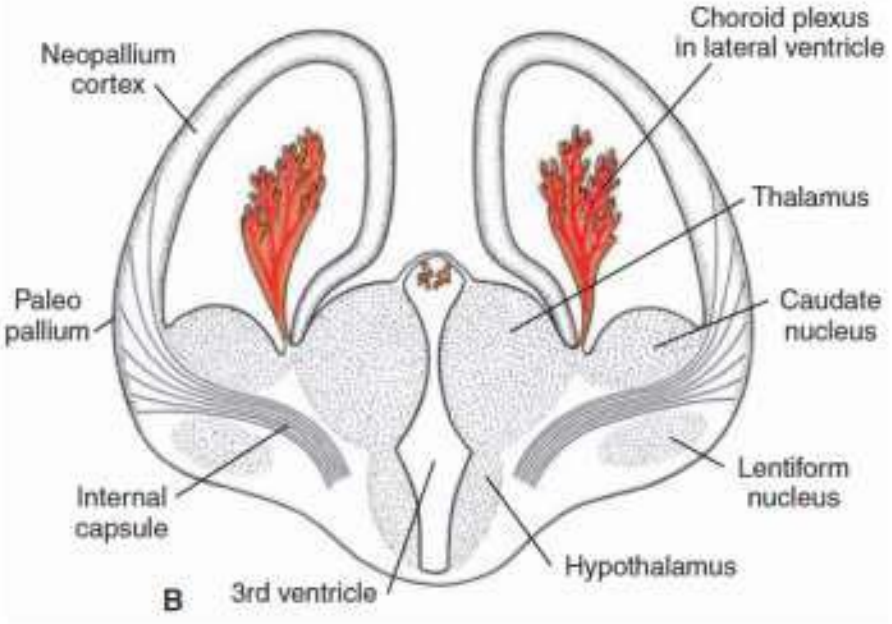
- At 10th week: The ***telencephalon*** consists of two lateral out pocketings, the ***cerebral hemispheres***, and a median portion, the ***lamina terminalis***

- In 4 month embryo: The ***lamina terminalis*** is used by the commissures as a connection pathway for fiber bundles between the right and left hemispheres (future ***Corpus Callosum***).

