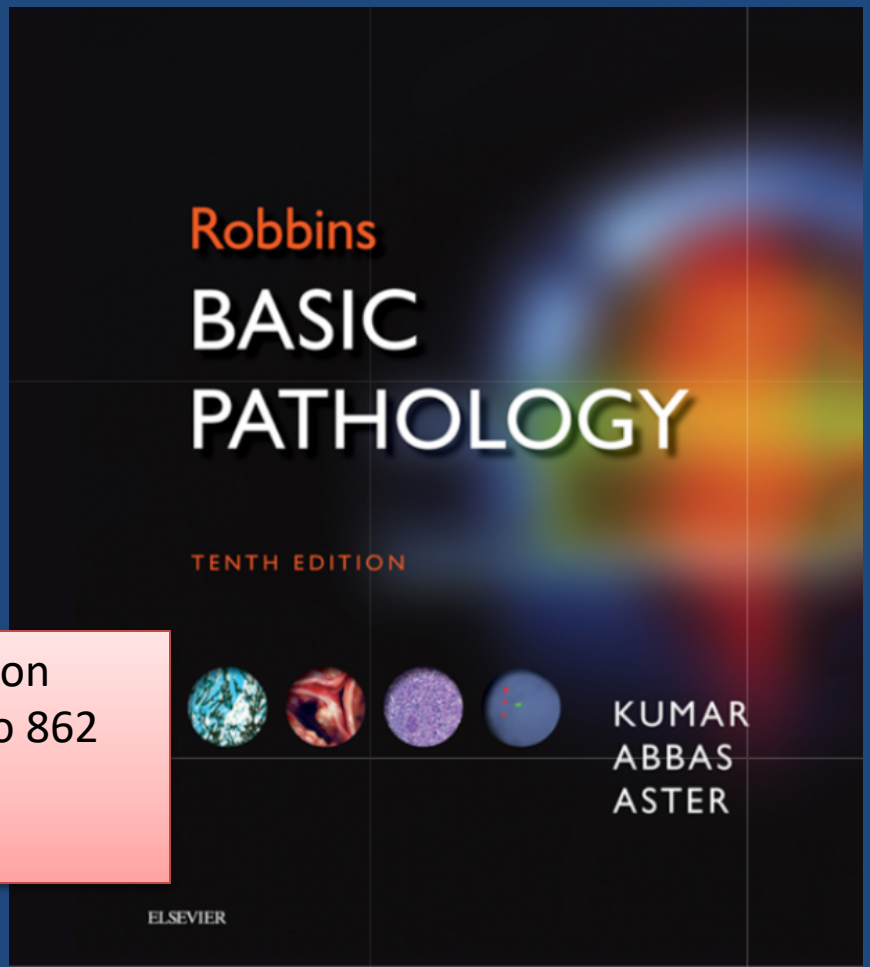
CNS 2020
Pathology

Congenital malformations and hydrocephalus

Maha Arafah



Congenital malfomation
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Hydrocephalus
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Objectives:

1. CNS congenital malformation

- Know the common types of congenital malformations of the CNS
- 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.

2. Hydrocephalus

- 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 **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

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

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

1. CNS congenital malformation

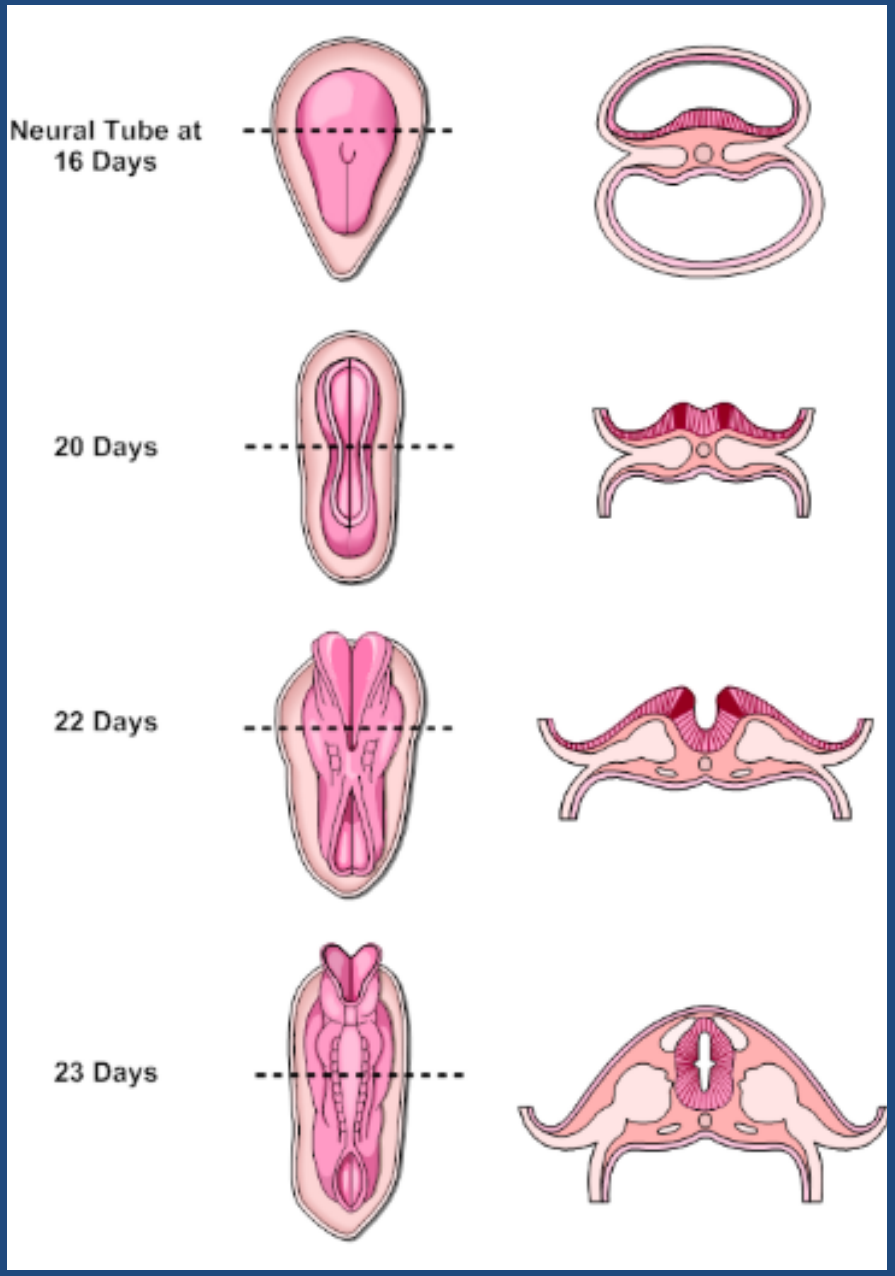
- The incidence of CNS malformations is estimated at 1% to 2%
- Malformations of the brain are more common in the setting of **multiple** birth defects
- Causes:

