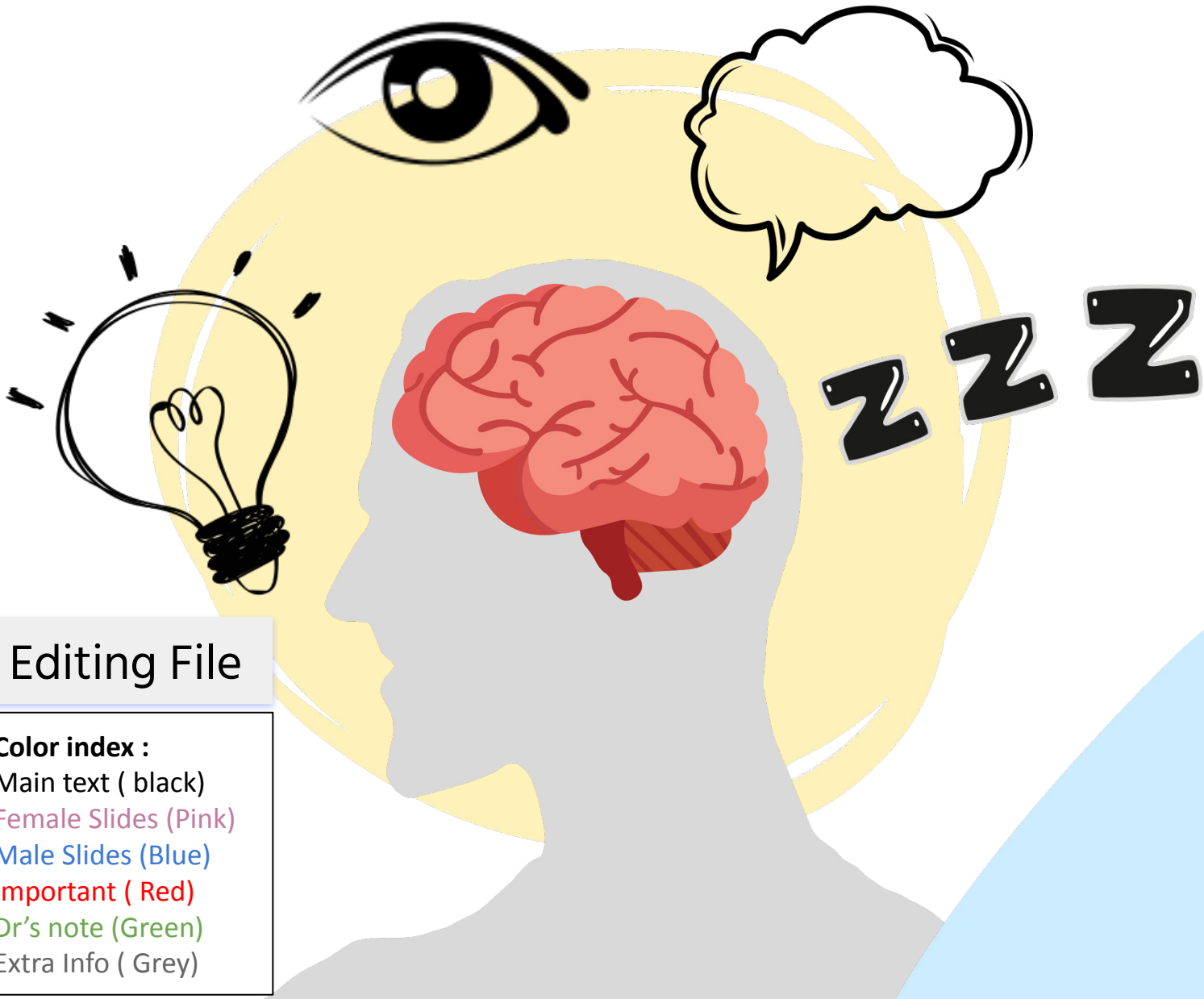
Congenital Malformations and Hydrocephalus



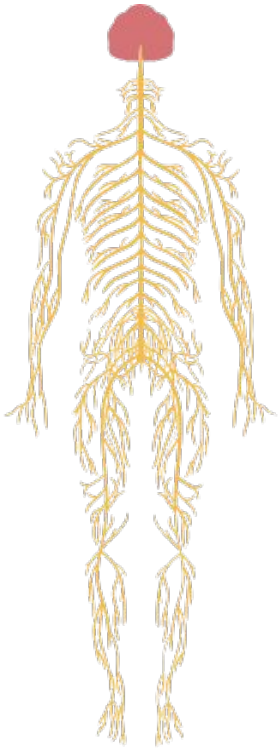
Editing File

Color index :
Main text (black)
Female Slides (Pink)
Male Slides (Blue)
Important (Red)
Dr's note (Green)
Extra Info (Grey)

Objectives

- Understand the mechanisms that lead to hydrocephalus
- List and classify the causes of hydrocephalus.
- Know the common types of congenital malformations and their pathological features.
- Correlate normal CNS development with the classification of congenital CNS malformations.
- Appreciate the role of folate deficiency as an etiological factor in neural tube defects and the role of alpha fetoprotein measurement in antenatal diagnosis of neural tube defects.