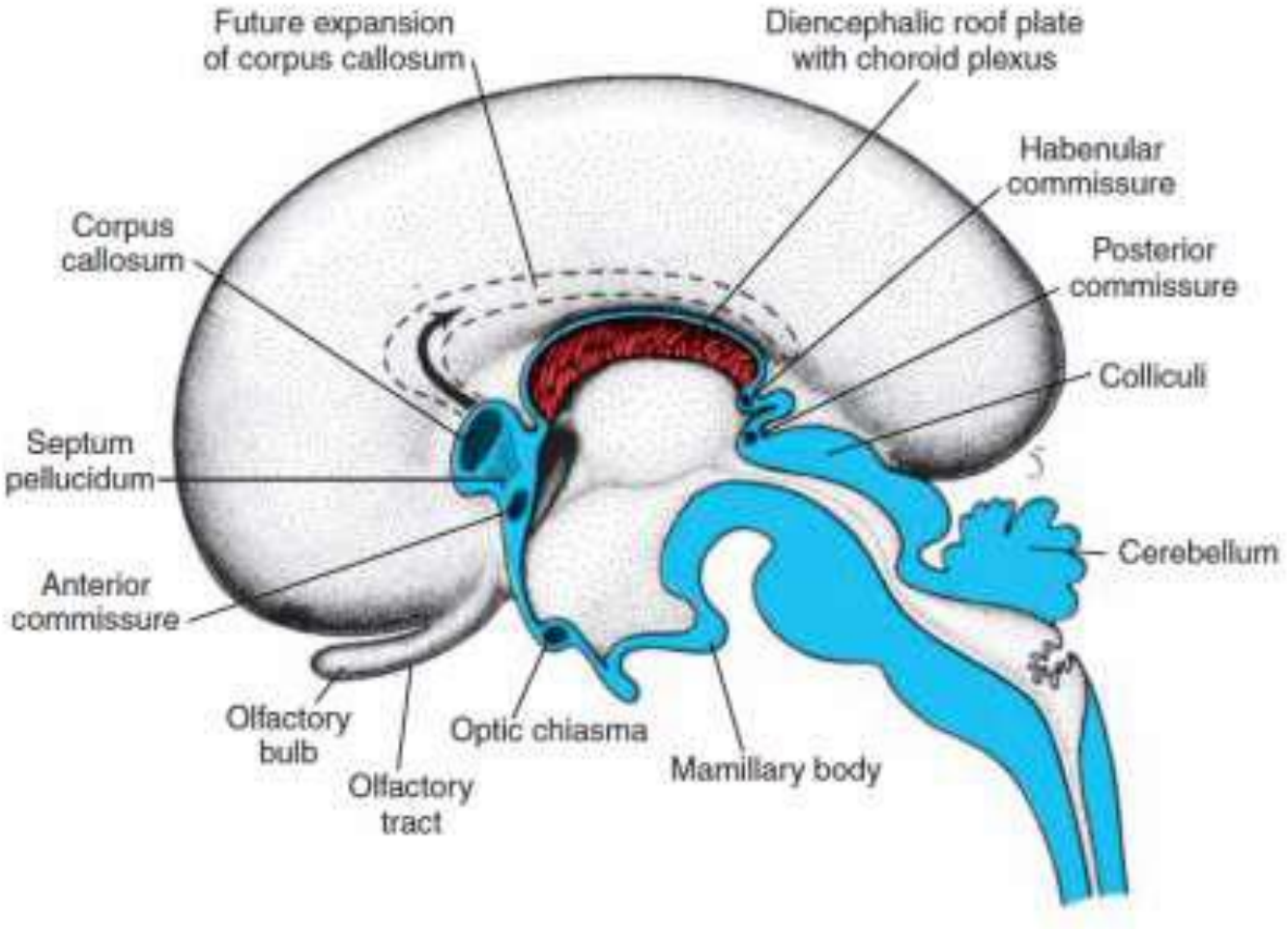

Mesencephalon
Rhombencephalic isthmus
Cerebral hemisphere
Intraventricular portion of rhombic lip
Cut edge of roof of 4th ventricle
Myelencephalon (medulla oblongata)
N. V
N. IX, X, XI
N. XII
Pontine flexure
N. VII, VIII
Olfactory bulb
Diencephalon (hypothalamic region)

10 Weeks Embryo





4 Month Embryo



Development of Cerebral Cortex

- ***In 7th to 9th month embryo:*** The cerebral outpocketings, expand and ***cover the lateral aspect of the diencephalon, mesencephalon, and metencephalon.***

- In addition, due to expanding in all directions, its medial wall becomes thin, flat and it is the site of choroid plexus of the lateral ventricle.

Development of Cerebral Cortex

- Continuous growth of the cerebral hemispheres in anterior, dorsal, and inferior directions results in the formation of ***frontal, parietal, temporal,*** and ***occipital*** lobes, respectively.

- The area between the frontal and temporal lobes becomes depressed and is known as the ***insula***.

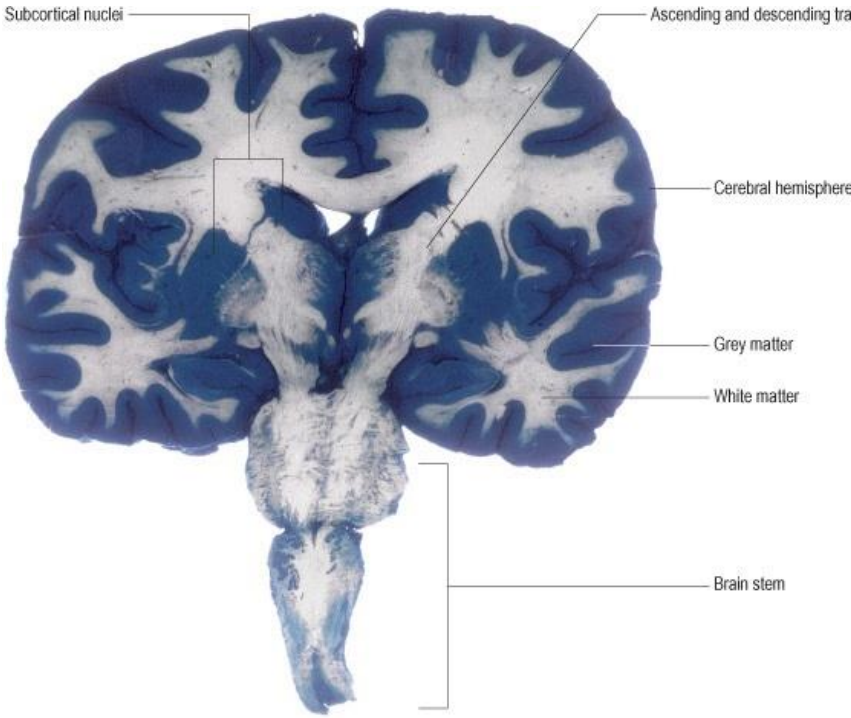
Development of Cerebral Cortex

- ***The wall of the telencephalon is formed of 3 layers:***

1. ***Ependymal*** (lining the cavity of the lateral ventricle.
2. ***Marginal:*** nerve fibers forming the white matter.
3. ***Mantel:*** nerve cells forming the grey matter.