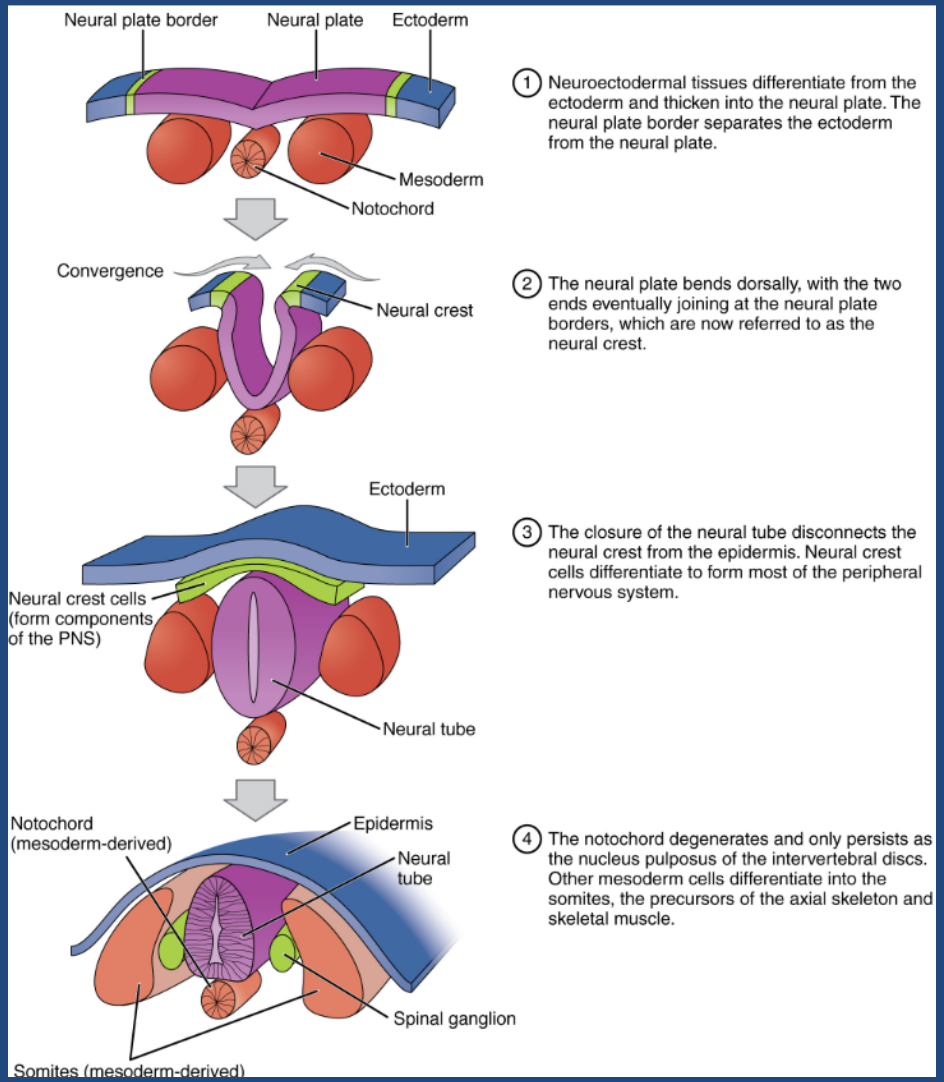
1. Prenatal or perinatal insults give rise to mental retardation, cerebral palsy or neural tube defects
   i. Various chemicals and infectious agents
   ii. Timing is important
   iii. May lead to failure of normal CNS development or tissue destruction
2. Mutations affecting genes that regulate the differentiation, maturation, or intercellular communication of neurons or glial cells

Definition and pathological changes in **neural tube defects:**

1. Spina bifida
2. Meningomyelocele
3. Anencephaly and encephalocele

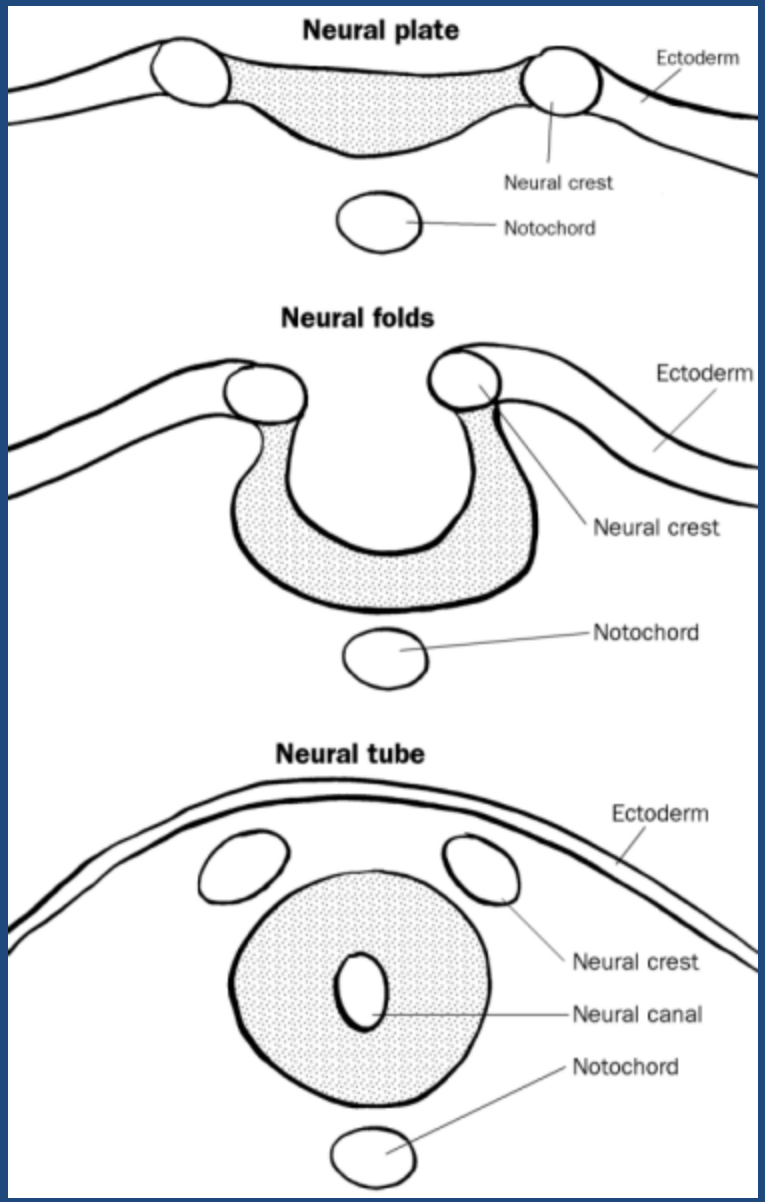
1. CNS congenital malformation





1. CNS congenital malformation

- 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



I. Neural tube defect

- The most frequent CNS malformations
- 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

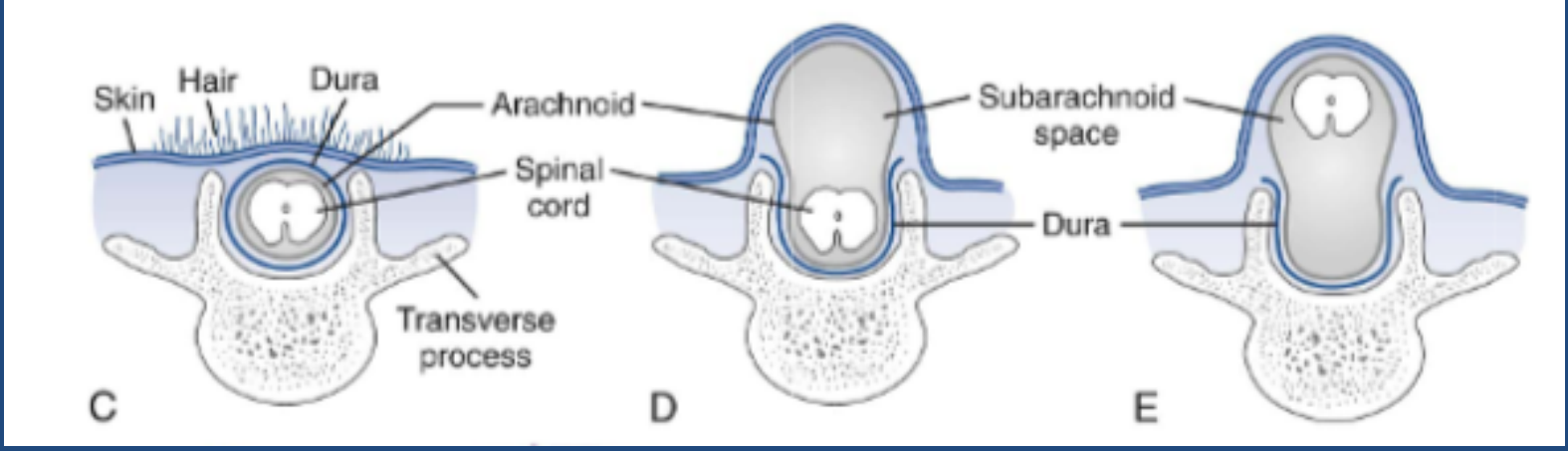
Neural tube defect

- Folate deficiency during the initial weeks of gestation is a risk factor
  - prenatal vitamins are aimed as administration of folate to women of child-bearing age reduces the incidence of neural tube defects by up to 70%
- 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

