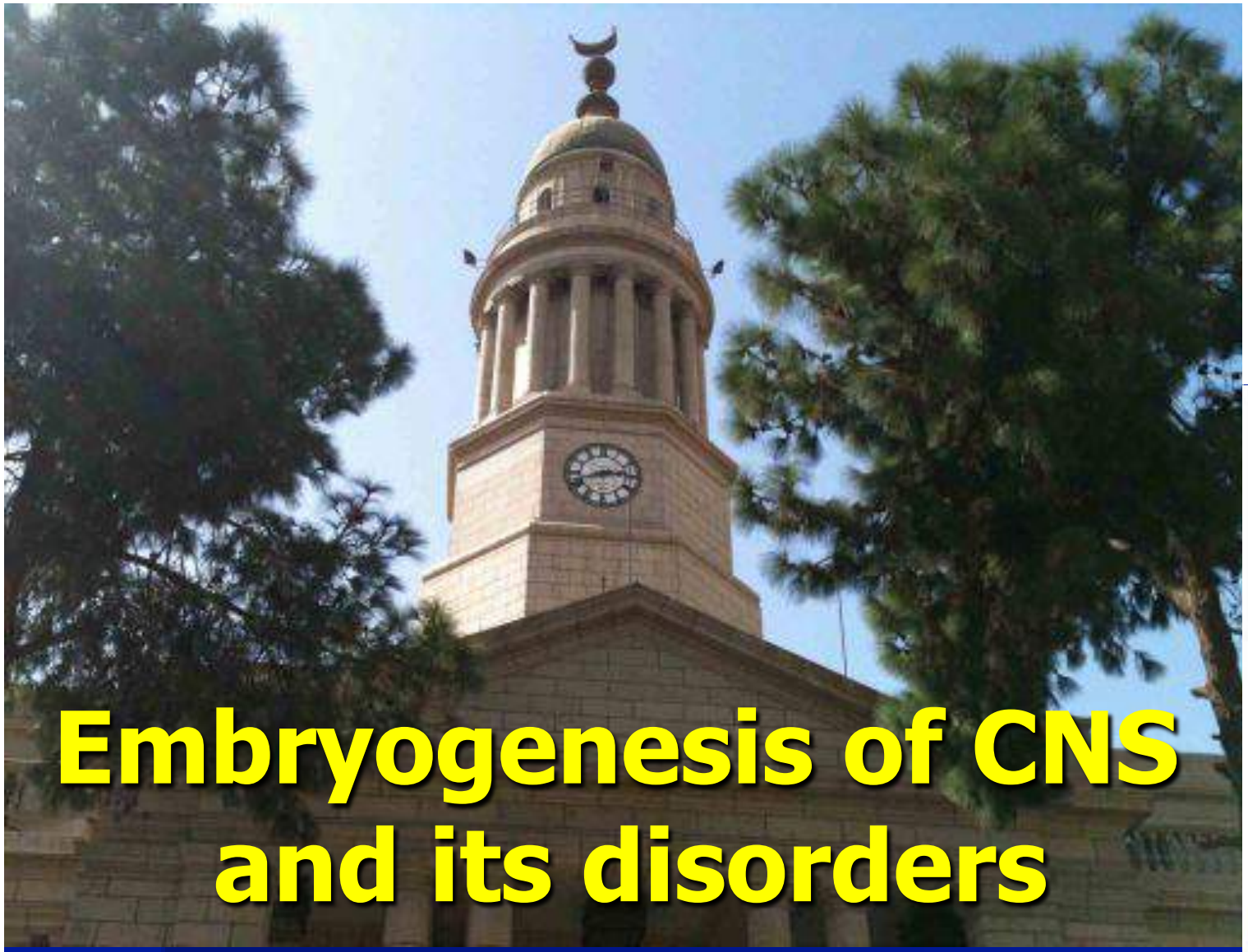

Embryogenesis of CNS and its disorders

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Associate Professor of Neurology

Cairo University

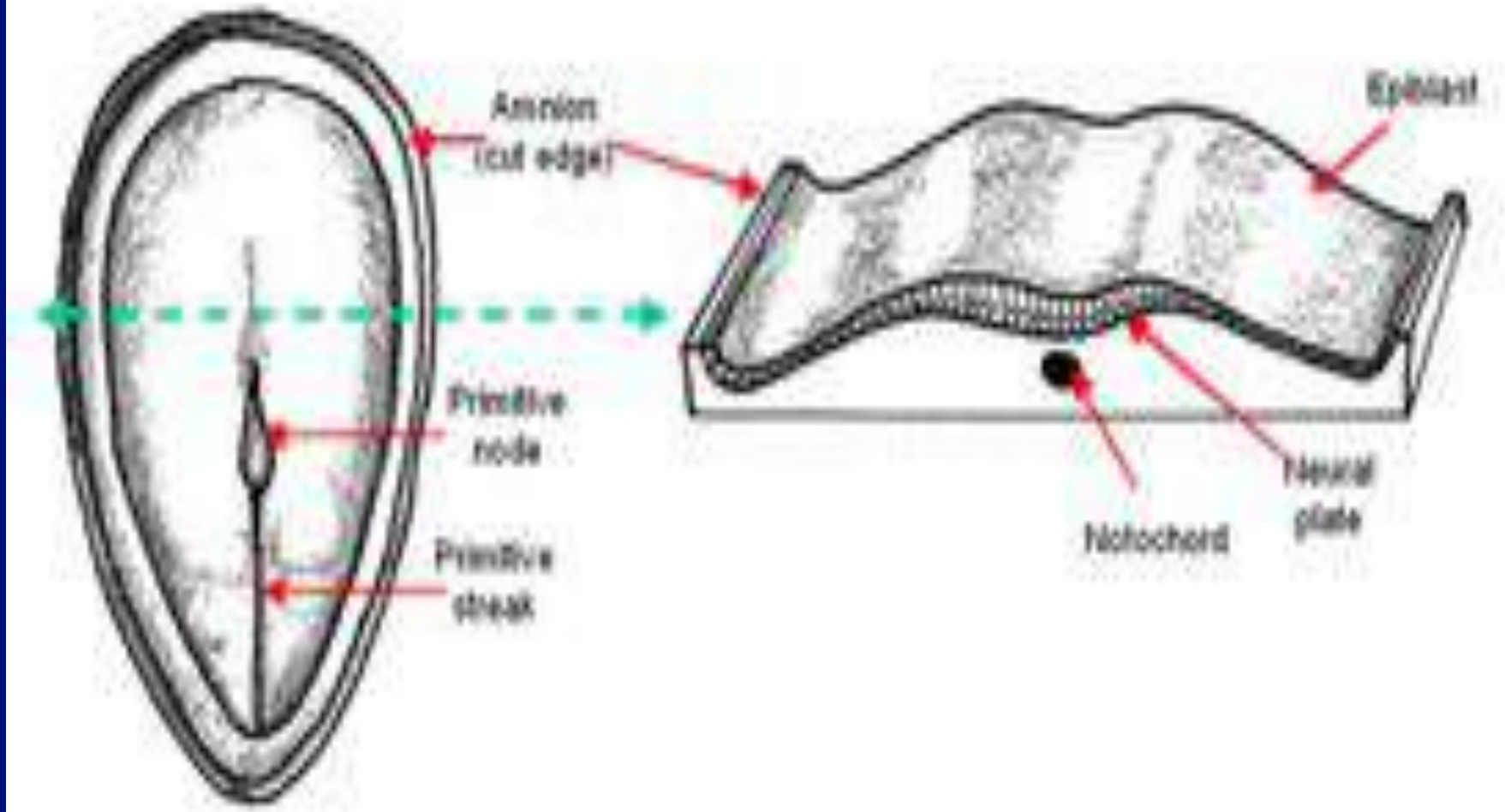

Embryological
developmental progress

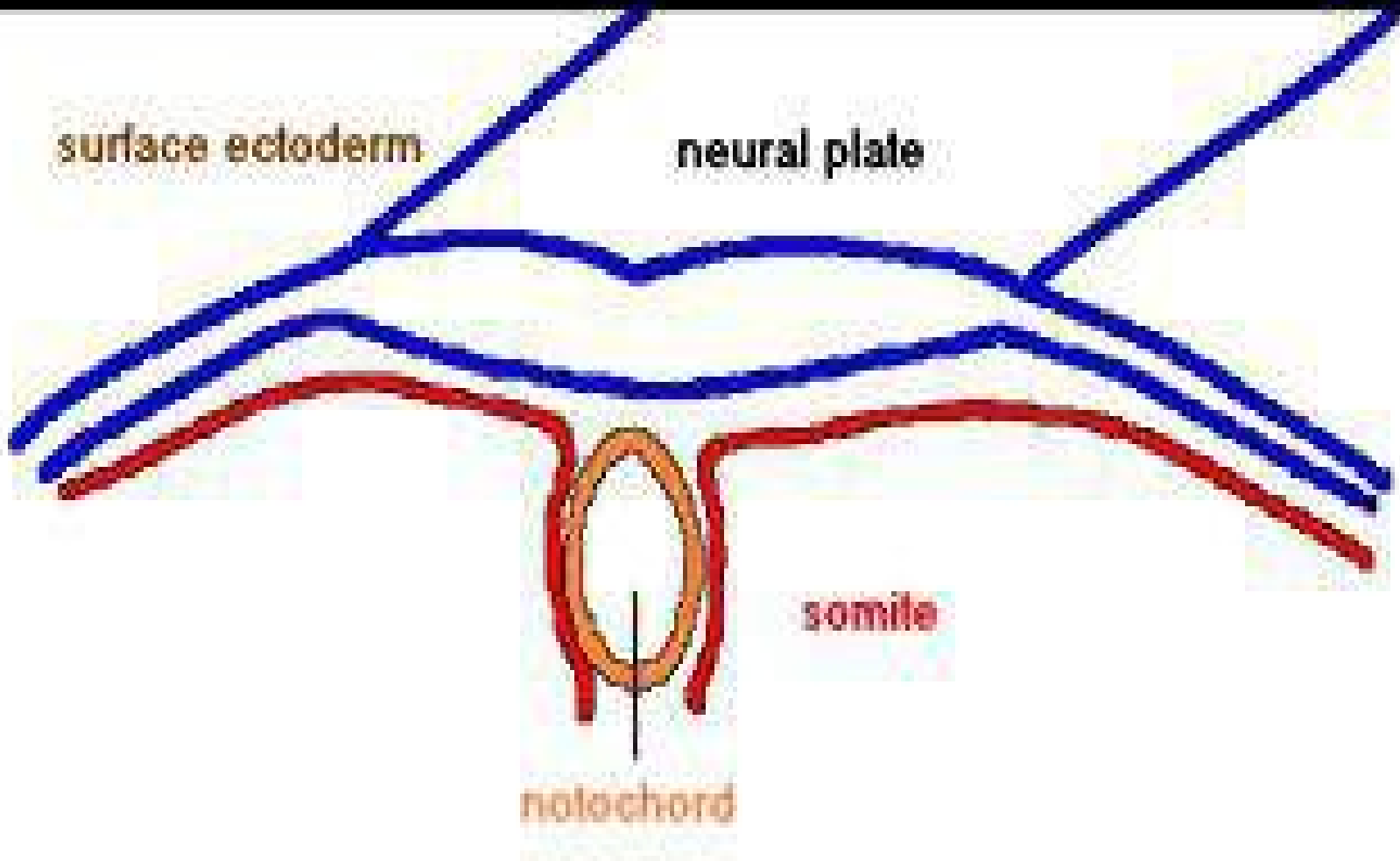
Stage I: Dorsal Induction

Formation and Closure of the Neural Tube(2-4 wks)

DR AMR HASAN AL HASANY

At 2 weeks


Amnion
(cut edge)
Primitive
node
Primitive
streak
Notochord


surface ectoderm
neural plate
somite
notochord

Development of the Neural Tube

Begins in the third week and is completed in the fourth week.

Induction: the notochord directs the overlying ectoderm to form the *neural plate.*

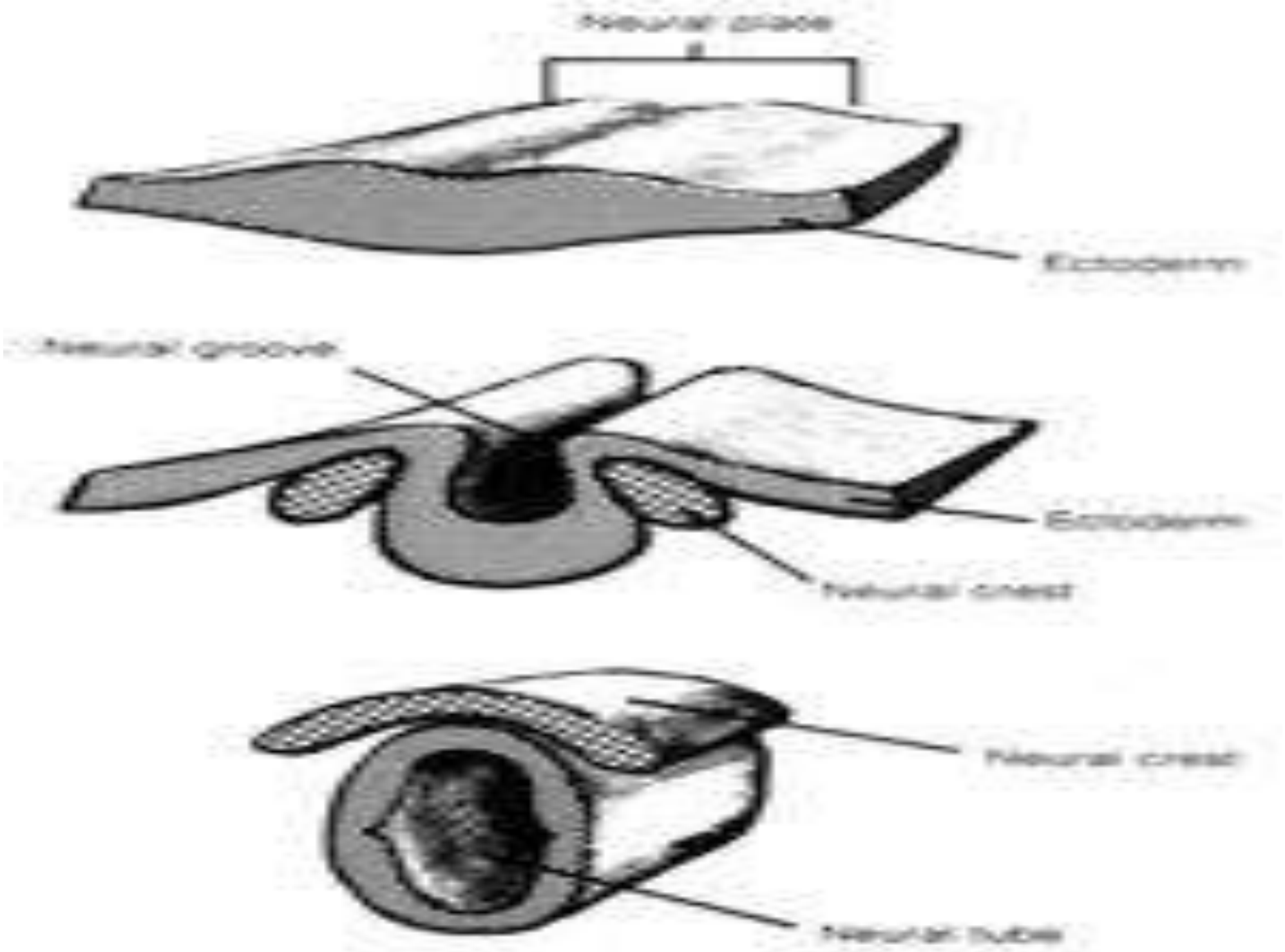
Neural fold: formed by thickening of the neural plate with elevation of its edges.

Development of the Neural Tube

Neural tube:

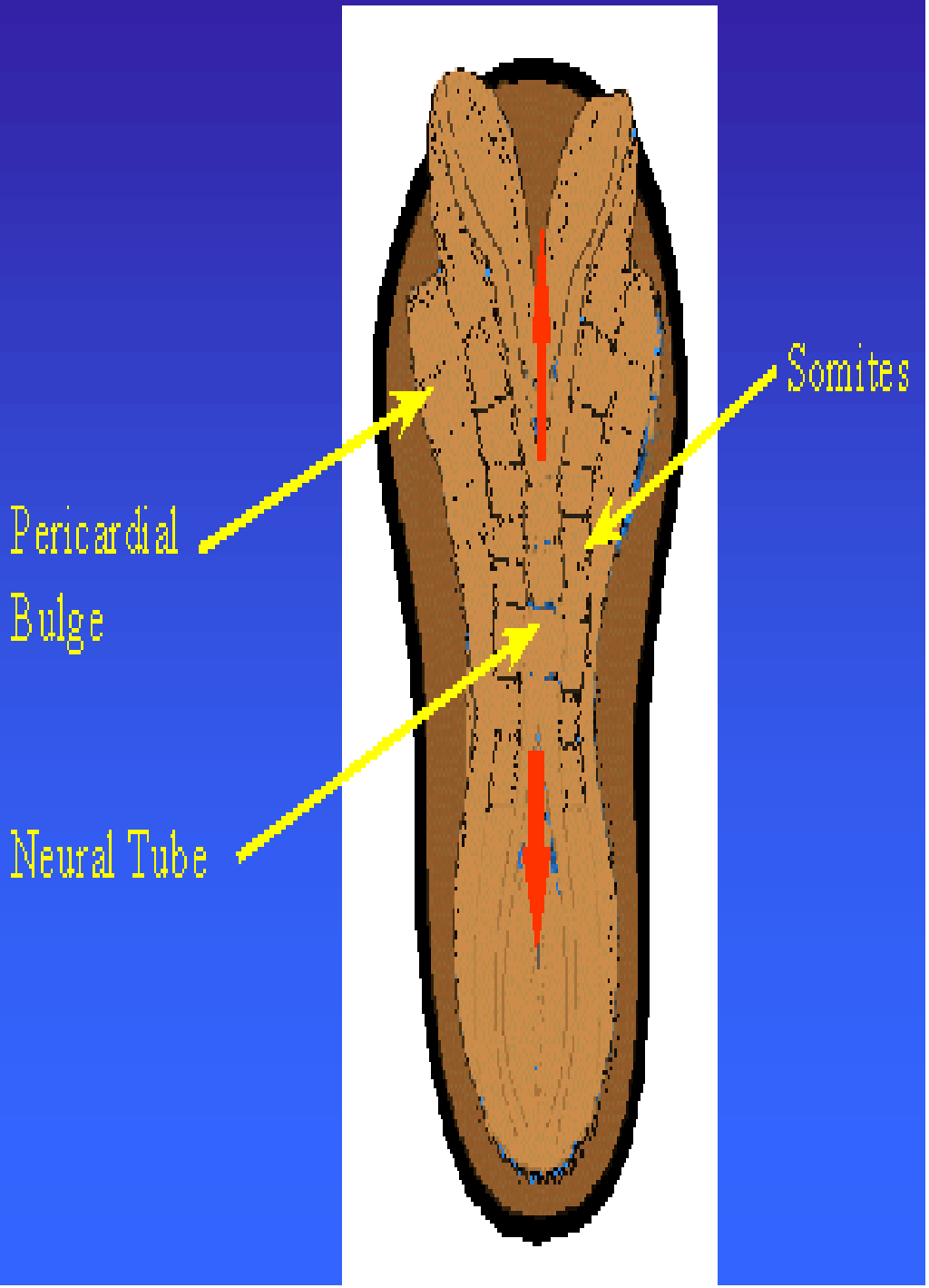
- The neural folds first contact each other to begin the formation of the neural tube.

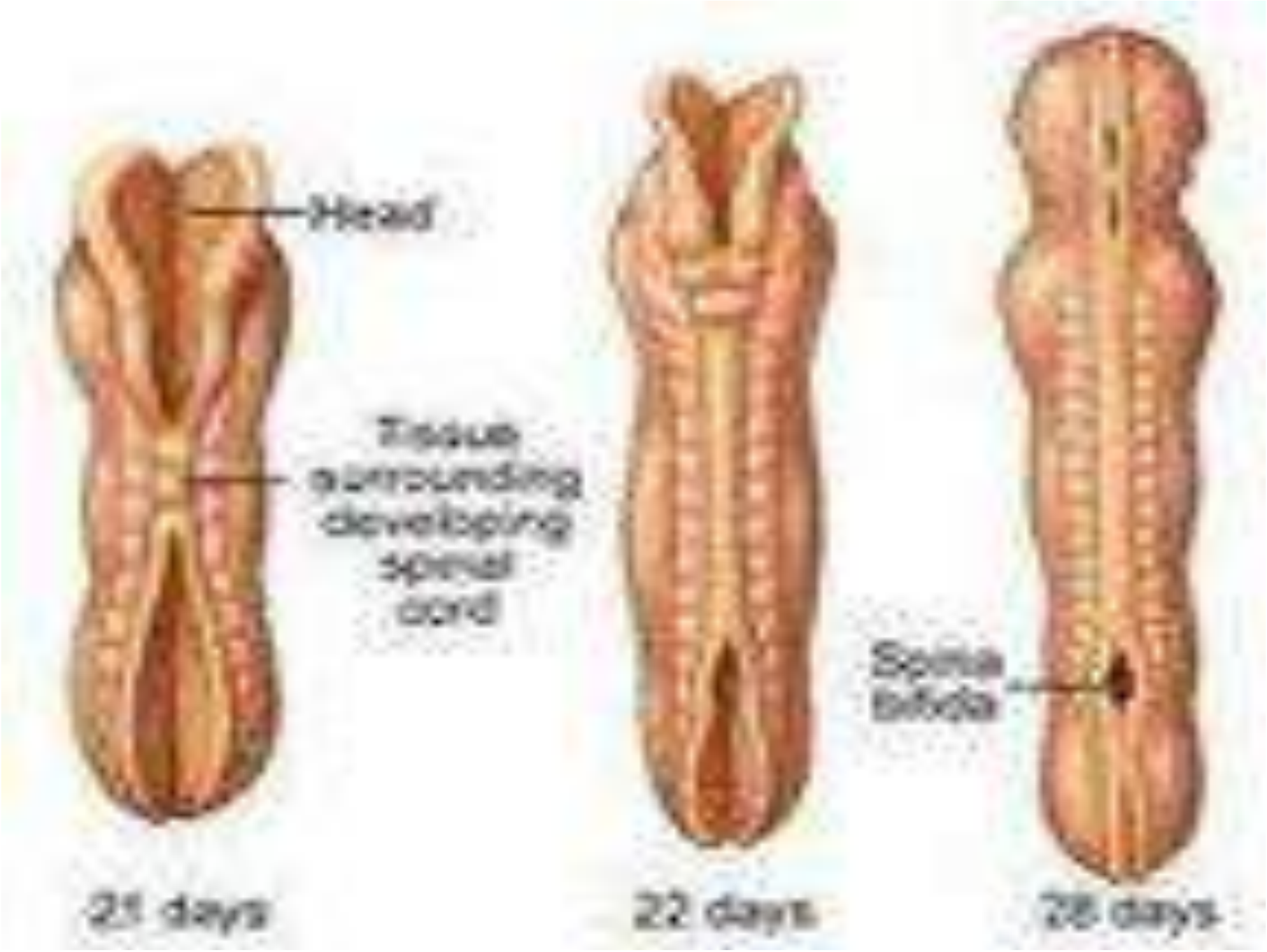
- This fusion initially takes place on the dorsal midline at what will become the cervical levels of the spinal cord. The fusion proceeds, zipper-like, in rostral and caudal directions.


Neural groove
Ectoderm
Neural groove
Ectoderm
Neural crest
Neural crest
Neural tube

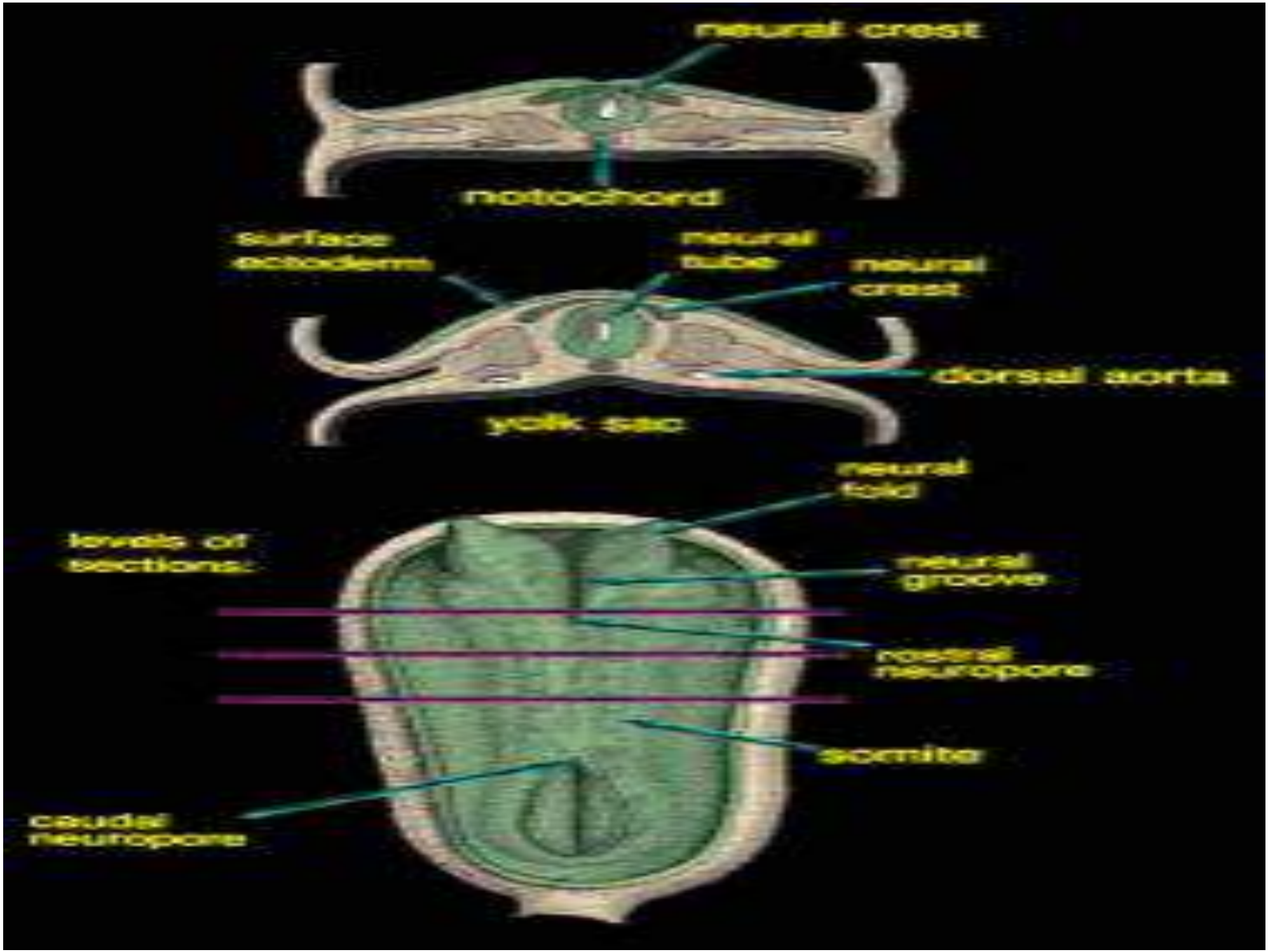
Tube closure

- 2/3 thickened to form future brain.
- 1/3 caudal form future spinal cord.
- Closes like a zipper starting in hind brain




Head
Tissue surrounding developing spinal cord
Spina bifida
21 days
22 days
28 days

Neural tube closure is followed by disjunction of cutenous and neural ectoderm


neural crest
notochord
surface ectoderm
neural tube
neural crest
dorsal aorta
yolk sac
neural fold
levels of sections:
neural groove
rostral neuropore
somite
caudal neuropore

Development of the Neural Tube

- During the process, the lumen of the neural tube, called the central canal, is open to the amniotic cavity both rostrally and caudally.
- The two openings in the neural tube connect the central canal with the amniotic cavity.
  - Anterior neuropore: closes at about 24 days and becomes the lamina terminalis.
  - Posterior neuropore: closes at about 26 days.

Neurulation: process by which CNS develops from a hollow structure called the neural tube.

Primary neurulation: most of the neural tube forms from the neural plate by a process of infolding called primary neurulation. This part of the neural tube will give rise to the brain and to the spinal cord through lumbar levels.

Secondary neurulation: the sacral and coccygeal segments of the spinal cord and their corresponding dorsal and ventral roots are formed secondary neurulation.

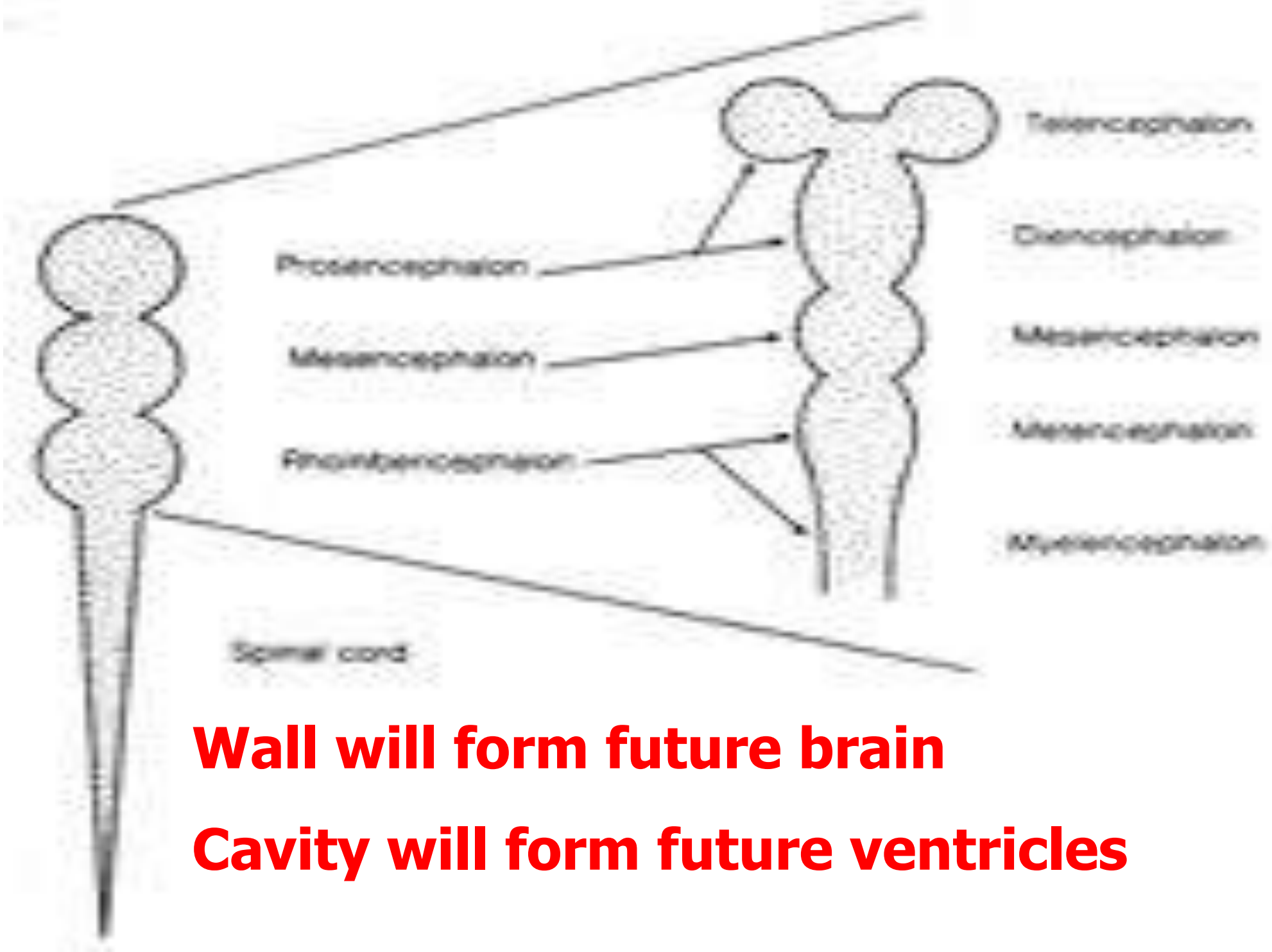
Neural Crest

Gives rise to:

- Pseudounipolar ganglion cells of the spinal and cranial nerve ganglia
- Schwann cells (neurolemmal sheath cells that form myelin in the PNS)
- Multipolar ganglion cells of the autonomic ganglia
- Leptomeninges (pia-arachnoid cells)
- Chromaffin cells of the suprarenal medulla
- Pigment cells (melanocytes)
- Odontoblasts (dentine-forming cells)
- Aorticopulmonary septum of the heart
- Parafollicular cells (calcitonin-producing C-cells)
- Skeletal and connective components of the pharyngeal arches

Stage 2: Ventral Induction

Formation of the Brain Segments and Face (5-10 wks)



