جامعة الملك سعود
King Saud University

Pathology
Teamwork 438

Lecture 7: Congenital malformations and 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 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

Black: original content
Red: Important
Blue: only found in boys slides

Dark orange: Doctor notes
Grey: Extra/Robbins
Pink: Only found in girls slides

Reviewed by Razan AlRabah & Ibrahim AlDakhil

Editing file

Lecture Content

Congenital Malformation

Forebrain Malformation

- Megalencephaly
- Microencephaly
- Lissencephaly

Neural Tube Defect

- Myelomeningocele
- Anencephaly
- Encephalocele

Posterior fossa Anomalies

- Arnold chiari syndrome

Hydrocephalus

- Definition
- CSF physiology
- Causes
- Types and locations

Congenital Malformation

Introduction

- The incidence of CNS malformation is estimated at 1% to 2%
- It gives rise to **mental retardation**, **cerebral palsy**, or **neural tube defect**.
- Malformation of the brain usually come with **several other birth defects**
- Because different part 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.

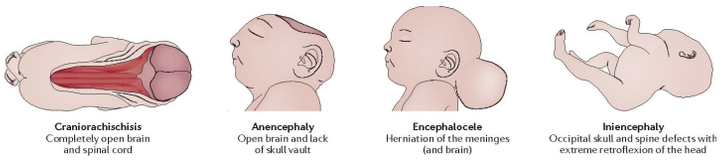
Etiology & pathogenesis

- The pathogenesis and etiology of many malformations remain unknown.
- However, it has **Genetic** and **Environmental** factor.

1. **Genetic factors:**
   - CNS malformation can be caused by Mutations affecting molecules in pathways of neuronal and glial:
     - Development
     - Migration recall that neurons can move from place to another.
     - Connection

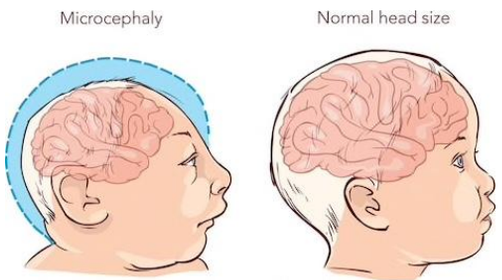
2. **Environmental Factors:**
   - Toxic compounds
   - Infectious agents

Forebrain Malformation



Megalencephaly

- The volume of the brain is abnormally **large**.
- Rare genetic disorder



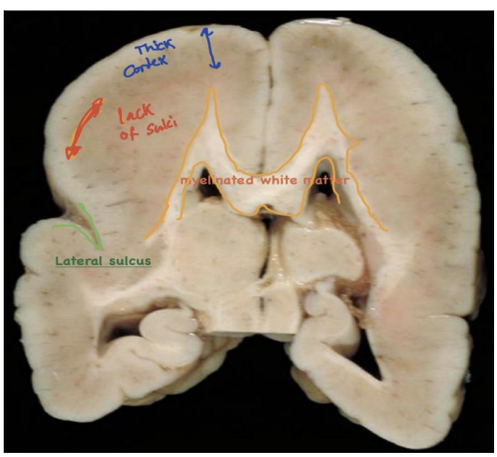
Microencephaly

- The volume of the brain is abnormally **small**.
- Usually associated with a small head (**microcephaly**)
- It is more common
- It occurs in a range of clinical settings **including:**
  - Chromosome abnormalities
  - Fetal alcohol syndrome
  - Human Immunodeficiency virus type-1 (HIV-1) and Zika virus infection acquired in utero.

- All of these causes lead to a disruption of the neuronal migration and differentiation.
- This causes less neurons going to the cerebral cortex.
- As well as, disruption of normal gyration and the architecture of the six-layered neocortical architecture.