Development of Cerebral Cortex

- ***As development proceeds the following changes occur:***



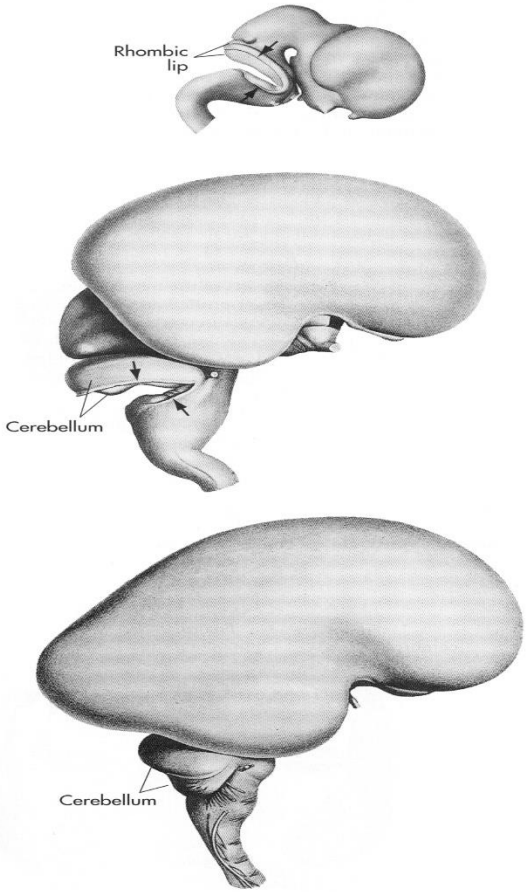
1. Most of the ***nerve cells migrate*** to the ***marginal layer*** forming the cerebral ***cortex***.

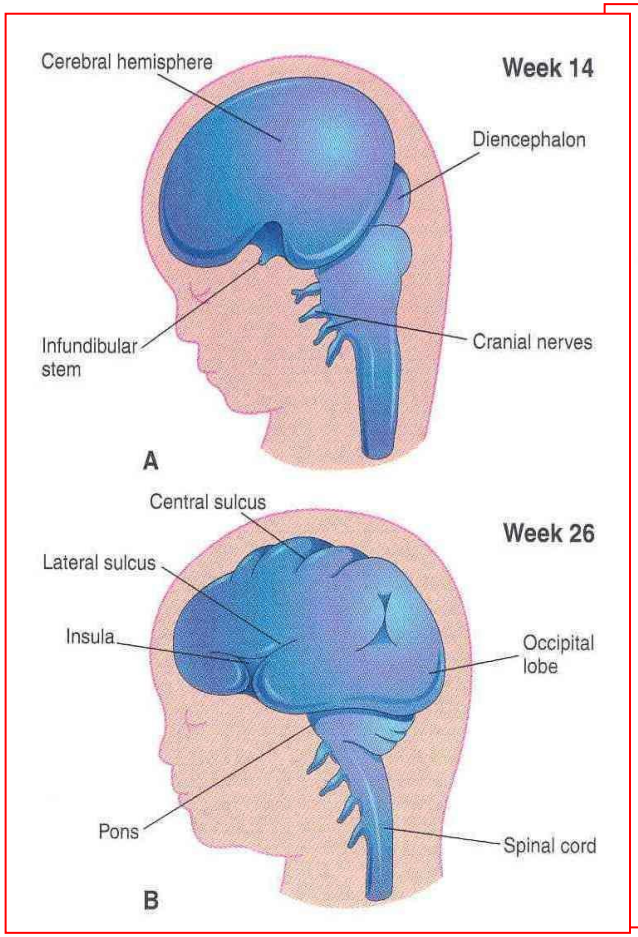
2. Some ***cells do not migrate*** and remains to form the ***basal ganglia***.