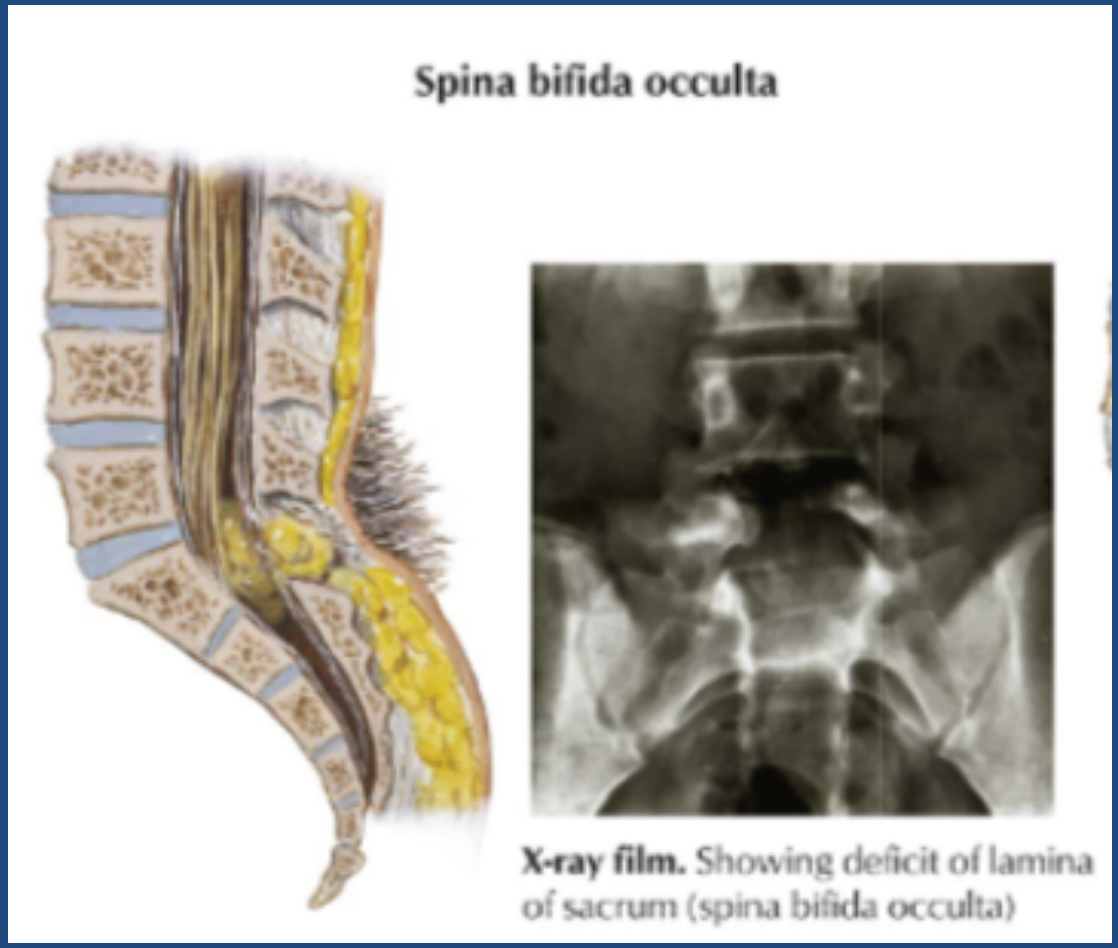
Neural tube defect

- The most common defects involve the posterior end of the neural tube, from which the spinal cord forms.
- These can range from asymptomatic bony defects *(spina bifida occulta)* to *spina bifida*, a severe malformation consisting of a flat, disorganized segment of spinal cord associated with an overlying meningeal outpouching.

