Congenital Malformations and Hydrocephalus

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Red: Doctors' and important notes.
Green: Team notes.

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 (leading to formation of a syndromes)

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 as well as the location.

Prenatal or perinatal insults may either cause:

- Failure of normal CNS development. e.g: folate deficiency →neural tube defect.
- Tissue destruction .e.g: in a fetal alcohol syndrome, Infections can also induce tissue destruction and cause congenital malformations, e.g: torch disease that is associated with a number of causative pathogens, like toxoplasma and rubella, even trauma to the baby in the uterus can cause tissue destruction and malformation.

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 e.g: neural tube
- connection (between different parts of the CNS)

Some migratory malformations cause the neuronal bodies to be situated in the white matter rather than gray, cause them to be centered in a germinal layer, or even cause them become patchy centers at different locations of the brain

Additionally, some toxic compounds and infectious agents are known to have teratogenic effects (e.g. led toxicity, cytomegalo virus, and rubella).

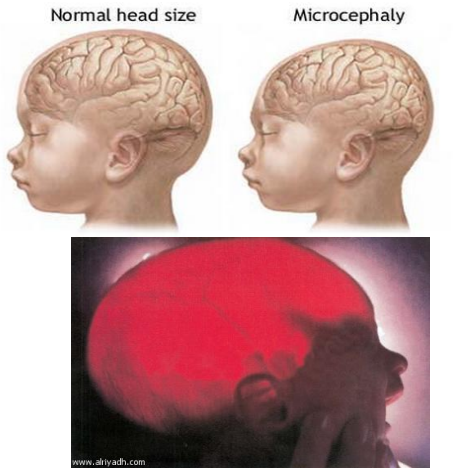
Malformations:

- Forebrain malformations
- Neural tube malformations
- Posterior fossa anomalies

1. Forebrain Malformations:

E.g megaloencephaly, microencephaly, and lissencephaly.

The volume of brain may be abnormally large (*megalencephaly*) or small (*microencephaly*).



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:

1. chromosome abnormalities (like with Edwards syndrome)
2. fetal alcohol syndrome
3. 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= microencephaly.

megaloencephaly means large brain material not large skull

Disruption of normal neuronal migration and differentiation during development can lead to a disruption of the normal gyration and architecture of the neocortex and its six layers.

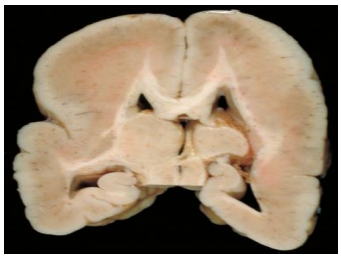
Lissencephaly (*agyria*) (***Liss*** means smooth) or, in case of more patchy involvement, *pachygyria* is characterized by an absence of normal gyration and a smooth-surfaced brain (flat). The cortex is abnormally thickened and is usually only four-layers (instead of six). Single-gene defects have been identified in some cases of lissencephaly.

- Cortical sulci are absent except, usually, except for the Sylvian fissure.
- The cortex is thick and consists of the molecular three neuronal layers.

Sylvian fissure (lateral fissure) : the deepest and most prominent of the cortical fissures; separates the frontal and parietal lobes from temporal lobes in both hemispheres

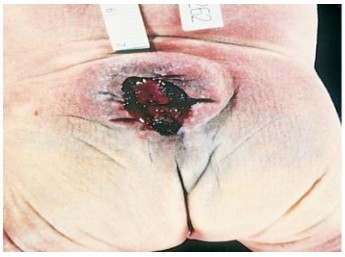
- The deepest of these layers is also the thickest and most cellular, presumably comprised of neurons that migrated a certain distance from the ventricles but failed to reach their normal destinations. So Lissencephaly is caused by defective migration.

- There is a small amount of myelinated white matter between the abnormal cortex and the ventricles.
- The cortex and the inner structures are formed of white matter and the gray matter is found abnormally between them.



2. Neural tube defect e.g. (spina bifida):

Normally: 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.



Meachnism : 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.

Risk factors: Folate deficiency during the initial weeks of gestation.

To reduce the risk factor: prenatal vitamins are aimed.

The early detection: of neural tube defects can be established by using a combination of ultrasound and maternal screening for elevated α-fetoprotein in the amniotic fluid.

- The overall recurrence risk in subsequent (following) pregnancies is 4% to 5%

Examples on neural tube defects:

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

Location: most commonly in the lumbosacral region.

Myelomeningocele:

Myelo *(spinal cord)****/meningo*** *(meanings)****/cele*** *(protruding outside)*

Clinical manifestations: - Patients have motor and sensory deficits in the lower extremities

- Problems with bowel and bladder control ⟶ 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. *encephalocele* is a diverticulum of malformed CNS tissue extending through a defect in the cranium. This may cause herniation of the brain, with or without symptoms.

