



Congenital malformation & hydrocephalus



Objectives:

- 1- Know the common types of congenital malformations of the CNS and have a basic knowledge of their pathological features.
- 2- Correlate CNS normal development with the classification of congenital CNS malformations.
- 3- 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.
- 4- Understand the various mechanisms that lead to the development of hydrocephalus.
- 5- 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.
- 2- Definition and pathological changes in forebrain anomalies:
- 3- Megalencephaly, microencephaly and lissencephaly, Microencephaly causes.
- 4- Definition and pathological changes in neural tube defects
- 5- Pathogenesis with special emphasis on the role of folate and alpha fetoproteins and their clinical significance.
- 6- Definition and pathological changes in posterior fossa anomalies: Arnold Chiari malformation.
- 7- Hydrocephalus: Definitions of normal pressure hydrocephalus, noncommunicating hydrocephalus and communicating hydrocephalus - Pathophysiology and etiology.

Black: Doctor's slides.

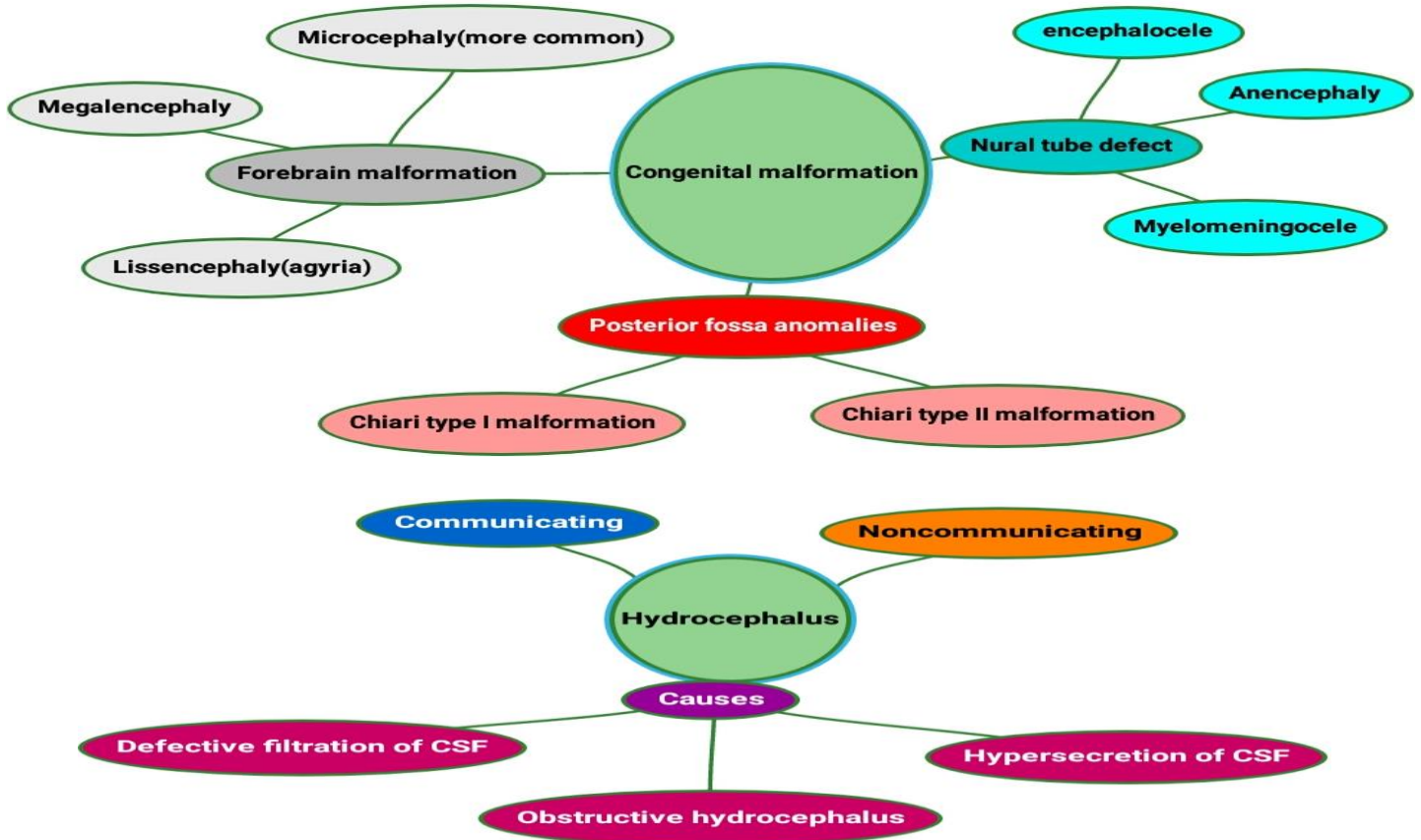
Red or black bold: important!

