Lecture Eight

Hydrocephalus & Congenital Malformations

*432 **Pathology** Team*

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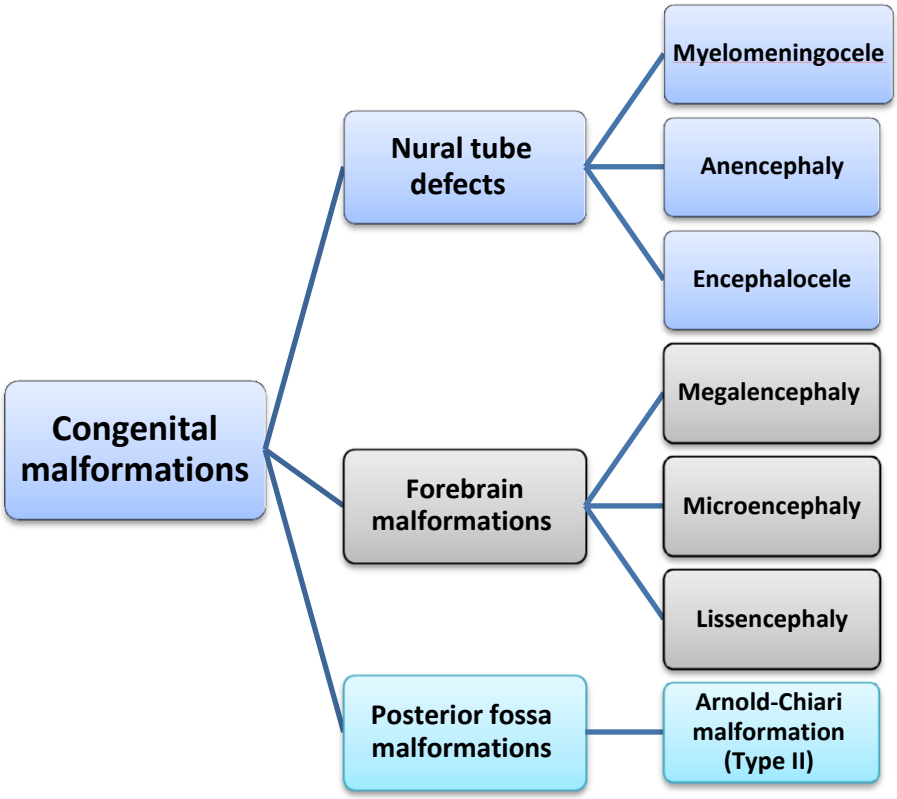
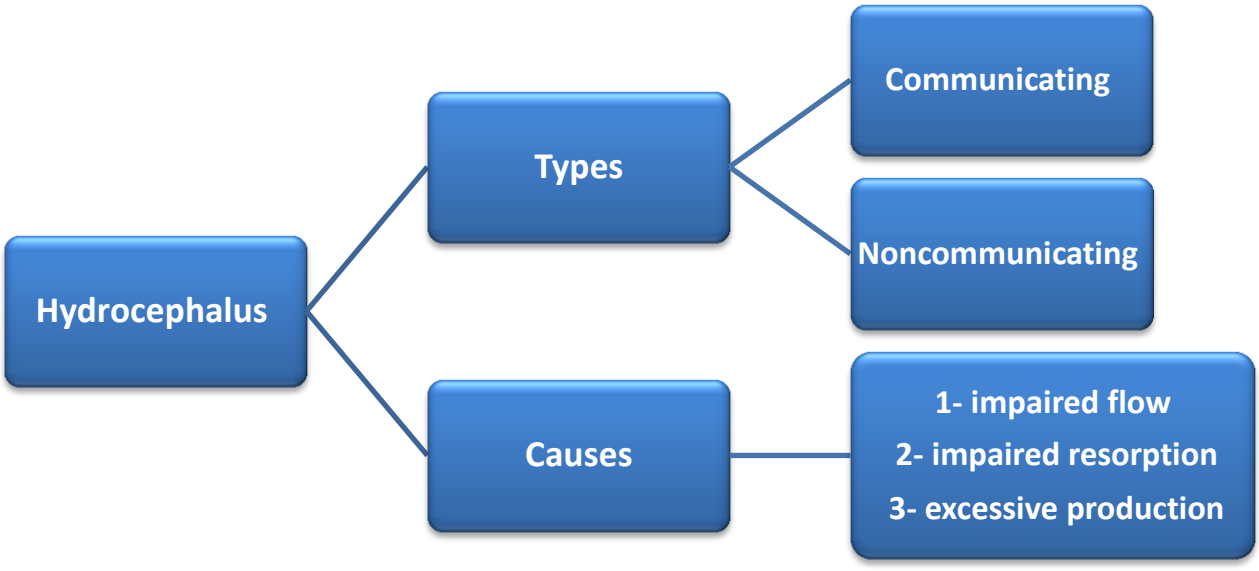
CNS Block

