# Congenital malformations and hydrocephalus

Pathology

# Objectives:

- Know the common types of congenital malformations of the CNS and have a basic knowledge of their pathological features.
- Correlate CNS normal development with the classification of congenital CNS malformations.
- Appreciate the role of folate deficiency as an etiological factor in neural tube defects and understand the role of Alpha feto-protein measurement and ultrasound in antenatal diagnosis of neural tube defects.
- Understand the various mechanisms that lead to the development of hydrocephalus.
- List and classify the main causes of hydrocephalus

# Key principles to be discussed:

1] CNS congenital malformation:

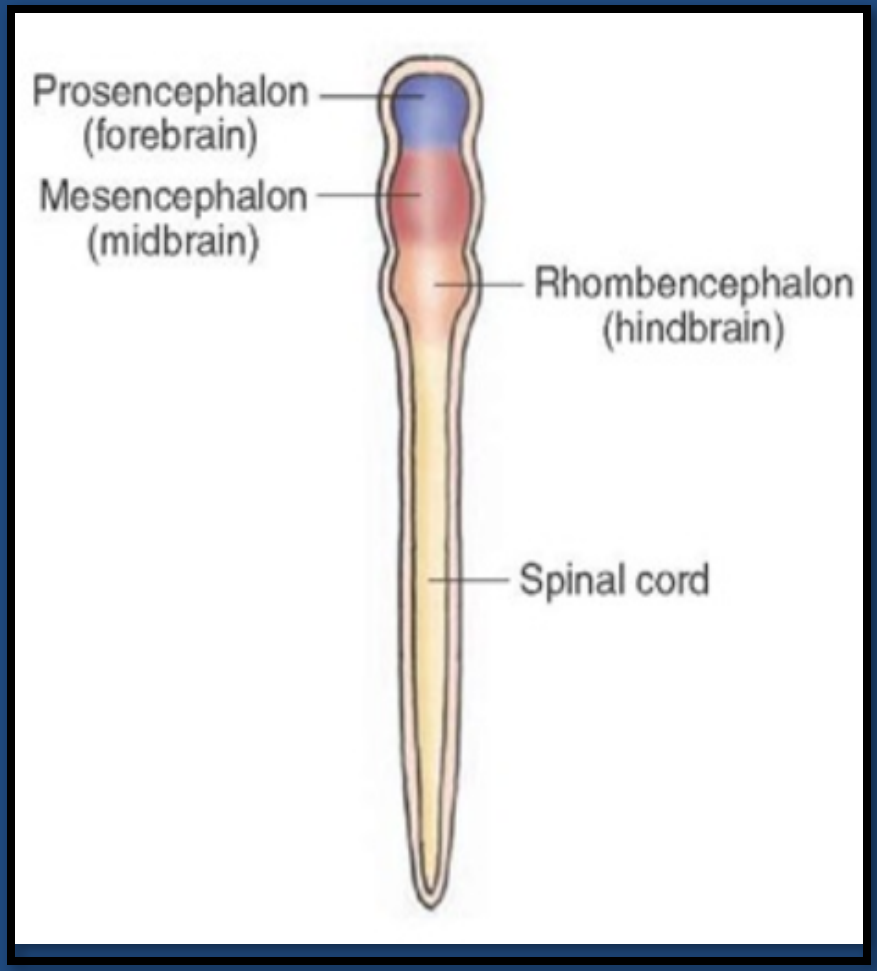
Incidence and introduction to the basic concepts behind the pathogenesis. These include genetic and environmental factors and the role of the stage of gestation development.

I. Definition and pathological changes in **forebrain anomalies:**
   a. Megalencephaly.
   b. Microencphaly and its causes.
   c. Lissencephaly

II. Definition and pathological changes in **neural tube defects:**
   a. Meningomyelocele
   b. Spina bifida
   c. Anencephaly and encephalocele

   Pathogenesis of neural tube defect with special emphasis on the role of folate and alpha fetoproteins and their clinical significance.

III. Definition and pathological changes in **posterior fossa anomalies**:
   a. Arnold Chiari malformation.


Prosencephalon
(forebrain)
Mesencephalon
(midbrain)
Rhombencephalon
(hindbrain)
Spinal cord

# Key principles to be discussed:

**2] Hydrocephalus:**

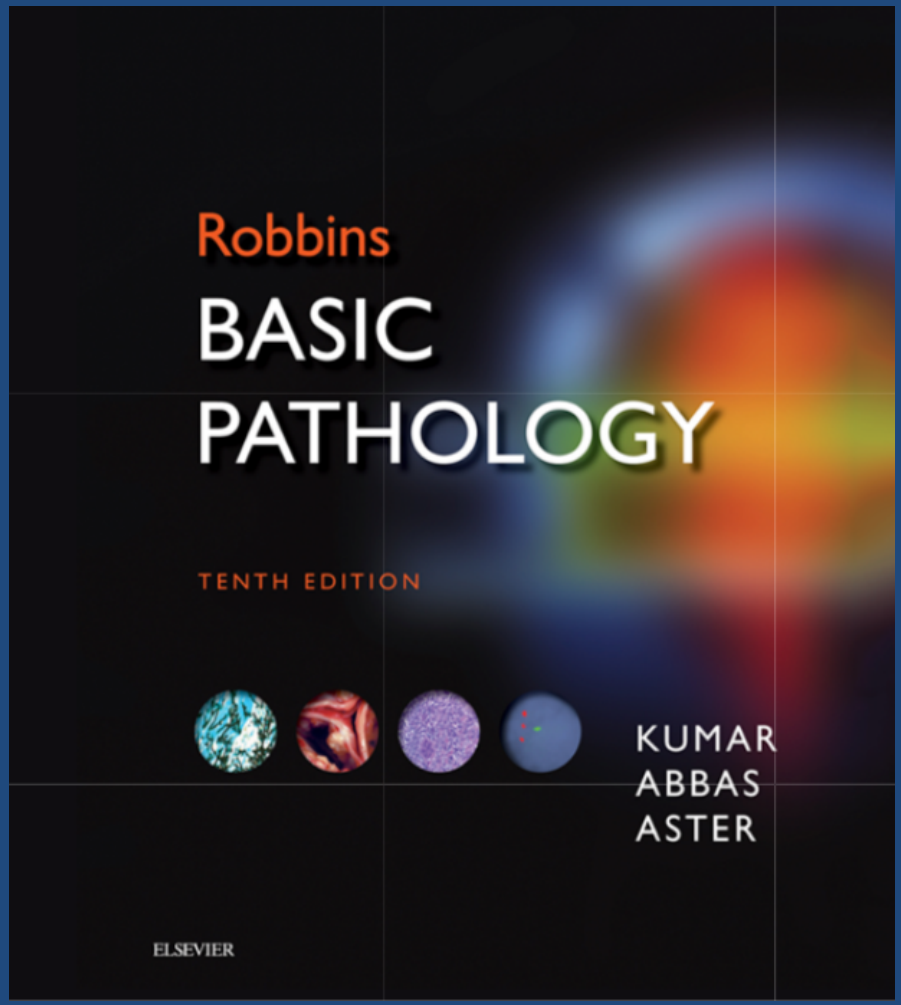
- **Definitions of normal pressure**
- **Hydrocephalus:**

  **noncommunicating hydrocephalus vs. communicating hydrocephalus**

- **Pathophysiology and etiology.**

Ref:

- CNS congenital malformation
  - Page: 860 to 862
- Hydrocephalus
  - Page: 851



# 1. Congenital malformations

- The incidence of CNS malformations is estimated at 1% to 2%
- Malformations of the brain are more common in the setting of **multiple** birth defects
- give rise to mental retardation, cerebral palsy, or neural tube defects

# 1. Congenital malformations

- Because different parts of the brain develop at different times during gestation (and afterwards), the timing of an injury will be reflected in the pattern of malformation
- Prenatal or perinatal insults may either cause:
  - failure of normal CNS development
  - tissue destruction

# 1. Congenital malformations

- Although the pathogenesis and etiology of many malformations remain unknown, both genetic and environmental factors are clearly at play:

1. Genetic factors:

CNS malformation can be caused by Mutations affecting molecules in pathways of neuronal and glial cells:

- Development
- Migration
- Connection

2. Environmental factors :

- Toxic compounds
- Infectious agents

# 1. CNS congenital malformation

**Forebrain Malformations:**

1. **Megalencephaly**
2. **Microcephaly**
3. **Lissencephaly**

# 1. Forebrain Malformations

## Megalencephaly and Microcephaly

- The volume of brain may be abnormally large (*megalencephaly*: rare genetic disorders) or small (*microencephaly, more common*). Microencephaly, is usually associated with a small head as well
- Microencephaly occurs in a wide range of clinical settings, e.g.: - chromosome abnormalities
  - fetal alcohol syndrome
  - human immunodeficiency virus 1 (HIV-1) infection acquired in utero
- All causes are associated with a decreased number of neurons destined for the cerebral cortex. Disruption of normal neuronal migration and differentiation during development can lead to a disruption of the normal gyration and six-layered neocortical architecture
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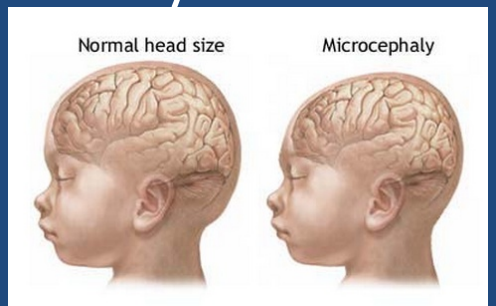
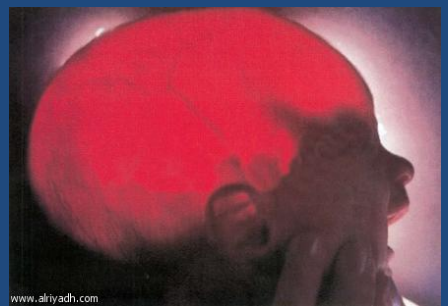
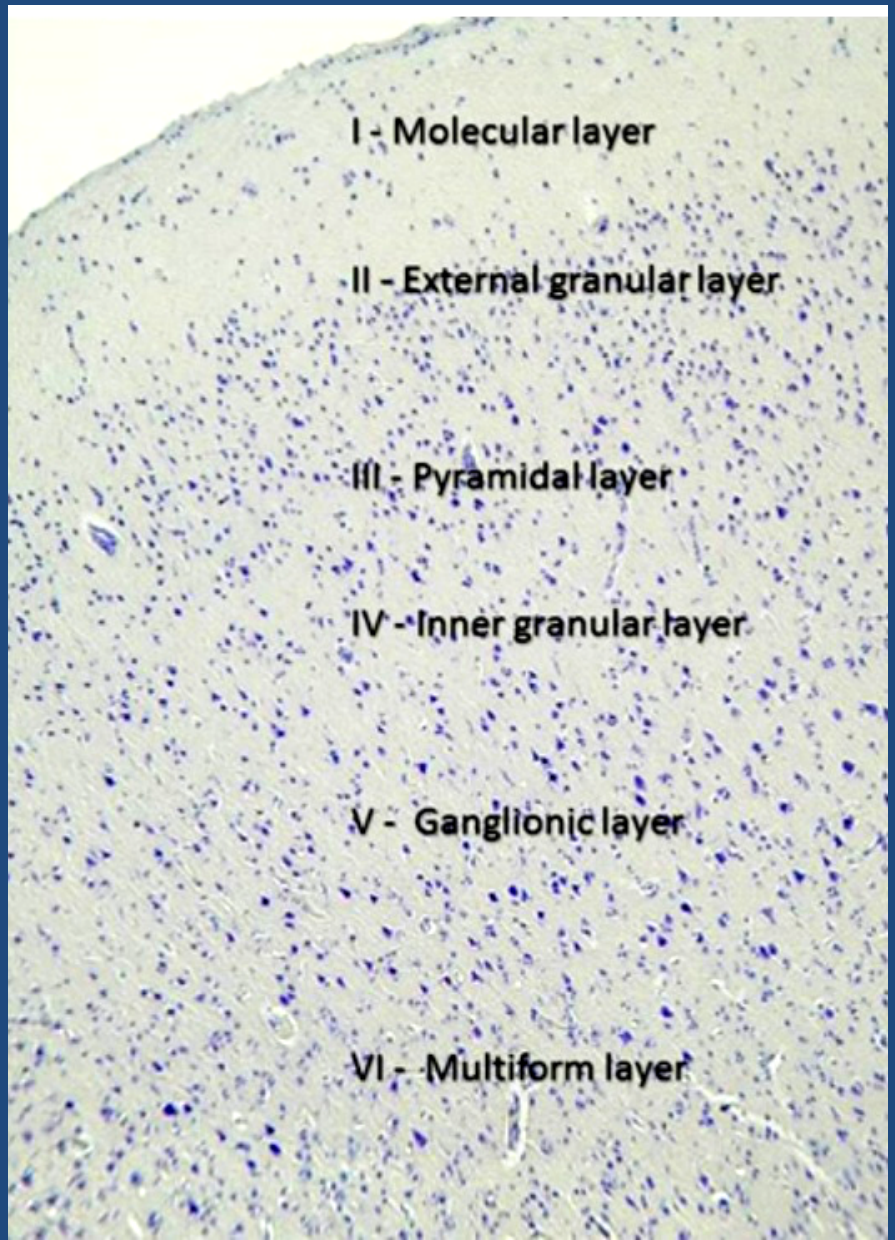


# Six-layered neocortical architecture

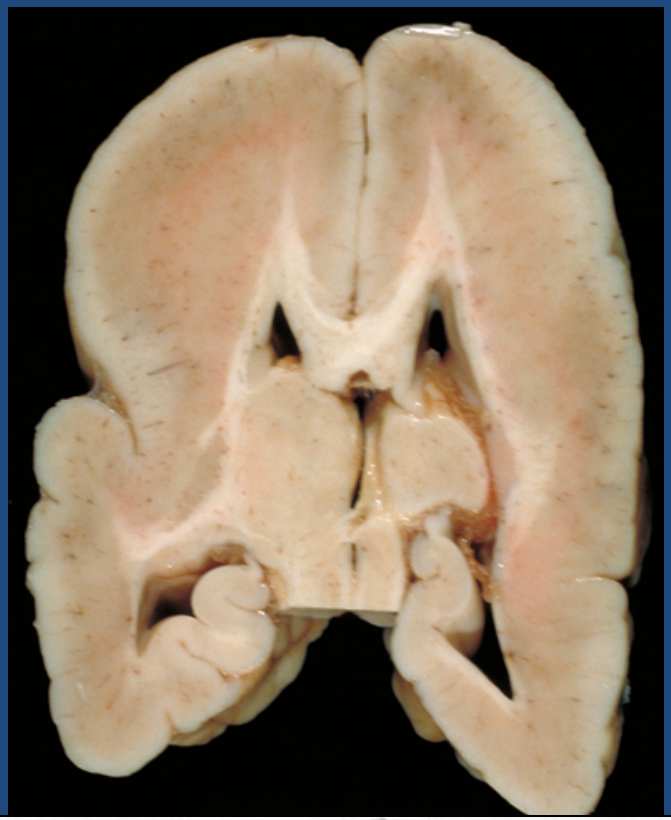


# 1. Forebrain Malformations
# *Lissencephaly*

- *Lissencephaly* (*agyria*) or, in case of more patchy involvement, *pachygyria* is characterized by an absence of normal gyration and a smooth-surfaced brain

The cortex is abnormally thickened and is usually only four-layered
Single-gene defects have been identified in some cases of lissencephaly.