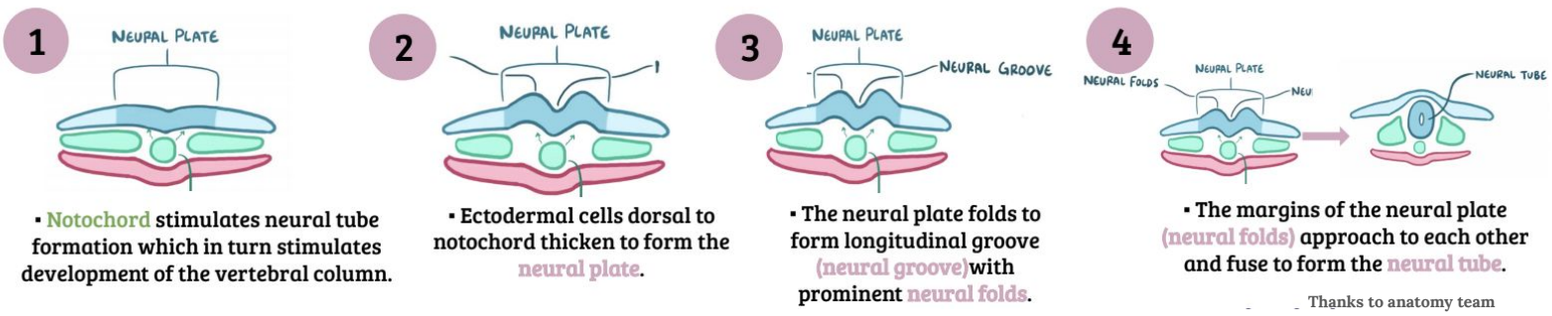
Lissencephaly (Agyria)

- Absence of normal gyration **except for the sylvian fissure**, a **smooth surfaced brain**.
- The cortex is **abnormally thickened** and is **only four layers** (one molecular and three neuronal).
  - The deepest layer is the thickest and most cellular. Made of cells that migrated from the ventricles but couldn't reach their destination.
  - Small amount of myelinated white matter between cortex and ventricle.
- Single-gene defects have been noted in some cases of lissencephaly.
- **Pachygyria;** a form of the disease which has more patchy involvement.



Embryo Recall: Neural Tube Defect (not important)

Stages of development:



1. ▪ Notochord stimulates neural tube formation which in turn stimulates development of the vertebral column.
2. ▪ Ectodermal cells dorsal to notochord thicken to form the neural plate.
3. ▪ The neural plate folds to form longitudinal groove (neural groove) with prominent neural folds.
4. ▪ The margins of the neural plate (neural folds) approach to each other and fuse to form the neural tube.

Thanks to anatomy team

Spina Bifida

Occulta

- Skin overlying it is intact.
- Sometimes covered by a tuft of hair.

Manifesta (cystic)

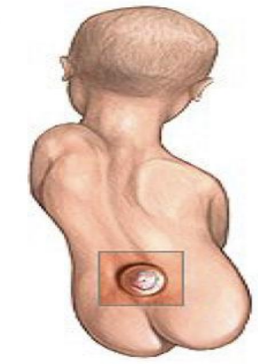
- Forebrain Spina bifida with meningocele
- **Spina bifida with meningomyelocele**
- Spina bifida with myeloschisis

You will only study these two, the rest you remember from embryo.

Note:
You will also learn anencephaly and encephalocele, however they are Neural tube defects not part of spina bifida.

