Nervous system

CNS

Brain

Spinal chord

PNS

Nerves

ganglia

1. White matter
2. Grey matter
3. Dendrite
4. Axon
5. Myelin
6. Neuropil

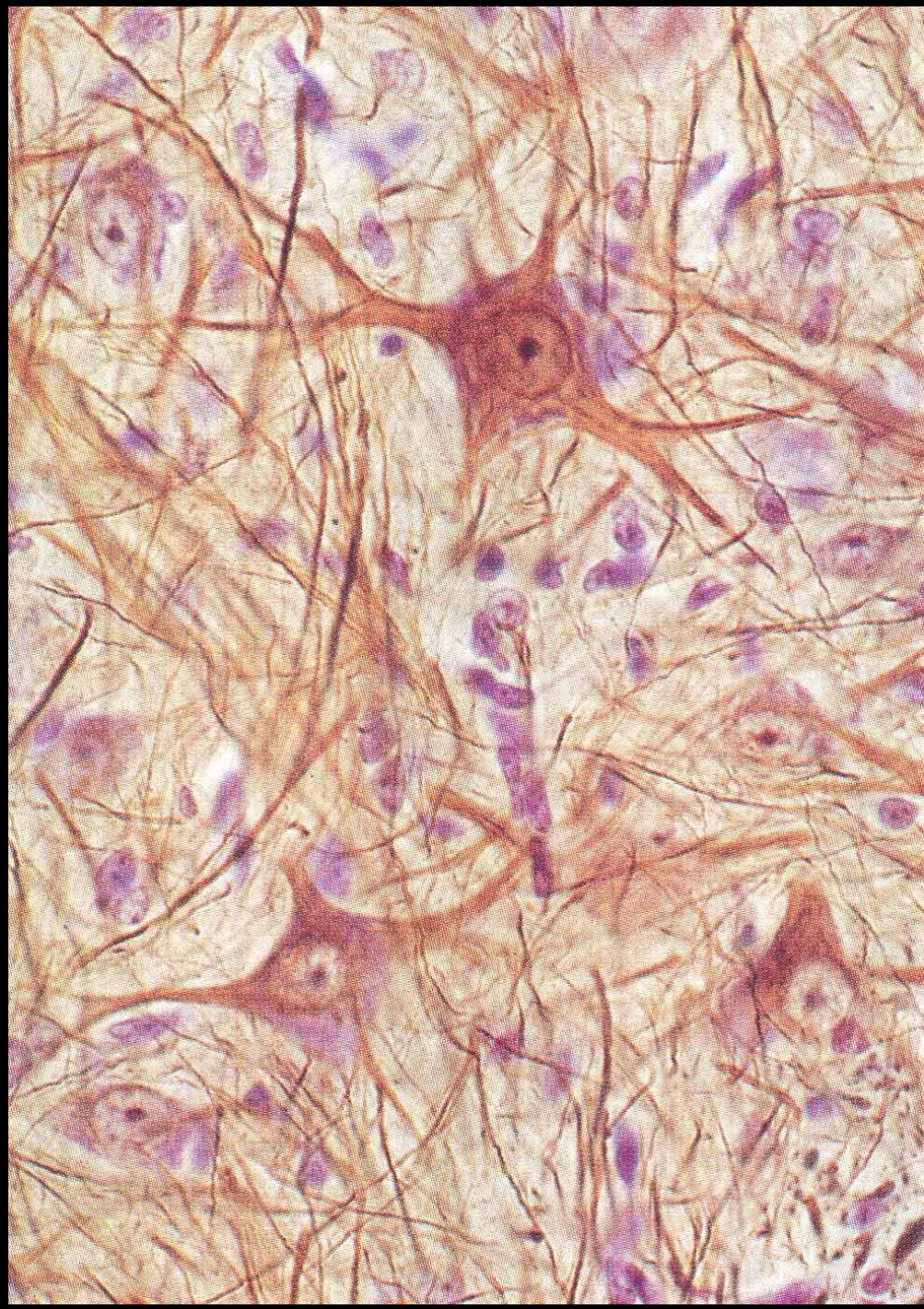
a) Can be either myelinized or non-myelinized
b) Is predominantly composed of neuronal processes
c) A mesh of glial and neuronal processes in the grey matter
d) Contains both cellular bodies and processes
e) Is practically always nonmyelinized
f) Lipid layer improving the conduction of signal along the axon

Cells

- neurons
- glial cells (neuroglia)

Extracelular matrix

- A little amount between the cells



GLIA

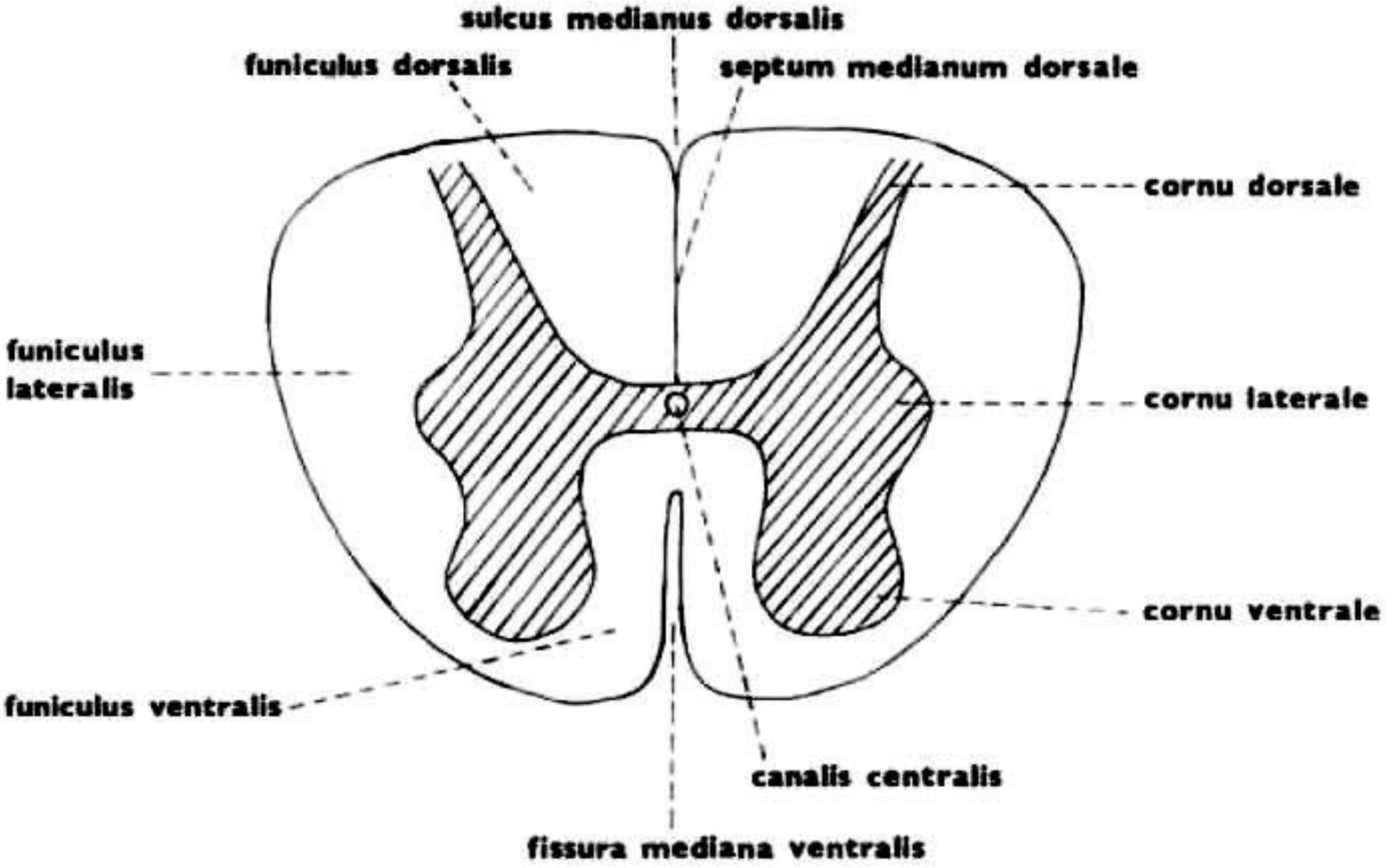
1. Neuroglia in CNS

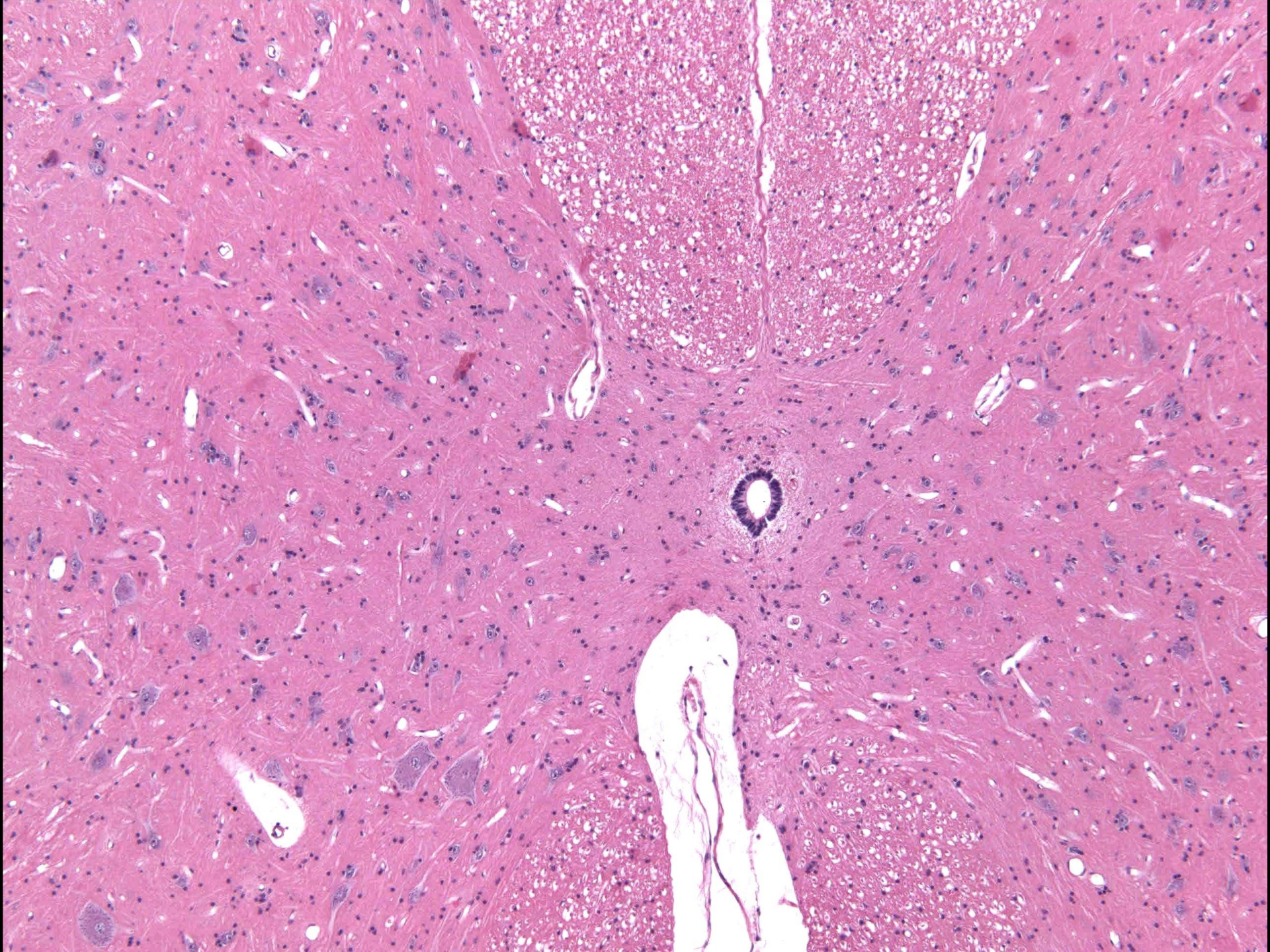
- **1. ependyma**
- **2. astrocytes**
  - **1. protoplasmic (grey matter)**
  - **2. fibrilar (white matter)**
- **3. oligodendrocytes (myelinization of axons)**
- **4. microglia**

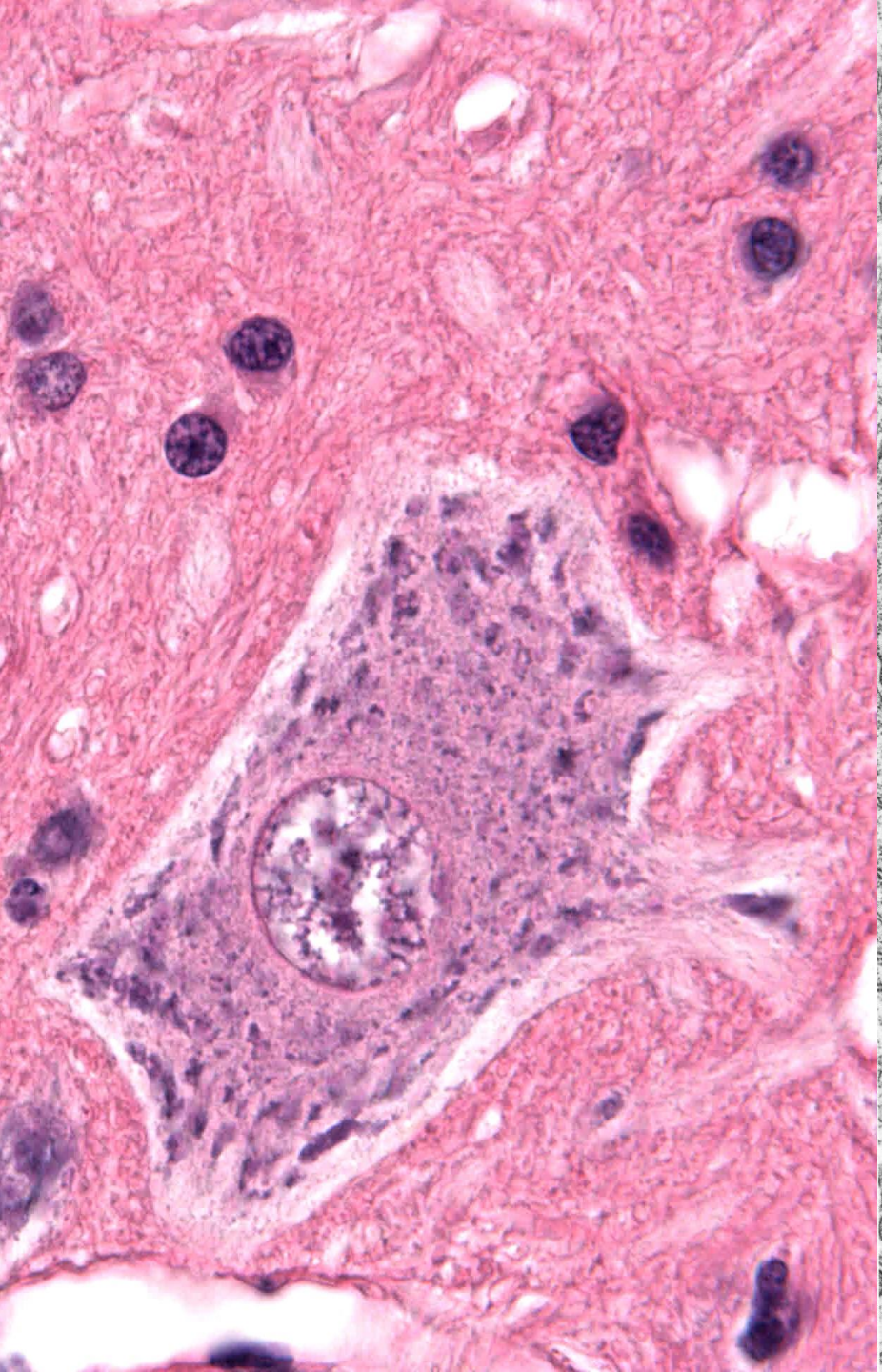
2. Neuroglia v PNS

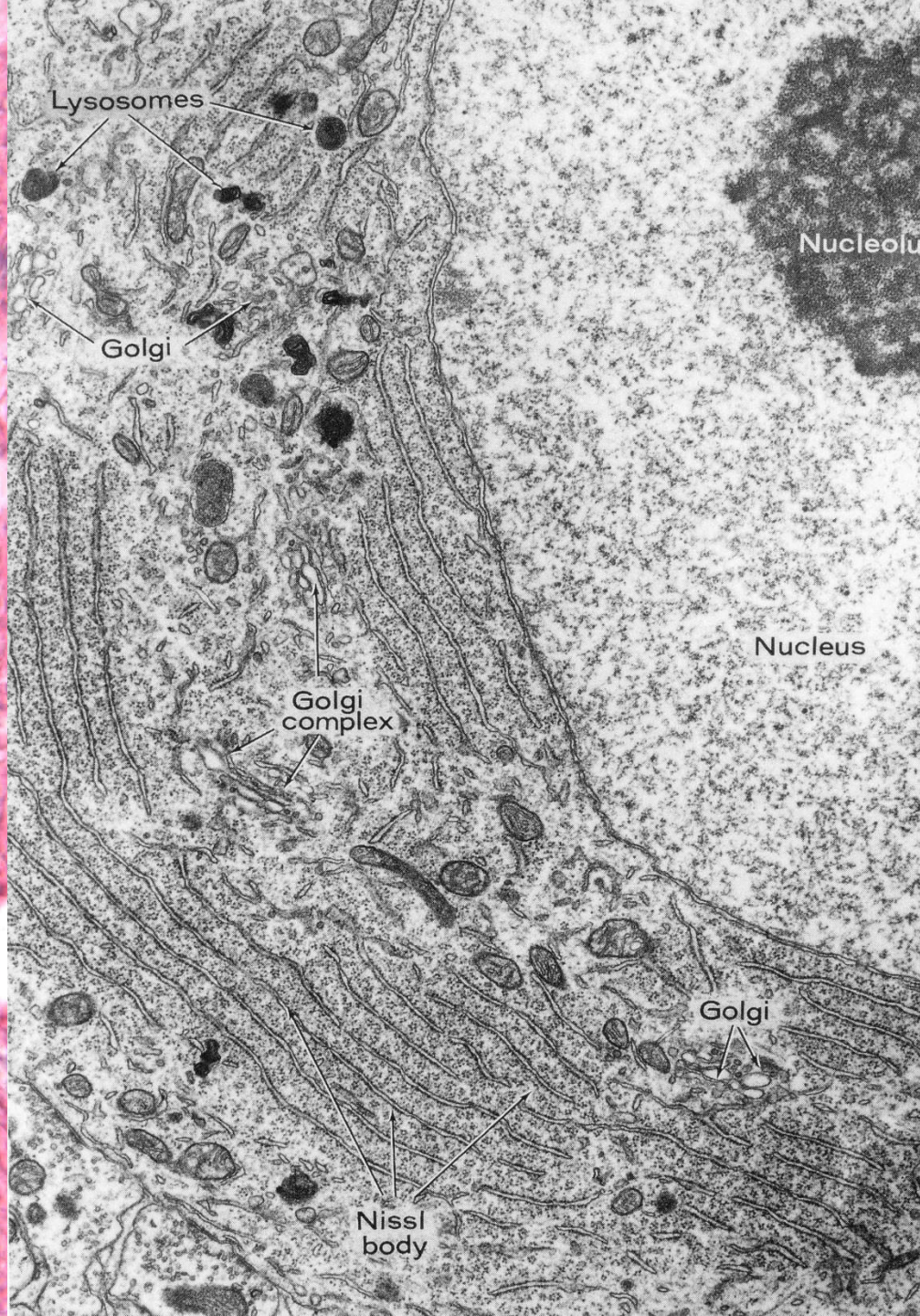
- **1. Schwann cells (myelinization of axons)**
- **2. satelite cells (cerebrospinal a autonomic ganglia)**

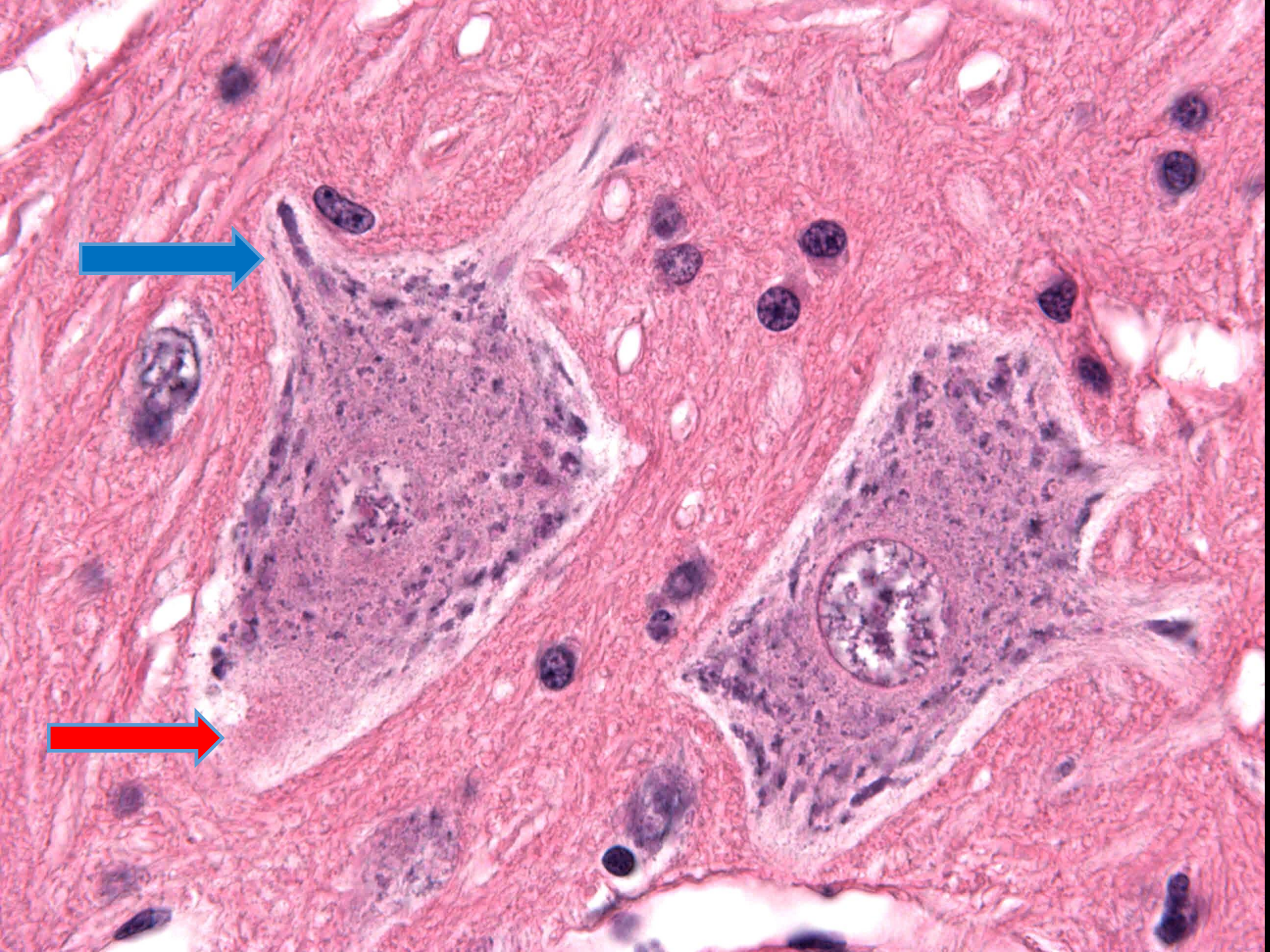
MEDULLA SPINALIS

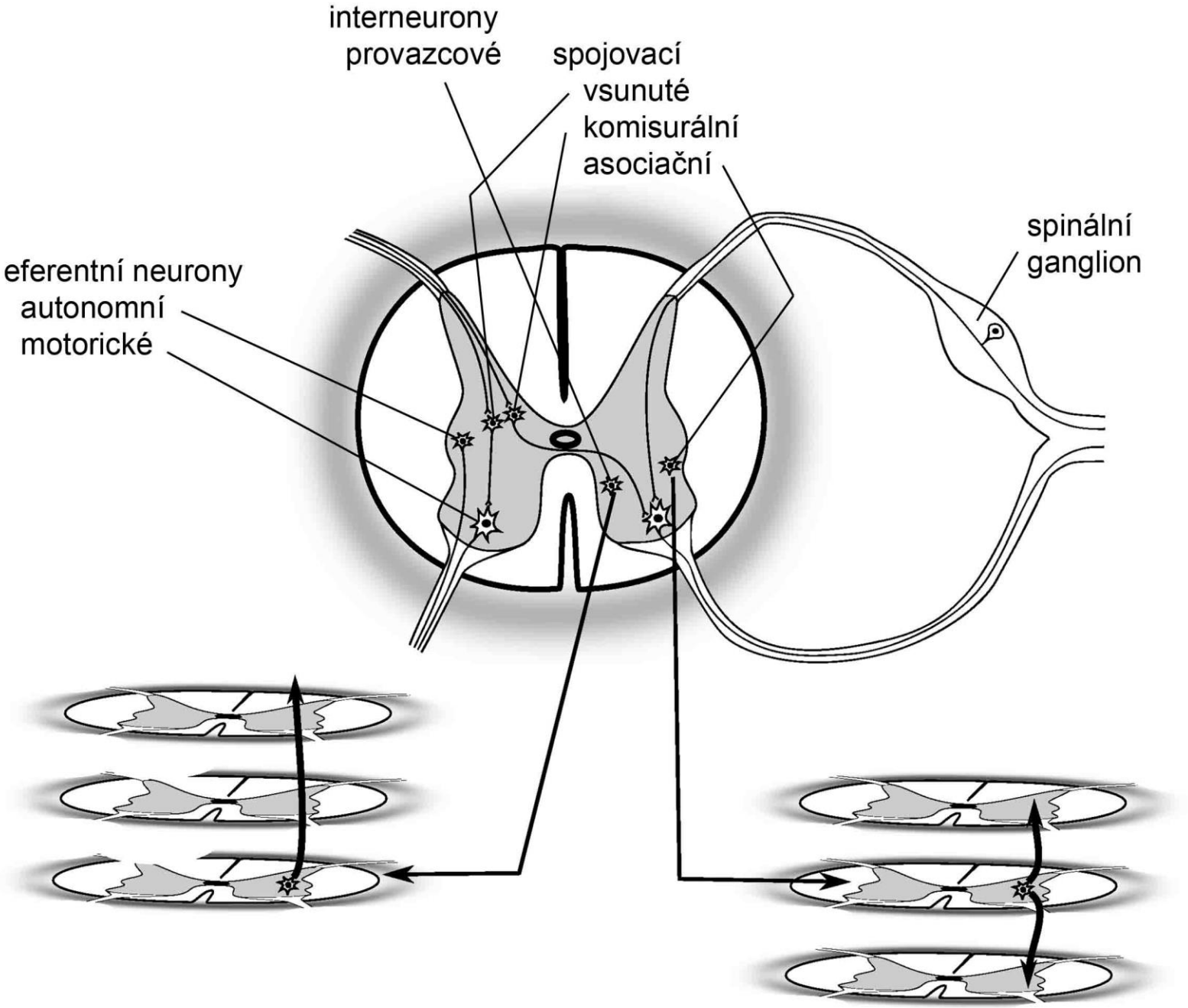







Lysosomes
Nucleolu
Golgi
Nucleus
Golgi
complex
Golgi
Nissl
body



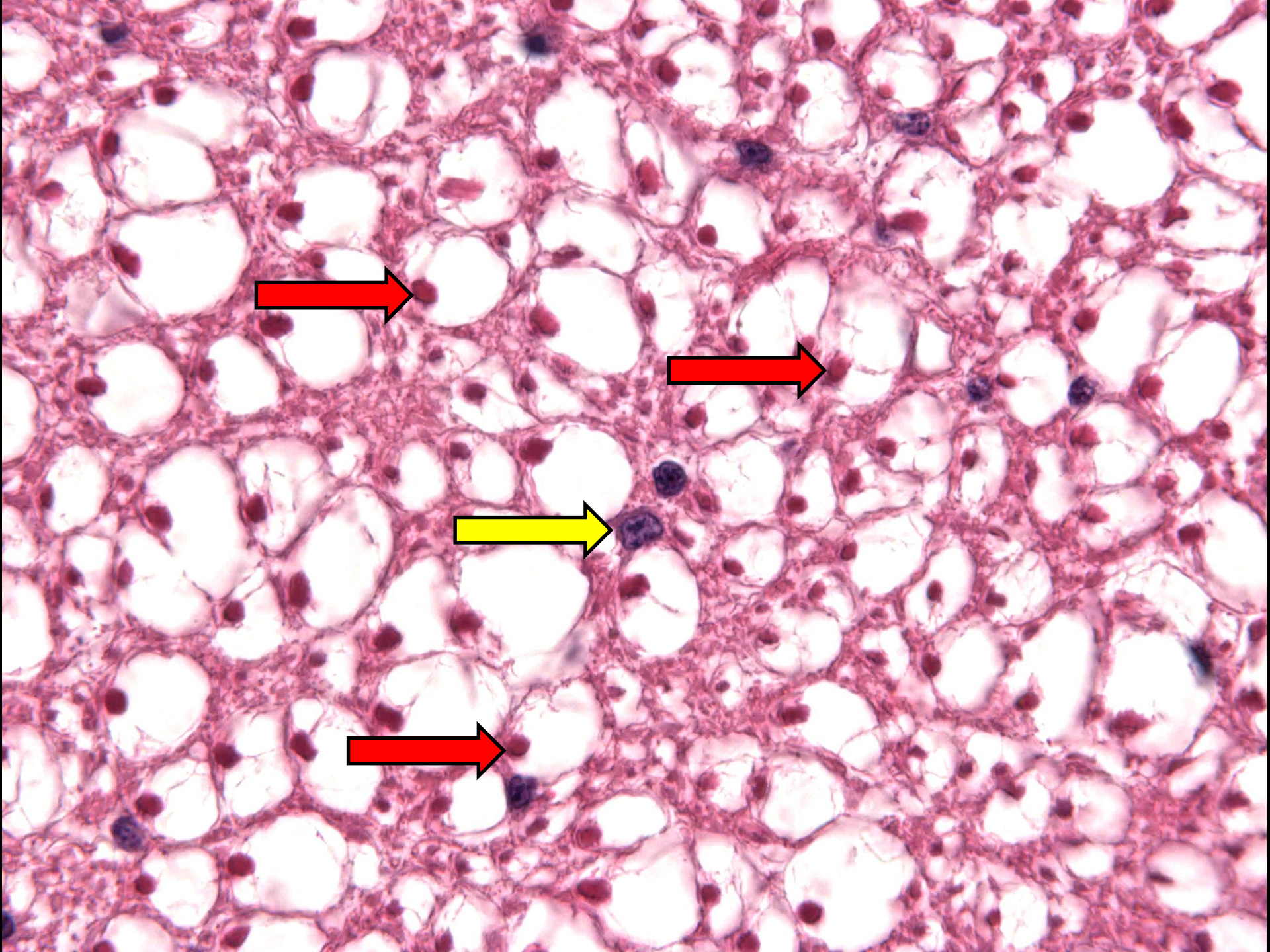

interneurony
provazcové
spojovací
vsunuté
komisurální
asociační
spinální
ganglion
eferentní neurony
autonomní
motorické

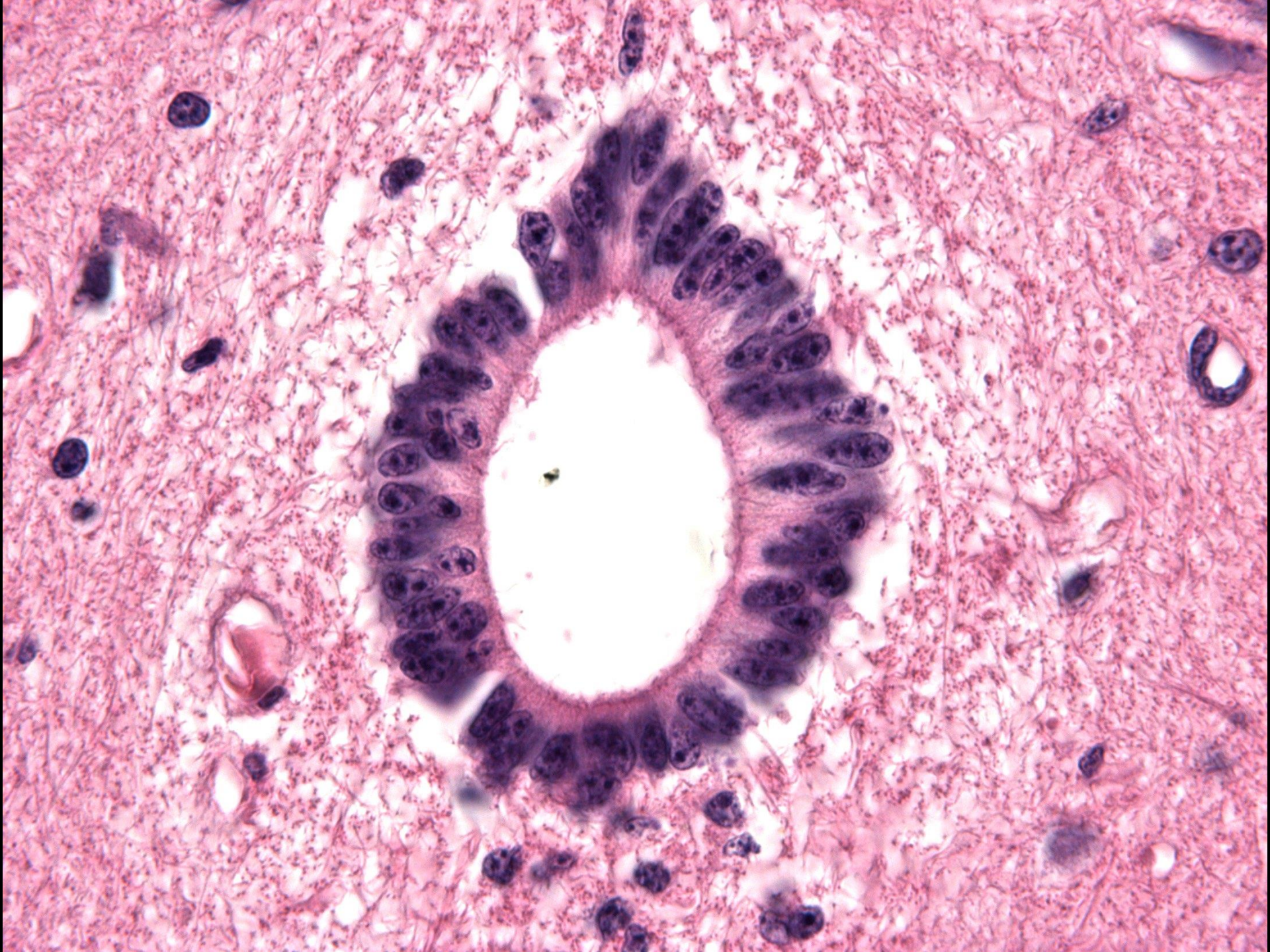
Quiz

1. Which viral disease affects the mononeurons of the spinal cord? Is it prevalent?

2. Which two neurons take part in the simplest reflex arches?

3. Which part of the brain or the spinal cord is affected by the multiple sclerosis? Which cranial nerve is often affected?