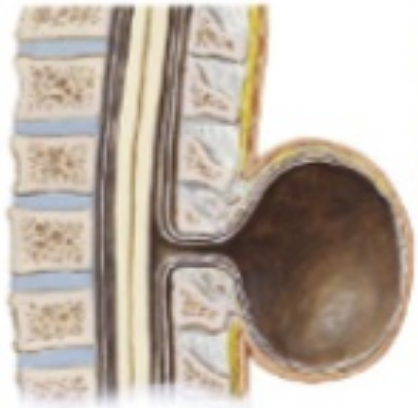


Neural tube defect
1. Spina bifida occulta

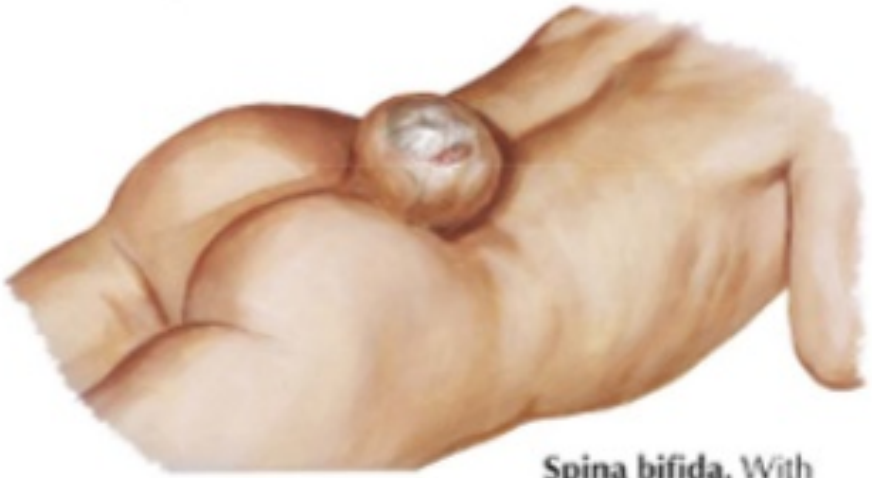
- Asymptomatic bony defects



Neural tube defect
Spina bifida



Meningocele

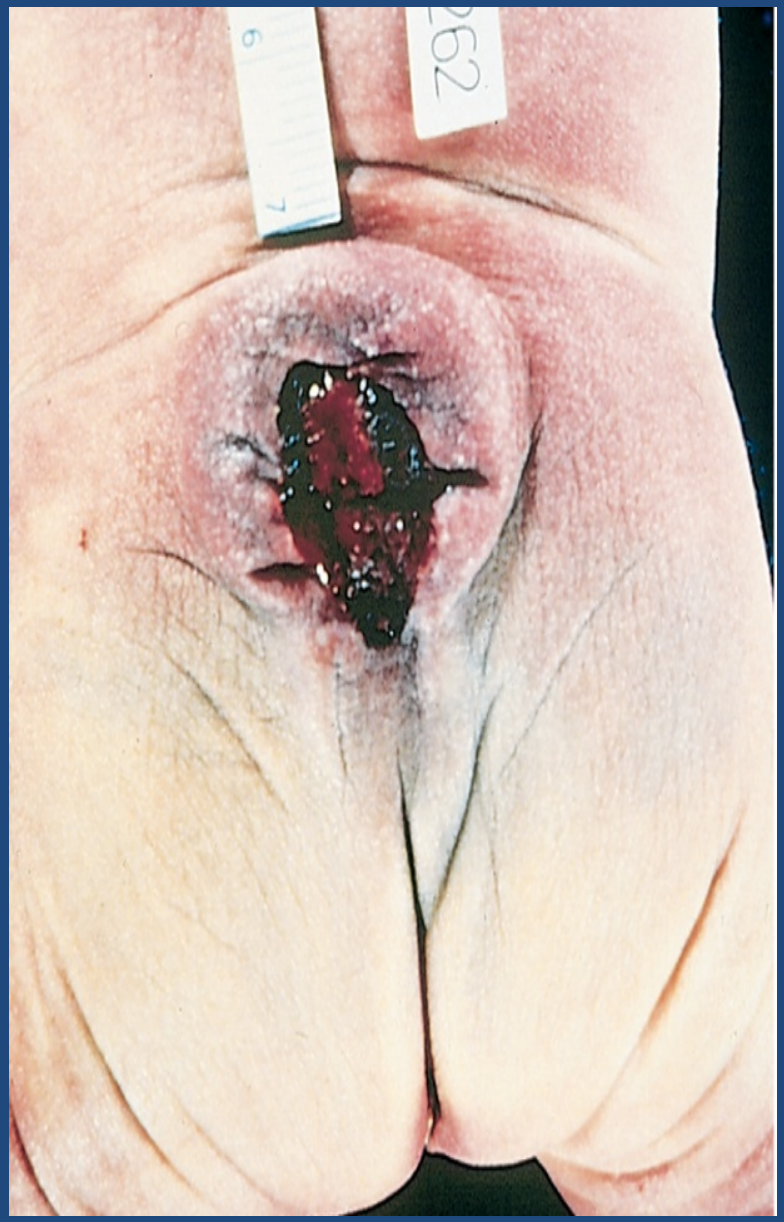


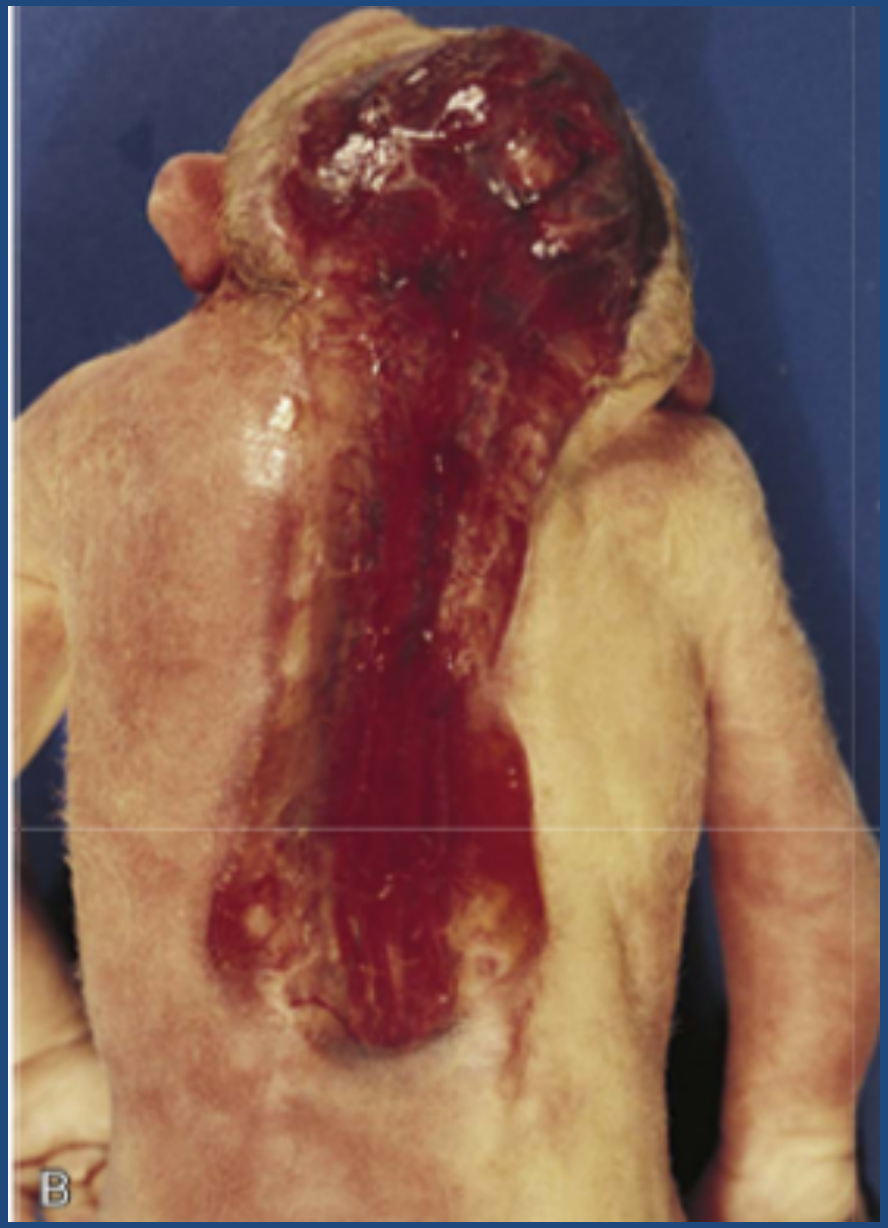
Spina bifida. With central cicatrix

Neural tube defect:
2. Meningomyelocele

- *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

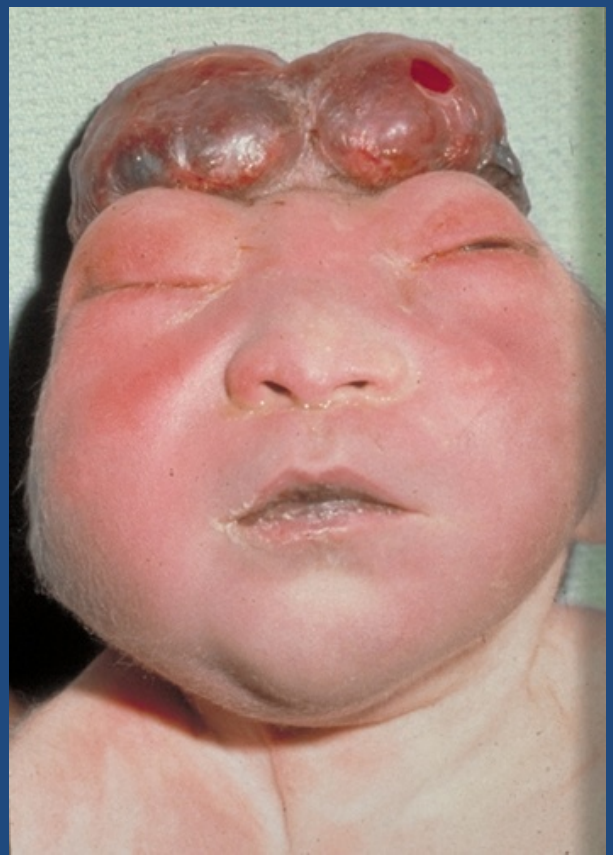
1. CNS congenital malformation

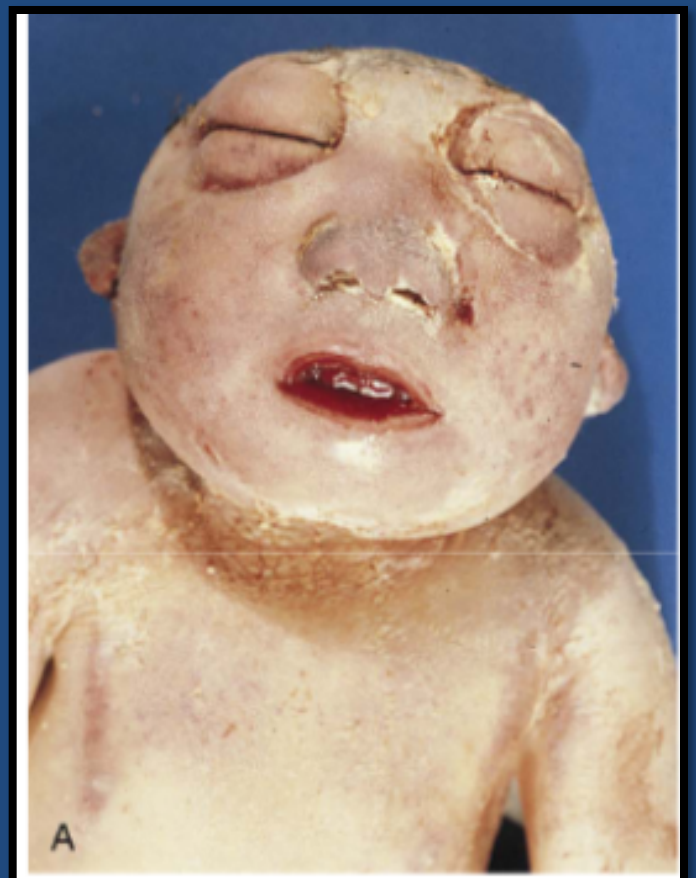




Neural tube defect:
3. Anencephaly and encephalocele