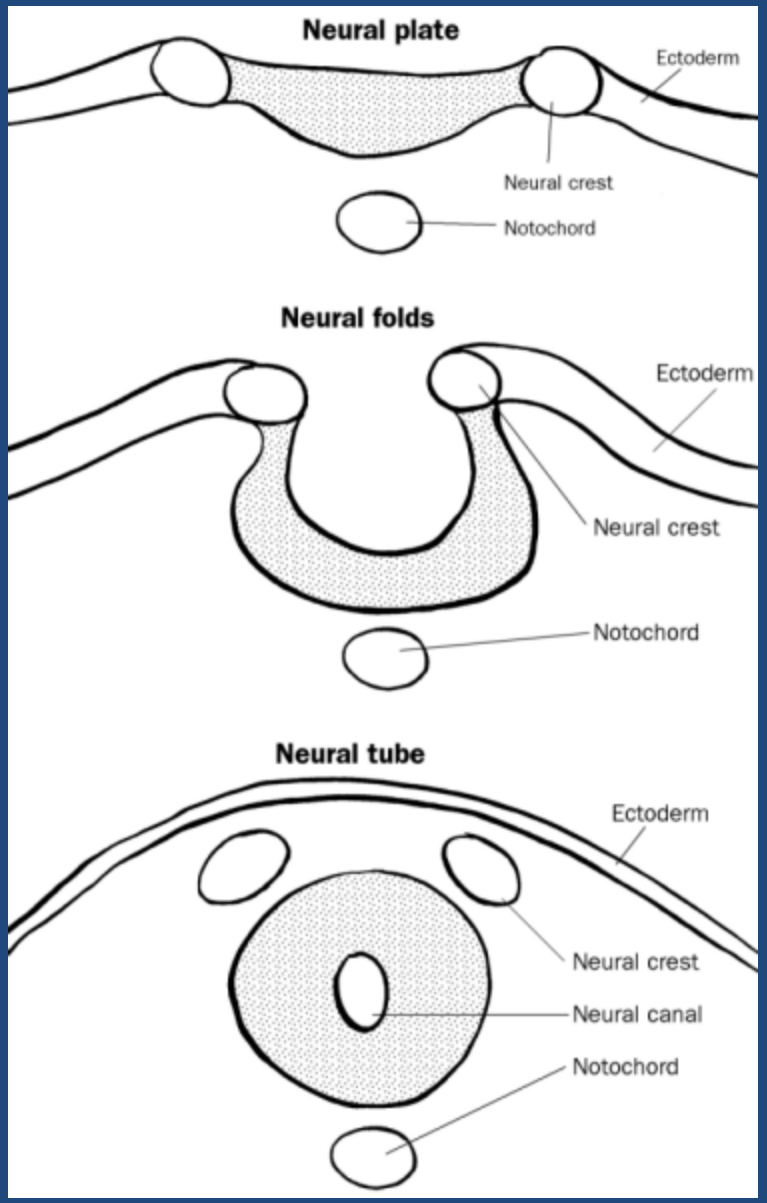
# 1. Forebrain Malformations: *Lissencephaly*

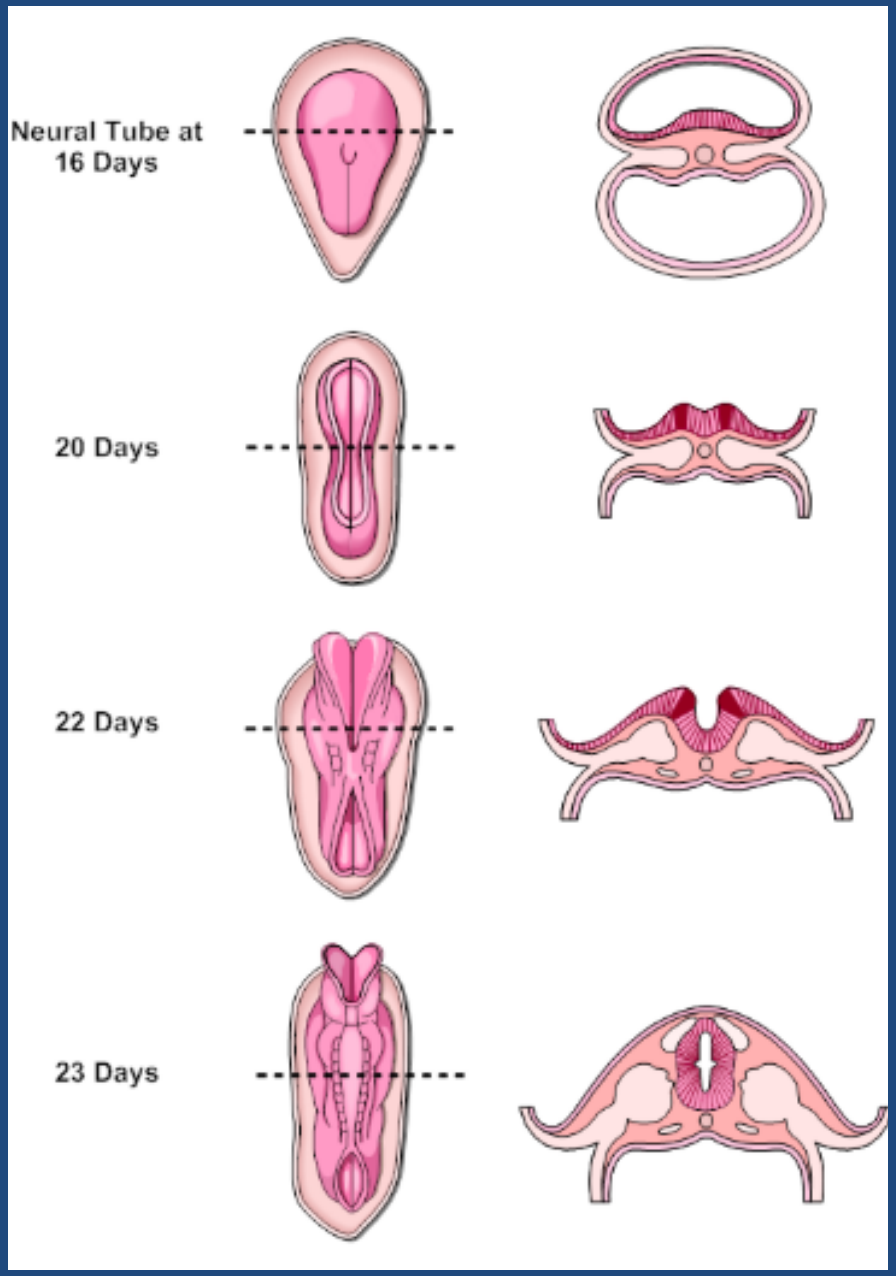


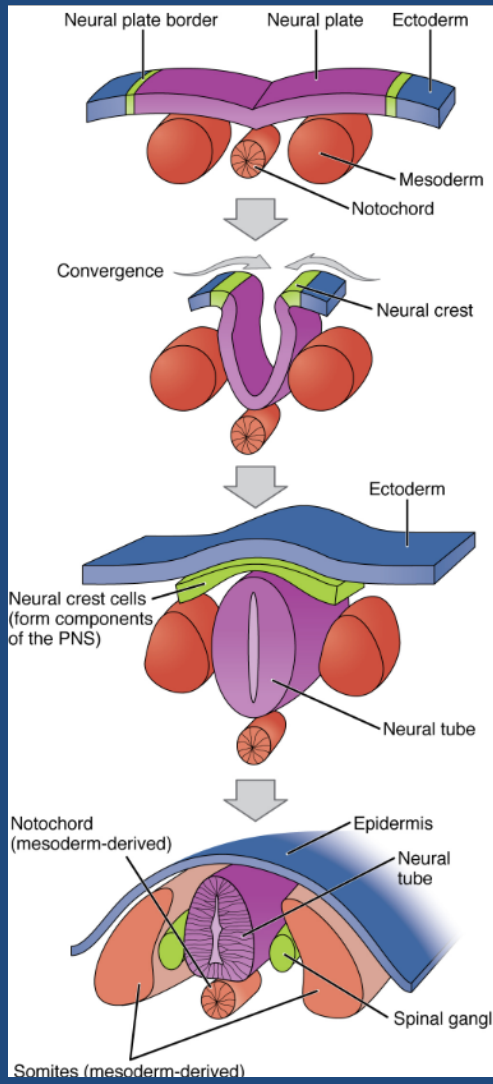
- Cortical sulci are absent except for the Sylvian fissure
- The cortex is thick and consists of the molecular and three neuronal layers
- The deepest of these layers is also the thickest and most cellular, presumably comprised of neurons that migrated a certain distance from the ventricles but failed to reach their normal destinations
- There is a small amount of myelinated white matter between the abnormal cortex and the ventricles

# 1. CNS congenital malformation

**Neural tube defect**


Neural plate
Ectoderm
Neural crest
Notochord
Neural folds
Ectoderm
Neural crest
Notochord
Neural tube
Ectoderm
Neural crest
Neural canal
Notochord




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.