Neural Tube Defect

Introduction



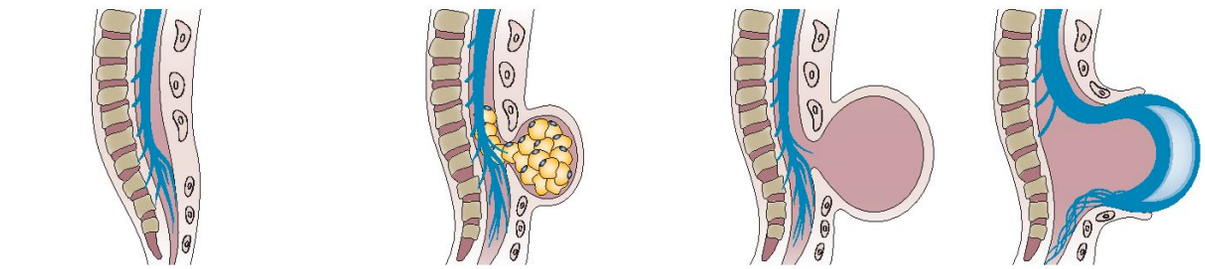
- Failure of a portion of the neural tube to close, or reopening after successful closure may lead to one of several malformations.
- All these malformations are **characterized by** abnormalities involving some combination of:
  - Neural tissue.
  - Meninges.
  - Overlying bone or soft tissues
- The most common defects involve the posterior end of the neural tube, from which the spinal cord forms.
- Collectively, neural tube defects are the most frequent CNS malformations

Risk Factors

- **Folate deficiency** during the initial weeks of gestation.
  - Prenatal vitamins are aimed, in part, at reducing this risk by up to 70%.
- The overall recurrence risk in subsequent pregnancies is 4% to 5%.

Diagnostic methods

- The combination of **ultrasound** and maternal screening for elevated **α-fetoprotein** *in serum and/or amniotic fluid* has increased in the early detection of neural tube defects.
- Increased maternal α-fetoprotein (AFP) in:
  - Meningocele.
  - Myelomeningocele.
  - But **not spina bifida occulta.**



Spina bifida occulta
Closed asymptomatic NTD in which some of the vertebrae are not completely closed

Closed spinal dysraphism
Deficiency of at least two vertebral arches, here covered with a lipoma

Meningocele
Protrusion of the meninges (filled with CSF) through a defect in the skull or spine

Myelomeningocele
Open spinal cord (with a meningeal cyst)

Neural Tube Defect

Diseases associated with Neural Tube Defects:

01

Spina bifida occulta

- **Asymptomatic** bone defect, caused by failure of fusion of the halves of vertebral arches.
- Skin overlying is intact, sometimes covered by a tuft of hair.

02

Myelomeningocele[1]

- Is an extension of CNS tissue through a defect in the vertebral column.
- Most commonly Occur in the **lumbosacral region.**

Symptoms

- Patients have **motor** and **sensory** deficits in the **lower** extremities.
- 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**.

03

Anencephaly[2]

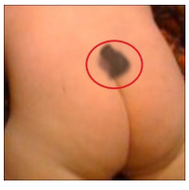
Anencephaly is a malformation of the **anterior end** of the neural tube, with absence of the brain and top of skull.

04

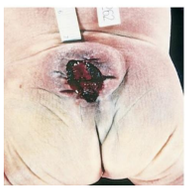
Encephalocele

- 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.

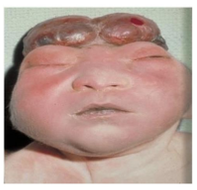
Spina bifida occulta



Myelomeningocele



Anencephaly



Encephalocele

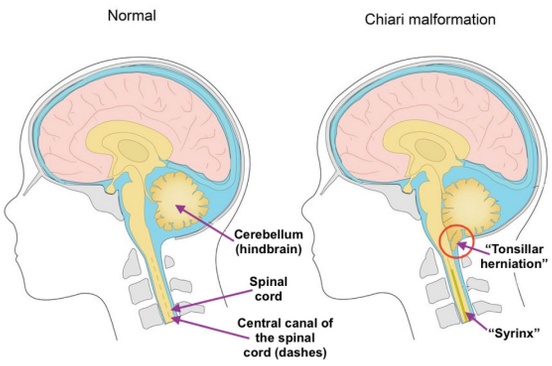
1- Meningo (meninges) , Myelo (spinal cord), Cele (hernia, cavity) ; it's a protrusion of meninges and spinal cord through a defect in the spine.
2- Encephaly (Brain), cephaly (head or skull)