- is a malformation of the anterior end of the neural tube, with absence of the brain and top of skull





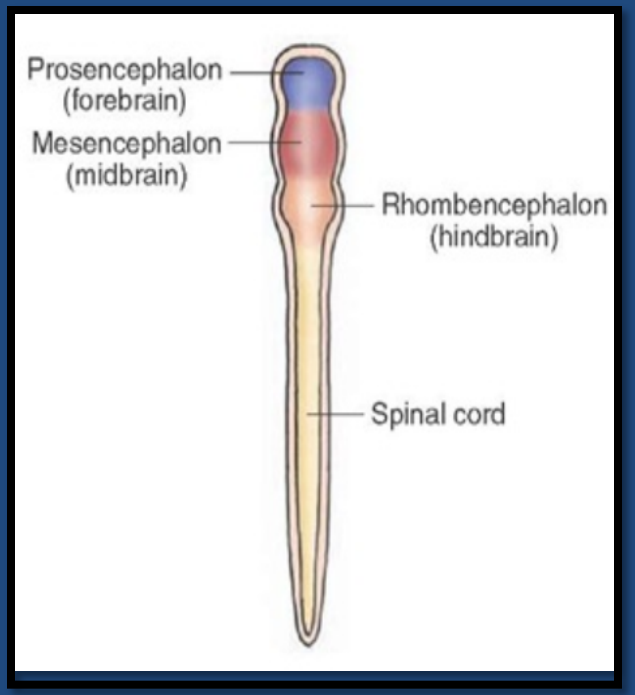
Neural tube defect:
3. Anencephaly and encephalocele

- 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

Encephalocele

II. Forebrain Malformations:

1. Megalencephaly
2. Microcephaly
3. Lissencephaly



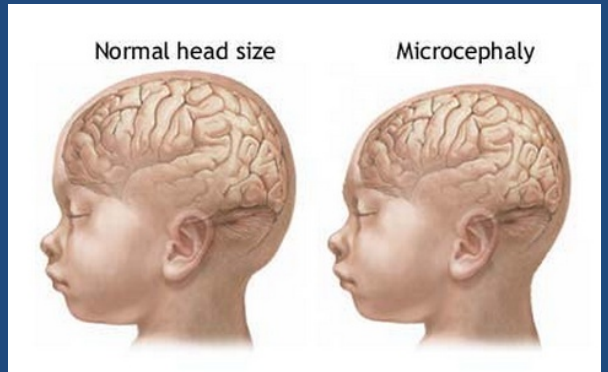
II. Forebrain Malformations
Megalencephaly and Microcephaly

- 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

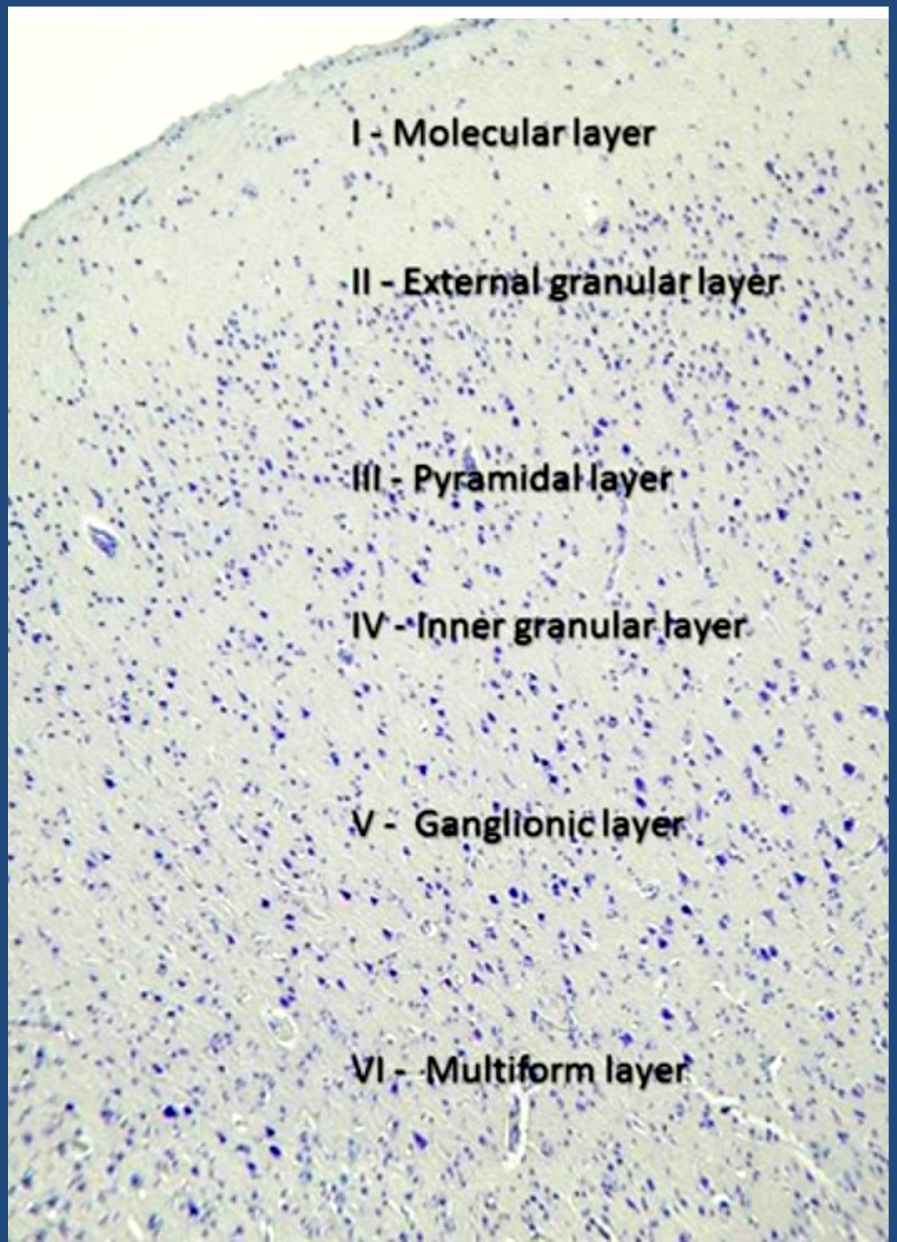
II. Forebrain Malformations
Microcephaly