# Neural tube defect

- Among the earliest stages in brain development is the formation of the neural tube, the inside of which will become the ventricular system and the wall of which will become the brain and spinal cord
- Failure of a portion of the neural tube to close, or reopening after successful closure, may lead to one of several malformations. All are characterized by abnormalities involving some combination of neural tissue, meninges, and overlying bone or soft tissues
- Collectively, neural tube defects are the most frequent CNS malformations

Increased maternal α-fetoprotein (AFP) in serum and/or amniotic fluid in anencephaly, meningocele, or myelomeningocele but

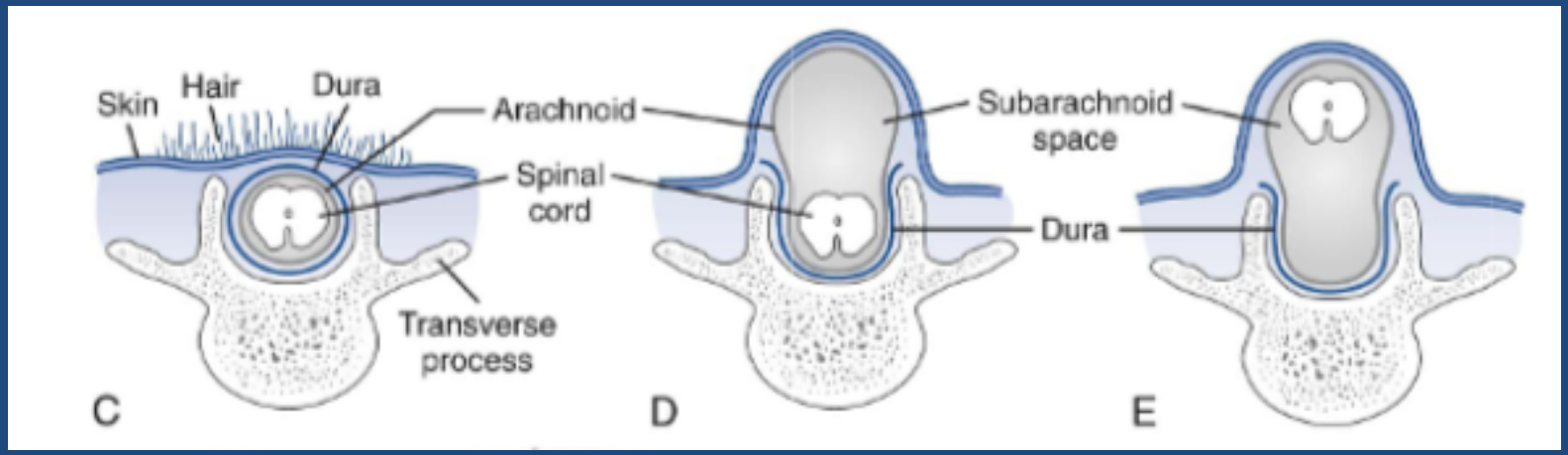
# Neural tube defect

- Folate deficiency during the initial weeks of gestation is a risk factor;
  - prenatal vitamins are aimed, in part, at reducing this risk
- The combination of ultrasound and maternal screening for elevated α-fetoprotein has increased the early detection of neural tube defects
- The overall recurrence risk in subsequent pregnancies is 4% to 5%

Increased maternal α-fetoprotein (AFP) in serum and/or amniotic fluid in anencephaly, meningocele, or myelomeningocele but not spina bifida occulta

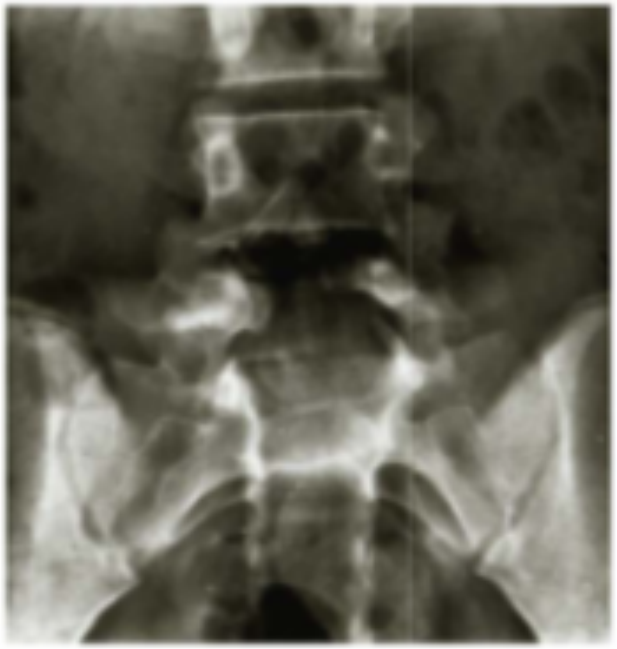
# Neural tube defect

- *Myelomeningocele* is an extension of CNS tissue through a defect in the vertebral column
- Occur most commonly in the lumbosacral region
- Patients have motor and sensory deficits in the lower extremities and problems with bowel and bladder control
  - The symptoms derive from the abnormal spinal cord in this region, often compounded by infections extending from thin or ulcerated overlying skin



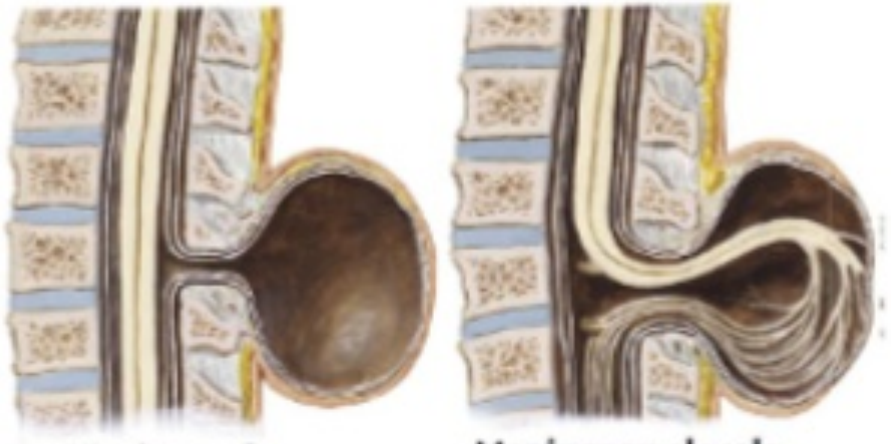
# Neural tube defect
# Spina bifida occulta