Wall will form future brain

Cavity will form future ventricles

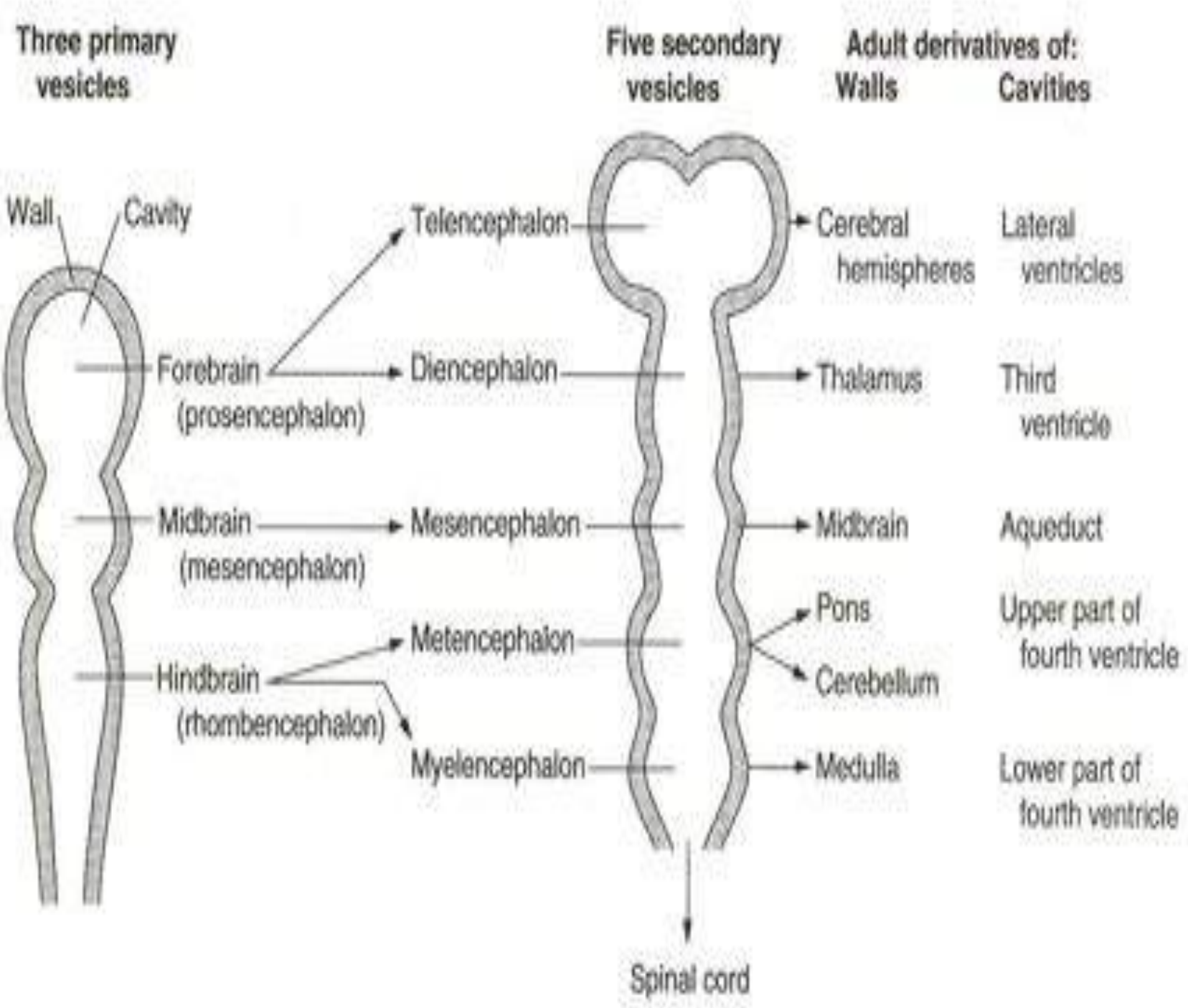
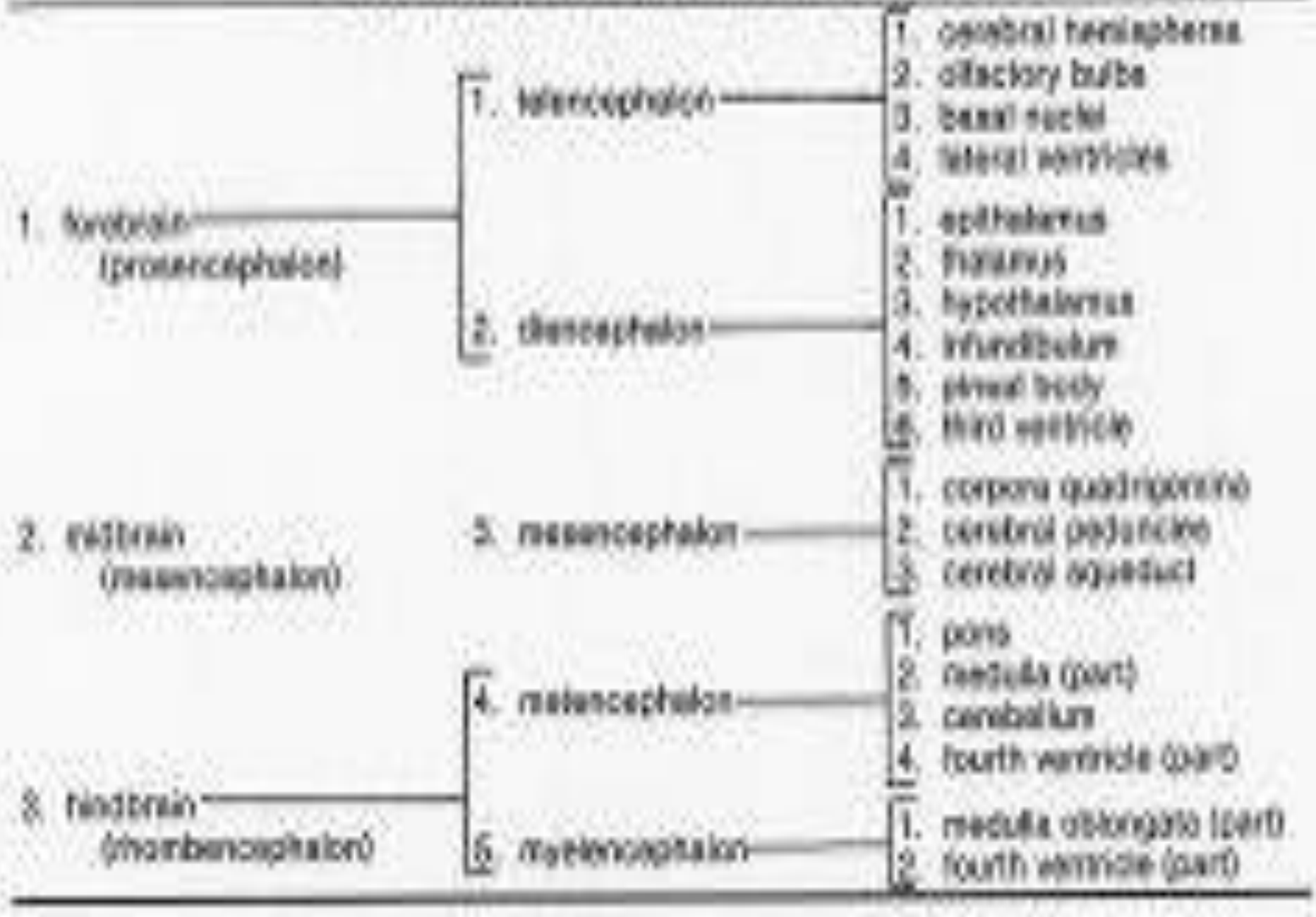
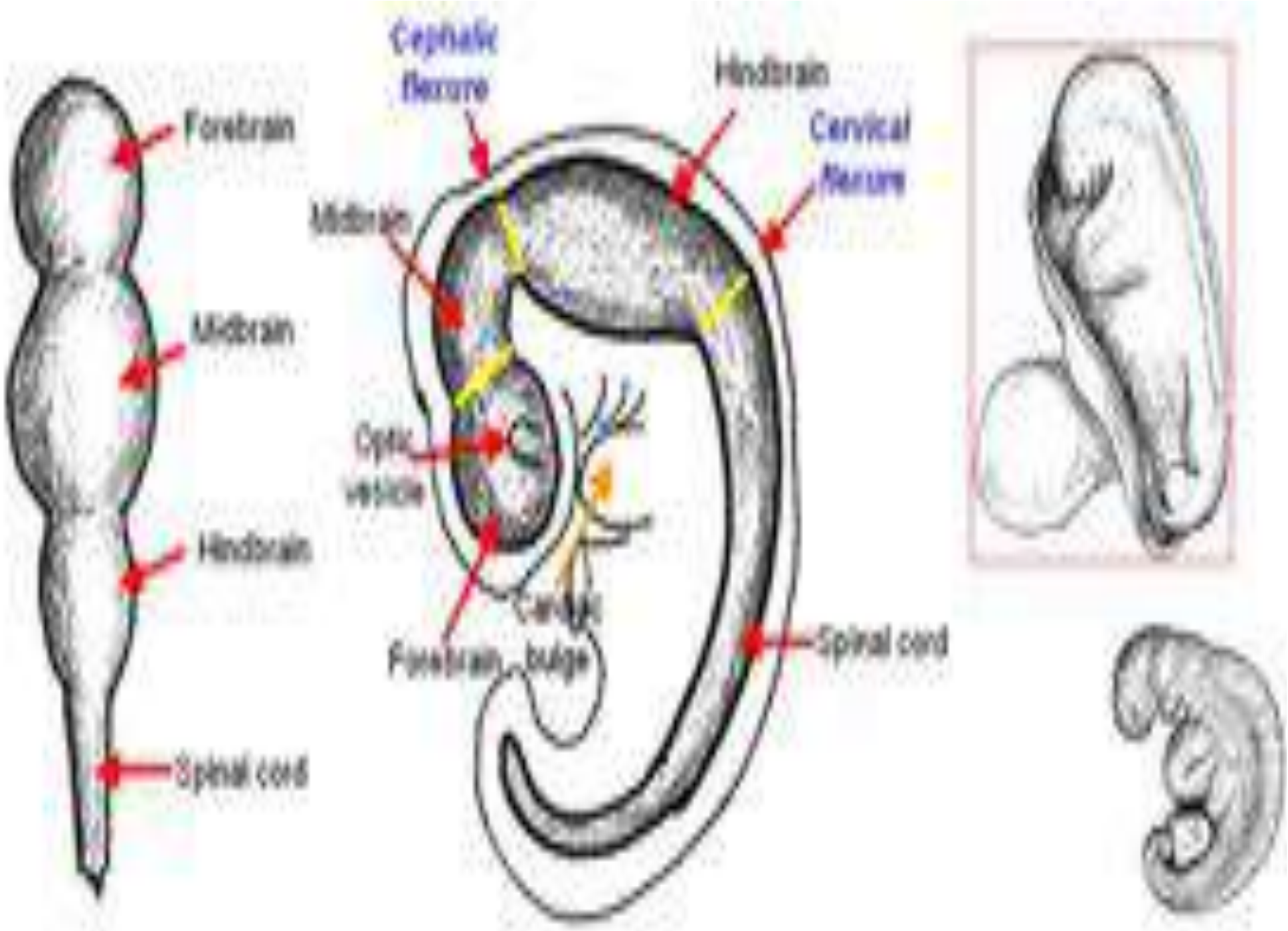
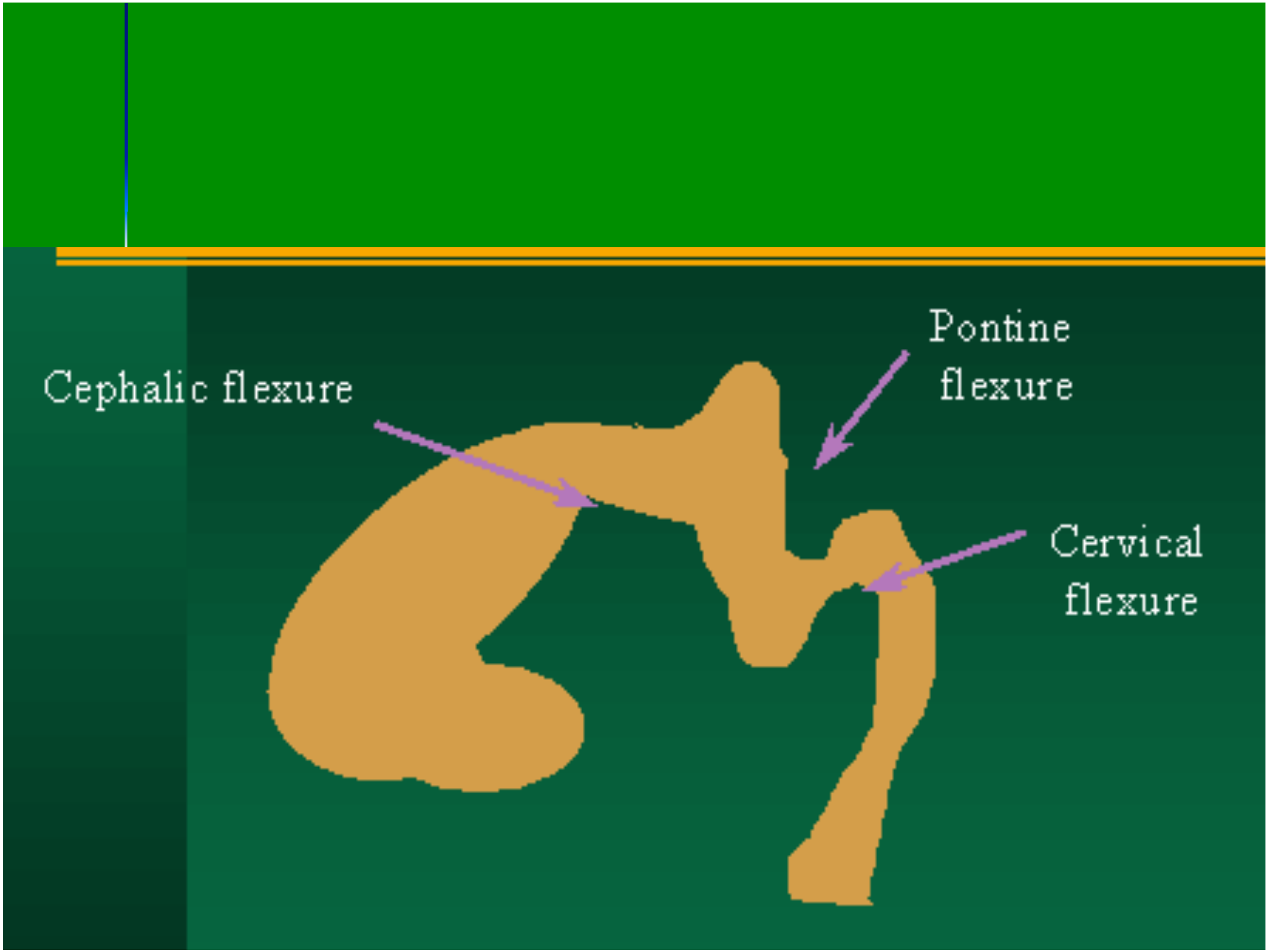

Three primary vesicles
Five secondary vesicles
Adult derivatives of:
Walls
Cavities
Wall
Cavity
Forebrain (prosencephalon)
Midbrain (mesencephalon)
Hindbrain (rhombencephalon)
Telencephalon
Diencephalon
Mesencephalon
Metencephalon
Myelencephalon
Cerebral hemispheres
Thalamus
Midbrain
Pons
Cerebellum
Medulla
Lateral ventricles
Third ventricle
Aqueduct
Upper part of fourth ventricle
Lower part of fourth ventricle
Spinal cord

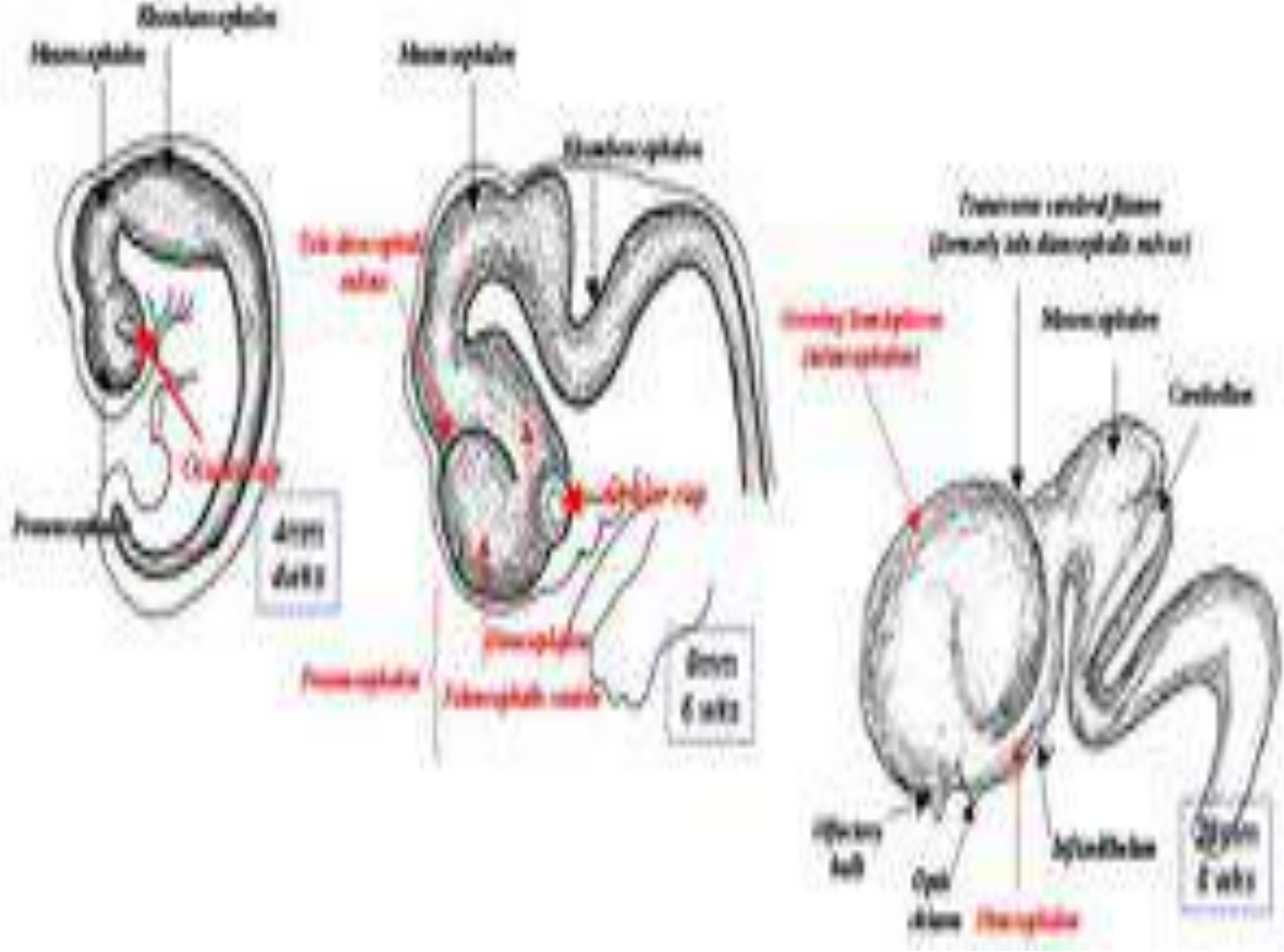
TABLE 1

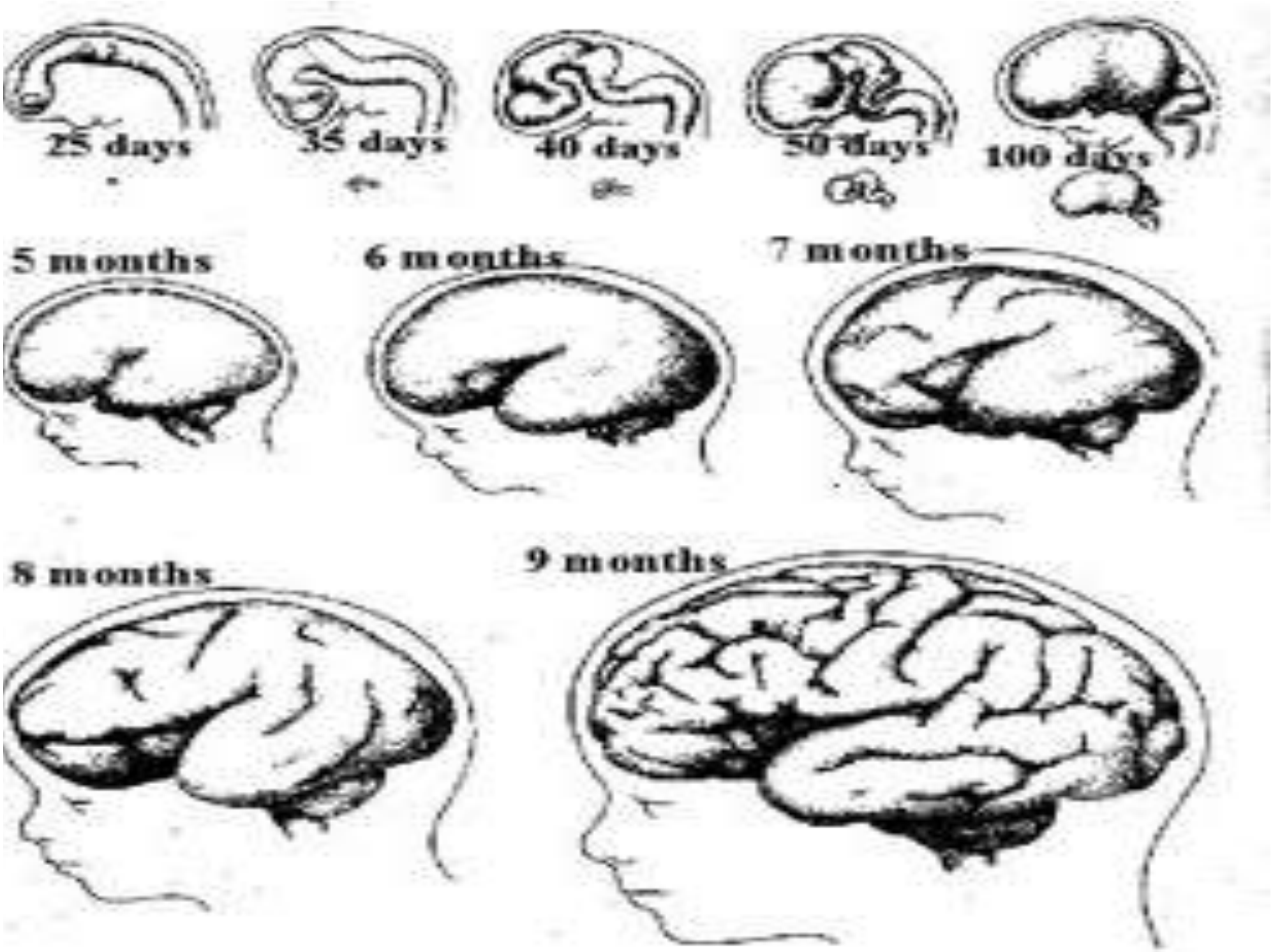
SUBDIVISIONS OF THE NERVOUS SYSTEM

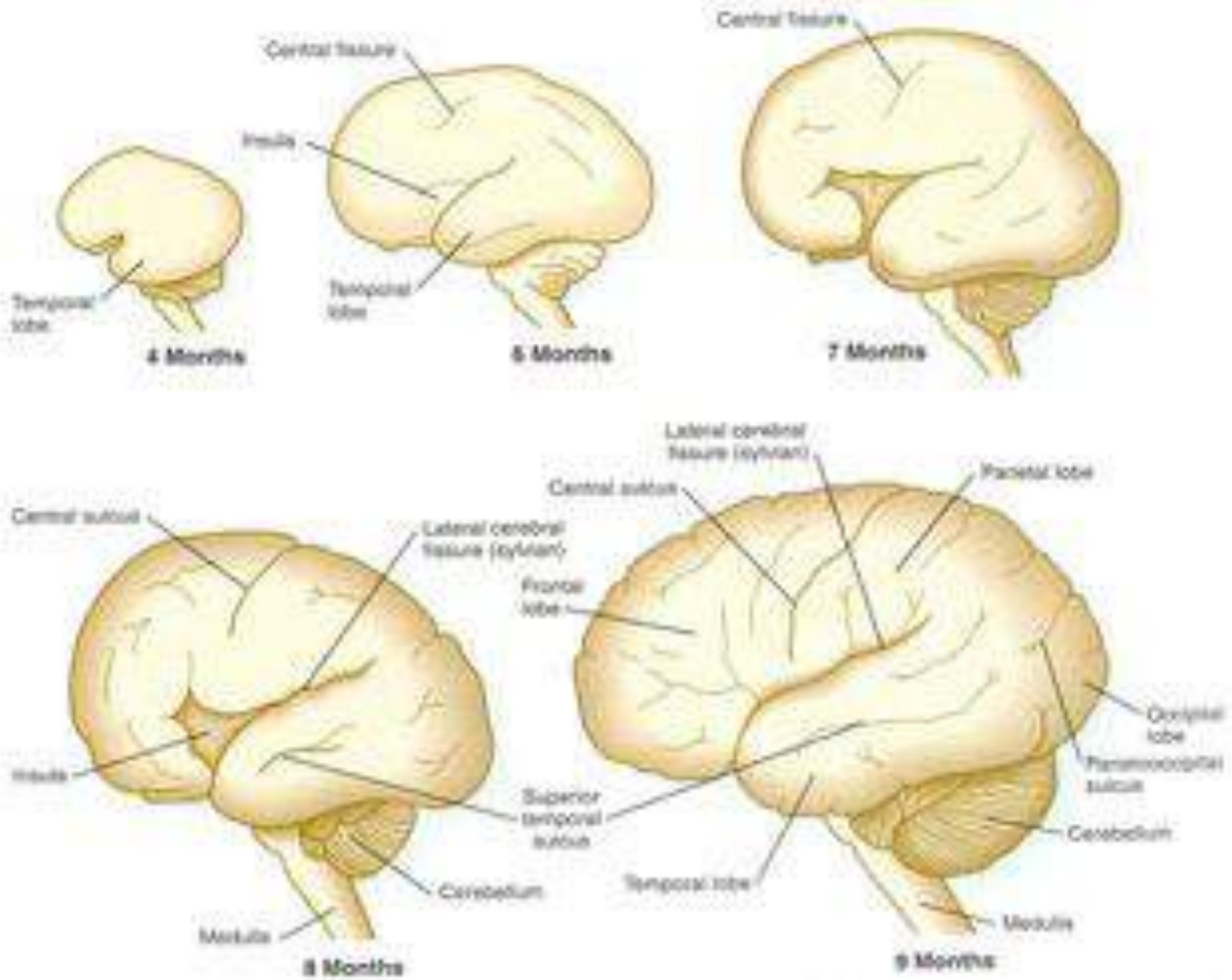



Forebrain
Midbrain
Hindbrain
Spinal cord
Cephalic flexure
Hindbrain
Cervical flexure
Midbrain
Optic vesicle
Forebrain
Cervical bulge
Spinal cord


Pontine
flexure
Cephalic flexure
Cervical
flexure




25 days
35 days
40 days
50 days
100 days
5 months
6 months
7 months
8 months
9 months


Central fissure
Insula
Temporal lobe
4 Months
Central fissure
Insula
Temporal lobe
6 Months
Central fissure
7 Months
Central sulcus
Lateral cerebral fissure (sylvian)
Insula
Superior temporal sulcus
Cerebellum
Medulla
8 Months
Lateral cerebral fissure (sylvian)
Central sulcus
Parietal lobe
Frontal lobe
Occipital lobe
Parietooccipital sulcus
Cerebellum
Temporal lobe
Medulla
9 Months

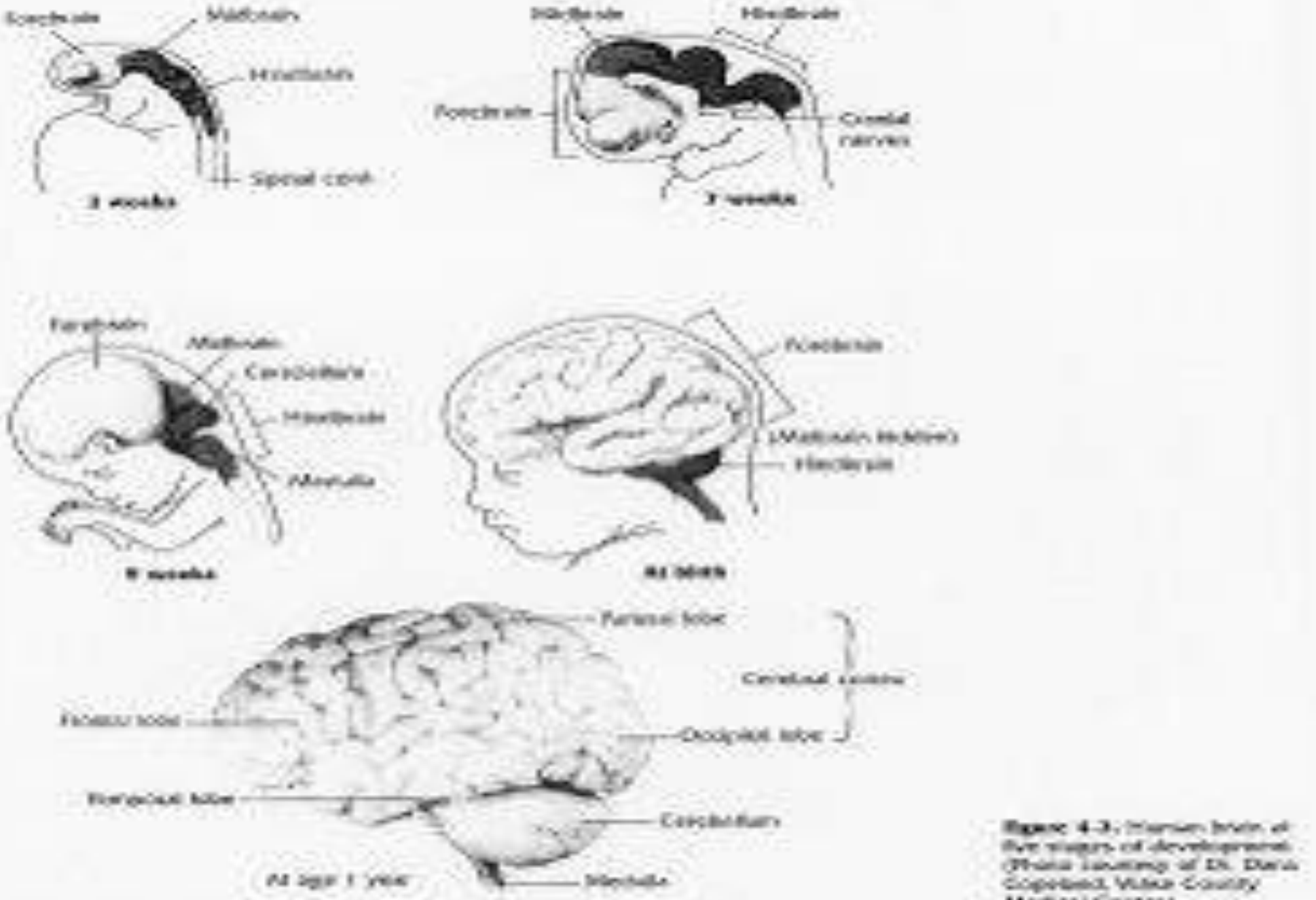
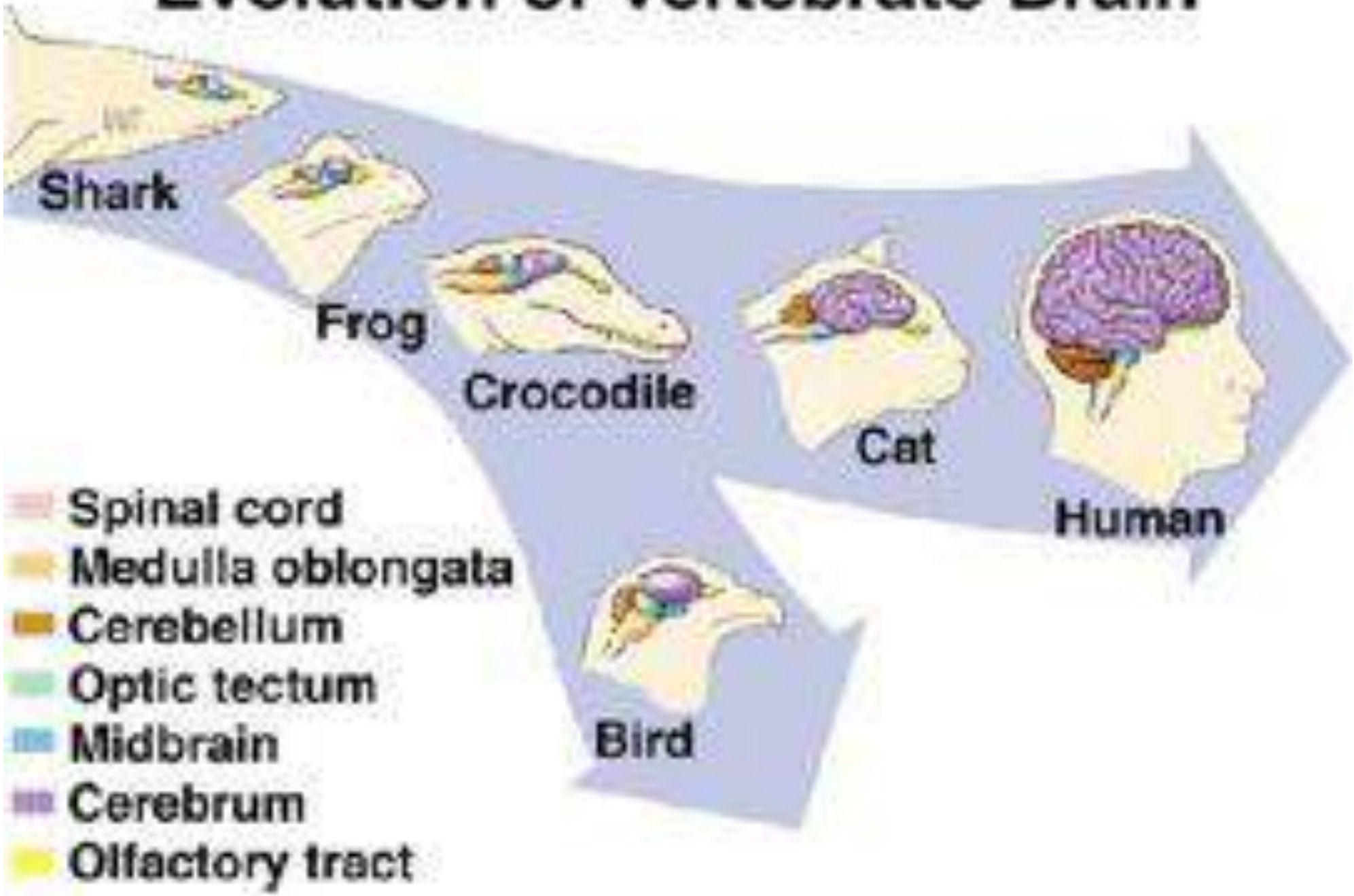


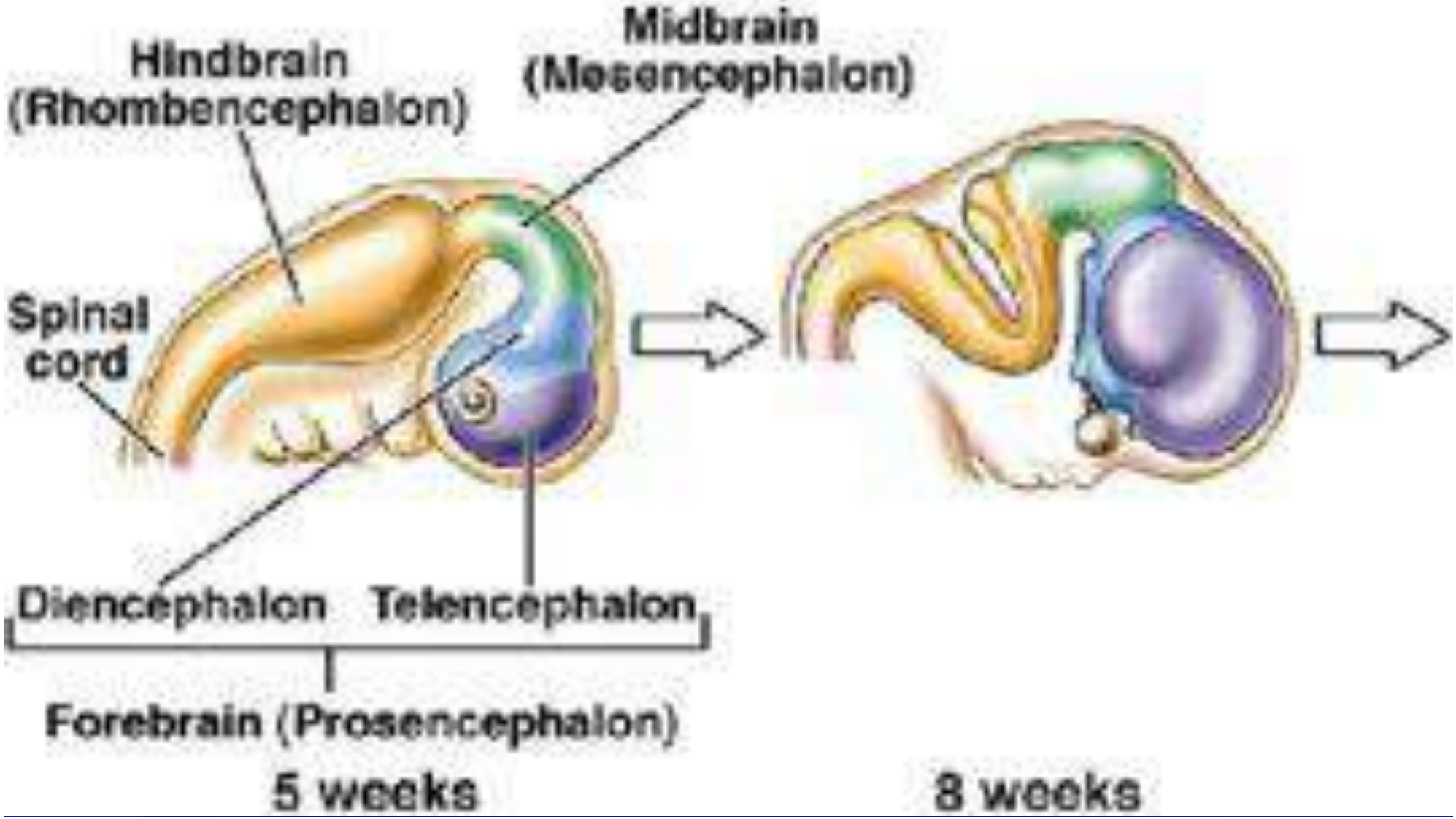
Figure 4-3. Human brain at five stages of development. (Photo courtesy of Dr. Dana Copeland, Wake County Medical Center.)

