MODULE: CLINICAL PATHOLOGY

UNIT: Disorders of Nervous System

By
Carey Francis Okinda
June 2016

UNIT OUTLINE

	Topic	Duration (hours)
1.	Introduction and Developmental Abnormalities	2
2.	Circulatory Disorders	2
3.	Head Injury	2
4.	Infections 1– Bacterial Infections	2
5.	Infections 2 - Viral; Fungal; Protozoal; Metazoal	2
6.	Disorders of the Spinal Cord	2
7.	Disorders of the PNS	1
8.	Metabolic and Toxic	1
9.	Tumours	1
	TOTAL	**15**

Lesson 1: INTRODUCTION & DEVELOPMENTAL ABNORMALITIES

Learning Outcomes

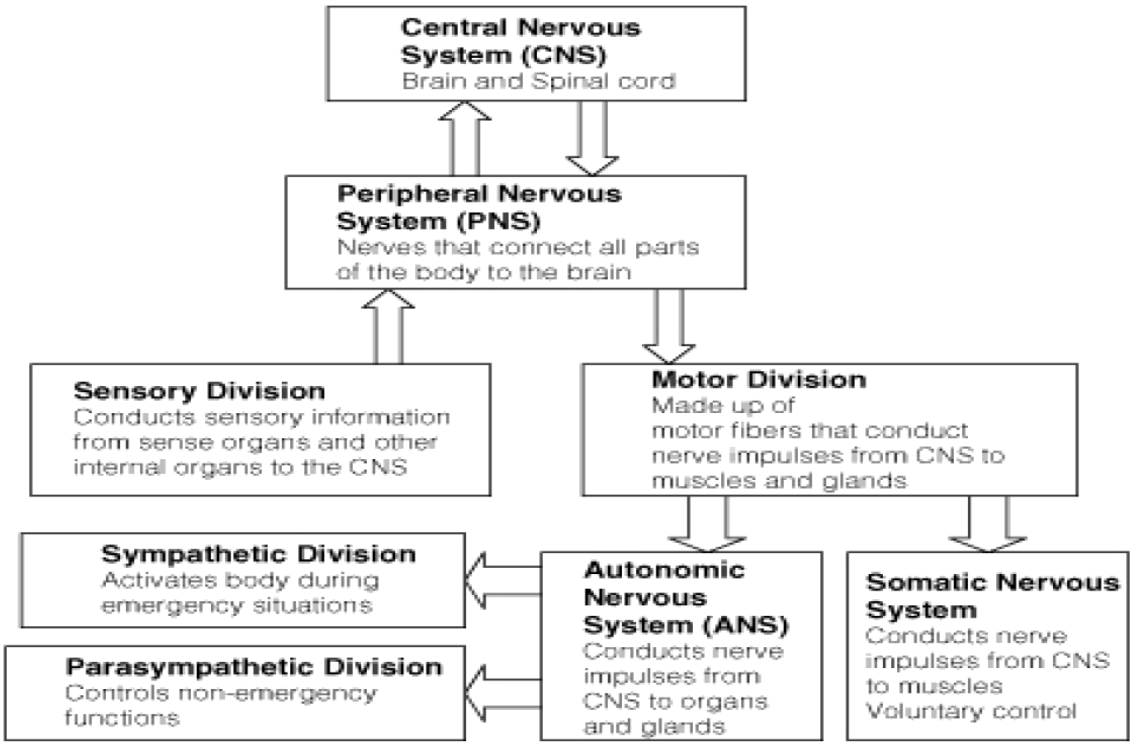
At the end of the lesson the learner should be competent to: -
1. Describe the pathophysiology & pathology of congenital malformations
2. Outline investigations in malformations and developmental abnormalities
3. Describe the complications of malformations and developmental abnormalities

1.0. INTRODUCTION

1.1. General Introduction

- It integrates and evaluates the information & initiates an outgoing response.
- NS is the most complex body system whose working determines our personality, intelligence and skills. It is specialized properties of irritability, conduction and integration
- The skull and vertebrae form a rigid compartment protecting the delicate CNS tissue
- This rigidity has serious disadvantages when pressure inside the skull increases e.g. an expanding lesion soon takes up the small reserves of the space available and the delicate brain tissues are progressively compressed, with very serious results

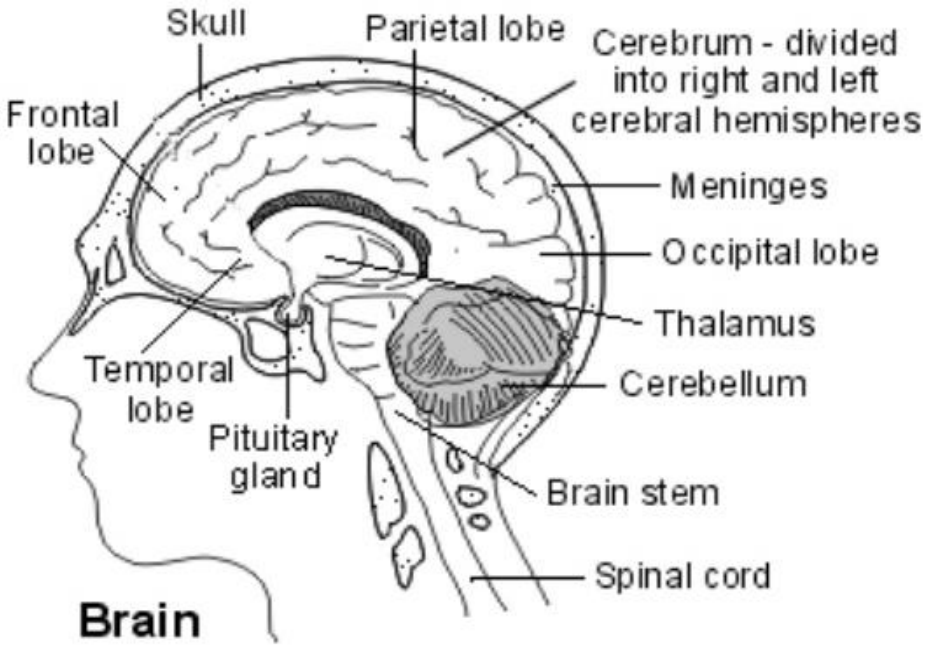
Diagram 1.1: Functional Organization of the Nervous System