**Spina bifida occulta**



**X-ray film.** Showing deficit of lamina of sacrum (spina bifida occulta)

# Neural tube defect
# Spina bifida

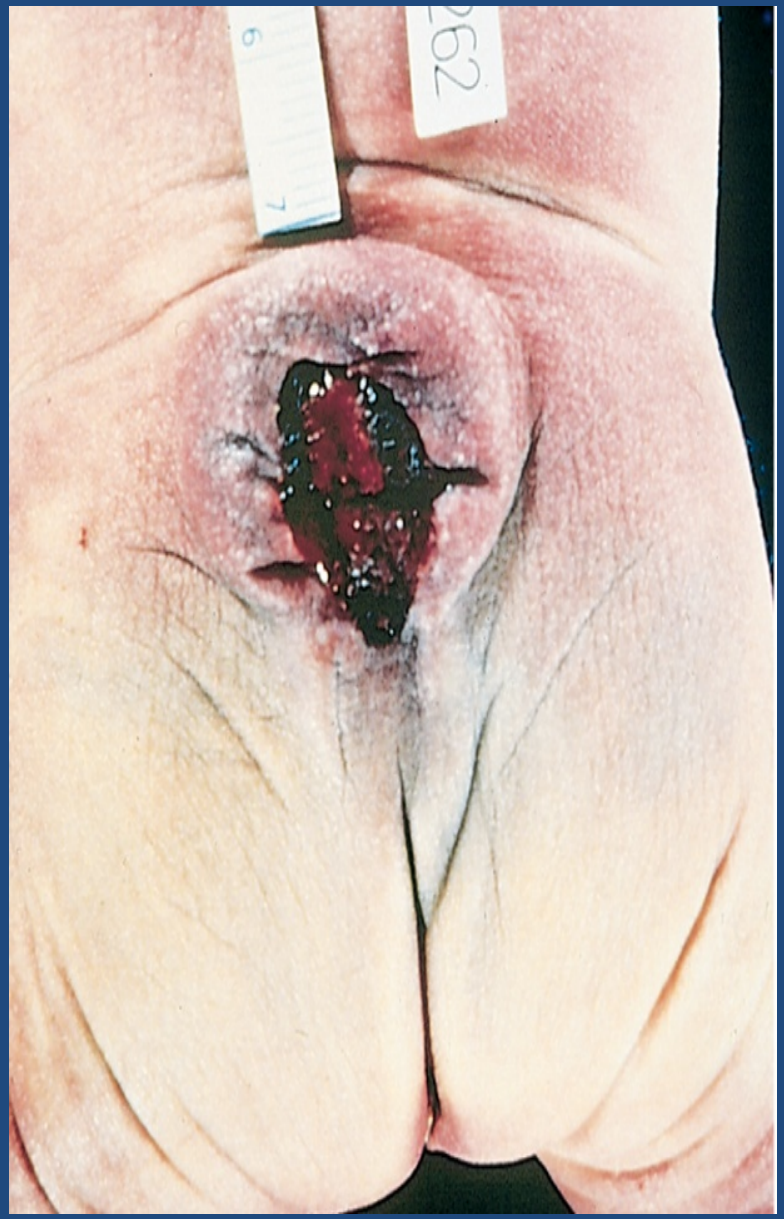


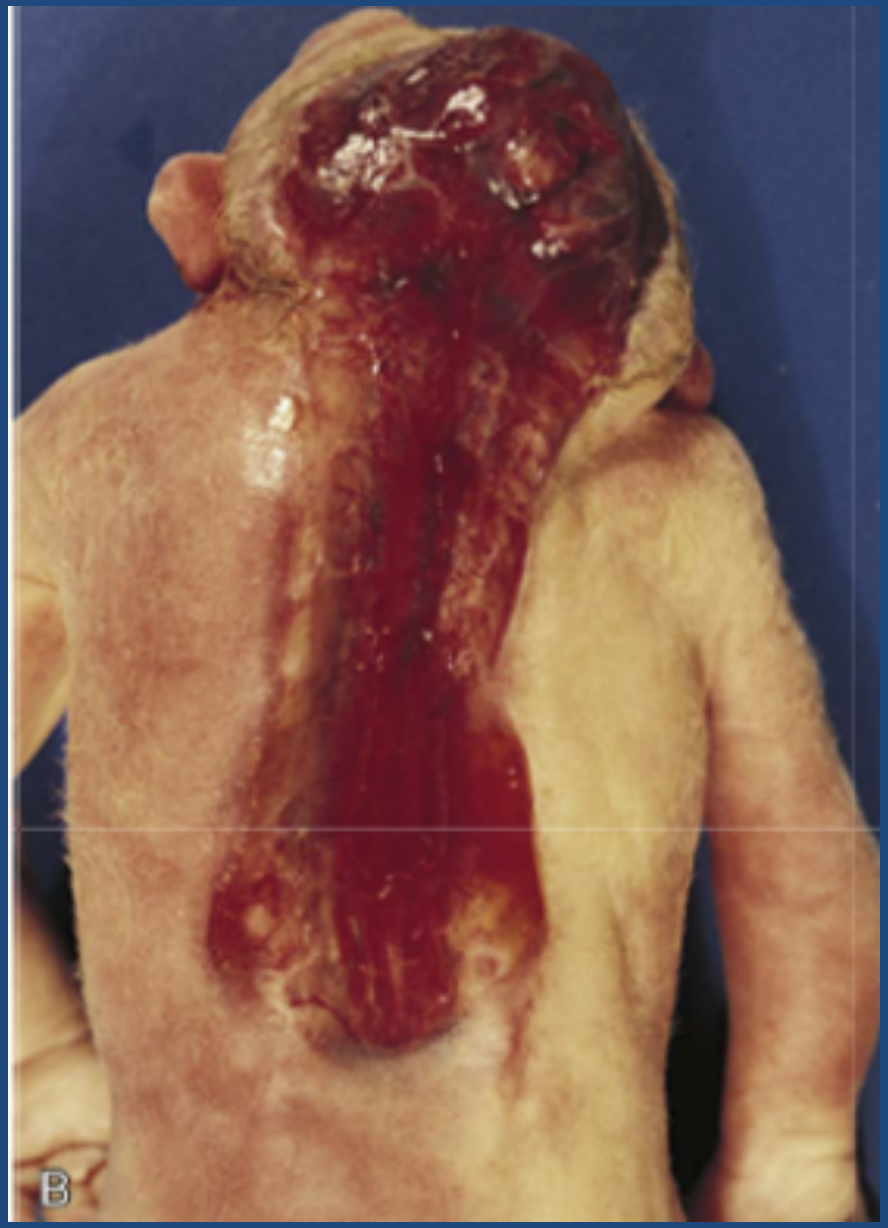
Meningocele



Meningomyelocele

**Spina bifida.** With central cicatrix

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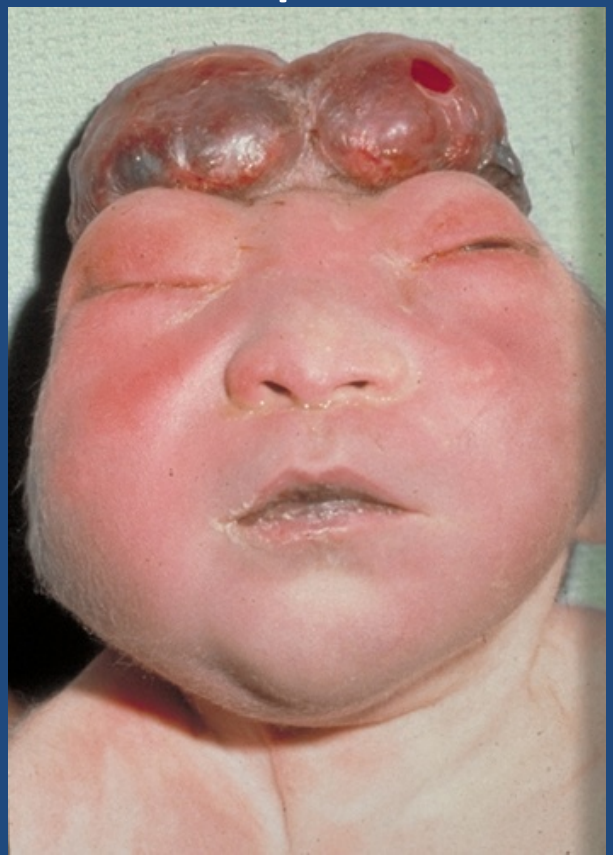
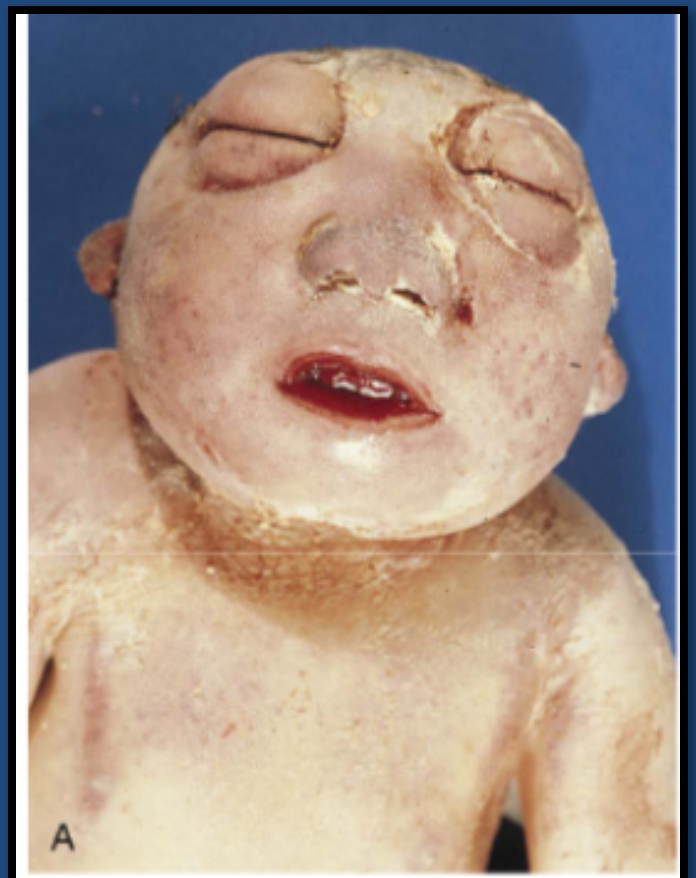
# Neural tube defect