If you want to read the lecture from Robbins [click here]



Overview

Osmosis Vid

Congenital Malformation

Neural Tube Defect

- Spina Bifida Occulta
- Myelomeningocele
- Anencephaly
- Encephalocele

Forebrain Malformation

- Megalencephaly
- Microencephaly
- Lissencephaly
- Polymicrogyria
- Arrhinencephaly
- Holoprosencephaly

Posterior Fossa Anomalies

- Type 1 Chiari malformation
- Type 2 Chiari malformation
- Dandy-Walker malformation

Hydrocephalus

Types

- Noncommunicating Hydrocephalus
- Communicating Hydrocephalus

Causes

- Hypersecretion of CSF
- Defective filtration of CSF
- Obstructive hydrocephalus

Congenital Malformations

Introduction

The incidence of CNS malformations is estimated at 1% to 2% and they are more common in the setting of multiple birth defects.

Clinically they give rise to mental retardation, cerebral palsy, or neural tube 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. Injury in the first stages of pregnancy will lead to more severe lesion and phenotypes.

Prenatal or perinatal insults may interfere Cause :
1. failure of normal CNS development.
2. Cause tissue damage & destruction

Causes

Although the pathogenesis and etiology of many malformations remain unknown, however, it has multiple factors:

Genetic Factors

Mutations affecting genes that regulate the :
1. differentiation & development
2. maturation & migration
3. intercellular communication & connection

of neurons or glial cells.

Environmental Factors

1. Toxic compounds (chemicals).
2. Infectious agents.

Neural Tube Defects

Introduction

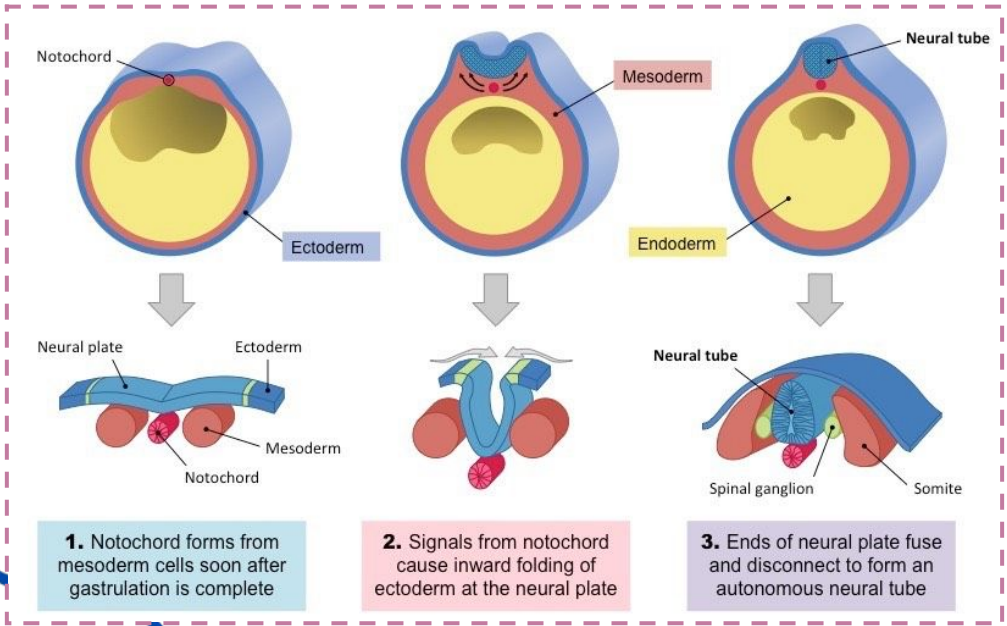
Neural tube defects are the most frequent CNS malformations.

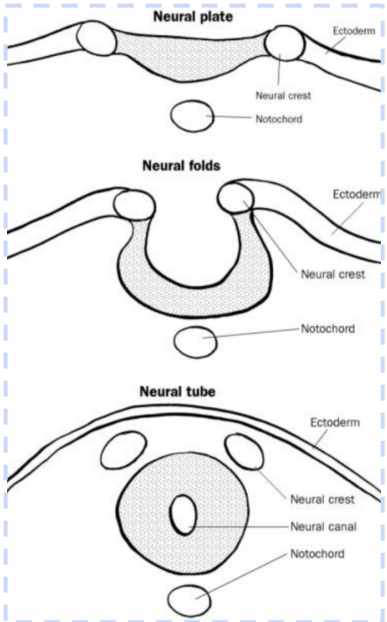
One of the earliest steps in brain development is the formation of the neural tube, which gives rise to the ventricular system, brain, and spinal cord.

Partial failure or reversal of neural tube closure may lead to several 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

All are characterized characterized by abnormalities involving neural tissue, meninges, and overlying bone or soft tissues

Brief Embryology





Neural Tube Defects

Risk Factors

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

Folate Deficiency

Folate deficiency during the first trimester (initial weeks of gestation)sharply increases risk through uncertain mechanisms and represents an important opportunity for prevention.