1.2. Central Nervous System (CNS)

- The CNS, which consists of the **brain and spinal cord**, is the structural and functional centre of the entire nervous system
- Basic functional unit is the neurone
- Neurones are arranged in organized neural networks determining the functions of the nervous system

Diagram 1.2: The CNS



Sensory Division – Sensory Receptors

- Many actions of NS are initiated by sensory experience emanating from sensory receptors
- Information from the sensory receptors can cause an immediate reaction from the brain or activate memory of the experience to determine the body reaction

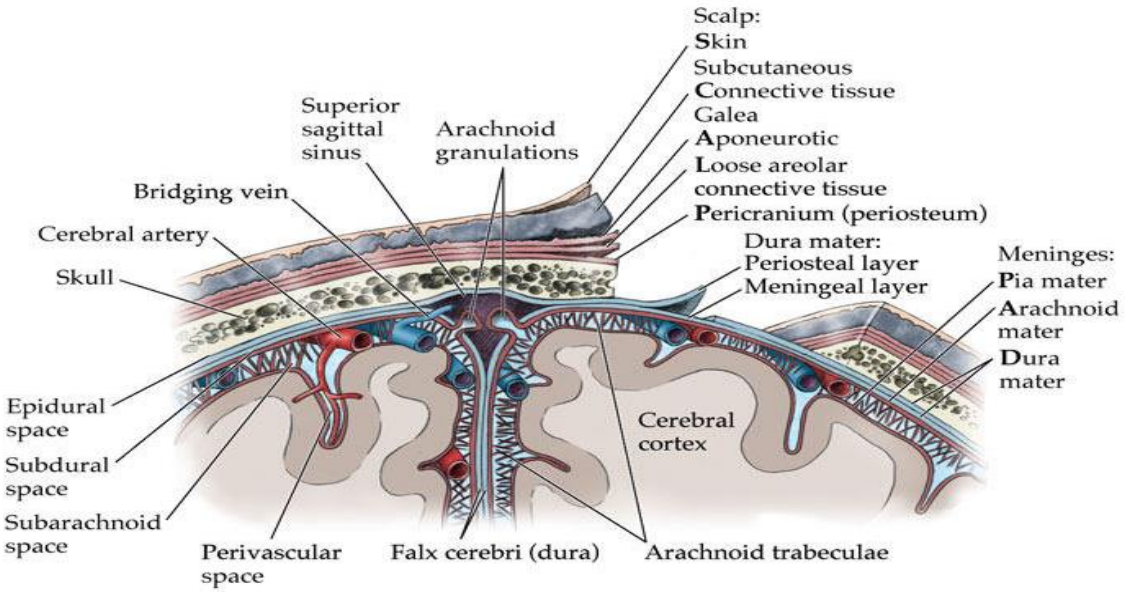
Motor Division – Effectors

- Controls bodily functions by controlling contraction of skeletal muscles and smooth muscles and in internal organs and secretion by both exocrine and endocrine glands

1.3. The Meninges

- Meninges cover the brain tissues and have CSF circulating freely in the subarachnoid space over the whole CNS surface and in the ventricular system
- Include the dura matter, pia matter and arachnoid matter
- CSF bathes and protects the brain

Diagram 1.3: Meninges



1.4. Peripheral Nervous System

- Consists of nerves that lie in the periphery
- Peripheral nerves include cranial and spinal nerves that consist of fibres that form incoming and outgoing information pathways
- PNS has 2 main subdivisions called the sensory (afferent) and the motor (efferent) nervous system that has all outgoing or efferent pathways
- Motor nervous system is further subdivided into somatic and autonomic nervous system (ANS) which is divided into sympathetic and parasympathetic nervous system

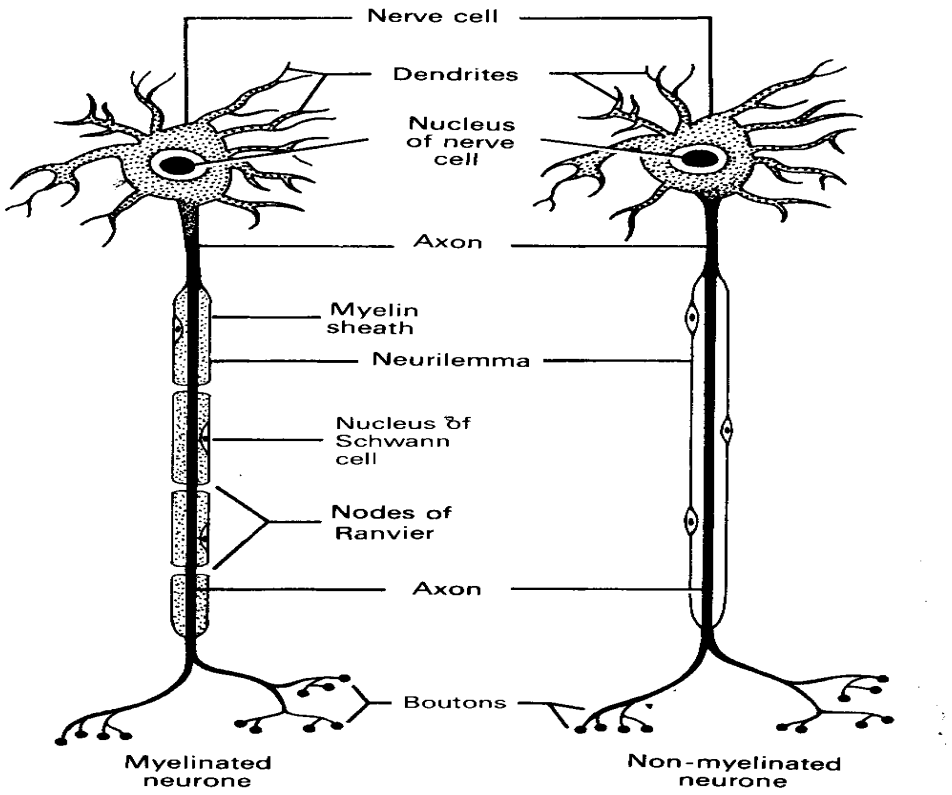
2.0. CELLS OF THE NERVOUS SYSTEM

- CNS is made up of two types of cells namely the neurones and neuroglia (glial cells)