Evolution of Vertebrate Brain

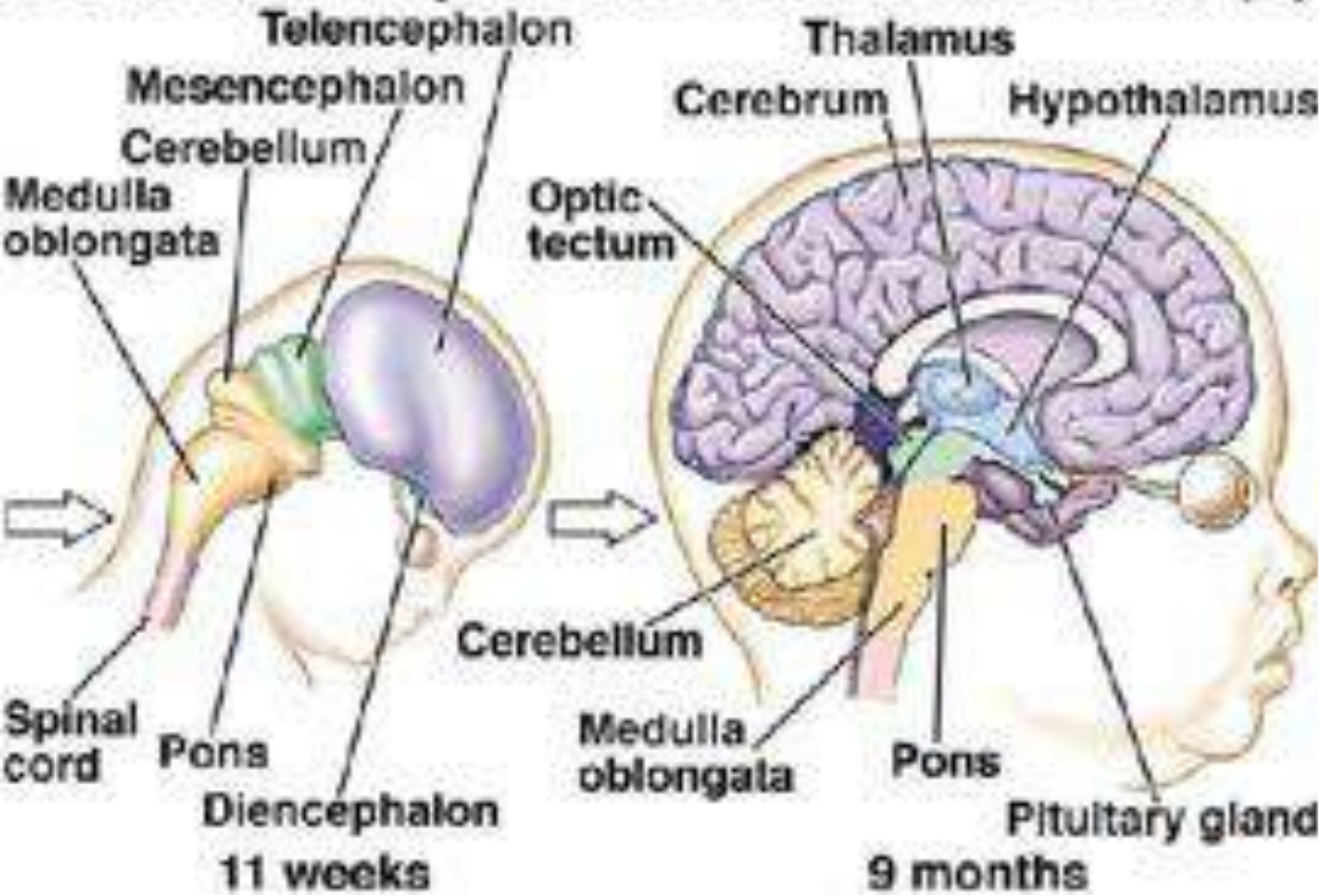


“ لقد خلقنا الانسان في
أحسن تقويم“
اية 4 سورة التين

Fetal Development of Human Brain (1)



Fetal Development of Human Brain (2)



Stage 3 :

Proliferation,differentiation ,

Histogenesis and Migration

(2-5 months)

1-Neural proliferation:

Germinal matrix formed lining lateral ventricles and third ventricle at about 7 weeks.

2-Neural differentiation:

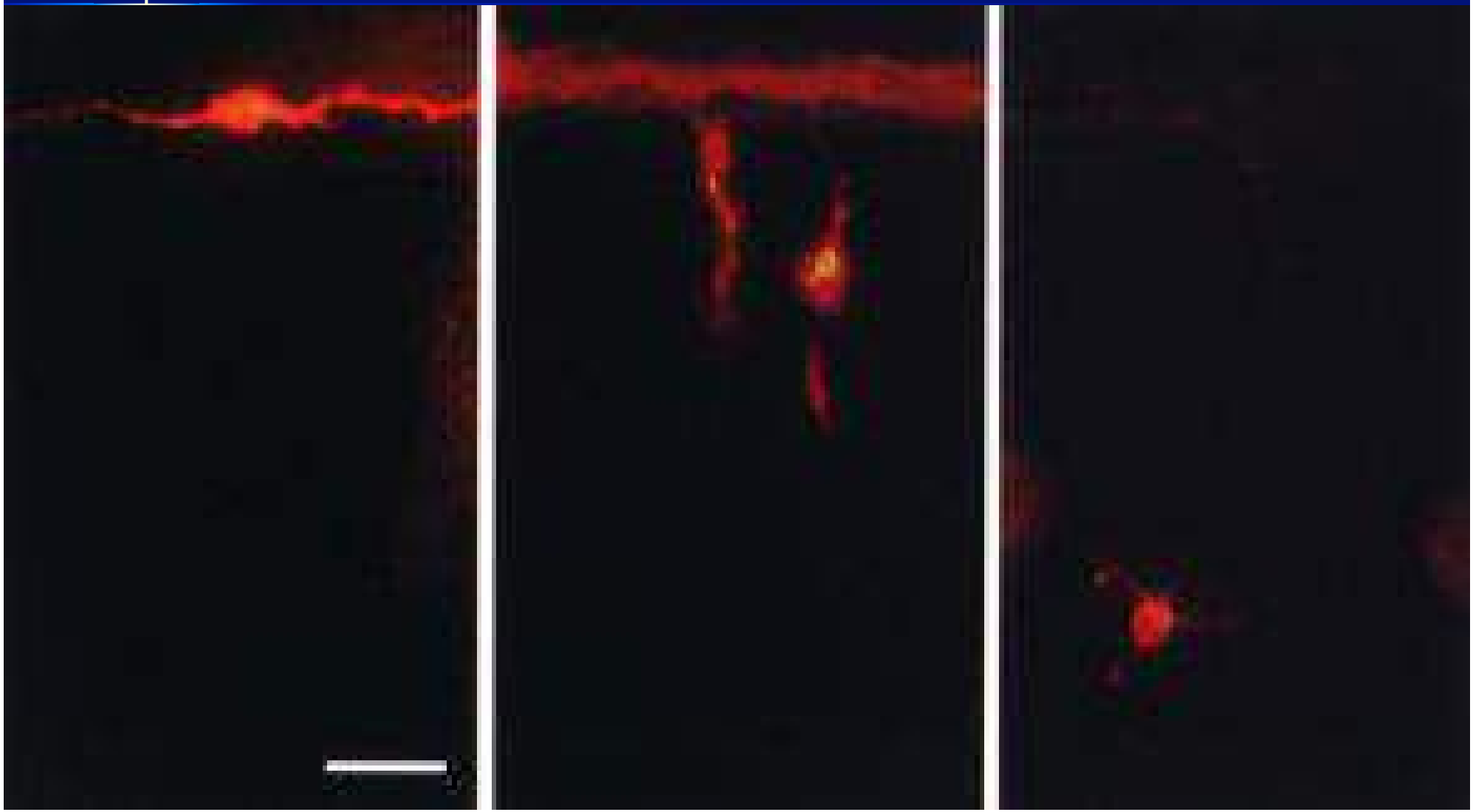
3-Neural migration

- Migrate peripherally along specialized radial glial fibres
- To cortex along inside-out fashion.

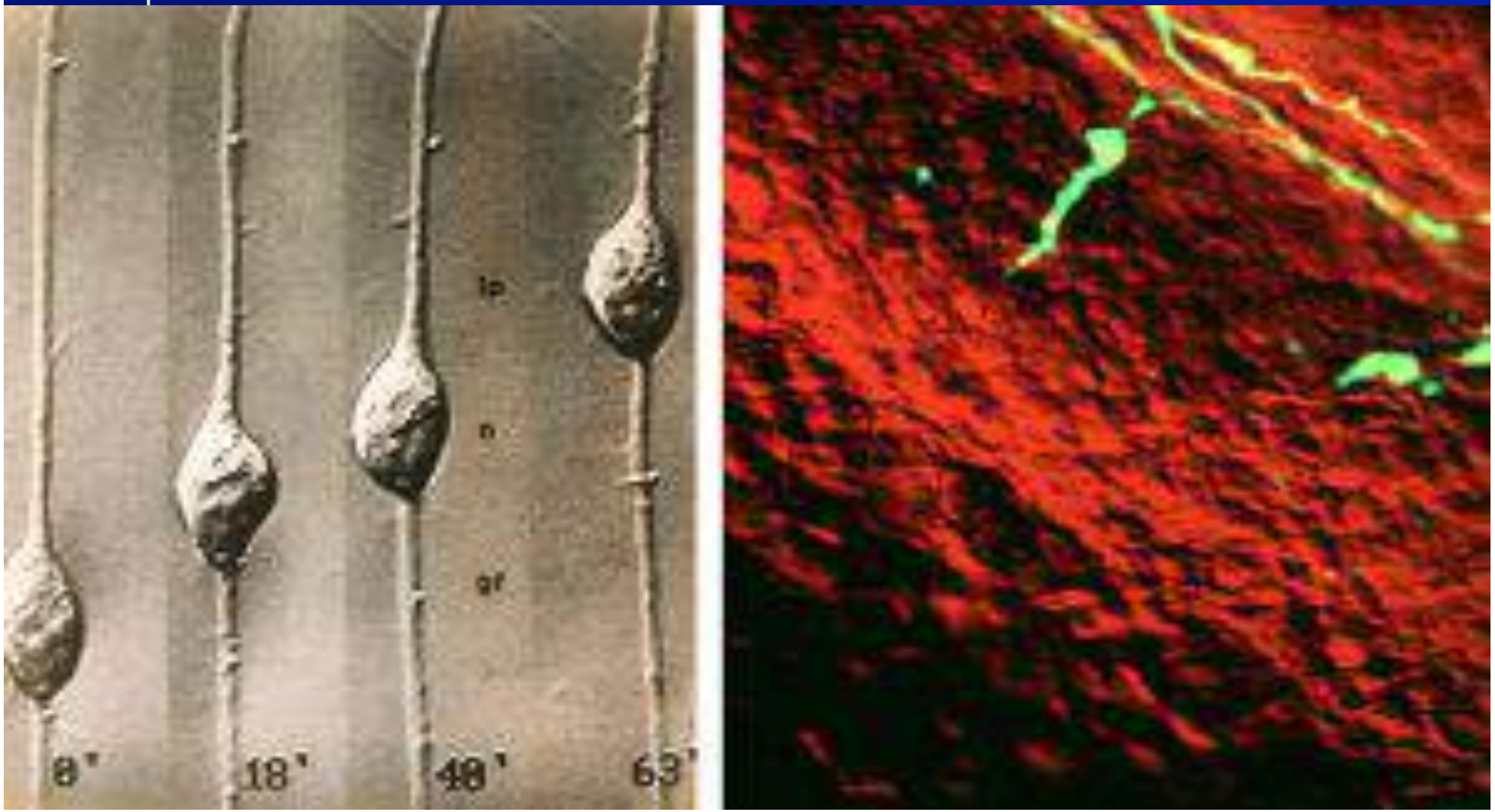
4- Cerebral Comissures:

Forms from front to back except rostrum forms **“last”**

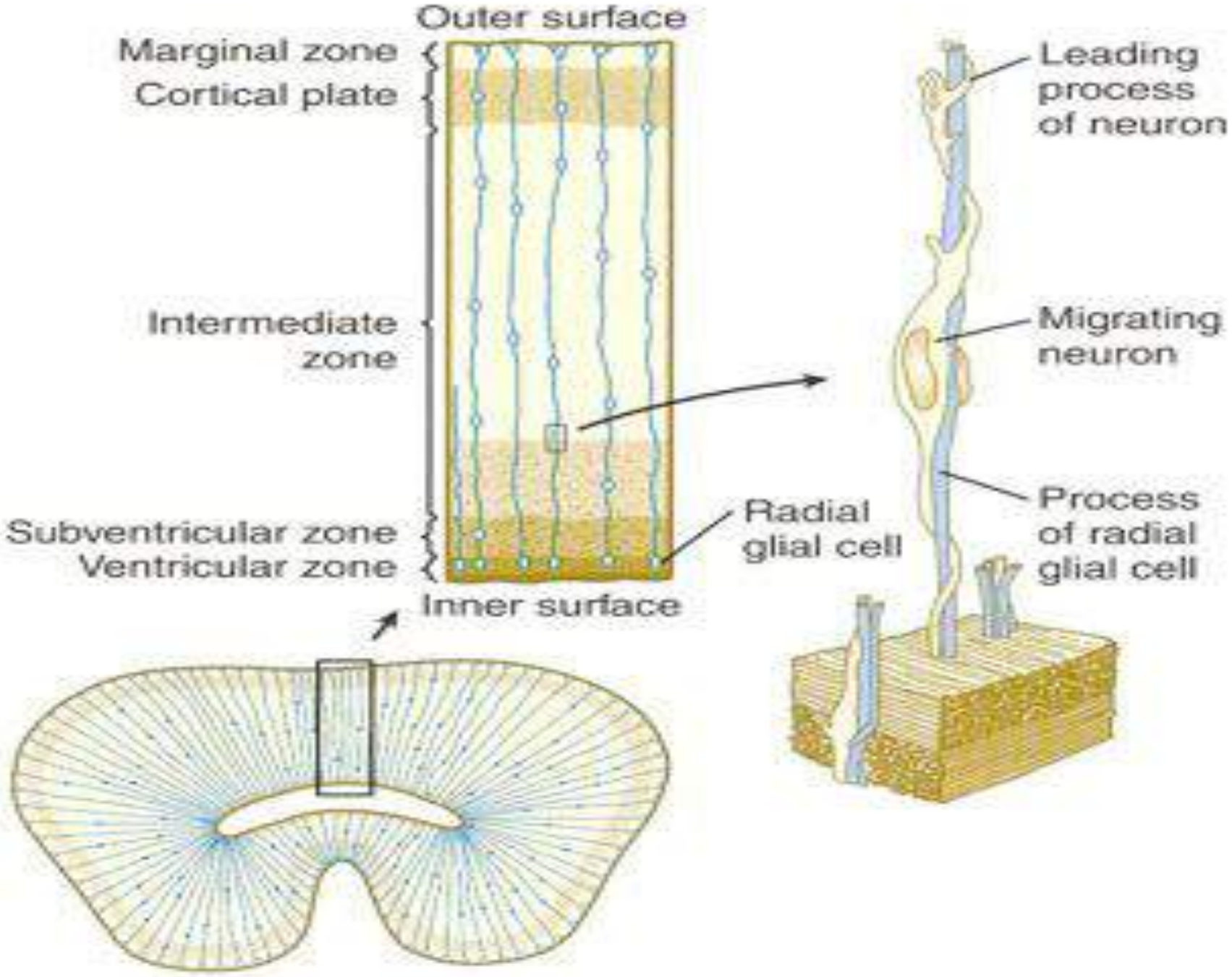
Neuronal migration

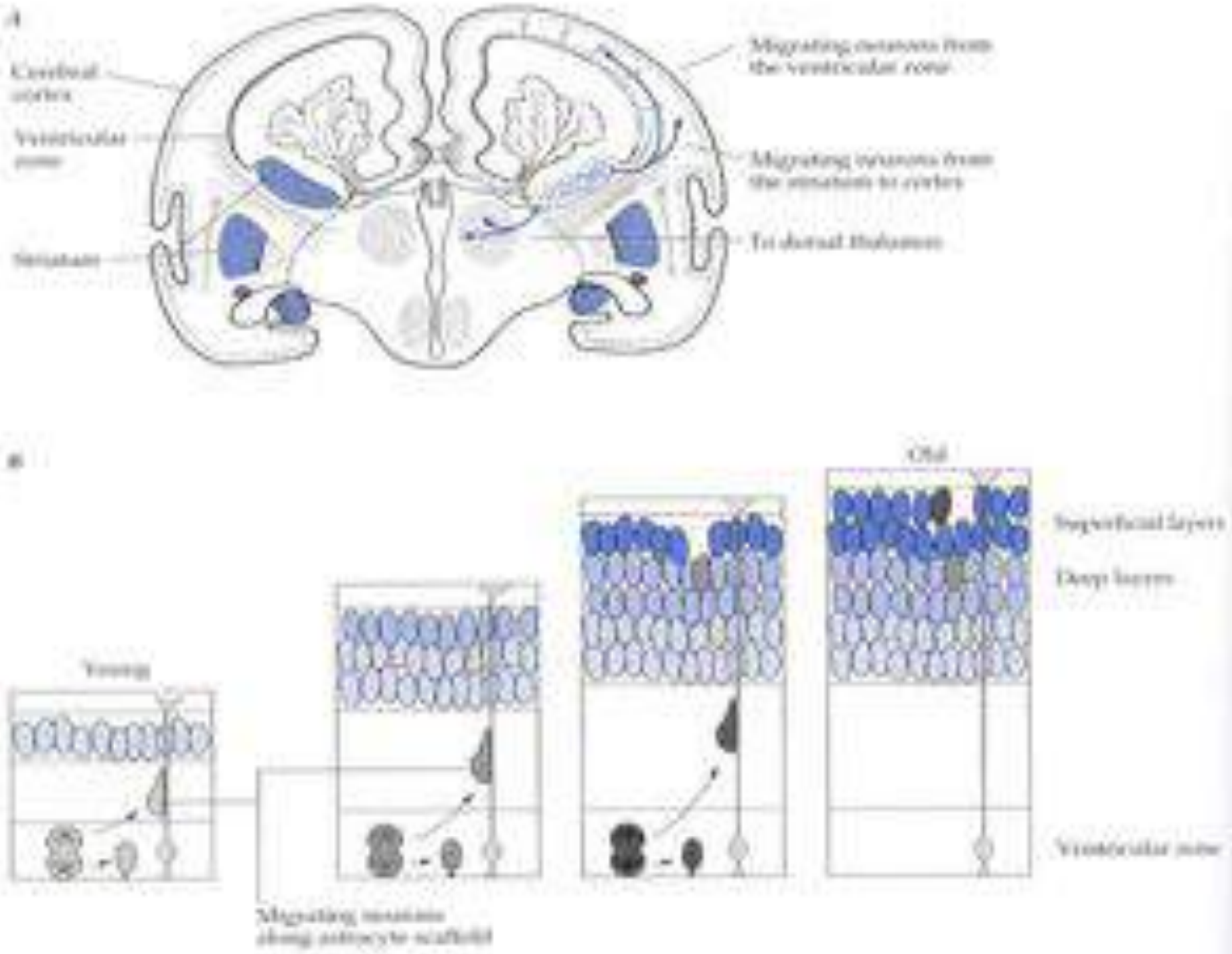


Neuronal migration




02-24-06
17:23:57


Outer surface
Marginal zone
Cortical plate
Intermediate zone
Subventricular zone
Ventricular zone
Inner surface
Radial glial cell
Leading process of neuron
Migrating neuron
Process of radial glial cell


A
Migrating neurons from the ventricular zone
Migrating neurons from the striatum to cortex
To dorsal thalamus
B
Old
Superficial layers
Deep layers
Ventricular zone
Migrating neurons along astrocyte scaffold

Stage 4: Myelination

- **Stage 4: Myelination**
  - Inferior to superior; posterior to anterior.
  - 5 - 15 months; matures by 3 years.
  - Failure: developmental delay, dysmyelinating disease

Myelination Milestones

- **Brain stem, cerebellum, posterior limb of internal capsule:** term birth.
- **Anterior limb internal capsule:** two months.
- **Splenium of the corpus callosum:** three months.

Myelination Milestones

- **Genu corpus callosum:** six months.
  - **Occipital white matter. Central:** five months (T1)/fourteen months (T2) Peripheral: seven months (T1)/fifteen months (T2) .
  - **Frontal white matter. Central:** six months (T1)/ sixteen months (T2) Peripheral: eleven months (T1)/eighteen months (T2)

Table 1. *Progress of myelination visible on MRI. Modified from (5, 7).*

Region	T1-weighted images	T2-weighted images
Dorsal brainstem	26-28 gw	27-30 gw
Middle cerebellar peduncle	Birth	Birth-2 mo
Cerebellar white matter	Birth-4 mo	3-5 mo
Posterior limb of the internal capsule		
anterior portion	First month	4-7 mo
posterior portion	Birth	Birth- 2 mo
Anterior limb of the internal capsule	2-3 mo	7-11 mo
Genu corpus callosum	4-6 mo	5-8 mo
Splenium corpus callosum	3-4 mo	4-6 mo
Occipital white matter		
central	3-5 mo	9-14 mo
subcortical	4-7 mo	11-15 mo
Frontal white matter		
central	3-6 mo	11-18 mo
subcortical	7-18 mo	14-30 mo
Centrum semiovale	2-4 mo	7-11 mo

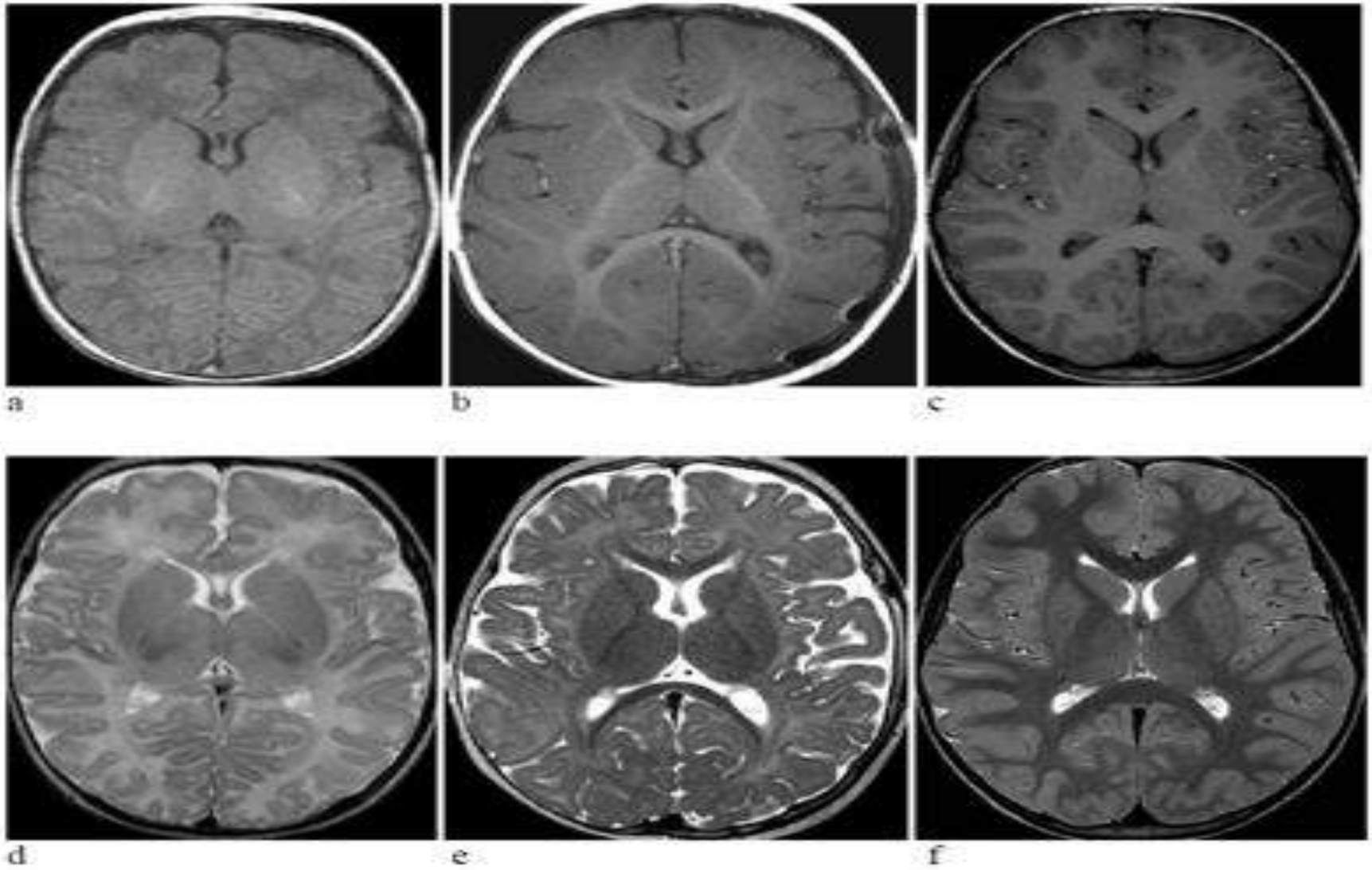
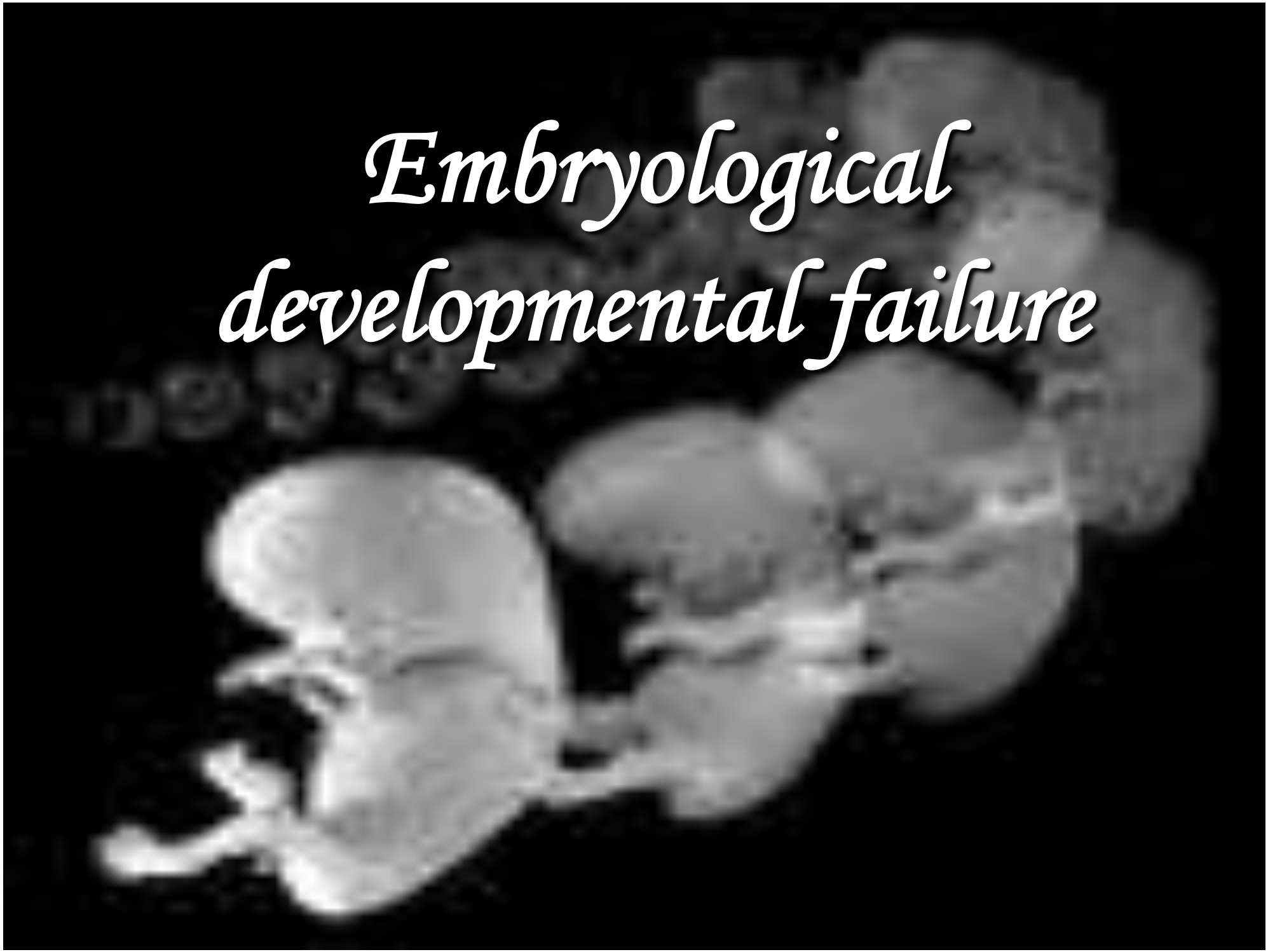


Figure 3. *Progress of myelination on T1-weighted (upper row) and T2-weighted (lower row) MRIs. In a newborn (a) and (d), the myelinated white matter is seen in the posterior limbs of the internal capsule. It appears hyperintense on T1-weighted images and hypointense on T2-weighted images. By the age of 8 months (b) and (e), the deep white matter is hyperintense on T1-weighted images, but the subcortical areas are still mostly unmyelinated. Hypointensity on T2-weighted images lags behind. By 24 months (c) and (f), the brain is fully myelinated on both T1- and T2-weighted images.*


Embryological
developmental failure

Congenital brain disorders

Embryological failure

Acquired lesions

Congenital brain disorders

Embryological failure

Acquired lesions

Stage 1: Dorsal Induction: Formation and Closure of the Neural Tube

- Weeks 3 - 4
- Three phases: Formation and Closure of the Neural Tube, Neurulation.