Green: Doctor's notes.

Grey: Extra.

Italic black: New terminology.

Lecture outlines:



Congenital malformations:

The incidence of CNS malformations, giving rise to mental retardation, cerebral palsy, or neural tube defects, is estimated at 1% to 2%.

- Malformations of the brain are more common in the setting of multiple birth defects. 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.

If one baby has a defect usually there is another defect.

- Prenatal or perinatal insults may either cause:

- Failure of normal CNS development.
- Tissue destruction. **It can be due to infection or toxins.**

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

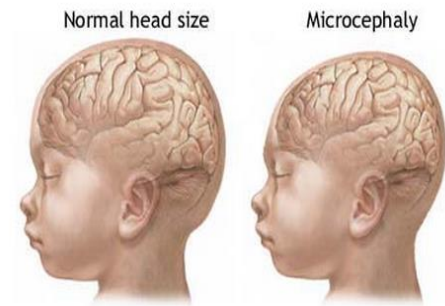
◇ CNS malformation can be caused by **Mutations** affecting molecules in pathways of **neuronal** and **glial**:

- Development.
 - Migration.
 - Connection.
- **Toxic** compounds and **Infectious agents** have teratogenic effects.

A) Forebrain Malformations:

The volume of brain may be:

1. Abnormally **large** (**Megalencepahly**).
2. **Small** (**Microencephaly**¹, **more common**). Microencephaly, is usually associated with a small head as well.



They can occur in a wide range of clinical settings, including:

- a. **Chromosomal abnormalities.**
- b. **Fetal alcohol syndrome.**
- c. **Human immunodeficiency virus 1 (HIV-1) infection acquired in utero.**

All causes are associated with:

1. A **decreased number of neurons** destined² for the cerebral cortex.
2. **Disruption of normal neuronal** migration and differentiation during development can lead to a disruption of the normal gyration and six-layered neocortical architecture.

- **Lissencephaly** (**Agyria**): كلها سموث مافي قايراي بالمره

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

- The cortex is abnormally thickened and is usually only four-layered.

The normal is six-layers.

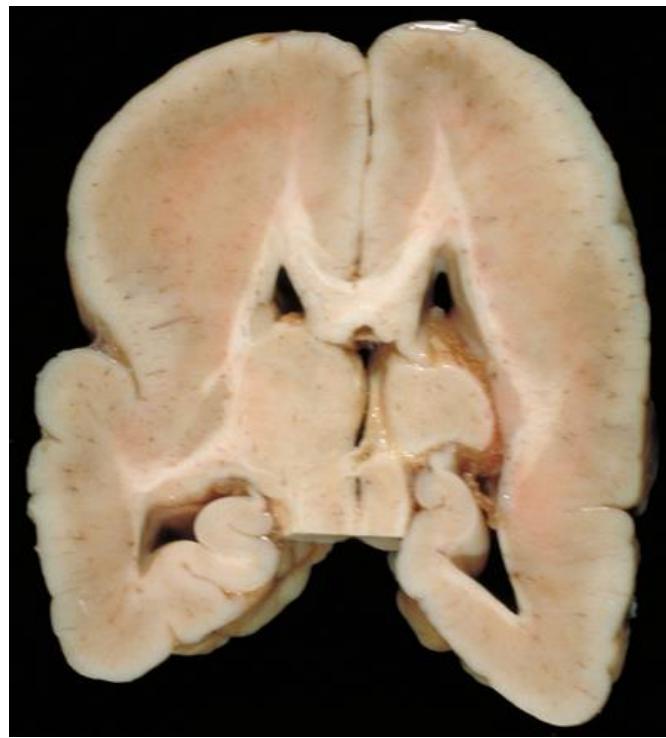
- **Single-gene defects** have been identified in some **cases of lissencephaly**.

