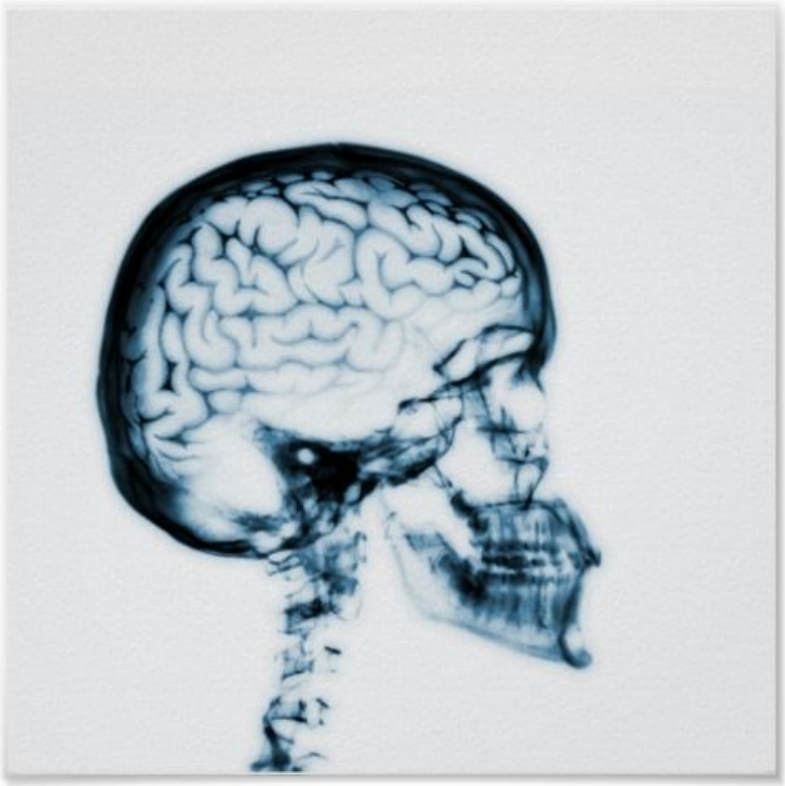
Congenital Malformation & Hydrocephalus



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 fetoprotein 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.**

Important note: **Please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: Pathology Edit**

Red: Important
Grey: Extra notes

Congenital malformations (Introduction).

The incidence of CNS malformations, giving rise to *mental retardation*, *cerebral palsy* (group of permanent movement disorders that appear in early childhood), or *neural tube defects*, is estimated at 1% to 2%.

- Because different parts of the brain develop at different times during gestation[1] (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.**

Prenatal: before birth; during or relating to pregnancy.
Perinatal: the period around childbirth, especially the five months before and one month after birth.

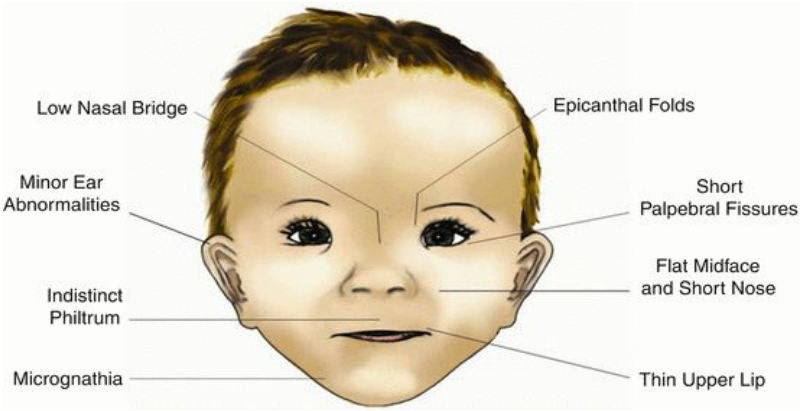
Although the pathogenesis and etiology of many malformations remain unknown, both genetic and environmental factors are clearly at play. CNS malformation can be caused by Mutations affecting molecules in pathways of neuronal and glial **Development, Migration[2] or connection.**

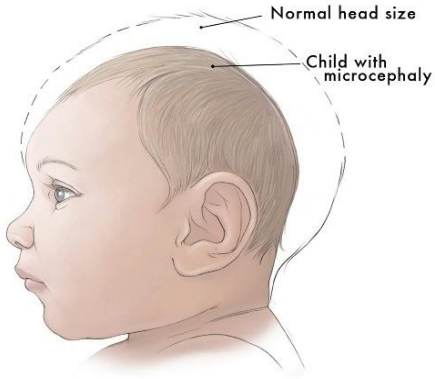
- **toxic compounds** & **infectious agents** are known to have **teratogenic effects[3].**

Forebrain Malformations.