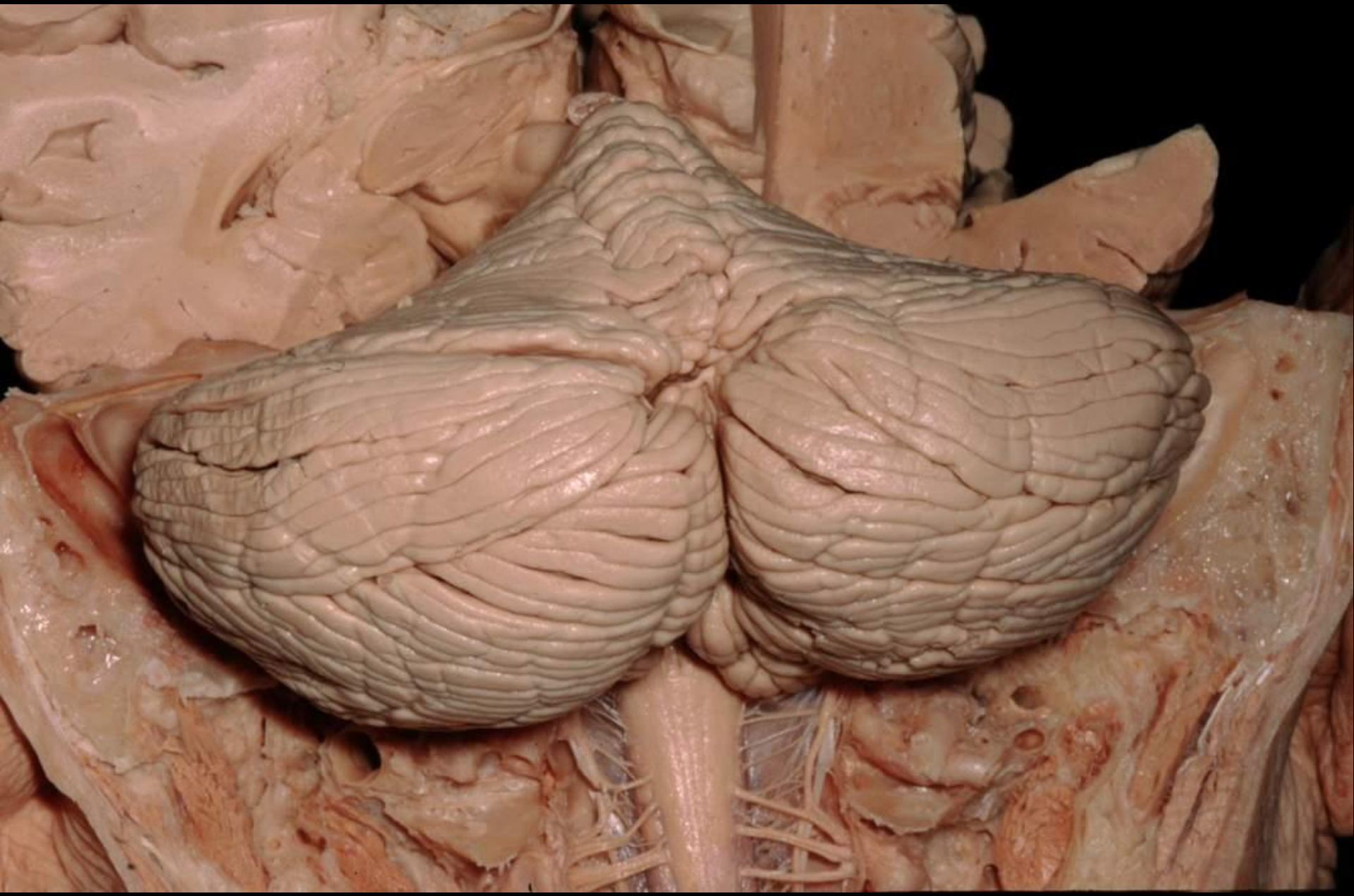


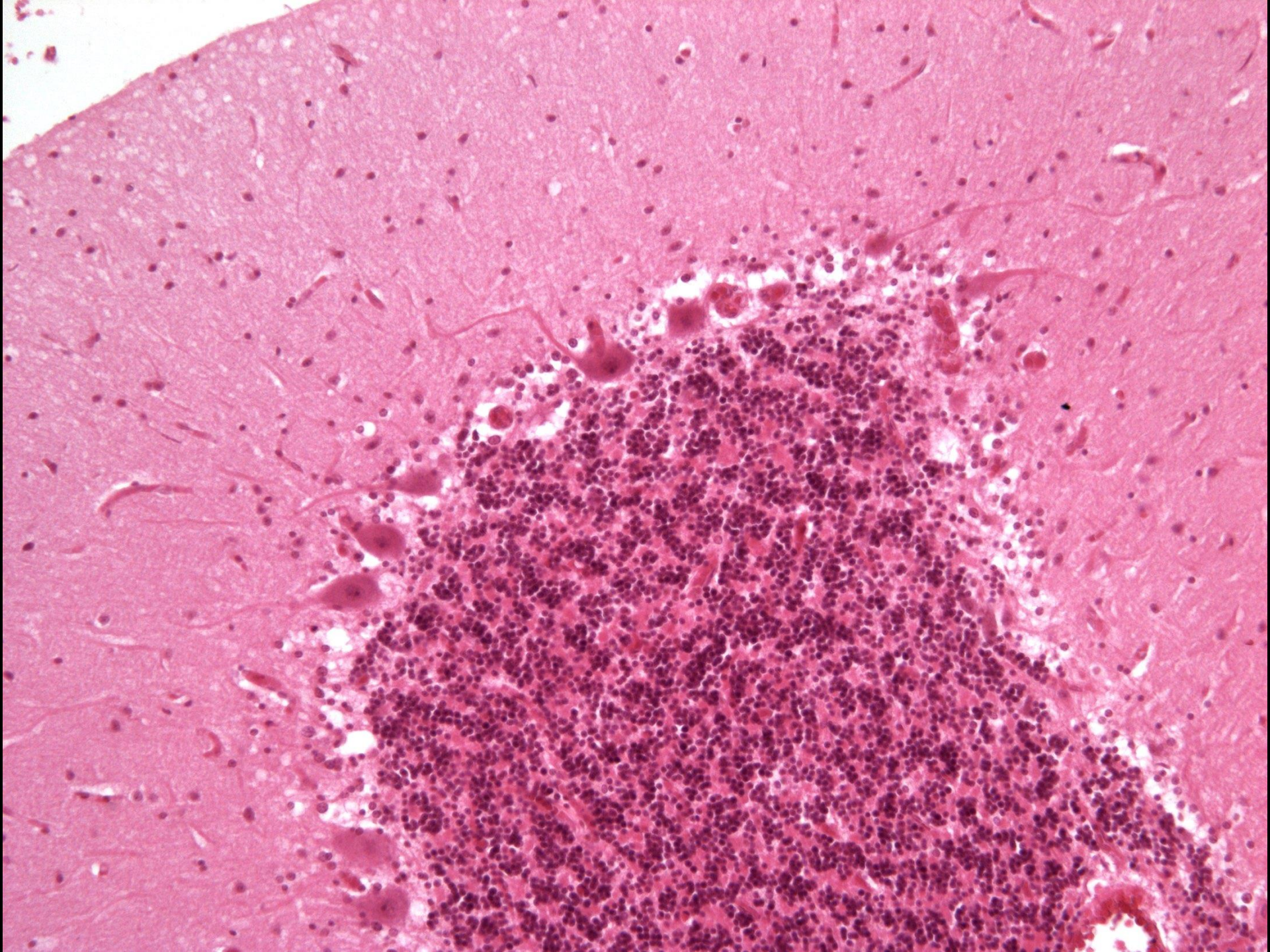


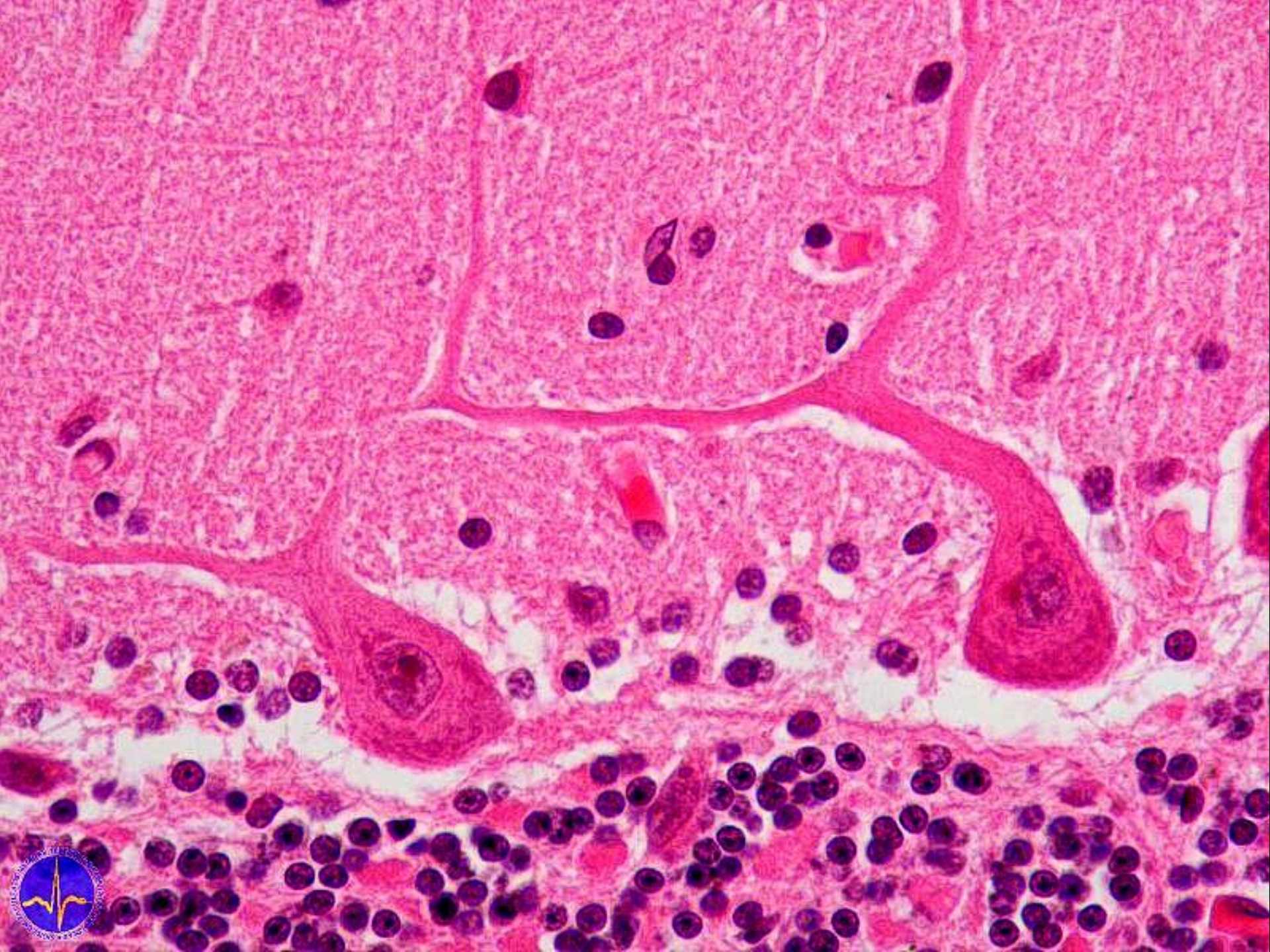
Spinal cord– summary

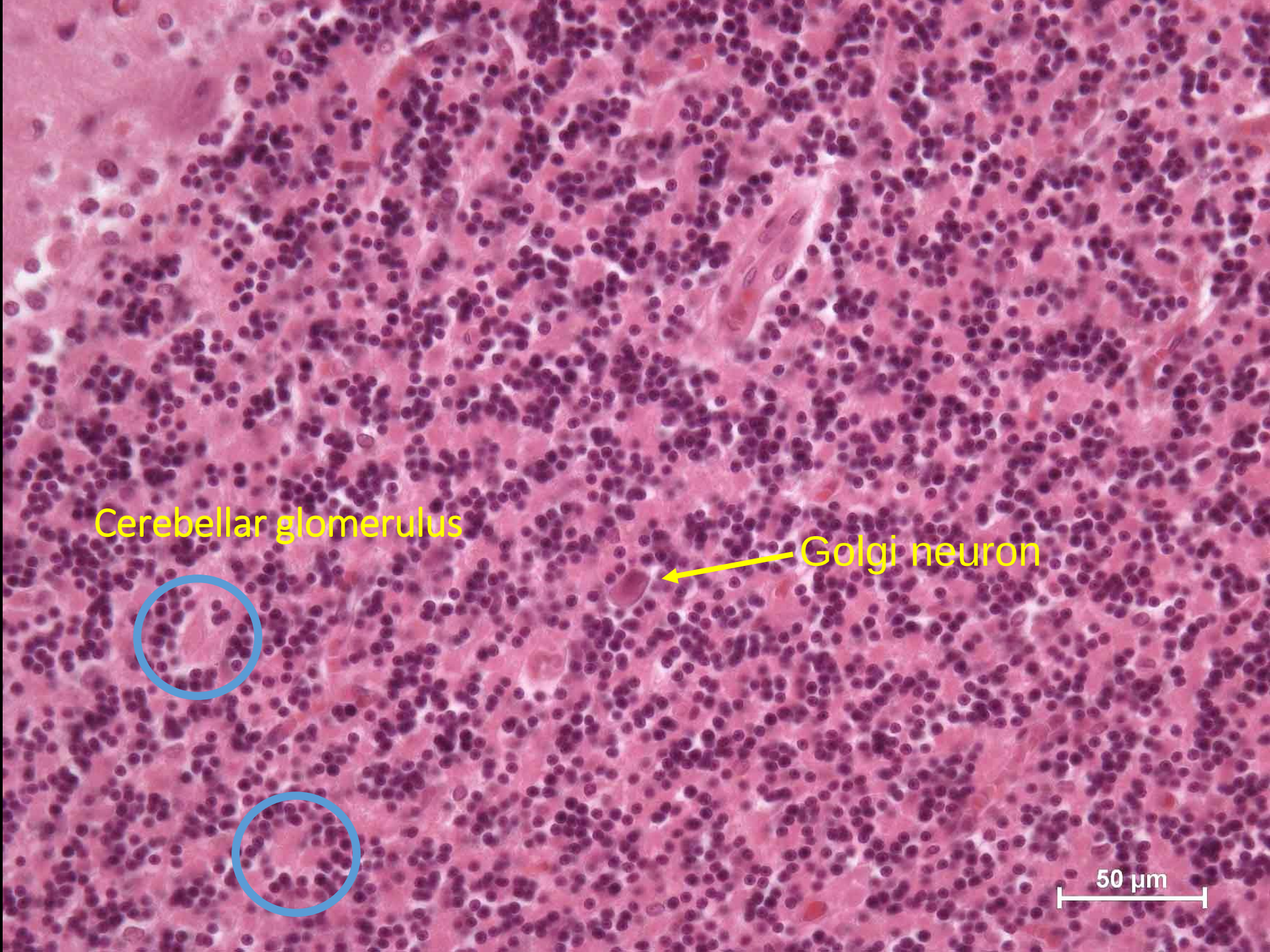
- The **white matter** is divided into **funiculi** dorsales, ventrales and laterales
- The **gray matter** contains bodies of neurons (many types of interneurons and motor neurons), we can divide it into anterior and posterior horns and intermediate zone (or in a more complex way into the Rexed laminae)
- The **interneurons** have a lot of functions (e.g. reflexes, coordination, relay of sensitive information…), the motor neurons directly control the muscles
- The **central canal** is lined by **ependyma**, these cells look like epithelium but they have some differences, for example they do not have a basal lamina

Cerebellum

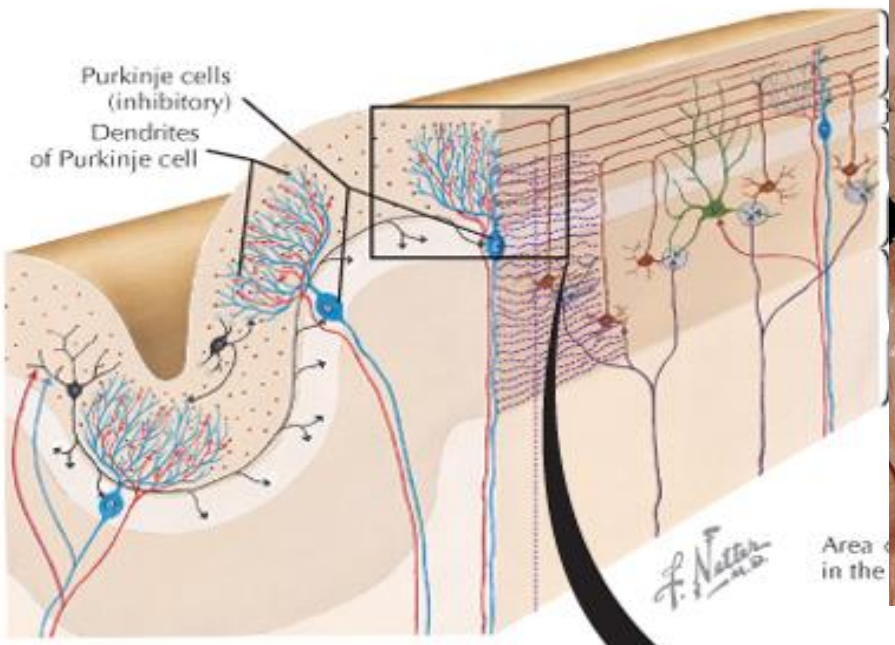


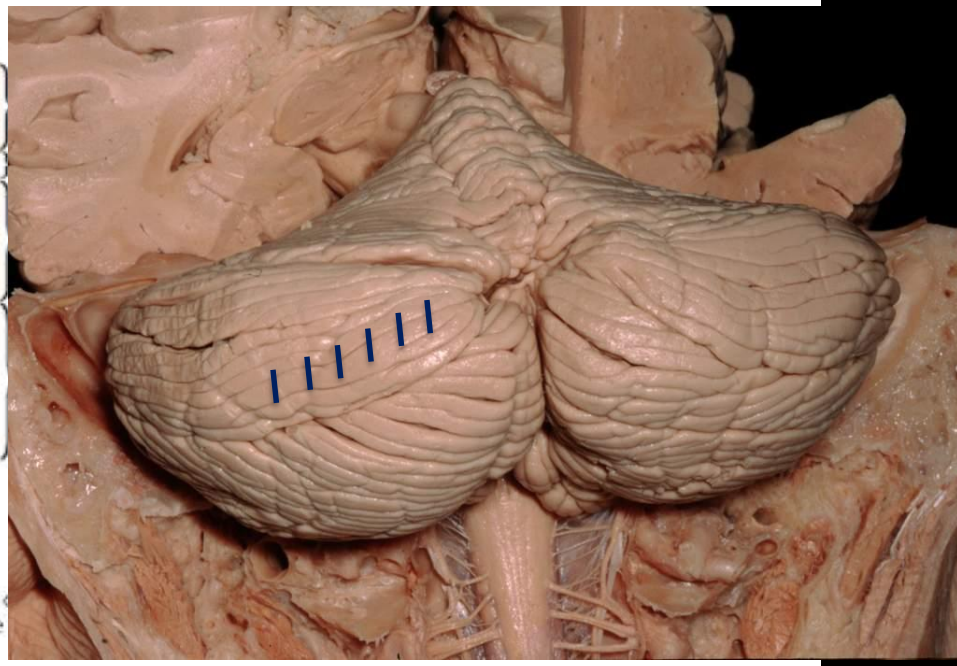





Cerebellar glomerulus
Golgi neuron
50 µm

▼ Types of neurons in the cerebellar cortex.

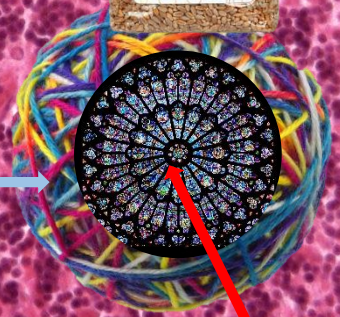




► **Immunocytochemical staining of Purkinje cells in the cerebellar cortex.** An antibody to parvalbumin selectively labels Purkinje cells, so that their cell bodies, basal axons, and elaborate apical fan-like dendritic tree are clear. 135×. *Immunoperoxidase-diaminobenzidine. (Courtesy of Dr. K. G. Baimbridge)*


SCI


CountryLife
Bio
PŠENICE
OZIMÁ



Cerebellum summary

Cortex cerebelli

- Stratum **moleculare** – basket and stellate cells
- Stratum **gangliosum** – Purkinje cells
- Stratum **granulare** – Golgi cells, granule cells

White matter

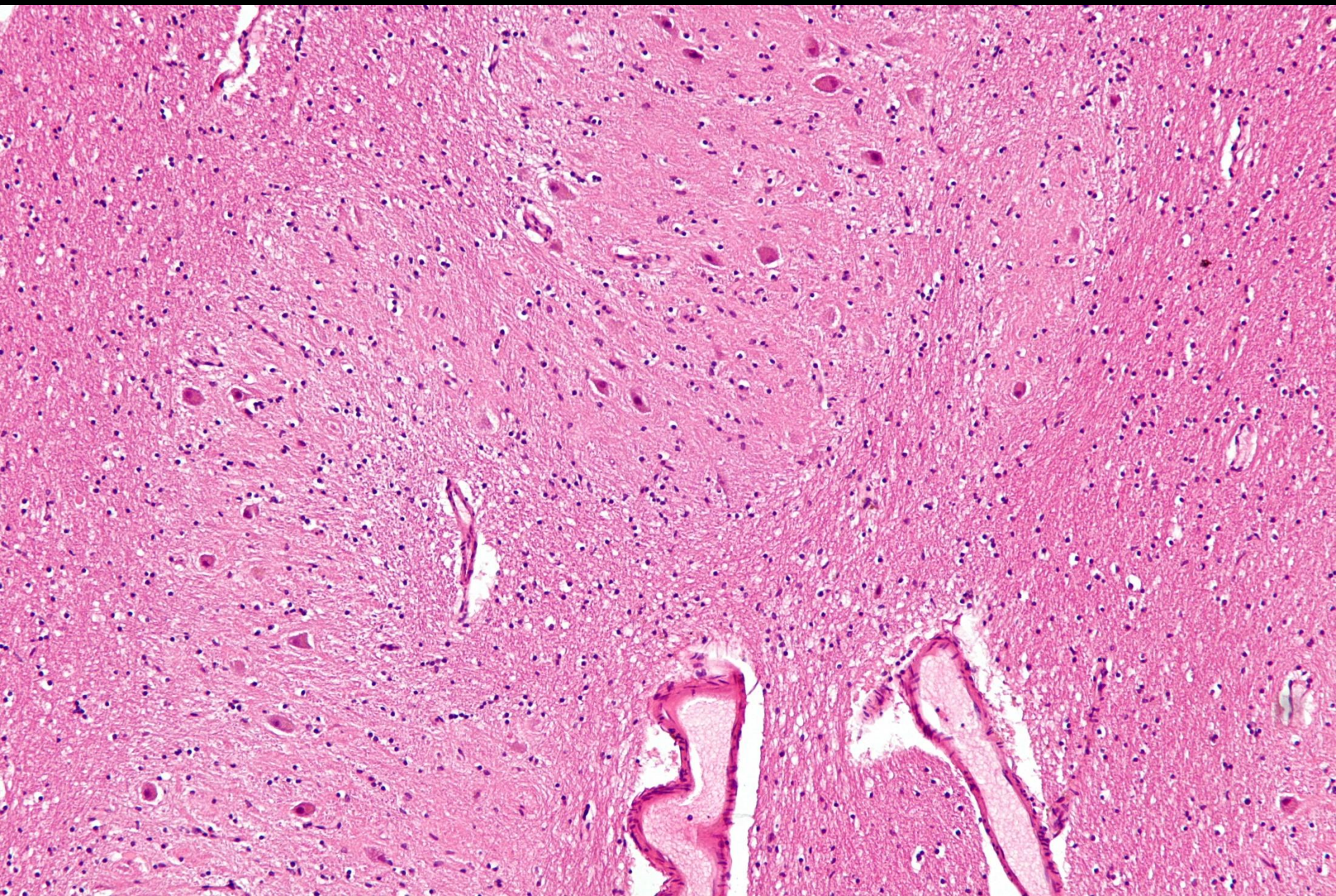
- Mossy fibers (most originate in nuclei pontis), climbing fibers (most originate in oliva inferior)
- **Purkinje cells axons** projecting to the cerebellar nuclei
- Axons of neurons from cerebellar nuclei

Nuclei of cerebellum

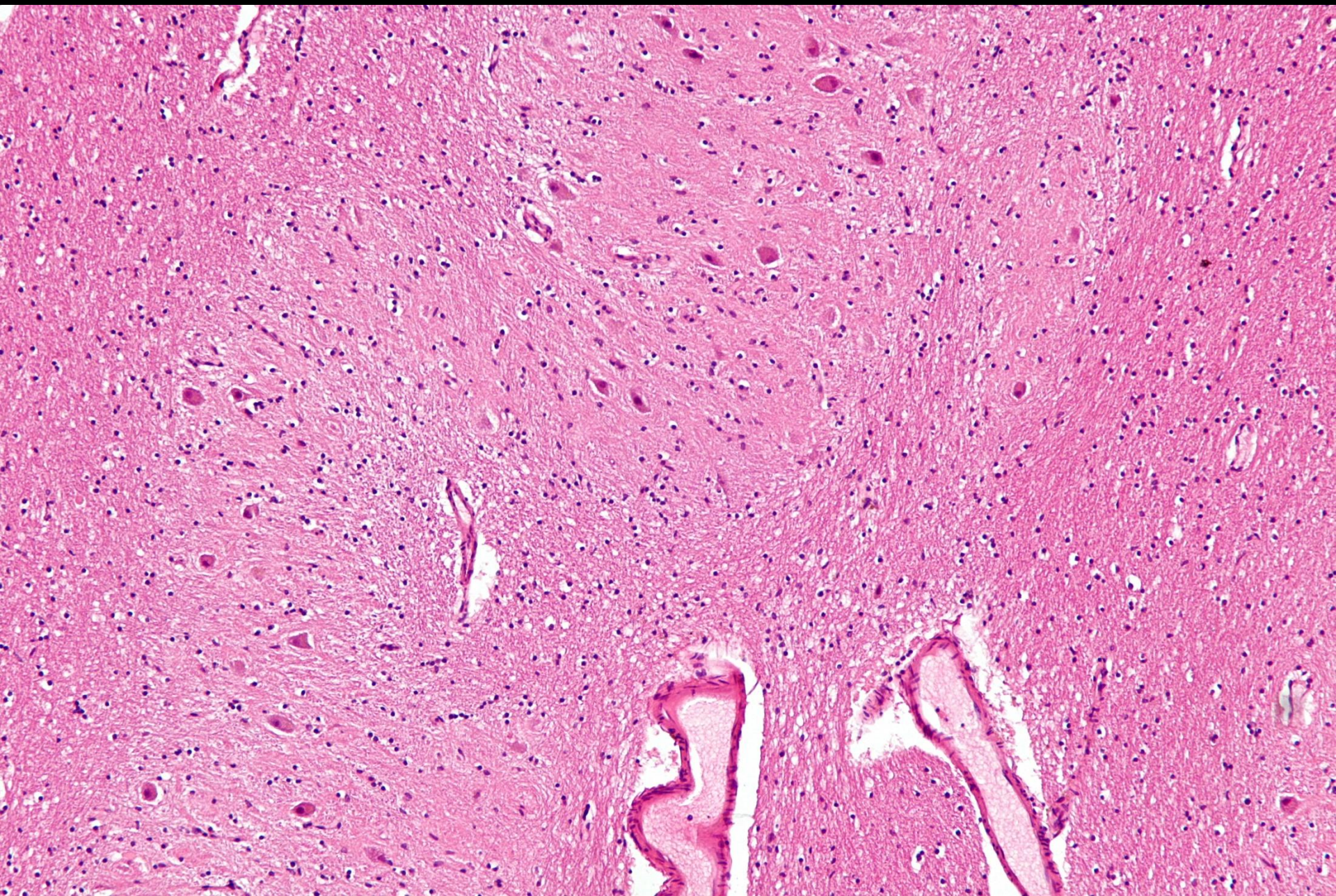
- Nucleus fastigii, nc. emboliformis, nc. globosus, nc. dentatus

5 neuron types, 4 nuclei, 3 cortical layers, 2 fiber types, 1 output

What is this?



Nucleus dentatus (from en.wikipedia.org)



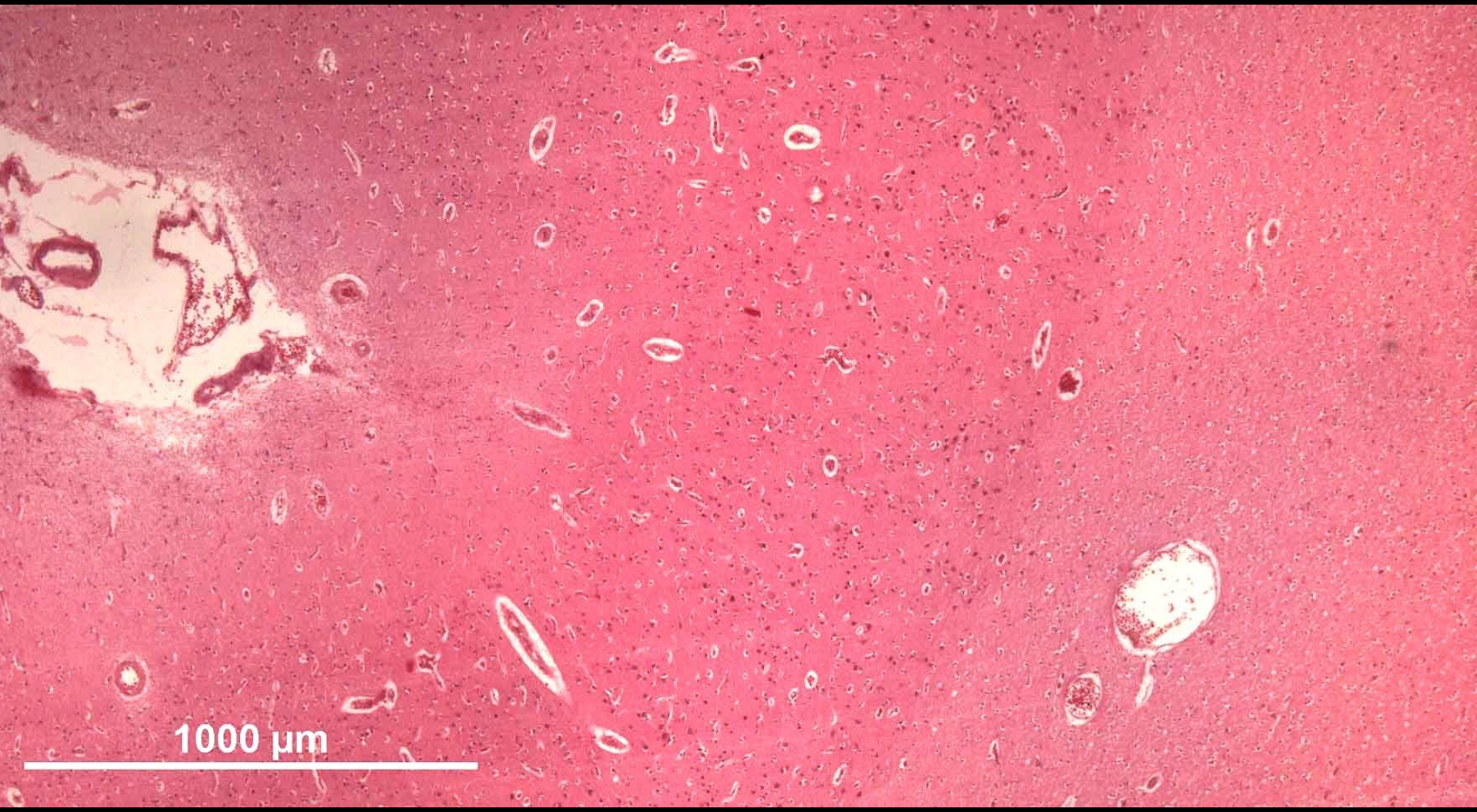
Quiz

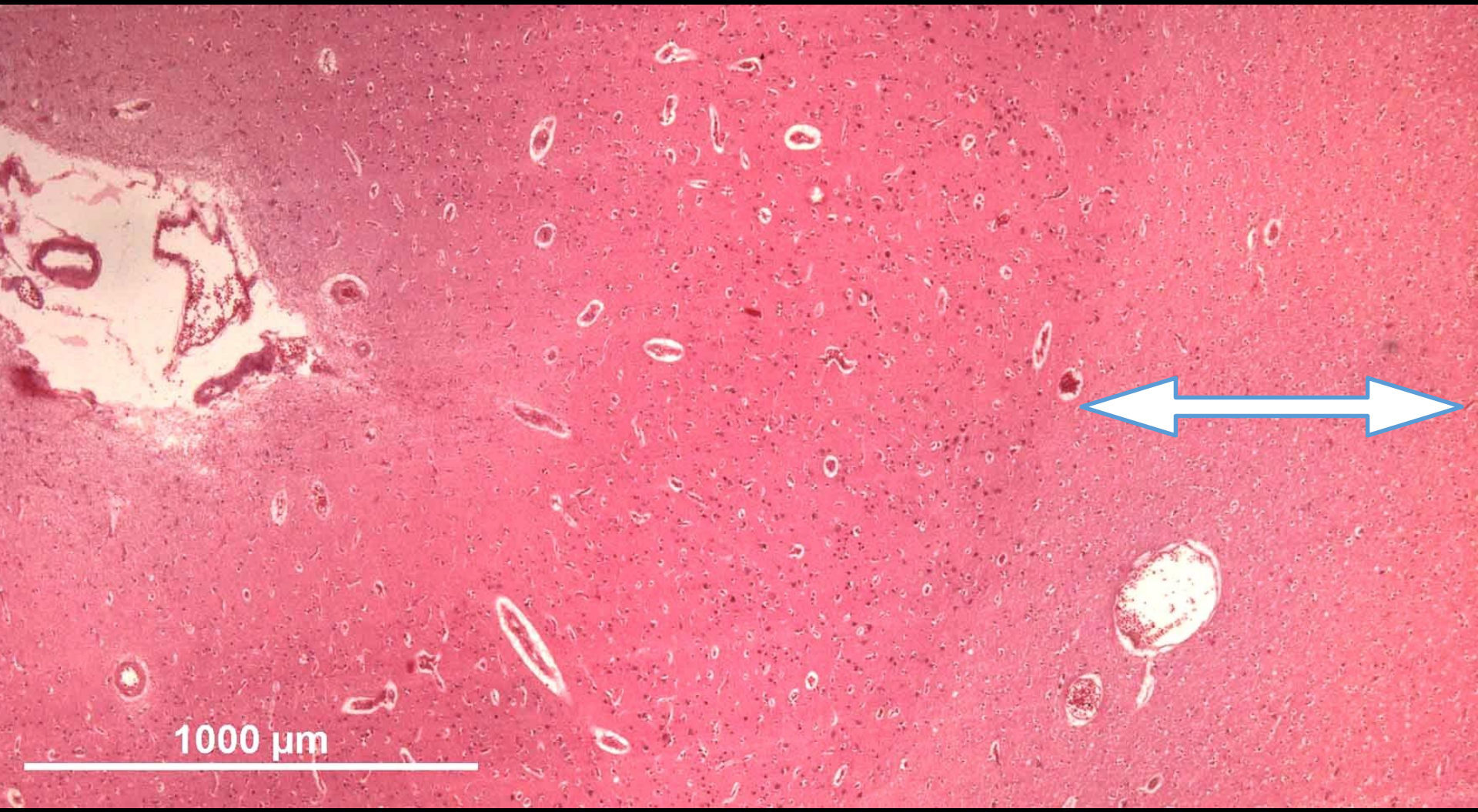
1. Order by number of the Purkinje cells, with which they form synapses: climbing fibers, basket cells, mossy fibers, parallel fibers

2. How does the cerebellar damage manifest clinically? Which commonly used addictive substance can cause the cerebellar syndrome?