- Microencephaly occurs in a wide range of clinical settings, e.g.:
  - chromosome abnormalities
  - fetal alcohol syndrome
  - human immunodeficiency virus 1 (HIV-1) and Zika virus 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

the six-layered neocortical architecture



Six-layered neocortical architecture



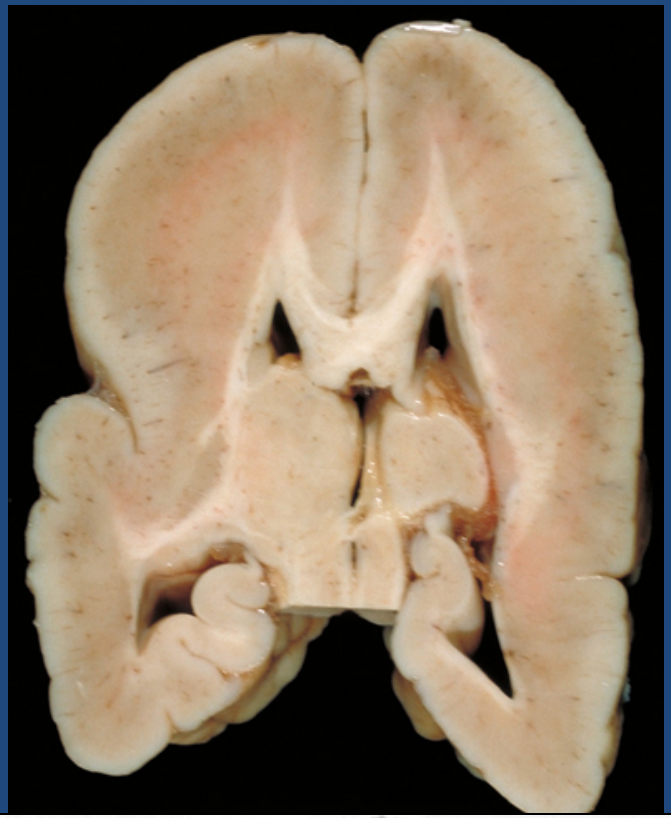
II. Forebrain Malformations

Lissencephaly

- *Lissencephaly* (*agyria*) is characterized by an absence of normal gyration and a smooth-surfaced brain
- *Pachygyria* is patchy involvement by an absence of normal gyration

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

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

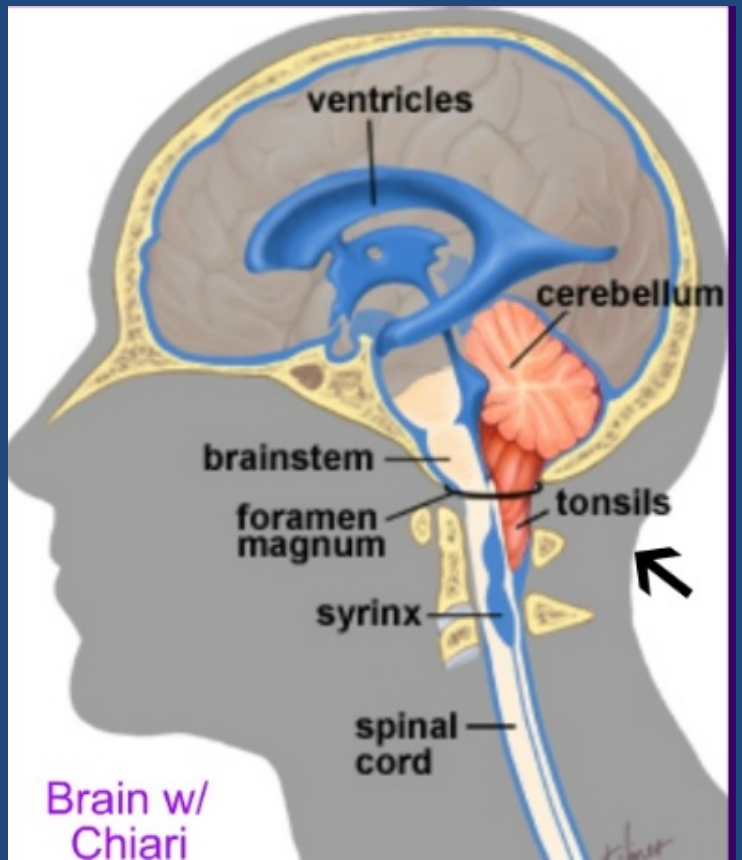
III. Posterior Fossa Anomalies:

Arnold-Chiari malformation

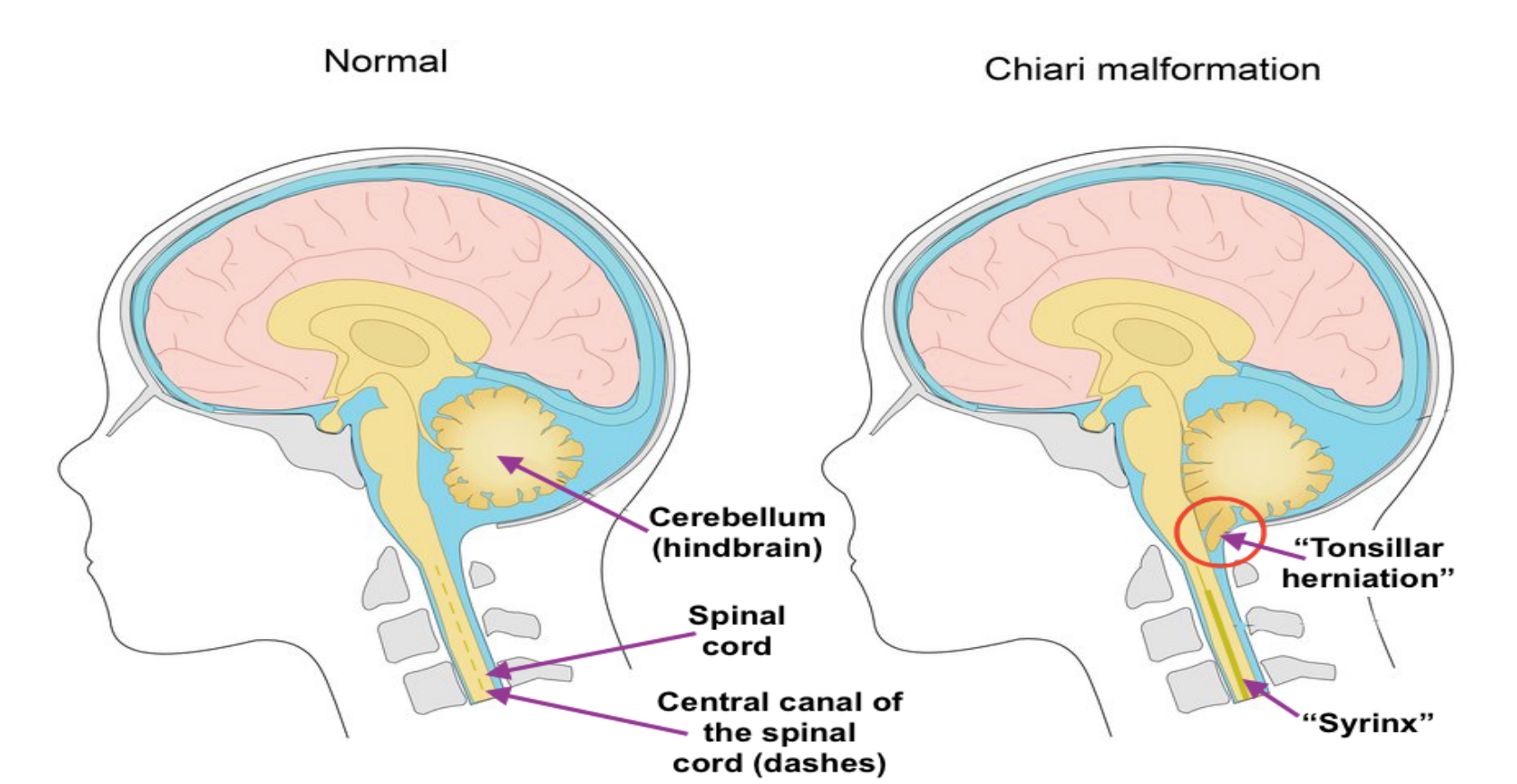
III. Posterior Fossa Anomalies

- 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*



In the *Chiari I malformation,* low-lying cerebellar tonsils extend through the foramen magnum at the base of the skull. This can lead to obstruction of CSF flow and compression of the medulla, resulting in symptoms of headache or cranial nerve deficits. Increasing the space for the tissue through neurosurgery can alleviate the symptoms

2. Hydrocephalus

- Definitions of normal pressure
- Hydrocephalus:

  noncommunicating vs.
  communicating hydrocephalus

- Pathophysiology and etiology.

2. Hydrocephalus

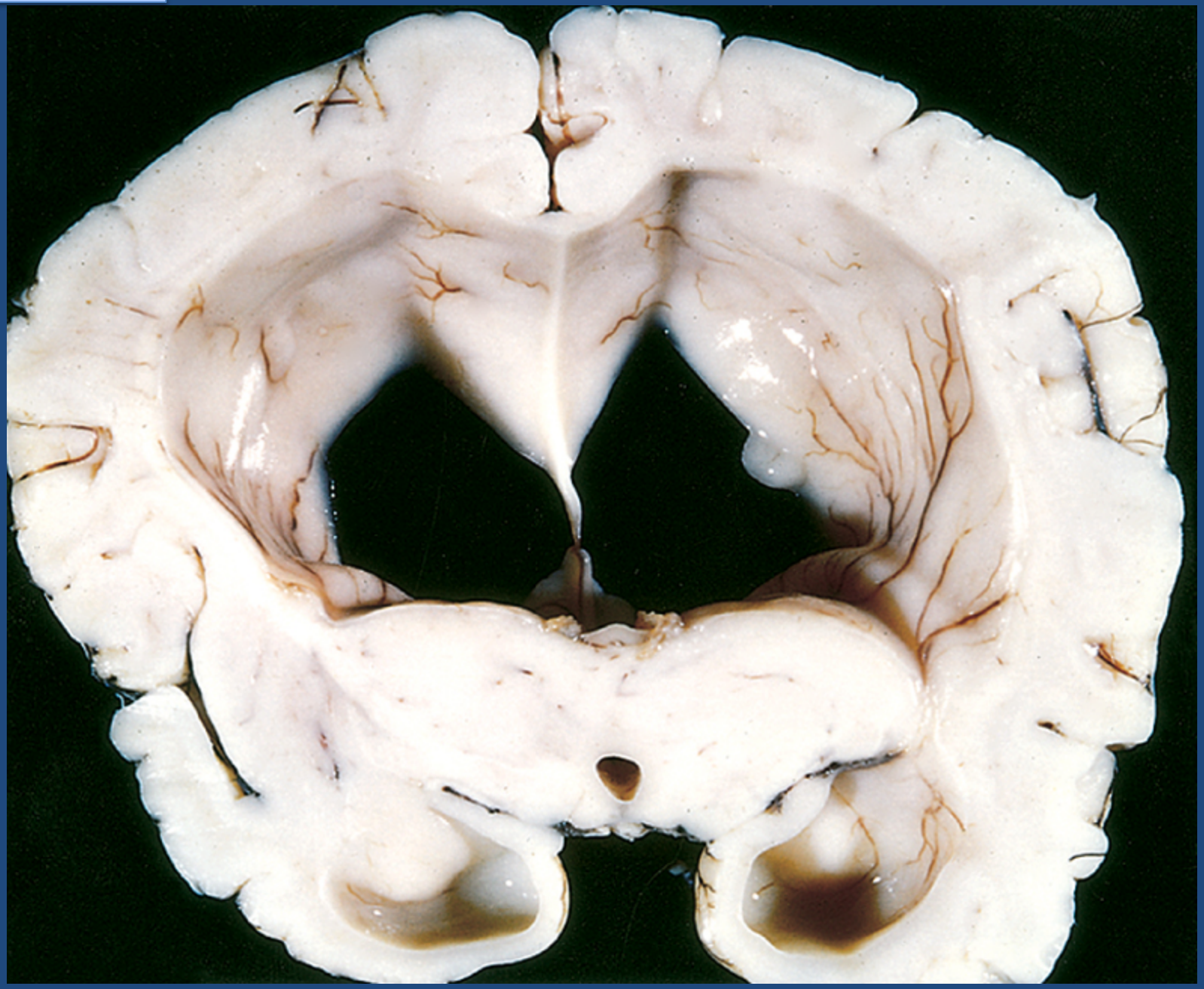
Hydrocephalus refers to an increase in the volume of the CSF within the ventricular system.