2.1. Neurones

- Are excitable cells that conduct impulses making the nervous system functions possible as they make up the wiring of the body's information circuit
- Have three principal parts namely the cell body (*soma*, *perikaryo*), dendrites (processes) and axon (nerve fibre)

Diagram 1:4: Neurones



2.2. Neuroglia or Glial Cells

- Neuroglia (glial cells) offer support functions and do not conduct impulses
- Form the bulk of the cells in the CNS accounting for 80 – 90%
- Support neurones physically and metabolically
- Include - astroglia (astrocytes), oligodendroglia (oligodendrocytes), microglia, Schwann cells, ependyma and satellite cells

3.0. CAUSES OF NERVOUS TISSUE INJURY

- Anoxia/hypoxia(ischaemia); hypoglycaemia; Infections; trauma; metabolic disturbances (e.g. Vitamin B_{12} deficiencies), poisons & toxins; aging; tumours; degeneration

4.0. NERVOUS TISSUE RESPONSE TO INJURY

- Depends upon the aetiological agent and pathological process (central chromatolysis, atrophy and degeneration of neurons and axons and intraneuronal storage of substances)
- Response of peripheral nerves to injury depends on the target of the insult
  - Schwann cell damage - results in loss of myelin (segmental degeneration)
  - Axon damage - results in axonal degeneration, some axonal regeneration and re-innervation of muscles
  - Pathology in skeletal muscles includes denervation atrophy and myopathy.

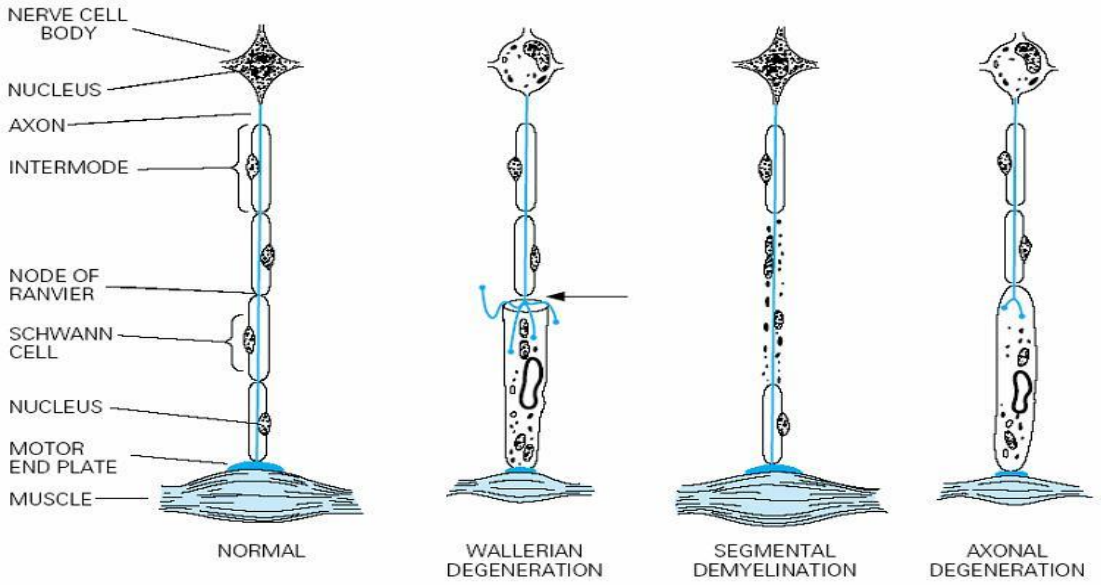
5.0. EFFECTS OF NEURONAL DAMAGE

- Depend on the rapidity of the changes which include
  - Rapid necrosis (associated with acute failure of function)
  - Slow atrophic changes (associated with gradual loss of function)
- Neuronal damage results in primary degeneration (necrosis and atrophy) and secondary degeneration in some situations where axon damage involves degeneration of the neurone as well

1) Degeneration of Axons

- Axonal damage exhibits retrograde degeneration or trans-synaptic degeneration
- Retrograde degeneration occurs when the main axon is damaged and the degeneration process proceeds to involve the cell body
- Following axonal resection two types of changes take place that is
  - Chromatolysis which occurs proximally in the cell body
  - Wallerian degeneration that occurs distally in the peripheral axon

Figure 1:5: Degeneration



- Most products of myelin breakdown are removed by macrophages within weeks and the Schwann cells proliferate to form cords of cells within the endoneural tubes
- These cords are necessary for re-innervation
- Myelin debris is phagocytozed and its staining properties changes largely due to production of cholesterol esters

2) Atrophy

- Axonal degeneration leads to loss of neural input to affected motor nit resulting in denervation atrophy
- Degeneration of muscle leads to breakdown of myosin and action with reduction in cell size and resorption of myofibrils but the cells remain viable.