3. What is the translation of the Latin words glomus and glomerulus? Try to list some structures of human body with this name.

Telencephalon


1000 µm

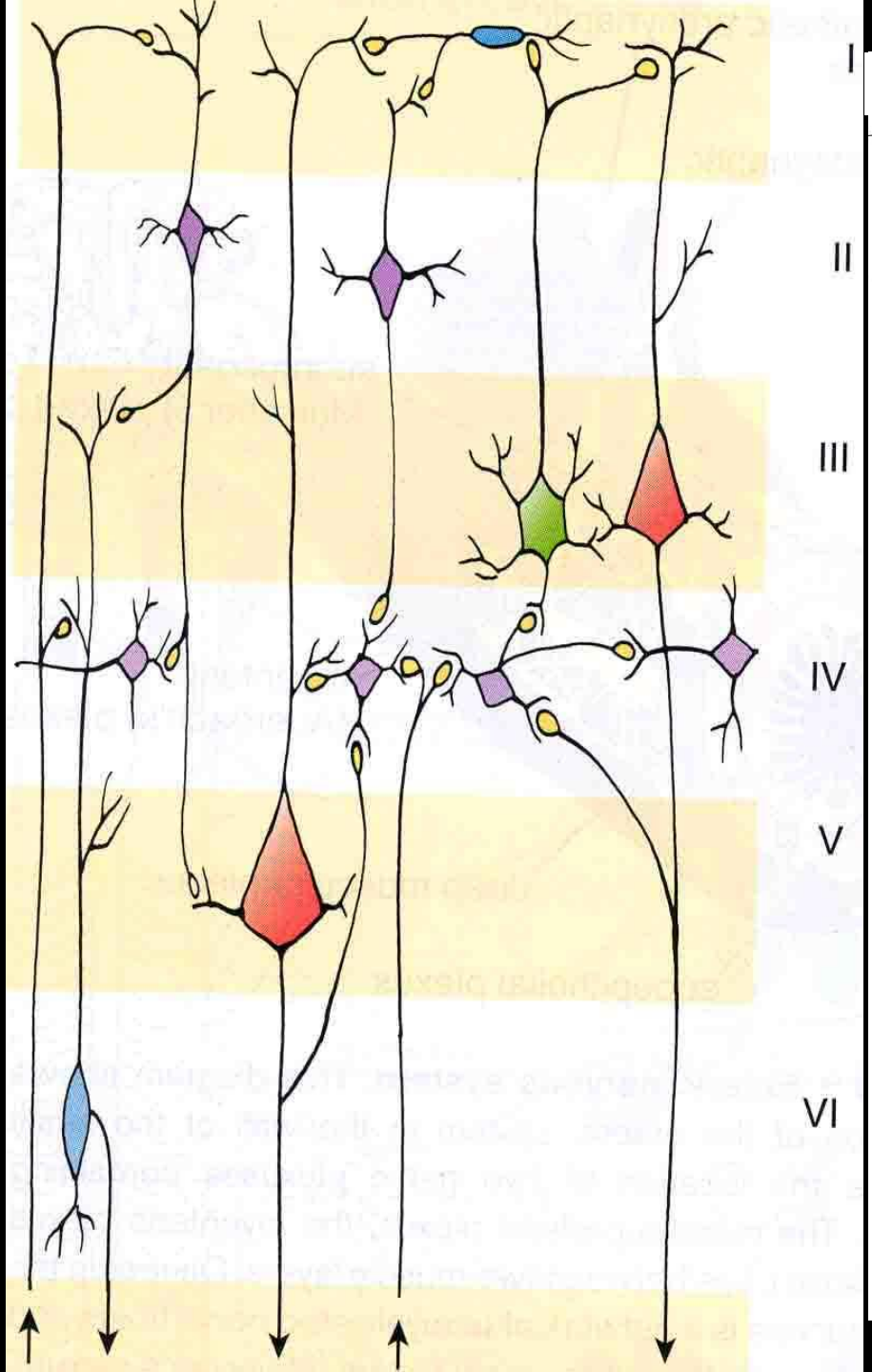

1000 µm

Neurons of the cortex

- **Excitatory** (70 - 80%, dendritic spines, **glutamate**)
  - **pyramid** (eferent neurons)
  - **Stellate cells with dendritic spines** (interneuron)

- **inhibitory** (20 - 30%, interneurons, usually no dendritic spines, **GABA**)

  - many types, basket cells are the most numerous



lamina

molecularis

granularis externa

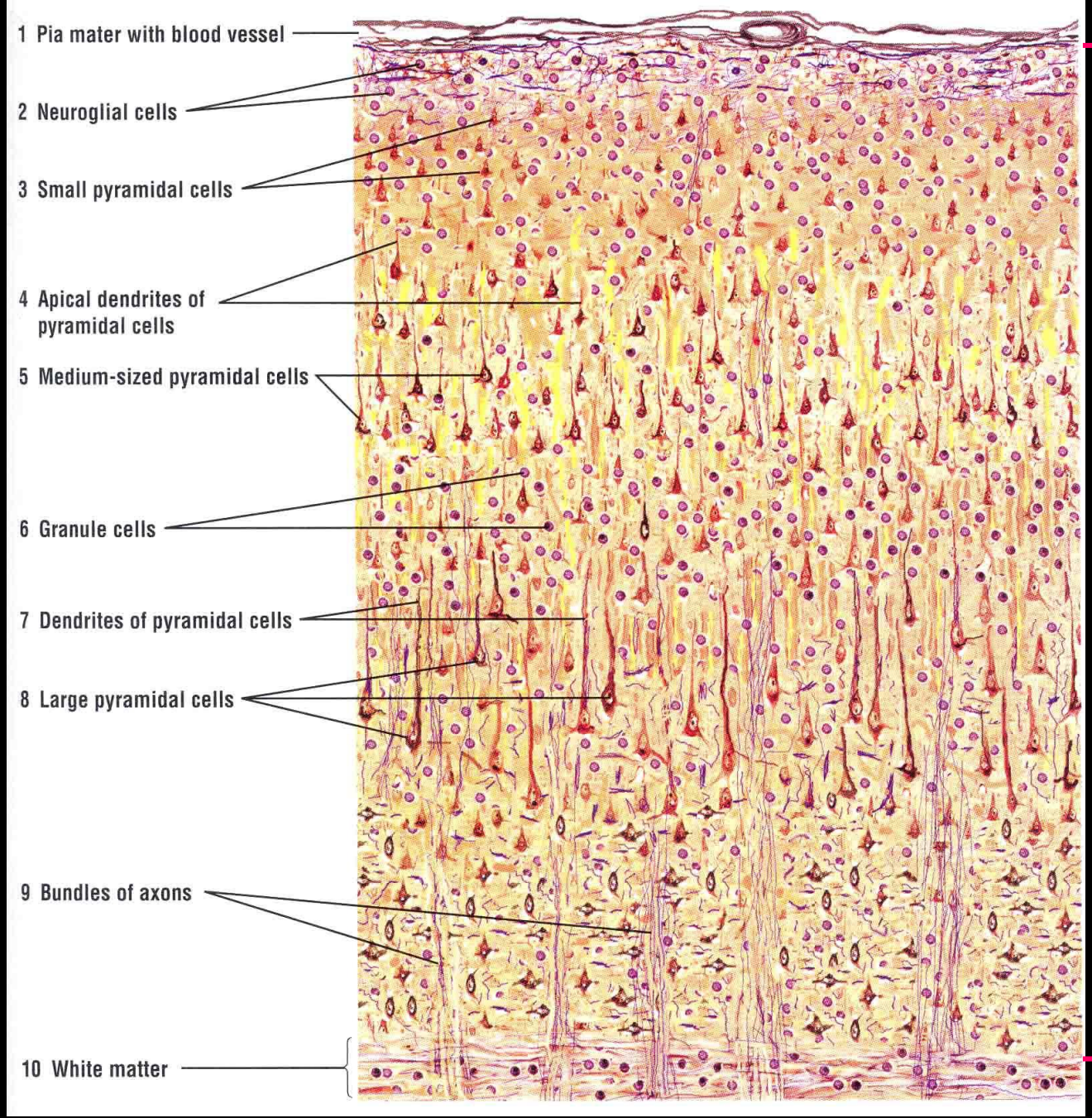
pyramidalis externa

granularis interna

pyramidalis interna

multiformis

Ross, M.H., Pawlina, W.: Histology: a text and atlas, 6th ed., Lippincott Williams & Wilkins, 2011
upraveno

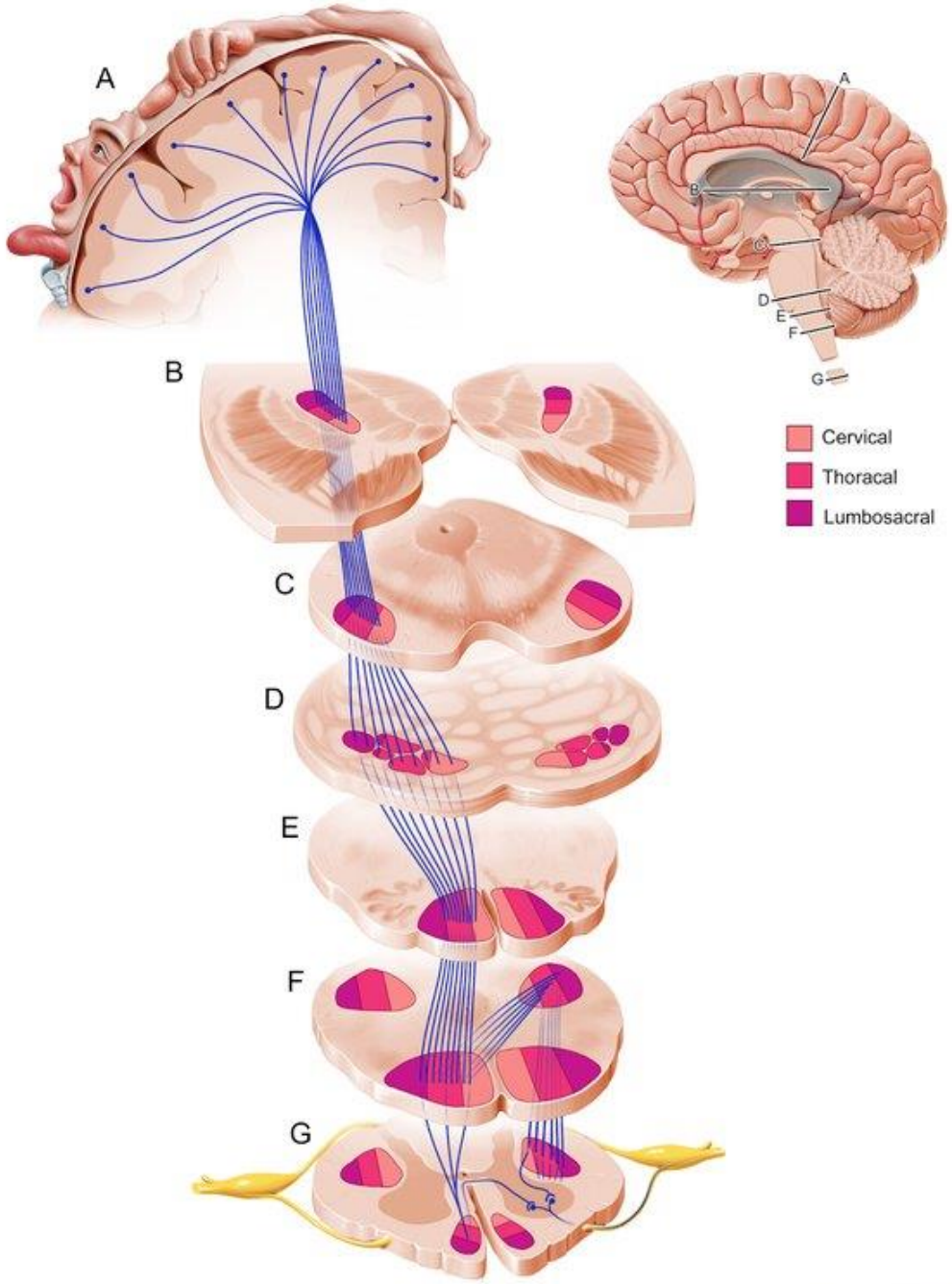

1 Pia mater with blood vessel
2 Neuroglial cells
3 Small pyramidal cells
4 Apical dendrites of pyramidal cells
5 Medium-sized pyramidal cells
6 Granule cells
7 Dendrites of pyramidal cells
8 Large pyramidal cells
9 Bundles of axons
10 White matter
Cortex (gray matter)
White matter

Quiz

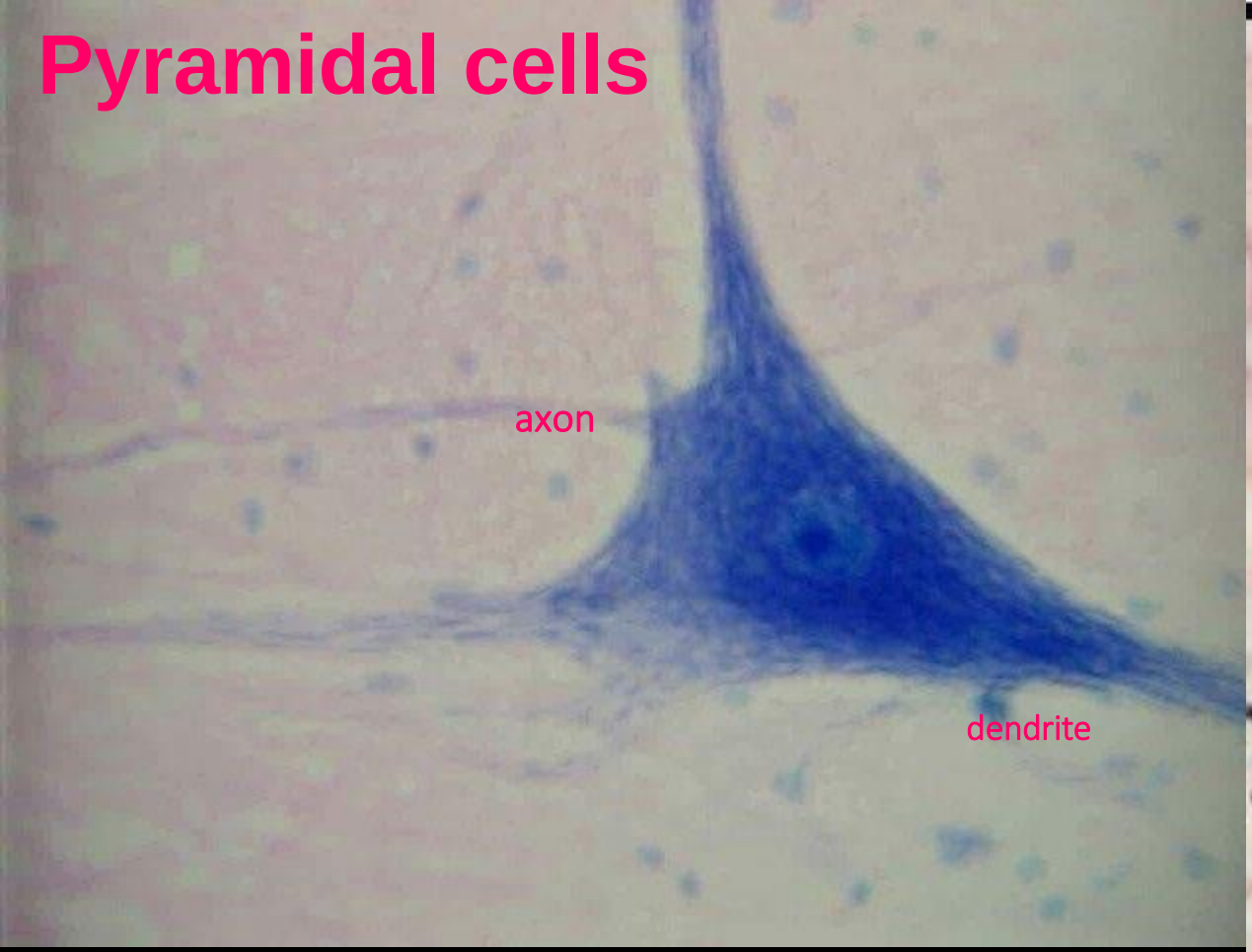
1. What is the percenatage of inhibitory neurons in mice? Is it more or less than in humans?

2. Can we find pyramid cell bodies in other layers than lamina pyramidalis externa et interna?

3. What is the main output of the cerebral cortex towards other cortical areas and subcortical structures?

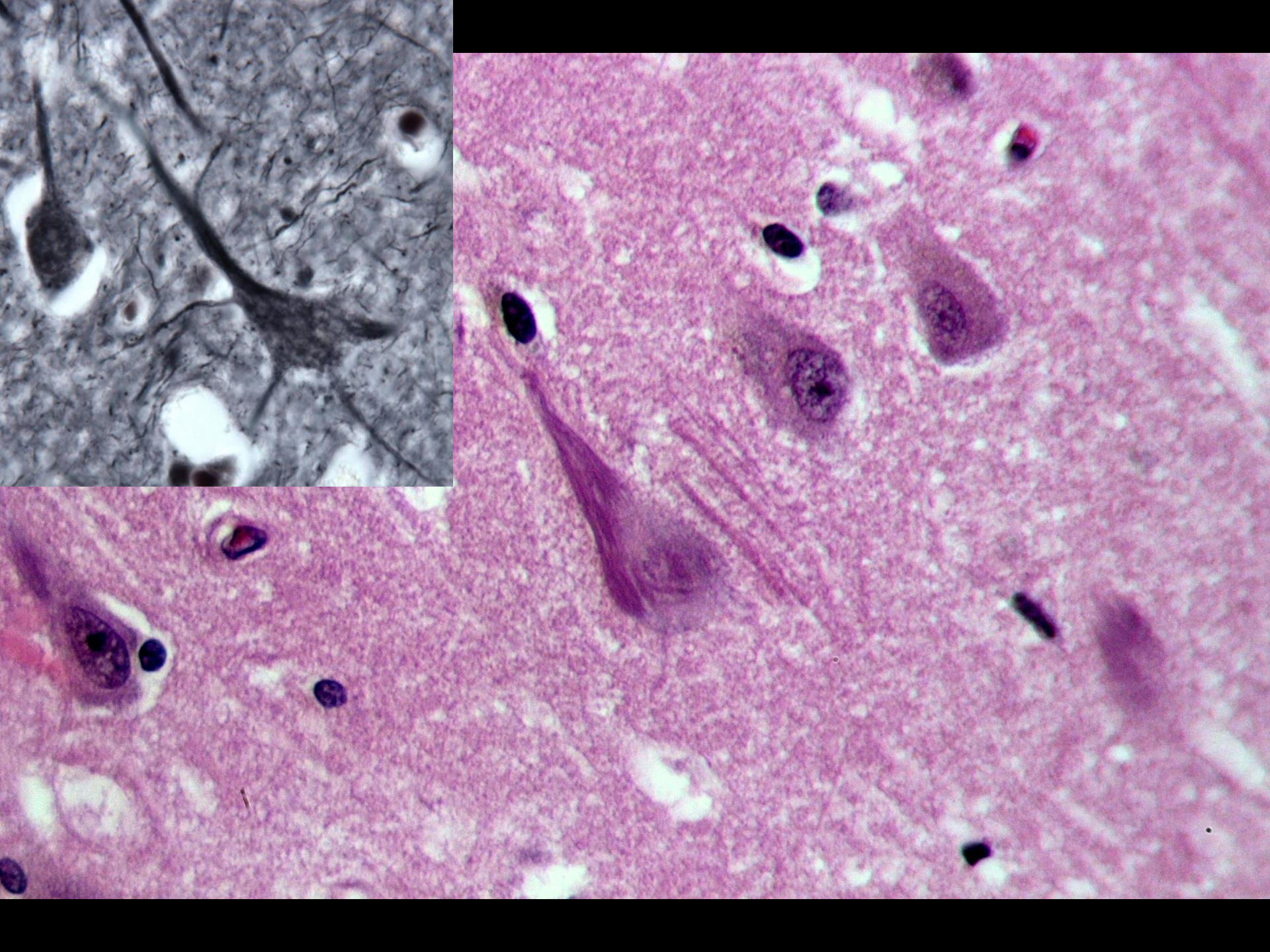


Pyramidal cells



Immunocytochemistry demonstrating intermediate filaments, NF protein

Silver impregnation



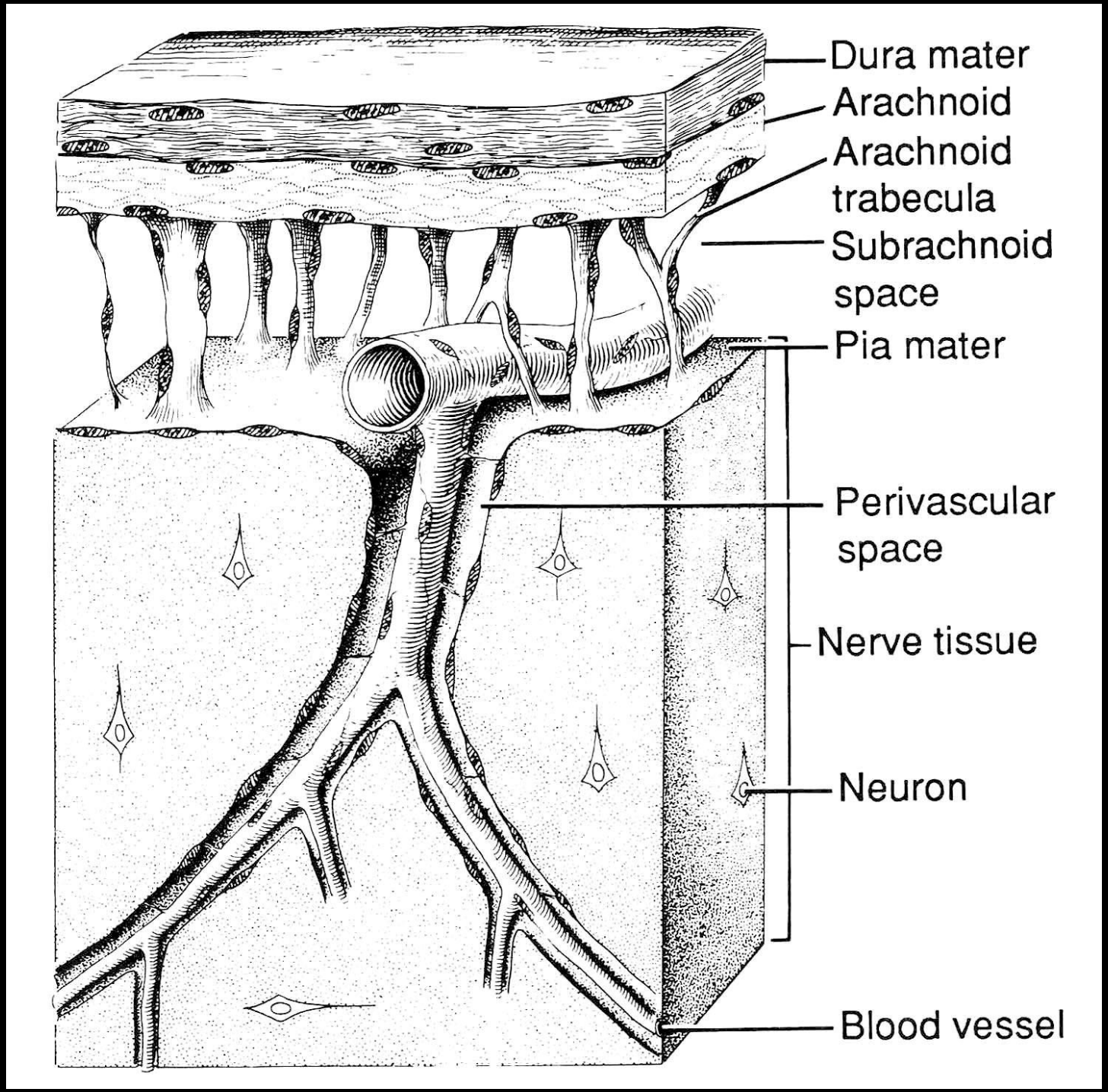
Cerebral cortex - summary

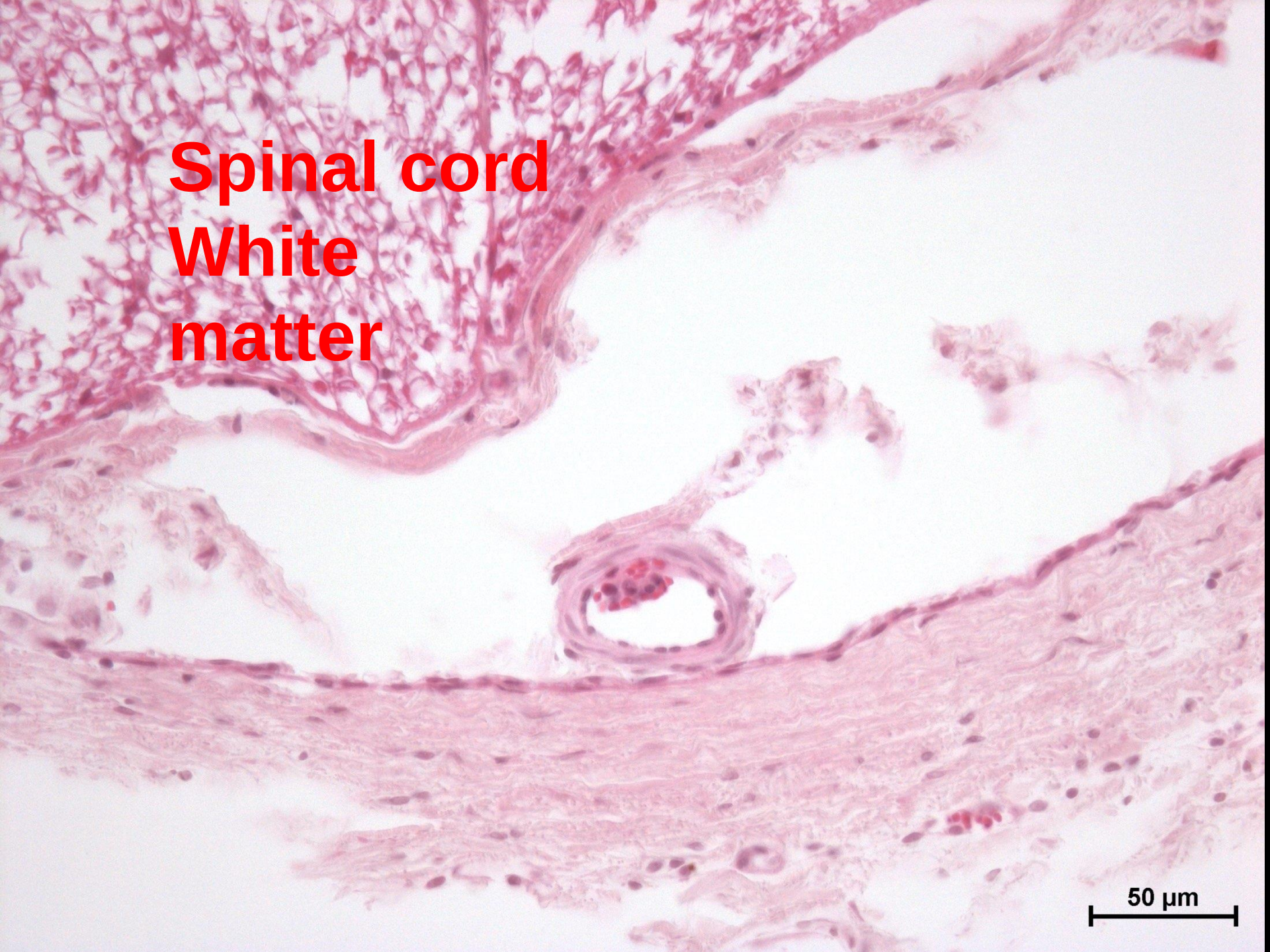
- Located on the surface of the brain, it can be divided into three layered **paleocortex** and **archicortex** and six layered **neocortex**
- Most cells are excitatory – **pyramidal** cells and **stellate cells with dendritic spines**
- There is a large variety of **inhibitory neurons**

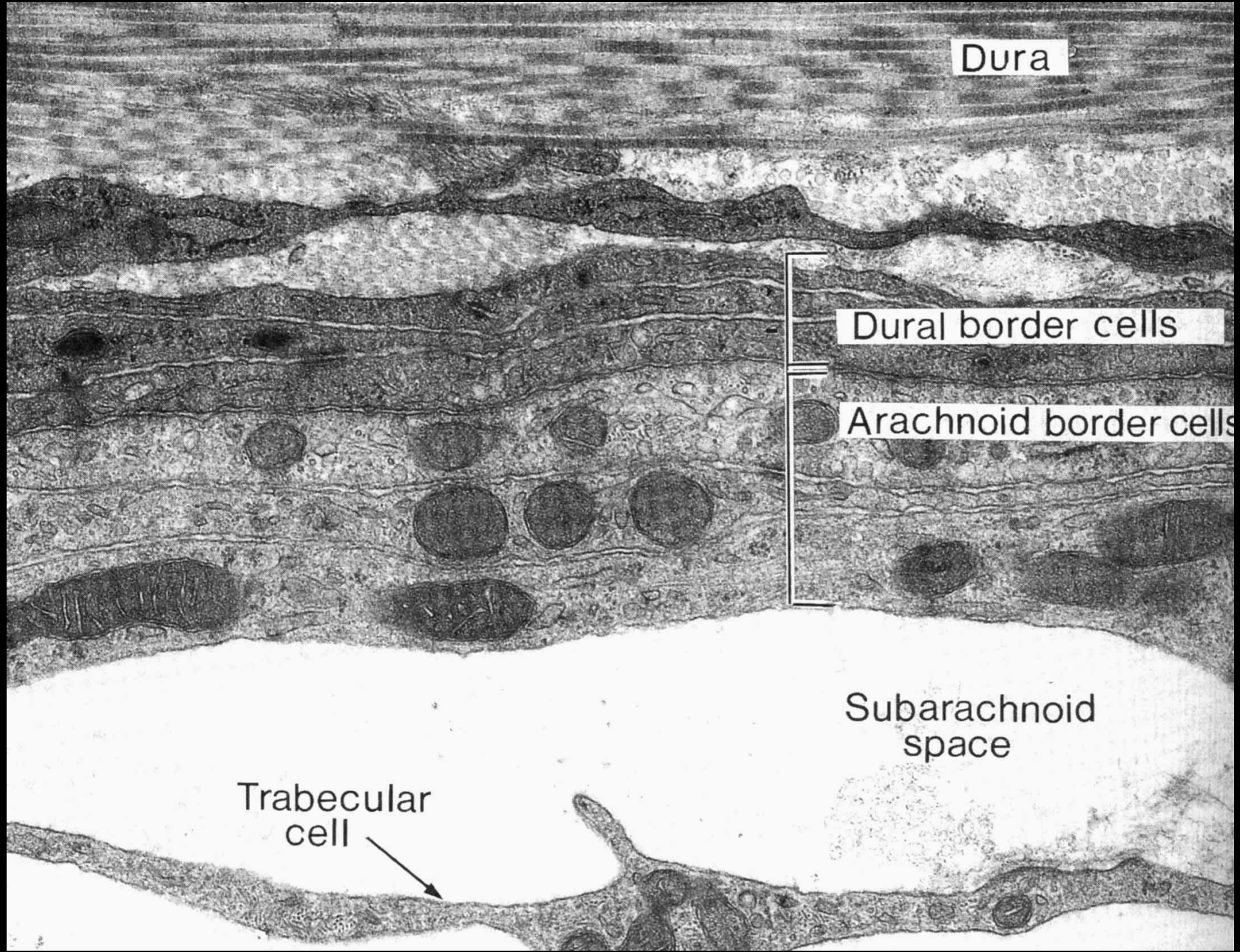
The six layers of neocortex are:

- Lamina I - **molecularis**: mostly neuronal processes
- Lamina II - **granularis externa**: small neurons
- Lamina III - **pyramidalis externa**: pyramidal cells dominate
- Lamina IV - **granularis interna**: small neurons
- Lamina V - **pyramidalis interna**: large pyramidal neurons (reaching 100 micrometers) dominate
- Lamina VI - **multiformis**: neurons of many types
- All layers contain a diverse population of inhibitory neurons
- Although the pyramidal layers are named after them, the pyramid cells are found throughout neocortex
- MGP GPM – the names are almost symetrical

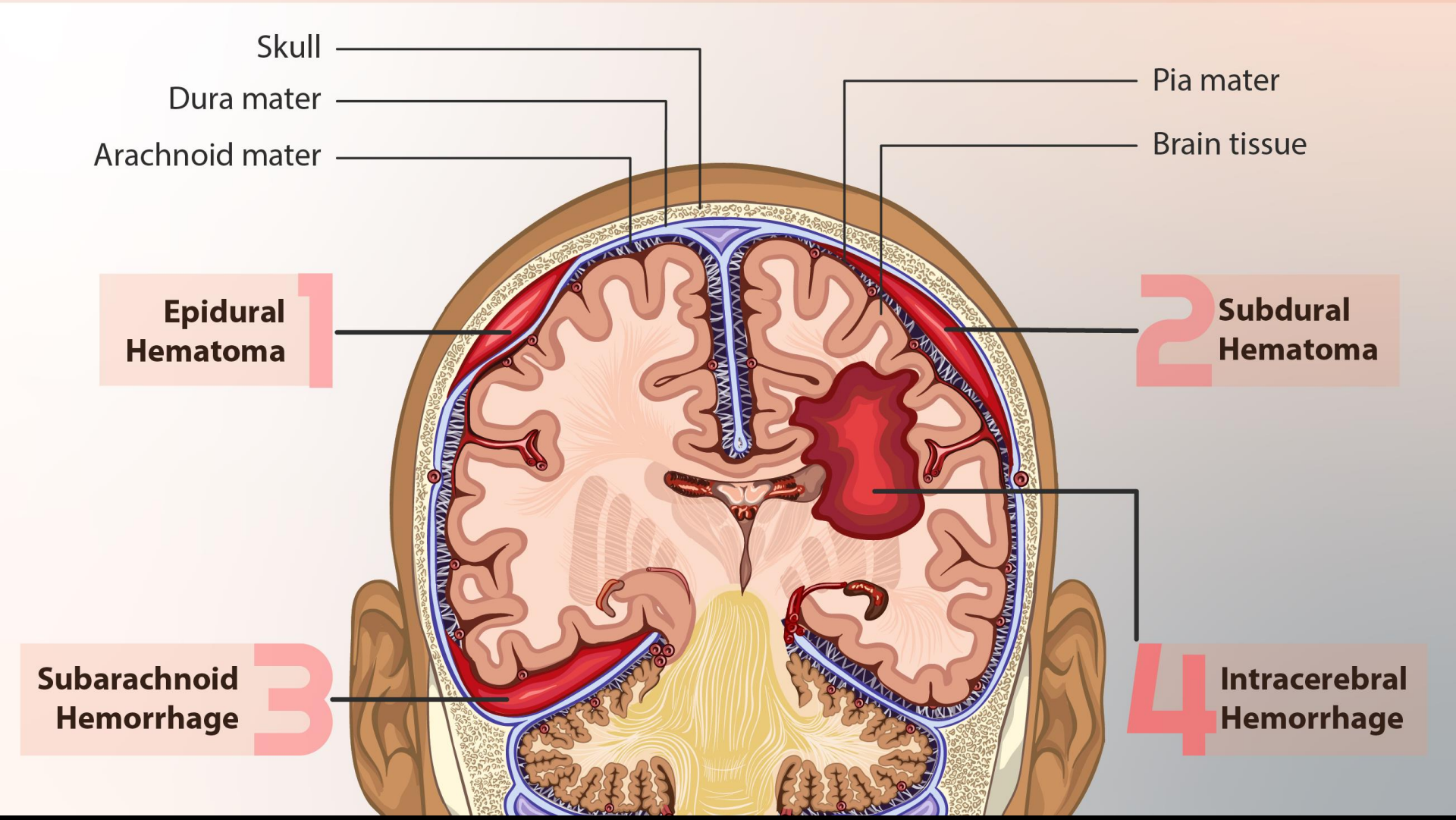
Meninges


Dura mater
Arachnoid
Arachnoid trabecula
Subrachnoid space
Pia mater
Perivascular space
Nerve tissue
Neuron
Blood vessel


Spinal cord
White
matter
50 µm


Dura
Dural border cells
Arachnoid border cells
Subarachnoid space
Trabecular cell

Types of brain hemorrhage



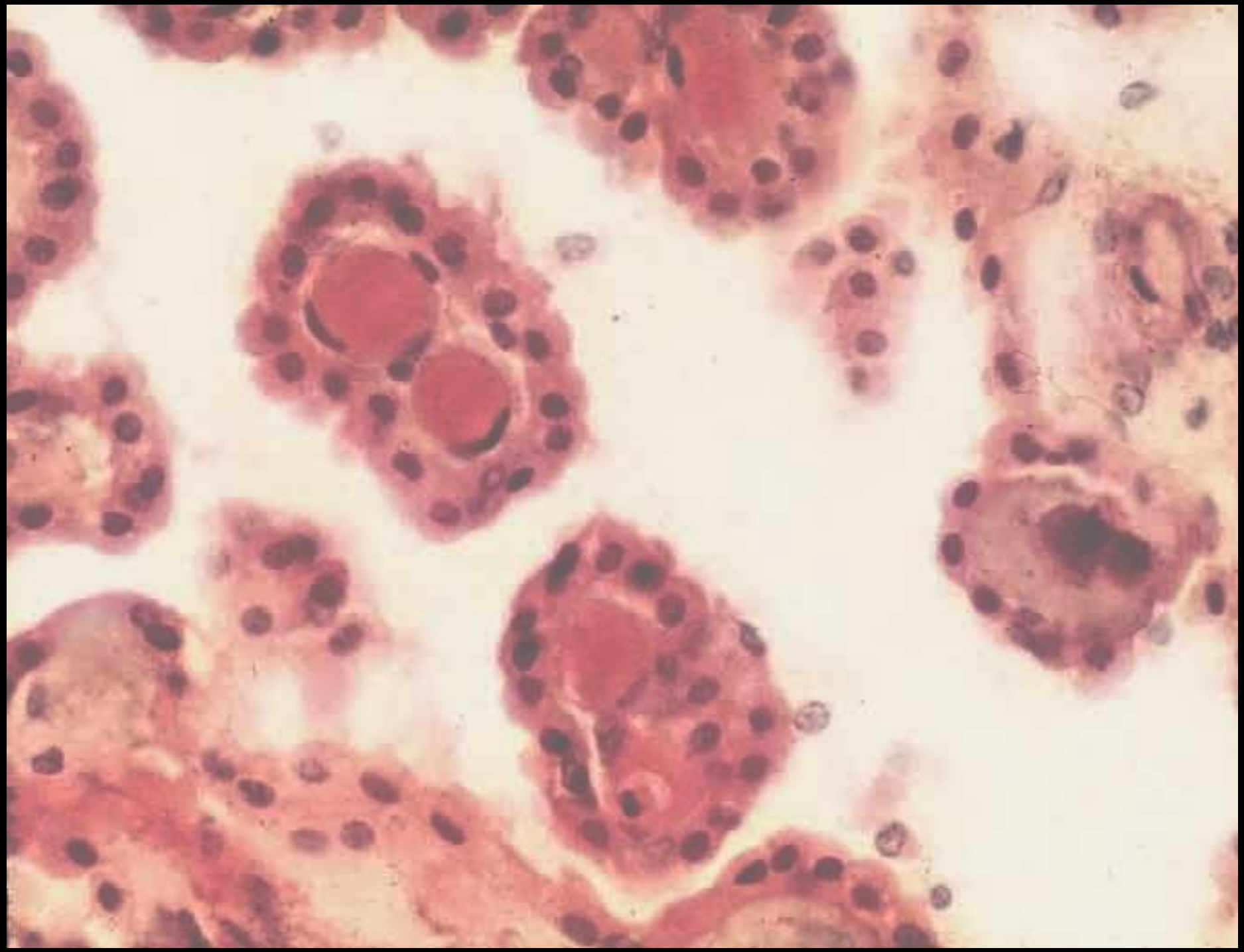
Quiz

1. What is a meningitis? What can cause it?

2. What are the presenting signs of a subarachnoid hemorrhage?

3. What groups of people are prone to develop the subdural hematoma? Why?

Plexus choroideus



Quiz

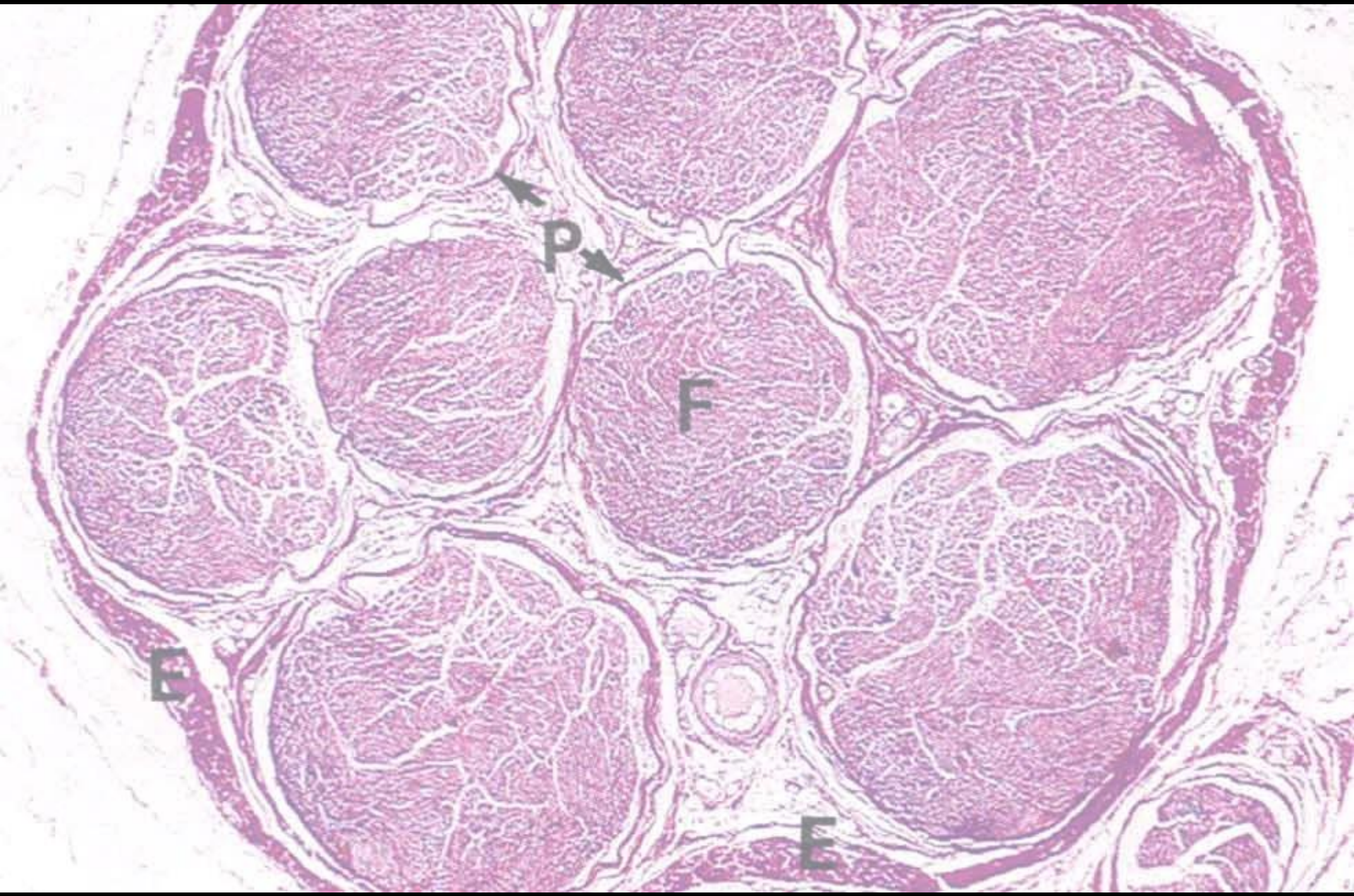
1. Describe CSF circulation. What happens, if there is an obstruction?

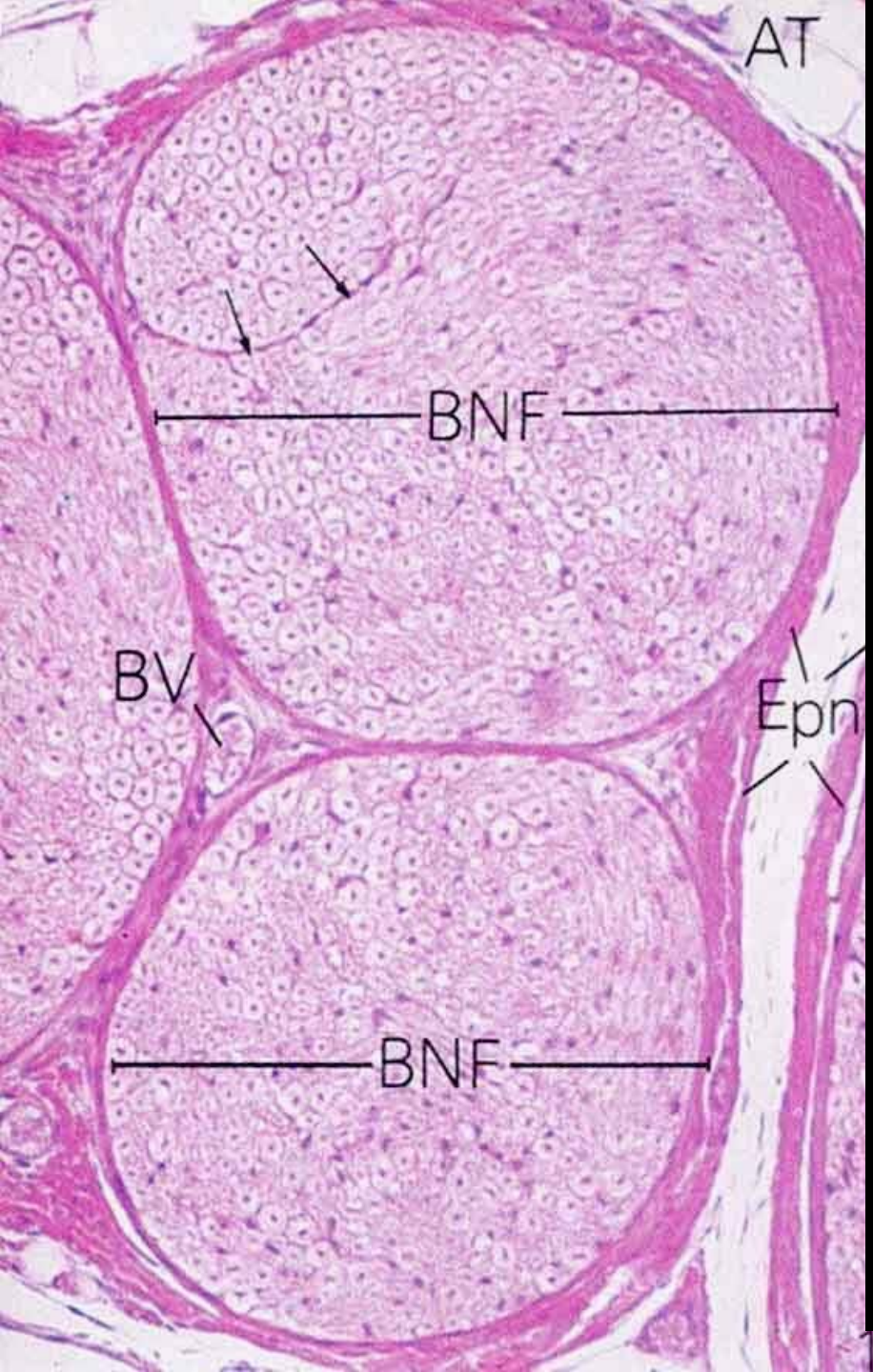
2. Compare the blood-brain barrier with the blood CSF barrier.

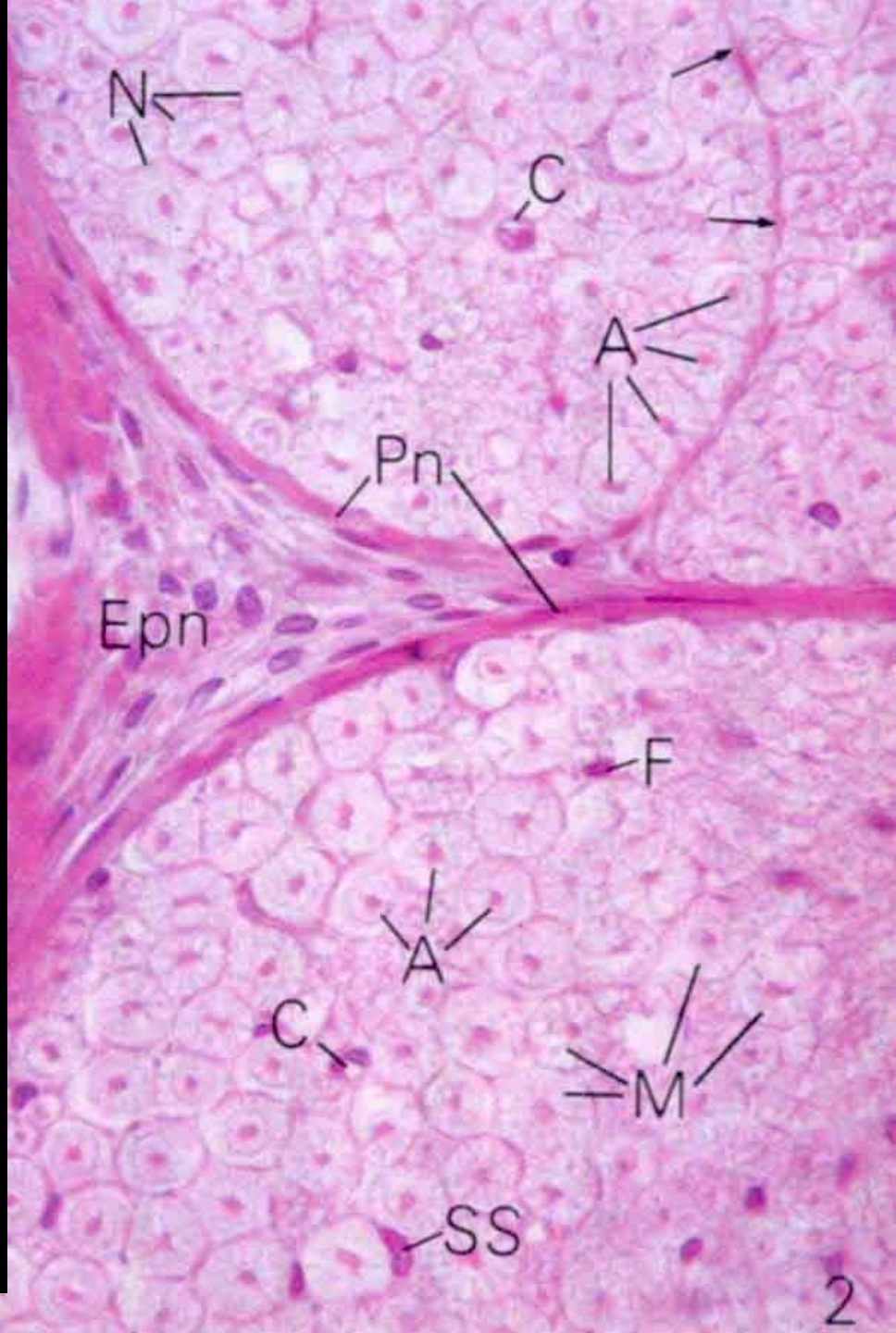
Meninges and choroid plexus

- **Dura mater –** dense collagenous tissue + dural border cells
- In skull it is continuous with periosteum, in spine there is a true epidural space containing vessel and adipose tissue
- **Arachnoid** - connective tissue containing arachnoid border cells, and trabeculae
- **Pia mater** se is a layer of highly vascularized connective tissue on the surface of the CNS bordered by lamina limitans gliae superficialis
- **Choroid plexus** is a highly vascular connective tissue forming villous structures in the ventricles, on the surface there is a columnar epithelium continuous with ependyma

PNS - nerves


P
F
E
E

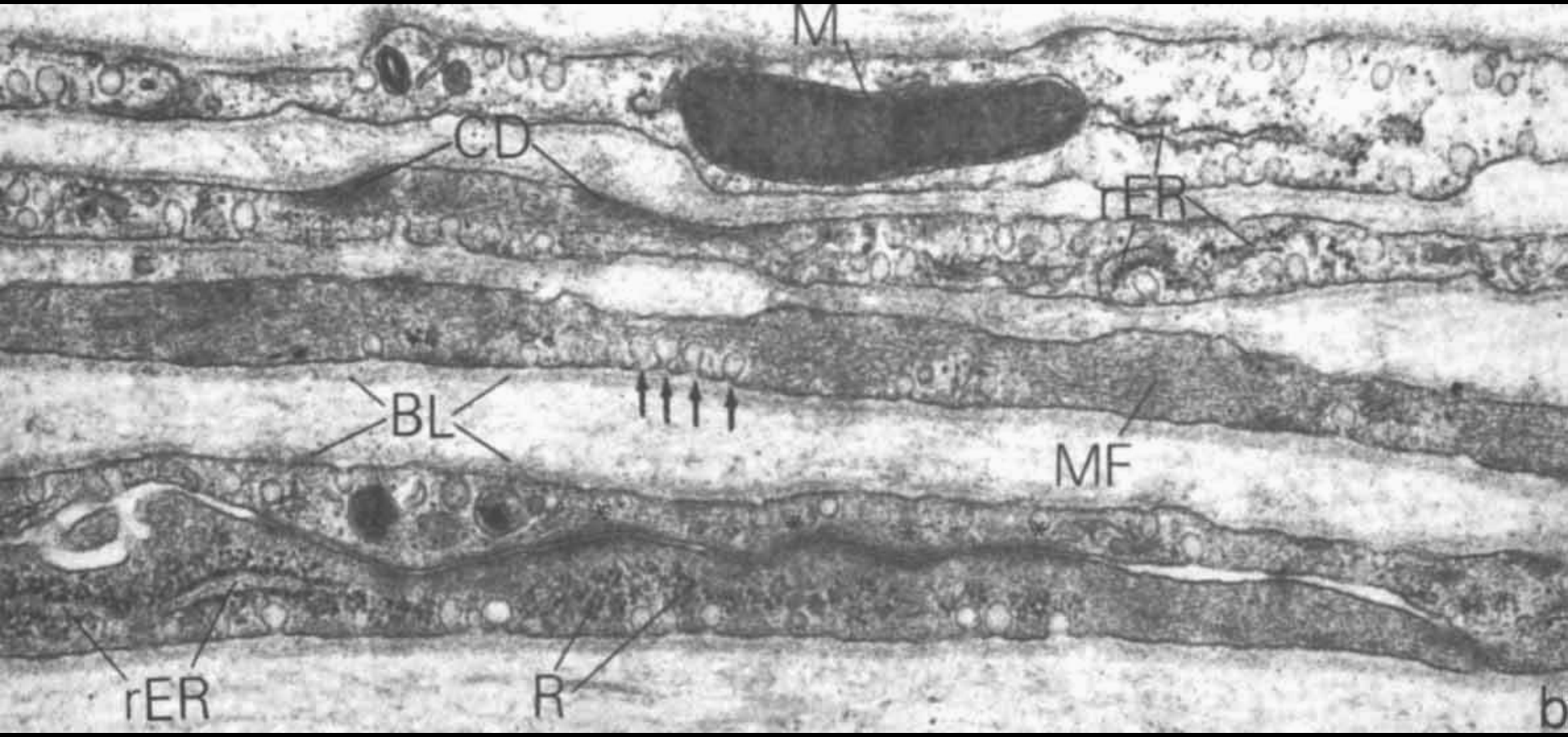

AT
BNF
BV
Epn
BNF


N
C
A
Pn
Epn
F
A
C
M
SS
2

S = Schwann cells

F = fibroblasts

Perineurium



Quiz

1. What happens to neurons when the nerve is severed? Can it regenerate? What happens with the innervated muscle?

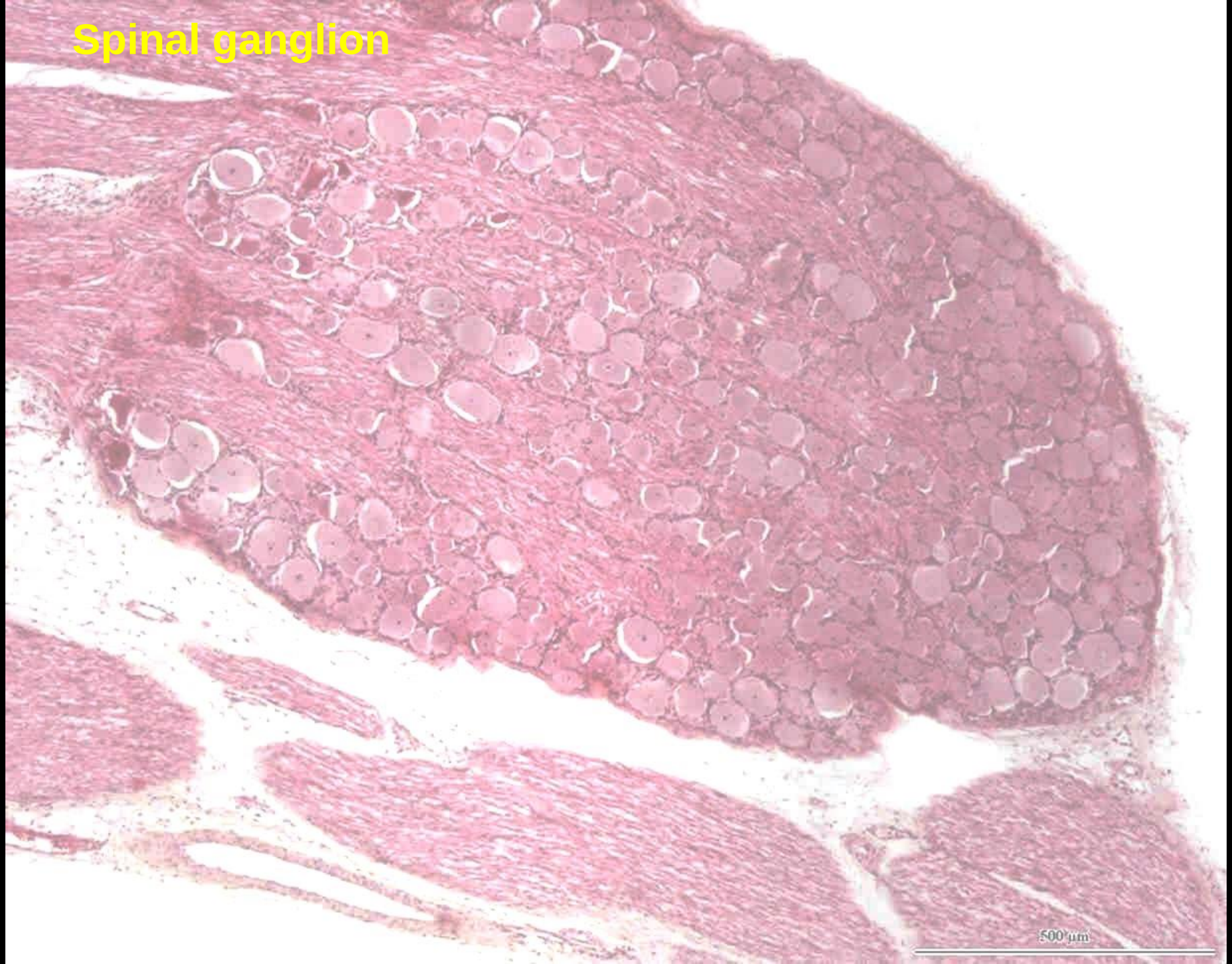
2. What is a schwannoma? Which cranial nerve is often affected?

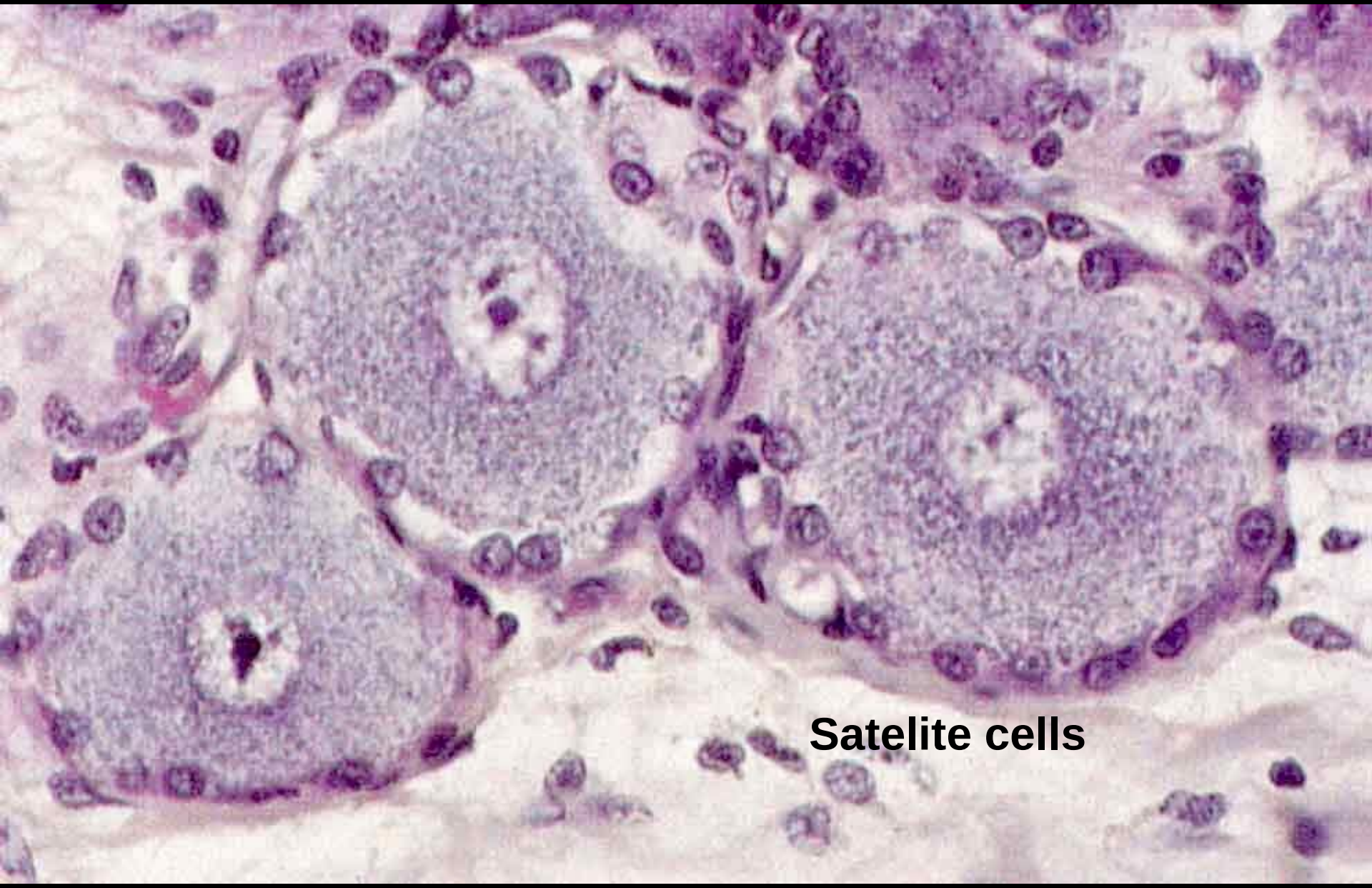
Nerves - summary

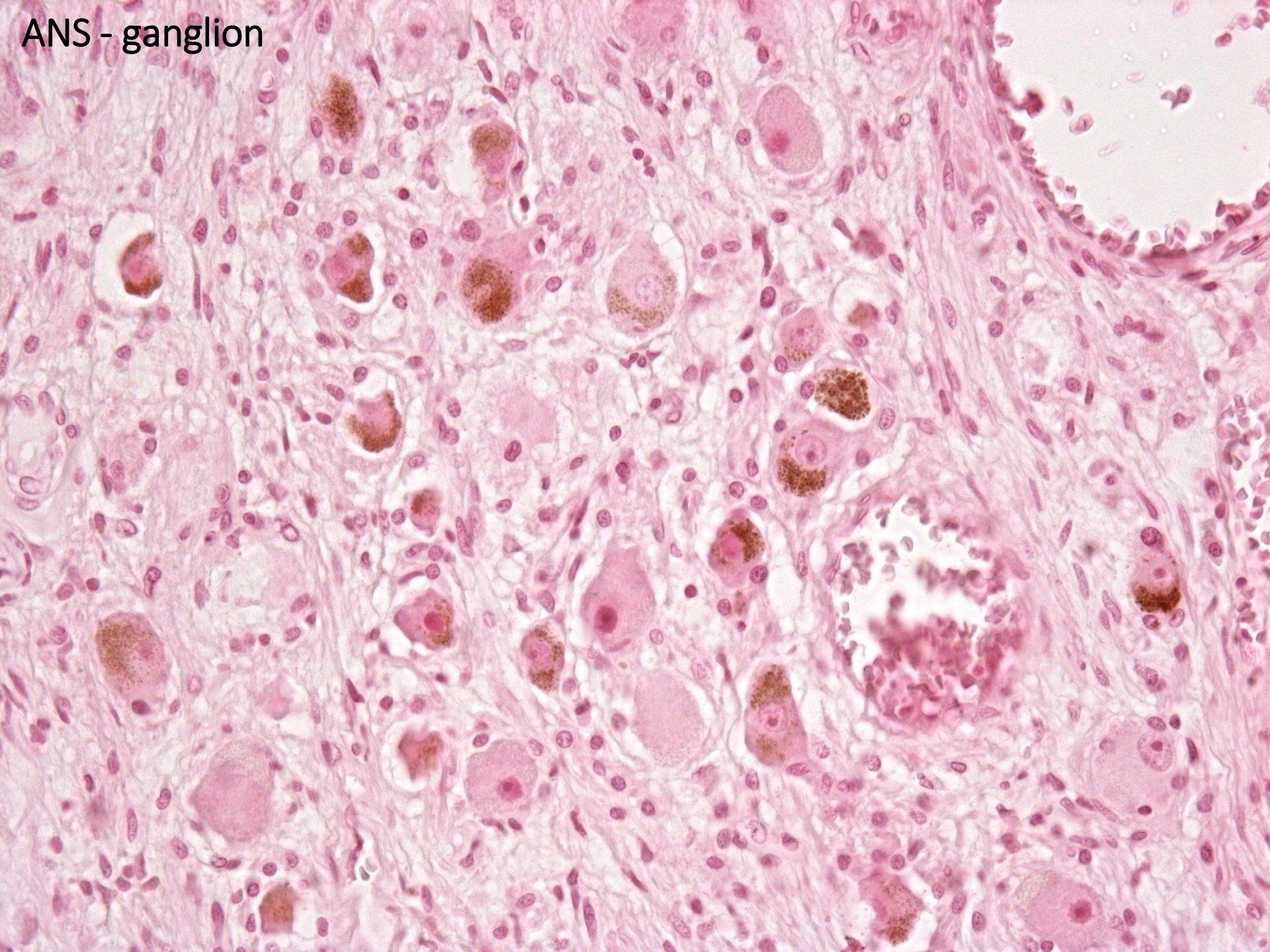
- Bundles of myelinized and non-myelinized **axons** with **Schwann cells** and surrounding **connective tissue**
- The cell bodies of neurons are not found in the nerves, the nuclei we see belong to Schwann cells and fibroblasts
- **Endoneurium** (reticular fibres and amorphous matter) and are surrounded by **perineurium** (several layers of special flat cells with epithelial and connective tissue features, together with fibroblasts and extracellular matrix including collagen and reticular fibres)
- The **epineurium** is located on the surface of the nerve and between the individual bundles, it is composed of collagenous connective tissue with relatively numerous blood vessels