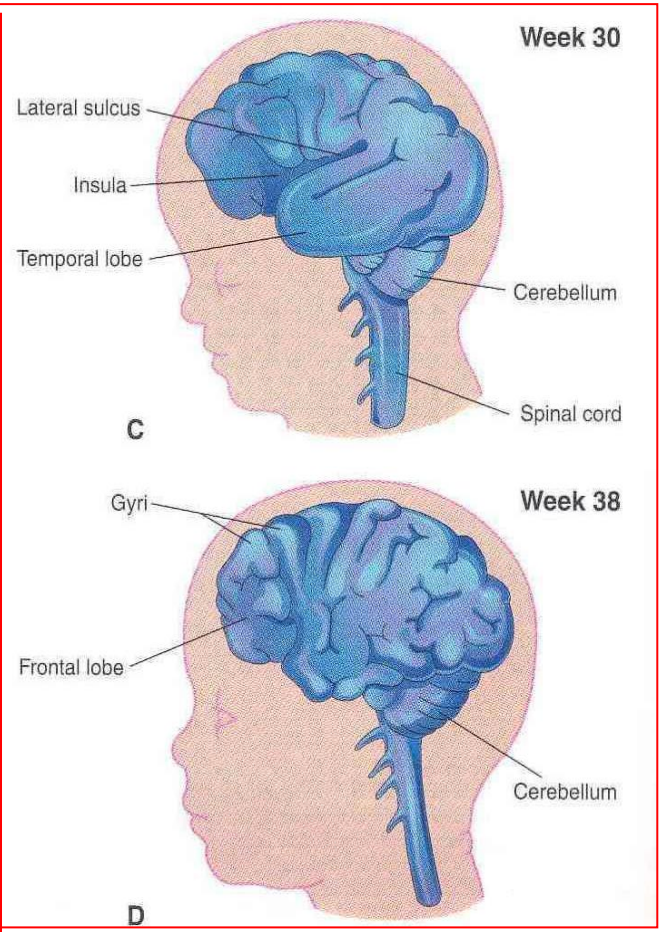
Development of Cerebral Cortex

- By the end of the ***3rd month*** the ***surfaces*** of the cerebral hemispheres ***are smooth***.

- By the ***4th month*** the grey matter grows faster than the white matter, so, the cortex becomes folded into gyri separated by sulci. The ***gyri and sulci*** effectively increase the surface area of the brain.


Rhombic lip
Cerebellum
Cerebellum


Cerebral hemisphere
Week 14
Diencephalon
Infundibular stem
Cranial nerves
A
Central sulcus
Week 26
Lateral sulcus
Insula
Occipital lobe
Pons
Spinal cord
B


Week 30
Lateral sulcus
Insula
Temporal lobe
Cerebellum
Spinal cord
C
Gyri
Week 38
Frontal lobe
Cerebellum
D

Development of the Diencephalon

- ***Consists of roof plate & 2 alar laminae without floor plate or basal laminae (thalamus has no motor efferent fibers).***