Color Index: female notes are in purple. Male notes are in Blue. **Red is important.** Orange is explanation.

Congenital Malformations & Hydrocephalus

Mind Map:





Congenital Malformations

General information :

- The incidence of CNS malformations, giving rise to mental retardation, cerebral palsy, or neural tube defects, is estimated at 1% to 2% (especially in the western population; due to alcohol and drug abuse).
- 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.

NOTE: Cerebral palsy: a condition marked by impaired muscle coordination (spastic paralysis) and/or other disabilities, typically caused by damage to the brain **(oxygen deprived one of the main causes) before or at birth.**

Pathogenesis:

Prenatal (before birth) or perinatal (after birth) insults may either cause:

1. **Failure of normal CNS development**
2. **Tissue destruction**

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:

1. **Development**
2. **Migration** of neurons
3. **Connection** between CNS and other parts of the body

(These processes and many others are programed in the genes, so if there's any mutation in the genes they'll be defected)

- Additionally, some toxic compounds and infectious agents are known to have teratogenic effects. (ex, HIV, measles , rubella , toxoplasmosis (from cats) , CMV)

"From Robbins"

Perinatal Brain Injury

A variety of exogenous factors can injure the developing brain. Injuries that occur early in gestation may destroy brain tissue without evoking reactive changes, sometimes making them difficult to distinguish from malformations. Brain injury occurring in the perinatal period is an important cause of childhood neurologic disability.

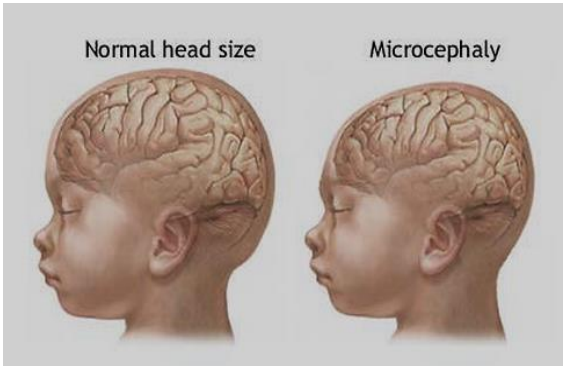
The two major types of injury that occur in the perinatal period are hemorrhages and infarcts. **These differ from the otherwise similar lesions in adults in terms of their locations and the tissue reactions they engender. In premature infants, there is an increased risk of *intraparenchymal hemorrhage* within the germinal matrix, most often adjacent to the anterior horn of the lateral ventricle. Hemorrhages may extend into the ventricular system and from there to the subarachnoid space, sometimes causing hydrocephalus. Infarcts may occur in the supratentorial periventricular white matter (*periventricular leukomalacia*), especially in premature babies. The residua of these infarcts are chalky yellow plaques consisting of discrete regions of white matter necrosis and mineralization. When severe enough to involve the gray and white matter, large cystic lesions can develop throughout the hemispheres, a condition termed *multicystic encephalopathy.***

1- Forebrain Malformations:

1/ Megalencephaly: The volume of brain may be abnormally large.

2/ Microencephaly: Small brain.

Microencephaly, by far the more common of the two, is usually associated with a small head as well.