Posterior Fossa Anomalies

- The most common malformations in posterior fossa result in either **misplaced or absent cerebellum.**
- Typically, these are associated with **hydrocephalus**

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

- Small posterior fossa
- Misshapen midline cerebellum
- Downward extension of vermis through the foramen magnum. Herniation causing 2ry hydrocephalus
- Hydrocephalus
- Lumbar myelomeningocele



Chiari type I malformation (Extra)

- Milder form, Low-lying cerebellar tonsils extend through the foramen magnum at the base of the skull.
- This can lead to partial 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

- Refers to the **accumulation of excessive CSF** within the ventricular system (hydro=water,cephalus=brain) .

Physiology of CSF: 🚃

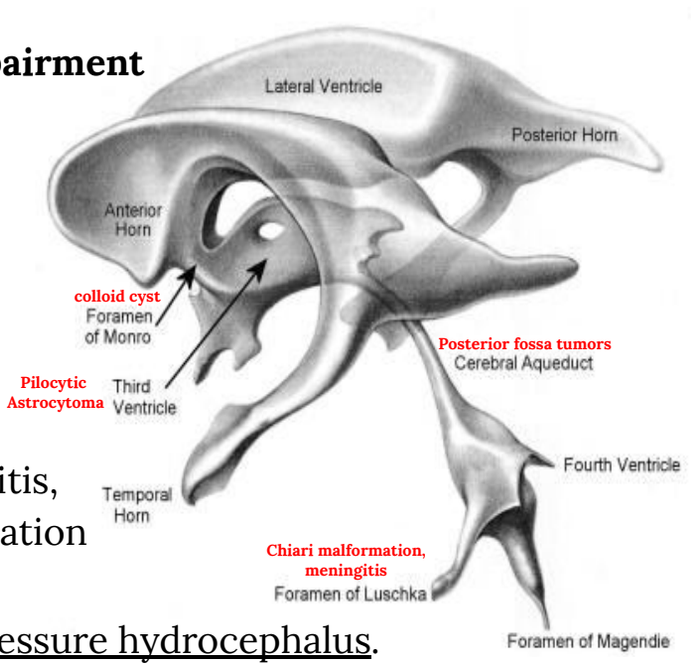
CSF is produced in the choroid plexus and exits the ventricular system through foramina of Luschka and Magendie → CSF then fills the subarachnoid space to cushion the CNS → The arachnoid granulations are responsible for the resorption of CSF → The balance between CSF generation and resorption keeps the volume of this fluid stable

What are the possible causes ?

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

1. **Hypersecretion of CSF**: e.g. choroid plexus tumor. (rare)

2. **Obstructive hydrocephalus** :
   - Obstruction of the **foramina of Monro**[1] 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** by:
     - Chiari malformation
     - **Meningitis**
     - **subarachnoid hemorrhage**
     - posterior fossa tumors



   - Fibrosis of the **subarachnoid space** e.g. meningitis, subarachnoid hemorrhage,meningeal dissemination of tumors .

2. **Defective filtration of CSF**: <u>postulated for low-pressure hydrocephalus</u>.

1- between the lateral ventricles and the third ventricle

Hydrocephalus

1 **Hydrocephalus in infancy**
Before closure of cranial suture

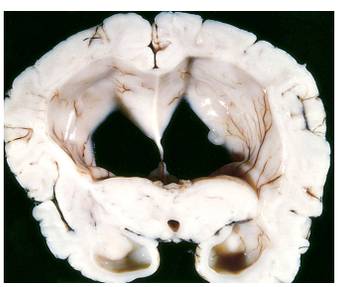
Enlargement of the head

2 **Hydrocephalus after fusion of suture**

Ventricles expand and increase intracranial pressure without a change in head circumference

Types of hydrocephalus

- **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 remainde does not. (Most commonly seen with masses at the foramen of **Monro** or **aqueduct of Sylvius**).