- prenatal vitamins are aimed, in part, at reducing this risk
- Administration of folate to women of child-bearing age reduces the incidence of neural tube defects by up to 70%.

Elevated maternal α-Fetoprotein (AFP)

Increased maternal α-fetoprotein (AFP) in serum and/or amniotic fluid in anencephaly, meningocele, or myelomeningocele but **not spina bifida occulta**. The combination of ultrasound imaging studies and maternal screening for elevated α-fetoprotein has increased early detection of neural tube defects.

Clinical Note

Major Risk factors in mothers that would cause neural tube defect

- Diabetes
- Obesity
- Medications : especially anti seizures medications for example anti epileptic drugs

Deep Focus Question

Pregnant lady with epilepsy what is the best drug for her condition ?

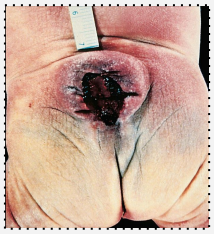
A. Lamotrigine
B. Valproate
C. Phenytoin
D. She should stop taking drugs !!

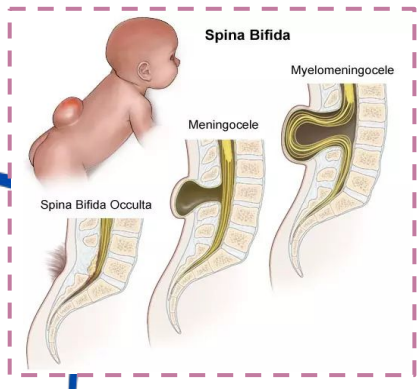
Answer: A , Pharmacology lecture

Neural Tube Defects

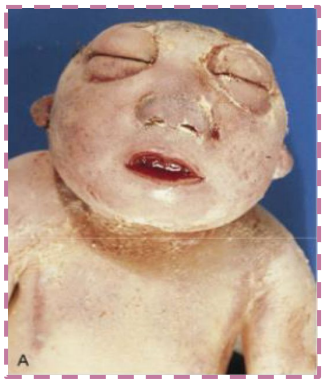
Osmosis Vid

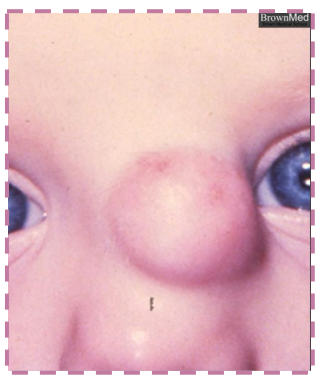
Types

Affecting the spinal cord	**spina bifida** [1]	◦ 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	
		Spina Bifida occulta	Asymptomatic bony defects
		Meningocele	protrusion of sac containing meninges & CSF (without the nerves root)
		Myelomeningocele 	◦ Is an extension of CNS tissue through a defect in the vertebral column that occurs most commonly in the **lumbosacral** region. ◦ **Symptoms:** 1. is derived from the abnormal spinal cord in this region, and are often compounded by infections extending from thin or ulcerated overlying skin 2. patients have motor and sensory deficits in the lower extremities & problems with bowel and bladder control.
Affecting the brain	**Anencephaly** [2]	◦ Is a malformation of the **anterior** end of the neural tube that leads to the absence of the forebrain and the top of the skull. ◦ Varying amounts of posterior fossa structures may be present.	
	Encephalocele [3]	◦ 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. ◦ When it occurs anteriorly, brain tissue may extend into the sinuses.	



[1]


[2]



[3]

Forebrain Malformations

Micronencephaly describes a group of malformations in which the volume of the brain is too small; usually its associated with a small head as well as (microcephaly).

Causes include:

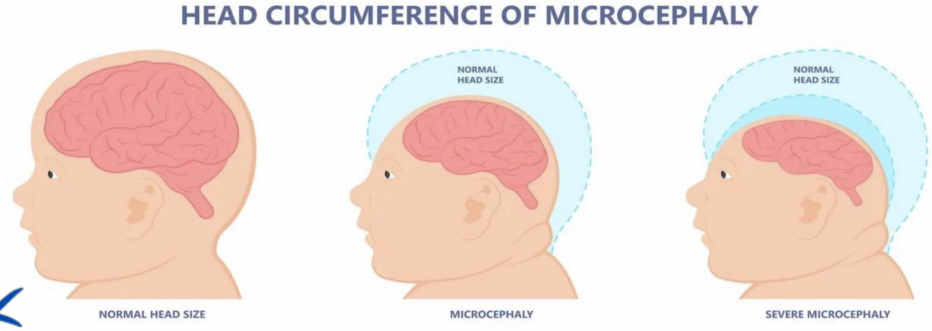
- chromosome abnormalities
- **fetal alcohol syndrome**
- Human immunodeficiency 1 **(HIV-1)** and Zika virus infections acquired in utero
- All causes are associated (unifying feature) with a **decreased number of neurons destined for the cerebral cortex.** Disruption of normal neuronal migration and differentiation during development can lead to a disruption of the normal gyration and six-layered neocortical architecture

Megalencephaly

- The volume of the brain may be abnormally large.
- Excessive brain volume that is always associated with a large head, is far less common and is mostly associated with rare genetic disorders.