Ganglia

Spinal ganglion




Satelite cells


ANS - ganglion

Ganglia – summary

- Groups of **neurons** embedded in encapsulated structures along the course of a peripheral nerve
- Neuron bodies are surrounded by special glial cells called **satellite cells**
- Sensory ganglia contain afferent **pseudounipolar** neurons and are located in the foramina intervertebralia at the **posterior spinal roots**, or along the course of the **cranial nerves**
- Ganglia of the eighth cranial nerve contain **bipolar neurons**
- Autonomic ganglia contain multipolar neurons
- **Sympathetic** ganglia are larger and located near the spine (paravertebral and prevertebral)
- **Parasympathetic** ganglia are located in the head region in the course of nerves III, VII, IX, X. Other small ganglia are located near the target organs, often intramurally
- A large **enteric nervous system** is sometimes distinguished as a separate part of the ANS

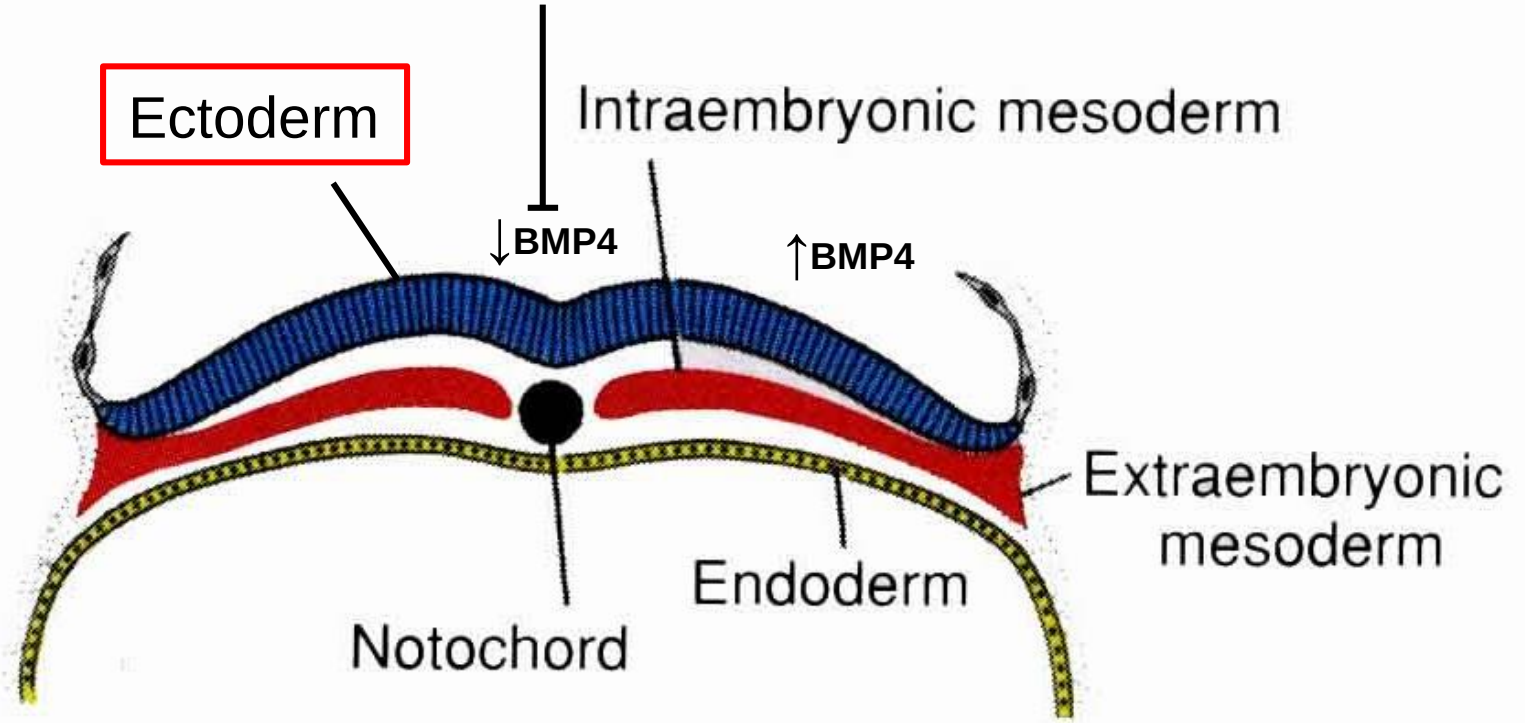
ORGANOGENESIS OF THE NERVOUS SYSTEM

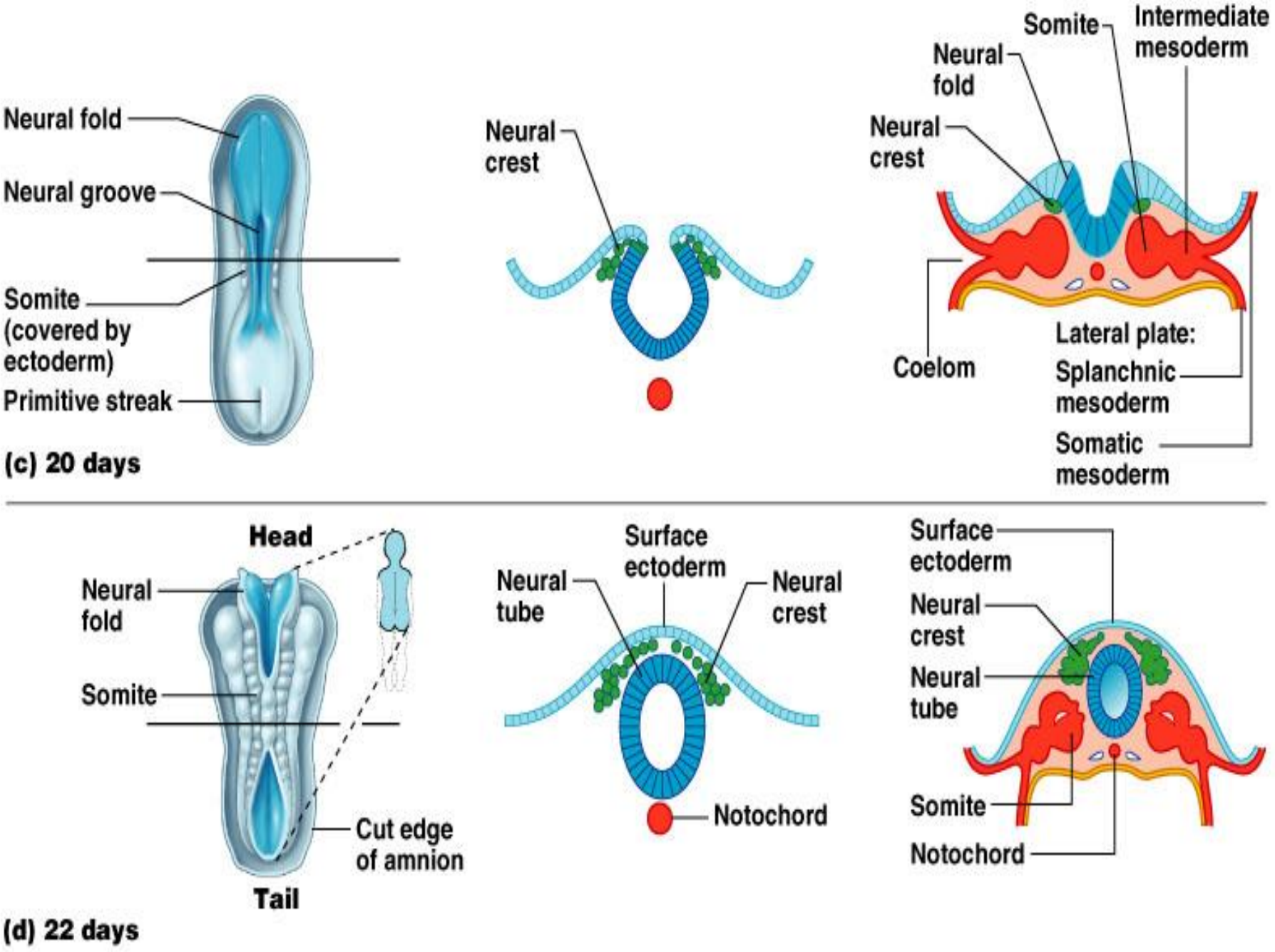
Embryology revision

1. Notochord
2. Neural plate
3. Neural crest
4. Neuroporus
5. Neuroepithelium
6. Sonic hedgehog

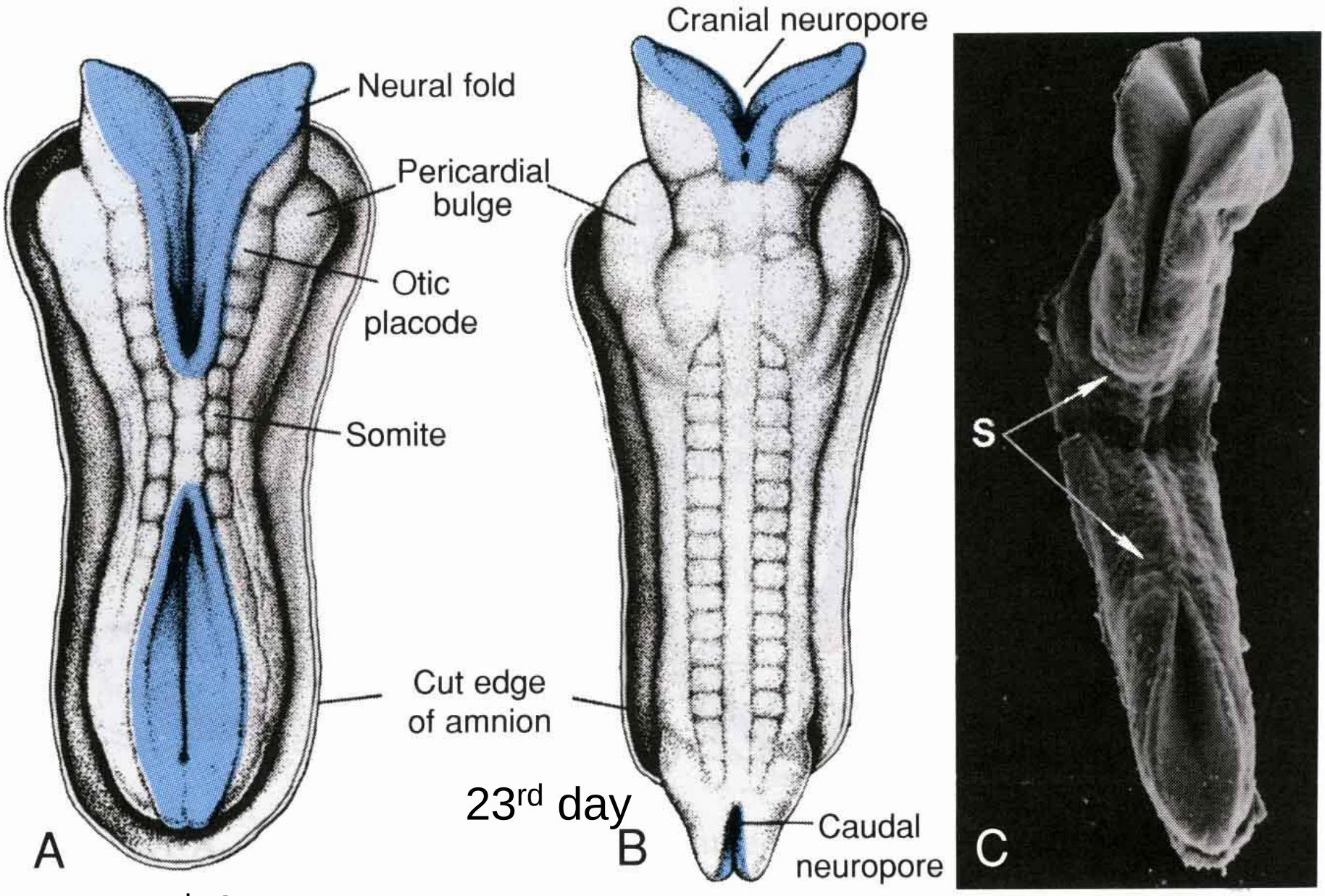
a) Arrangement of cells in the neural tube
b) Structure in the centre of the body important for signaling
c) The opening at the end of the neural tube
d) Cell population separating during neurulation
e) Signaling molecule involved in almost everything
f) Part of the ectoderm from which the nervous system develops

DEVELOPMENT OF NEURAL TUBE
NEURULATION


Ectoderm
Intraembryonic mesoderm
↓BMP4
↑BMP4
Extraembryonic mesoderm
Endoderm
Notochord


Neural fold
Neural groove
Somite (covered by ectoderm)
Primitive streak
(c) 20 days
Neural crest
Somite
Intermediate mesoderm
Neural fold
Neural crest
Coelom
Lateral plate:
Splanchnic mesoderm
Somatic mesoderm
Head
Neural fold
Somite
Cut edge of amnion
Tail
(d) 22 days
Surface ectoderm
Neural tube
Neural crest
Notochord
Surface ectoderm
Neural crest
Neural tube
Somite
Notochord

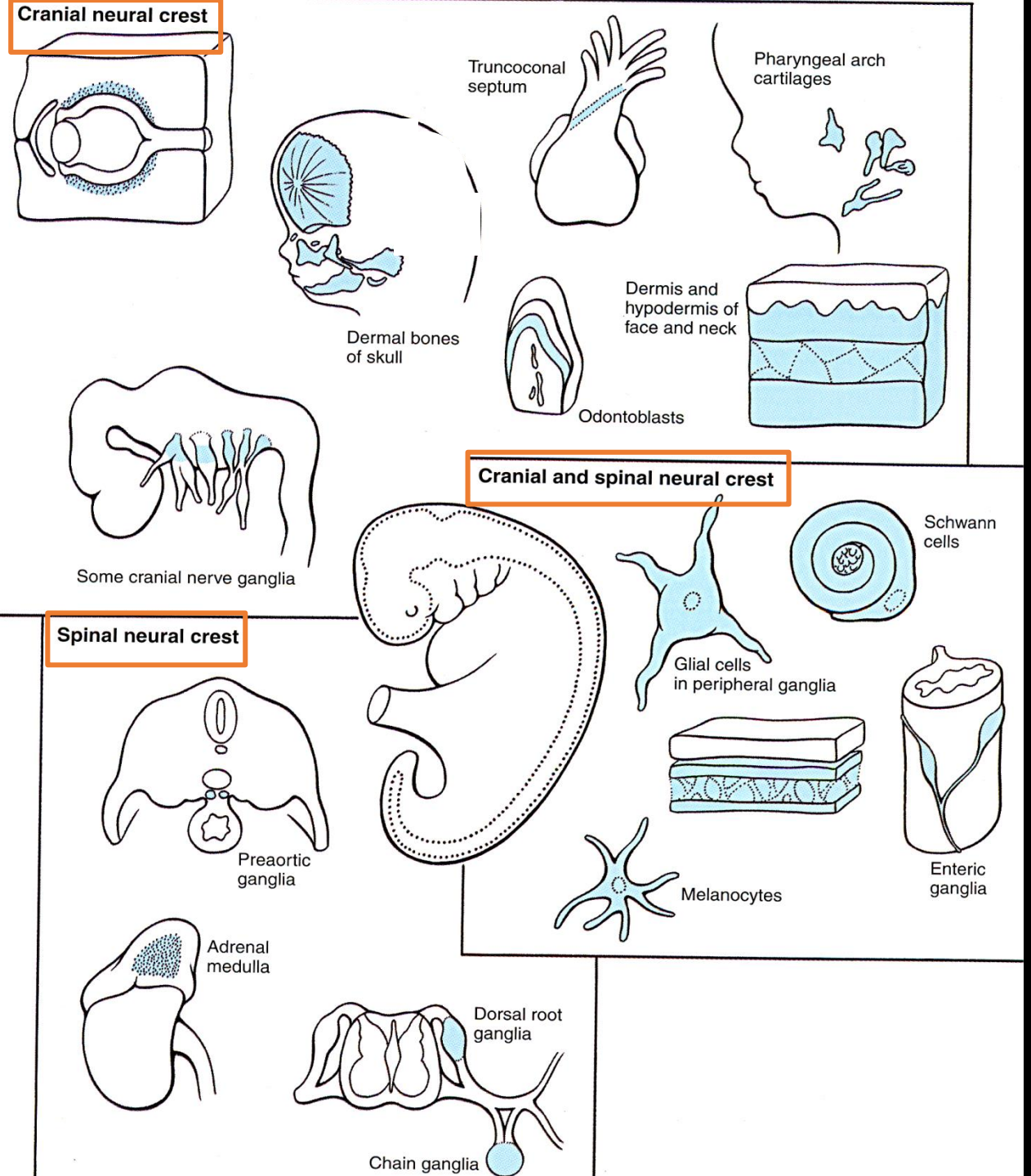
Closes at days 24 – 25



22nd day

23rd day

Closes at days 26 - 28

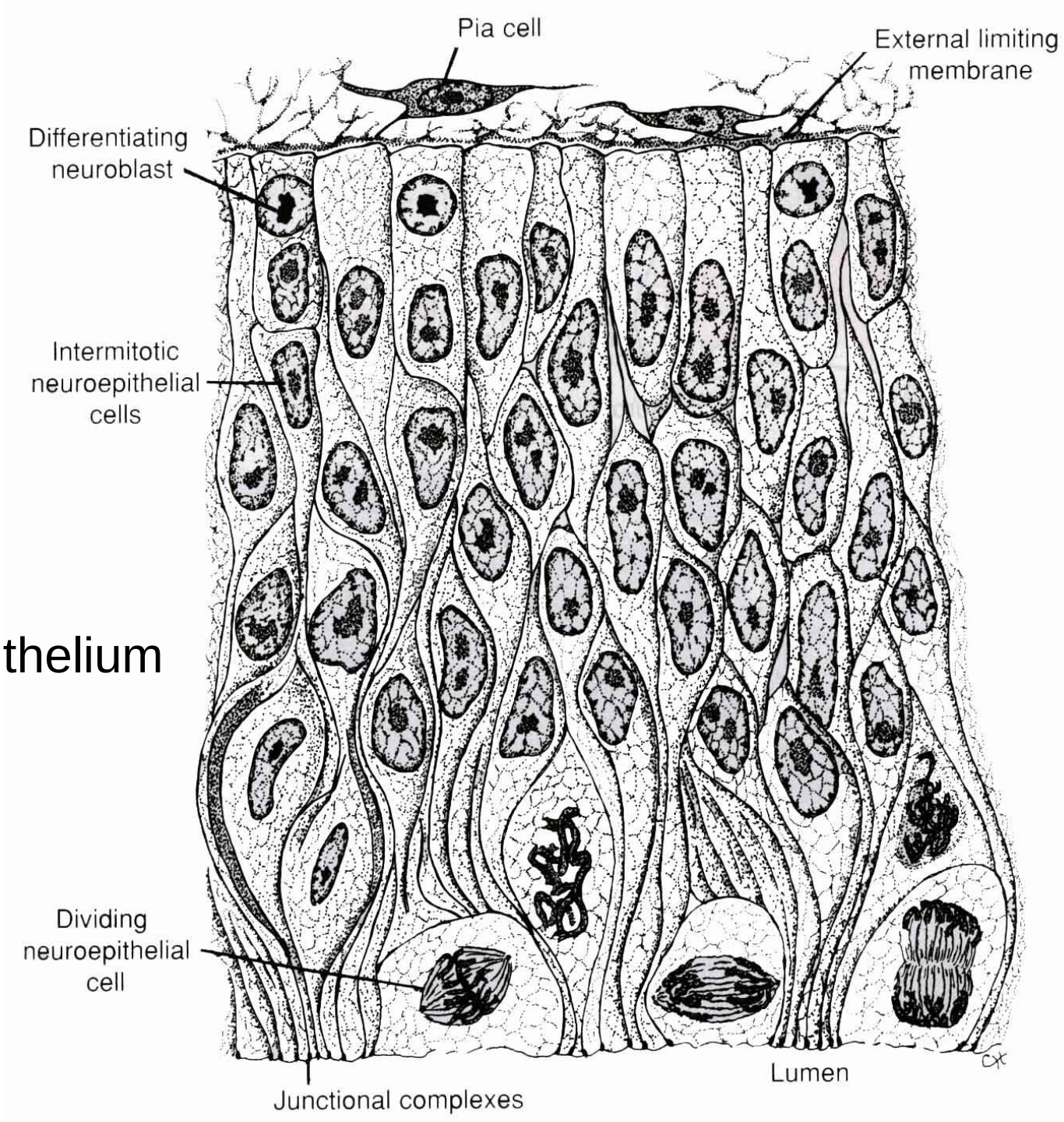

Cranial neural crest
Truncoconal septum
Pharyngeal arch cartilages
Dermal bones of skull
Dermis and hypodermis of face and neck
Odontoblasts
Some cranial nerve ganglia
Cranial and spinal neural crest
Schwann cells
Glial cells in peripheral ganglia
Spinal neural crest
Preaortic ganglia
Melanocytes
Enteric ganglia
Adrenal medulla
Dorsal root ganglia
Chain ganglia

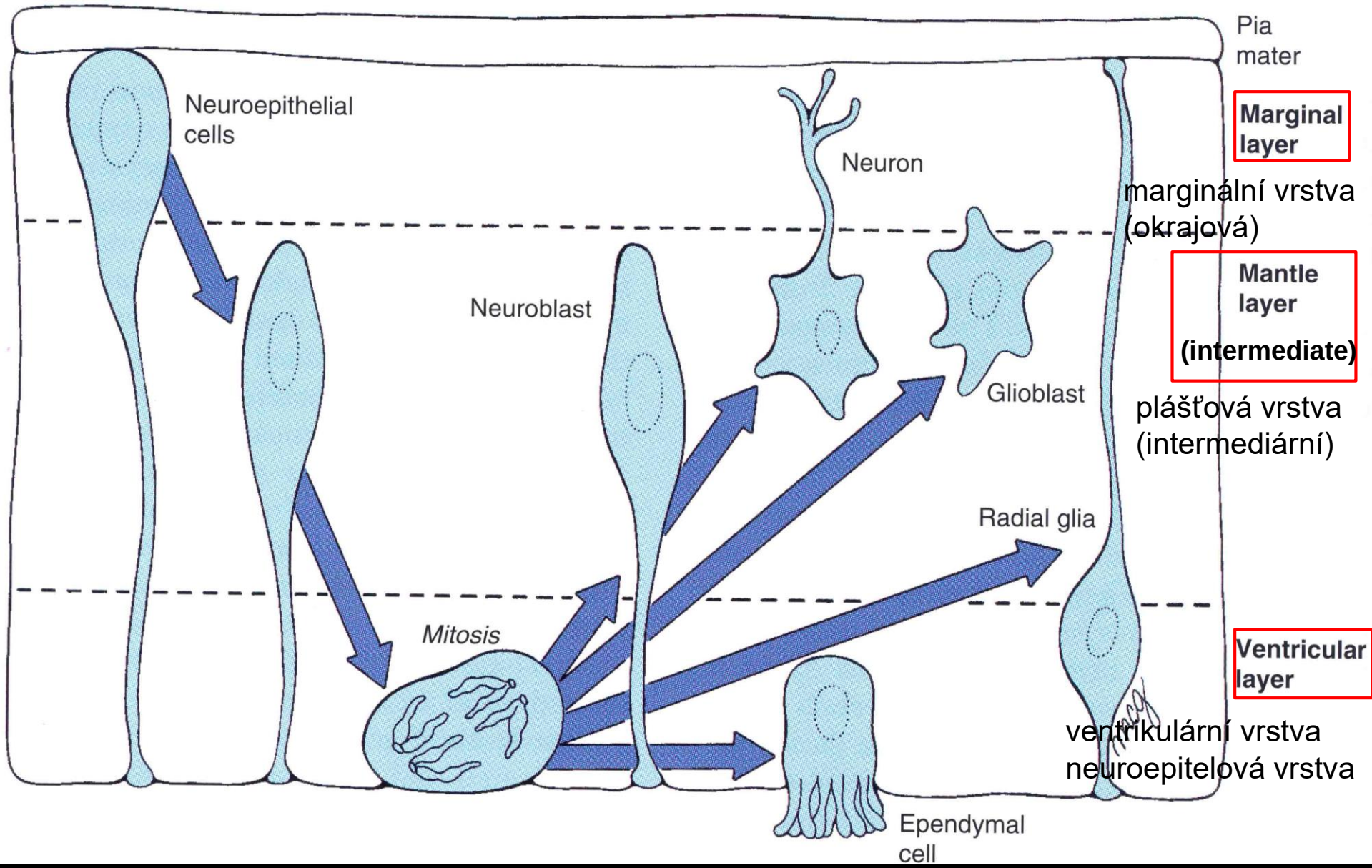
Origin of the neural tube – neurulation

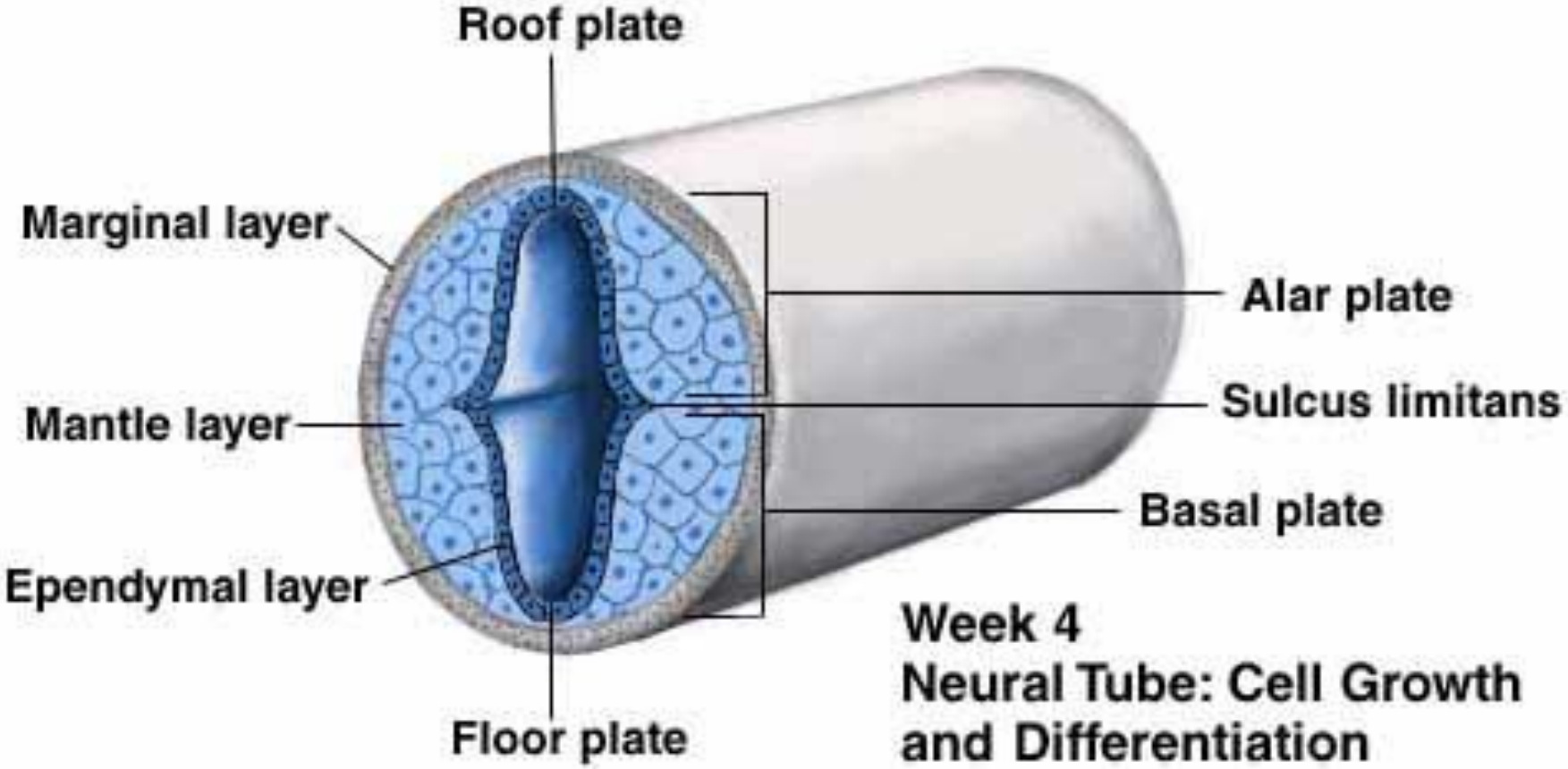
- After **gastrulation**, the part of the ectoderm close to the midline differentiates into a neural plate
- Lateral edges of the **neural plate** increase to form **neural folds**, while the **neural groove** deepens in the centre
- This process continues until the **neural folds fuse** dorsally - a roof plate is formed
- The process starts in the occipitocervical region (rhombencephalon and cervical spinal cord), then it spreads caudally and cranially, with the **caudal neuroporus closing last** (days 26-28)
- Some of the cells of the neural folds undergo epithelial-mesenchymal transformation to form the **neural crest**, this important population then contributes to e.g. PNS, head and neck connective tissue, cardiac septation, odontoblasts, skin melanocytes, adrenal medulla...