Neural tube defects

(Failure of fusion or dysraphias)

- Complete or regional disturbance in continuity of neural tube structures and their coverings

1.Open defects (Neurulation defects)

Neural tissue is exposed to the environment or covered only with a thin membrane

- Anencephaly
- Open spina bifida (myelocele;meningomyelocele)

Neural tube defects

2. Closed defects (postneurulation defects)

Neural tissue is covered by normal skin

- Encaphalocele
- Closed spina bifida (meningocele; occult spinabifida)
- Split cord malformations (diastematomyelia;diplomyelia)

3. Arnold-Chiari malformation

Neural tube defects

1. Cranioschisis

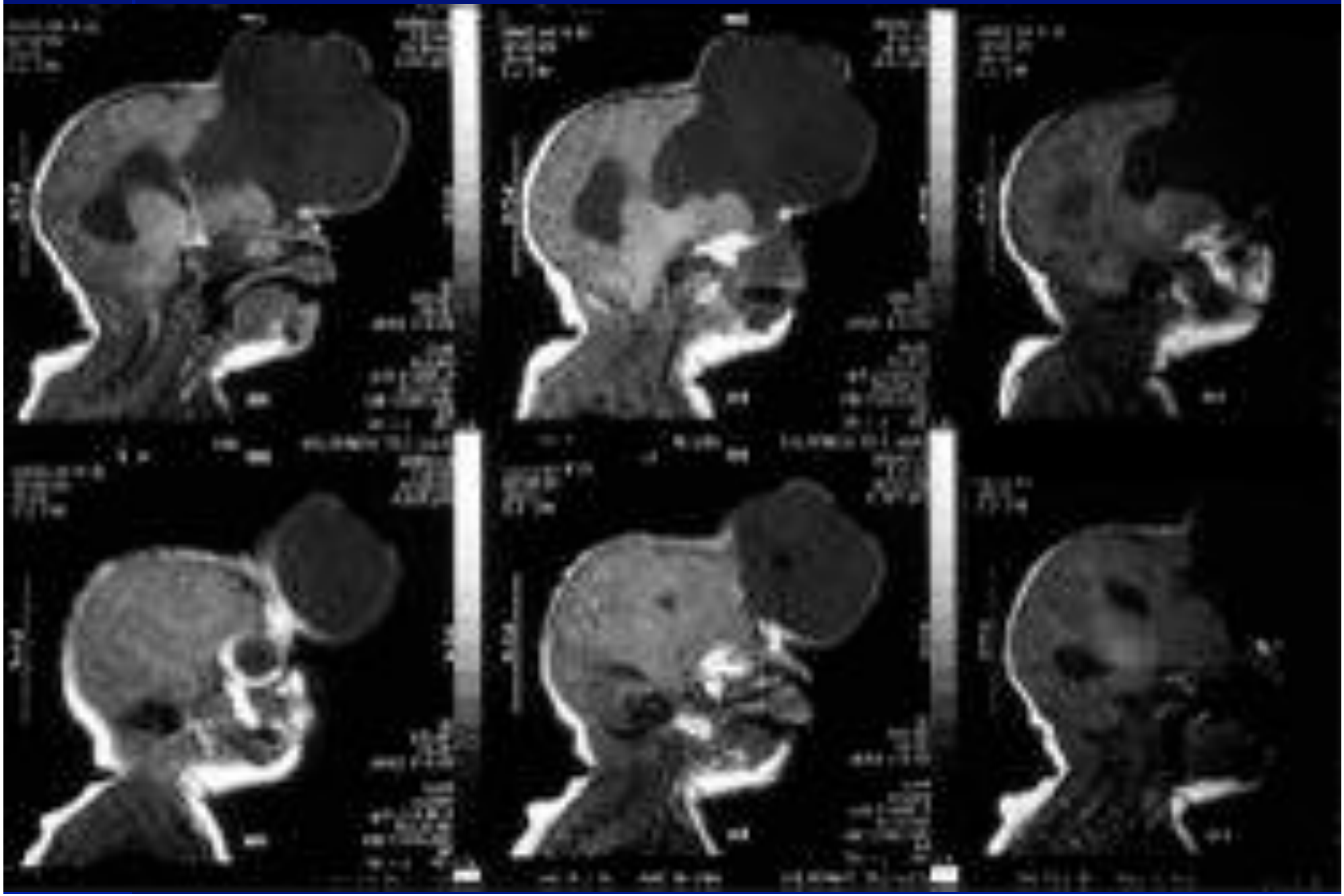
- Anencephaly
- Encephalocele
- Meningocele

2. Rachischisis

- Spina bifida
- MyeloMeningocele
- Meningocele

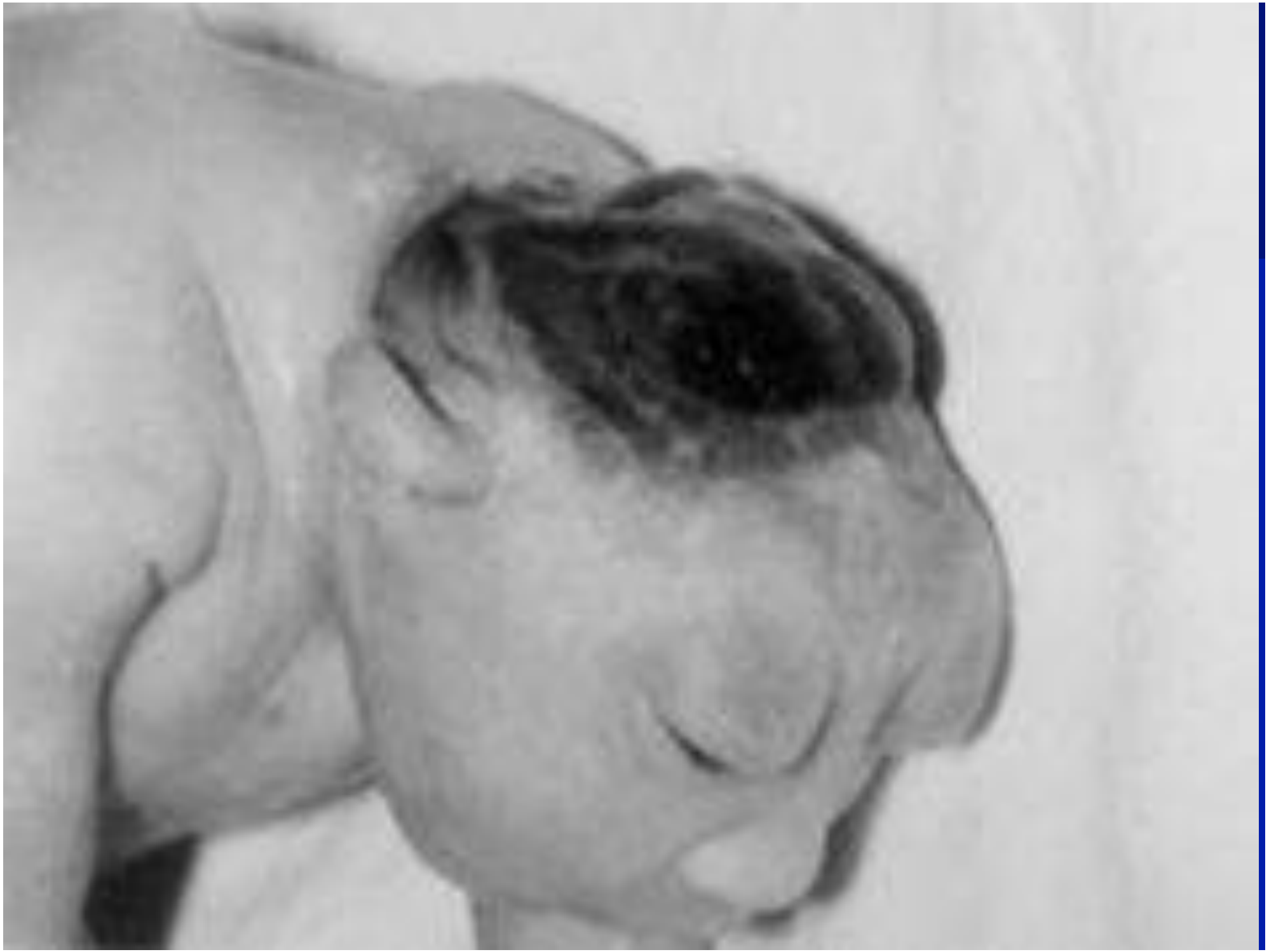
3. Arnold-Chiari malformation

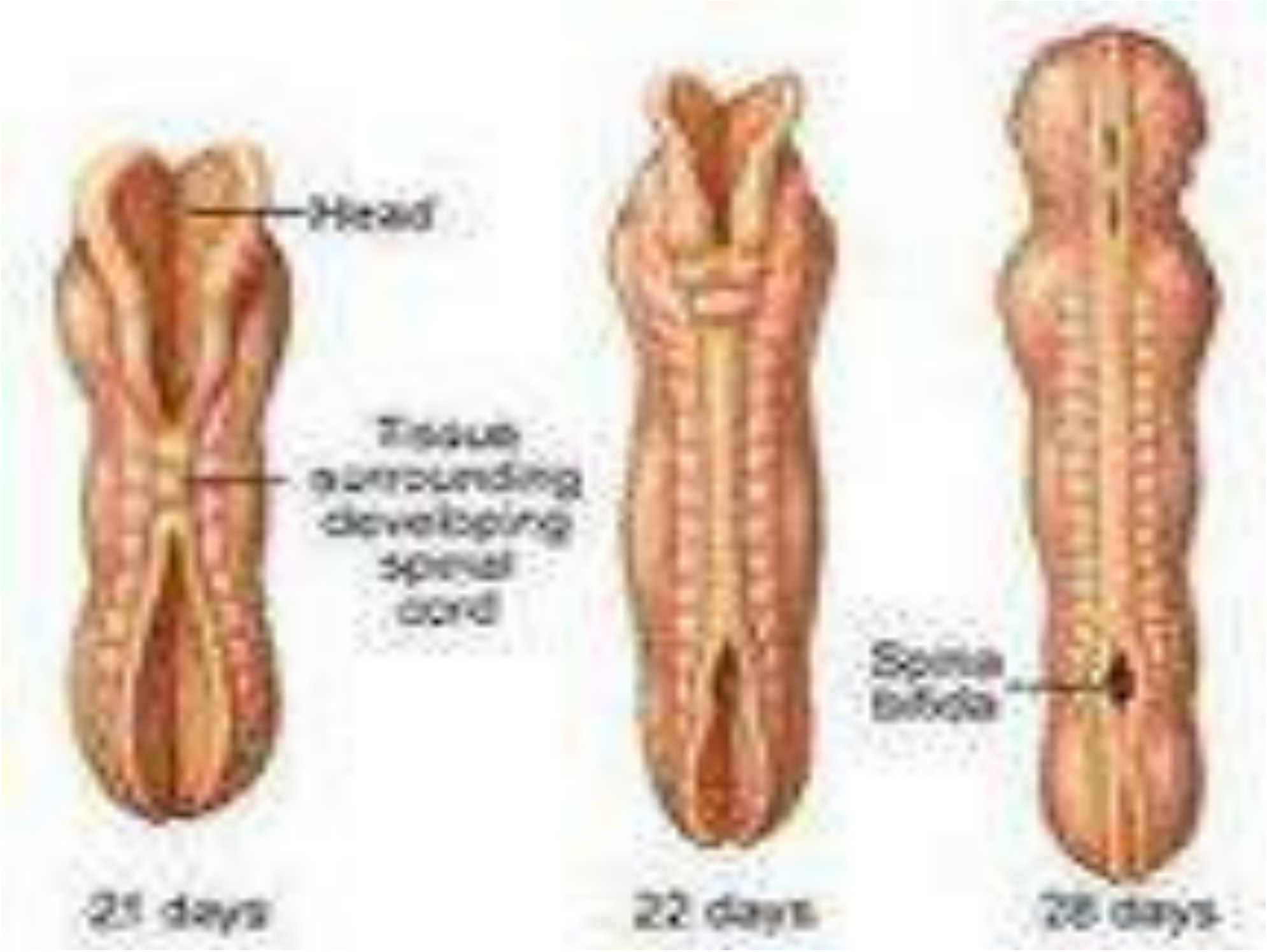
Encephalocele

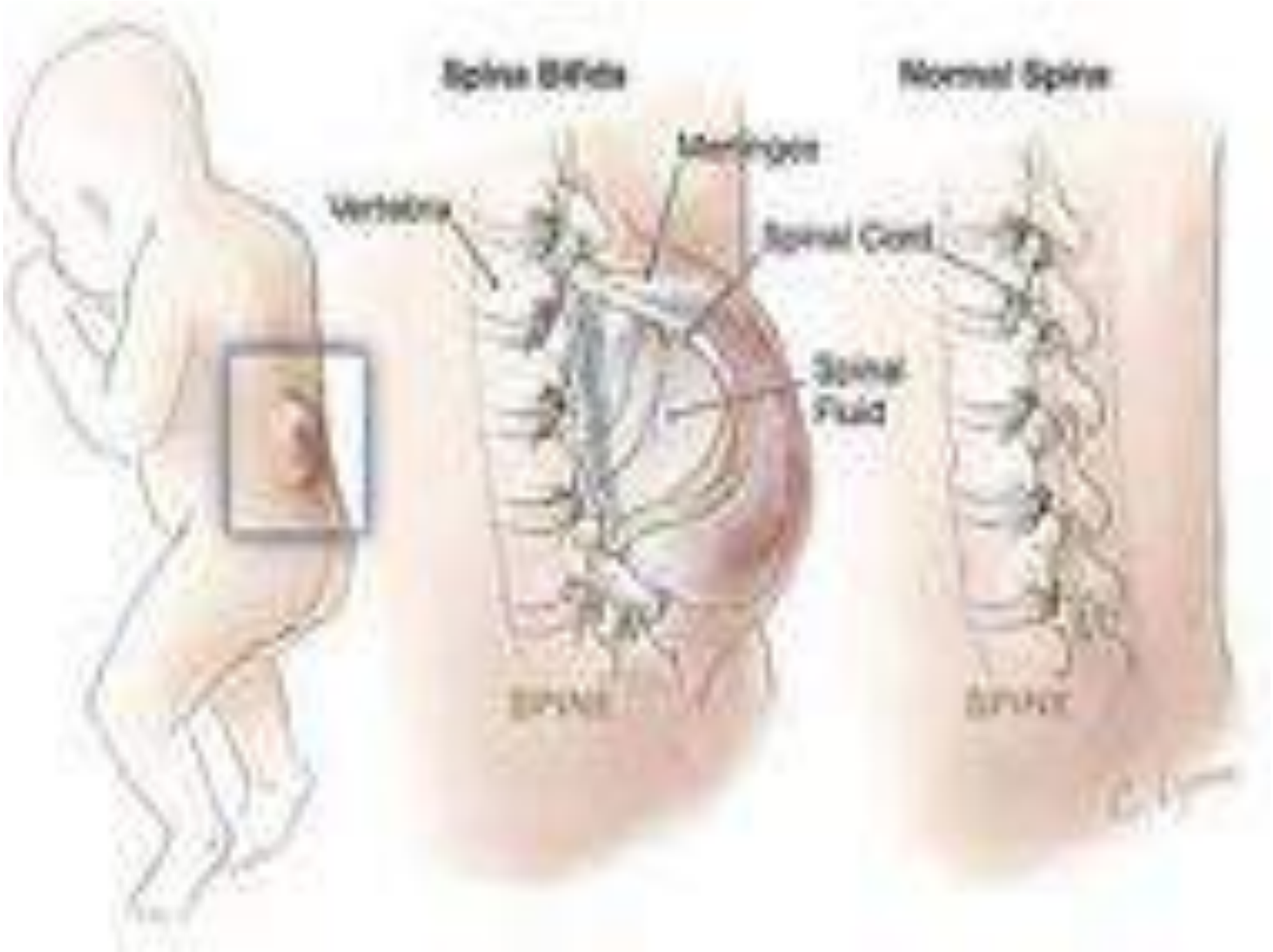


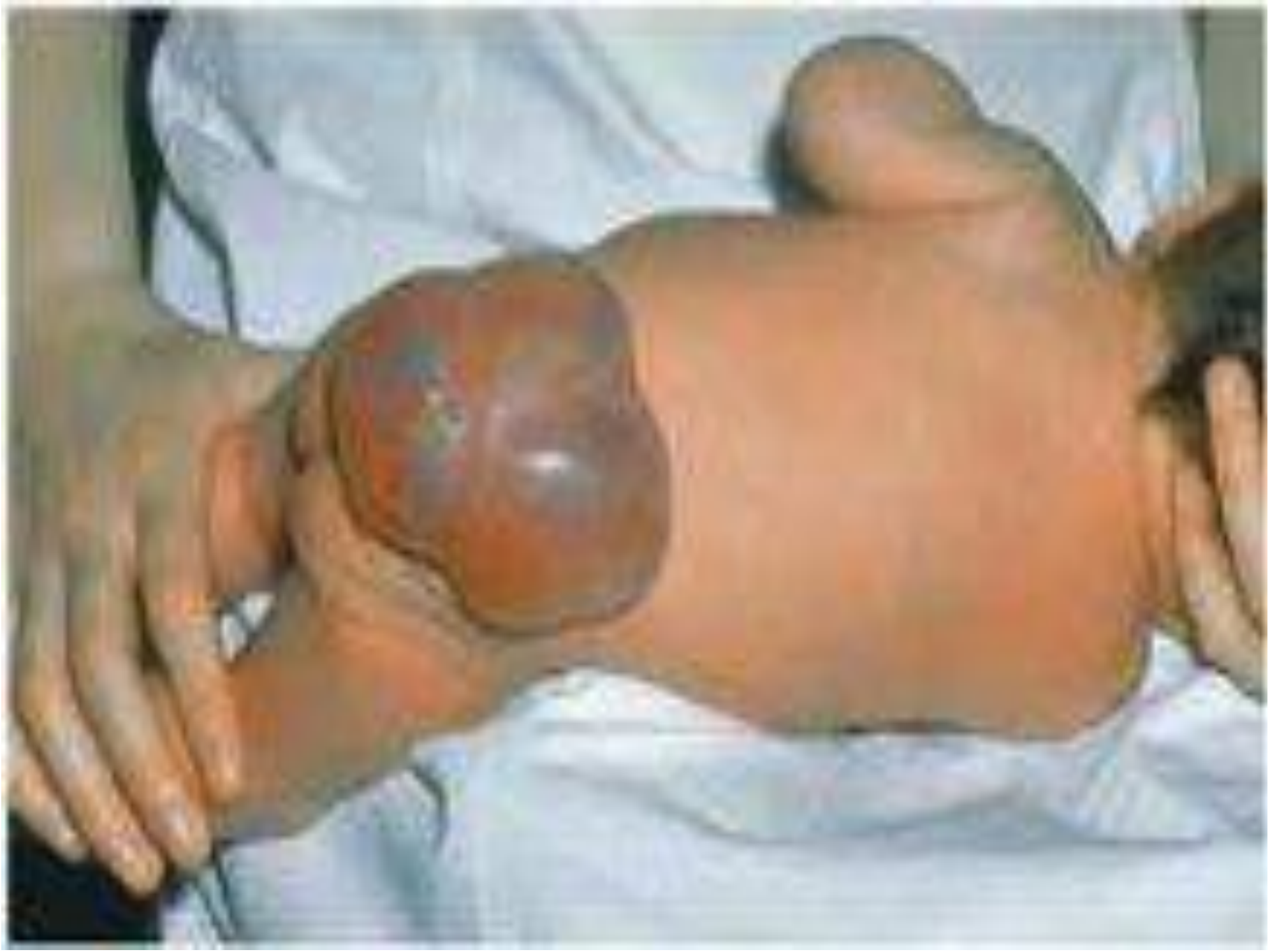
Anencephaly

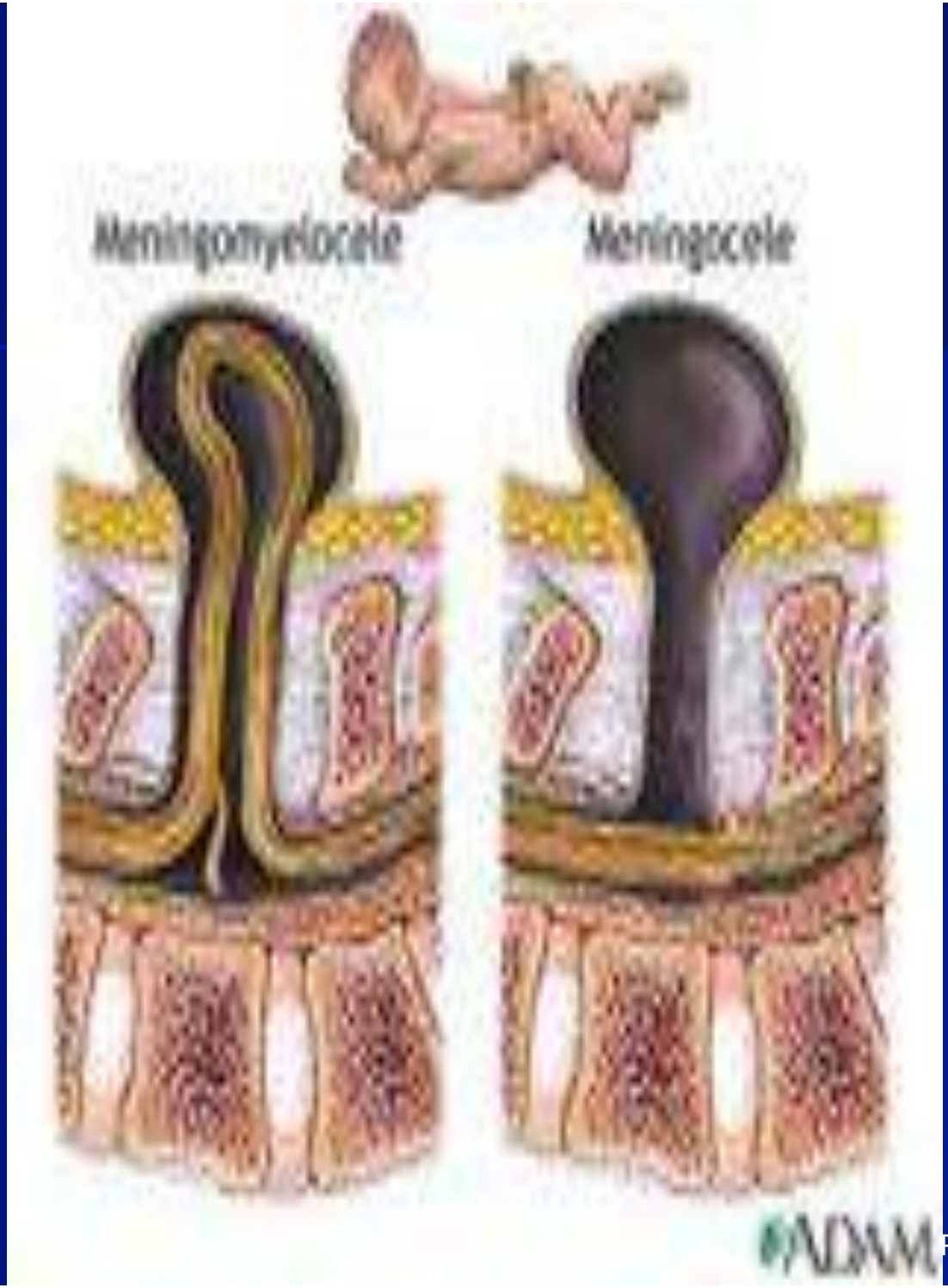
- Failure of the brain and skull development.
- Most severe anomaly.
- Ultrasound diagnosis as early as twenty weeks.
- Polyhydramnios, high alpha fetoprotein.
- Death.

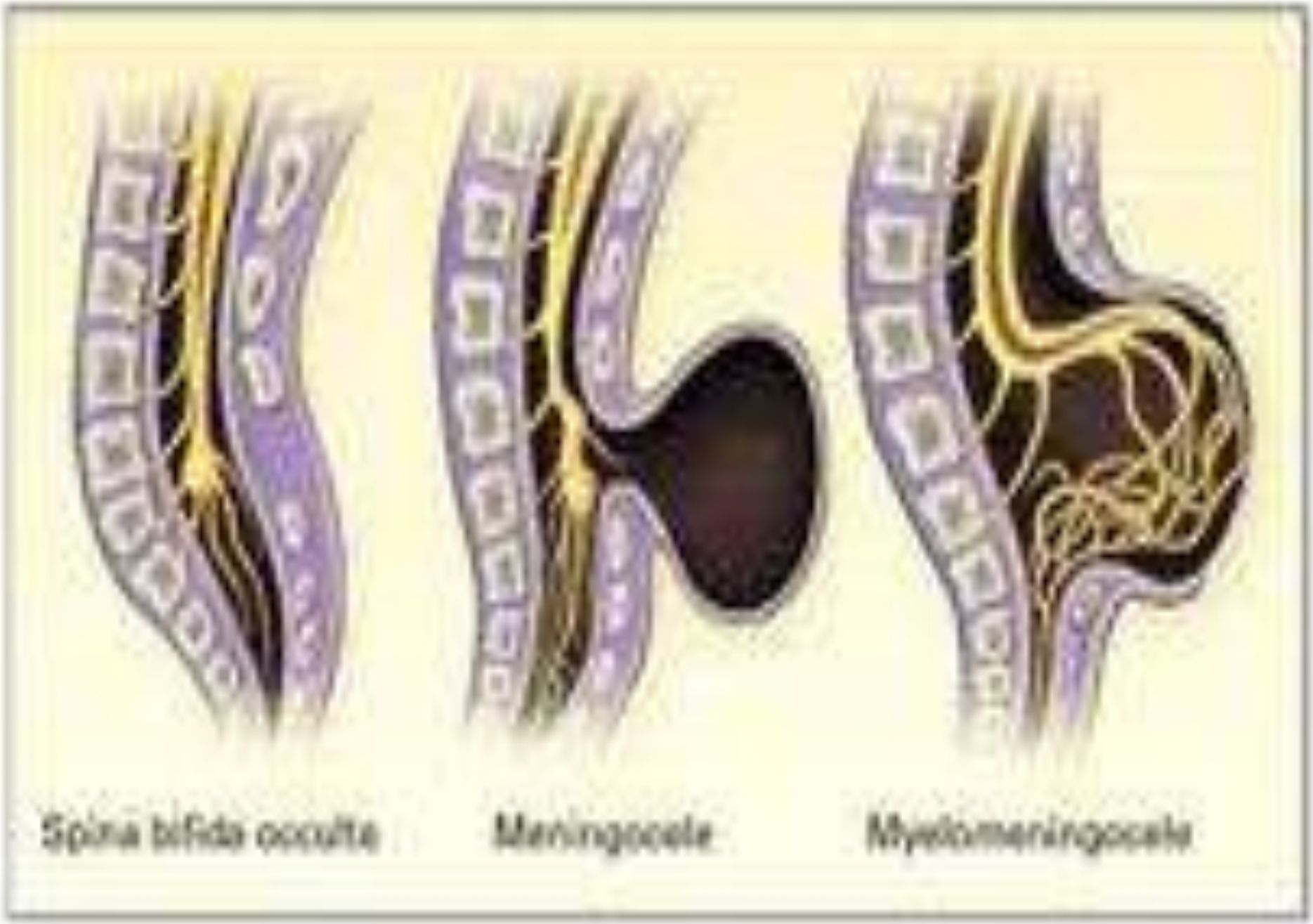


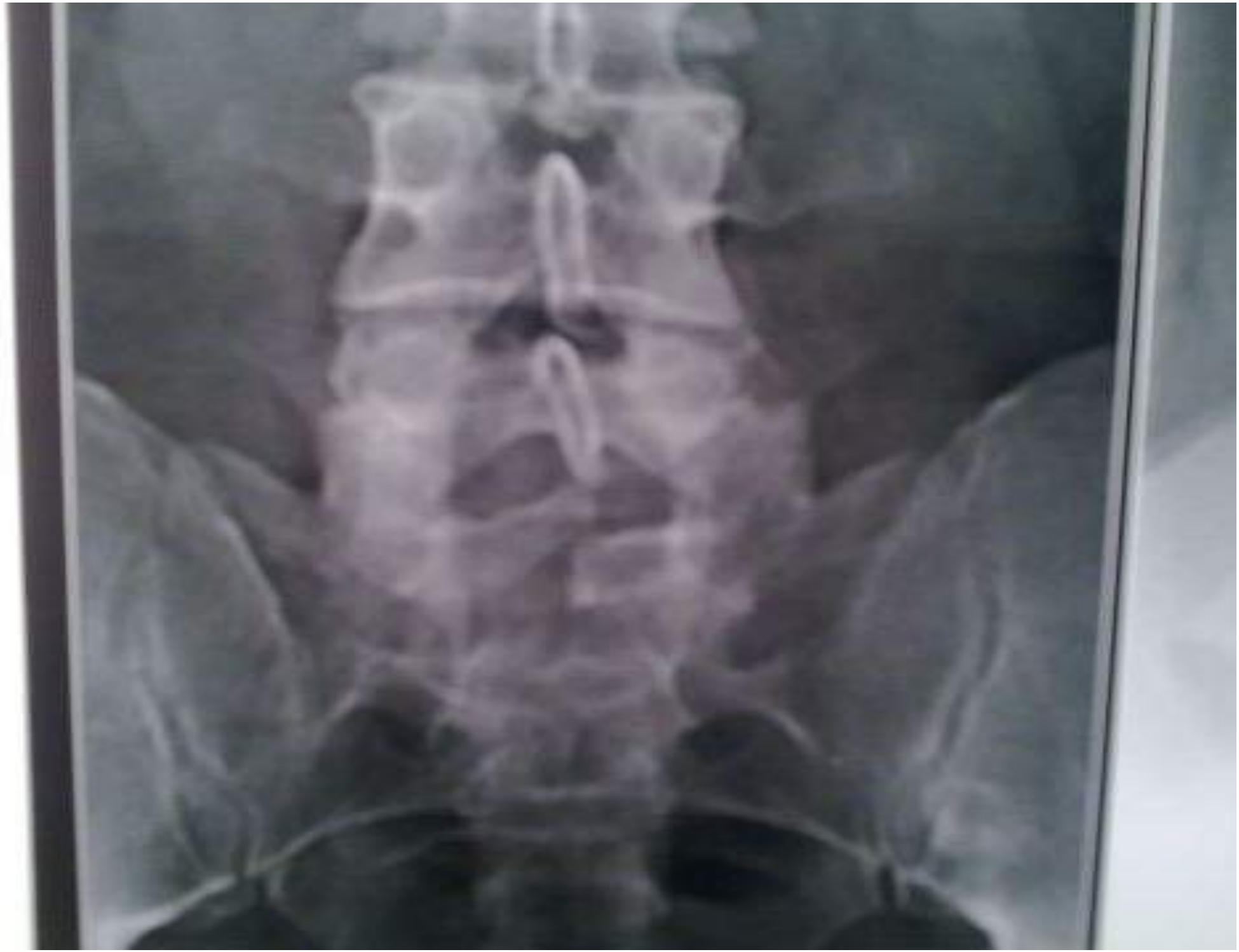

Head
Tissue surrounding developing spinal cord
Spina bifida
21 days
22 days
28 days