Microcephaly

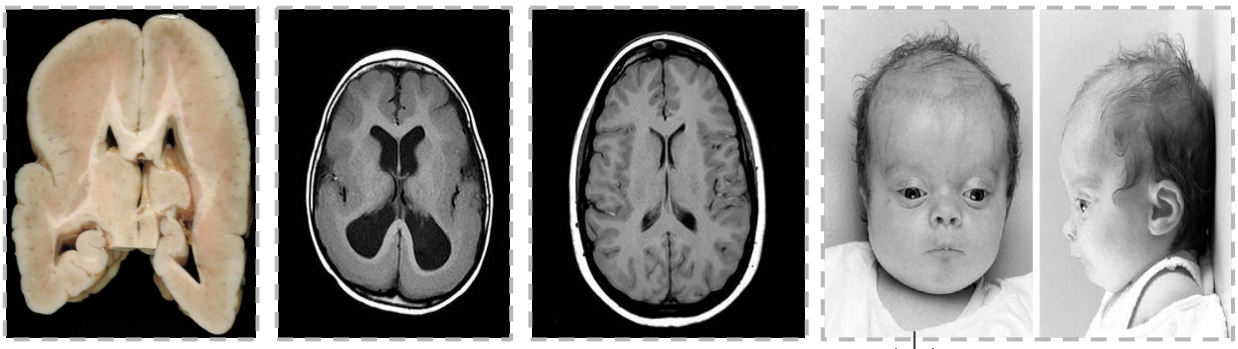
- Describes the group of malformations in which the volume of brain is too small.
- More common and is usually associated with a small head as well.



Forebrain Malformations Cont.

Lissencephaly

- Loss of gyri (Agyria) or in case of more patchy (partial) involvement
- Increased number of **irregularly formed gyri** (polymicrogyria)
- 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
- **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



OB \ GYN Note

Abnormalities usually take place in the 4th week , at that time the mother may not know she is pregnant & doesn't take the folic acid supplement so as precaution folic acid is embedded in breakfast cereals

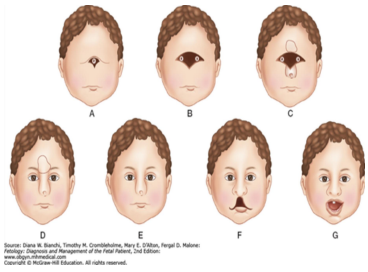
Extra INFO

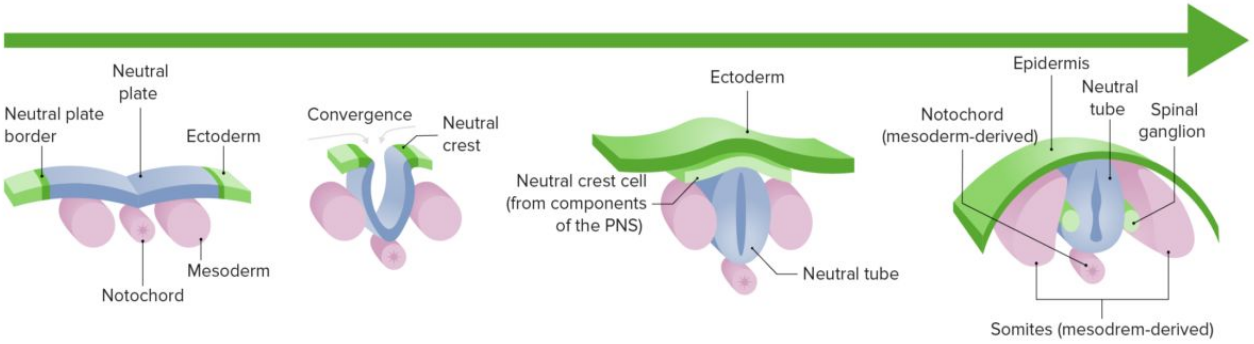
Forebrain Malformations are seen in trisomy 13 patau syndrome

Forebrain Malformations Cont.

Holoprosencephaly

- Characterized by disruption of normal midline patterning
- Mild forms show absence of the olfactory bulbs and related structures (arrhinencephaly)
- In severe forms, the brain is not divided into hemispheres or lobes, and there may be facial midline defects such as cyclopia.





Deep Focus Question

A failure of the neural folds to close in time can prevent the vertebrae from forming properly but not cause displacement of nervous tissue or the dura mater. How would this congenital defect be classified?

A. Spina bifida occulta
B. Meningocoele
C. Anencephaly
D. Microcephaly

Answer: A

Deep Focus Question

What information can an anatomic screen provide?