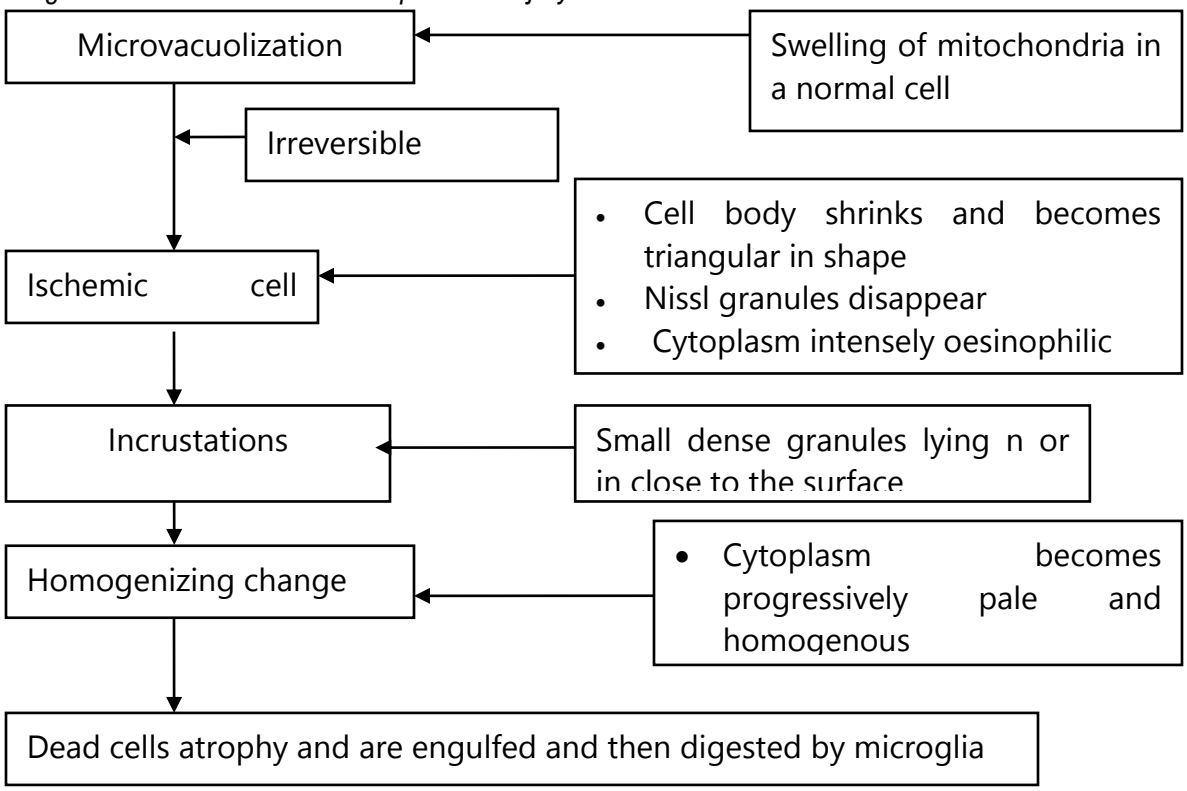
3) Phagocytosis

- Follows cell death and involves removal of damaged tissue by phagocytic resident microglial cells supplemented by recruitment of monocytes from blood.

4) Gliosis

- Astrocytes become activated to fulfil metabolic roles in protecting neurones. After death of cells and removal by phagocytes, damaged areas are replaced by proliferation of astrocytes forming a **glial scar**.

Diagram 1.6: Nervous Tissue Response to injury



6.0. MALFORMATIONS & DEVELOPMENTAL ABNORMALITIES

- Occur in 2 – 3% of all infants at birth with about 1/3 involving the central nervous system
- Result from inherited and acquired factors that play havoc on the genetic composition
- Important factors include
  i) Genetic factors include genetic factors e.g. chromosomal abnormalities
  ii) 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 (folic acid) and foetal hypoxia

1) 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 Klenefelter's syndrome (XXY) and Turner's syndrome (XO) are also associated with mental retardation
- Down's syndrome (trisomy 21)
  - Occurs due to non-disjunction during meiosis in one of the parents
  - Most common chromosomal disorder
  - Commonest cause of mental retardation and the brain is usually small

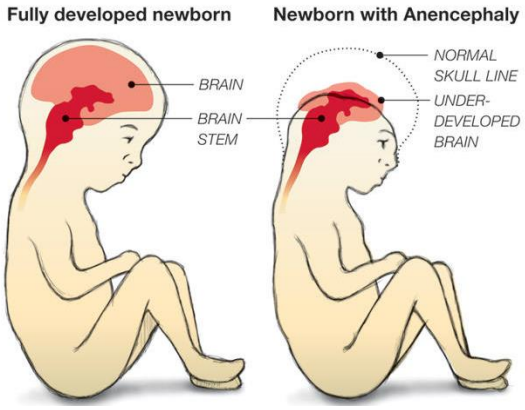
2) Neural Tube Defects

- Occur due to damage during the 4th week of foetal development as a result of genetic and environmental factors
- Can be diagnosed pre-natally by presence of increased feto proteins level in blood and increased amniotic fluid on ultra sound scan.

i) Anencephaly

- Affects more females than males in the ratio of 3:1
- Head is retroflexed and appears to sit on the shoulders with the cranial vault missing and a flattened base of the skull
- Brain is underdeveloped with lack of the fore brain; represented by disorganized mass of glia, malformed brain and choroid plexus
- Neural tube fails to close properly and the developing brain and spinal cord are exposed to the amniotic fluid that surrounds the foetus resulting in tissue degenerate thus large parts of the brain (cerebrum and cerebellum) are missing
- These regions are critical for thinking, hearing, vision, emotion, & coordinating movement
- The bones of the skull are also missing or incompletely formed
- Almost all babies die before birth or within a few hours or days after birth

Diagram 1.7: Anencephaly



ii) Spinal Bifida

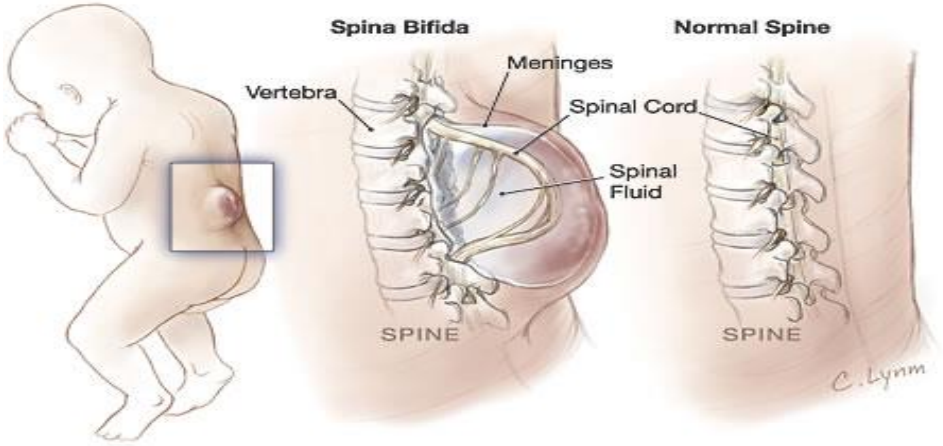
- Result from failure of fusion (incomplete closure) of neural arches are called **spina bifida and** one or more of the vertebral arches (rachiochisis)

- The vertebral defect is associated with defect in the neural tube structures and their coverings
- A portion of the neural tube fails to develop or close properly. The bony defect may be of varying degrees. Majority of these malformations occur in the lumbosacral region.

