***DEVELOPMENTAL ABNORMALITIES***

***INTRODUCTION***

Developmental abnormalities of the nervous system occur in 2 – 3% of all infants at birth of which about 1/3 involve the central nervous system. The malformations are the result of inherited and acquired factors that play havoc on the genetic composition. The important factors include genetic factors include genetic factors, chromosomal abnormalities and environmental factors such as maternal infections (rubella, cytomegalovirus), irradiation (during first 4 months of pregnancy), foetal-alcohol syndrome, drugs e.g. thalidomide, tobacco, vitamin deficiencies and foetal hypoxia. The central nervous system is susceptible to malformations throughout its various phases of development. The teratogenic effects of an agent depend on its nature, gestation and genetic background of the individual.

***CHROMOSOMAL ABNORMALITIES***

Important chromosomal abnormalities include those where there is extra chromosomal material e.g. Trisomy 13, 18 and 21 which are associated with mental retardation. Sex chromosomes’ disorders such as Kleinfelter’s syndrome (XXY) and Turner’s syndrome (XO) are also associated with mental retardation. Down’s syndrome is a trisomy 21 disorder that occurs due to non-disjunction during meiosis in one of the parents. It is the most common chromosomal disorder and it is the commonest cause of mental retardation. The brain is usually small.

***NEURAL TUBE DEFECTS***

Defects of the neural tube occur due to damage during the 4th week of foetal development as a result of genetic and environmental factors. The defects can be diagnosed pre-natally by presence of increased -feto proteins level in blood and increased amniotic fluid on ultra sound scan.

**Anencephaly**

Anencephaly affects more females than males in the ratio of 3:1. The head is retroflexed and appears to sit on the shoulders with the cranial vault missing and a flattened base of the skull. The brain is represented by disorganized mass of glia, malformed brain and choroids plexus. The area ***cerebrovaseulosa*** that sits on the base of the skull is covered by a thin smooth membrane. It results form failure of neural tube closure.

**Spinal Bifida**

Defects of the spinal cord resulting from failure of fusion (incomplete closure) of neural arches are called **spina bifida**. Spina bifida are malformations of the vertebral column involving incomplete embryologic closure of one or more of the vertebral arches (rachiochisis). The vertebral defect is associated with defect in the neural tube structures and their coverings. The bony defect may be of varying degrees. Majority of these malformations occur in the lumbosacral region.

Diagram a – Muirs 848

***Spina Bifida Occulta***

In spina bifida occulta there is only vertebral bone defect with no abnormality of the spinal cord and its meninges. It is seen in 175 of normal adults where it appears as absence of one or more spinous processes radiologically. It is limited to the lumbosacral region. The site of the bone defect is marked by a small dimple covered by skin which may show abnormal pigmentation (mole), a hairy patch or a dermal sinus. In majority of the cases spina bifida occulta is asymptomatic but neurological disturbances may develop in adult life.

Diagram b – Muirs 848

***Spina Bifida Cystica***

In spina bifida cystica, the vertebral bony defect is large and the spinal cord and its meninges appear as a distinct cystic swelling over the affected site as revealed through the skin defect. The defect in the skin allows herniation of the meninges or the spinal cord or both. Herniation of the meninges alone through the bony defect results in formation of a **meningocele** which is less common (10 – 20%) and involves only meninges, vertebral arches and the skin. the herniation sac consists of the dura and arachnoid. The spinal cord is virtually normal.

**Myelomeningocele** which is the commonest (80 – 90) is a more serious condition that involves herniation of meninges and the abnormal spinal cord or its roots through the defect and is attached to the posterior wall of the sac. The dura and the skin in the sac are deficient. Other abnormalities associated with this malformation are syringomyelia (myelocele) or diastematomyelia. In syringomyelia there is defective closure of the spinal canal so that the sac consists of an open flat neural tissue plate without skin covering and the cerebral spinal fluid (CSF) leaks through it.

Myelomeningocele and myelocele are associated with poor quality of life due to varying degrees of neurological defects. The sequelae include bladder and bowel dysfunction (incontinence), motor and sensory defects (flaccid areflexic weakness of the legs), paraplegia, lumbar kyphosis and moderate-to-severe mental retardation.