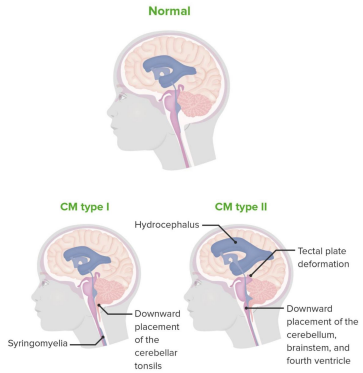
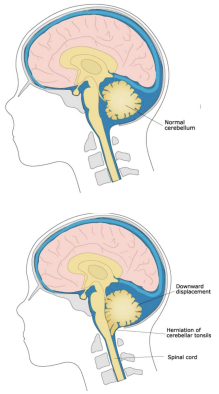
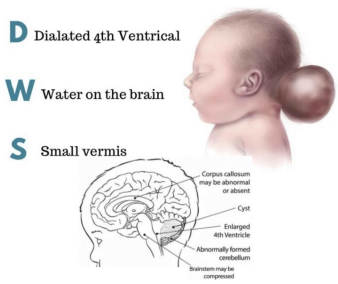
A. Confirmation of whether or not the baby will be vaginally delivered
B. Possibility of the baby having Down Syndrome
C. Diagnosis of the baby having spina bifida
D. Indication of the baby having anatomical and genetic abnormalities

Answer: A

Posterior Fossa Anomalies

Osmosis Vid

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

-	Description	Picture
Chiari type I: FEMALES SLIDES	• Far milder • Has low-lying cerebellar tonsils that extend through the foramen magnum • Excess tissue in the foramen magnum results in partial obstruction of CSF flow and compression of the medulla • Symptoms of headache or cranial nerve deficits	
Arnold-Chiari Malformation (Chiari Type II Malformation) (Males' Dr.: the only example included in your curriculum)	• combines a small posterior fossa with a **misshapen** midline cerebellum • **Downward extension of vermis through the foramen magnum** • **Hydrocephalus** • Lumbar myelomeningocele typically are also present. (greater complexity with increased pressure)	
Dandy-Walker Malformation FEMALES SLIDES	characterized by an enlarged posterior fossa, absence of the cerebellar vermis, and a large midline cyst (water in the brain)	

Cerebrospinal Fluid (CSF)

1 produced by the choroid plexus within the ventricles

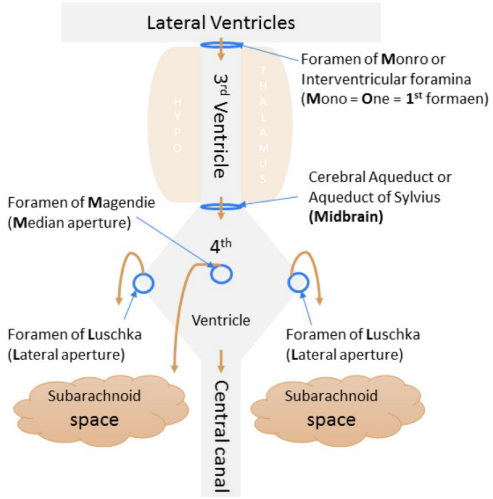
2 cerebrospinal fluid (CSF) circulates through the ventricular system

3 exits through 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

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



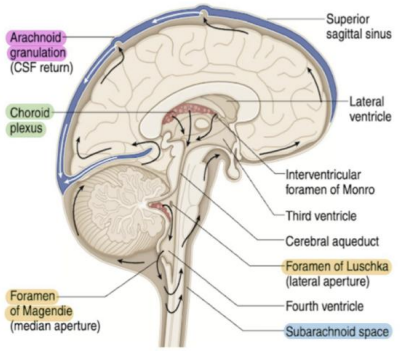


Figure III-3-2. Sagittal Section of the Brain

interventricular foramen of Monro cerebral aqueduct
Lateral ventricles → third ventricle → fourth ventricle → subarachnoid space
(via foramina of Luschka and foramen of Magendie)

Deep Focus Question

The failure of prosencephalon to develop into two hemispheres is known as...

A. diencephalon.
B. ...telencephalon.
C. ...anencephaly.
D. ...holoprosencephaly.

Answer: D

Deep Focus Question

Neurulation takes place in which of the following time periods?

A. Third trimester
B. Early in the second trimester
C. First week
D. Three to four weeks

Answer: D

HYDROCEPHALUS

Definition

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

If hydrocephalus develops in:

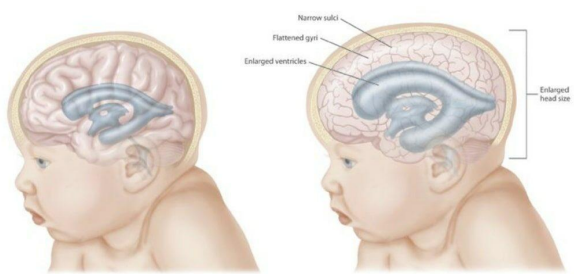
Infancy	Before closure of cranial sutures	Head is **enlarged**
Adults	After fusion of cranial sutures	Expanded ventricles and ICP ↑ but NO change in head circumference

Deep Focus Question

What is TRUE regarding hydrocephalus?