Risk Factors

- Race
- Family genetic lines.
- Folate, vitamin B-9, deficiency
- Anti-seizure medications (interference with folic acid utilization)
- Diabetes and obesity are associated risk factors.

Diagram 1.8: Spina Bifida

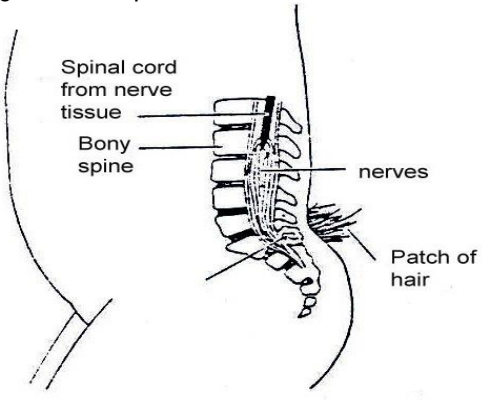


Types

a) Spina Bifida Occulta

- There is only vertebral bone defect with no abnormality of the spinal cord and its meninges
- It is limited to the lumbosacral region
- 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
- Majority are asymptomatic but neurological disturbances may develop in adult life
- Indications include abnormal tuft of hair; collection of fat; small dimple or birthmark and slight to pronounced skin discoloration

Diagram 1:9: Spina Bifida



b) Spina Bifida Cystica

- 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
- Defect in the skin allows herniation of the meninges or the spinal cord or both

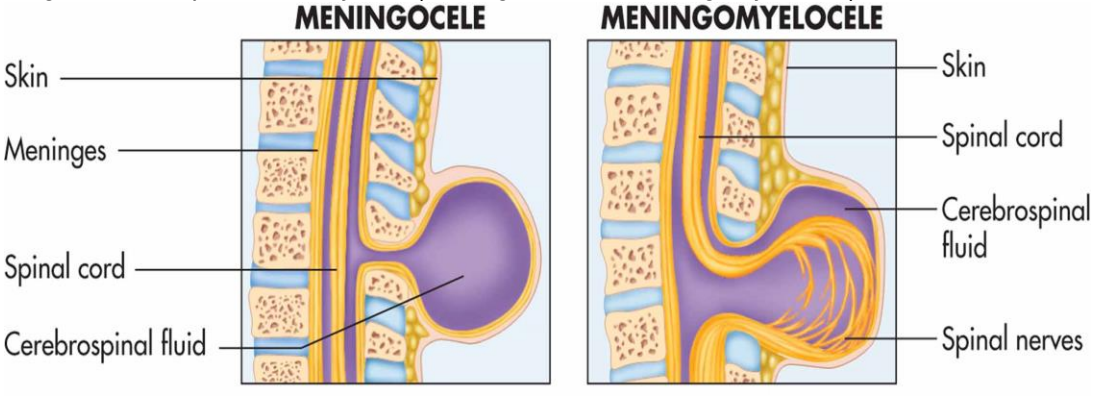
Meningocele

- Involves herniation of the meninges alone through the bony defect (involves only meninges, vertebral arches and the skin)
- Herniation sac consists of the dura and arachnoid

Myelomeningocele (Meningomyelocele)

- Involves herniation of meninges and abnormal spinal cord or its roots through the defect and is attached to the posterior wall of the sac
- Dura and the skin in the sac are deficient
- Myelomeningocele and myelocele are associated with poor quality of life due to varying degrees of neurological defects
- Sequelae include bladder and bowel dysfunction, motor and sensory defects, paraplegia, lumbar kyphosis and moderate-to-severe mental retardation

Diagram 1:10: Spina Bifida Cystica (Meningocele and Meningomyelocele)



- Associated with malformation such as 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

Syringomyelia and Syringobulbia

- A syrinx is a fluid filled cavity in the cord (**syringomyelia**) or brain stem (**syringobulbia**)
- The syrinx is surrounded by glial tissue
- The cavity may communicate with spinal canal and is lined with ependymal cells
- Involvement of the lateral spinothalamic tract result in clinical effects such as loss of pain and temperature sensation in the affected region due to trauma, ischaemia and tumours and cause compression of the white matter tracts resulting in neurological disability
- Clinical features are due to compression of spinal nerve tracts resulting in wasting of intrinsic muscles of the hands, spastic weakness in the legs, loss of pain and temperature sensation but with preservation of touch.