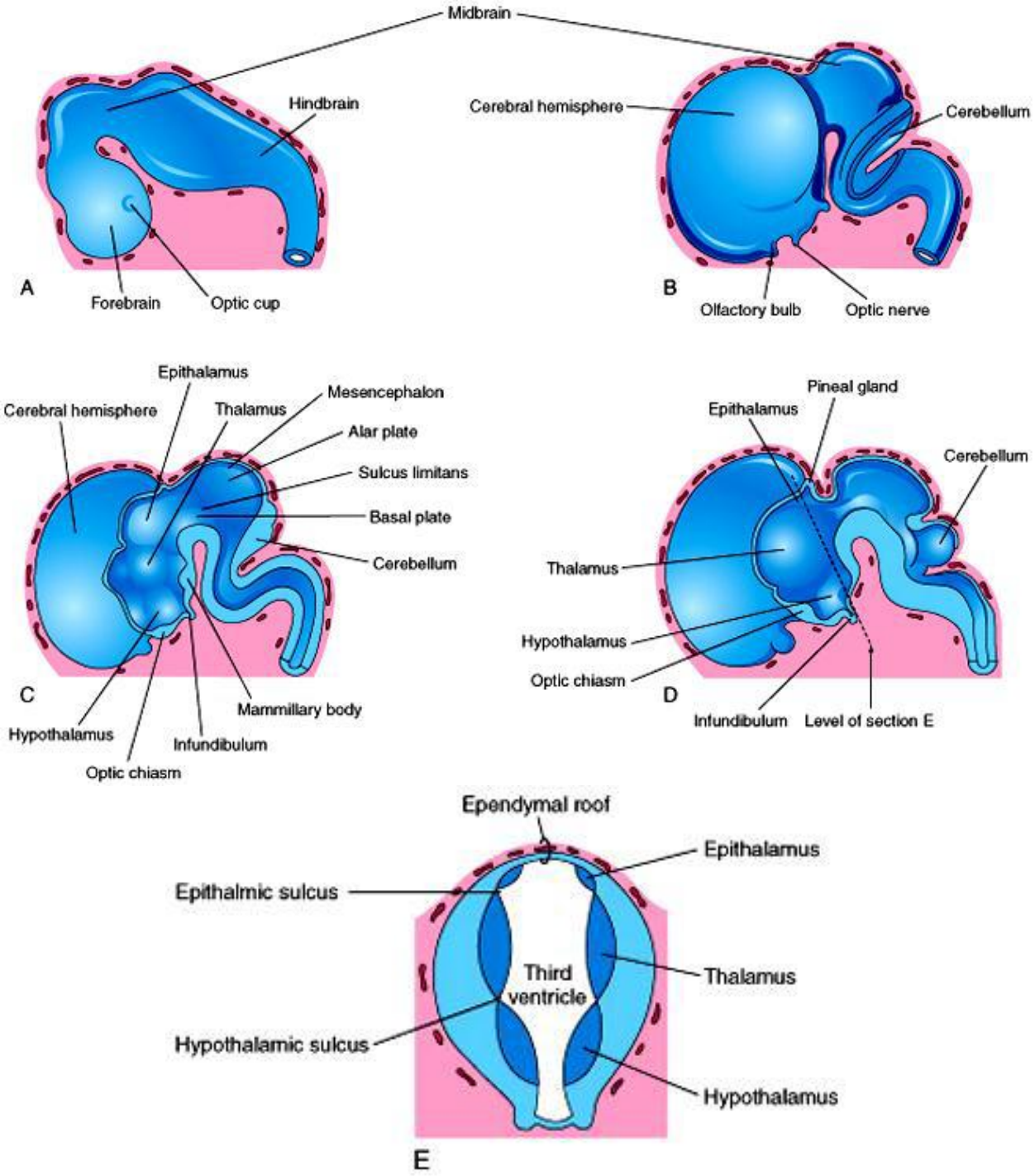
- Its cavity: ***the 3rd ventricle***

- Its alar lamina becomes divided by a **hypothalamic sulcus** into thalamus & hypothalamus.

Development of the Diencephalon

- Thus, the hypothalamic sulcus does not correspond to the sulcus limitans.

- An evagination of the roof plate leads to the pineal body. The rest of the roof plate (ependyma) is covered by vascular mesenchyme that forms the ***choroid plexus of 3rd ventricle.***


Midbrain
Hindbrain
Forebrain
Optic cup
A
Cerebral hemisphere
Cerebellum
Olfactory bulb
Optic nerve
B
Epithalamus
Cerebral hemisphere
Thalamus
Mesencephalon
Alar plate
Sulcus limitans
Basal plate
Cerebellum
Mammillary body
Hypothalamus
Infundibulum
Optic chiasm
C
Pineal gland
Epithalamus
Cerebellum
Thalamus
Hypothalamus
Optic chiasm
Infundibulum
Level of section E
D
Ependymal roof
Epithalamus
Epithalmic sulcus
Third ventricle
Thalamus
Hypothalamic sulcus
Hypothalamus
E

Development of the Diencephalon

1. ***Pineal gland:*** sleep-wake cycle, secretes melatonin

2. ***Epithalamus:*** masticatory and swallowing functions

3. ***Thalamus:*** major relay of sensory input to cerebral cortex

Development of the Diencephalon

4. ***Hypothalamus:*** master regulatory center (autonomic and endocrine) and also limbic system (emotion & behavior)

5. ***Hypophysis/infundibulum***: posterior pituitary gland, secretes ADH and oxytocin