A. It cause an expansion of the ventricular system.
B. It is due to increasing the cortex mass.
C. There are 3 major types; communicating, non-communicating, and mixed.
D. It is due to increased absorption of CSF.
E. It is due to decreased production of the CSF.

Answer: A



HYDROCEPHALUS

Causes

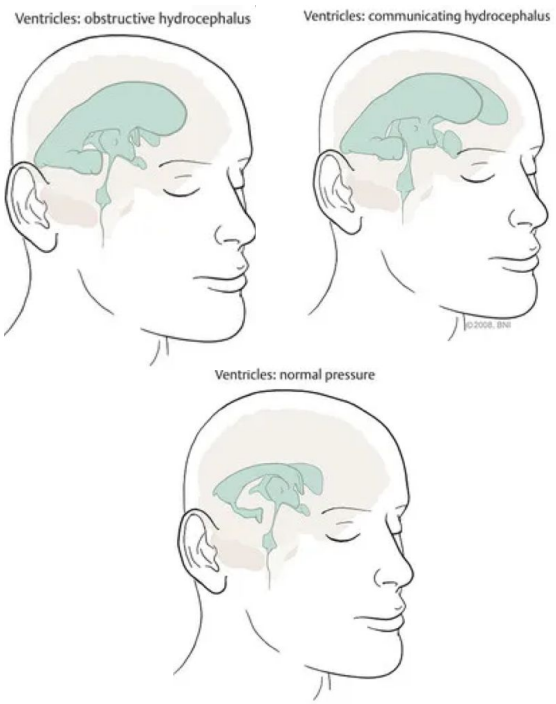
Hypersecretion of CSF e.g.choroid plexus tumor

Defective filtration of CSF (low-pressure hydrocephalus)
trauma, infection(not properly understood)

Obstructive hydrocephalus
- Obstruction of the foramen 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** (absence) and posterior fossa tumors
-Obstruction of the foramina of Luschka or impairment of flow from the fourth ventricel e.g (Chiari malformation, meningitis, subarachnoid hemorrhage, posterior fossa tumors)
- Fibrosis of the subarachnoid space e.g. meningitis, subarachnoid hemorrhage, meningeal dissemination of tumors

Types

Non-Communicating	Communicating
There is a localized obstacle to the flow of CSF within the ventricular system	The entire ventricular system is enlarged.
ONLY a portion of the ventricles enlarges while the remainder does NOT	usually caused by reduced CSF absorption.
e.g., mass obstructing foramen of Monro or compressing the cerebral aqueduct.(Sylvius)	—



FEMALES SLIDES

HYDROCEPHALUS EX VACUO

It is a compensatory increase in CSF volume (hydrocephalus ex vacuo) which occurs secondary to a loss of brain volume from any underlying cause (e.g., infarction, neurodegenerative disease).

In such settings, the hydrocephalus merely reflects the primary disorder and is of no clinical significance.

Deep Focus Question

What are the classic neuroimaging findings of normal pressure hydrocephalus?

A. Cortical atrophy with ventricular enlargement
B. Ventriculomegaly in the absence of atrophy
C. Atrophy of the corpus callosum and scattered white matter enhancement
D. Periventricular enhancement (Dawson fingers)

Answer: B

Deep Focus Question

Which of the following would be a cause of hydrocephalus?

A. Aqueductal block.
B. Decreased CSF production
C. Decreased irrigation of the brain
D. Diffuse axonal injury

Answer: A

Deep Focus Question

A disturbance in which of the following would NOT contribute to the development of hydrocephalus?

A. Absorption of CSF
B. Biochemical composition of CSF
C. Flow of CSF
D. Communication between ventricles

Answer: B

Keywords

Spina bifida : Due to Folate deficiency	occulta	• bony defect • Normal α-fetoprotein
	Myelomeningocele	• extension of CNS tissue • lumbosacral region. • infections & ulceration • Motor and sensory deicits • elevated α-fetoprotein
	Meningocele	• protrusion of sac • Contain meninges & CSF • elevated α-fetoprotein
Anencephaly	• anterior end of the neural tube malformation • absence of the forebrain & the skull	
Encephalocele	• extension of CNS • defect in the cranium . • occipital region or the posterior fossa.	
Forebrain Malformations : Due to : -chromosome abnormalities -fetal alcohol syndrome --(HIV-1) and Zika virus	Megalencephaly	• Large head
	Microencephaly	• Small head
	Lissencephaly	• loss of gyro • Smooth surface of the brain
	Holoprosencephaly	• Undivided hemispheres • absence of the olfactory bulb
Posterior Fossa Anomalies	Arnold Chiari Type II	• Downward extension of vermis • Hydrocephalus • Lumbar myelomeningocele
	Arnold Chiari Type I	• low-lying cerebellar tonsils
	Dandy-Walker Malformation	• enlarged posterior fossa • absence of the cerebellar vermis • large midline cyst
Hydrocephalus	• head enlargement (infant) , increase ICP (adults) • Hypersecretion Or Defective filtration of CSF Or Obstruction • Non Communicating : localized obstacle eg.atresia of Sylvius • Communicating : ventricular system is enlarged	

MCQ

Elevated maternal α-fetoprotein In serum is an indication of?