Advanced hydrocephalus.
Clinical appearance

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

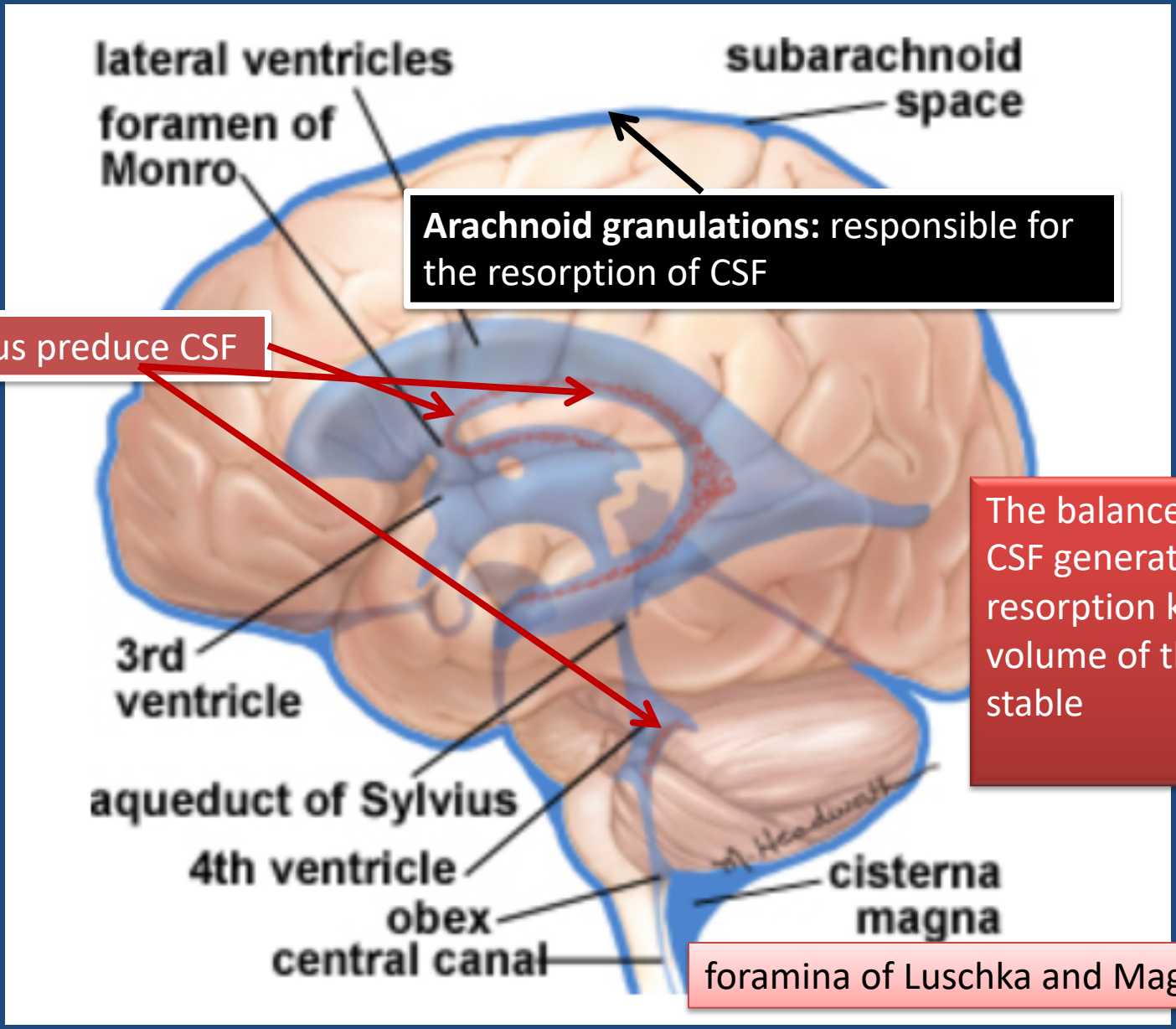


Cerebrospinal fluid (CSF)

- CSF is produced by the choroid plexus within the ventricles, it 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

Cerebrospinal fluid (CSF)



The balance between CSF generation and resorption keeps the volume of this fluid stable

Causes:

- 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

Two types:

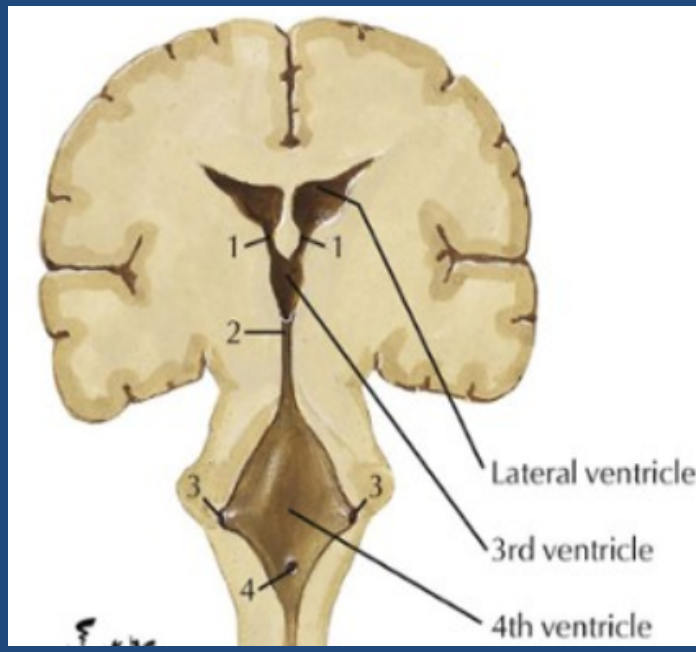
communicating and non communicating

- 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

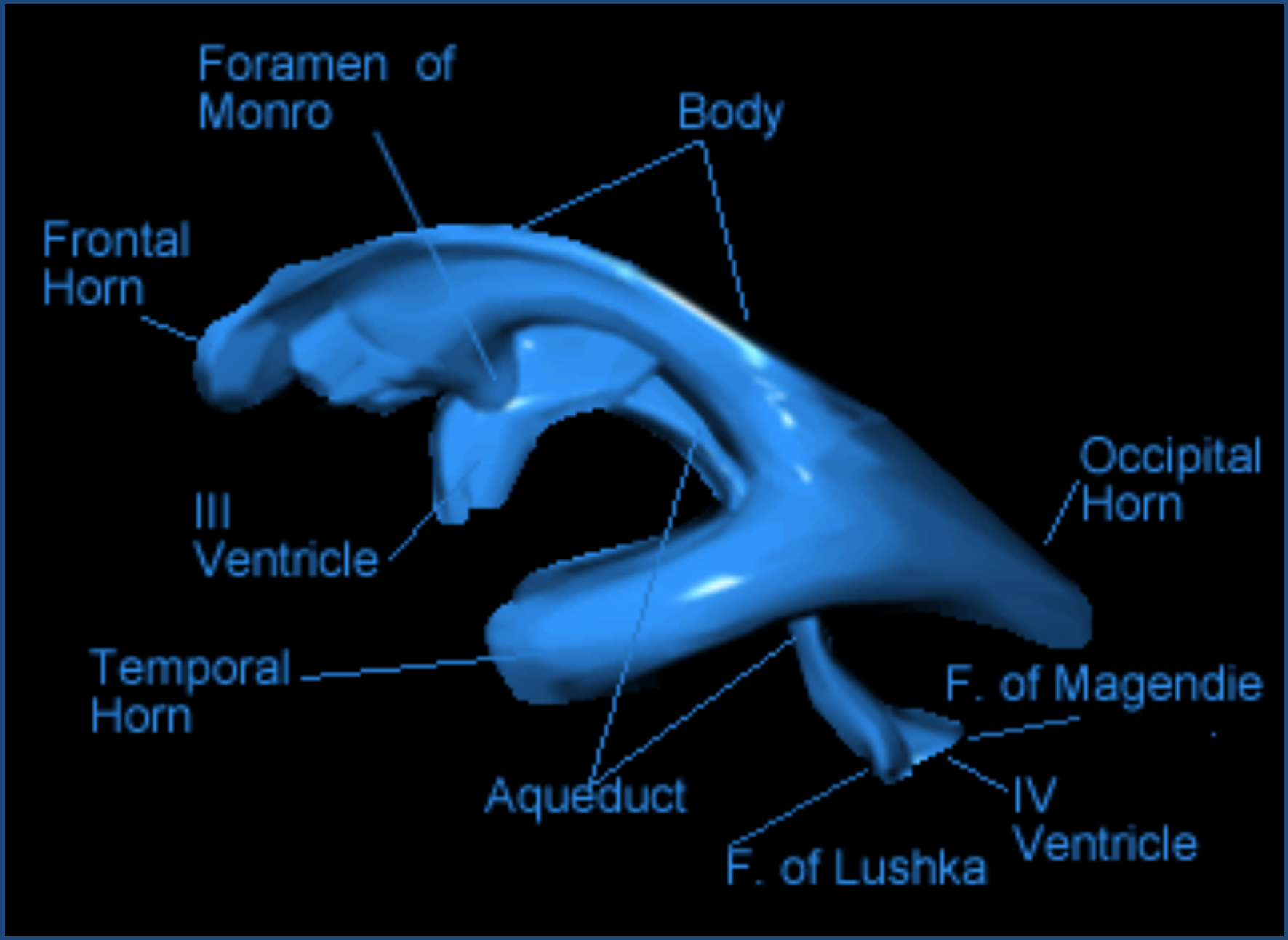
What can cause hydrocephalus?

1. **Hypersecretion of CSF**: e.g. choroid plexus tumor
- **2. Obstructive hydrocephalus**
- **3. Defective filtration of CSF: postulated for low-pressure hydrocephalus**



Causes of 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


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.

A compensatory increase in CSF volume *(hydrocephalus ex vacuo)* may occur secondary to a loss of brain volume from any underlying cause (e.g., infarction, neurodegenerative disease)