3) Malformations of the Cerebellum

Arnold-Chiari Malformations

- Malformations of the brain involving the brain stem, cerebellum and base of skull
- 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
- The major components of the Arnold-Chiari malformation include: -
  i) 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. Displacement includes part of the 4th ventricle
  ii) 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
- 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

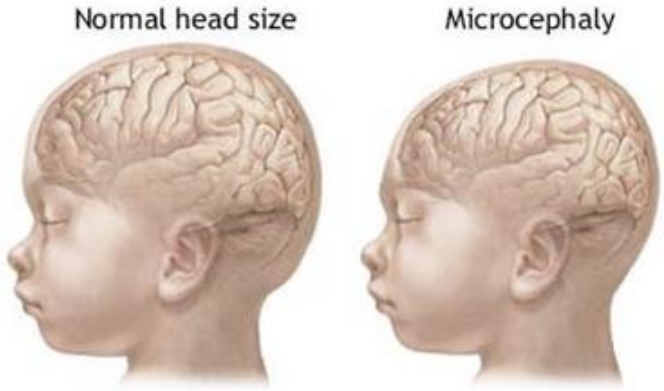
4) Malformations of Whole Brain

- Common and result from many disease processes of genetic, chromosomal and environmental origin

1) Microcephaly

- A condition with brain weighing less than 1000 gm in adults or less than 2 standard deviation mean normal weight for age and sex
- Results from degeneration, destructive or congenital conditions
- Causes include - congenital infections (rubella, toxoplasmosis, cytomegalovirus), toxins, irradiation, metabolic disorders and chromosomal abnormality

Diagram 1.11: Microcephaly



2) Megalencephaly

- 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

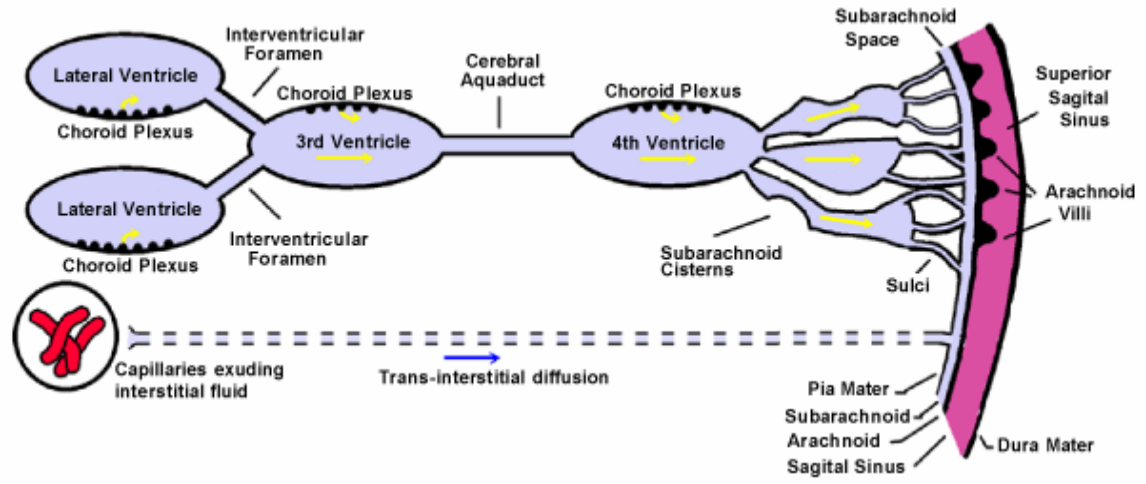
5) Hydrocephalus

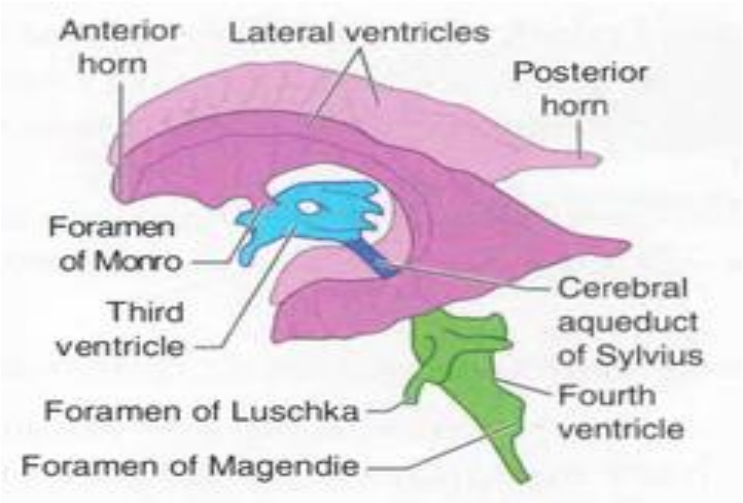
- Is increased CSF volume within the cranial cavity accompanied by dilatation of ventricles
- Can be
  - i) Internal hydrocephalus - increased volume of CSF is within the ventricular system which becomes enlarged (dilated) and associated with increased intracranial pressure
  - ii) External hydrocephalus, excess CSF collects in the subarachnoid space
  - iii) Communicating hydrocephalus - CSF can flow freely from the ventricular system
  - iv) Non-communicating hydrocephalus - CSF does not circulate in the ventricular system

Cerebrospinal Fluid (CSF) – Source and Circulation

- 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
- 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
- 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
- CSF is then absorbed into the blood by the arachnoid villi present along the dural venous sinuses.

Diagram 1.12: CSF Formation, Circulation and absorption

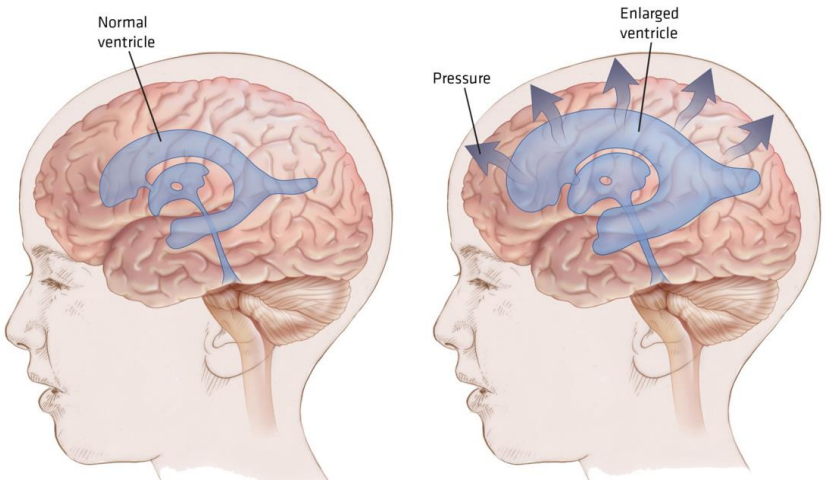




Causes of Hydrocephalus

1) Inherited - myelodysplasia, atresia of foramen of Monro, neural tube defects (encephalocele, spina bifida), genetic abnormalities (aqueduct stenosis, Dandy-Walker complex), cerebral and spinal malformations
2) Acquired - tumours, meningitis, infection, haemorrhage, arachnoid cyst, posterior fossa cyst, traumatic brain (TBI) injury and idiopathic