A- Myelomeningocele

B- Multiple sclerosis

C- Astrocytoma grade III

D- Hydrocephalus

Which of the following pathological CNS findings is consistent with Arnold chiari disease?

A- Agenesis of the corpus callosum

B- Lissencephaly

C- Downward displacement of medulla and cerebral tonsils

D- Microcephaly

A 2 year old baby came to the ER suffering from myelomeningocele, hydrocephalus, small posterior fossa , what is the most likely anomaly?

A- Chiari I

B- Chiari II

C- Dandy walker

D- Microcephaly

Which of the following is the most frequent CNS malformation?

A- Posterior fossa anomalies

B- Arnold-Chiari

C- Hydrocephalus

D- Neural tube defects

1-A / 2-C / 3-B / 4-D

MCQ

A newborn has a Frog-like appearance which is absence of the forebrain and the top of the skull , which of the following

A- Encephalocele

B- Anencephaly

C- Spina bifida

D - Hydrocephalus

Which of the following is associated with arnold chiari type 2 malformation?

A- Anencephaly

B- Lumbar myelomeningocele

C- Anterior anencephaly

D- Meningocele

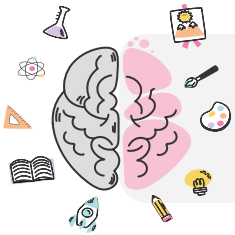
Following a cesarean section delivery, a newborn was found to have herniated of spinal cord tissue through sacral skin, radiology showed two vertebral defects.Which of the following are associated with newborn condition?

A- Arnold chiari malformation

B- Myelomeningocele

C- Spina bifida occulta

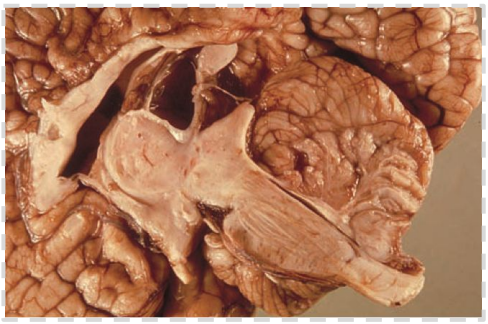
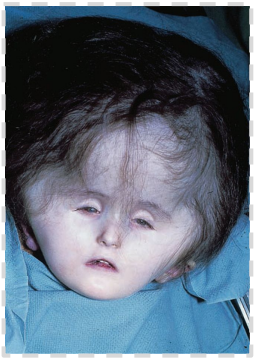
D- Hydrocephalus



Need a SUMMARY ? Click here

1- B / 2- B / 3- B

Cases

1.A female neonate is noted at birth to have a gross deformity of her lower back. Examination of the subcutaneous lesion reveals disorganized neural tissue with entrapment of nerve roots. What is the appropriate diagnosis?			
A.Meningocele	B.Meningomyelocele	C.Spina bifida occulta	D.Syringomyelia
2.The parents of the neonate described in Question 1 ask about the risks for similar birth defects in their future offspring. You mention that supplementation of the maternal diet can reduce the incidence of neural tube defects. What is this important dietary supplement?			
A.Folic acid	B.Niacin	C.Thiamine	D.Vitamin B6
3.A male neonate is noted at birth to have paralysis of the lower limbs. The infant fails to thrive and expires. The brainstem and cerebellum are examined at autopsy (shown in the image). What is the diagnosis? 			
A.Anencephaly	B.Arnold-Chiari malformation	C.Holoprosencephaly	D.Lissencephaly
4.A female neonate is noted to have a pronounced enlargement of her head (shown in the image). She develops convulsions. MRI reveals excessive accumulation of cerebrospinal fluid, ventricular enlargement, and atrophy of the cerebral cortex. This developmental birth defect was most likely caused by which of the following mechanisms of disease? 			
A.Atresia of the aqueduct of Sylvius	B.Birth trauma	C.Congenital brain tumor	D.Oligohydramnios