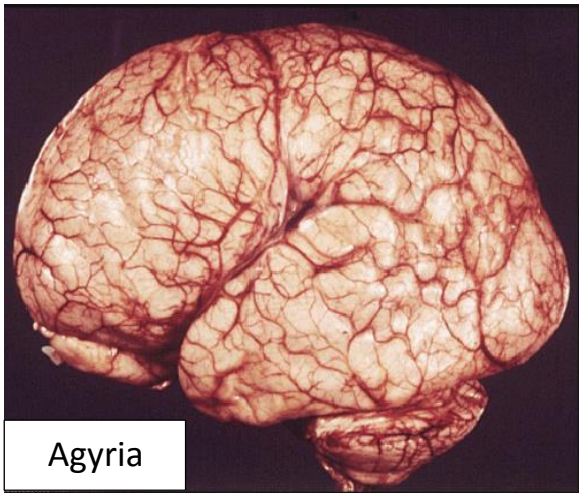
It can occur in a wide range of clinical settings, including:

- Chromosome abnormalities
- Fetal alcohol syndrome (a spectrum of characterized dysmorphic features and development defects resulting from maternal alcohol intake during pregnancy).
- Human immunodeficiency virus 1 (hiv-1) 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 **six-layered** neocortical architecture.

3/ Lissencephaly (agyria)=smooth brain or, in case of more patchy involvement, *pachygyria* (thick gyri) is characterized by an absence of normal gyration and a smooth-surfaced brain (in severe cases of pachygyria the brain appears smooth due to enlargement of gyri and loss of sulci).

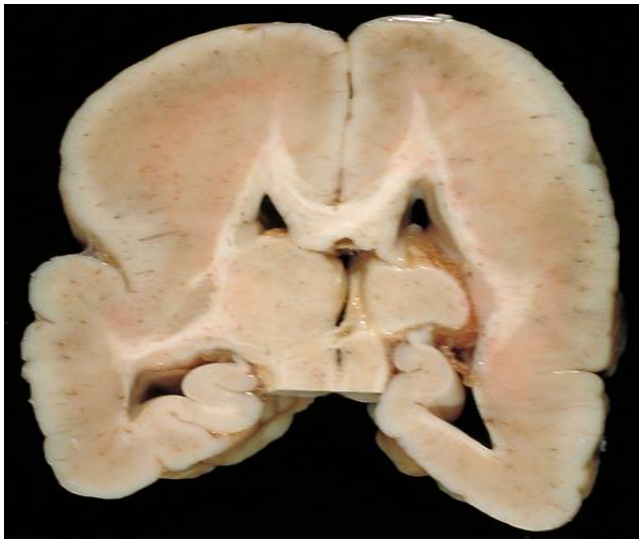

Pachygyria


Agyria

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

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

(Picture):

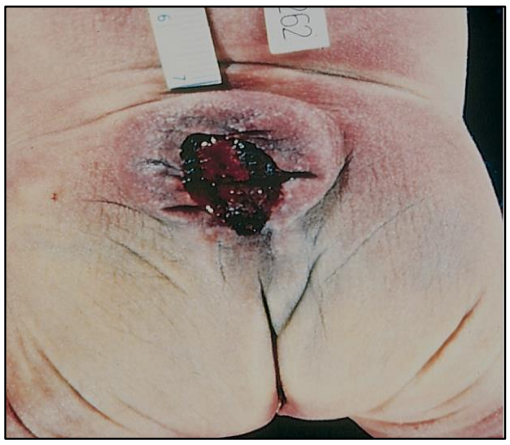


- Cortical sulci are absent except, usually, for the Sylvian fissure
- The cortex is thick and consists of the molecular and three neuronal layers (some cases four layers and some three, depends on the patient and severity)
- The deepest of these layers is also the thickest and most cellular, presumably comprised of neurons that migrated a certain distance from the ventricles but failed to reach their normal destinations (defect in migration).
- There is a small amount of myelinated white matter between the abnormal cortex and the ventricles.

2- Neural Tube Defects:

- 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, menginges, and overlying bone or soft tissues.
- Collectively, neural tube defects are the most frequent CNS malformations

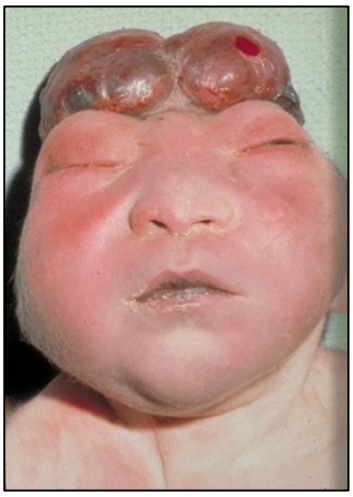
IN spinal cord



(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 (accompanied with infection)

IN the brain



- At the other end of the developing brain, ***anencephaly*** is a malformation of the anterior end of the neural tube, with absence of the brain and top of skull (picture).
- 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.**

NOTE From ROBBINS:

Folate deficiency **during the initial weeks of gestation also increases risk through uncertain mechanisms; of clinical importance, prenatal vitamins containing folate can reduce the risk of neural tube defects by up to 70%. The combination of imaging studies and maternal screening for *elevated α-fetoprotein* has increased the early detection of neural tube defects.**

3- 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

From ROBBINS

The far milder *Chiari type I malformation* 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, with symptoms of headache or cranial nerve deficits often manifesting only in adult life. Surgical intervention can alleviate the symptoms.