Diagram 1:13: Hydrocephalus



Mechanisms of Hydrocephalus

- In hydrocephalus, the volume of CNS is increased and the ventricles are dilated. In majority of the cases there is an increase in intracranial pressure
- Three main mechanisms
  1) Overproduction of CSF
     - The choroid plexus secretes more CSF to compensate for any external leak, but overproduction is not a cause of hydrocephalus
  2) Obstruction of the flow of CSF (commonest)
     - Sites particularly vulnerable to obstruction are the aqueduct of Sylvius, foramina of Magendi and Luschka and the subarachnoid space between the midbrain and forebrain (interposition of tentorium cerebelli)
  3) Defective or deficient reabsorption
     - Normally CSF is absorbed into venous sinus via the arachnoid granulation
     - Existence of pathology such as scarring following inflammation, haemorrhage obliterates the absorption sites reducing their absorption capacity.

CLASSIFICATION

- Classified into **primary** and **secondary** hydrocephalus

Primary Hydrocephalus

- Most common where there is actual increase in the volume of CSF within the cranial cavity with increased intracranial pressure
- Commonest mechanism is obstruction to the flow of CSF (**obstructive hydrocephalus)**

- Terms non-communicating & communicating hydrocephalus denote site of obstruction
- Because of the ventricular enlargement that occurs there is a reduction in the bulk of white matter in the cerebral hemispheres
- 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 inter-ventricular foramen of Munro or the aqueduct in the midbrain produces hydrocephalus rapidly

Non-communicating Hydrocephalus

- Site of obstruction of CSF flow pathway is in the 3rd ventricle or at the exit foramen in the 4th ventricle
- 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
   - Stenosis of the aqueduct of Sylvia; Arnold-Chiari malformation; Progressive gliosis of the aqueduct; Intra-uterine meningitis
2. Acquired non-communicating hydrocephalus (occurs from an expanding lesion within the cranial cavity: -
   a) Tumours adjacent to the ventricular system e.g. ependyoma, choroid plexus papilloma and medulloblastoma
   b) Inflammatory lesions e.g. cerebral abscess and meningitis
   c) Haemorrhage – parencymal haemorrhage, intraventricular haemorrhage, epidural haematoma and subdural haematoma

Communicating Hydrocephalus

- Obstruction to CSF flow is in the subarachnoid space at the base of the brain and 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
- 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

- 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
- Also called **hydrocephalus ex vacuo**.

Pathologic Changes

Gross

- Ventricular dilatation, thinning and stretching of the brain, engorged scalp veins overlying the enlarged head and open fontanelles

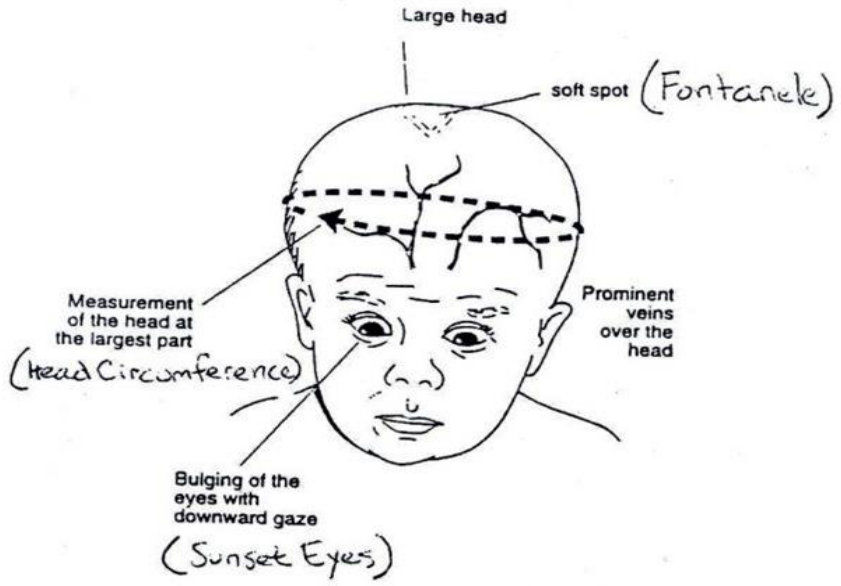
Microscopy

- Damage to ependymal lining of the ventricles and periventricular interstitial oedema

CLINICAL FEATURES

- Variable and depends on many factors such as age of onset, nature of lesion causing obstruction and duration and rate of increase of intracranial pressure.

Diagram 1:14: Hydrocephalus



Infants

- Accelerated enlargement of the head
- Anterior fontanel –wide open and bulging
- Scalp vein are dilated
- Broad forehead
- Eyes may deviate downwards (sunset eyes sign)
- Long tract signs – brisk tendon reflexes, spasticity and clonus (especially of the lower extremities)

Older children

- Cranial sutures partially closed
- Skull percussion – "cracked pot" – **Macewen sign** – indicates separation of sutures

DIAGNOSIS

1. History
2. Physical examination
3. Plain Skull X-ray
4. CT scan
5. MRI

What are the important parameters in these investigations?

COMPLICATIONS

- What are the complications of hydrocephalus?
- What are the differences between acute and chronic hydrocephalus?