HISTOGENESIS OF CNS

neuroepithelium



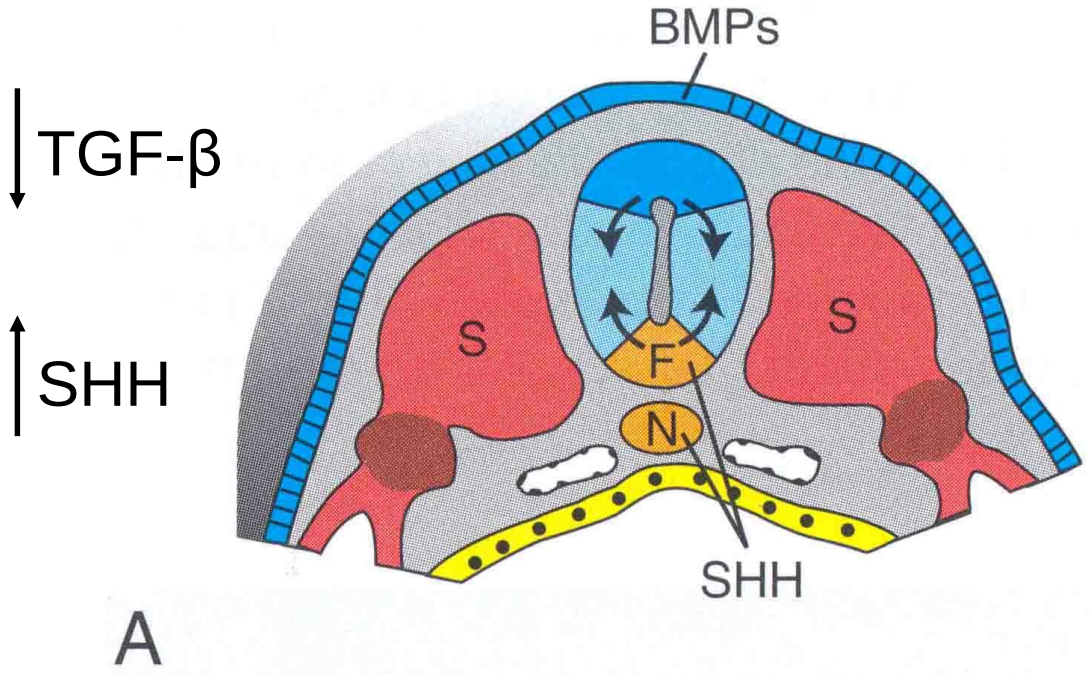

Pia mater
Marginal layer
marginální vrstva (okrajová)
Mantle layer
(intermediate)
plášťová vrstva (intermediární)
Ventricular layer
ventrikulární vrstva neuroepitelová vrstva
Neuroepithelial cells
Neuron
Neuroblast
Glioblast
Radial glia
Mitosis
Ependymal cell


Roof plate
Marginal layer
Alar plate
Sulcus limitans
Mantle layer
Basal plate
Ependymal layer
Floor plate
Week 4
Neural Tube: Cell Growth
and Differentiation

Cytodifferentiation in the CNS

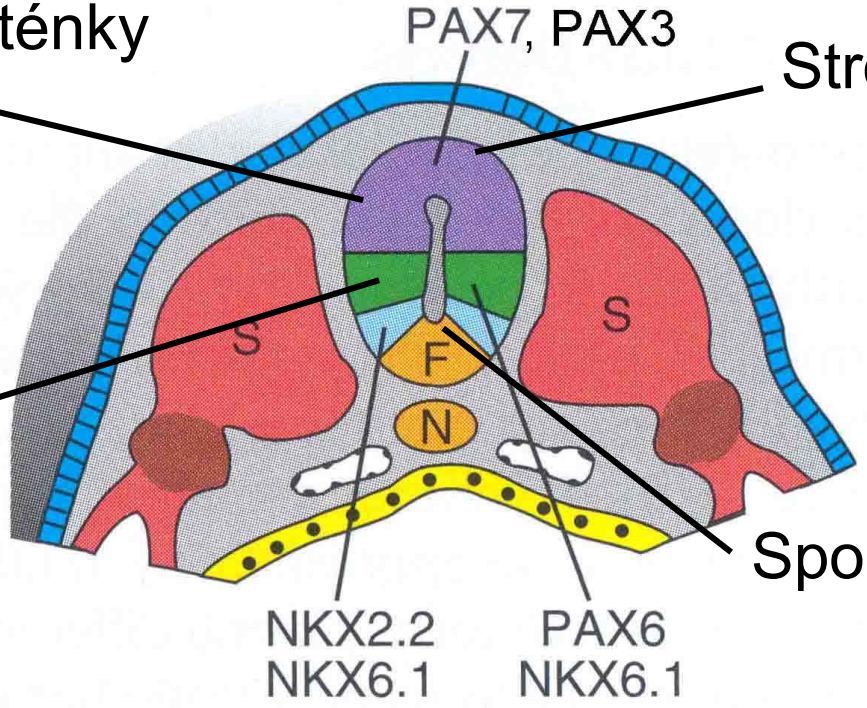
- Begins after the closure of the neural tube
- The wall of this tube is initially composed of a layer of **neuroepithelium**, where initially the the radial-glia-like morphology predominates
- Mitosis takes place in the **ventricular zone** (zone closest to the central canal)
- The first newly formed population are **neuroblasts** (young neurons) migrating into the **mantle zone**, which is the precursor of the grey matter
- Neuroblasts grow their processes to form the **marginal zone**, which eventually develops into the white matter
- The migration of neurons is facilitated by the radial glia
- The next (i.e. later-forming) population are the **glioblasts**, which give rise to oligodendrocytes and astrocytes
- **Microglia** are cells related to macrophages, they do not originate in neuroepithelium

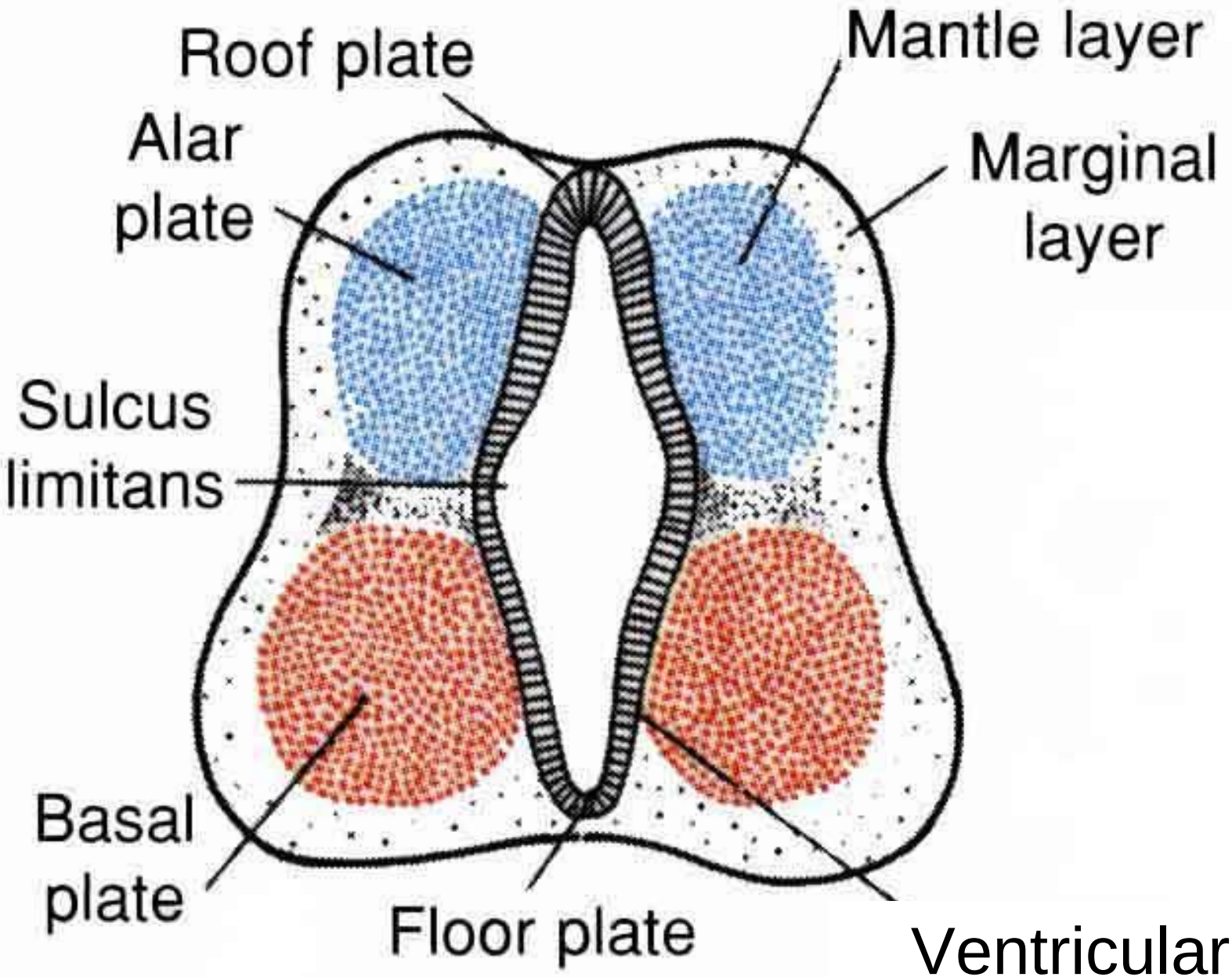
DEVELOPMENT OF THE SPINAL CORD

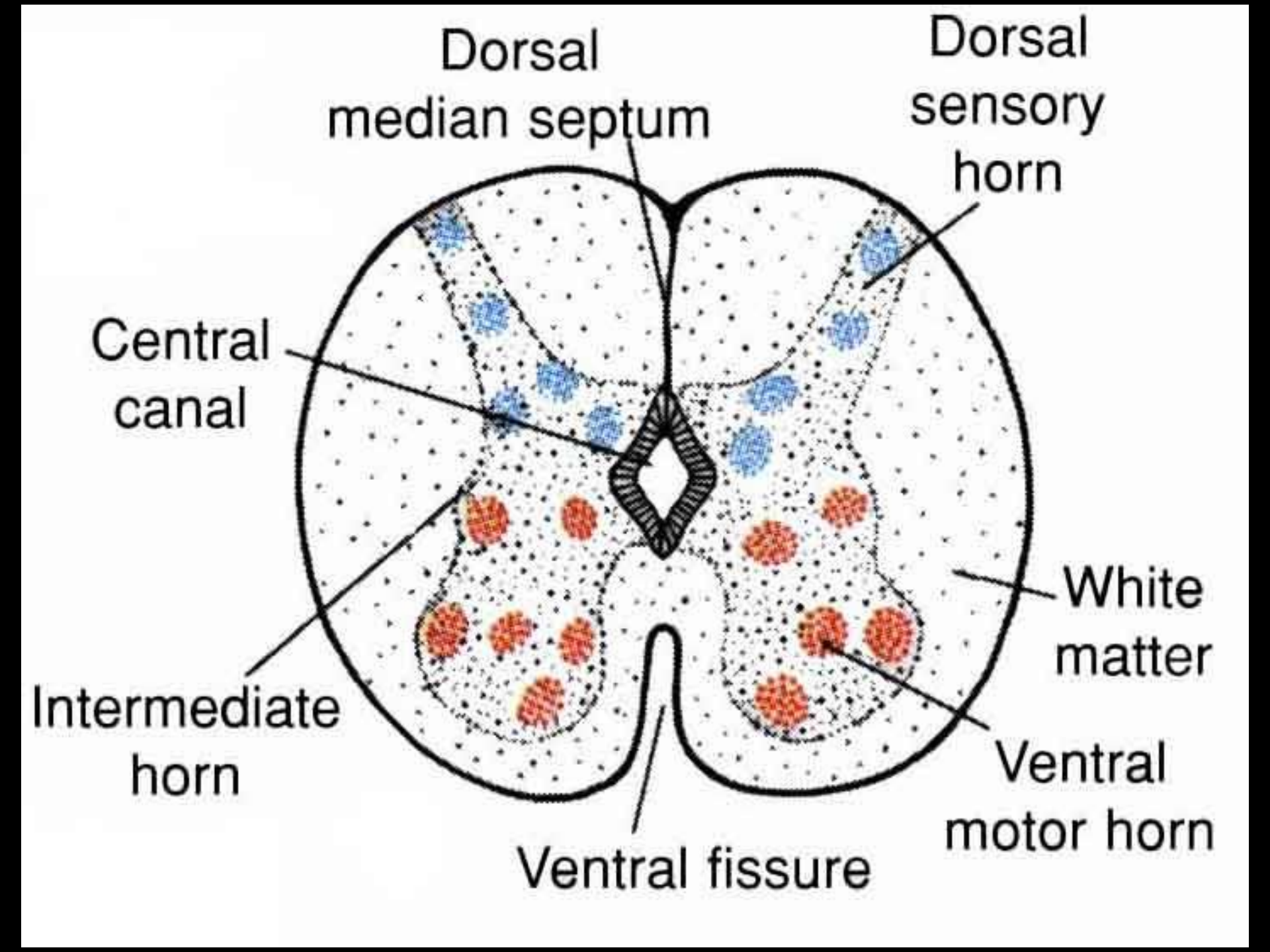


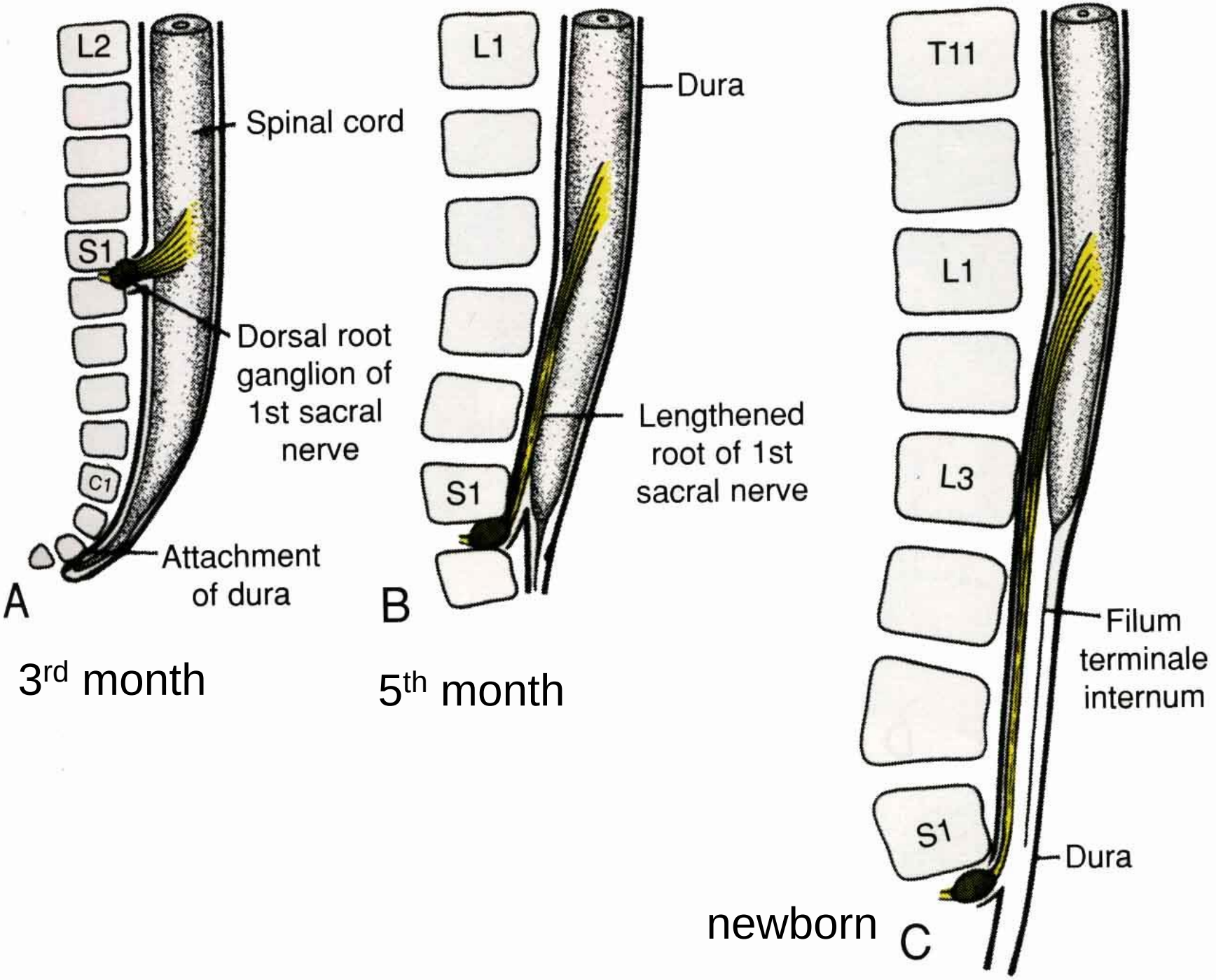
Alární (dorzální) ploténky

Bazální (ventrální) ploténky (zelená i modrá oblast)




Roof plate
Mantle layer
Alar plate
Marginal layer
Sulcus limitans
Basal plate
Floor plate
Ventricular layer


Dorsal
median septum
Dorsal
sensory
horn
Central
canal
White
matter
Intermediate
horn
Ventral
motor horn
Ventral fissure


L2
Spinal cord
S1
Dorsal root ganglion of 1st sacral nerve
C1
Attachment of dura
A
3rd month
L1
Dura
Lengthened root of 1st sacral nerve
S1
B
5th month
T11
L1
L3
Filum terminale internum
S1
Dura
newborn
C

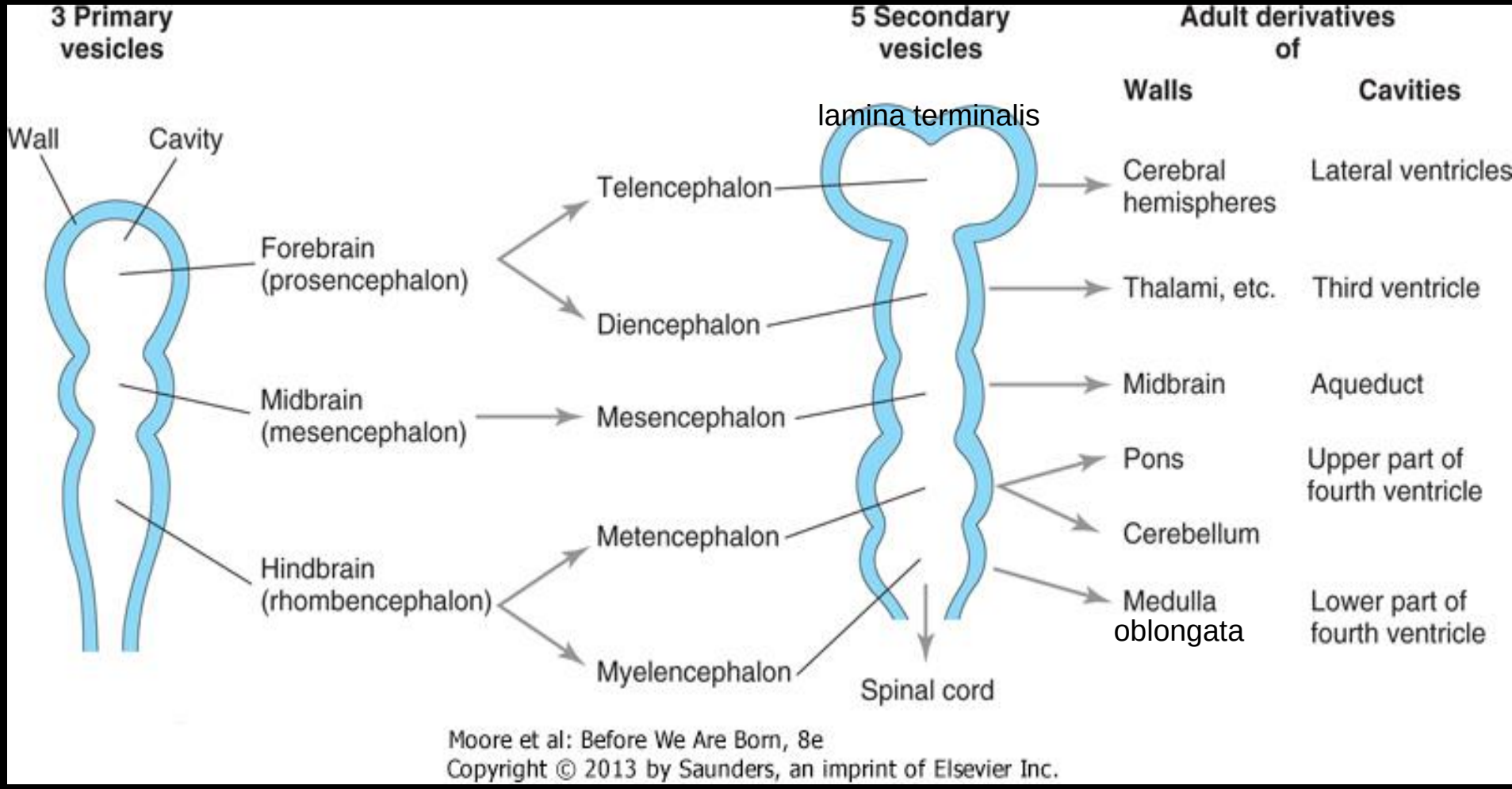
Development of the spinal cord – summary

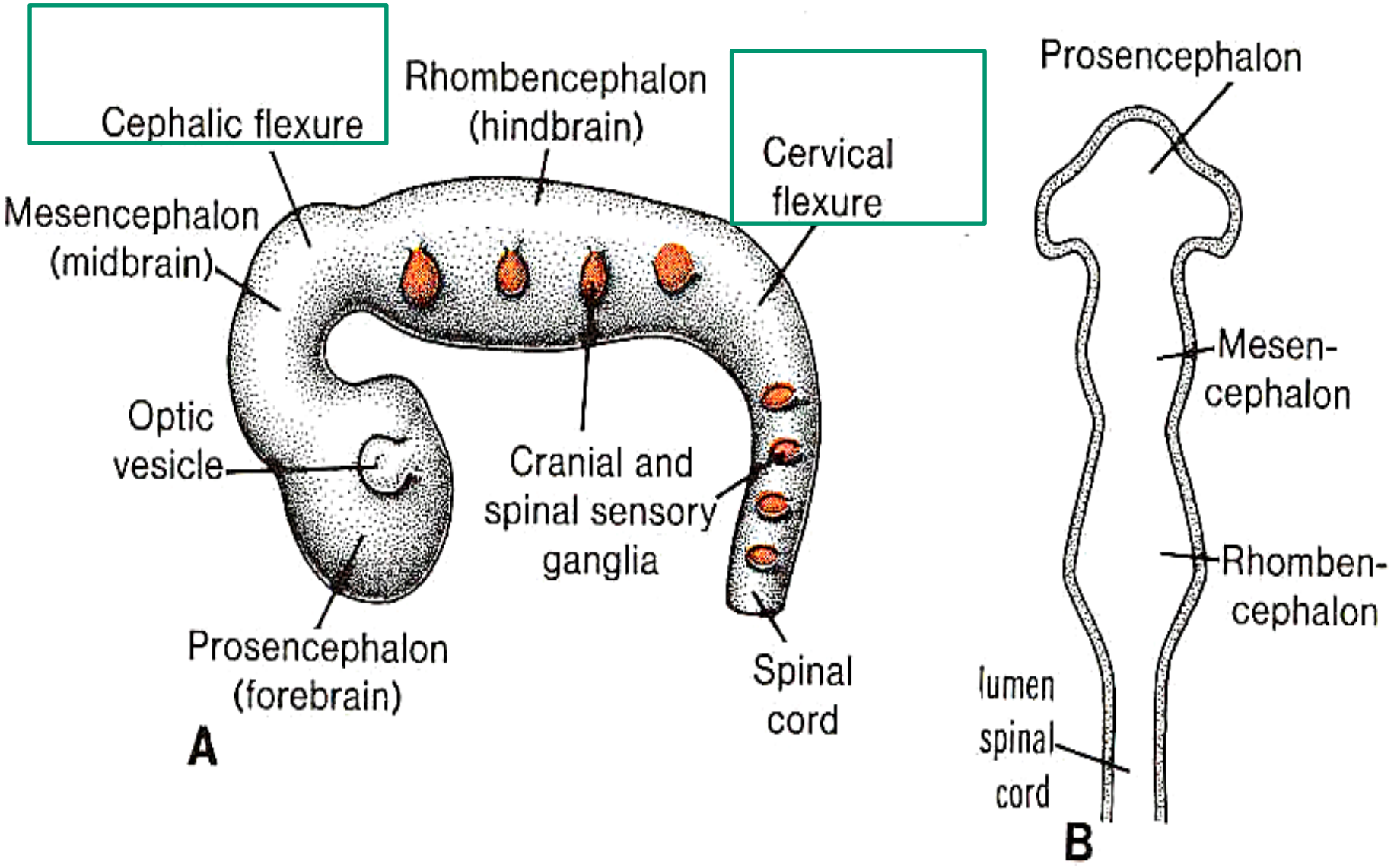
- At the end of the 4th week, the neurons of the mantle zone divide into paired **basal** (ventral) and **alar** (dorsal) plates, which are separated by the **sulcus limitans**
- Dorsally, the neural tube is closed by the **roof plate**, ventrally by the **floor plate**
- **Motor neurons** develop from the **basal plate**, its more dorsal part gives rise to efferent sympathetic and parasympathetic neurons in the thoracolumbar and sacral regions
- The **alar plate** develops into **interneurons**
- Thus, in simplified terms, the posterior horns of the grey matter arise from the alar, while the anterior horns arise from the basal plate
- The white matter arises from the marginal zone and contains neuronal processes

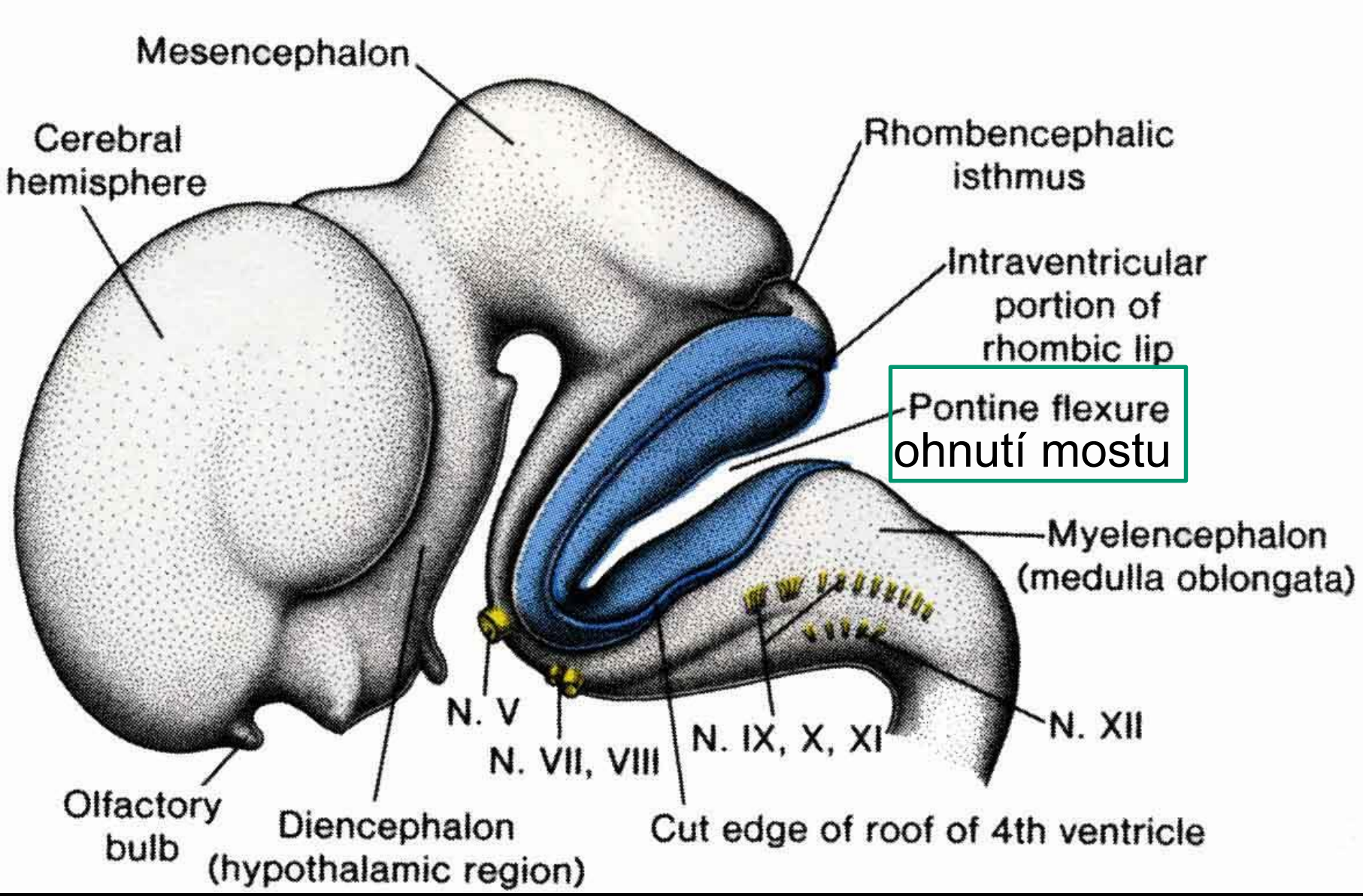
BRAIN DEVELOPMENT

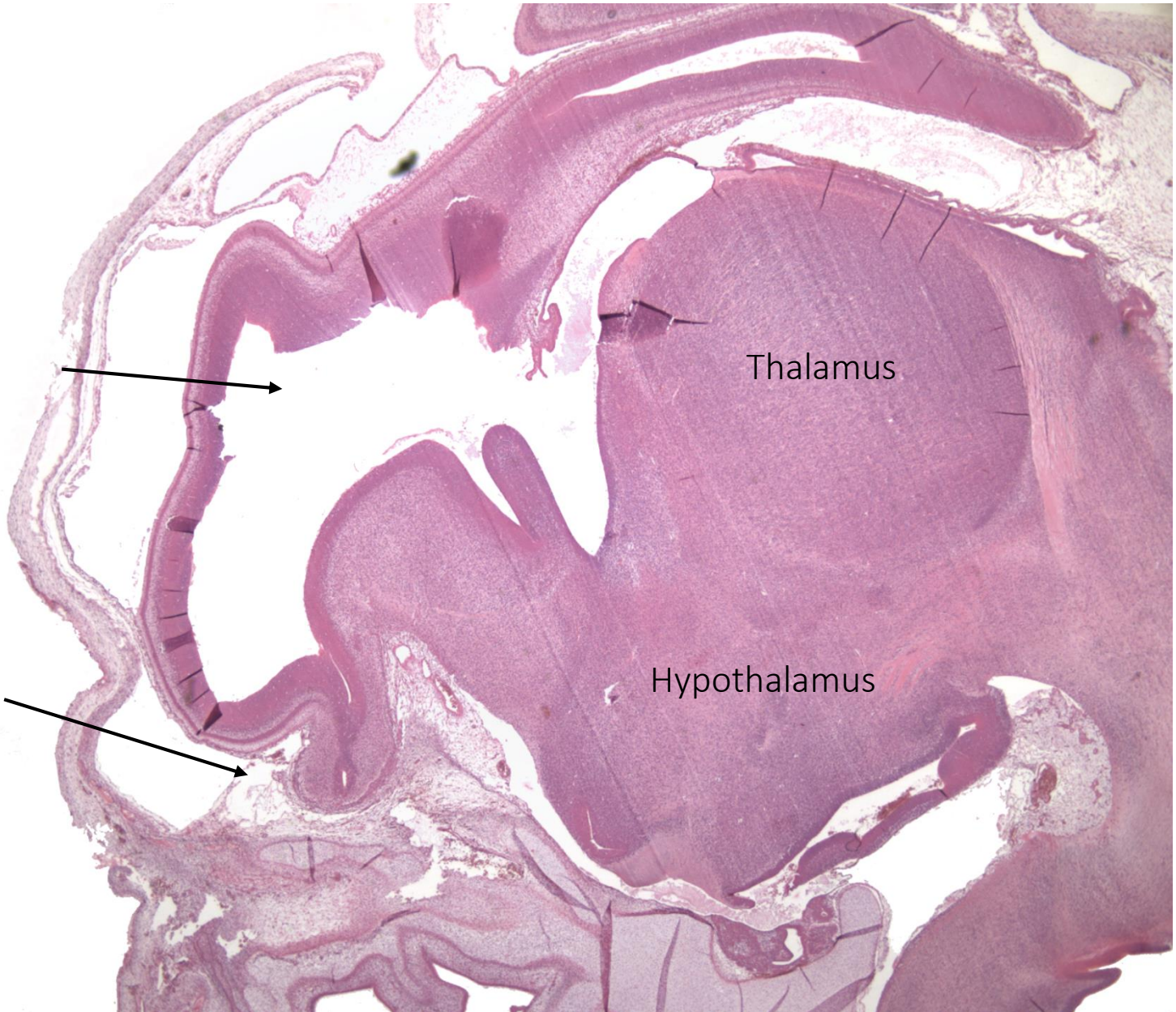
4. týden

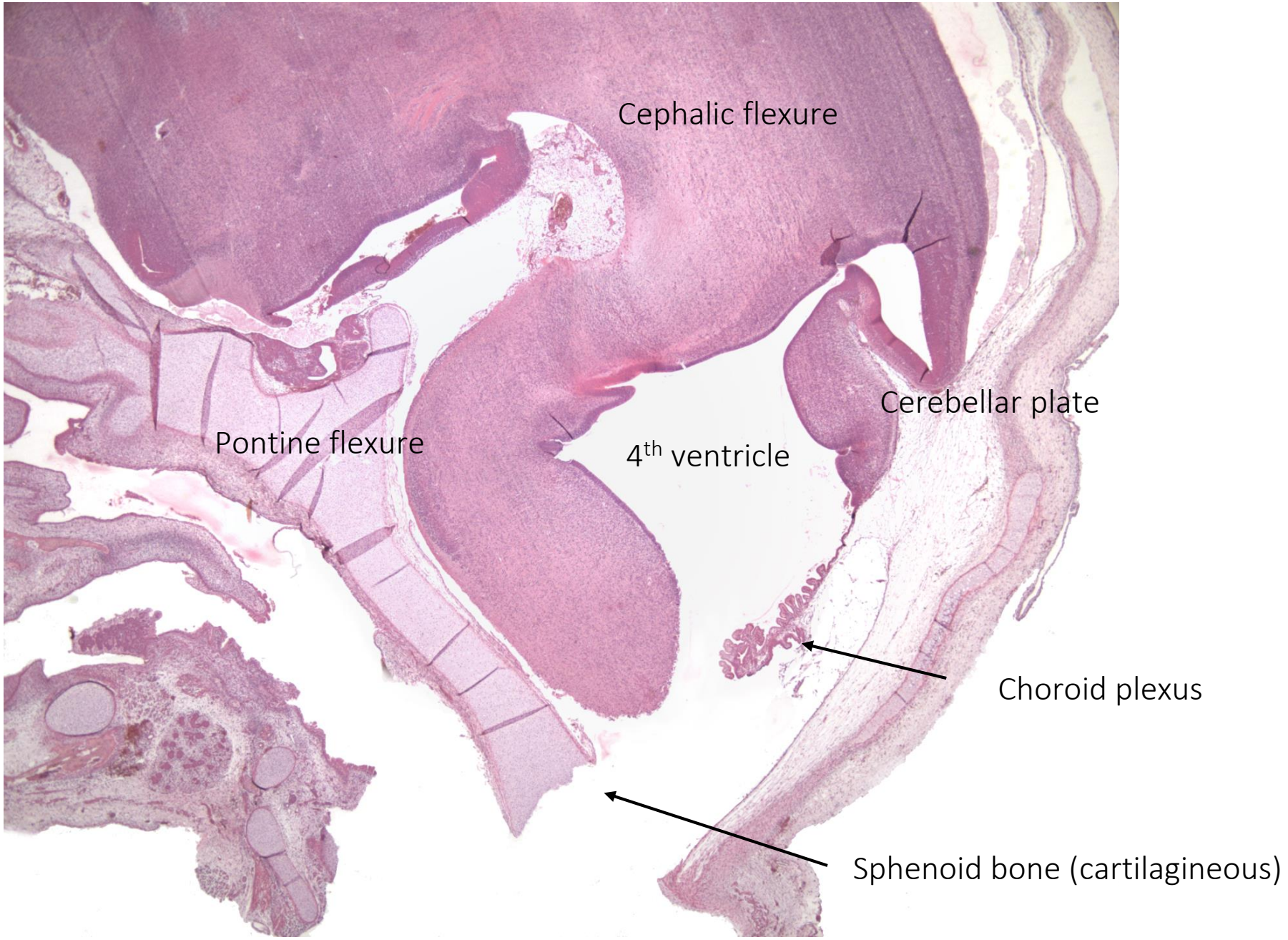
5. týden



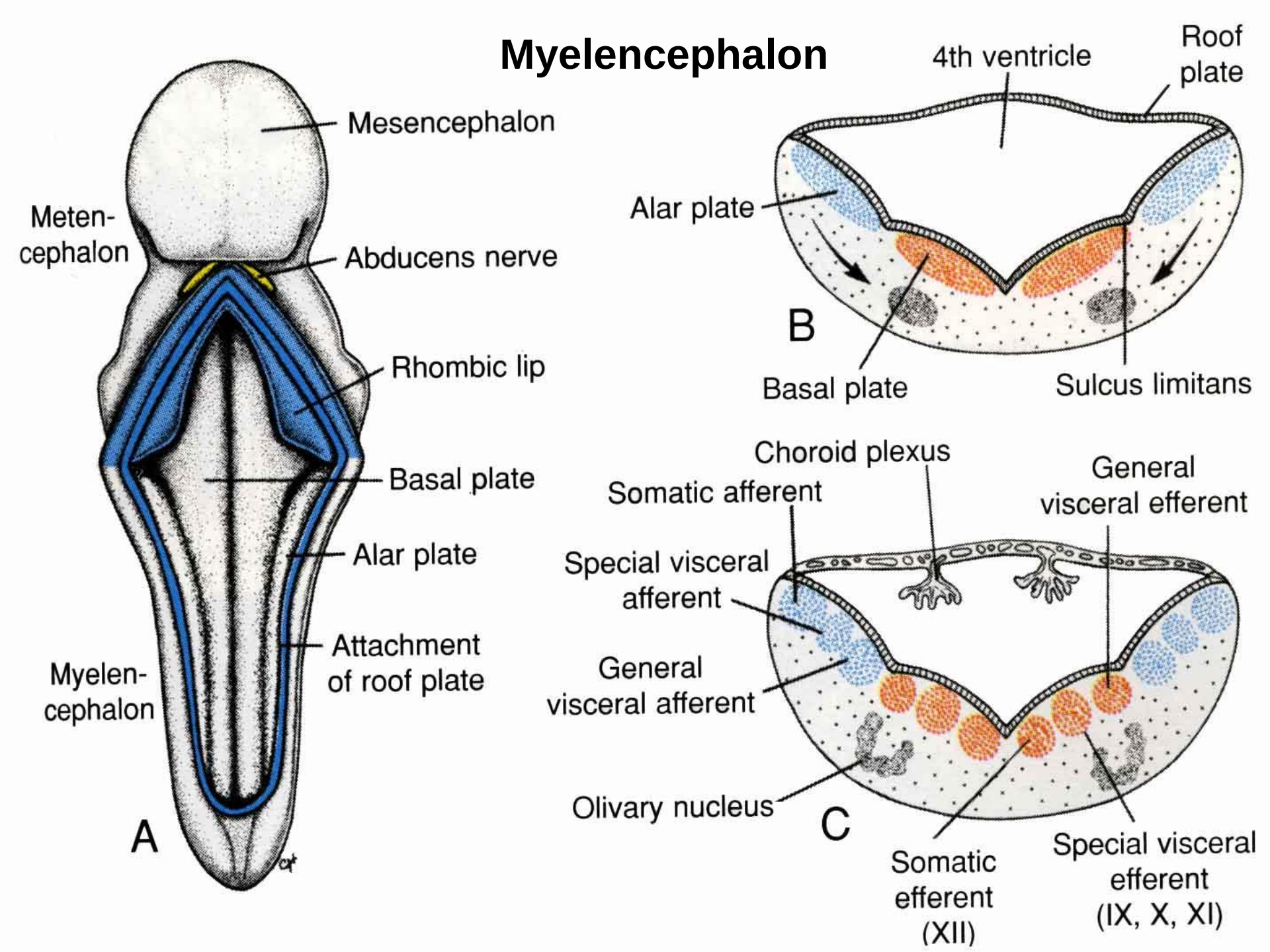

Cephalic flexure
Rhombencephalon
(hindbrain)
Cervical
flexure
Mesencephalon
(midbrain)
Optic
vesicle
Cranial and
spinal sensory
ganglia
Prosencephalon
(forebrain)
Spinal
cord
A
Prosencephalon
Mesen-
cephalon
Rhomben-
cephalon
lumen
spinal
cord
B