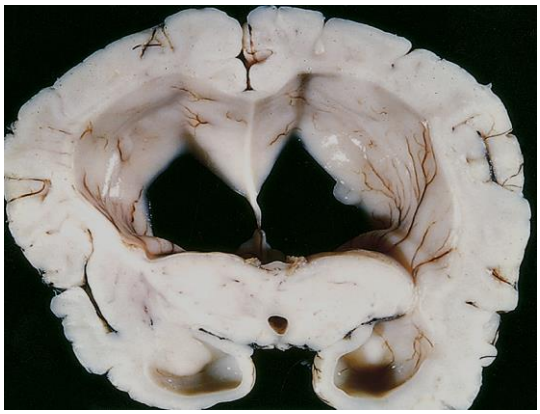
Syndromes characterized by "missing" cerebellar tissue include *Dandy-Walker malformation,* characterized by an enlarged posterior fossa, absence of the cerebellar vermis, and a large midline cyst, and *Joubert syndrome,* in which there is absence of the vermis and brain stem abnormalities resulting in eye movement problems and disrupted respiratory patterns. A range of recessive genetic lesions have been found to cause Joubert syndrome, with many involving alterations of the primary cilium.

Hydrocephalus:

- ***Normally,*** 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.

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.
- When hydrocephalus develops in infancy before closure of the cranial sutures, there is enlargement of the head (protrude forehead).
- Hydrocephalus developing after fusion of the sutures, in contrast, is associated with expansion of the ventricles and increased intracranial pressure (could lead to herniation), without a change in head circumference.
- 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. This pattern is referred to as ***noncommunicating hydrocephalus*** and is 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 reabsorption of CSF.



- Abnormal buildup of cerebrospinal fluid (CSF) in the ventricles of the brain.
- It can result from congenital and acquired etiologies.
- The fluid is often under increased pressure (but not always) and can compress and damage the brain.

Causes:

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

NOTE: Colloid cyst: it's a benign cyst in the 3rd vent. mostly near the foramina of Monro. If it's enlarged, it causes obstruction to the CSF circulation which leads to sudden death (Most common cause of sudden death in young people)

Homework!

Meningocele:

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

Polymicrogyria:

a developmental anomaly of the brain marked by development of numerous small convolutions (microgyri), causing mental retardation.

Microcephaly: Small head (skull).

Microencephaly: Small brain.

Hydrocephalus Ex Vacuo:

Hydrocephalus due to loss or atrophy of brain tissue (a compensatory mechanism in case of AD).

Summary (from Robbins Basic Pathology)

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.

Questions from Pathology Recall book

1/ neural tube defects are associated with an increase in what in the maternal serum?
α- fetoprotein

2/ what are 3 possible reasons for neural tube defects?
- Presence of pathological state in utero at time of neural tube closure (metabolic, nutritive, toxic, or infective causes)
- Faulty implantation of placenta
- Genetic abnormalities

3/ what malformation can be associated with lumbar spina bifida?
Arnold-Chiari malformation

4/ what is the most sever neural tube defects?
Anencephaly

5/ what is the difference between communicating and noncommunicating hydrocephalus?
Communicating: CSF can freely flow between ventricles and spinal subarachnoid space.
Noncommunicating: The flow of CSF is obstructed between the ventricles and spinal subarachnoid space, causing proximal dilation of the ventricular system.

6/ what can often be seen in infants with hydrocephalus?
Marked enlargement of the skull.

7/ why does this enlargement occur?
Cranial sutures are not closed yet.

8/ what is Arnold-chiari malformation?
Caudal displacement of medulla and cerebellum through foramen magnum into the cervical vertebral canal. It can be associated with lumbar spina bifida.

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*Good Luck ^_^*