- At the other end of the developing brain, *anencephaly* is a malformation of the anterior end of the neural tube, with absence of the brain and top of skull





# Neural tube defect

- An *encephalocele* is a diverticulum of malformed CNS tissue extending through a defect in the cranium
- It most often involves the occipital region or the posterior fossa

# 1. CNS congenital malformation

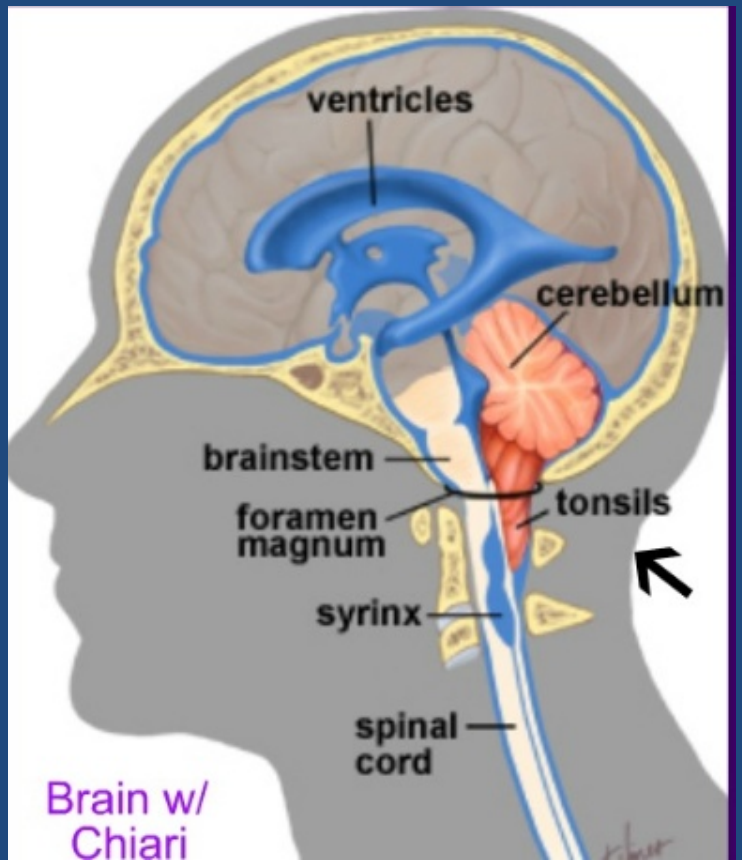
Posterior Fossa Anomalies:

*Arnold-Chiari malformation*

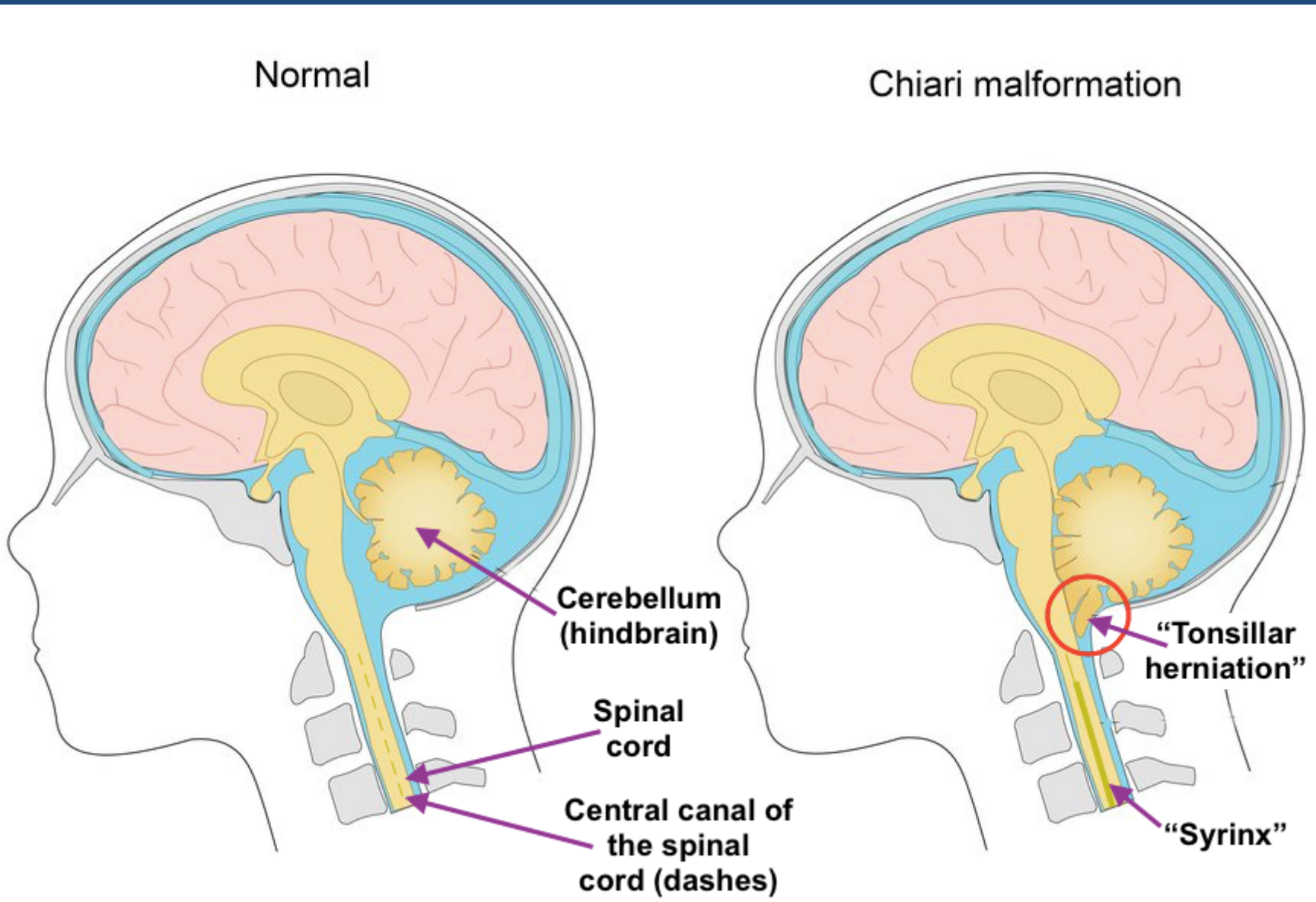
# Posterior Fossa Anomalies

- The most common malformations in this region of the brain result in either misplaced or absent cerebellum
- Typically, these are associated with hydrocephalus
- The *Arnold-Chiari malformation* (Chiari type II malformation) consists of:

**•A small posterior fossa**
**•A misshapen midline cerebellum**
**•Downward extension of *vermis* through the foramen magnum**
**•Hydrocephalus**
**•A lumbar myelomeningocele**