¹ Microencephaly: small brain, Microcephaly: small head

² Prepared.

- Morphology:

- Cortical **sulci are absent except**, usually, 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.**

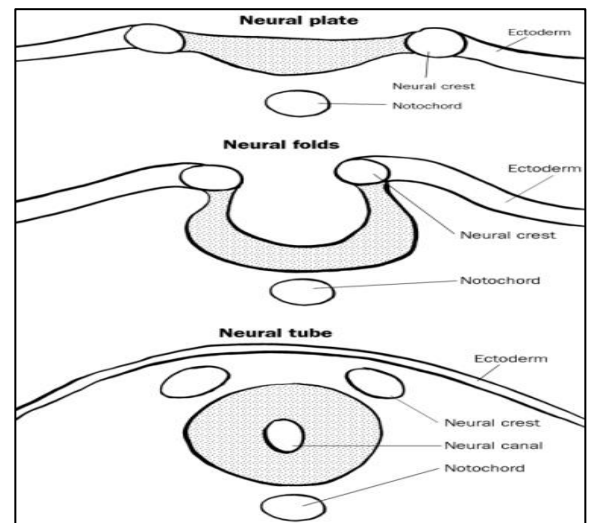


- Lack of sulci.
- Thick cortex and flat surface.
- Loss of sulci and gyri contour.

B) Neural tube defect: The ectoderm did not close.

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.



Every word is important!

- **Folate deficiency** during the **initial weeks** of gestation³ is a risk factor; prenatal vitamins are aimed, in part, at reducing this risk.

Pregnant woman must take Folic acid.

- The combination of **ultrasound and maternal** screening for **elevated α -fetoprotein** has **increased** the **early detection of neural tube defects.**

يرتفع هذا البروتين بدم الأم إذا كان البيبي عنده هذا النوع من الديقكتس.

³ Pregnancy.

- The overall recurrence risk in subsequent pregnancies is 4% to 5%.

Diseases associated with Neural Tube defects:

1- **Myelomeningocele**⁴ 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. (At the other end of the developing brain)

3- **Encephalocele**: is a diverticulum⁵ of malformed CNS tissue extending through a defect in the **cranium**

It can happen in small openings in the nose and around the ear.

- It most often involves the **occipital** region or the posterior fossa.

Myelomeningocele



Encephalocele (Extra)



Anencephaly



c) **Posterior Fossa Anomalies:** Could be: 1- Enviromintal. 2- Genetics.

The most common malformations in this region of the brain result in either **misplaced or absent cerebellum**. Typically, these are associated with **hydrocephalus**.



⁴ Myelo = Spinal cord, Meningo = Meninges, Cele = Herniation فتاق

⁵ An abnormal fluid filled sac.

The *Arnold-Chiari malformation*:

Chiari type II malformation Most common	Chiari type I malformation (Extra)
<p>Consist of:</p> <ul style="list-style-type: none"> • A small posterior fossa. • A misshapen midline cerebellum. • Downward extension of <i>vermis</i> through the foramen magnum. • Hydrocephalus. (because it close or Obstruct the aqueduct) • A lumbar myelomeningocele. <p style="text-align: right;">عادتها الدكتوراة ألف مرة:!</p>	<ul style="list-style-type: none"> • 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.

Hydrocephalus: Hydro: water. Cephalus: in the brain.

Is the accumulation of excessive CSF within the ventricular system.

- **Most cases** occur as a consequence of **impaired flow** or **impaired resorption of CSF**.