Location: It most often involves the occipital region or the posterior fossa .

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 (discussed later).

Examples:

Chiari type(I) malformation	**The *Arnold-Chiari malformation* (Chiari type (II)) commonest**
- 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.	- A small posterior fossa. - A misshapen midline cerebellum. - Downward extension of *vermis* through the foramen magnum. - Hydrocephalus. - A lumbar myelomeningocele.

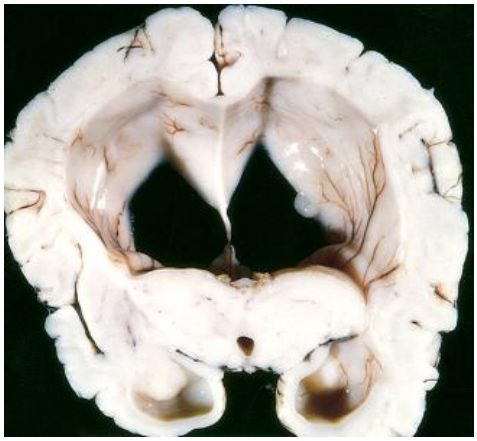
Hydrocephalus

Definition:

Hydrocephalus refers to the accumulation of excessive CSF within the ventricular system.

In normal circulation:

- 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



Coronal section of the brain showing hydrocephalus with dilated lateral ventricles

Hydrocephalus occurs as a result of:

- in Most cases :as a consequence impaired resorption of CSF (obstruction)
- in rare instances: (e.g., tumors of the choroid plexus), overproduction of CSF may be responsible

When hydrocephalus develops:

Before closure of the cranial sutures	after fusion of the sutures
- Infants. - Result in enlargement of the head.	- Adults. - Associated with expansion of the ventricles and increased intracranial pressure→herniation→death without a change in head circumference.

There are two types of 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. This pattern is referred to as:

Noncommunicating Hydrocephalus (obstruction) commonest	**Communicating Hydrocephalus (no obstruction)**
Most commonly seen with masses at the **formamen of Monro** or **aqueduct of Sylvius**.	All of the ventricular system is **enlarged**; here the cause is most often **reduced resorption** of CSF.

What can cause hydrocephalus?

In general, Obstruction can be duo to: Infection, inflammation, tumor, or congenital abnormalities.

1. **Hypersecretion of CSF**: e.g. choroid plexus tumor
2. **Obstructive hydrocephalus**:
   - Obstruction of the foramina of Monro e.g. colloid cyst (usually happens in young people). Obstruction of the foramina of Monro enlarges the third ventricle.
   - Obstruction of the third ventricle e.g. pilocytic astrocytoma
   - Obstruction of the aqueduct e.g. aqueductal stenosis (atresia) (congenital malformations of the aqueduct itself) and posterior fossa tumors
   - Obstruction of the foramina of Luschka or impairment of flow from the fourth ventricle such in 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.

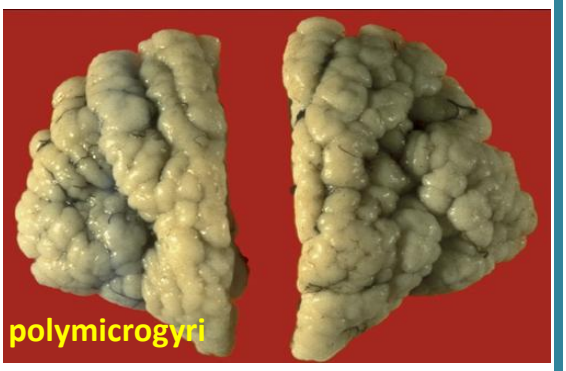
Low-pressure hydrocephalus: appears to be a more acute form of normal pressure hydrocephalus. The pressure in this case does not get high enough to allow the CSF to drain in a shunt system

How can we treat it? *Using a **shunt** (if it's infected can cause **membranoproliferative glomerulonephritis** → deposition of **IgM**.)*

HOMEWORK:

Define: meningocele → Meningocele is a form of spina bifida, where the meninges of the spine protrude out of the vertebrae into a sac that appears on the back.

Define: polymicrogyria → polymicogyria is characterized by an increased number of irregularly formed gyri that result in an irregular bumpy or cobblestone –like surface these changes can be focal or widespread. The normal cortical archeticture can be alterd in different ways and adjacent gyri often show fusion of the superficial (molecular) layer.



What is the difference between microcephaly and microencephaly?

Microcephaly is a rare neurological condition in which an infant's head is significantly smaller than the heads of other children of the same age and sex. Microencephaly: is a condition where the the brain itself is small. So Microcephaly is small head and Microencephaly: is small brain substance.

Define: hydrocephalus ex vacuo → (It is only a descriptive term). The term hydrocephalus ex vacuo refers to dilation of the ventricular system with a compensatory increase in CSF volume secondary to a loss of brain parenchyma.