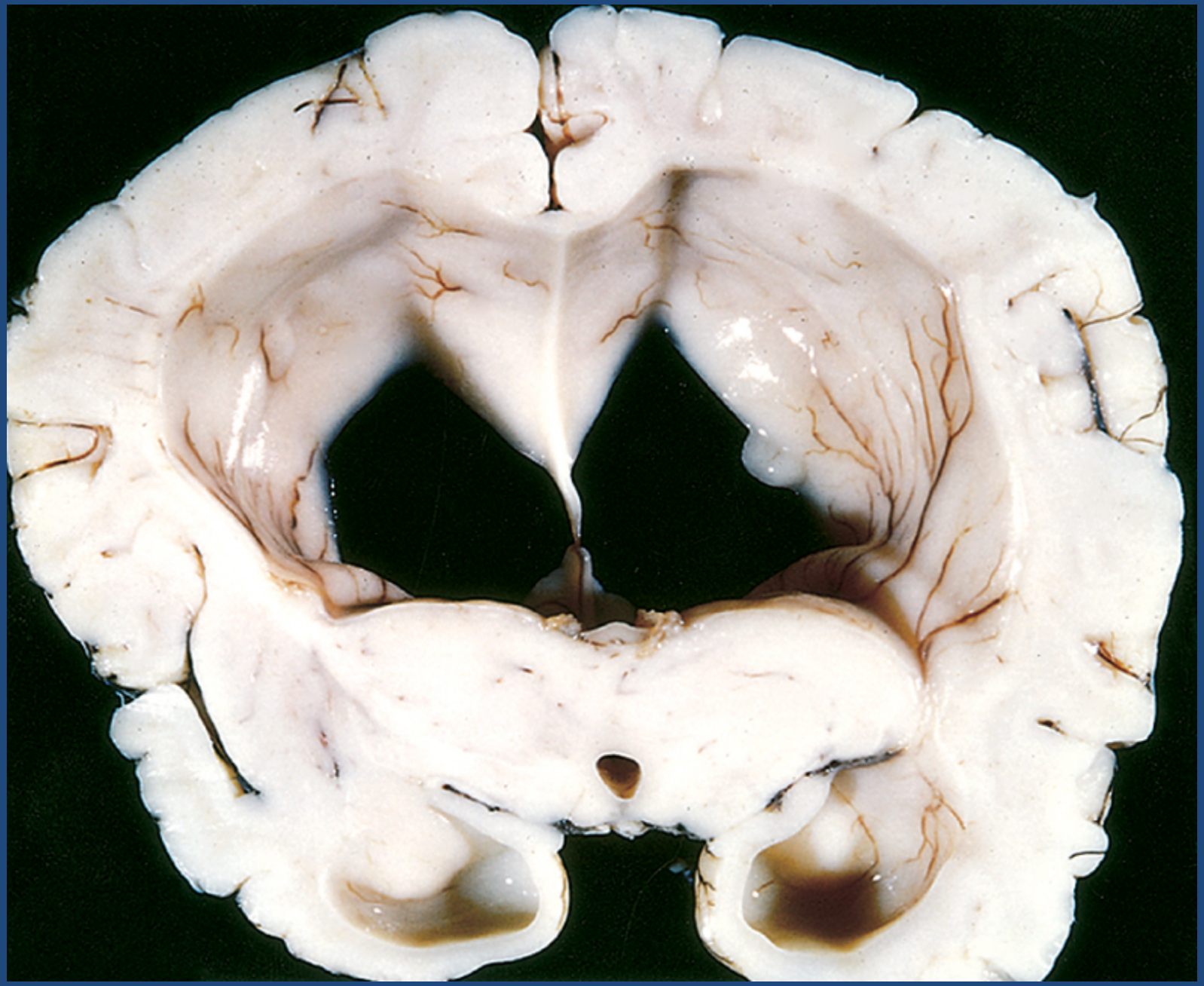


# The *Arnold-Chiari malformation*



# 2. Hydrocephalus

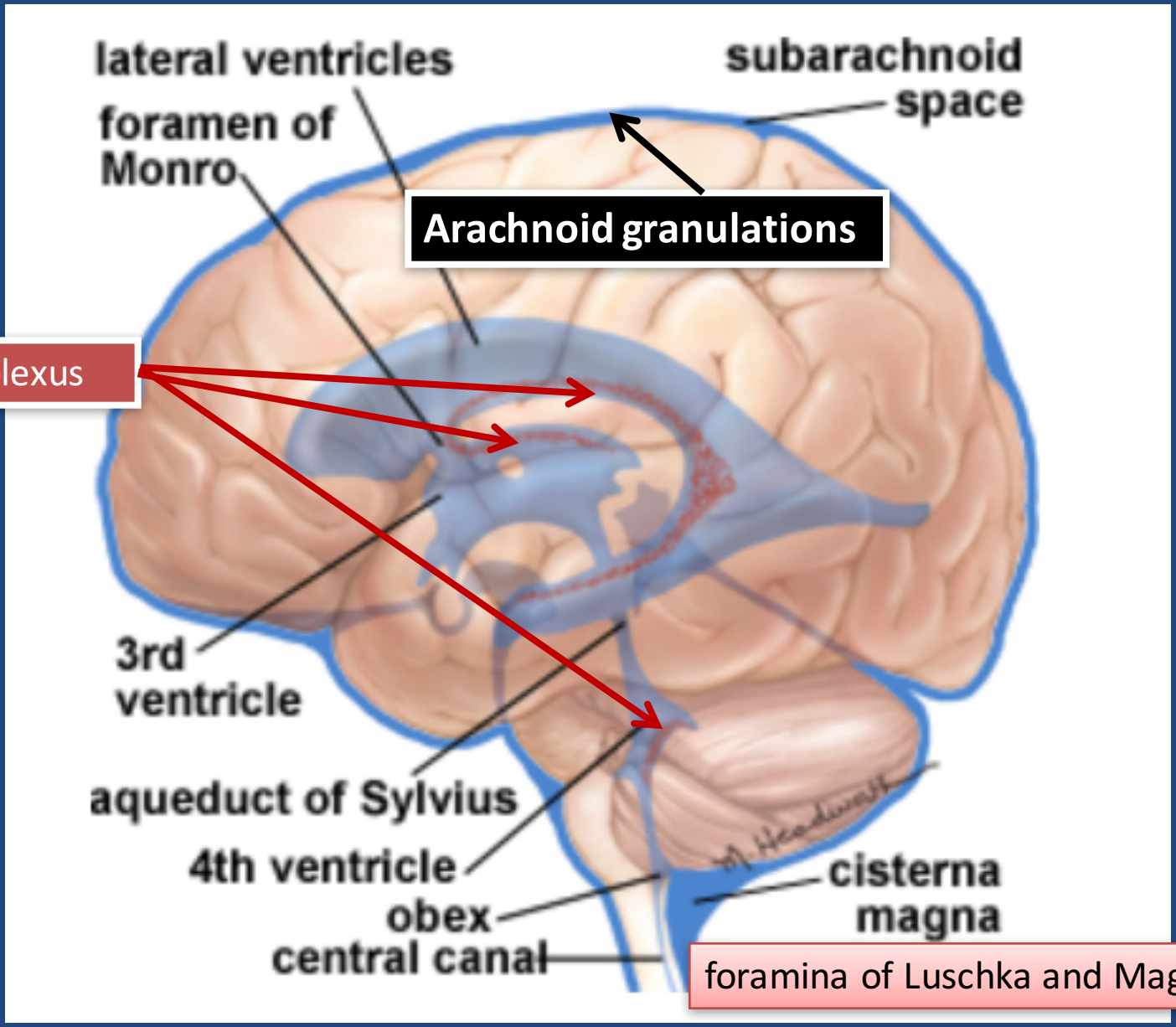
**Advanced hydrocephalus.**
Clinical appearance



# 2. Hydrocephalus Cerebrospinal fluid (CSF)

- After being produced by the choroid plexus within the ventricles, CSF circulates through the ventricular system and exits through the foramina of Luschka and Magendie
- CSF fills the subarachnoid space around the brain and spinal cord, contributing to the cushioning of the nervous system within its bony confines
- The arachnoid granulations are responsible for the resorption of CSF
- The balance between CSF generation and resorption keeps the volume of this fluid stable