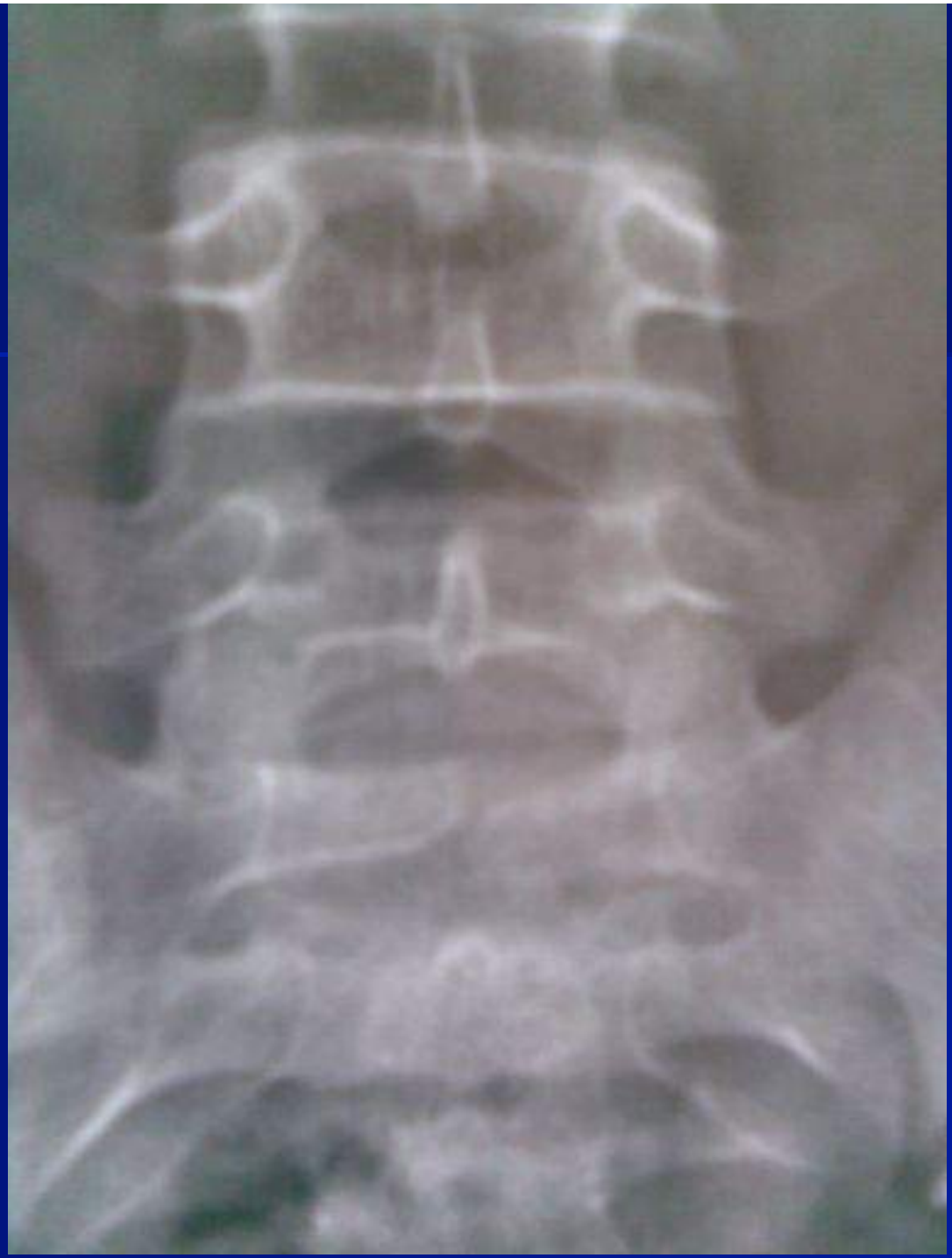

Spina Bifida
Normal Spine
Meninges
Vertebra
Spinal Cord
Spinal Fluid
SPINE
SPINE



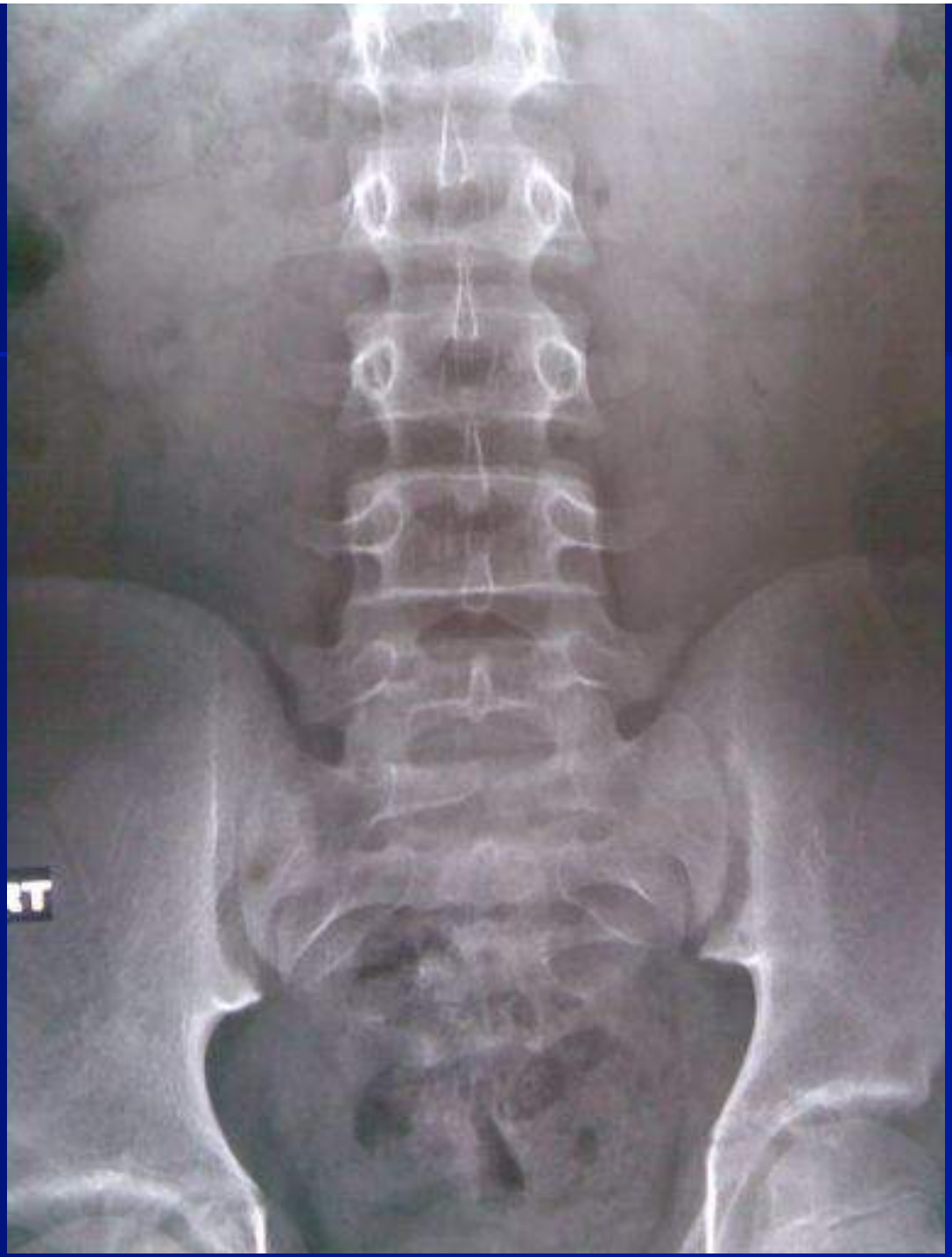

Meningomyelocele
Meningocele


Spina bifida occulta
Meningocele
Myelomeningocele

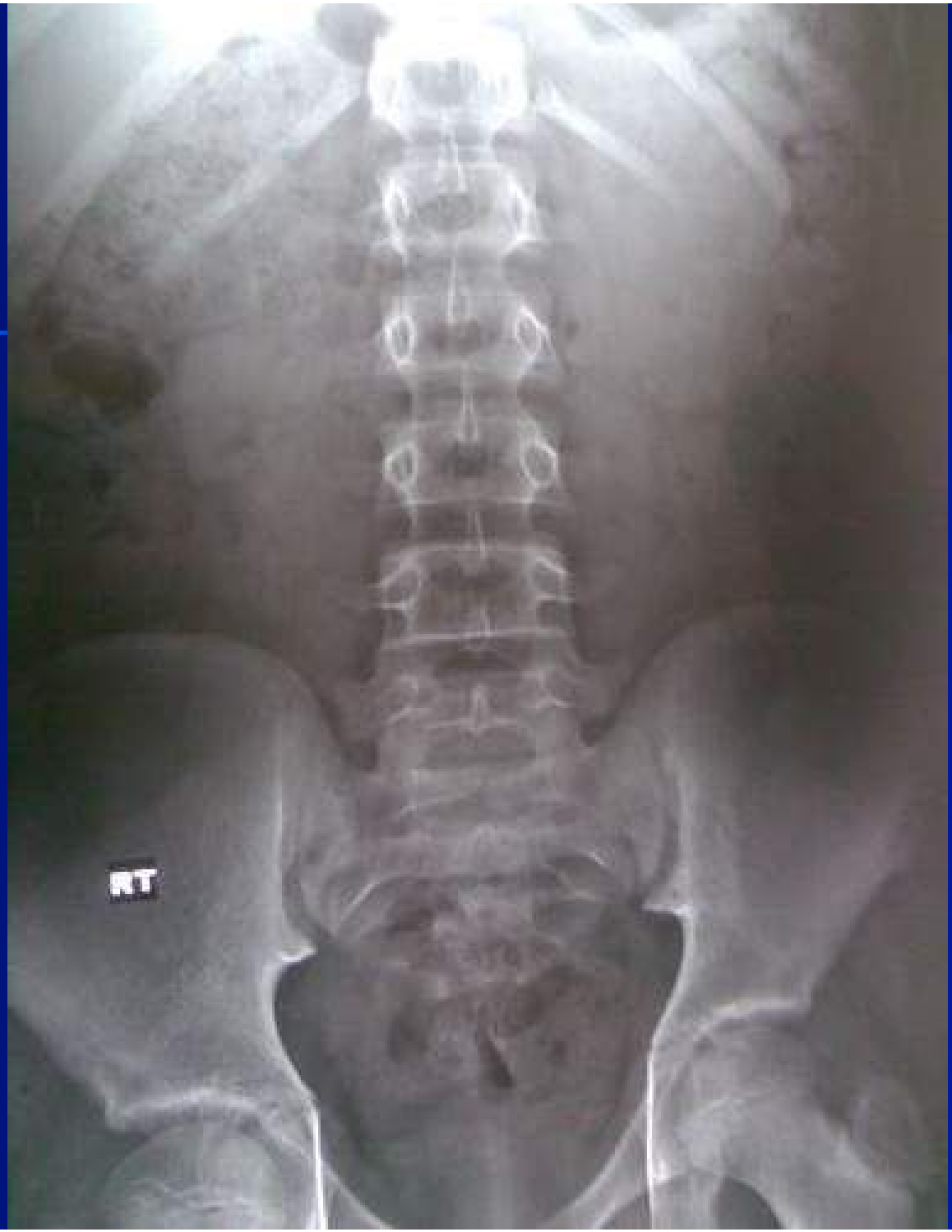




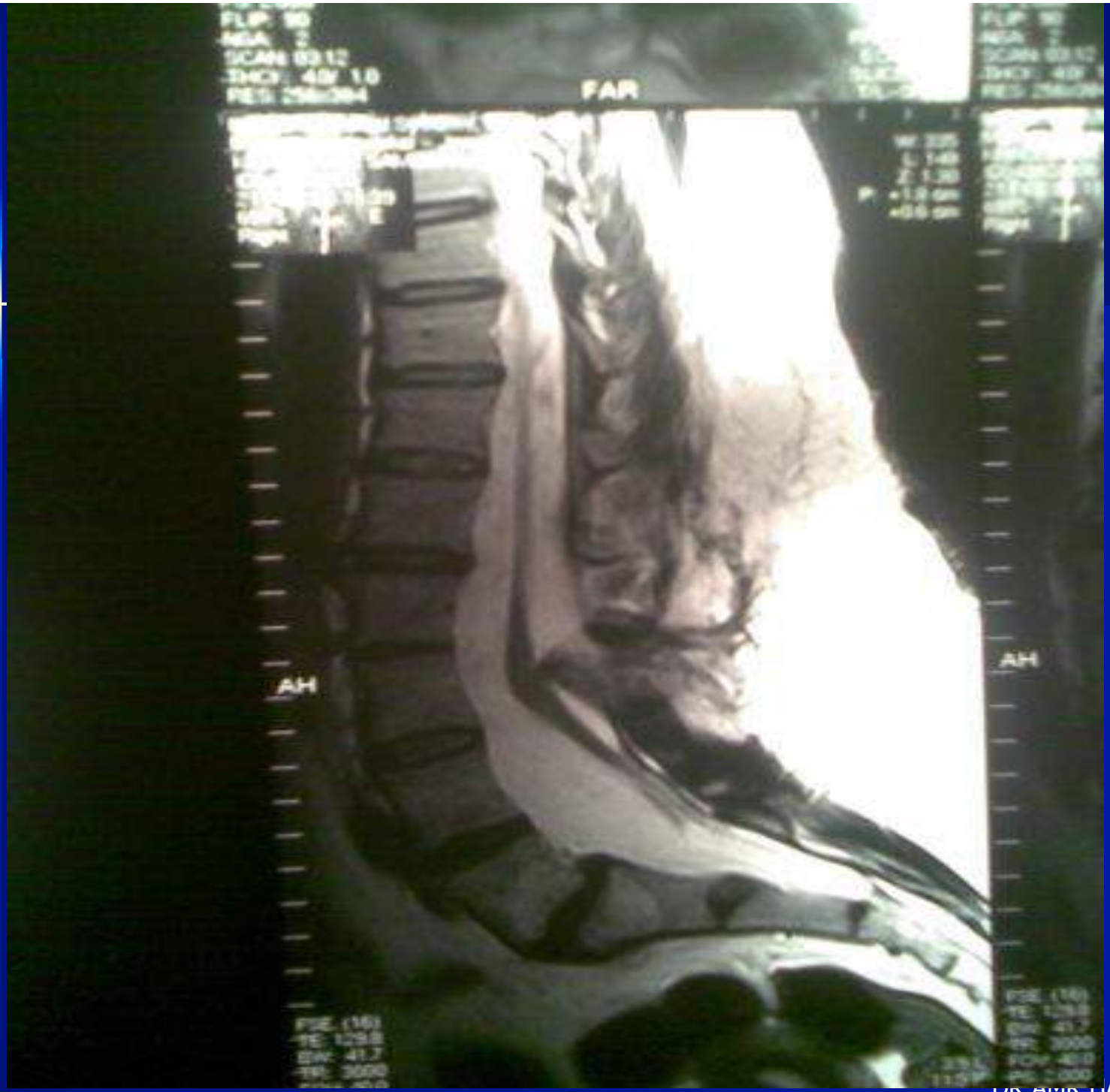
DR AMR HASAN AL HASANY



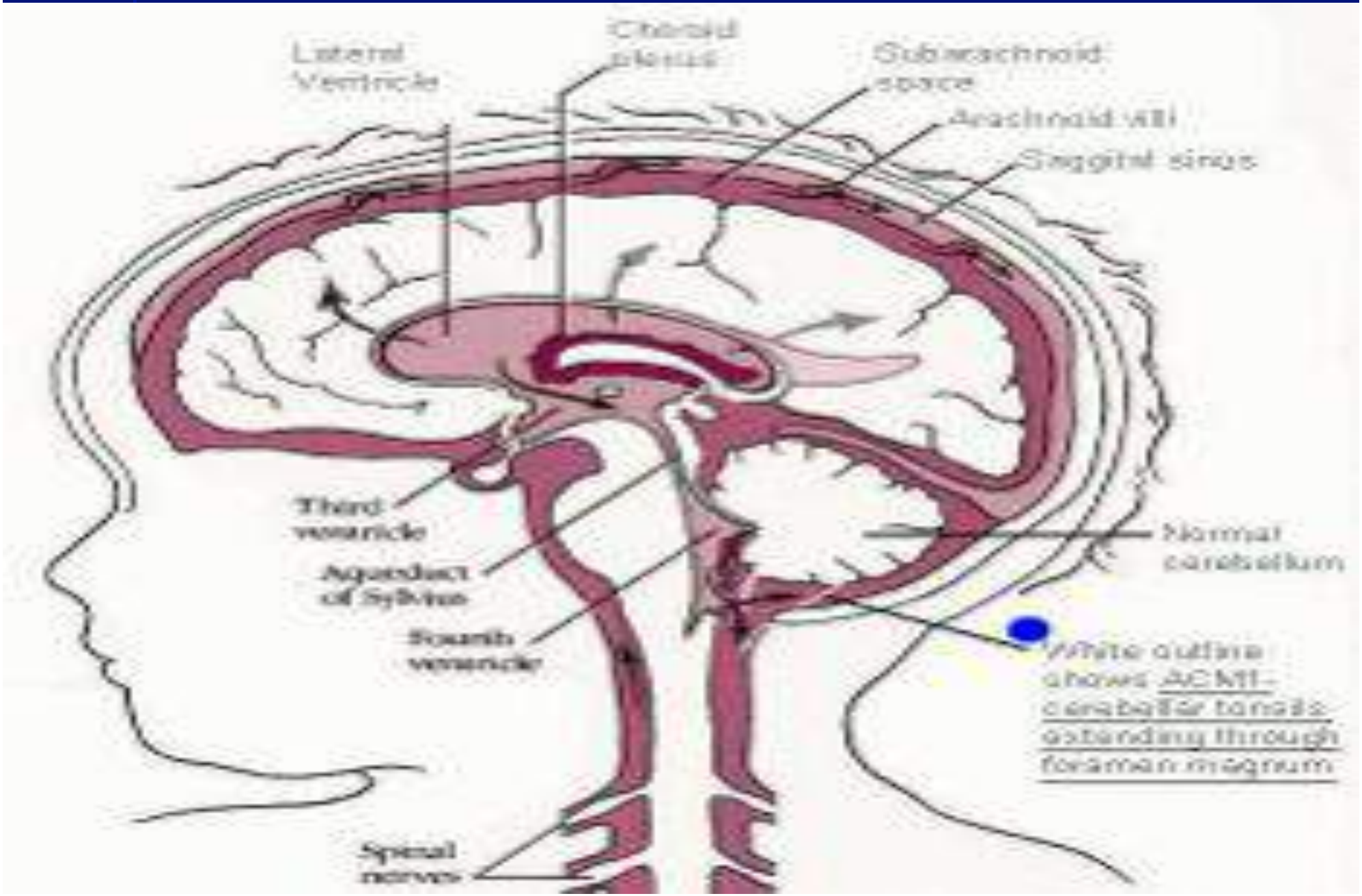
DR AMR HASAN AL HASANY



DR AMR HASAN AL HASANY


FAR
AH
AH

Chiari malformations



Chiari Malformation

- It was first described by **Hans Chiari**, Austrian pathologist, (1851-1914) in 1891 .
- In this and subsequent papers Chiari also credited **Julius Arnold** (1835-1915) Professor of Anatomy at Heidelberg, on the grounds of a previous publication by Arnold believed by him to be of a Chiari II malformation.
- It is a condition where there is herniation of the hindbrain into the upper cervical spine. This is classified into

TYPE I

There is herniation of the Cerebellar tonsils into the upper cervical canal.

TYPE II

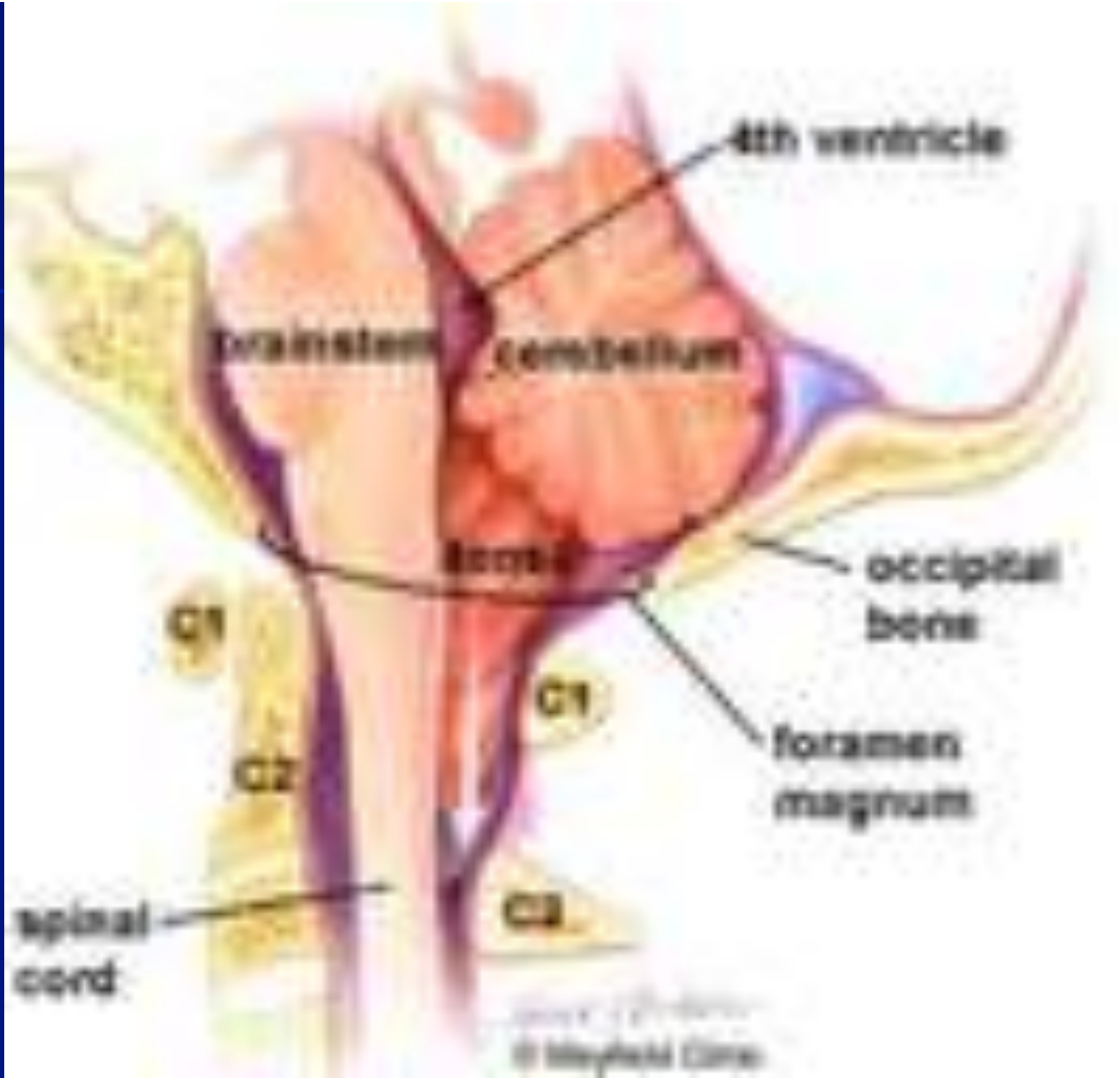
Migration of the medulla oblongata and 4th ventricle into the upper cervical canal.

TYPE III

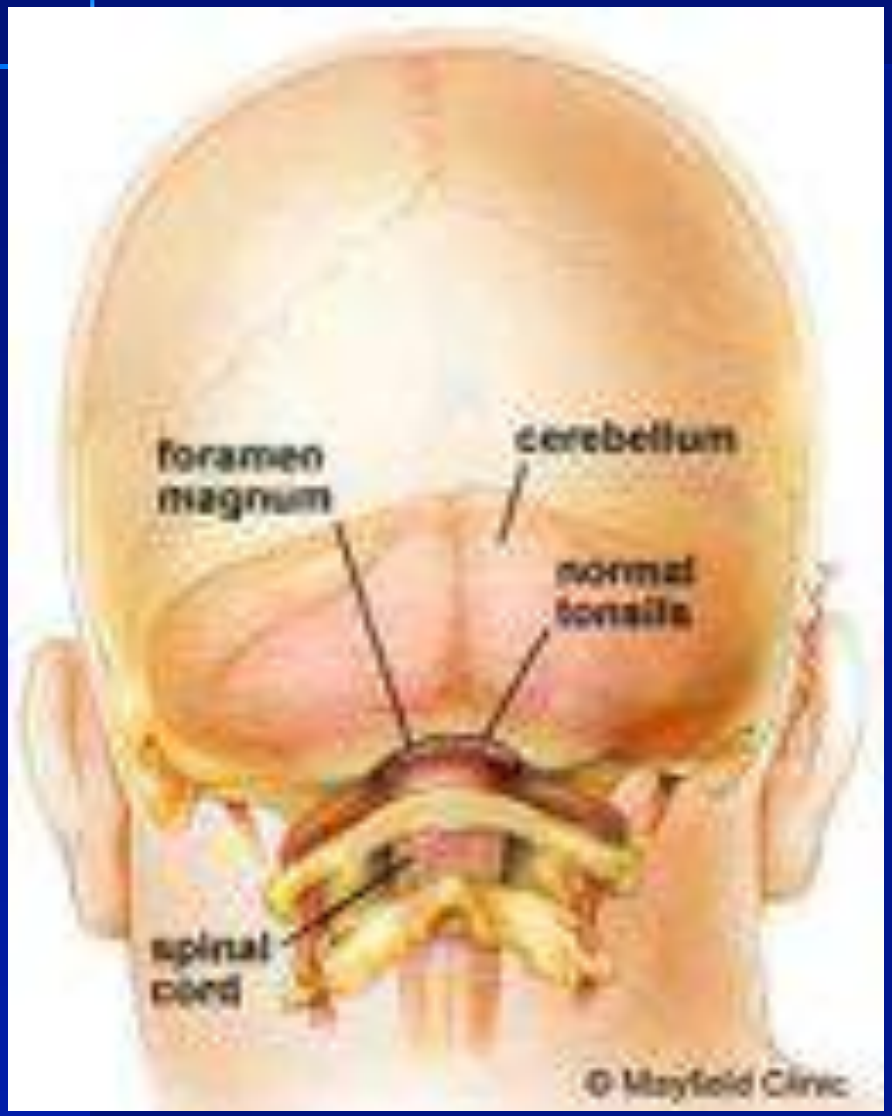
Displacement of the entire cerebellum and the 4th ventricle into the upper cervical canal.

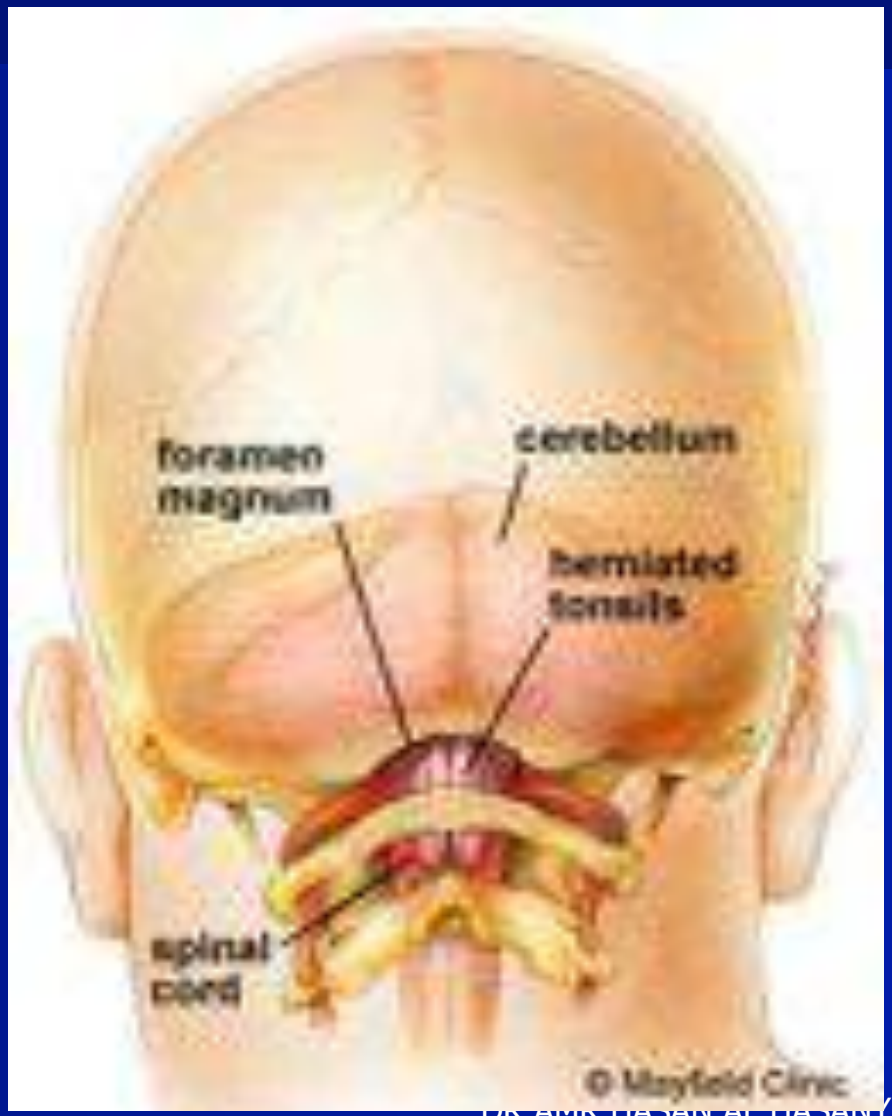
Chiari I

Chiari I

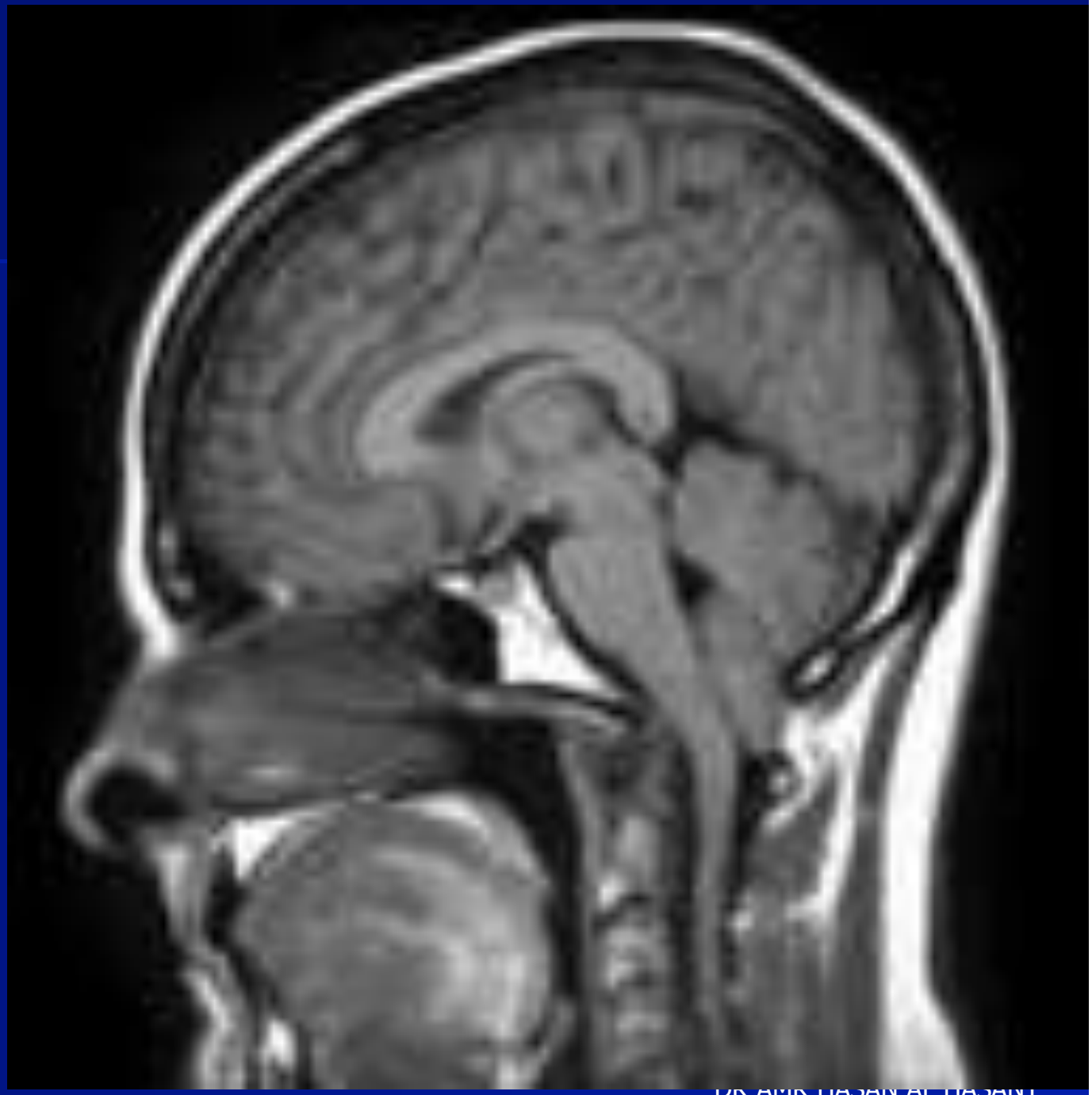

4th ventricle
brainstem
cerebellum
occipital bone
foramen magnum
C1
C2
C3
spinal cord

Chiari I

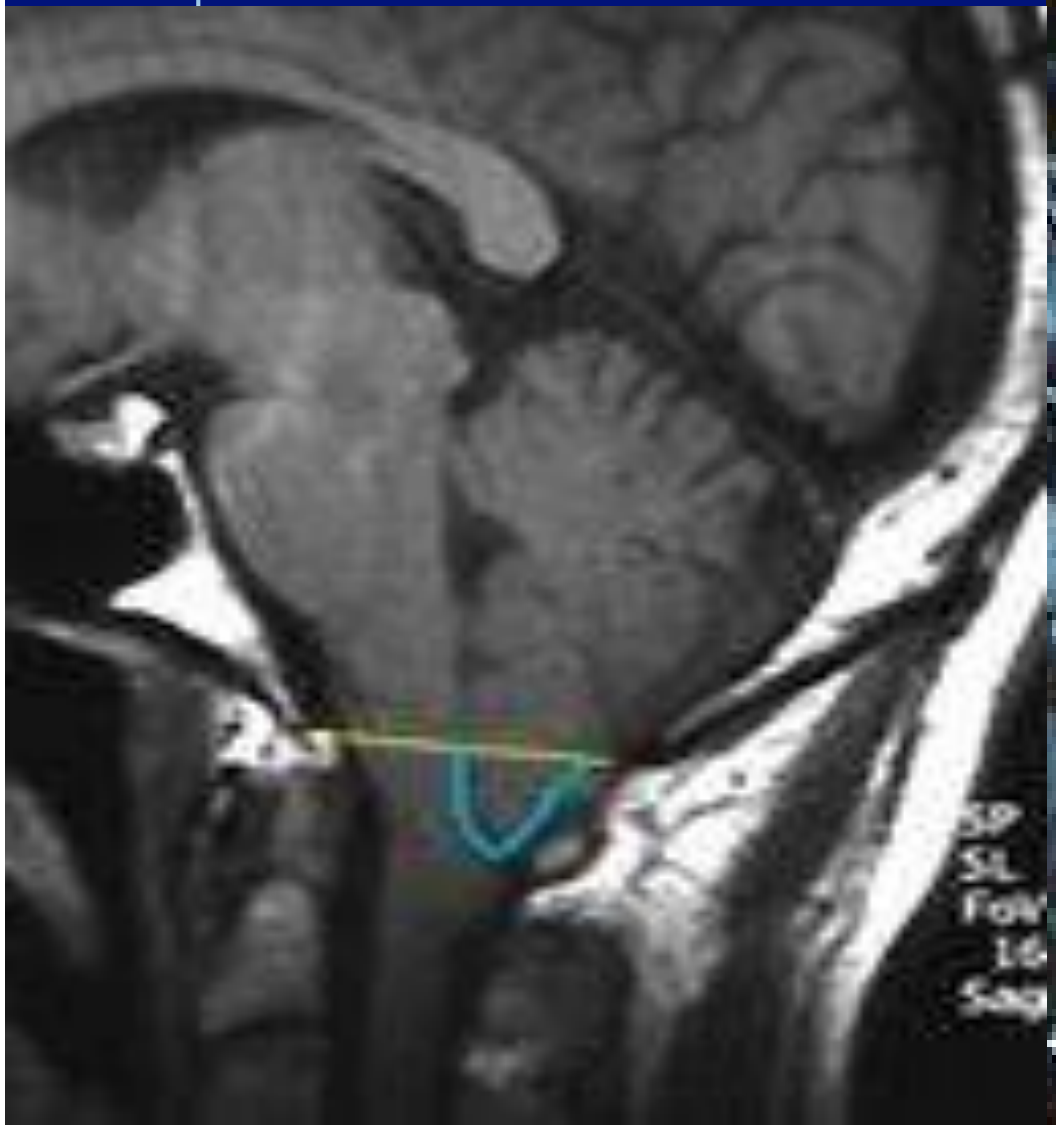

foramen magnum
cerebellum
normal tonsils
spinal cord
© Mayfield Clinic

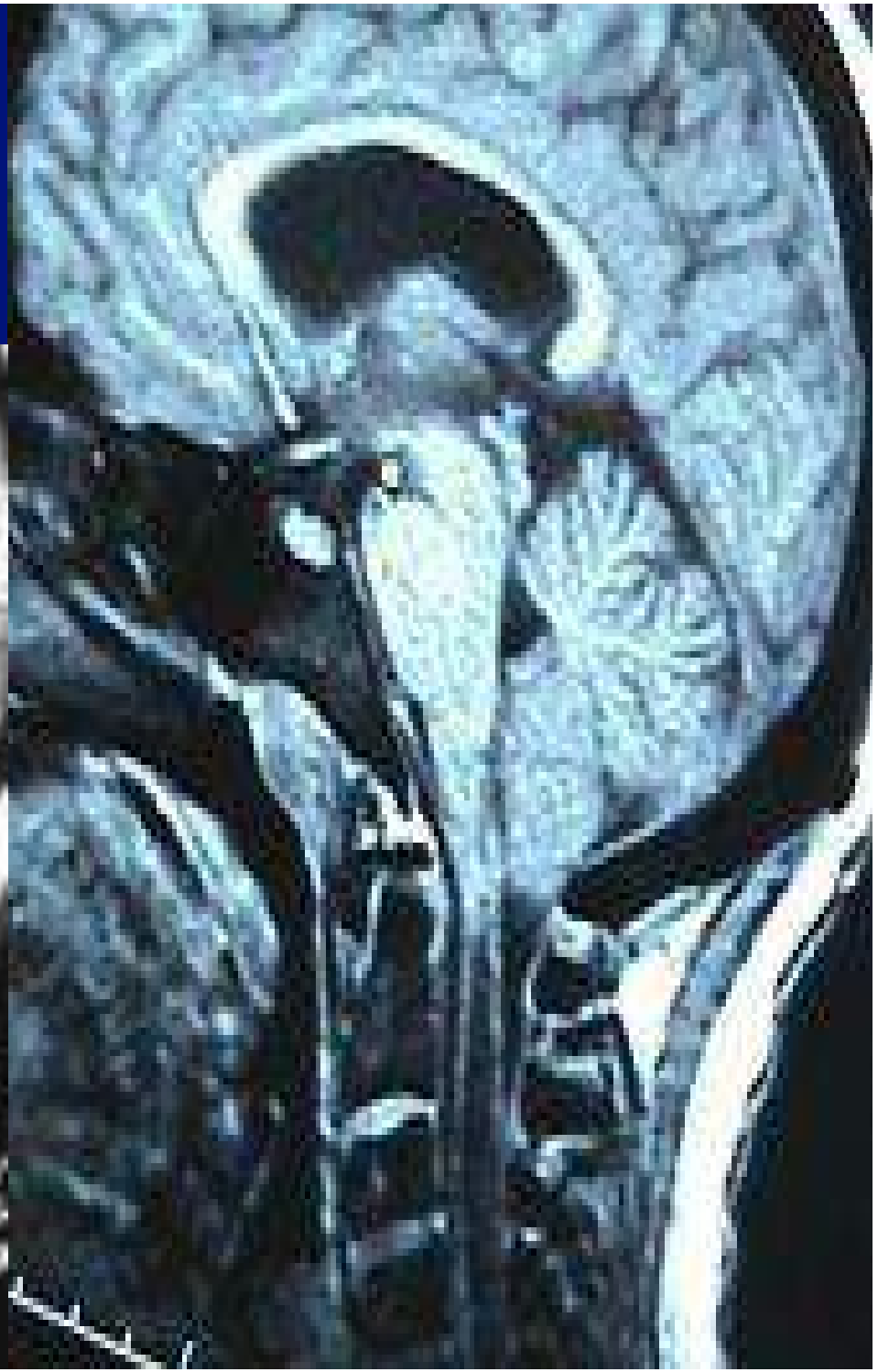

foramen magnum
cerebellum
herniated tonsils
spinal cord
© Mayfield Clinic

Chiari I

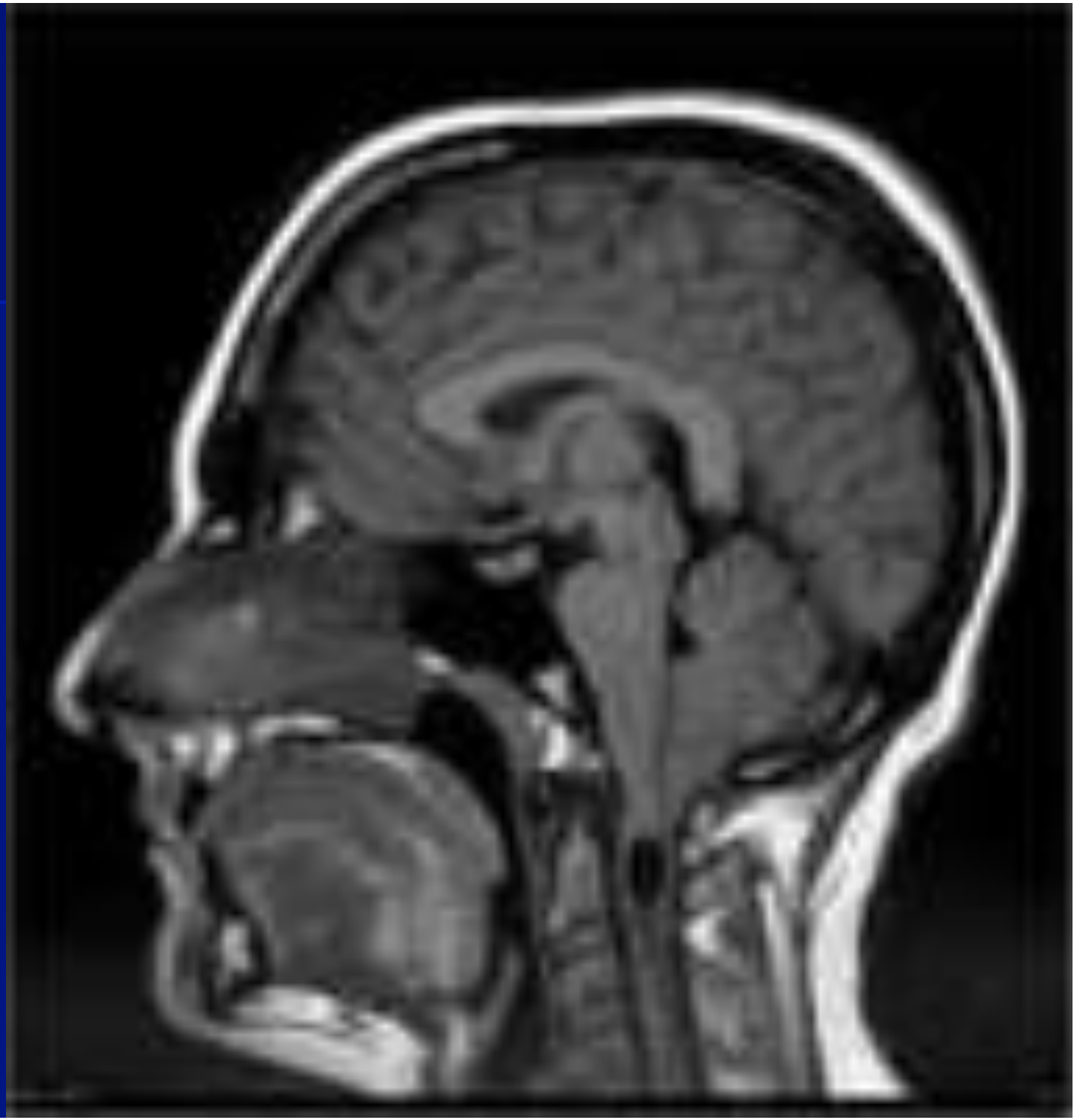


Chiari I





Chiari I with syrinx



Associated anomalies are:

- Spinal cord: syrinx 20-40%.
- Ventricles: mild to moderate hydrocephalus 20-25%
- Skeletal anomalies: basilar invagination 25-50%

Arnold Chiari II

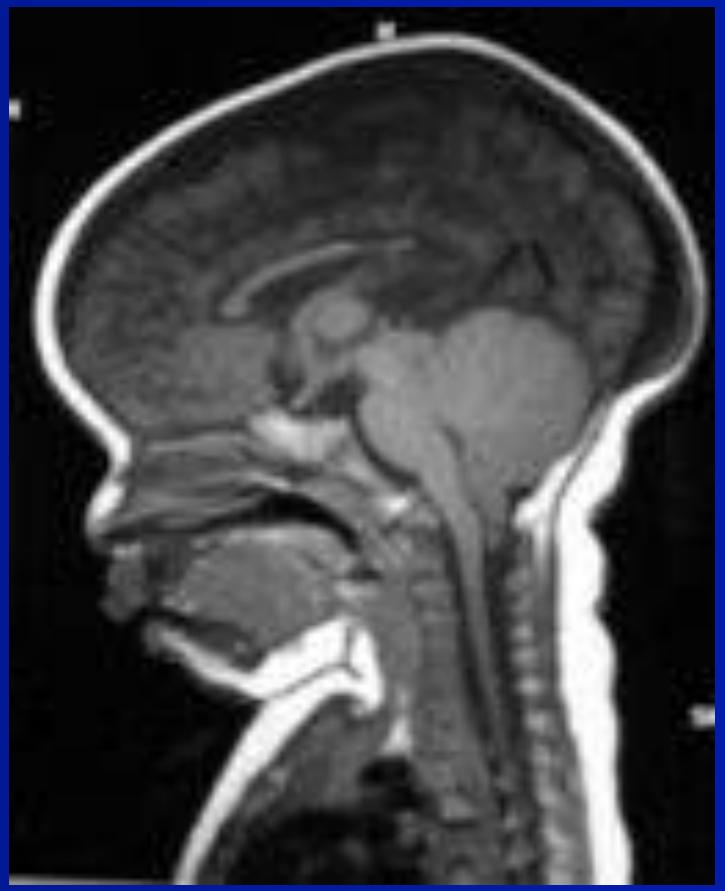
<u>Complex anomaly:</u>

Skull and dura

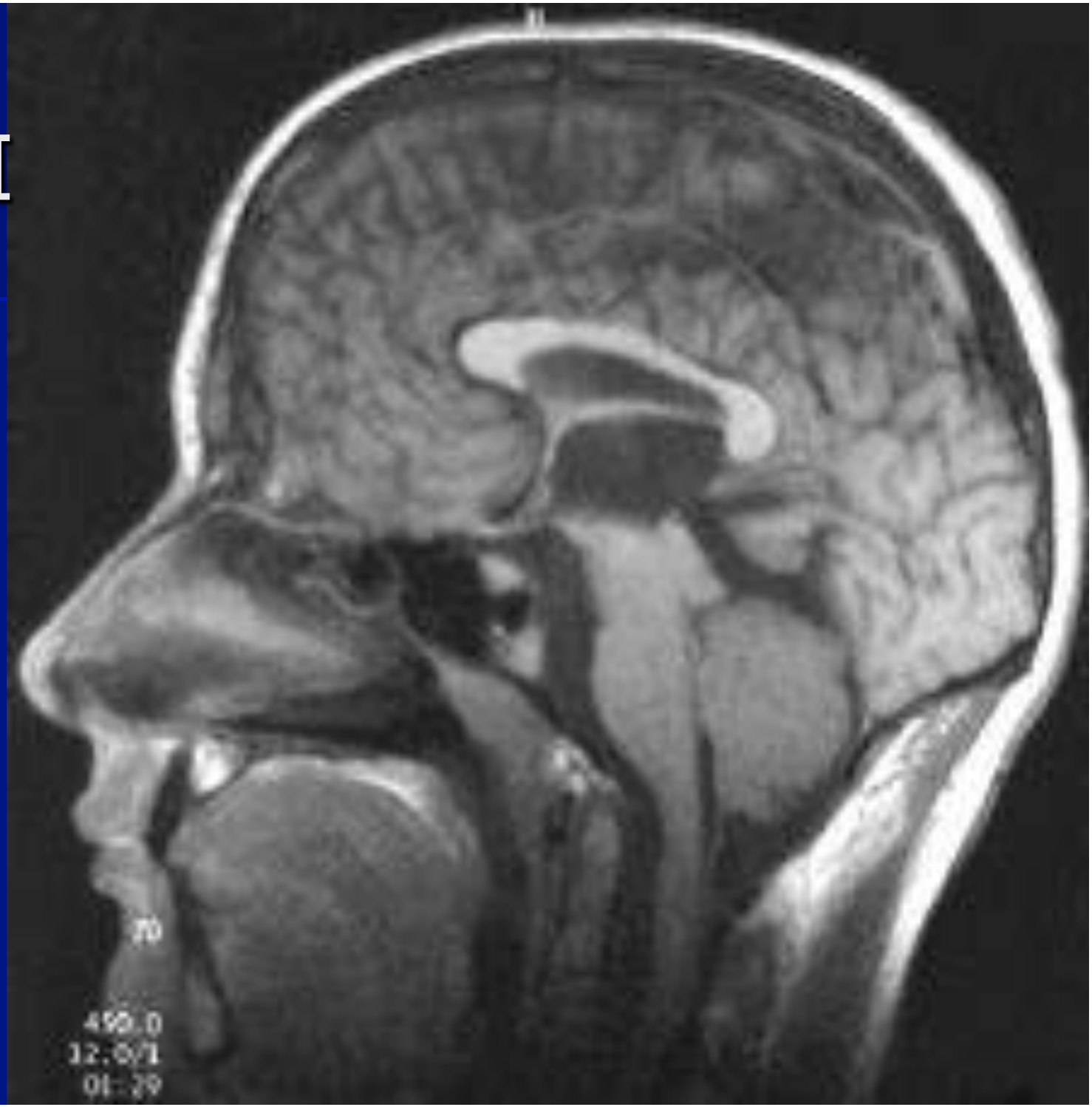
Brain

Spine

cord



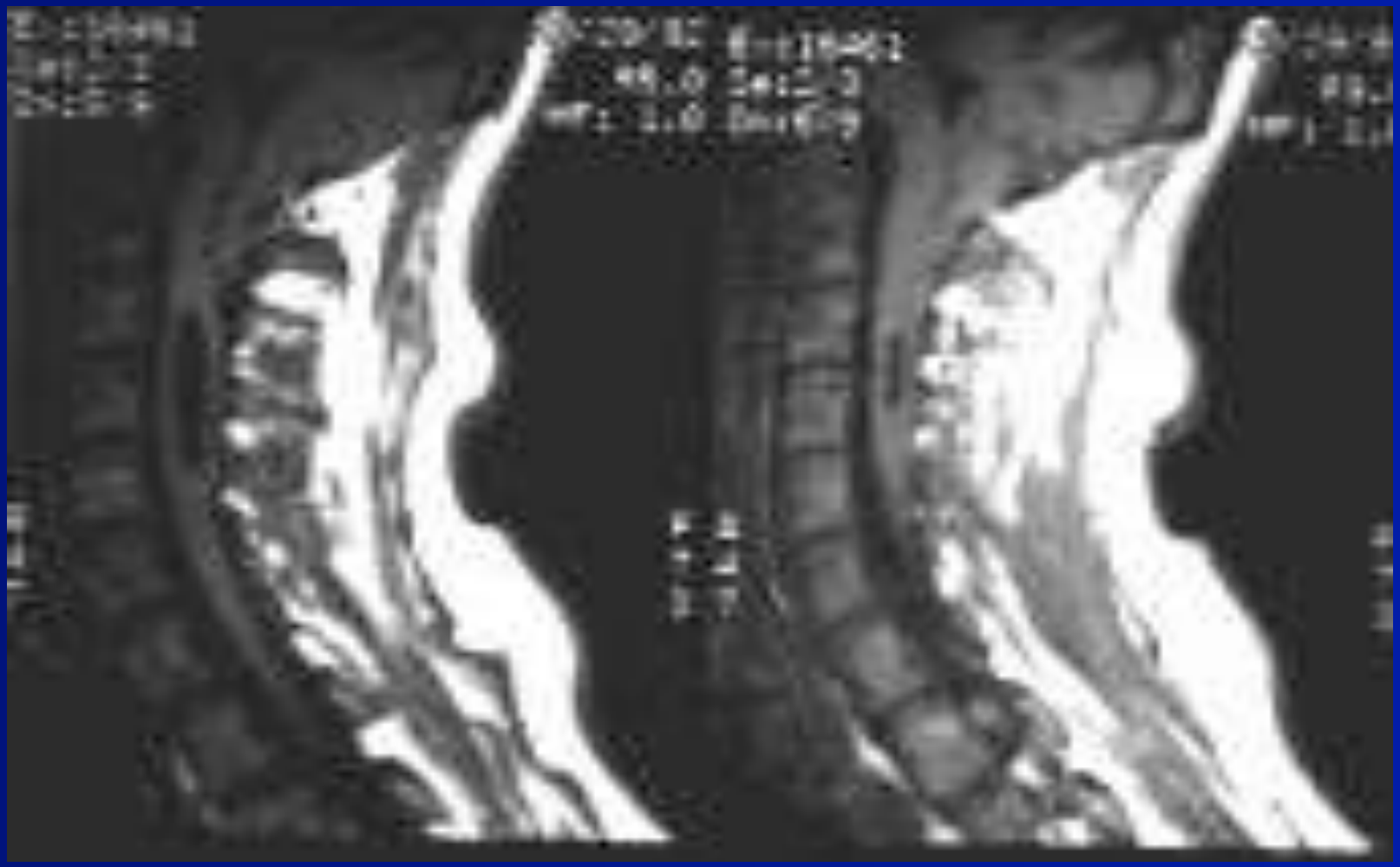
Chiari II



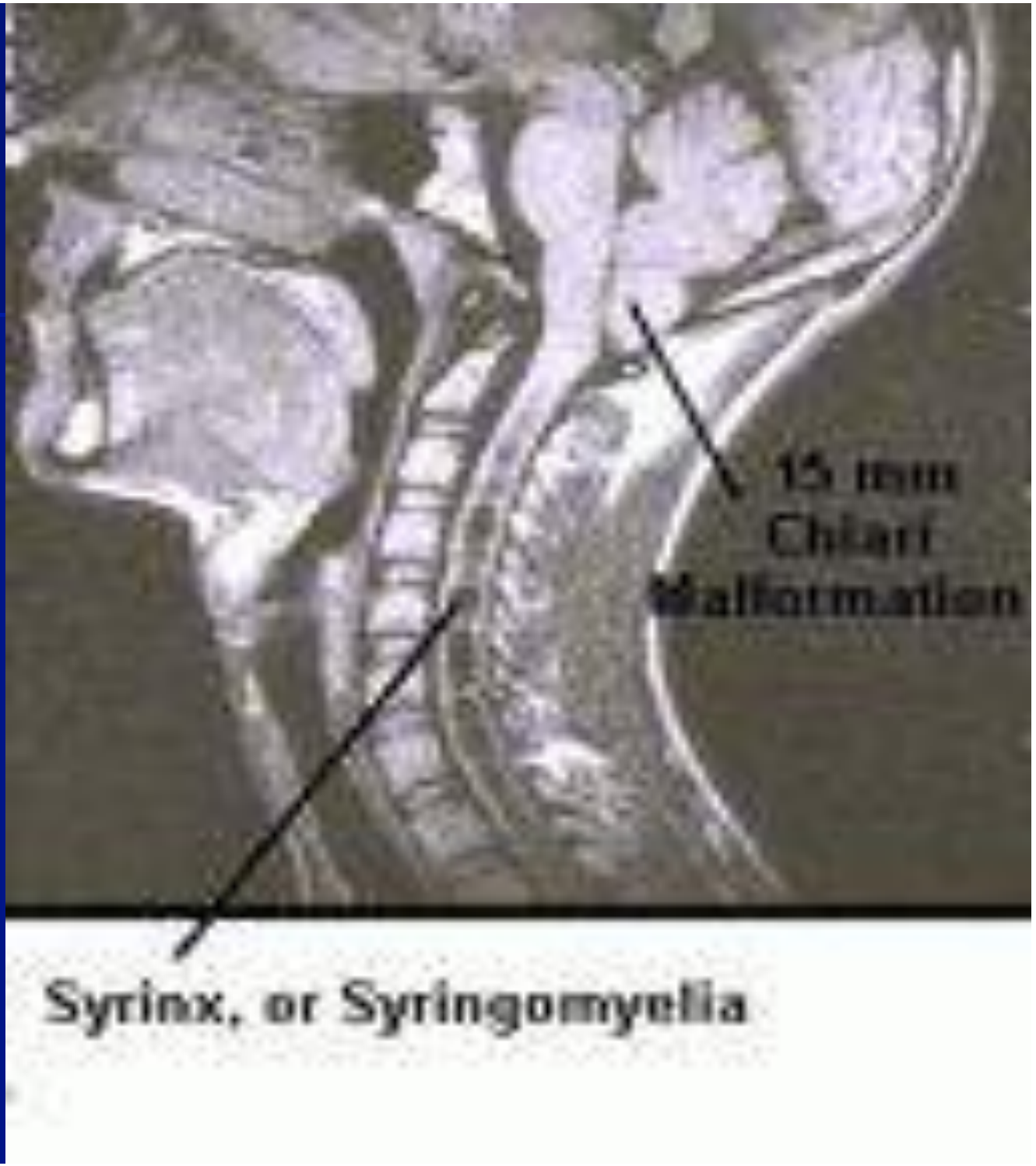
Chiari II

- Myelomeningoceleis present in nearly all patients with a Chiari II malformation
- Hydrocephalus 90% of cases .
- Aqueductal stenosis is seen in 50%
- Medullary kink.
- Corpus callosum agenesis.
- Polymicrogyria.
- Syringomyelia

Arnold Chiari II with syrinx

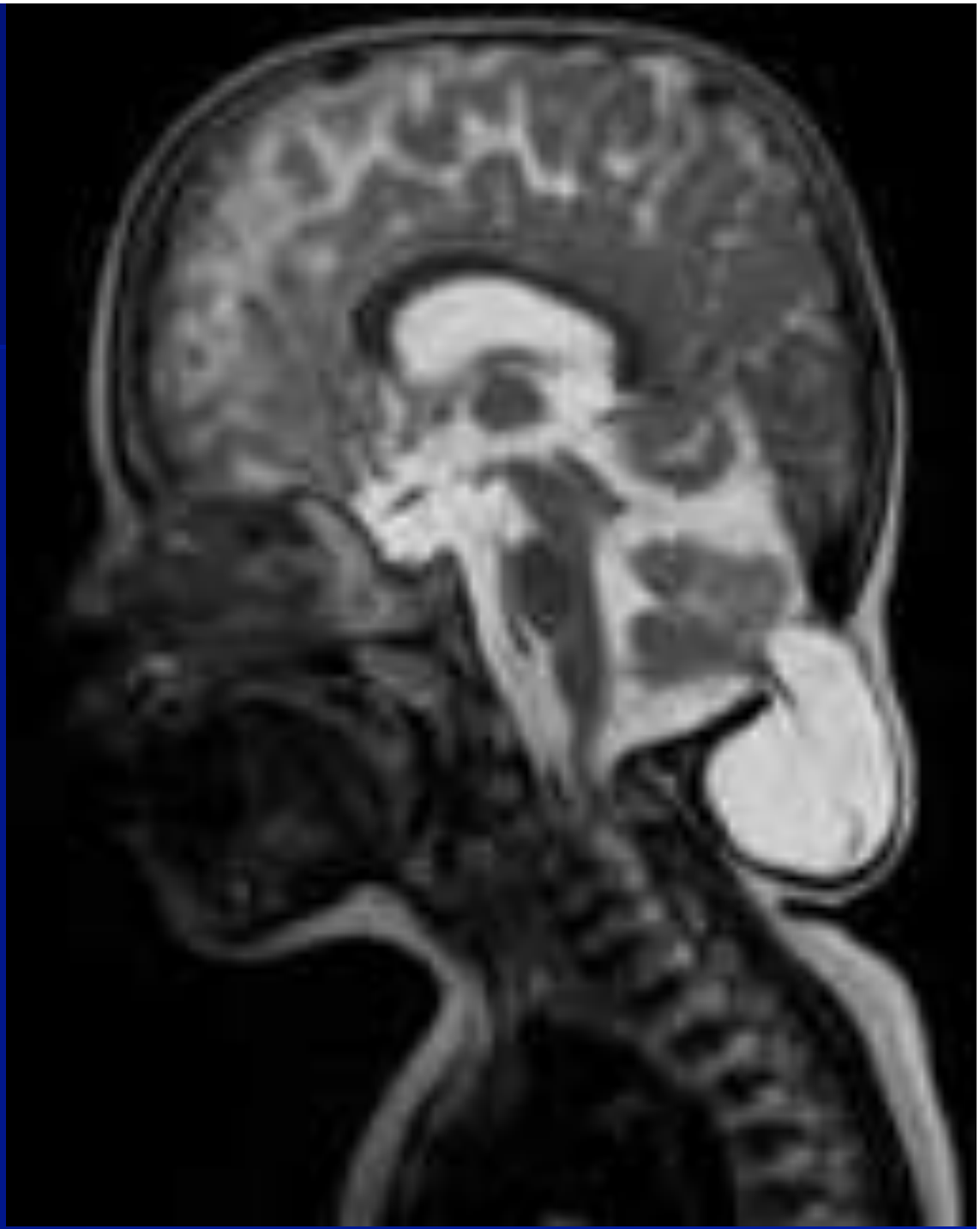


Chiari II with syrinx



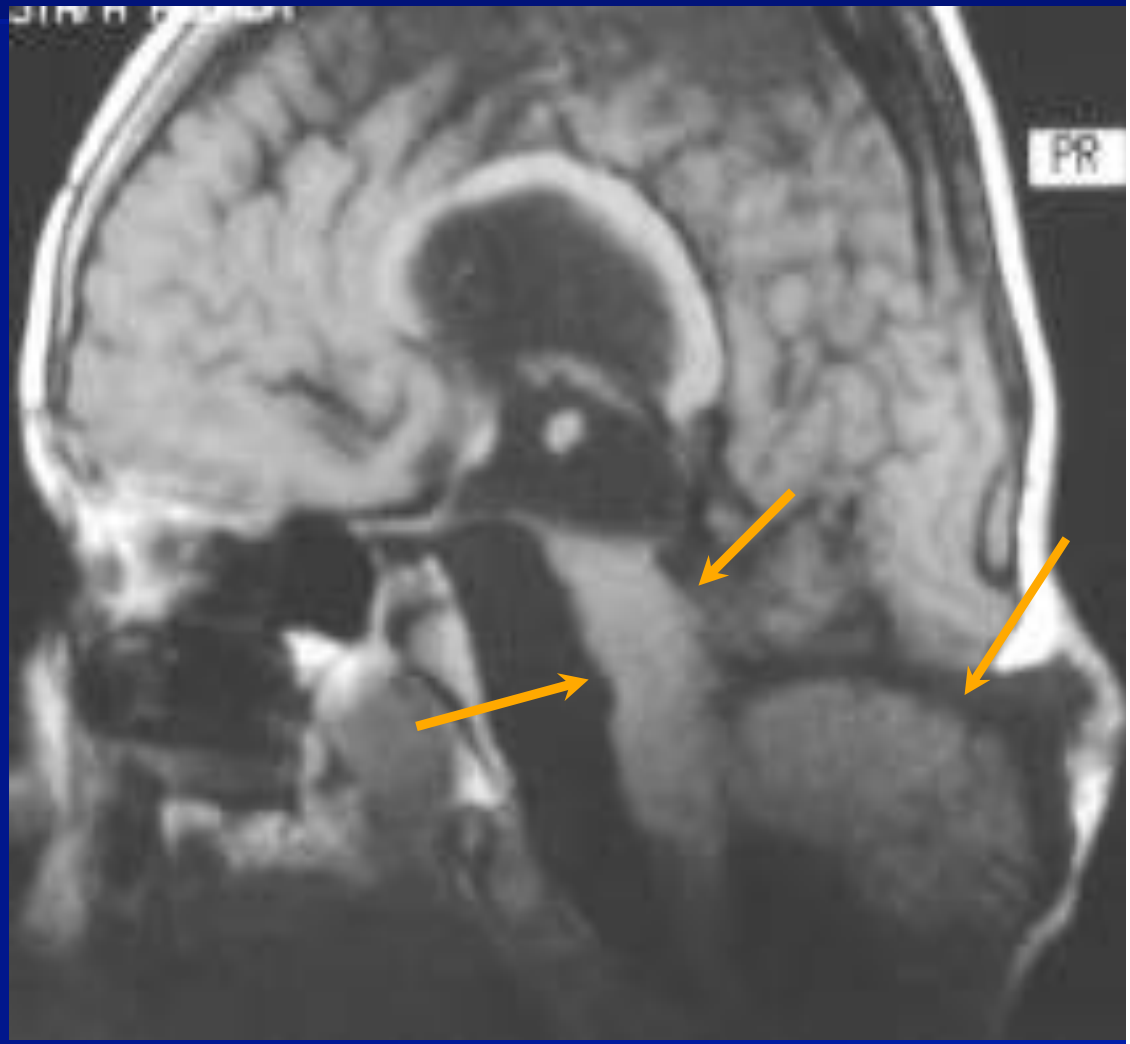
Chiari III:

Cervical occipital encephalocele that contains cerebellum.



Chiari III:

Cervical occipital encephalocele that contains cerebellum.



Chiari IV

Severe cerebellar hypoplasia.

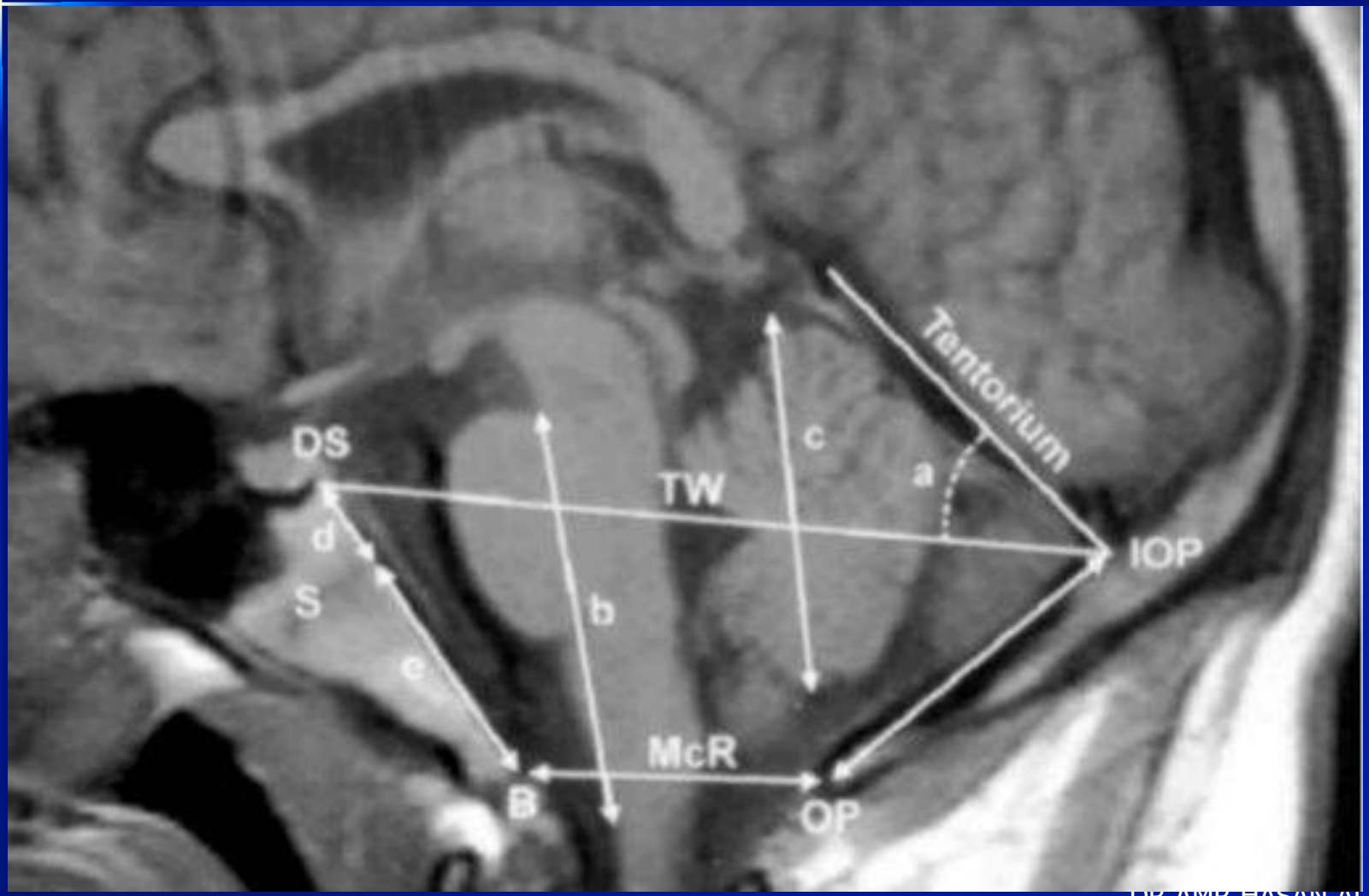
Chiari type 0

a newly identified form of Chiari, describes the absence (or a “zero” herniation) of the tonsils below the foramen magnum.

Yet Chiari 0 includes the presence of both symptoms and a syrinx in the spinal cord.

This new type is under study and controversial.

Chiari type 0



Stage 2: Ventral Induction: Formation of the Brain Segments and Face

- Weeks 5-10
  - Three vesicles (prosencephalon, mesencephalon, and rhombencephalon) form the cerebrum, mid-brain, cerebellum, and lower brain stem.
- Division into two hemispheres.

Stage 2: Ventral Induction: Formation of the Brain Segments and Face

Failure:

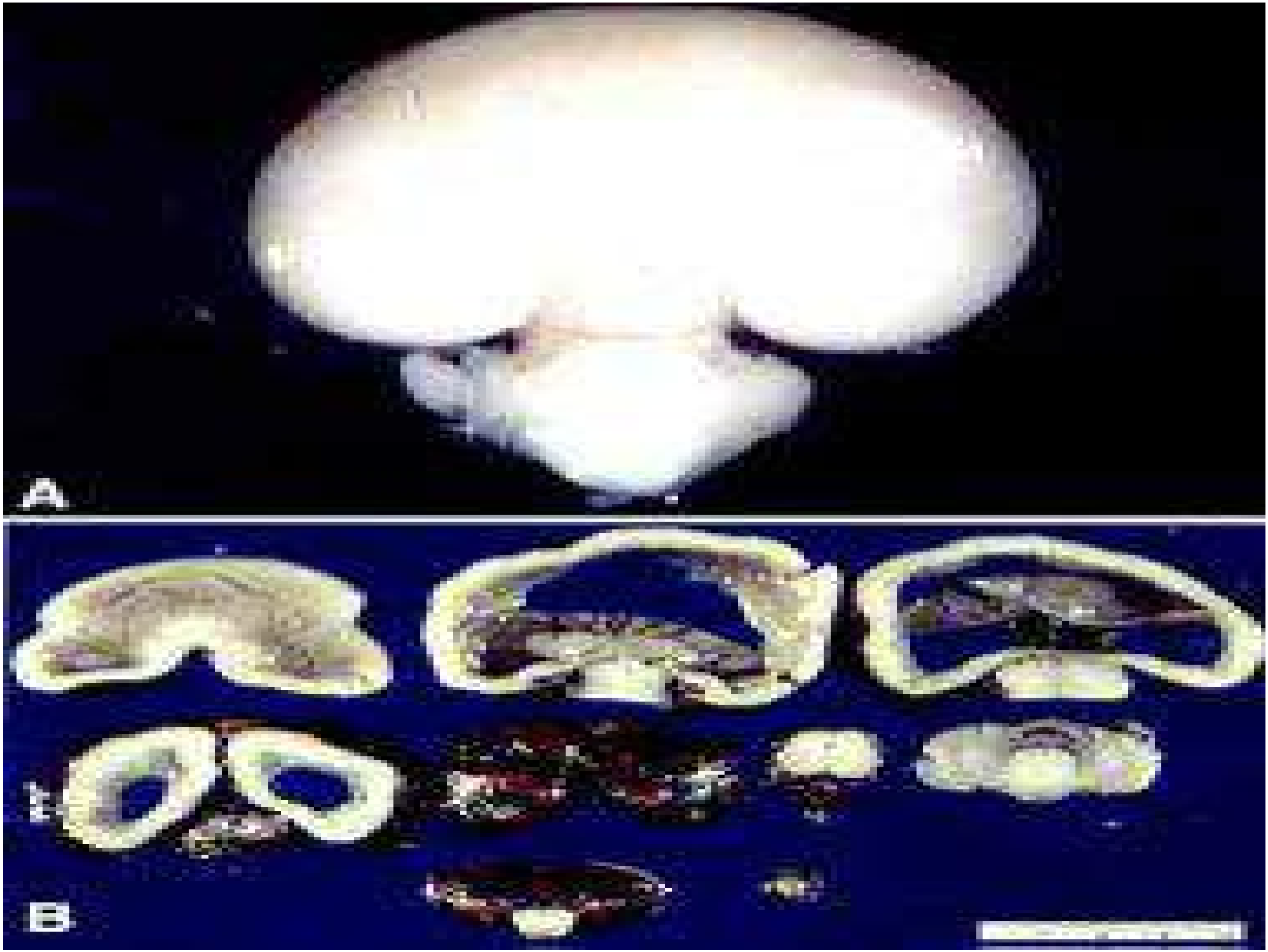
- Holoprosencephalies
- Dandy Walker
- Facial anomalies

- Basilar invagination
- K.F. syndrome
- Sprengel deformity

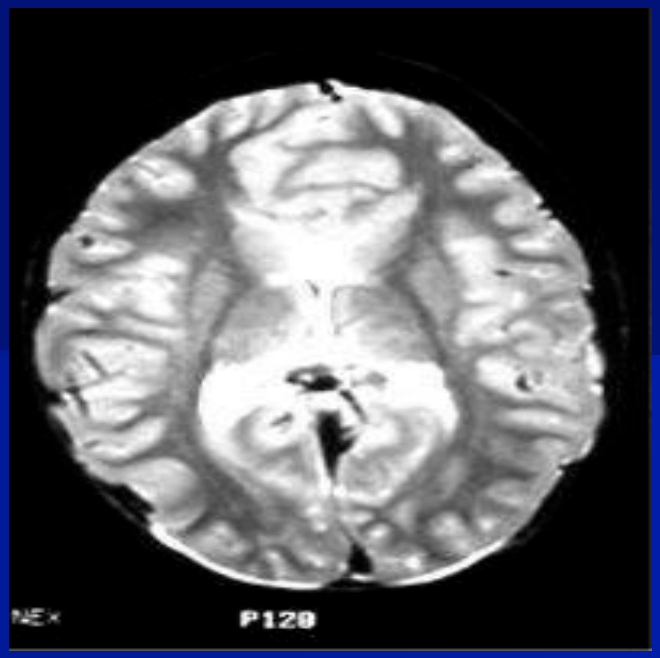
Holoprosencephalies

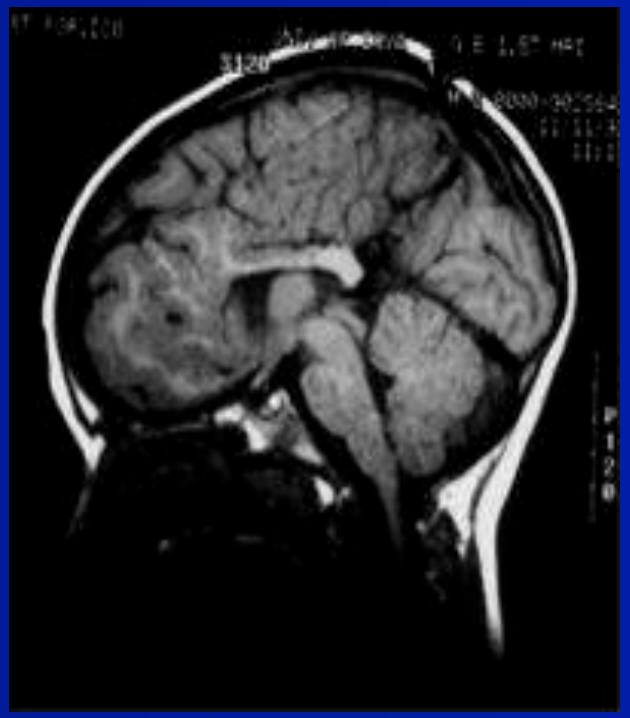
Failure to separate into two hemispheres.