Dilated lateral ventricles seen in a coronal section through the mid-thalamus.

- **Communicating hydrocephalus**
  In communicating hydrocephalus all of the ventricular system is enlarged; here the cause is most often **reduced resorption of CSF**.

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:

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

Summary

Congenital Malformation		
Forebrain malformation	**Megalencephaly**	- The volume of brain is abnormally enlarged. - Less common and associated with rare genetic disorders.
	Microencephaly	- Brain is small in volume and usually associated with small head (more common). It can occur due to: **1-** Chromosomal abnormalities **2-** Fetal Alcohol syndrome **3-** HIV-1 - All causes are associated with decreased number of neurons.
	Lissencephaly	- Abnormal Absence of gyration and smooth-surfaced brain. - The cortex is abnormally thickened and usually four layers. - Absence of sulci except for sylvian sulcus. - There is a small amount of myelinated white matter between the ventricles and the Abnormal cortex.
Neural tube defect	**Myelomeningocele**	- The **most common** in CNS malformation. - Extension of CNS tissue out of the spinal cord. - Associated with elevated **alpha-fetoprotein and folate deficiency.** - Affect lumbosacral region result in dysfunctioning in lower extremities and bladder.
	Anencephaly	- Failure of fusion of Anterior end of neural tube
	Encephalocele	- A diverticulum of malformed CNS tissue extending from a defect in the cranium. - Usually involve occipital fossa and occipital region.
Posterior Fossa Anomalies		- It usually result in misplaced or absent cerebellum. - Associated with Arnold chiari type II ○ **1-Misshapen cerebellum** ○ **2-Small posterior fossa** ○ **3-Secondary hydrocephalus** ○ **4-lumbar myelomeningocele** - Downward extension of vermis into the foramen magnum.

Hydrocephalus	
Types	**Non-communicating** (presence of obstruction e.g masses in foramen of monro) **Communicating** hydrocephalus (impaired resorption) Or can be : - Before infancy and closure of sutures (enlarged head). - After fusion of sutures (no change in head circumference).
Causes & areas	- Hypersecretion e.g **tumor of choroid plexus** - Obstruction of foramen of monro e.g **colloid cyst** - Obstruction of third ventricle e.g **pilocytic astrocytoma**

Quiz

Q1 :In general, the incidence rate of congenital malformation of CNS is considered which of the following?

A) common
B) rare
C) Medium well
D) Determined only numerically

Q2: Which one of the following malformation is associated with disrupted migration of primitive neuron cells during the early stages of development of CNS?

A) microencephaly
B) Megalencephaly
C) Spina bifida occulta
D) Polymicrogyria

Q3 : A thick cortex with abnormal neuronal layering is seen in?

A) pachygyria
B) Megalencephaly
C) Microencephaly
D) All of above

Q4 : The most common cause of obstructive hydrocephalus in children?

A) Tuberous sclerosis
B) Posterior fossa tumors
C) Meningitis
D) Glioma

Q5 : Which one of the following is most common CNS anomaly?

A) Anencephaly
B) Arnold chiari II
C) Posterior end of neural tube defect
D) Microencephaly

Q6: Which term describe an irregular increase in numbers of gyri:

A) polymicrogyria
B) Holoprosencephaly
C) Chiari type I
D) Pachygyria

Q7: Which one of the following features is associated with type II chiari malformation?

A) Asymptomatic
B) Presence of herniation
C) Association with syringomyelia
D) Primary hydrocephalus

Q8: Which one of the following tumors are associated with third ventricle obstruction?

A) Ependymoma
B) Medulloblastoma
C) Pilocytic astrocytoma
D) Tumors of choroid plexus

1-A 2-A 3-A 4-B 5-C 6-A 7-B 8-C

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Thank you