# Cerebrospinal fluid (CSF)



# 2. Hydrocephalus

- *Hydrocephalus* refers to the accumulation of excessive CSF within the ventricular system
- Most cases occur as a consequence of impaired flow or impaired resorption of CSF
- In rare instances (e.g., tumors of the choroid plexus), overproduction of CSF may be responsible

# 2. Hydrocephalus

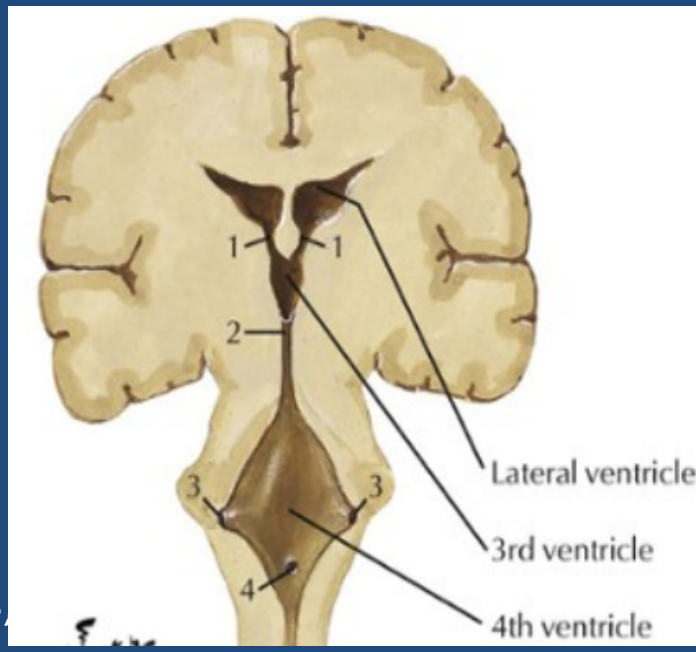
- When hydrocephalus develops in infancy before closure of the cranial sutures → enlargement of the head
- Hydrocephalus developing after fusion of the sutures →expansion of the ventricles and increased intracranial pressure, without a change in head circumference

# 2. Hydrocephalus

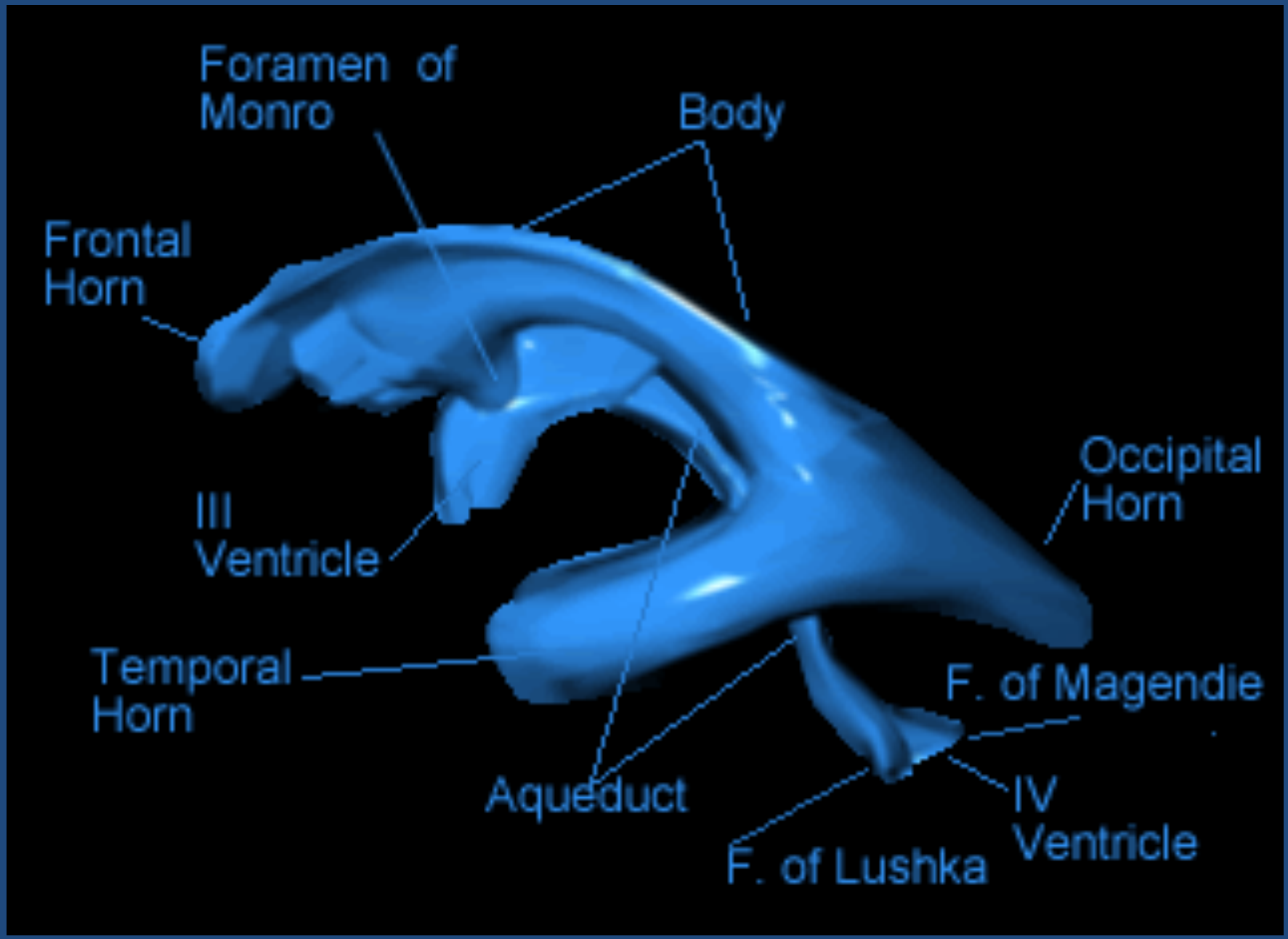
- If there is an obstacle to the flow of CSF within the ventricular system, then a portion of the ventricles enlarges while the remainder does not → *noncommunicating hydrocephalus*
  - most commonly seen with masses at the formamen of Monro or aqueduct of Sylvius
- In *communicating hydrocephalus* all of the ventricular system is enlarged; here the cause is most often reduced resorption of CSF

# 2. What can cause hydrocephalus?

1. **Hypersecretion of CSF**: e.g. choroid plexus tumor
2. **Obstructive hydrocephalus**
   - Obstruction of the foramina of Monro e.g. colloid cyst
   - Obstruction of the third ventricle e.g. pilocytic astrocytoma
   - Obstruction of the aqueduct e.g. aqueductal stenosis or atresia and posterior fossa tumors
   - Obstruction of the foramina of Luschka or impairment of flow from the fourth ventricle (Chiari malformation, meningitis, subarachnoid hemorrhage, posterior fossa tumors)
   - Fibrosis of the subarachnoid space e.g. meningitis, subarachnoid hemorrhage, meningeal dissemination of tumors




3. **Defective filtration of CSF**: postulated for low-pressure hydrocephalus


Foramen of Monro
Body
Frontal Horn
III Ventricle
Occipital Horn
Temporal Horn
F. of Magendie
Aqueduct
IV Ventricle
F. of Lushka

# Take home messages:

- Malformations of the brain can occur because of genetic factors or external insults.
- The timing of the injury will determine the pattern of the injury, based on the type of developmental processes occurring at the point of injury.
- Patterns of malformation include alterations in the closure of the neural tube, proper formation of the separate portions of the neural tissue, and migration of neurons to the appropriate locations.
- Hydrocephalus is an increase in CSF volume within all or part of the ventricular system.

# HOMEWORK

- Define: meningocele.
- Define: polymicrogyria.
- What is the difference between microcephaly and microencephaly?
- Define: hydrocephalus ex vacuo.