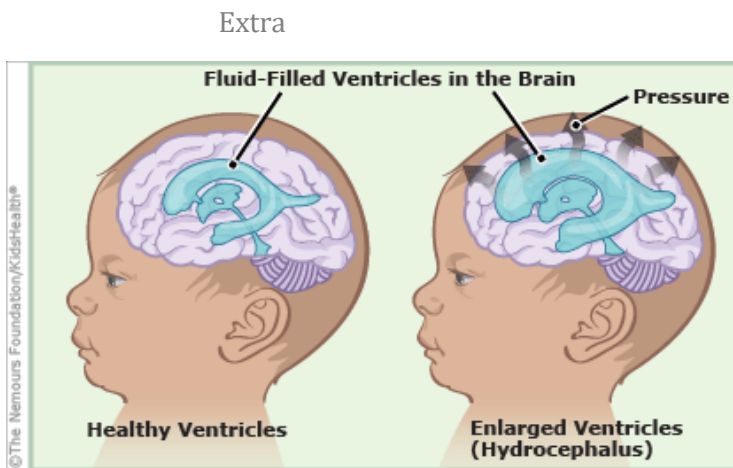
*تنسأل كثير!

- In rare instances (e.g., tumors of the choroid plexus), **overproduction of CSF** may be responsible.

- When hydrocephalus develops in infancy **before closure** of the cranial sutures → **enlargement of the head**. Which will lead to Macrocephaly, because they have flexible sutures.

- Hydrocephalus developing **after fusion** of the sutures → **expansion of the ventricles and increased intracranial pressure**, without a change in head circumference.

ما يكبر الهيد هنا لأن السوتشرز سگروا خلاص.



- Physiology of CSF:

- After being 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.

- Types of hydrocephalus:

a) *Noncommunicating hydrocephalus*: Focal. مطرح إنلارجد و مطرح لا، يعني فوق كبير و تحت لا

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.

- Most commonly seen with masses at the foramen of Monro or aqueduct of Sylvius.

يعني تسكر التدفق من اللاتيرال فينتركلز لتحت و نسّميه عادةً
"Flow abnormality"

b) *Communicating hydrocephalus*: Enlarged كله

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**:

- Obstruction of the **foramina of Monro**⁶ e.g. **colloid cyst**^{7*}.
- Obstruction of the third ventricle e.g. **pilocytic astrocytoma**.
- Obstruction of the aqueduct e.g. **aqueductal stenosis** or atresia⁸ and posterior fossa tumors.

*Very common, benign but can obstruct foramina of monro and lead to Death.

⁶ The interventricular **foramina** (or **foramina of Monro**) are channels that connect the paired lateral ventricles with the third ventricle at the midline of the brain.

⁷ It's a benign tumor but can cause death of patient.

- Obstruction of the foramina of Luschka or impairment of flow from the fourth ventricle (**Chiari malformation Type II**, meningitis, subarachnoid hemorrhage, posterior fossa tumors).
- Fibrosis of the subarachnoid space e.g. meningitis⁹, subarachnoid hemorrhage, meningeal dissemination of tumors.

3) **Defective filtration of CSF:** postulated¹⁰ for low-pressure hydrocephalus.

CSF is not absorbed, usually seen in patients in ICU.

*Homework

- Define:

❖ **Meningocele:**

Protrusion of the membranes of the brain or SC through a defect in the cranium or spinal column.

❖ **Polymicrogyria:**

Characterized by increased number of irregularly formed gyri that result in a bumpy surface.

❖ **hydrocephalus ex vacuo:**

An enlargement of cerebral ventricles and subarachnoid spaces, and is usually due to brain atrophy (as it occurs in dementias).

- What is the difference between microcephaly and microencephaly?

Microcephaly: Small head (skull).

Microencephaly: Small brain.

*Questions:

Q1: Myelomeningocele is mainly a defect associated with:-

A. Spinal cord.

B. Choroid plexus.

C. Vertebral column.

D. Anterior end of neural tube.

(C) Is the correct answer

⁸ Absence or abnormal narrowing of an opening.

⁹ Because it will cause inflammation, and this inflammation lead to granulation tissue (which is a fibrotic mass).

¹⁰ Assume.