- Lobar:
- Semi lobar:
- Alobar:
- Septal optic dysplasia:

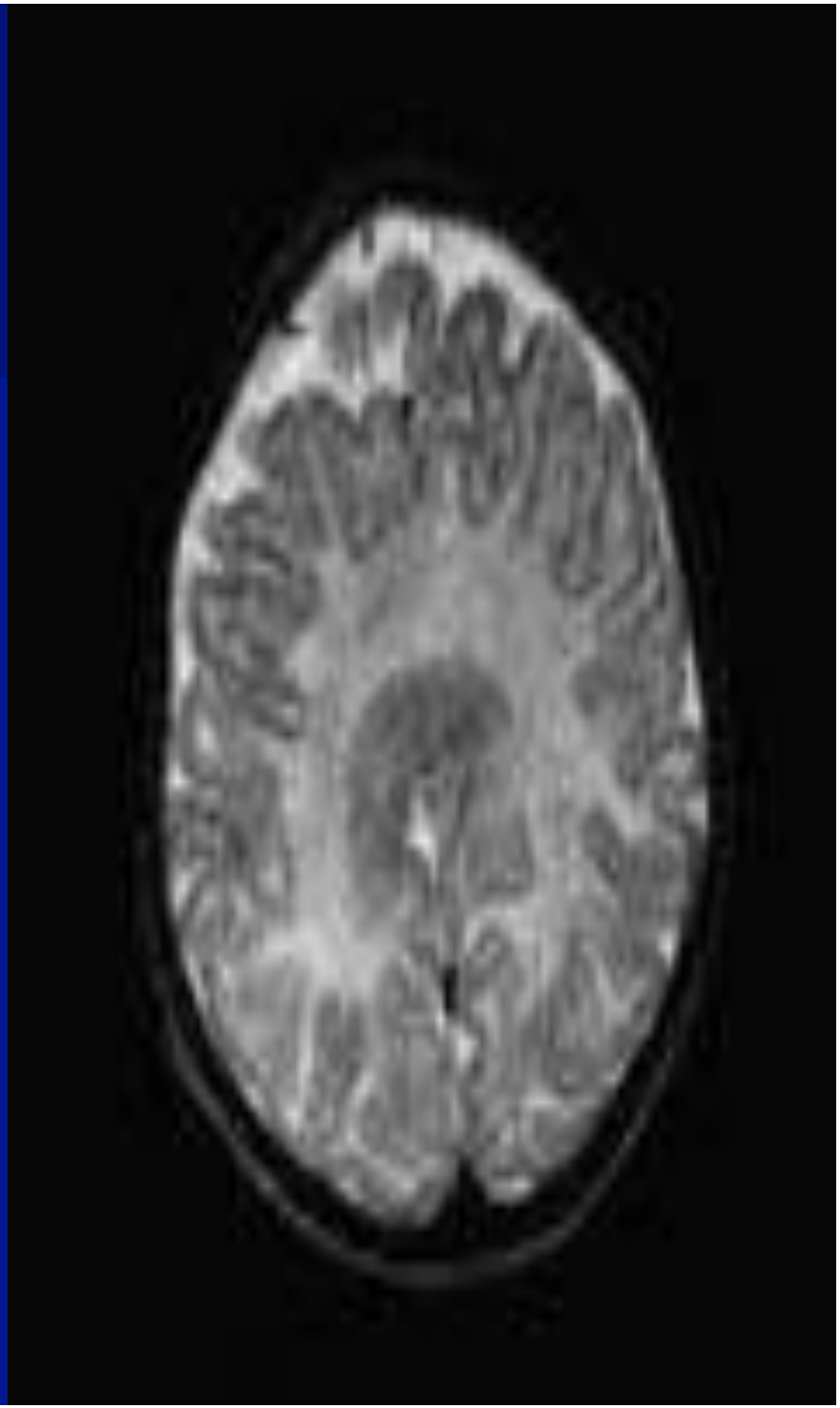

A
B

- **Lobar:** fusion of only anterior inferior frontal lobes. Otherwise the brain appears to be quite normal except for lack of septum pellucidum.

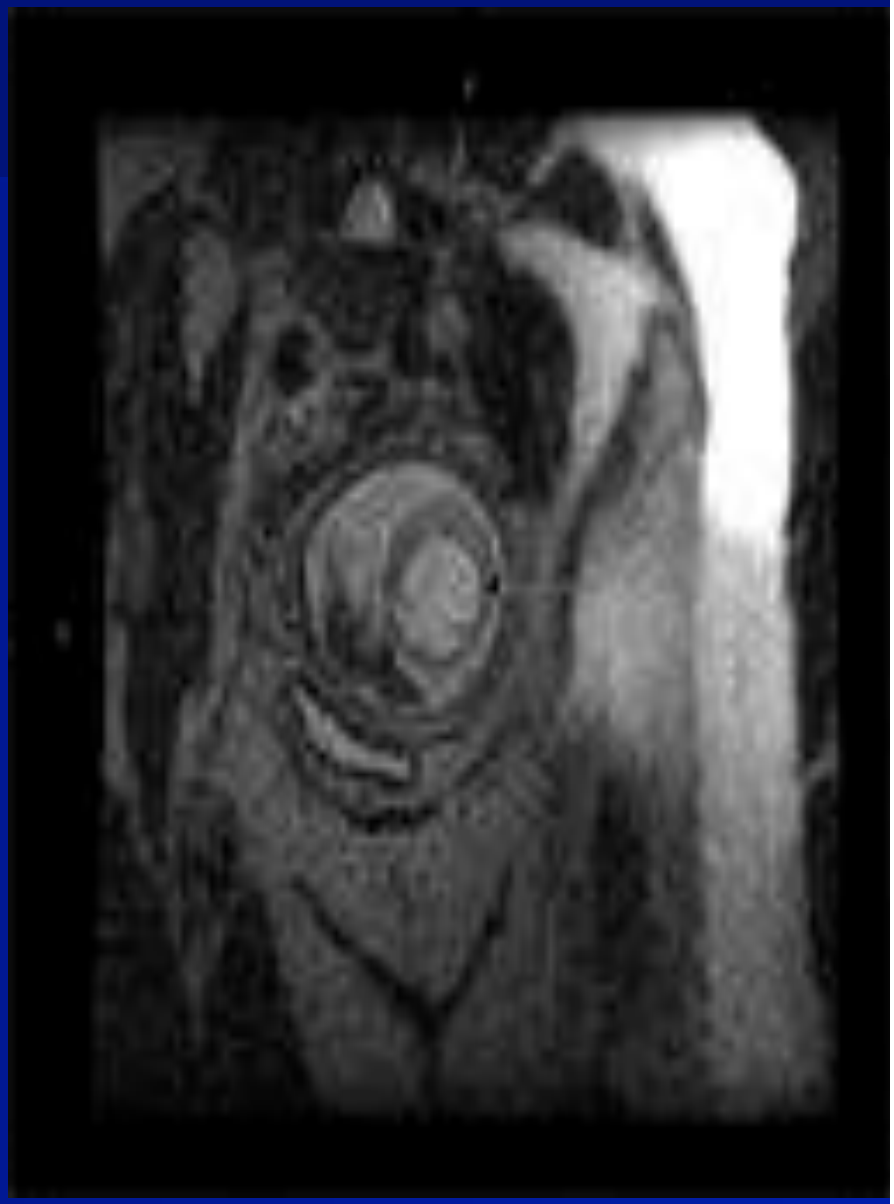


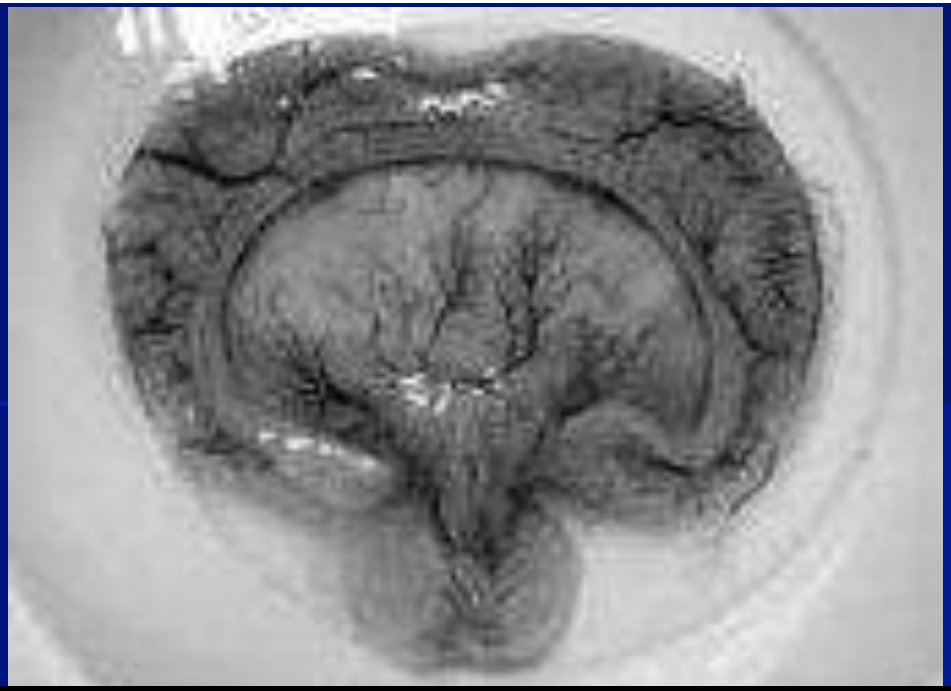


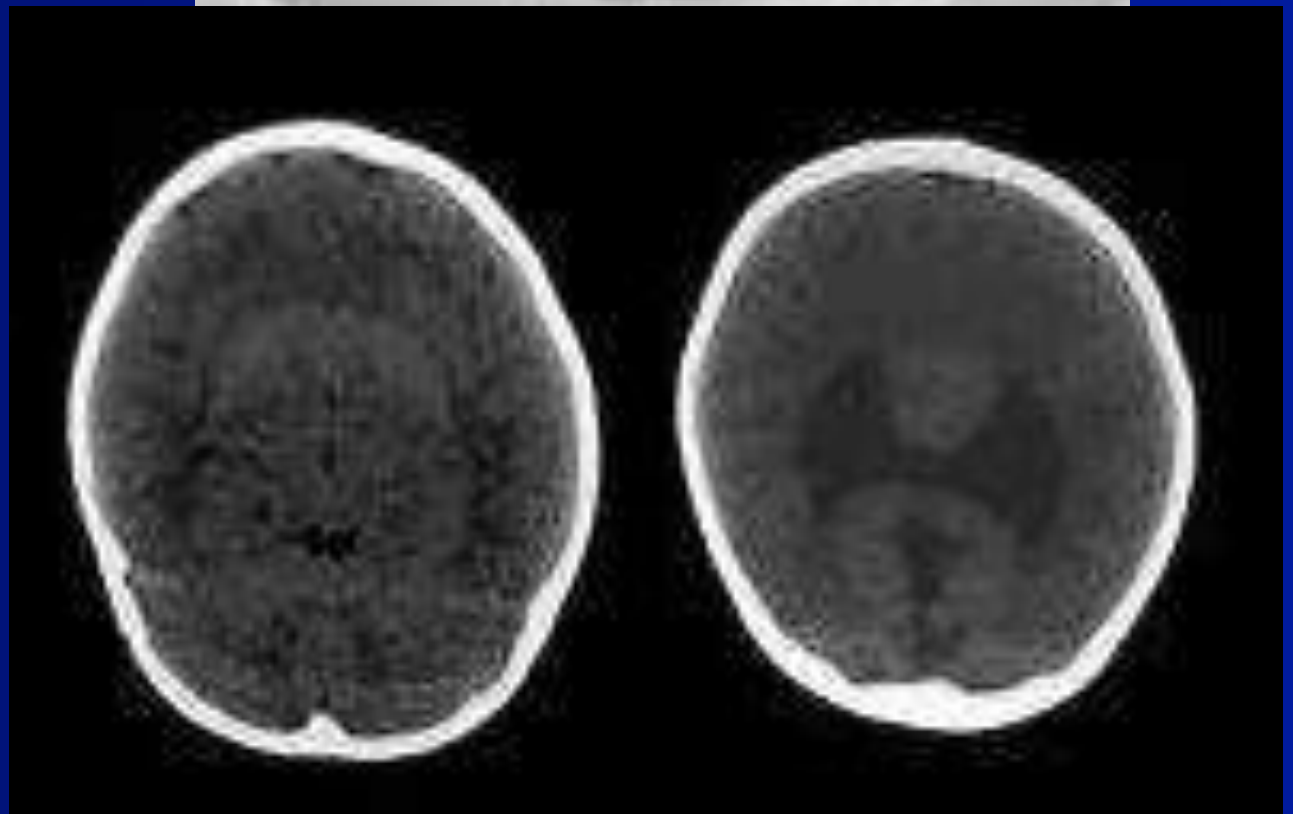
- **Semi lobar:** Partial separation of the posterior occipital and temporal lobes. Frontal brain is fused, thalami partially fused.



- **Alobar: complete failure, no falx, single mono-ventricle, fused thalami.**







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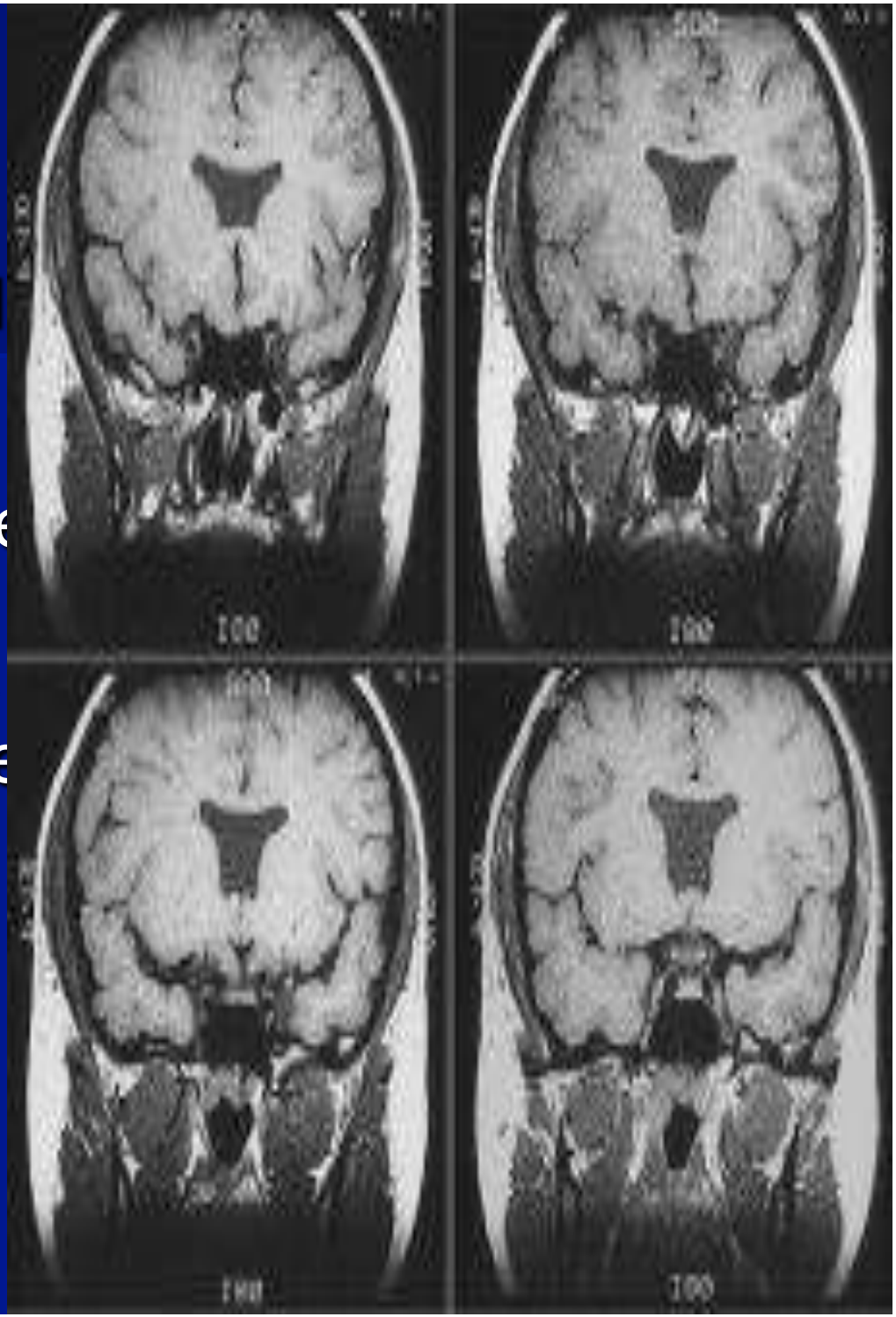
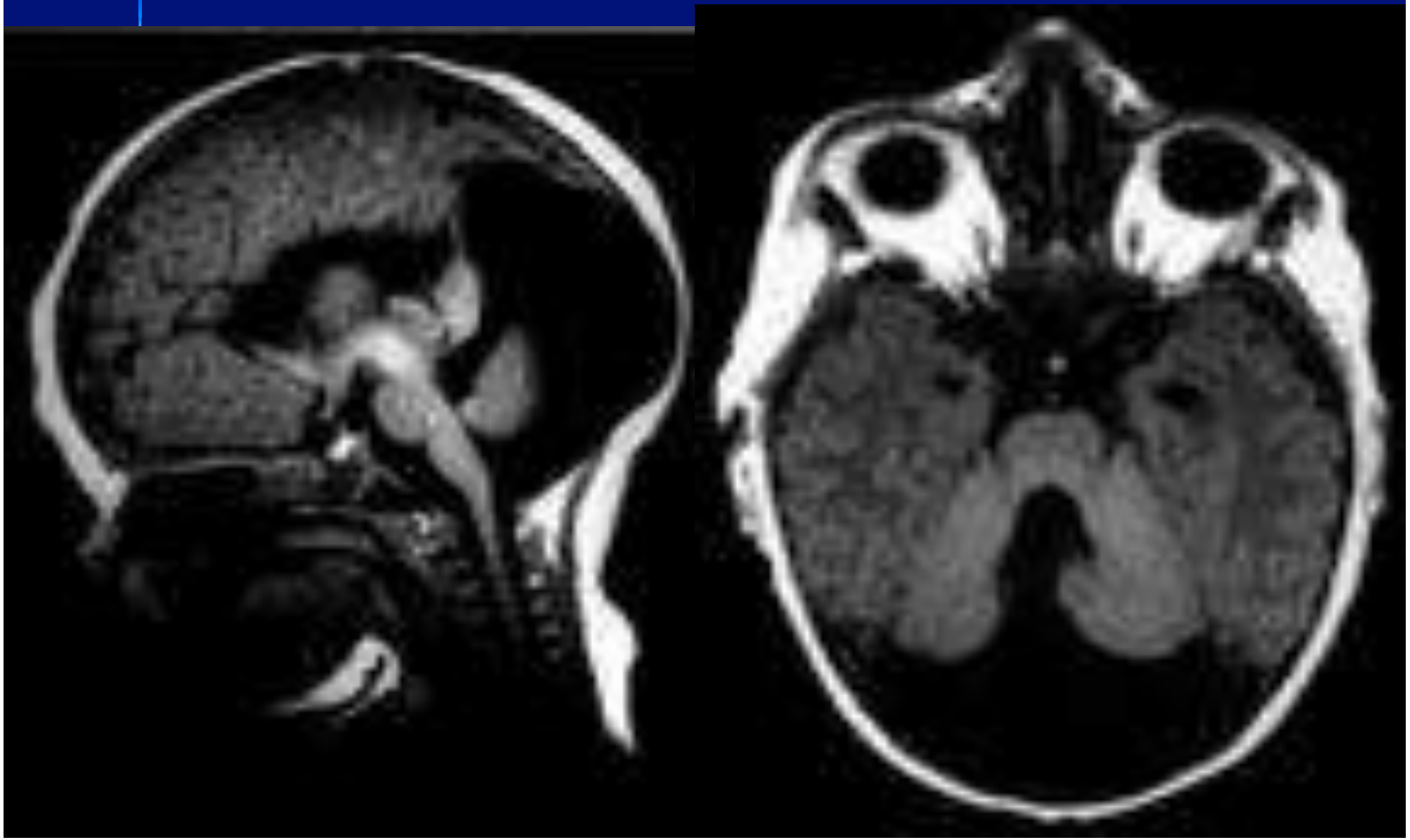
- **Septal optic dysplasia:** most mild form in which there is no septum pellucidum and the optic nerves are very atrophic.
- Schizencephaly may be present in 50% of these cases.
- Corpus callosum agenesis may also be seen.



Dandy Walker

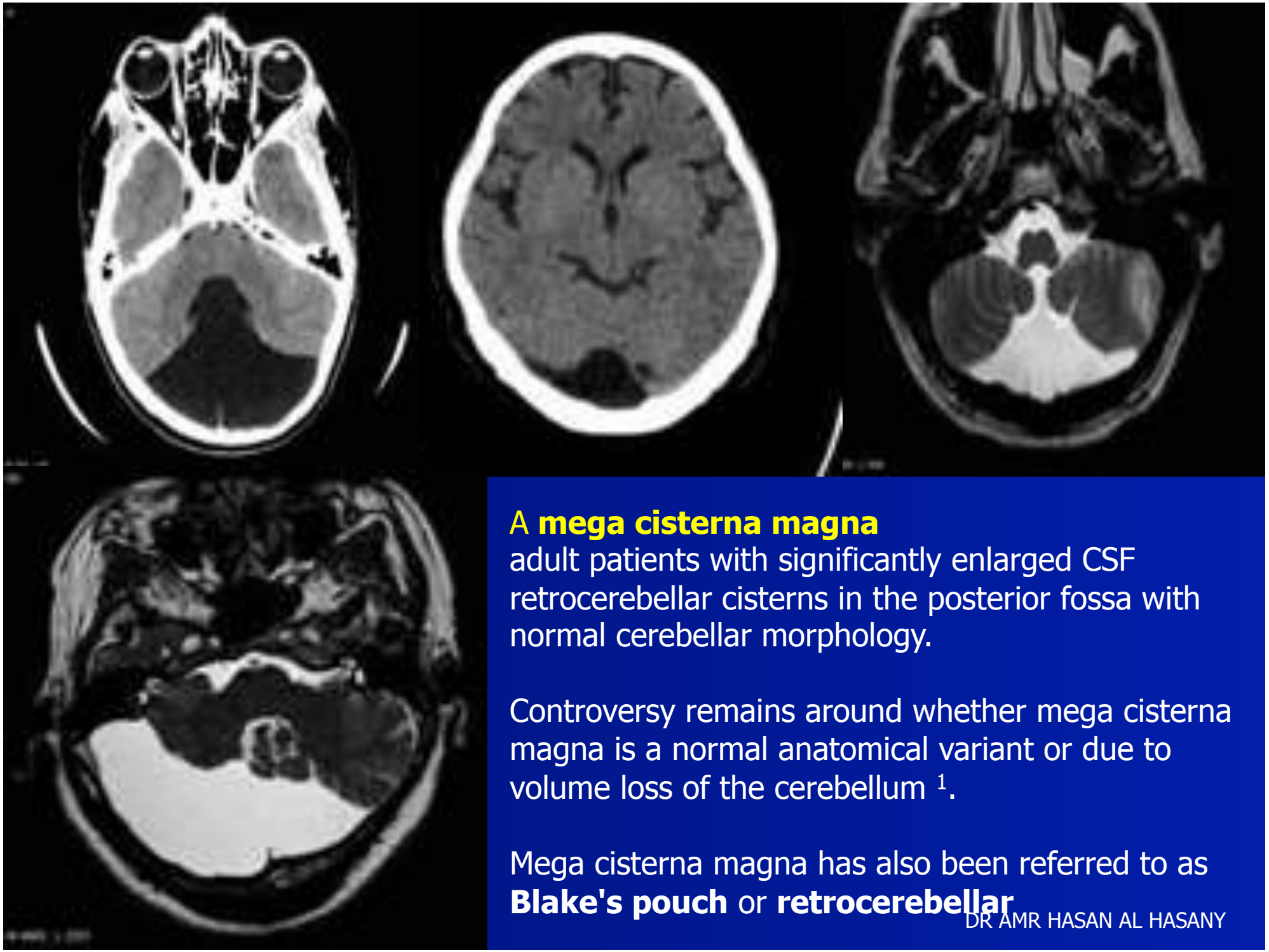
- Defective development of the roof of the fourth ventricle.
- Posterior fossa cyst (cystic dilation of 4th ventricles); hydrocephalus 80%.
- Large posterior fossa,absent falx in the posterior fossa.
- cerebellar hypoplasia.
- The most common accompanying cerebral anomaly is callosal hypogenesis, present in as much as 32% of affected patients

Dandy Walker



Dandy Walker

- D.D.: arachnoid cyst, mega cisterna magna, inflammatory cyst, dermoid cyst,



A **mega cisterna magna**
adult patients with significantly enlarged CSF retrocerebellar cisterns in the posterior fossa with normal cerebellar morphology.

Controversy remains around whether mega cisterna magna is a normal anatomical variant or due to volume loss of the cerebellum [1].

Mega cisterna magna has also been referred to as **Blake's pouch** or **retrocerebellar**

Facial Anomalies

- Often found with alobar holoprosencephaly, corpus callosal agenesis.
- Usually midline.
- Hypertelorism, hypotelorism, cleft palat,

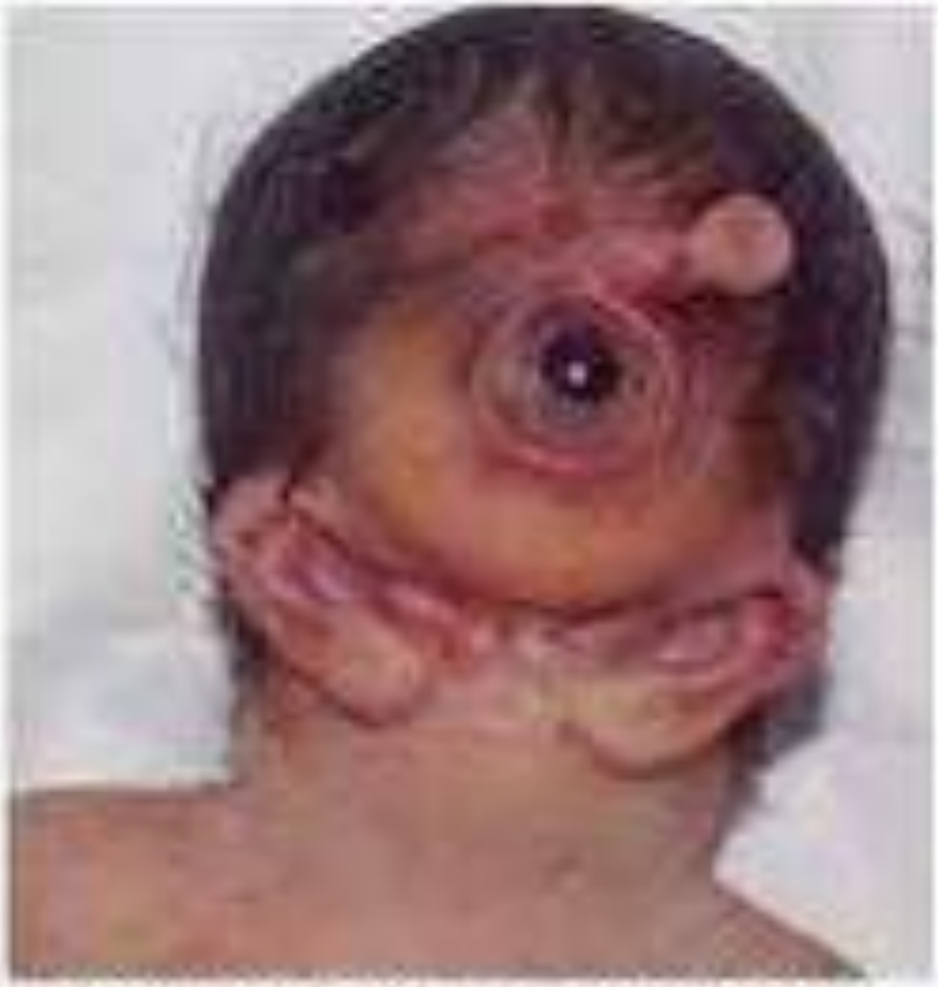


Foto 1. Ausencia de maxilar inferior, fusión de pabellones auriculares (sinotia)

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THANK YOU

Congenital brain disorders

Embryological failure

Acquired lesions

Congenital brain disorders

Embryological failure

Acquired lesions

Acquired Lesions

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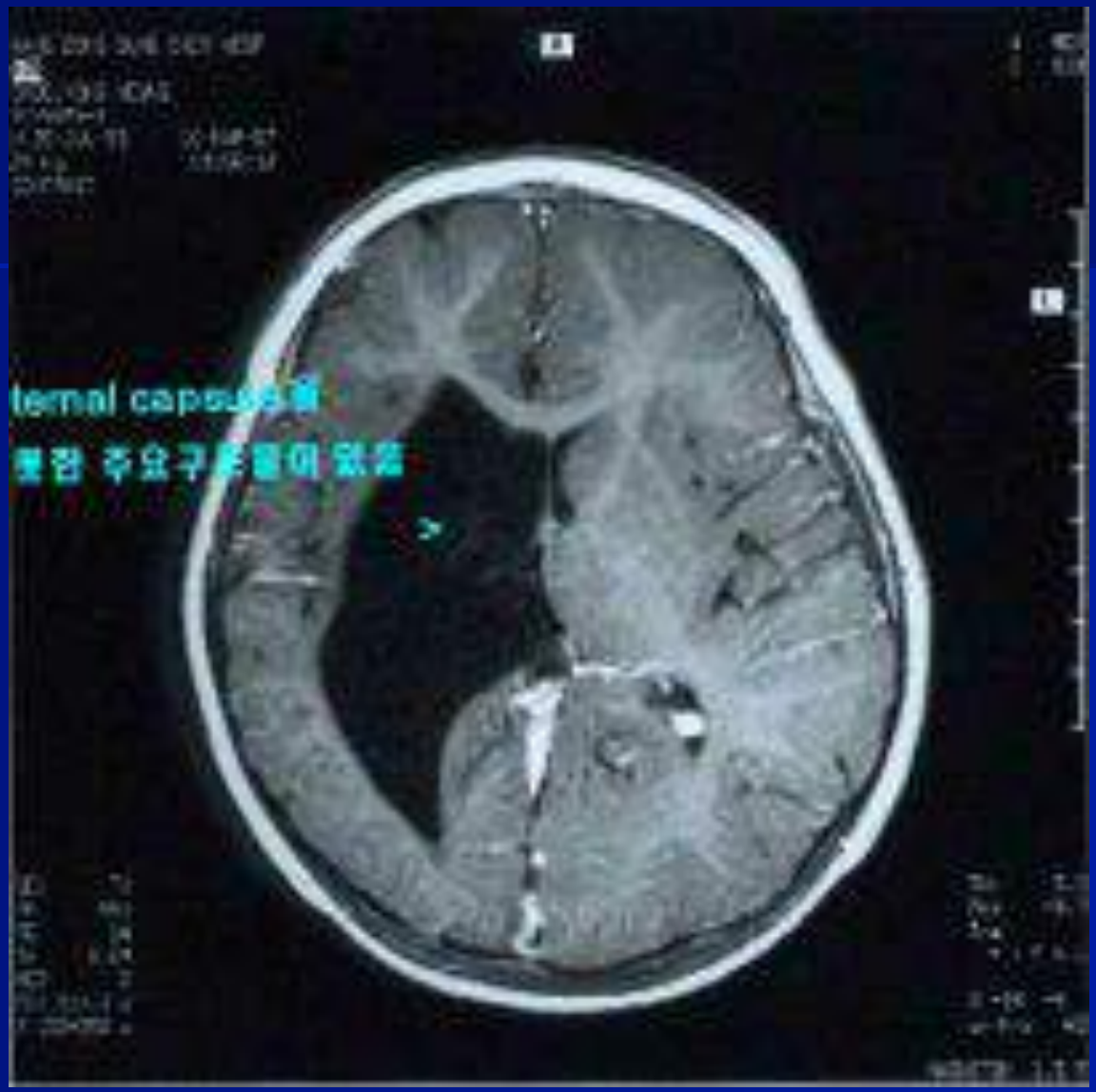
Acquired Lesions

- Destructive.
- Hypoxic.
- Toxic.
- Inflammatory.
- Other.

Hypoxic Destructive Lesions

Porencephaly:

- cyst in the brain that communicates with the ventricle or the subarachnoid space.
- Probably due to neonatal infarct, trauma, or infection.