The forebrain malformation can be divided into **three** types:
1- megalencephaly: The volume of brain may be abnormally **large**.
2- microcephaly (more common): The volume of brain may be abnormally **small** and usually associated with small head.

- **These two types can occur in a wide range of clinical settings, including:**
  a. Chromosome abnormalities.
  b. Fetal alcohol syndrome.
  c. Human immunodeficiency virus 1 (HIV-1) infection acquired in utero.





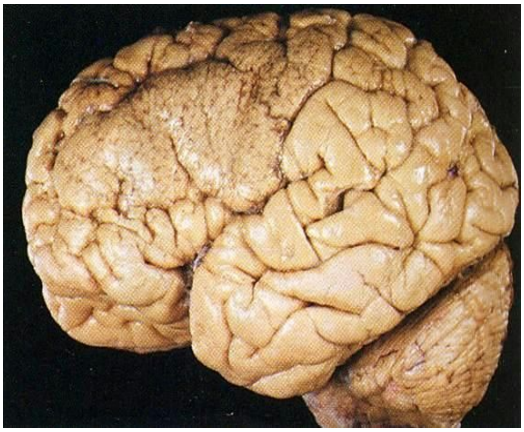
Fetal alcohol syndrome

These two types are associated with:

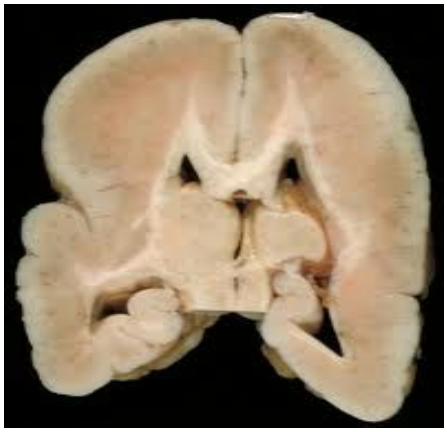
- Decreased number of neurons of cerebral cortex.
- Disruption of normal neuronal migration and differentiation during development which can lead to a disruption of the normal **gyration** and **six-layered neocortical architecture**.

[1] Gestation = فترة الحمل
[2] movement from one part of something to another
[3] Teratogenic effects = تأثيرات جينية على الجنين

3- Lissencephaly (agyria): is characterized by an absence of normal gyration and a smooth-surfaced whole brain (see pic 1)**, or sometimes called Pachygyria in case of more patchy involvement** (see pic 2)**.**



Pic1. Cortical sulci are absent except usually, for the **Sylvian fissure**.



Pic 2. Patchy involvement

- The cortex is abnormally thickened and is usually only **3 or 4-layered**
- Single-gene defects have been identified in some cases of lissencephaly.
- Cortical sulci are absent except, usually, for the **Sylvian fissure** (lateral fissure)
- There is a small amount of myelinated white matter between the abnormal cortex and the ventricles.

Neural tube defect.

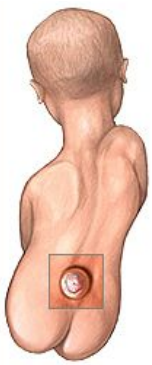
Among the earliest stages in brain development is the formation of the neural tube, the inside of which will become the ventricular system and the wall of which will become the brain and spinal cord.

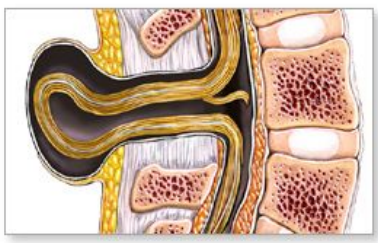
Failure of a portion of the neural tube to close, or reopening after successful closure, may lead to one of several malformations, All are characterized by abnormalities involving some combination of neural tissue, meninges, and overlying bone or soft tissues.