Herniation of brain tissue and meninges through a midline defect in the cranial cavity in the region of the occipital bone or fronto-ethmoid junction may result in encephalocele and cranial meningocele. It affects more females than males. At the occipital region the encephalocele protrudes through either the foramen magnum or squamous occipital bone.

Diagram c, d, e Muir’s 848

***Syringomyelia and Syringobulbia***

Syringomyelia and Syringobulbia are characterized by development of a syrinx or tubular cavity in the spinal cord and medulla respectively. The cavity may be fusiform or irregular. It begins with grey matter of spinal cord dorsal to the central canal. The syrinx is surrounded by glial tissue. The cavity may communicate with spinal canal and is lined with ependymal cells. Fibres of lateral spinothalamic tract and involvement in the cavity result in clinical effects such as loss of pain and temperature sensation in the affected region.

***MALFORMATIONS OF THE CEREBELLUM***

**Arnold-Chiari Malformations**

These are malformations of the brain involving the brain stem, cerebellum and base of skull as described by Arnold-Chiari. The primary problem is elongation of the medulla and part of the vermis of the cerebellum resulting from failure of pontine flexture to form. Four abnormalities have been described of which type II lesion which is also called Arnold-Chiari malformation is the most common and severe malformation of the central nervous after encephalopathy.

In the Arnold-Chiari malformation, there is an abnormality of the hind brain and cerebellum associated with a lumbar myelomeningocele and hydrocephalus. The major components of the Arnold-Chiari malformation include: -

1. Caudal displacement and distortion of the medulla which appears narrow, S-shaped and elongated with much of it lying below the level of the foramen magnum. The displacement includes part of the 4th ventricle
2. Displacement of vermis of the cerebellum through the foramen magnum into the upper portion of the spinal cord. There is lengthening and herniation of cerebellum vermis and cerebellar tonsils through the foramen magnum resulting in formation of a mass over the upper cervical cord.

These abnormalities result in stenosis of the aqueduct or obstruction of the foramina of Luschka and Magendie resulting in internal hydrocephalus. The downward displacement of the brain stem into the cervical canal and affects the lower cranial nerves and cervical nerve roots run a cephalad course from their point of origin.

Other features include shallow malformed posterior fosa, low insertion of tentorium and thickened and fibrotic meninges at the herniated tissue and exit at foramina of the fourth ventricle.

***MALFORMATIONS OF WHOLE BRAIN***

These are common and result from many disease processes of genetic, chromosomal and environmental origin.

***Microcephaly***

Microcephaly is a condition with the brain weighing less than 1000 gm in adults or less than 2 standard deviation mean normal weight for age and sex. It results from degeneration, destructive or congenital conditions.

*Causes*

1. Congenital infections
   1. Rubella
   2. Toxoplasmosis
   3. Cytomegalovirus
2. Toxins
3. Irradiation
4. Metabolic disorders
5. Chromosomal abnormality

***Megalencephaly***

The brain weighs more than 1700 gm or more or more than 2.5 standard deviation of mean normal for age and sex. It may be primary or secondary. Secondary megalencephaly is due to metabolic disorders.

***HYDROCEPHALUS***

Hydrocephalus means increased volume of cerebrospinal fluid (CSF) within the cranial cavity accompanied by dilatation of the ventricles. In **internal hydrocephalus** the increased volume of CSF is within the ventricular system which becomes enlarged (dilated). Internal hydrocephalus is associated with increased intracranial pressure. In **external hydrocephalus**, excess CSF collects in the subarachnoid space.

If the CSF can flow freely from the ventricular system to the subarachnoid space, this is described as **communicating hydrocephalus** and if it does not circulate then it is called **non**-**communicating** **hydrocephalus**. **Compensatory hydrocephalus** (ex vacuo) occurs when the increased volume of CSF is compensatory to loss of brain tissue.

**Cerebrospinal Fluid (CSF) – Source and Circulation**

The total volume of CSF produced is 120 – 150 mls. It is mainly produced by choroid plexus in the two lateral, 3rd and 4th ventricles and a small portion is formed on the surface of the brain and spinal cord.