6. ***Optic cup:*** retina of eye

Ventricular System

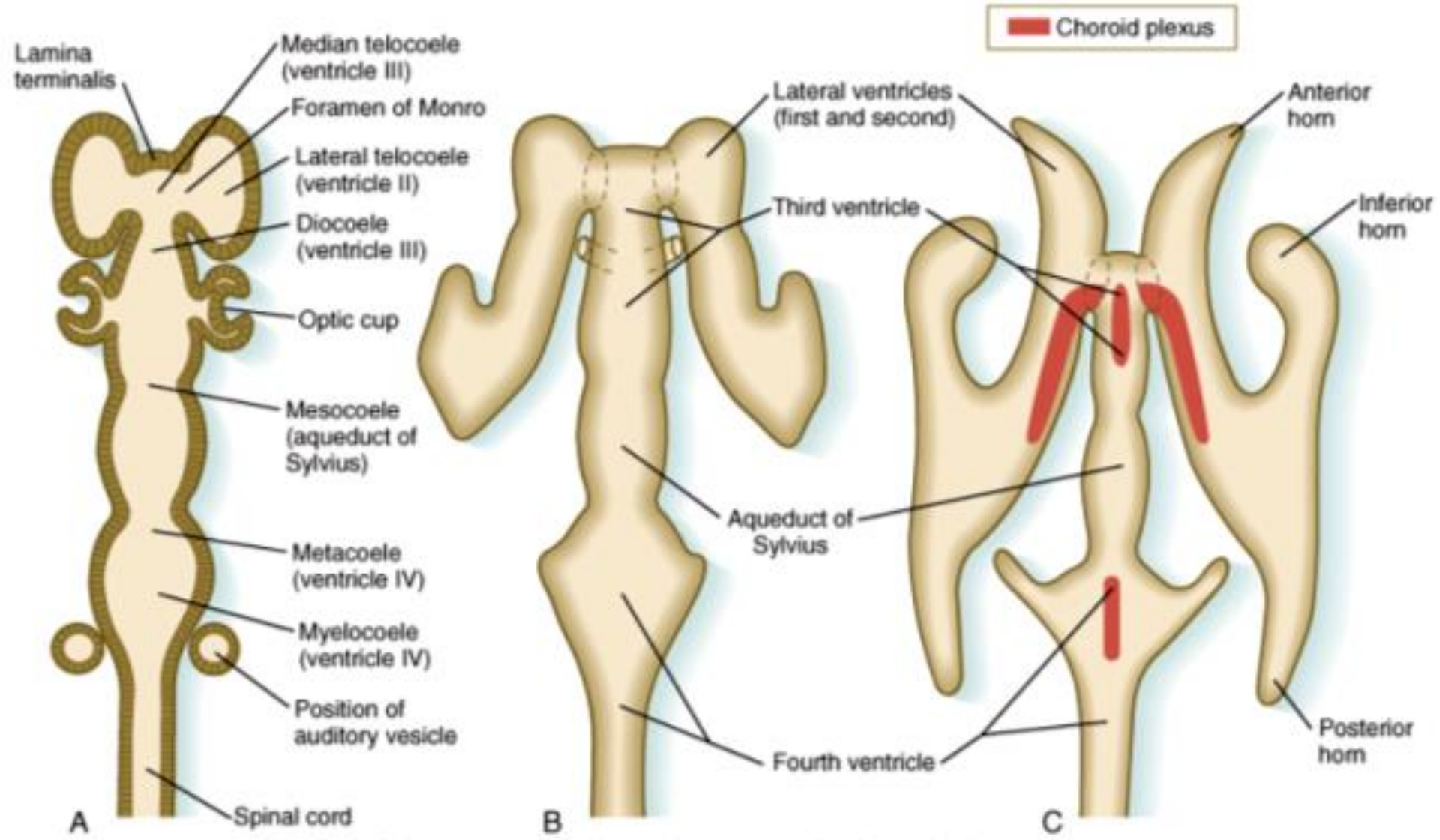
- **The lumen of the spinal cord, the central canal, is continuous with that of the brain vesicles.**

- The cavity of the ***rhombencephalon*** is the ***fourth ventricle***, that of the ***diencephalon*** is the ***third ventricle***, and those of the ***cerebral hemispheres*** are the ***lateral ventricles***.

Ventricular System

- The ***lumen*** of the ***mesencephalon*** connects the ***third*** and ***fourth ventricles***.

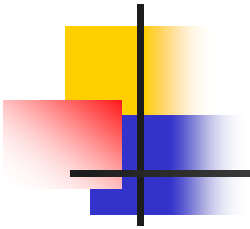
- This lumen becomes very narrow and is then known as the ***aqueduct*** of ***Sylvius***. Each lateral ventricle communicates with the third ventricle through the interventricular foramina of Monro .



- For further inquiries ***PLZ*** feel free to contact at any time through email

gamaltaha@med.asu.edu.eg

gamal.abdelhady@yu.edu.jo



Thank You