Q2: 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 (negative -). 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.
- B. Decrease in the number of neurons.
- C. Hydrocephalus.
- D. Anencephaly.

(B) Is the correct answer

Q3: What is the most severe neural tube defect?

- A. Anencephaly.
- B. Meningocele.
- C. Encephalocele.
- D. Hydrocephalus.

(A) Is the correct answer

Q4: Colloid cyst tumor can cause which of the following conditions:

- A. Communicating hydrocephalus.
- B. Non-Communicating hydrocephalus.
- C. Defective filtration of CSF.
- D. Hypersecretion of CSF.

(B) Is the correct answer

Q5: If hydrocephalus develops in adults will lead to:

- A. Head shrinkage.
- B. Head enlargement.
- C. Narrowing of the ventricles.
- D. Increased intracranial pressure.

(D) Is the correct answer

Q6: What malformation can be associated with lumbar spina bifida?

- A. Anencephaly.
- B. Encephalocele.
- C. Arnold-chiari Type II.
- D. Arnold-chiari Type I.

(C) Is the correct answer

Q7: Neural tube defects are associated with an increase in which of the following proteins in maternal serum?

- A. S100 protein.
- B. Alpha-Fetoprotein.
- C. Beta-Fetoprotein.
- D. Gamma-Fetoprotein.

(B) Is the correct answer

Q8: All of the following are causes that could lead to obstructive Hydrocephalus except?

- A. Low-pressure hydrocephalus.
- B. Meningitis.
- C. Subarachnoid hemorrhage.
- D. Pilocytic astrocytoma.

(A) Is the correct answer

*Summary

Forebrain Malformation

Megaloencephaly	Microencephaly	Lissencephaly (agyria)
The volume of brain may be abnormally large.	brain is small and usually associated with a small head (more common). It can occur due to: 1-Chromosome abnormalities. 2-Fetal alcohol syndrome. 3- (HIV-1) infection acquired in utero. All causes are associated with a <u>decreased number of neurons</u> destined for the cerebral cortex.	Is characterized by an absence of normal gyration leading to a smooth-surfaced brain. The cortex is abnormally thickened and is usually only four-layered (normal is six). Sylvian fissure is intact There is a small amount of myelinated white matter between the abnormal cortex and the ventricles.

Neural Tube Defects

- They are **Most frequent (CNS) malformations.**
- Can be detected by elevated α -fetoprotein in amniotic fluid
- **Folate deficiency** during the initial weeks of gestation is a risk factor.

Myelomeningocele	Anencephaly	Encephalocele
An extension of CNS tissue through a defect in the vertebral column involving (Spinal cord + Meninges).	A malformation of the anterior end of the neural tube, with absence of the brain and top of skull.	Diverticulum of malformed CNS tissue extending through a defect in the cranium it most often involves the occipital region or the posterior fossa.
Occur most commonly in the lumbosacral region.		
Motor and sensory deficits in the lower extremities.		
Problems with bowel and bladder control.		
Infections extending from thin or ulcerated overlying skin.		

Posterior Fossa Anomalies.

Most common malformations in this region of the (brain) associated with hydrocephalus.

Arnold-Chiari malformation type II.

Hydrocephalus

Accumulation of excessive CSF

Causes:

- (Tumors of the choroid plexus)
- Obstruction of the foramina of Monro (colloid cyst)
- Obstruction of the 3rd ventricle (Pilocytic astrocytoma)

When hydrocephalus is in (infancy) **before closure of the cranial sutures** it causes **enlargement of the head.**

When hydrocephalus is in (adult) **after fusion of the sutures** it cause expansion of the ventricles and increased intracranial pressure.

Non-communicating hydrocephalus	communicating hydrocephalus
Portion of the ventricles enlarges while the remainder does not.	<u>All</u> of the ventricular system is enlarged. the cause is most often reduced reabsorption of CSF.
Commonly seen with masses at the foramen of Monro or aqueduct of Sylvius.	

"اللهم لا سهل إلا ما جعلته سهلاً و أنت تجعل الحزن إذا شئت سهلاً"



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