The CSF formed in the lateral ventricles flows through the foramina of Munro to the 3rd ventricle and from here it flows through the aqueduct of Sylvias to the 4th ventricle. The CSF then passes through the foramina of Magendi and Luschka of the 4th ventricle to reach the subarachnoid space of the brain and spreads through the subarachnoid space over the surface of the spinal cord. The CSF is then absorbed into the blood by the arachnoid villi present along the dural venous sinuses.

Diagram CSF Circulation

**Classification and Aetiopathogenesis**

Hydrocephalus is classified into **primary** and **secondary** hydrocephalus. Primary hydrocephalus is more common. The commonest cause of hydrocephalus is ventricular enlargement secondary to cerebral atrophy. In such cases hydrocephalus is not associated with increased intracranial pressure. Hydrocephalus of acute onset with increased is commonly due to obstruction to the free flow of CSF.

**PRIMARY HYDROCEPHALUS**

In primary hydrocephalus thee is actual increase in the volume of CSF within the cranial cavity with increased intracranial pressure.

The aetiological mechanisms of primary hydrocephalus are: -

1. Obstruction to the flow of CSF
2. Overproduction of CSF
3. Deficient reabsorption of CSF

The commonest mechanism is obstruction to the flow of CSF hence the term **obstructive** **hydrocephalus** in entertained. The terms non-communicating and communicating hydrocephalus are used to denote the site of obstruction. Because of the ventricular enlargement that occurs there is a reduction in the bulk of white matter in the cerebral hemispheres. The site of obstruction is more important than the nature or size of obstruction e.g. a small lesion in a critical site adjacent to an interventricular foramen of Munro or the aqueduct in the midbrain produces hydrocephalus rapidly.

**Non-communicating Hydrocephalus**

In non-communicating hydrocephalus, the site of obstruction of CSF flow pathway is in the 3rd ventricle or at the exit foramen in the 4th ventricle. The ventricular system enlarges and CSF cannot pass into the subarachnoid space. Obstruction of CSF at the foramen of Munro results in enlargement of one lateral ventricle while that at the 3rd ventricle or the aqueduct results in enlargement of both ventricles. Obstruction at the exit of the 4th ventricle results in enlargement of the entire ventricular system.

***Causes***

1. Congenital non-communicating hydrocephalus
   1. Stenosis of the aqueduct
   2. Arnold-Chiari malformation
   3. Progressive gliosis of the aqueduct
   4. Intra-uterine meningitis
2. Acquired non-communicating hydrocephalus

Occurs from an expanding lesion within the cranial cavity: -

* 1. Tumours adjacent to the ventricular system e.g. ependyoma, choroid plexus papilloma and medulloblastoma
  2. Inflammatory lesions e.g. cerebral abscess and meningitis
  3. Haemorrhage – parencymal haemorrhage, intraventricular haemorrhage, epidural haematoma and subdural haematoma

**Communicating Hydrocephalus**

In communicating hydrocephalus obstruction to CSF flow is in the subarachnoid space at the base of the brain. It results in enlargement of the entire ventricular system but CSF flows freely between dilated ventricles and the spinal cord and that is why it is called communicating hydrocephalus. The causes of communicating hydrocephalus are non-obstructive.

***Causes***

1. Overproduction of CSF – choroid plexus papilloma
2. Deficient reabsorption of CSF – post meningitis, dural sinus thrombosis and sequelae of subarachnoid haemorrhage (the arachnoid granulations may be partly obliterated by macrophages containing haemosiderin).

**SECONDARY HYDROCEPHALUS**

Secondary hydrocephalus is less common and is defined as compensatory increase in CSF due to loss of neural tissue without increase in intracranial pressure e.g. flowing cerebral atrophy and infarction.

**Pathologic Changes**

***Gross***

* Ventricular dilatation
* Thinning and stretching of the brain
* Engorged scalp veins overlying the enlarged head
* Open fontanelles

***Microscopy***

* Damage to ependymal lining of the ventricles
* Periventricular interstitial oedema