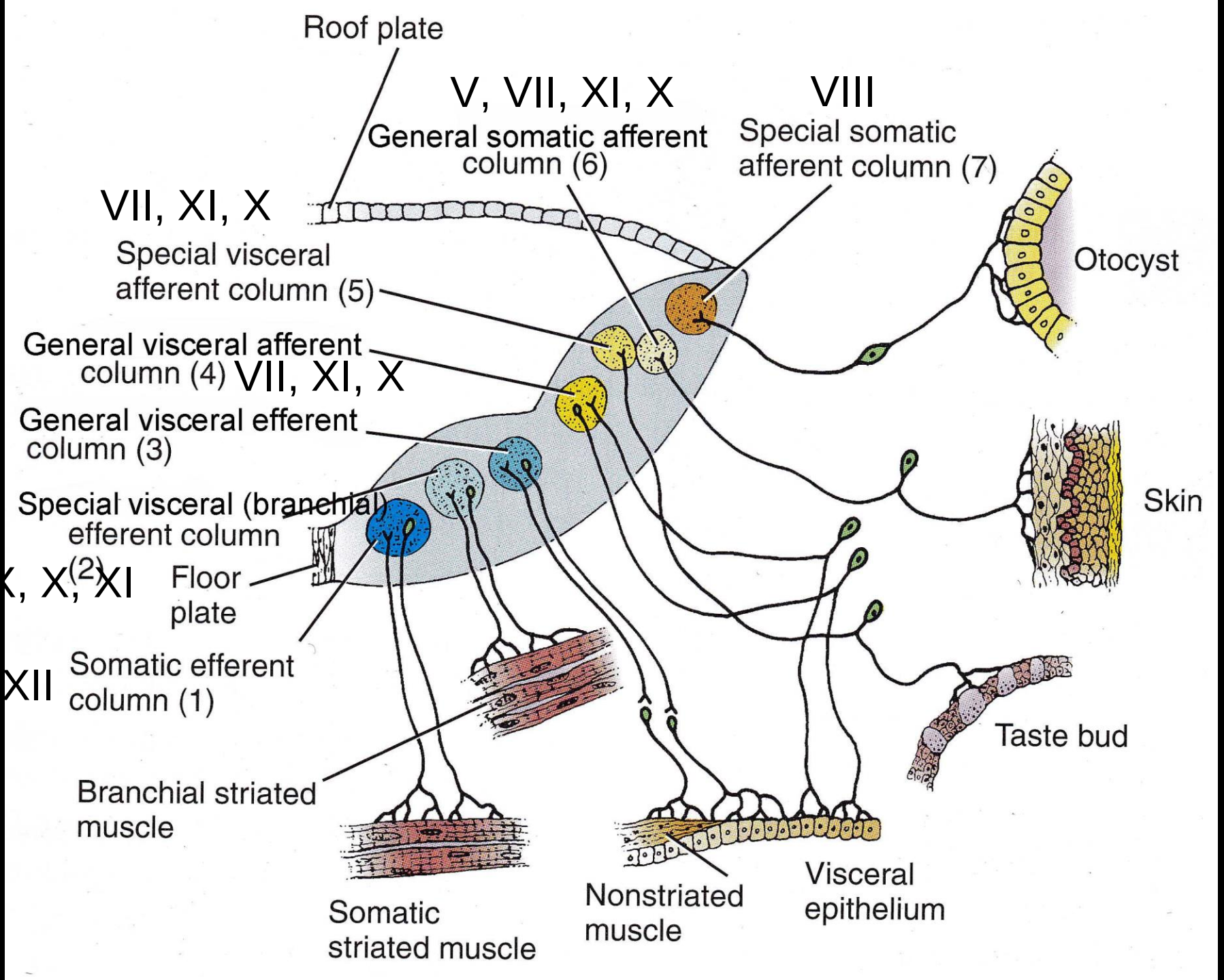

Mesencephalon
Cerebral hemisphere
Rhombencephalic isthmus
Intraventricular portion of rhombic lip
Pontine flexure
ohnutí mostu
Myelencephalon (medulla oblongata)
N. V
N. VII, VIII
N. IX, X, XI
N. XII
Olfactory bulb
Diencephalon (hypothalamic region)
Cut edge of roof of 4th ventricle

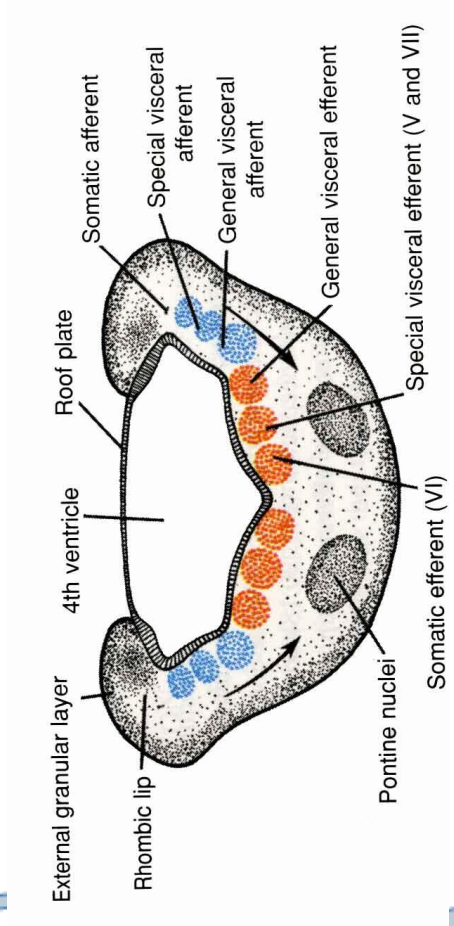

Lateral ventricle
Thalamus
Olfactory bulb
Hypothalamus

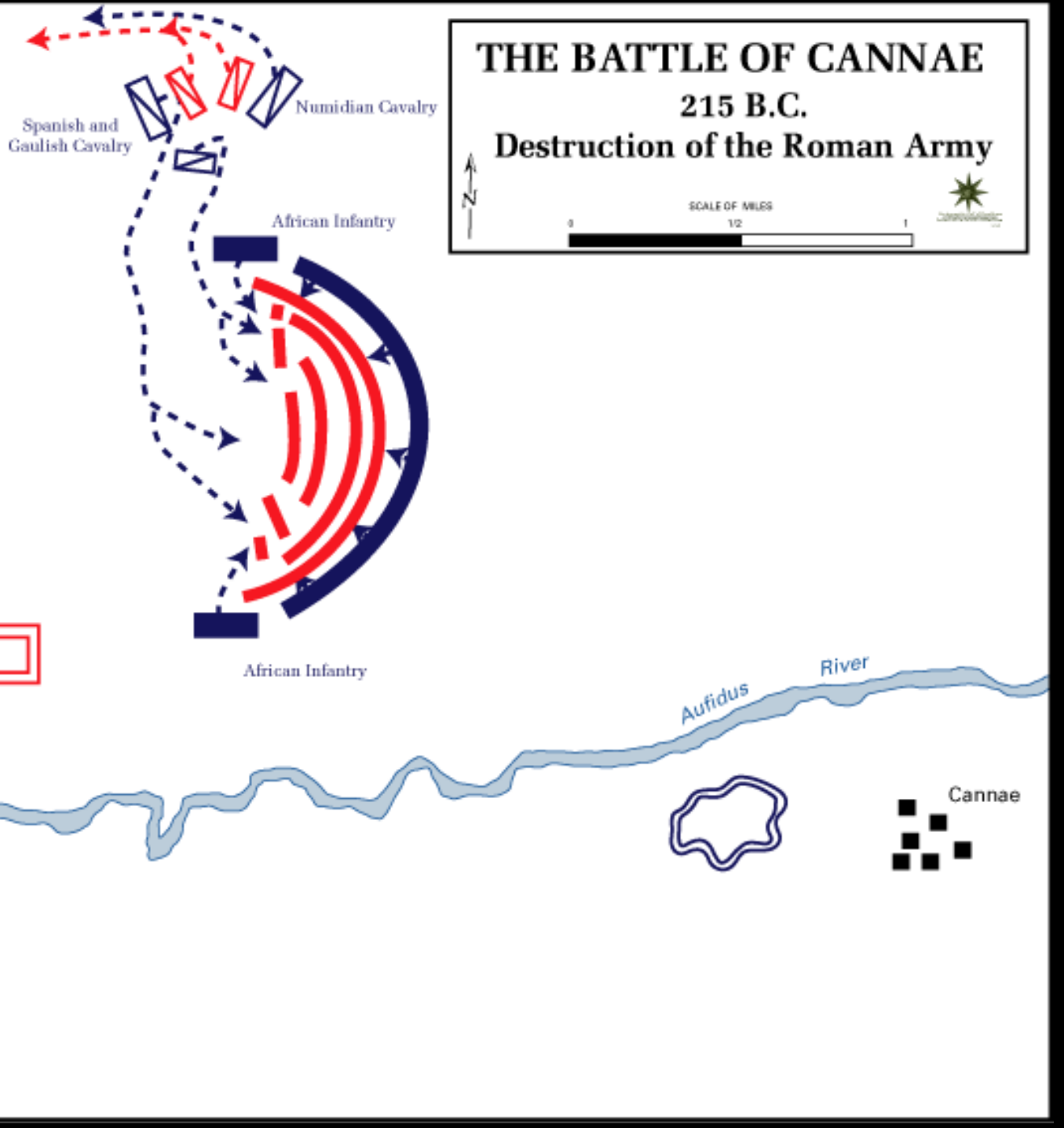

Cephalic flexure
Pontine flexure
4th ventricle
Cerebellar plate
Choroid plexus
Sphenoid bone (cartilagineous)

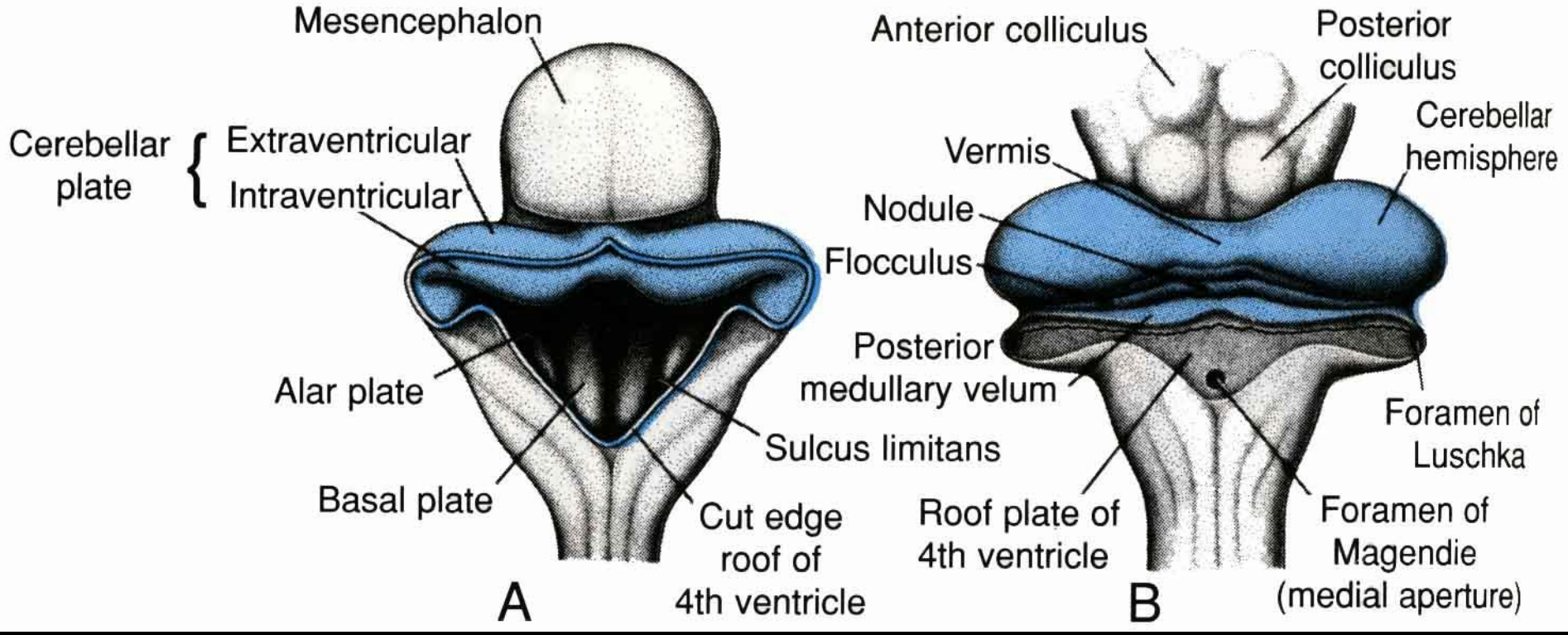
Myelencephalon

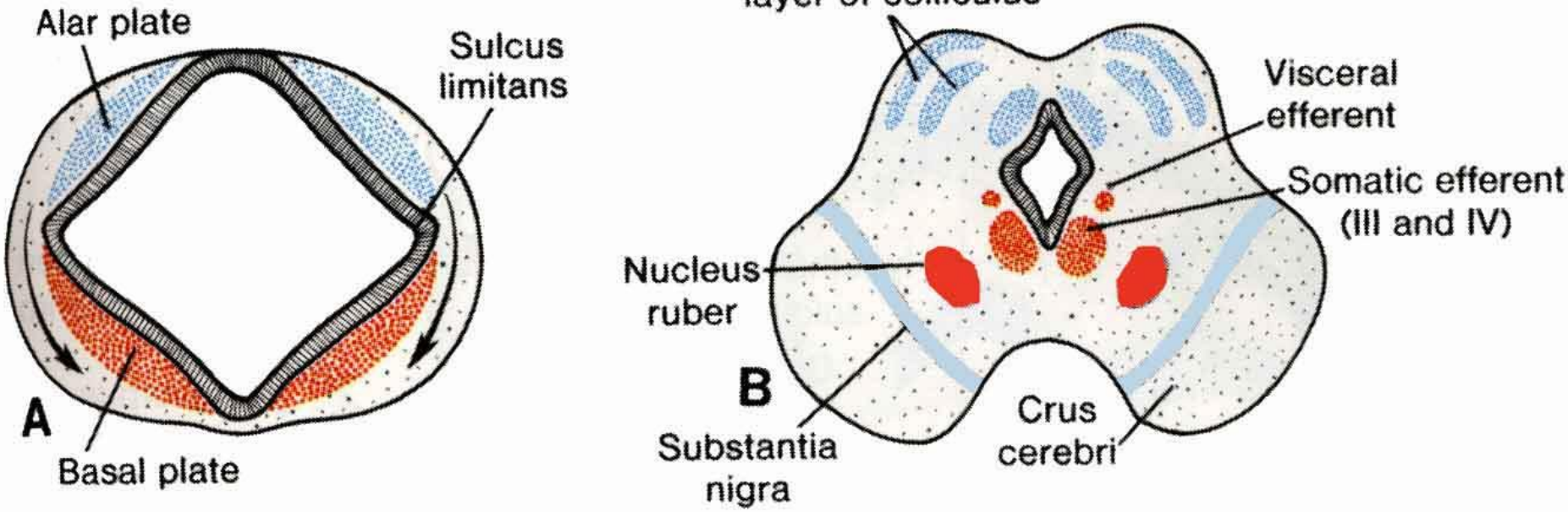


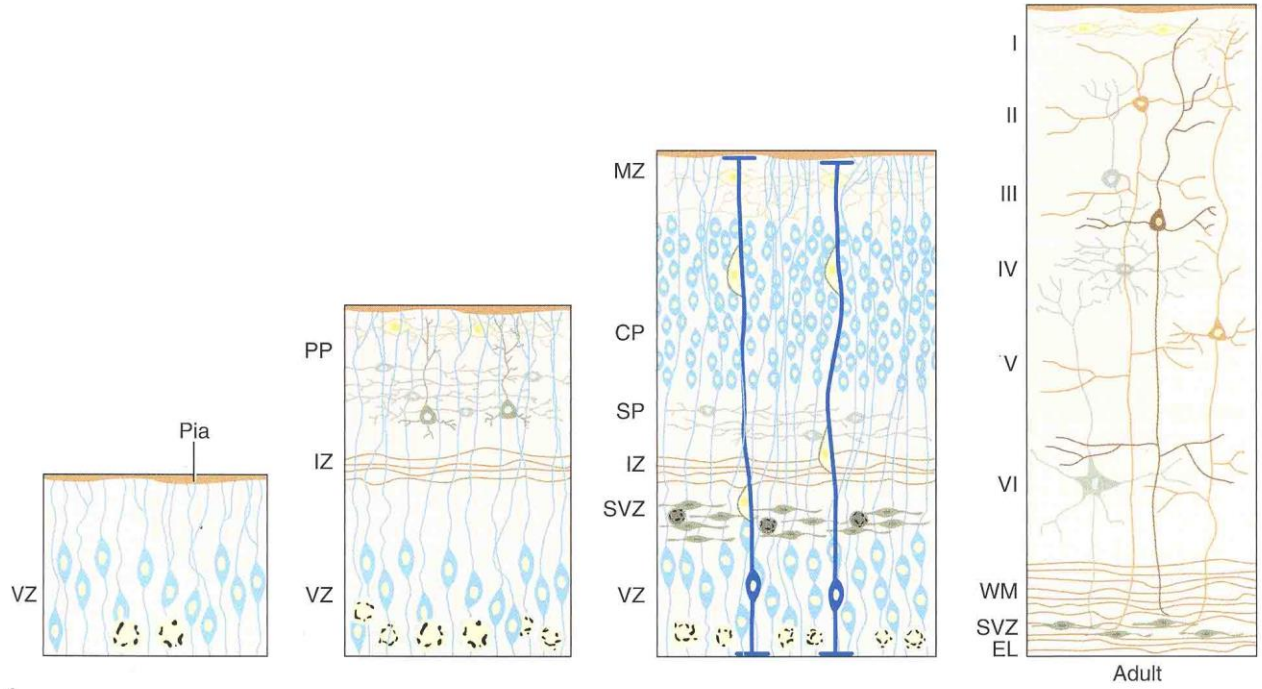

Roof plate
V, VII, XI, X
General somatic afferent column (6)
VIII
Special somatic afferent column (7)
VII, XI, X
Special visceral afferent column (5)
Otocyst
General visceral afferent column (4)
VII, XI, X
General visceral efferent column (3)
Special visceral (branchial) efferent column (2)
Skin
X, XI
Floor plate
XII
Somatic efferent column (1)
Taste bud
Branchial striated muscle
Somatic striated muscle
Nonstriated muscle
Visceral epithelium


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

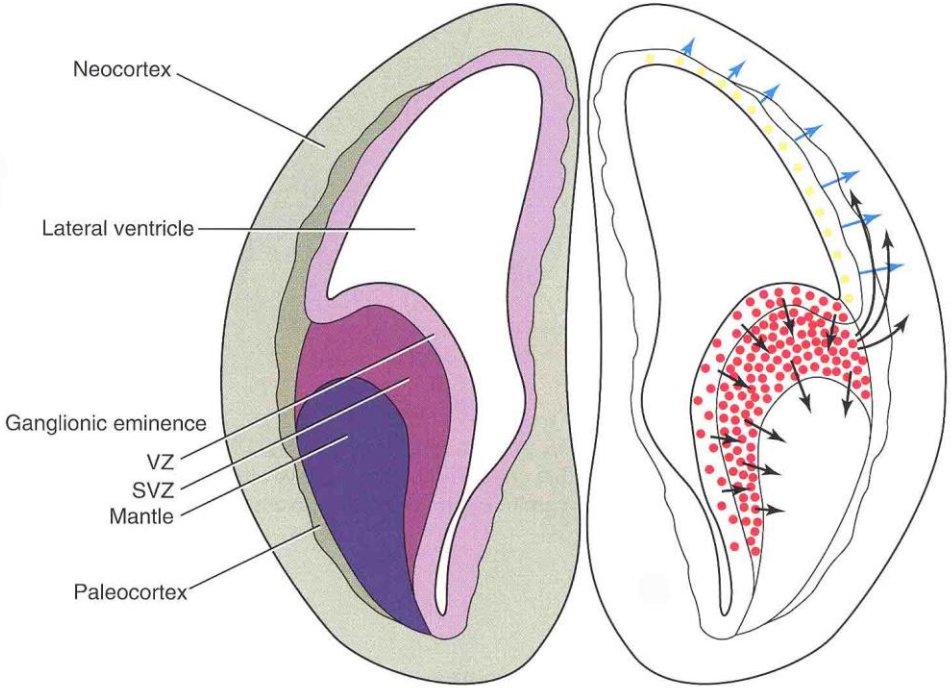

THE BATTLE OF CANNAE
215 B.C.
Destruction of the Roman Army
N
SCALE OF MILES
0
1/2
1
Spanish and Gaulish Cavalry
Numidian Cavalry
African Infantry
African Infantry
Aufidus River
Cannae


Mesencephalon
Cerebellar plate
Extraventricular
Intraventricular
Alar plate
Basal plate
Sulcus limitans
Cut edge roof of 4th ventricle
A
Anterior colliculus
Posterior colliculus
Cerebellar hemisphere
Vermis
Nodule
Flocculus
Posterior medullary velum
Foramen of Luschka
Roof plate of 4th ventricle
Foramen of Magendie (medial aperture)
B

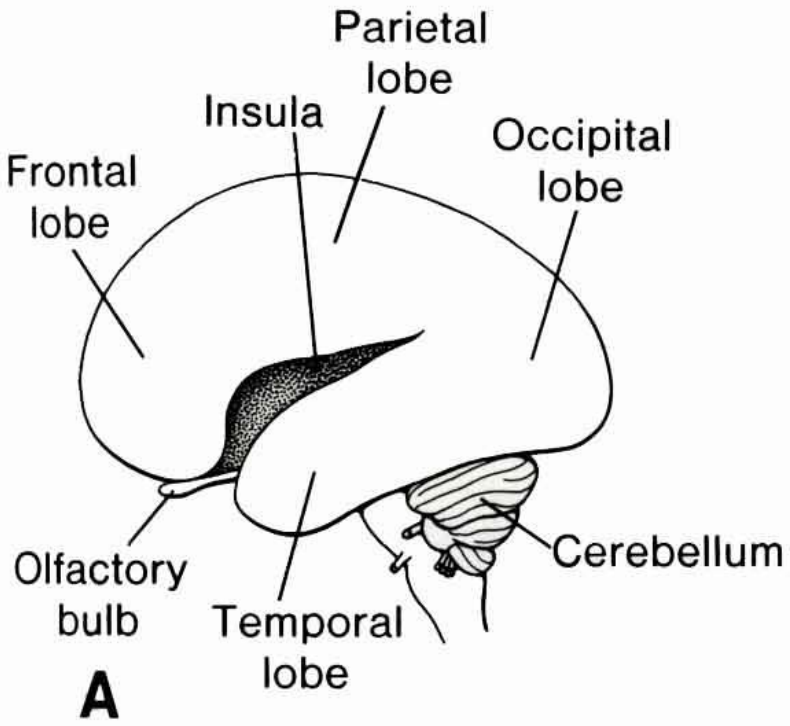

Alar plate
Sulcus limitans
A
Basal plate
Stratified nuclear layer of colliculus
Visceral efferent
Somatic efferent (III and IV)
Nucleus ruber
B
Substantia nigra
Crus cerebri


Pia
VZ
PP
IZ
VZ
MZ
CP
SP
IZ
SVZ
VZ
I
II
III
IV
V
VI
WM
SVZ
EL
Adult

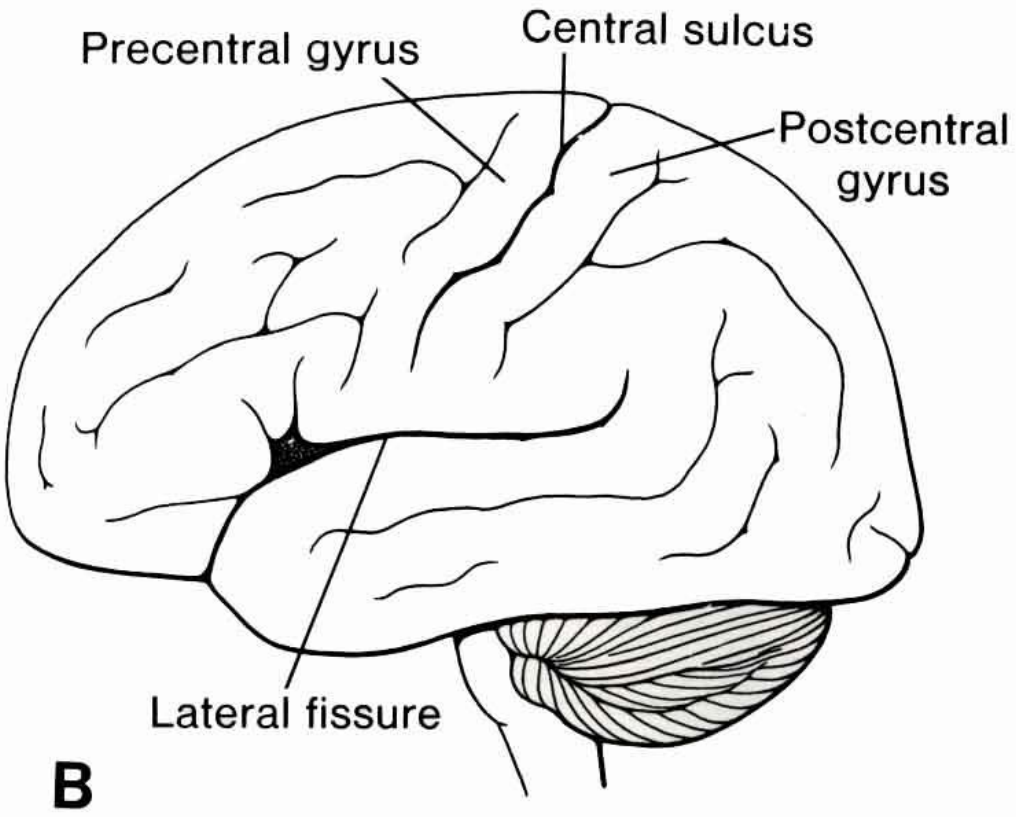
A


Neocortex
Lateral ventricle
Ganglionic eminence
VZ
SVZ
Mantle
Paleocortex

B



7 months



9 months

Brain development - summary

- The 3 primary brain vesicles (**rhombencephalon, mesencephalon and prosencephalon**) divide into 5 secondary brain vesicles (**myelencephalon, metencephalon, mesencephalon, diencephalon, telencephalon**)
- The cervical and cephalic felexures are also formed, pontine flexure develops later

Rhombencephalon

- The roof plate of the rhombencephalon covers the **fourth ventricle**
- The myelencephalon corresponds to the **medulla oblongata**, the basal plate and the alar plate each form 3 groups of neurons that become **cranial nerve nuclei** and other association nuclei
- The **metencephalon** is divided into the **pons** (basic organization similar to the medulla oblongata), and the **cerebellum**, which is a derivative of the alar plate and gradually grows over the roof plate

Brain development - summary

Mesencephalon

- Even in the mesencephalon, the basic division into derivatives of the basal and alar plates is approximately preserved
- The basal plate develops into the tegmentum, containing the somato- and visceromotor nuclei of **nerves III and IV**
- The alar plate develops into a tectum with two pairs of **colliculi** (corpora quadrigemina)

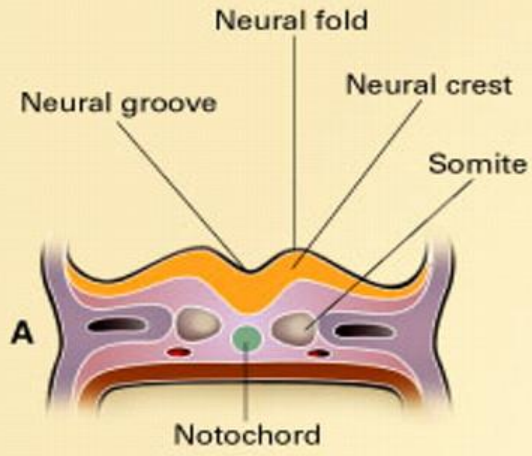
Prosencephalon

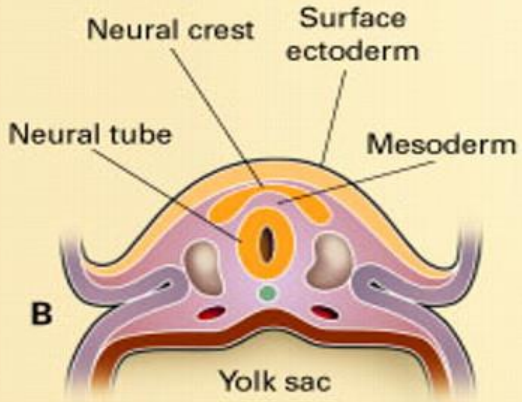
- The **prosencephalon** is thought to be a derivative of the alar plate with no significant contribution from the basal plate
- The **diencephalon** gives rise to the hypothalamus, the thalamus and the epithalamus (including glandula pinealis)
- The thalamus grows the most of these, the opposite masses even join together by so-called thalamic adhesions (massa intermedia)
- The diencephalon also gives rise to the two **optic cups** and the infundibulum – the precursor of the **neurohypophysis**