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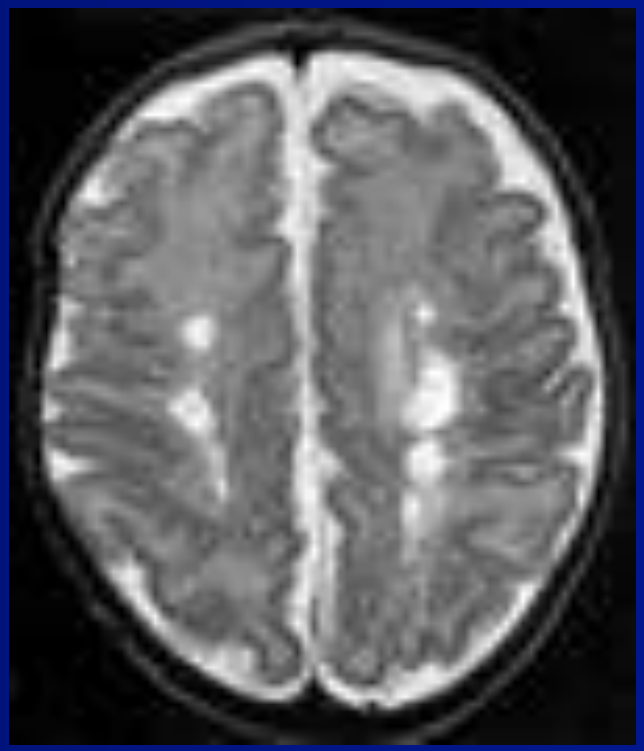
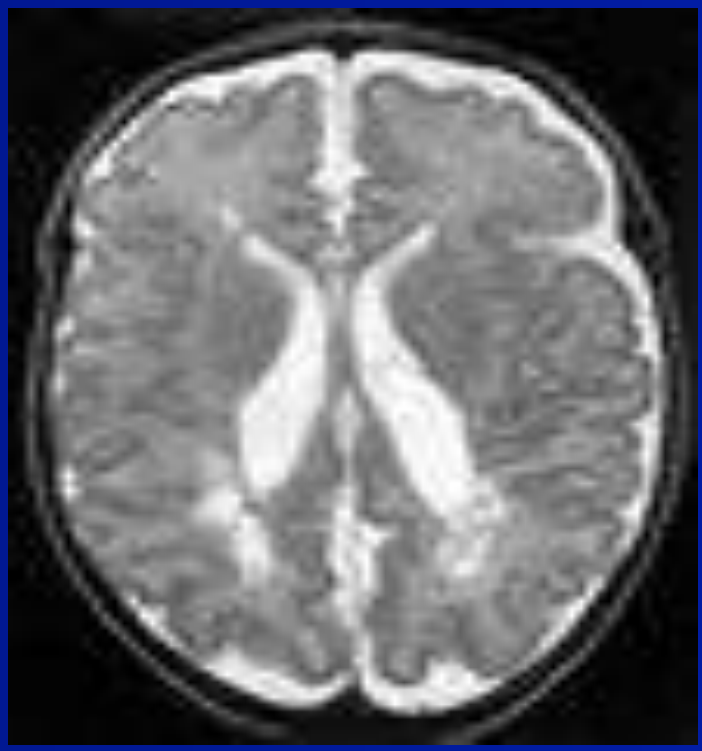
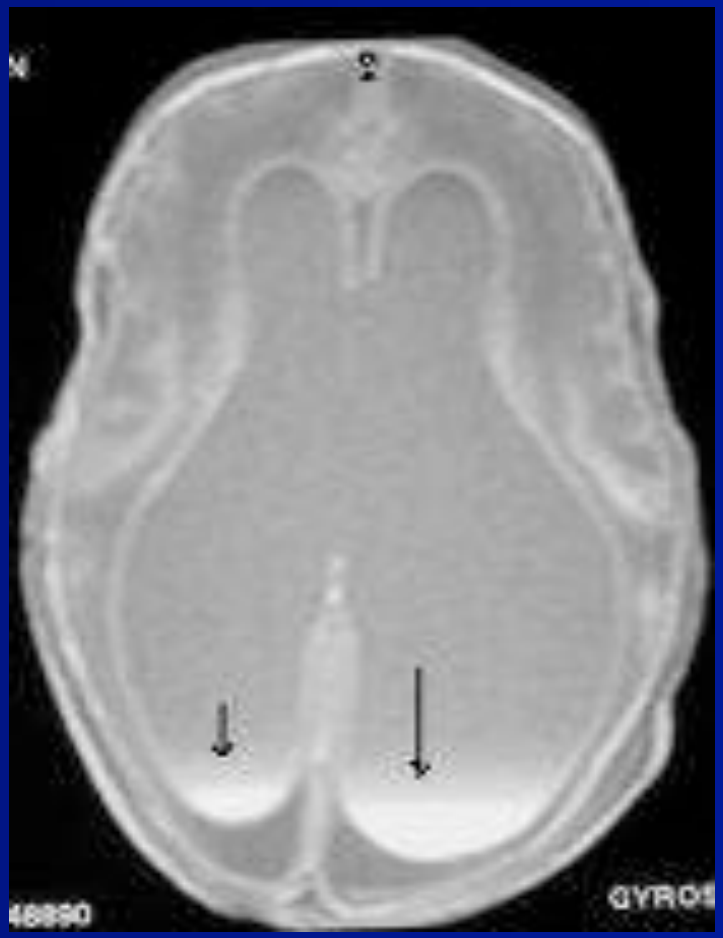
Periventricular Leukomalacia





- **Nonspecific white matter changes**

Germinal Matrix Hemorrhage (Complication of prematurity)

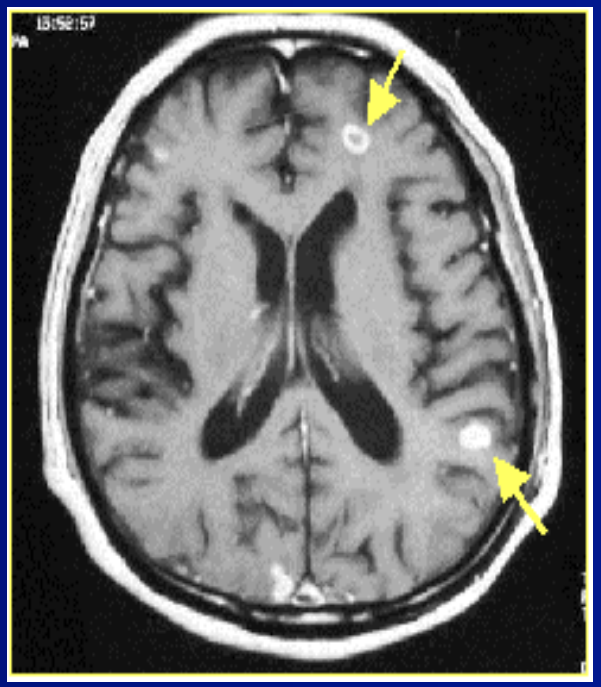


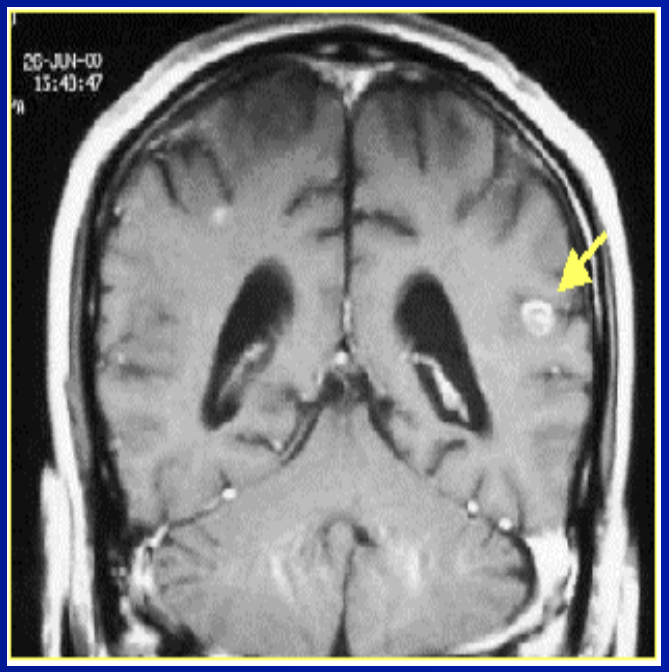
Destructive Lesions:

Congenital Infections

- TORCH ()
- Aids
- Other

TOXOPLASMOSIS





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- Cerebral palsy is defined as "an umbrella term covering a group of non-progressive, but often changing, motor impairment syndromes secondary to lesions or anomalies of the brain arising in the early stages of development."

- The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior and/or a seizure disorder

- Many preconceptional, prenatal and perinatal factors (oxidative damage, perinatal hypoxia/ ischemia and maternal infection among others) are known to be associated with brain injury

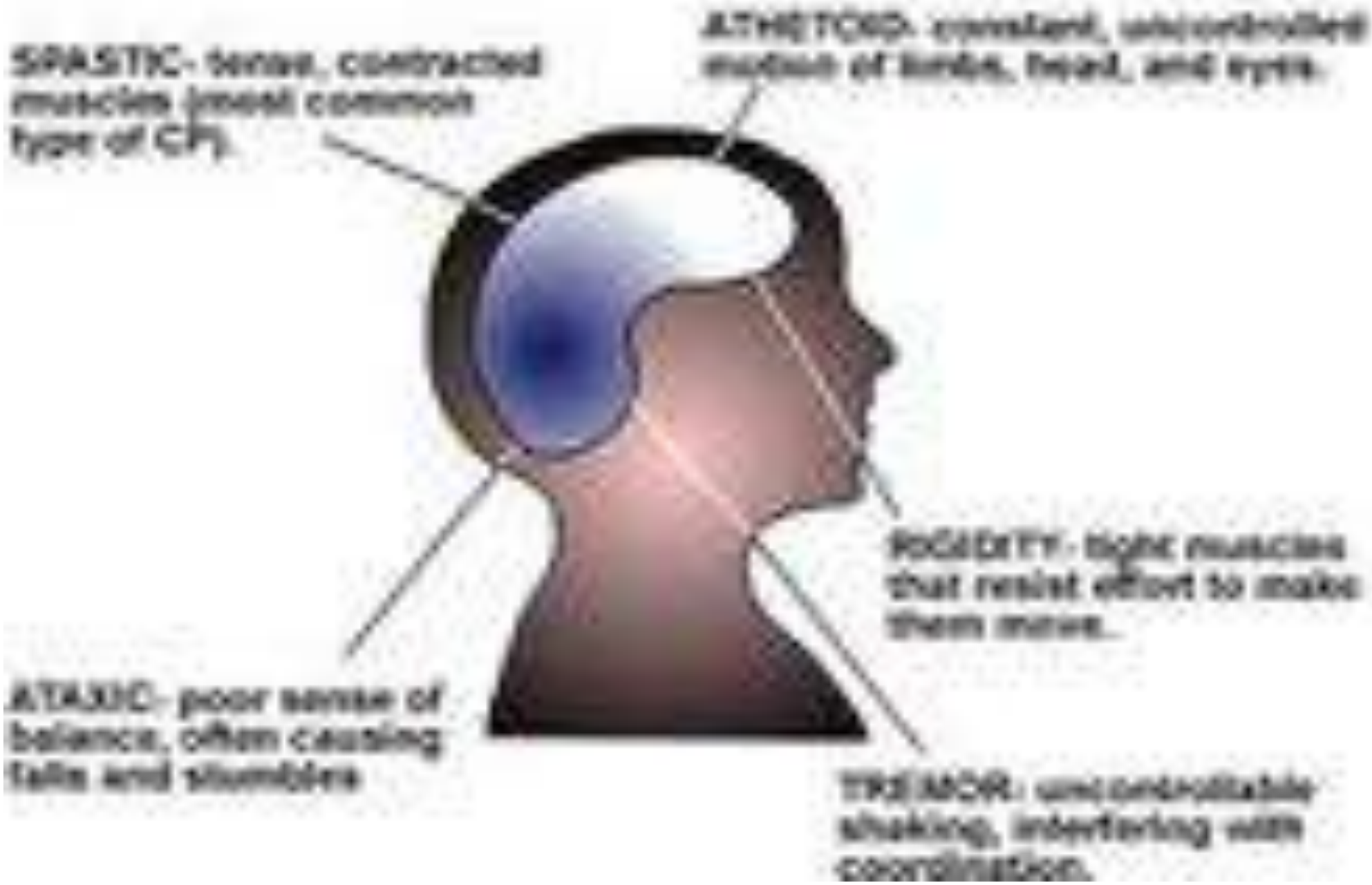
- Cerebral palsy has traditionally been classified on the basis of the type of motor disorder. The revised classification now in use defines 3 main categories of motor disorder, as follows:

I. Spastic : 70-80 %

II. Dyskinetic : 10-15 %

III. Ataxic : < 5 %

TYPES OF CEREBRAL PALSY



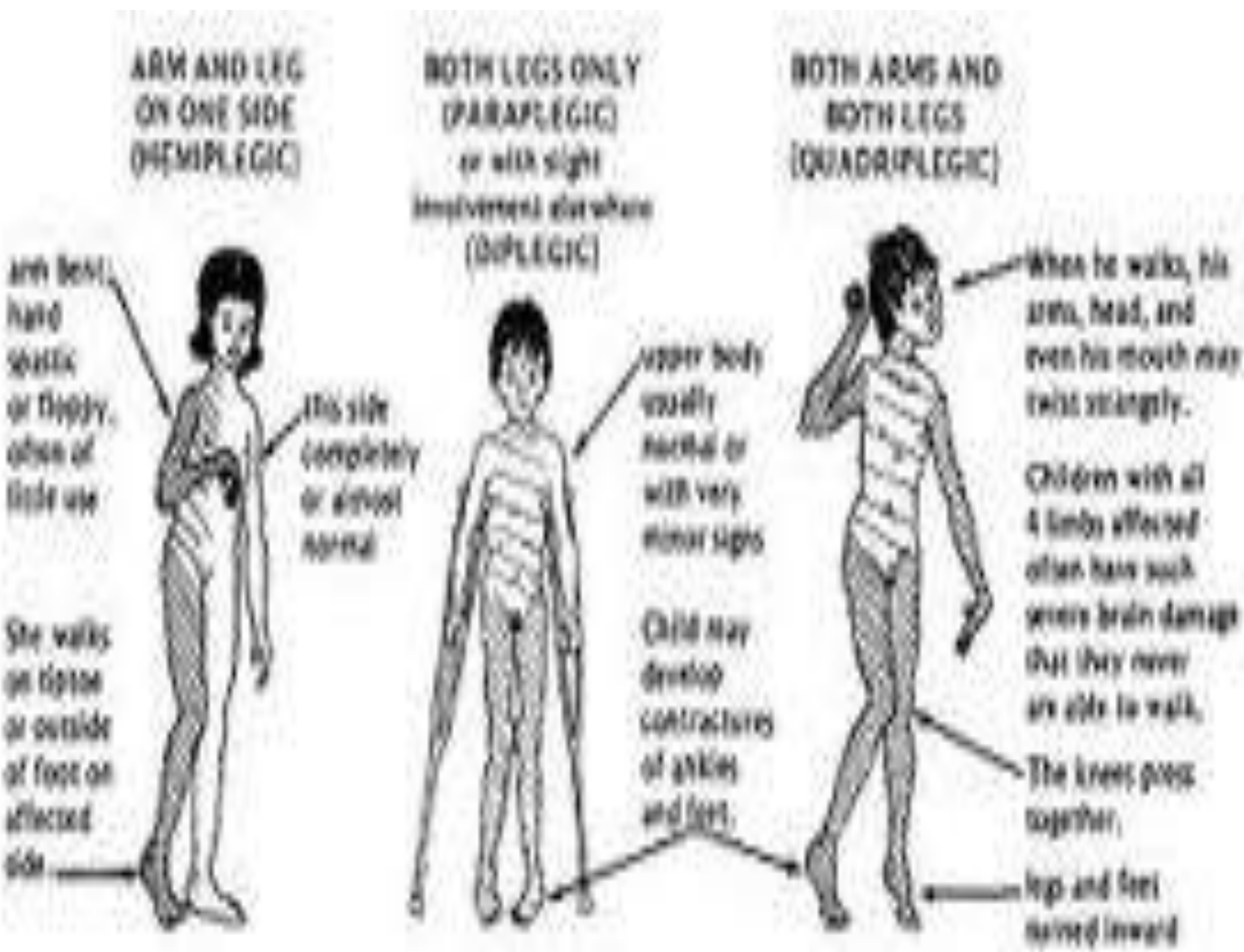
- There are also mixed types. Spastic cases are further classified ***(Christine et al., 2007)*** according to involvement of the extremities, as follows:

i. Quadriplegia : 10-15%

ii. Diplegia : 30-40%

iii. Hemiplegia : 20-30%

iv. Monoplegia : Rare.


ARM AND LEG ON ONE SIDE (HEMIPLEGIC)
arm and leg have spastic or floppy, often of little use
this side completely or almost normal
She walks on tiptoe or outside of foot on affected side
BOTH LEGS ONLY (PARAPLEGIC) or with slight involvement elsewhere (DIPLEGIC)
upper body usually normal or with very minor signs
Child may develop contractures of ankles and feet.
BOTH ARMS AND BOTH LEGS (QUADRIPLEGIC)
When he walks, his arms, head, and even his mouth may twist strangely.
Children with all 4 limbs affected often have such severe brain damage that they never are able to walk.
The knees cross together.
legs and feet turned inward

- **Physical therapy**
- **Occupational therapy**
- **Nutritional counseling**
- **Orthotic devices** such as ankle-foot orthoses (AFOs)
- **Speech therapy**

- **Hyperbaric oxygen therapy**
- Use of an astronaut suit to promote independent mobility *(Rosenbaum, 2003).*
- Hippotherapy

- **Regenerative medicine** is the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage or congenital defects ***(Mason and Dunnill, 2008).***
- **Stem cell therapy** based on a stem cell transplantation, that is aimed directly to augmenting reparative abilities of an injured brain, opens new opportunities in the cerebral palsy treatment ***(Velièkoviæ, 2006)***.

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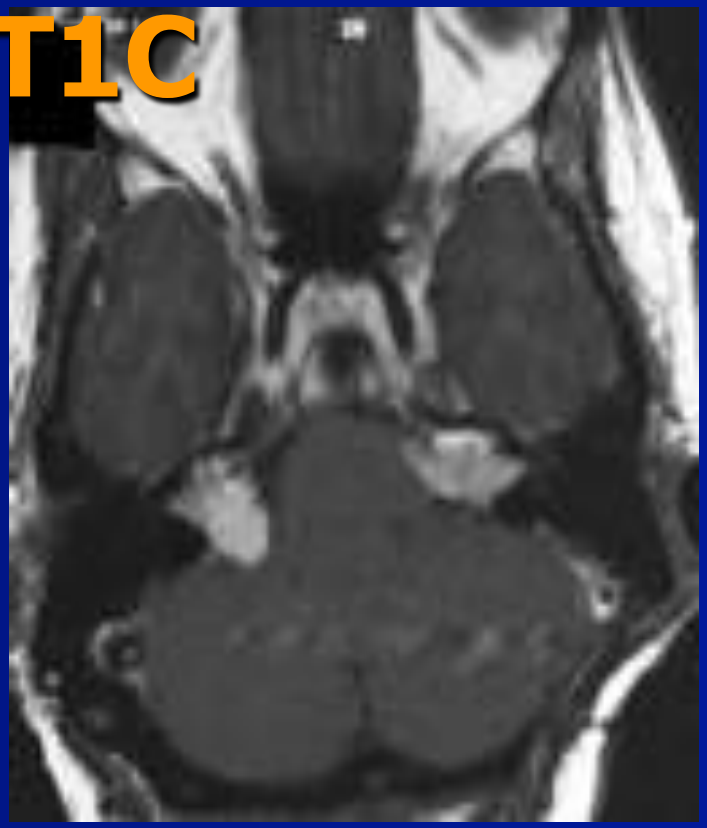
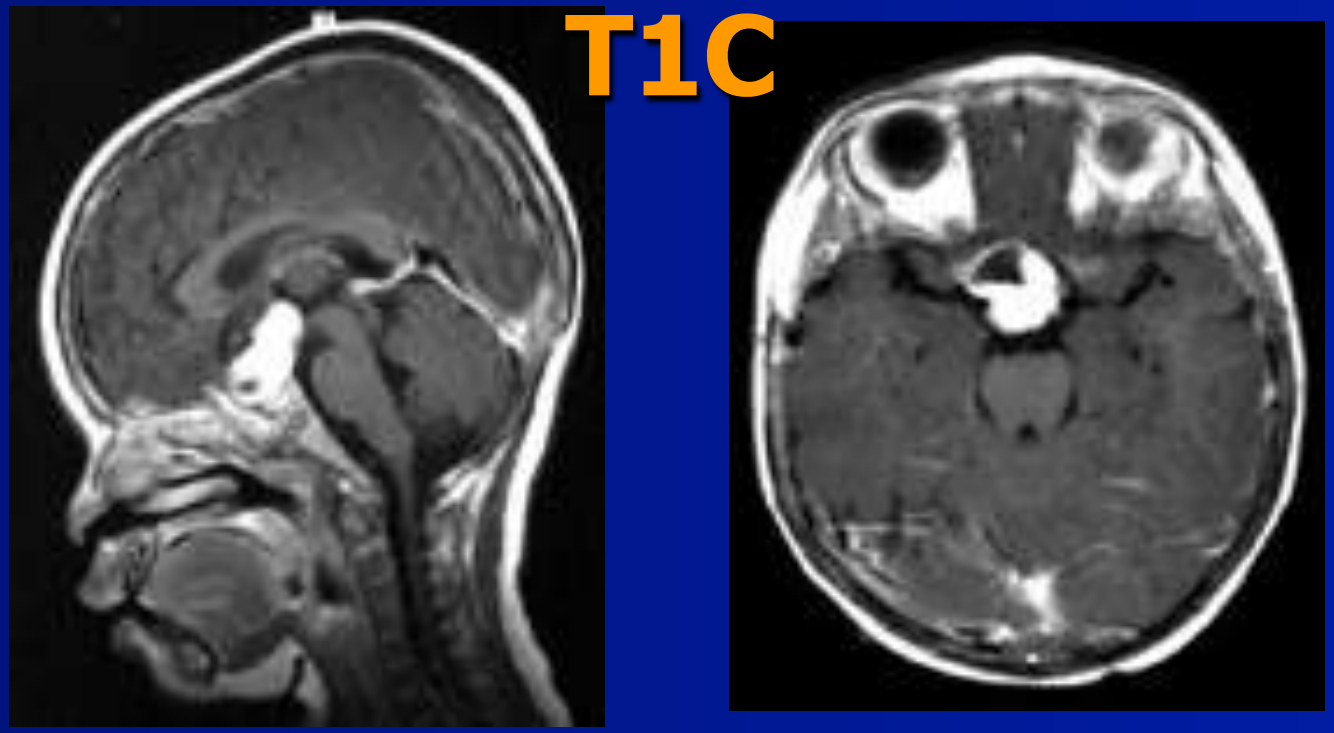
Phakomatosis

- ✓Neurofibromatosis Type I.
- ✓Neurofibromatosis Type II.
- ✓Tuberous Sclerosis.
- ✓Von Hippel Lindau.
- ✓Sturge Weber.
- ✓Others.

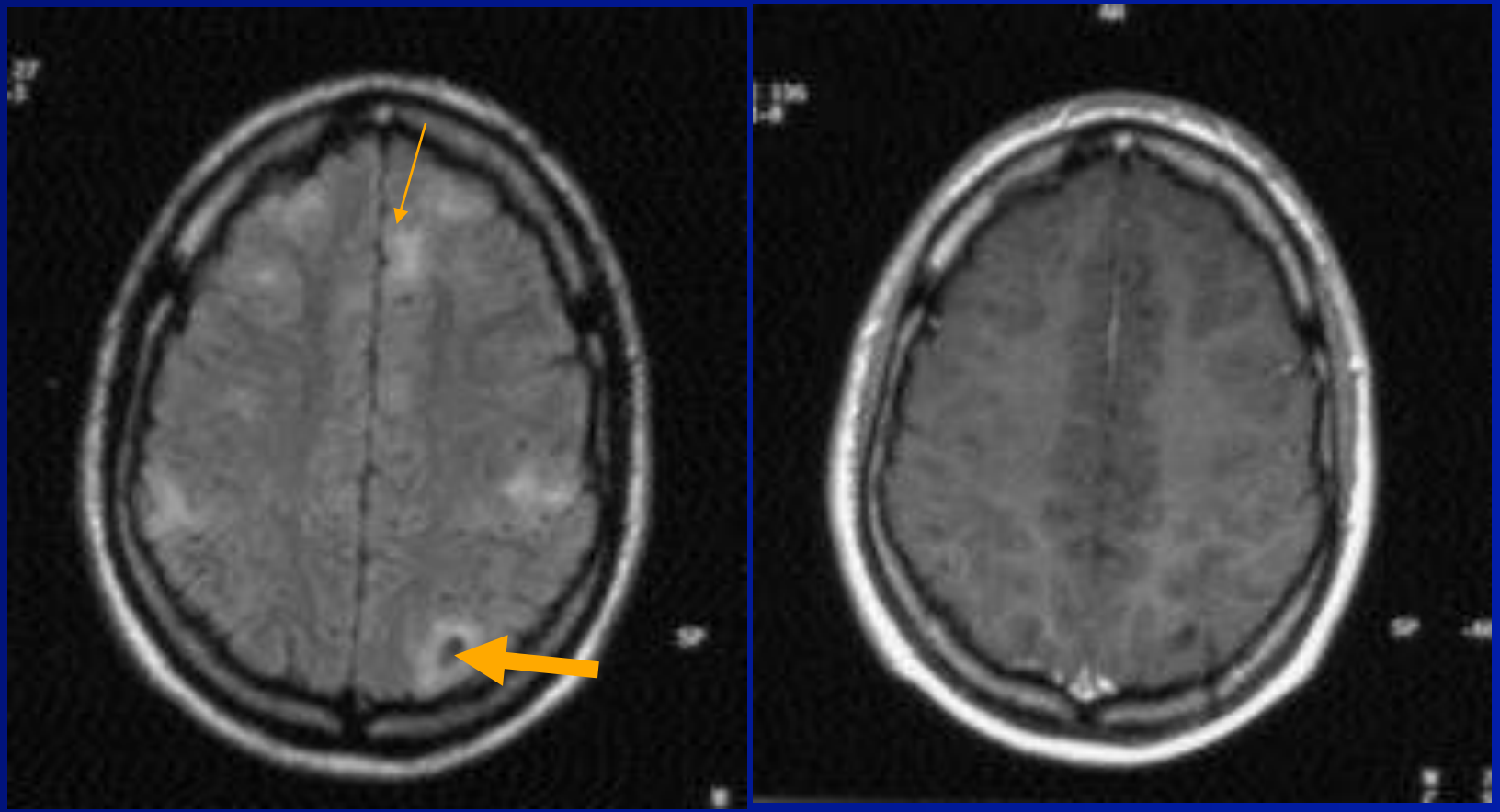
Neurofibromatosis Type II



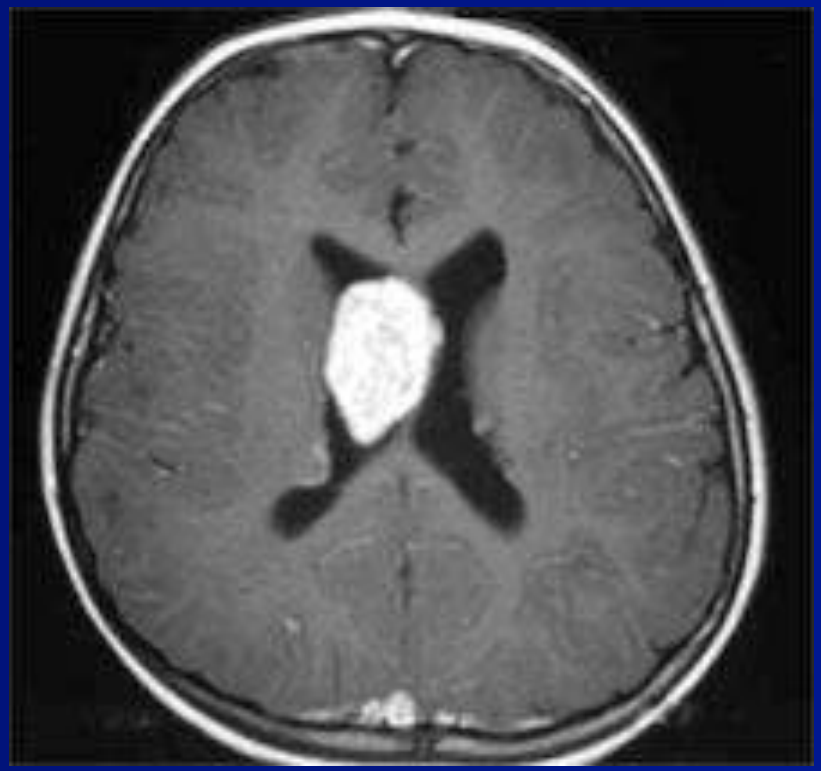
Neurofibromatosis Type I.

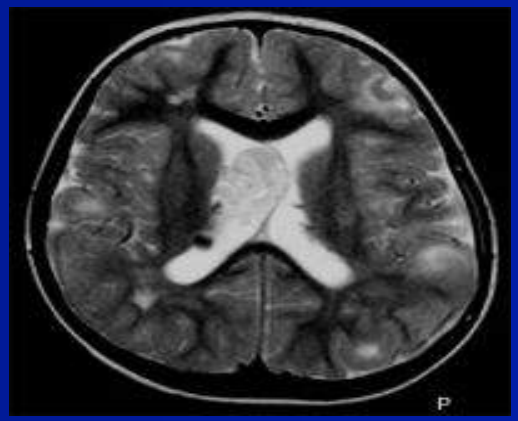


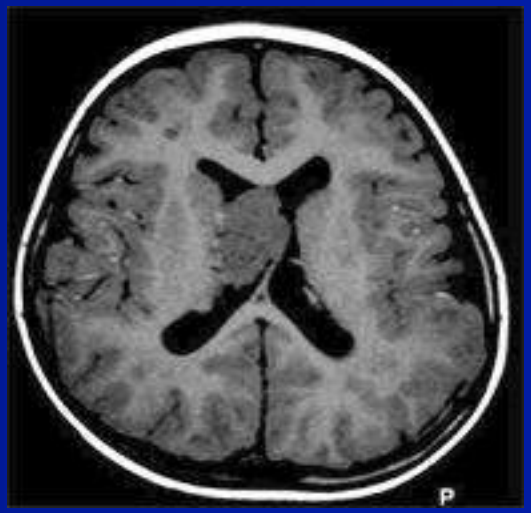
Tuberous sclerosis



Giant cell astrocytoma in a patient with tuberous sclerosis







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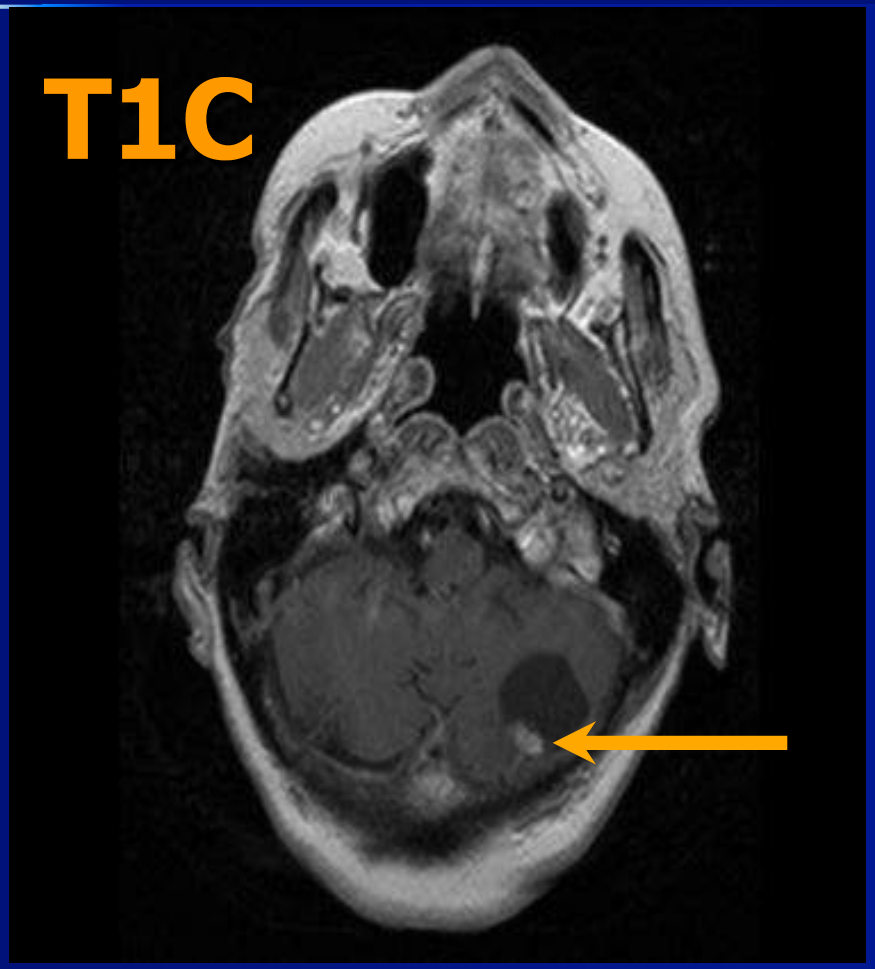
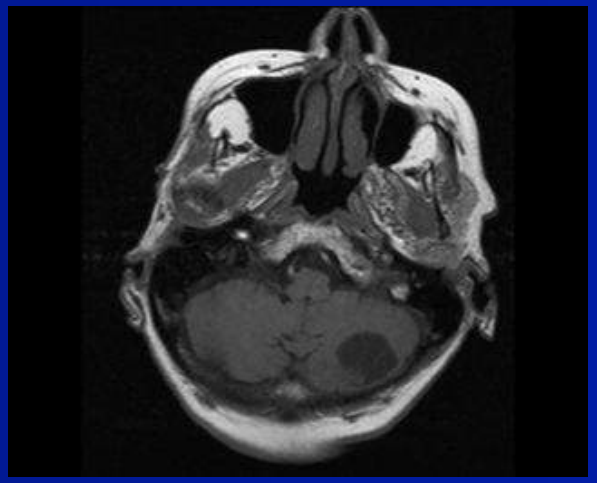
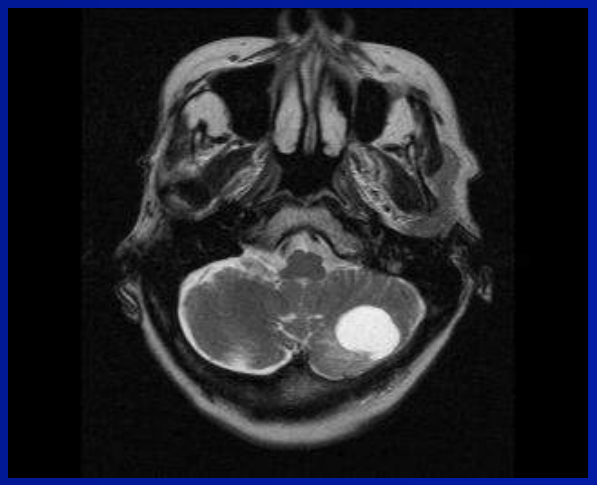
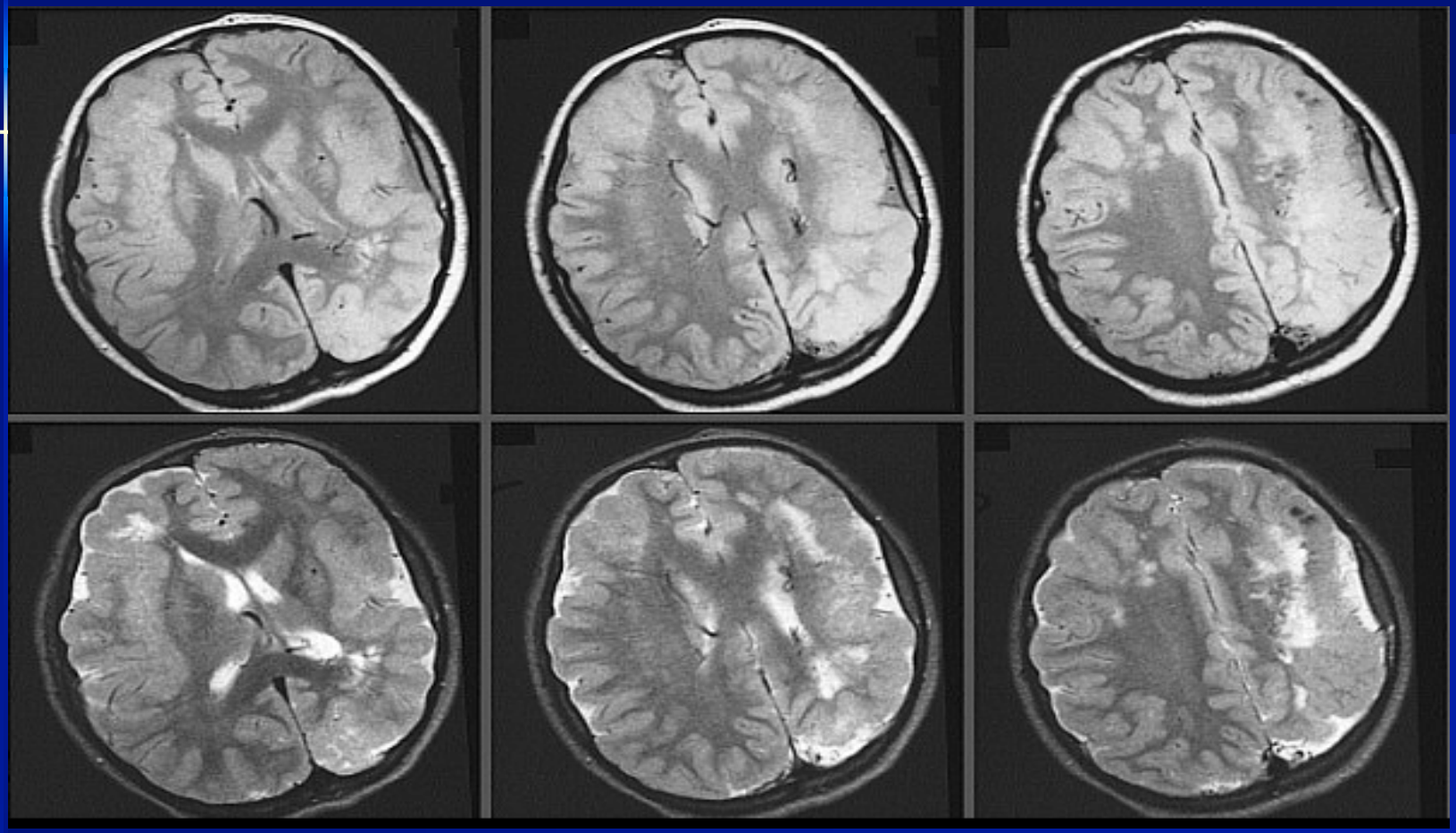
von Hippel-Lindau disease.







Sturge-Weber syndrome



high signal intensity within subcortical and periventricular white matter of left frontal and parietal lobes. dilated subependymal veins are obvious. thickened cortex overlying the left parietal lobe.abnormally high signal intensity within the white matter of the right frontal lobe. On T2- foci of cortical hypointensity suggesting calcification.

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