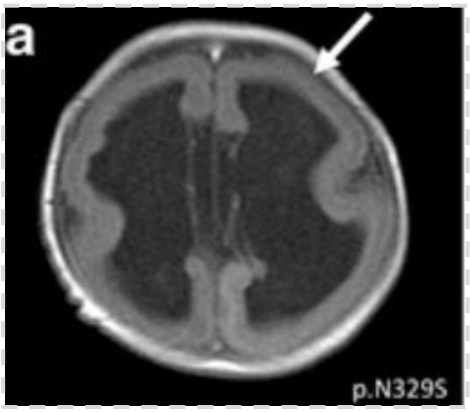
1-B / 2-A / 3-B / 4-A

NEED EXPLANATION ? CLICK HERE

Cases

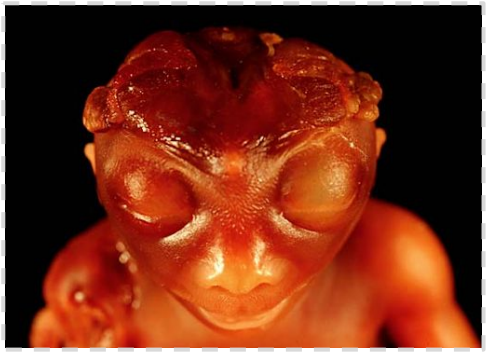
EXTRA CASES REQUIRE EXTRA INFO

1.A 6-month-old infant boy is brought to the pediatrician by his mother. The patient's mother delivered the child at home and did not receive consistent prenatal care. The patient's weight and head circumference are <5th percentile. An examination of the head is consistent with microcephaly. He is noted to have severe developmental delay with attainment of few milestones in speech, gross motor, and fine motor development. The infant cannot roll over or lift his head. An MRI of the brain is obtained and shown :



A.Dandy-Walker syndrome	B.Holoprosencephaly	C.Anencephaly	D.Lissencephaly

2.An 18-year-old woman, gravida 1, para 1, comes to the labor and delivery unit in active labor. She did not receive prenatal care. The estimated gestation age is 25 weeks based on last menstrual period. The mother did not take prenatal vitamins. She did not use tobacco, alcohol or illicit drugs during the pregnancy. Twenty minutes later, she gives birth to a stillborn male. An autopsy is performed and reveals the following: A defect in which of the following processes during embryogenesis most likely led to this condition?



A.Failure of fusion of the lateral palatine shelves	B.Failure of the facial processes to fuse	C.Failure of neuropore to close	D.Failure of neural crest cell migration

3.A 23-year-old woman comes to the labor and delivery unit in active labor. An hour later, she gives birth to a stillborn infant. The patient states that she did not receive consistent prenatal care. An autopsy of the infant reveals cyclopia and cleft palate. Examination of the brain shows fused cerebral hemispheres. This condition was most likely caused by failure of differentiation of which of the following anatomical structures?

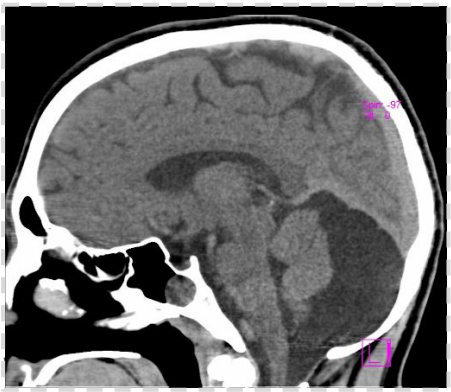
A.Diencephalon	B.Rhombencephalon	C.Mesencephalon	D.Prosencephalon

1- D/ 2-C / 3- D

NEED EXPLANATION ? CLICK HERE

Cases

EXTRA CASES REQUIRE EXTRA INFO

4.A 1-hour-old boy is being evaluated in the nursery due to a hairy patch on the lower back. He was born to a 24-year-old primigravida who did not receive prenatal care. The patient's mother took prenatal vitamins throughout the pregnancy and did not use tobacco, alcohol, or illicit drugs. The patient's vitals are within normal limits. Physical examination shows a comfortable infant moving all 4 limbs spontaneously. Rectal examination reveals normal anal sphincter tone. Examination of the lower back shows a small, flat, hairy patch. Palpation of the area reveals a gap. Which of the following is the most likely diagnosis?			
A.Meningomyelocele	B.Spondylolisthesis	C.Syringomyelia	D.Spina bifida occulta
5.1-hour-old newborn girl is being evaluated in the nursery. She was born to a 23-year-old woman who did not receive prenatal care and has no significant past medical history. The patient's mother smoked 1 pack of cigarettes per day throughout the pregnancy and did not drink alcohol. The patient's mother did not take prenatal vitamins. The patient's vitals are within normal limits. On physical examination, the infant is in no acute distress. Physical examination shows a raw, red lesion on the lower back. Anal sphincter tone is 0 (normal = 3), indicating no discernible pressure. The infant can move the upper extremities but not the lower extremities. Which of the following is the most likely diagnosis?			
A.Myelomeningocele	B.Tethered cord syndrome	C.Myeloschisis	D.Anencephaly
6.A 4-week-old newborn boy is brought to the emergency department by his parents due to irritability and difficulty feeding over the past few days. He was born through normal vaginal birth and delivery to a 24-year-old primigravida woman who did not receive prenatal care. The patient's family history is unremarkable. The patient's temperature is 37.0°C (98.6°F), pulse is 70/min, respirations are 40/min, and blood pressure is 120/80 mmHg. On physical examination, frontal bossing and prominent scalp veins are noted. Generalized spasticity is present in all limbs. Examination of the skin shows a hair patch over the lower back MRI of the brain is obtained and shown below: 			
A.Chiari I malformation	B.Dandy-Walker malformation	C.Lissencephaly	D.Chiari II malformation

4-D/ 5-A / 6-B

PATHOLOGY TEAM

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