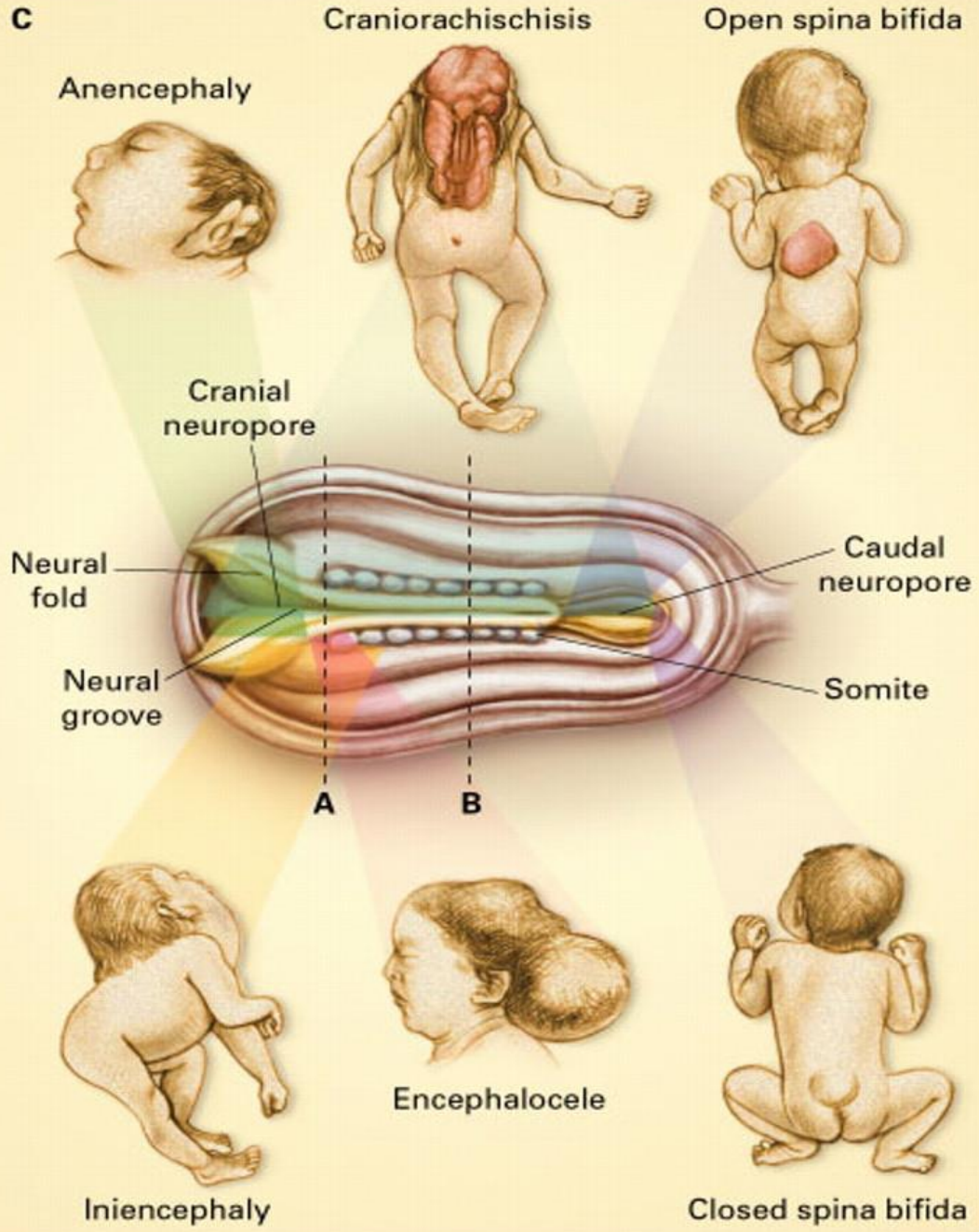
Brain development - summary

Prosencephalon

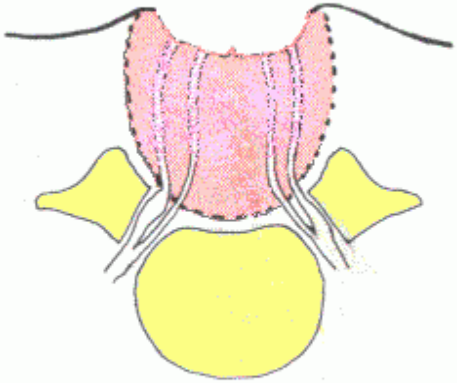
- The **telencephalon** arises from two spherical swellings on the sides of the prosencephalon, which gradually overgrow the diencephalon and thus become the **cerebral hemispheres**
- Lateral cerebral ventricles initially occupy most of the volume of the hemispheres, but their proportion decreases as the telencephalon grows
- The choroid fissure remains on the medial side of the hemisphere, where the pia mater inserts into the plexus choroideus of the **lateral ventricle**
- Histogenesis of the cerebral cortex is a complex process involving several migratory waves from the **ventricular** and **subventricular** zones and from **ganglionic eminences** located on the ventral side of the hemisphere
- By the 7th month, the hemisphere is already in the **lobation** stage and in the following months the hemispheres undergo **gyrification**
- The brain grows to its final size at about 7 years

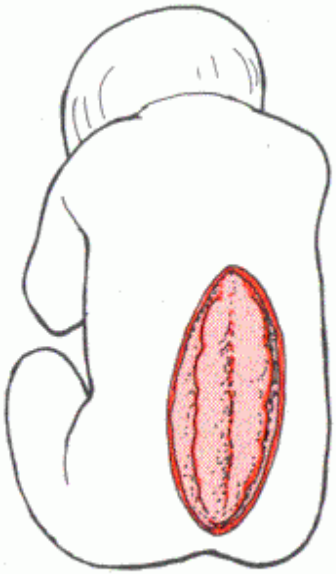

Neural fold
Neural groove
Neural crest
Somite
A
Notochord


Neural crest
Surface ectoderm
Neural tube
Mesoderm
B
Yolk sac

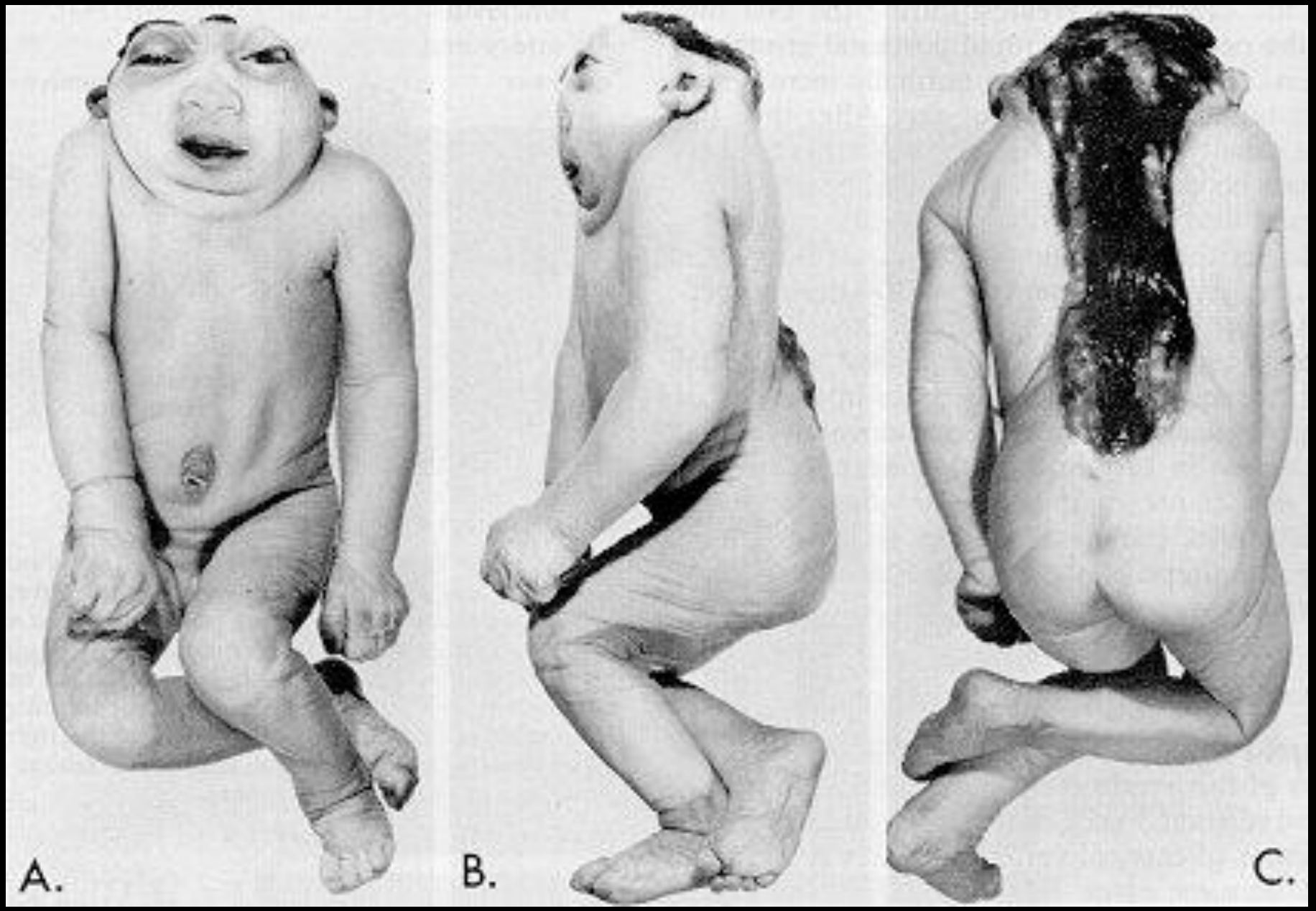

C
Craniorachischisis
Open spina bifida
Anencephaly
Cranial neuropore
Neural fold
Caudal neuropore
Neural groove
Somite
A
B
Encephalocele
Iniencephaly
Closed spina bifida

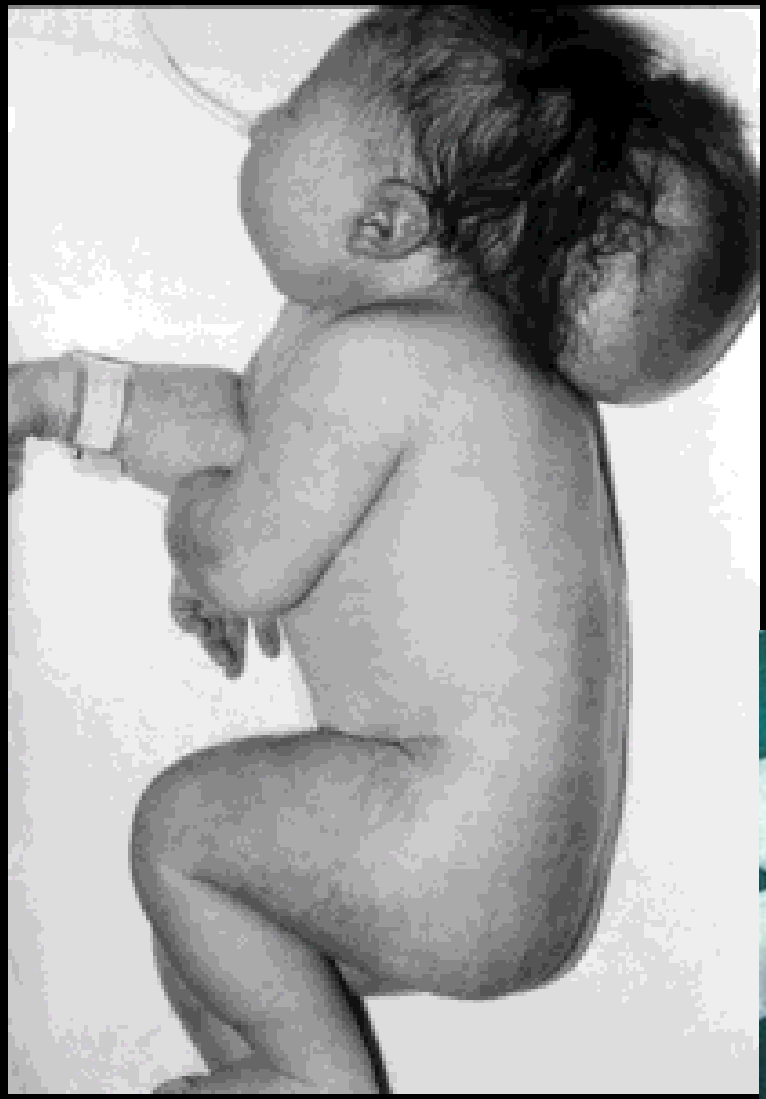
MYELOSCHISIS

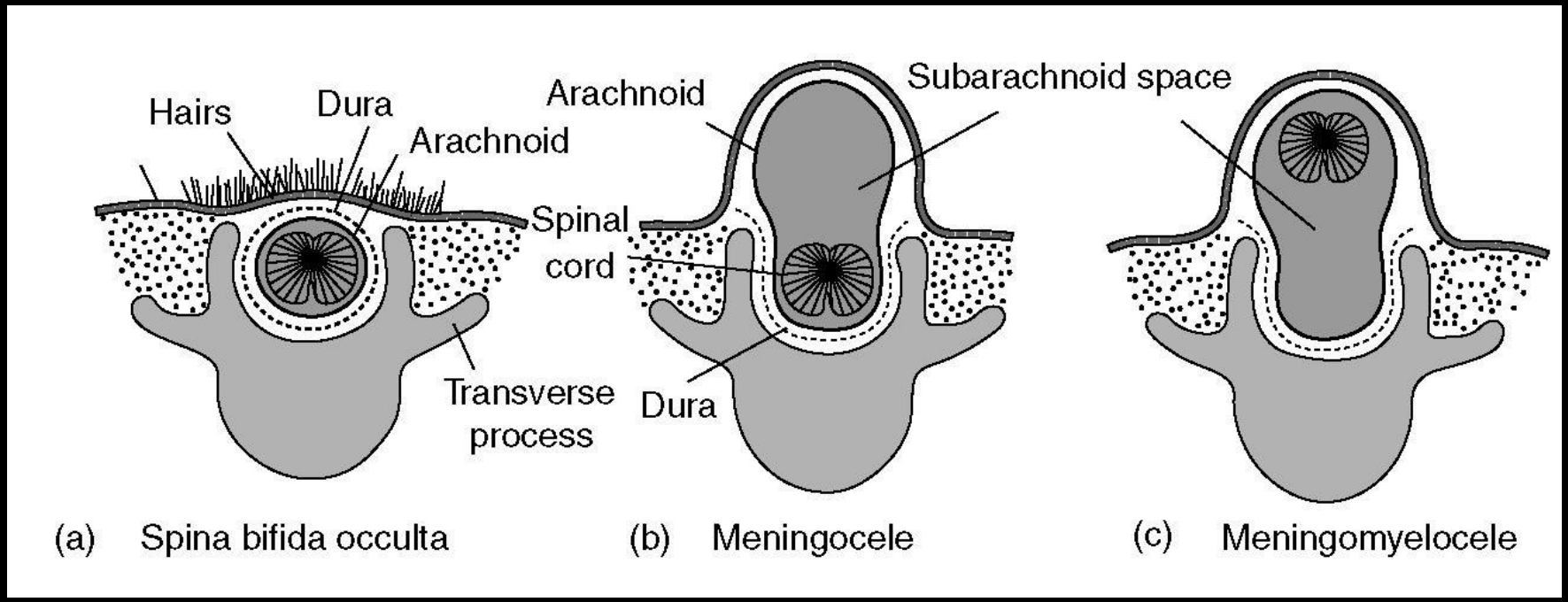


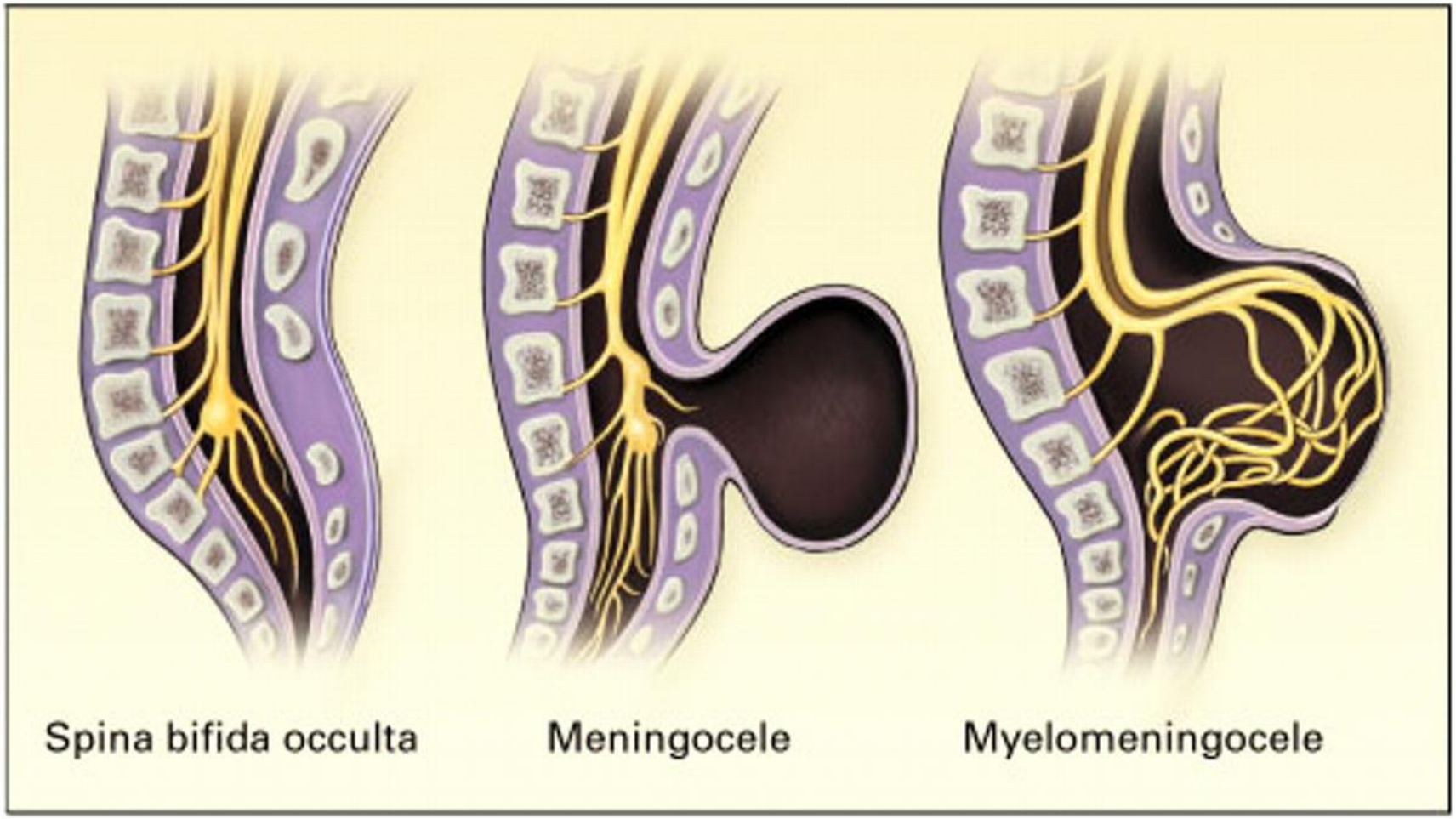


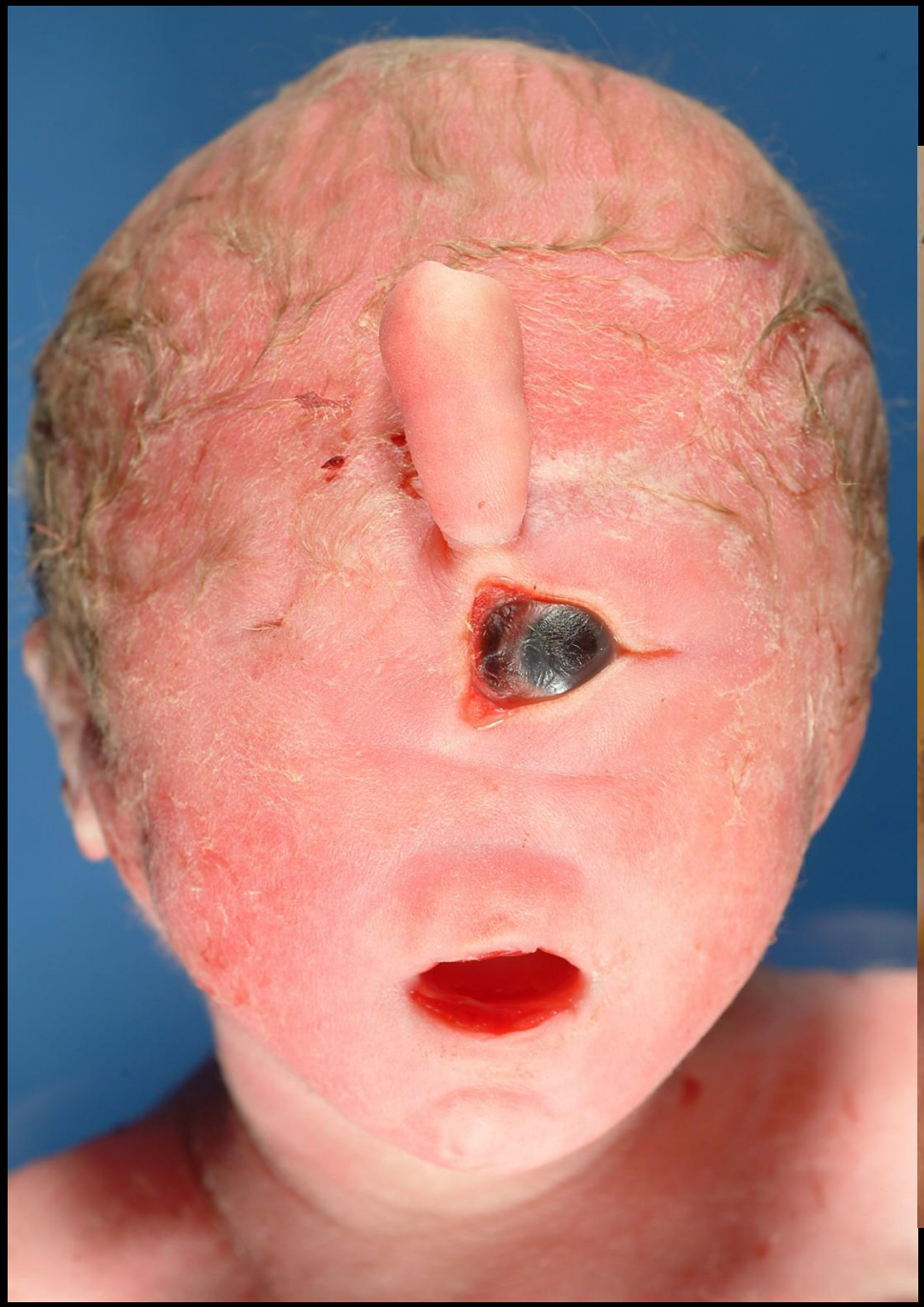
Missing: Roof plate
Vertebral arch
Skin


A.
B.
C.



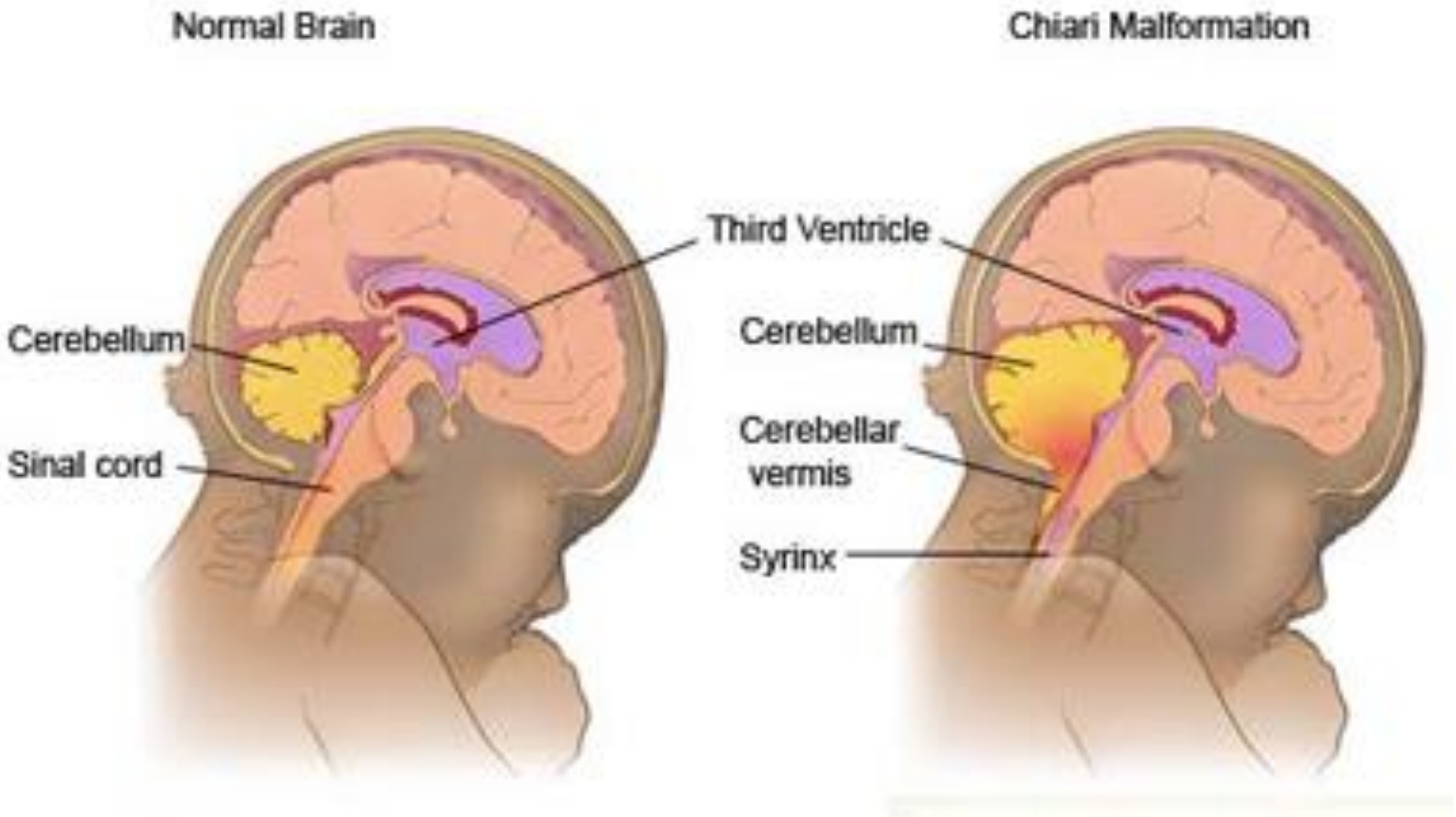

Hairs
Dura
Arachnoid
Spinal cord
Transverse process
Arachnoid
Subarachnoid space
Dura
(a) Spina bifida occulta
(b) Meningocele
(c) Meningomyelocele


Spina bifida occulta
Meningocele
Myelomeningocele

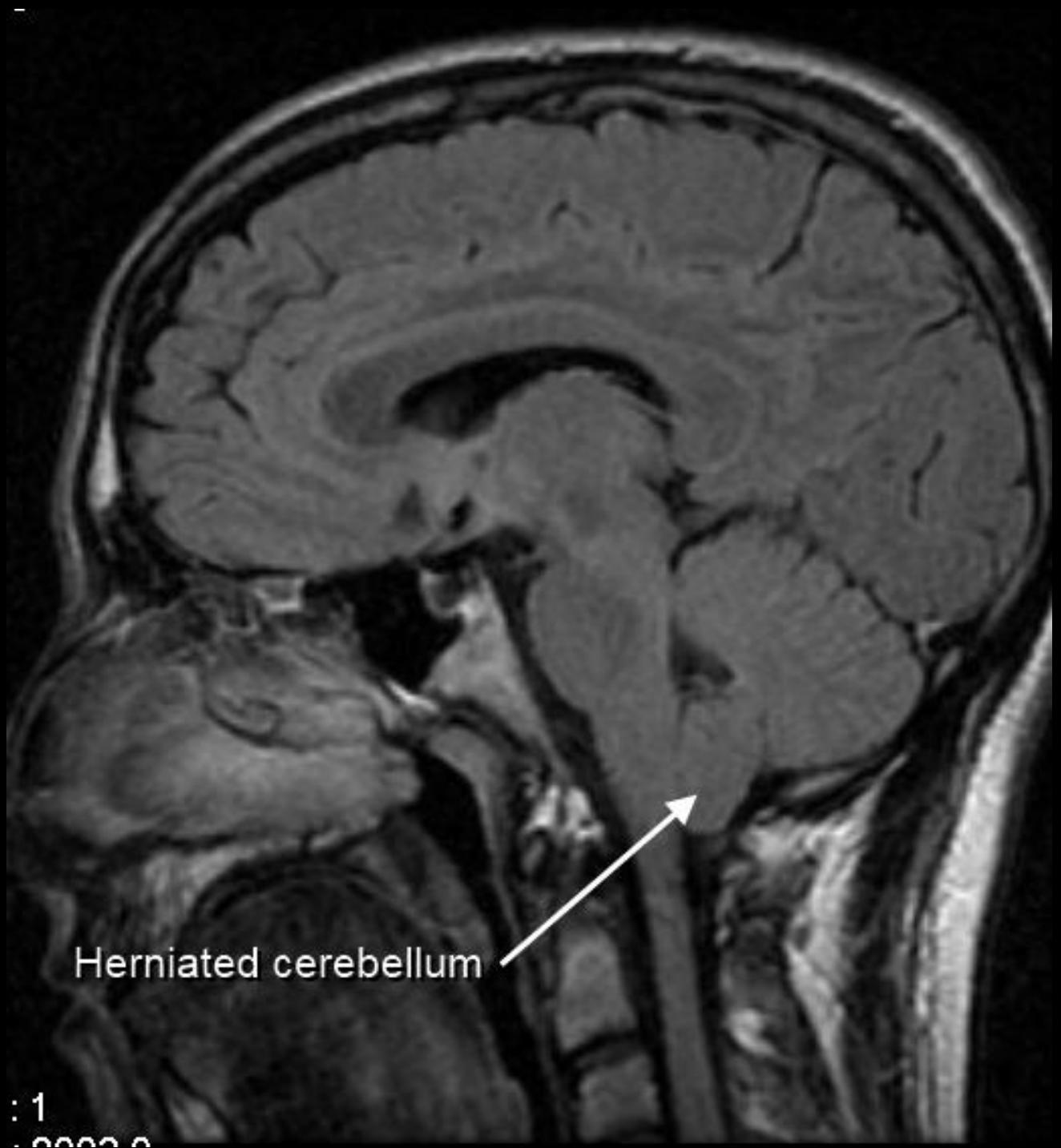



A

Chiari (Arnold-Chiari) malformace



- **dystopie** mozečku a oblongáty **do páteřního kanálu**, která se klinicky projevuje hydrocefalem.


Herniated cerebellum

Developmental disorders of the nervous systém - closure defects

- **Anencephaly**, **craniorachischisis** and **myeloschisis** form a group of neural tube closure defects, survival is severely limited
- In spina bifida the spinal canal is not closed often leading to **meningocele** or **meningomyelocele**; these defects are usually associated with neurological disability of varying degrees
- **Encephalocele** is a protrusion of brain through the defect in the skull; the prognosis here also depends on the size of the defect
- Elevated levels of **alpha-fetoprotein** in maternal blood serum play a role in prenatal diagnosis
- **Spina bifida occulta** is a defect in which the defect of the spinal canal is only slightly visible, in the area of the lesion we can find the so-called neurocutaneous signs (pigmentation, hair, angioma, retracted skin...), it occurs in up to 2% of people

Developmental disorders of the nervous system – holoprosencephaly

- **Holoprosencephaly** is caused by failure of the prosencephalon to divide into two halves, manifested by neurological deficit and craniofacial malformations (**cyclopia, synophthalmia, proboscis**), most patients do not survive the first year
- There are also milder variants with incomplete hemispheric division and milder facial stigmatisation, here the prognosis is better, but with severe neurological and cognitive deficits
- The frequency of the defect is reported to be around 1:10000 births, but up to 1:250 in spontaneous abortions

Developmental disorders of the nervous system - Chiari malformation

- **Chiari malformation** is characterized by herniation of the **cerebellar tonsils** and sometimes part of the brainstem into the foramen magnum, often accompanied by **hydrocephalus** or **syringomyelia**
- There are several anatomically and clinically distinct subtypes, often accompanied by other defects (e.g. meningomyelocele)

Once upon a time, in the world of the cerebellum, there lived three characters: Purkinje Cell, Small Granular Cell, and Mossy Fiber. Purkinje Cell was known for his sophistication and grace, always dressed to the nines and never at a loss for words. Small Granular Cell, on the other hand, was a free-spirited and energetic type, often seen skipping and humming a tune.

Small Granular Cell had feelings for Purkinje Cell but didn't know how to express them. So, she started sending him messages via parallel fibers, hoping to catch his attention. Every day, Purkinje Cell would receive a message from Small Granular Cell, expressing her love and admiration for him.

Meanwhile, Mossy Fiber had been in love with Small Granular Cell for a long time. He knew that she loved receiving messages via a rosette in a glomerulus, so he started sending her messages every day, expressing his love and admiration for her.

As the days passed, Purkinje Cell was receiving messages from Small Granular Cell and Mossy Fiber was sending messages to her as well. Purkinje Cell was flattered by Small Granular Cell's messages but was unsure of how to respond, while Mossy Fiber was eager for a response from Small Granular Cell.

One day, Purkinje Cell decided to confront Small Granular Cell and ask her about her feelings for him. Meanwhile, Mossy Fiber decided to ask her about her feelings for him as well. The three of them met and discussed their feelings for each other.

Small Granular Cell was in a dilemma as she had feelings for both Purkinje Cell and Mossy Fiber. After much thought, she suggested that they all go on a triple date and see where this leads them. Purkinje Cell and Mossy Fiber agreed, and the three of them went on a triple date.

The date was a success, and they all had a great time. They went to the park, had a picnic, and played games. In the end, Small Granular Cell realized that she loved both Purkinje Cell and Mossy Fiber equally and couldn't choose between them.

So, she suggested that they all be friends and continue to send each other messages via parallel fibers and a rosette in a glomerulus. From that day on, the three of them became the best of friends and had many more adventures together in the world of the cerebellum. They all lived happily ever after, spreading love and joy wherever they went.

The end.