- Neural tube defects are the **most frequent CNS malformations.**

Folate deficiency during the initial weeks of gestation is a risk factor, so 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





Diseases associated with Neural Tube defects:

1- Myelomeningocele: is an extension of CNS tissue through a defect in the **vertebral column.**

- They 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, and are often compounded by infections extending from thin or **ulcerated** overlying skin.

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

3- 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

Posterior Fossa Anomalies.

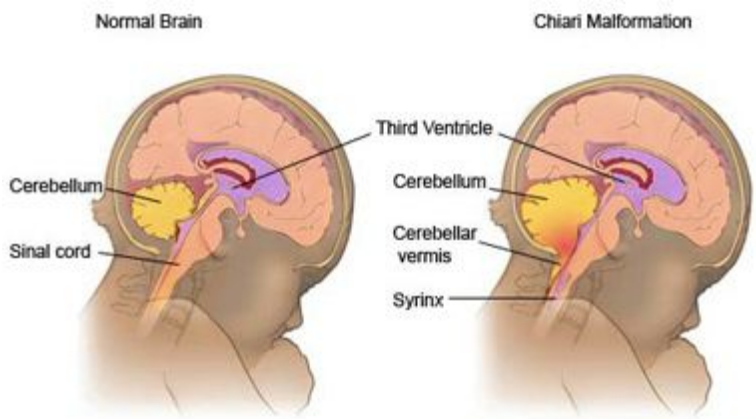
The most common malformations in this region of the brain result in either **misplaced or absent cerebellum.**

- Typically, these are associated with hydrocephalus.

The Arnold-Chiari malformation (Chiari type II malformation) consists of:

Chiari malformations are structural defects in the cerebellum. That's the part of the brain that controls balance. Some people with Chiari malformations may have no symptoms.

1. A small posterior fossa.
2. A misshapen midline cerebellum.
3. Downward extension of vermis through the foramen magnum.
4. Hydrocephalus.
5. A lumbar myelomeningocele.



Hydrocephalus.

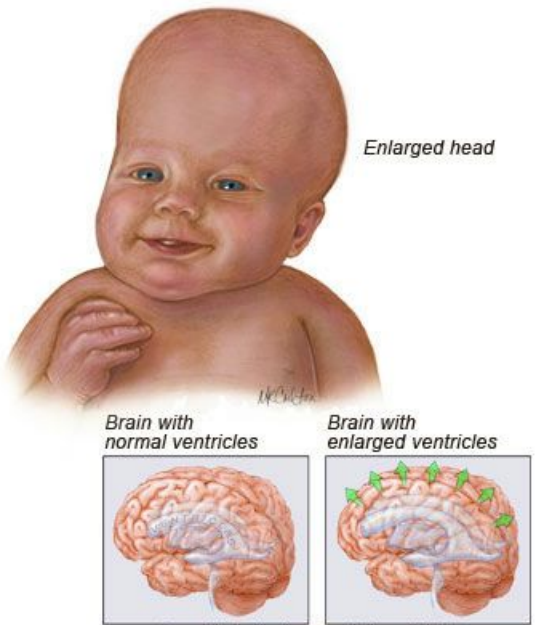
It is the accumulation of excessive CSF within the ventricular system (Hydro=water, cephalus=brain).

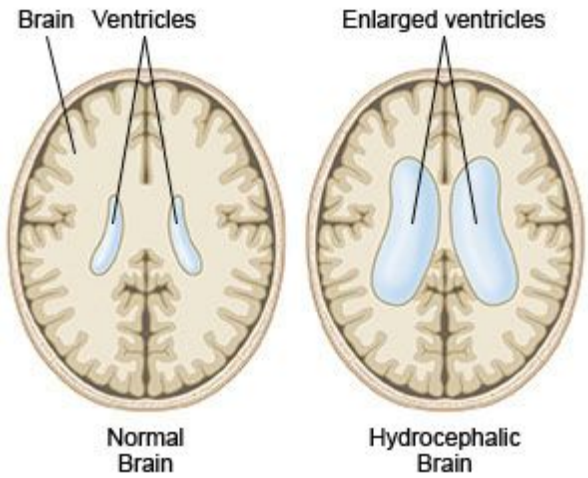
- **Cerebral edema** is the accumulation of excess fluid within the brain parenchyma.
- Both lead to increase in intracranial pressure that can damage brain tissue by either by decreasing perfusion or through herniation.

Normal physiology of CSF:

- After CSF is produced by the choroid plexus within the ventricles, cerebrospinal fluid (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.

- Most cases of hydrocephalus occur as a consequence of impaired **flow** or impaired **resorption** of CSF.
- In rare cases (e.g., tumors of the choroid plexus), overproduction of CSF may be responsible.





➔ If hydrocephalus develops in **infancy before closure of the cranial sutures**, **the head enlarges.**

➔ If hydrocephalus developing **after** fusion of the sutures (Adults) that will lead to **expansion of the ventricles and increased intracranial pressure**, without a change in head circumference.

Types of Hydrocephalus:

1. **Noncommunicating 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**, and it is most commonly is caused by masses obstructing the foramen of Monro of or compressing aqueduct of Sylvius (cerebral aqueduct)
2. **Communicating hydrocephalus:** entire ventricular system is enlarged, it is usually caused by **reduced resorption of CSF**.

Causes 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.

Summary.

Edema, Herniation, and Hydrocephalus

- Cerebral edema is the accumulation of excess fluid within the brain parenchyma. Hydrocephalus is defined as an increase in CSF volume within all or part of the ventricular system.
- Increases in brain volume (as a result of increased CSF volume, edema, hemorrhage, or tumor) raise the pressure inside the fixed capacity of the skull.
- Increases in pressure can damage the brain either by decreasing perfusion or by displacing tissue across dural partitions inside the skull or through openings in the skull (herniations).

Congenital Malformations and Perinatal Brain Injury

- Malformations of the brain can occur because of genetic factors or external insults.
- The developmental timing and position of the injury determine its pattern and characteristics.
- Various malformations stem from failure of neural tube closure, improper formation of neural structures, and altered neuronal migration.
- Perinatal brain injury mostly takes one of two forms: (1) hemorrhage, often in the region of the germinal matrix with the risk of extension into the ventricular system; and (2) ischemic infarcts, leading to periventricular leukomalacia.

Homework.

1-Define: meningocele: protrusion of the membranes of the brain or SC through a defect in the cranium or spinal column.

2-Define: polymicrogyria: characterized by increased number of irregularly formed gyri that result in a bumpy surface.

3-What is the difference between microcephaly and microencephaly? Microcephaly: Small head (skull). Microencephaly: Small brain.

4-Define: hydrocephalus ex vacuo. an enlargement of cerebral ventricles and subarachnoid spaces, and is usually due to brain atrophy (as it occurs in dementias)

MCQs.

Q1: A pregnant female comes to you for her ultrasound. On the screen you can see that the brain is shrunken compared to the size it should be at this point of her pregnancy. You run an HIV test and it is (-). you revise the history and it turns out that she "enjoys" the occasional evening drink after work. Which of the following based upon this case would you expect to see within the fetus' brain:
A) Spina bifida as well
B) A decrease in the number of neurons
C) Anencephalus

Q2: During your OB/GYN rounds, a female gave birth to a baby with arnold chiari. what you would expect to see in that baby:
A) Anencephalus
B) Myelomeningocele
C) Microcephaly
D) Myeloschisis

Q3: If a female gives birth to a baby with microcephaly, the first infectious cause that would come to you mind would be:
A) HIV
B) TB
C) Brucella
D) Toxoplasmosis

Q4: The pattern of CNS malformation depends on the region of the brain which primarily depends on:
A) Location of injury
B) Timing of development
C) Alcohol consumption

Q5: The volume of the brain may be abnormally small is the description of which of the following:
a) Magelencephaly
b) Microcephaly
c) Lissencephaly

Q6: Which of the following is NOT associated with megalencephaly and microcephaly?
a) Increased number of neurons of cerebral cortex
b) Disruption of normal neuronal migration and differentiation
c) Can both occur in fetal alcohol syndrome

Q7: Myelomeningocele is mainly a defect associated with:
a) Spinal cord
b) Choroid plexus
c) Vertebral column
d) Anterior end of neural tube

Q8: If hydrocephalus develops in infancy:
a) Scoliosis
b) Increased intracranial pressure
c) Head shrinkage
d) Head enlargement

1:B, 2:B, 3:A, 4:B, 5:B, 6: A, 7:C, 8:D

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