Lesson 2: CIRCULATORY (CEREBROVASCULAR) DISORDERS

Learning Outcomes

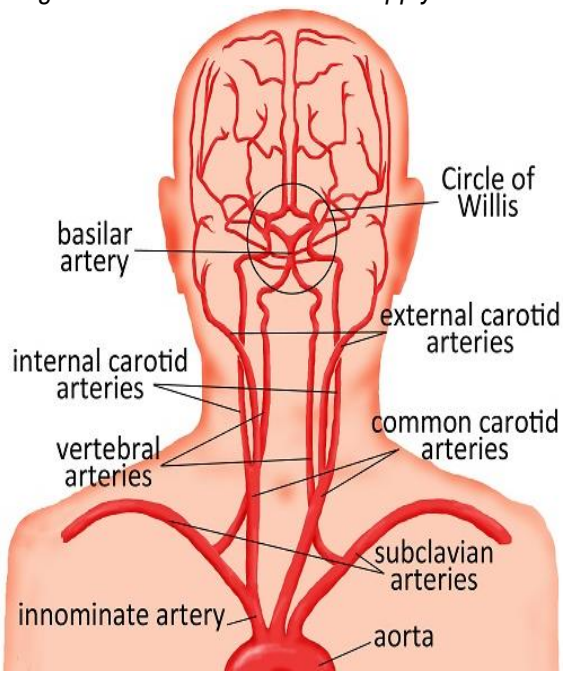
At the end of the lesson the learner should be able to: -

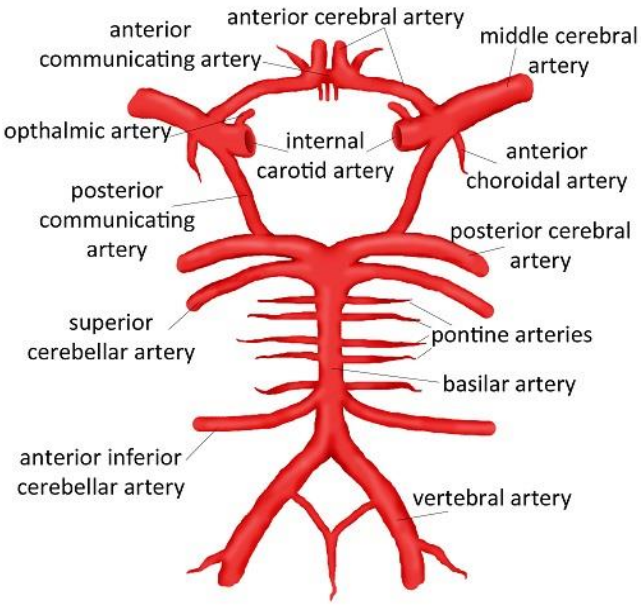
1. Describe the causes and effects of cerebrovascular disorders (CVA)

1.0. INTRODUCTION

- CVDs are diseases in which one or more of the blood vessels of the brain are involved in the pathologic process e.g. stroke is a sudden disturbance of cerebral function of vascular origin and accounts for many cases of severe disability and death
- Hypoxia/ischaemia & intracranial haemorrhage are important & common causes of brain damage

Diagram 2.1: Review of Blood Supply to the Brain





2.0. CEREBROVASCULAR DISORDERS

- Include increased intracranial pressure (ICP), cerebral oedema, cerebral ischaemia & Infarction, brain damage due to cardiac arrest, cerebrovascular accident (CVA)/stroke and cerebral haemorrhage
- Pathologic mechanisms commonly implicated include - *thrombosis, embolism, and vessel rupture, hypoxia, hypertensive arteriosclerosis, atherosclerosis, arteritis, trauma, aneurysm and developmental malformations*
- Pathological process results in 2 main types of parenchymal diseases of the brain namely-
  1) Ischaemic brain damage
     a. Generalized reduction in blood flow resulting in global hypoxia causING ischaemic encephalopathy
     b. Local vascular obstruction resulting in infarcts
  2) Intracranial haemorrhage
     a. Intracerebral haemorrhage – haemorrhage into the brain parenchyma
     b. Subarachnoid haemorrhage – haemorrhage into the subarachnoid space

2.1. Increased Intracranial Pressure (ICP)

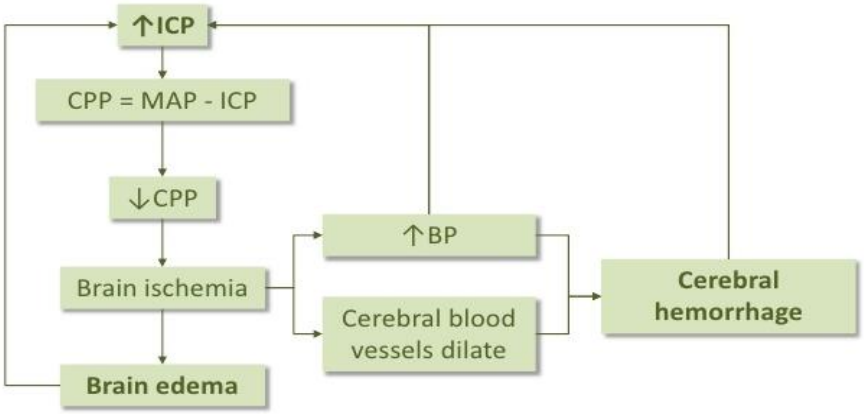
Introduction

- The normal ICP ranges between 5– 20 mmHg (0.7–1.2 kPa or 60–180mm H_2O)
- Increased ICP occurs due to the presence of an expanding lesion and/or due to obstruction of the free flow of CSF which results in hydrocephalus.
- ICP increases due to 2 general causes
  i) An expanding intracranial lesion
     - May occur within the
       a. Brain substance (intracerebral) - haemorrhages and haematomas (traumatic or spontaneous), infarction and tumours – primary cerebral tumours and secondary tumours
       b. In the meninges (meningeal) - haemorrhages and haematomas – extradural, subdural and subarachnoid
  ii) Obstruction to flow of the CSF (hydrocephalus)
- The situation of ICP is usually aggravated by development of cerebral oedema
- Severity of the effects of ICP is influenced by the size of the lesion and rapidity of expansion of the lesion.

Pathophysiology

- Intracranial pressure is a process and not an event
- Secondary injury can be more damaging than primary injury
- Main mechanisms include trauma (contusion and diffuse axonal injury), stroke, masses and oedema

Diagram 2.2: Pathophysiology of ICP



Progress of Increased Intracranial Pressure (ICP)

- Involves 4 stages - stages of total compensation, partial compensation, decompensation and vasomotor paralysis

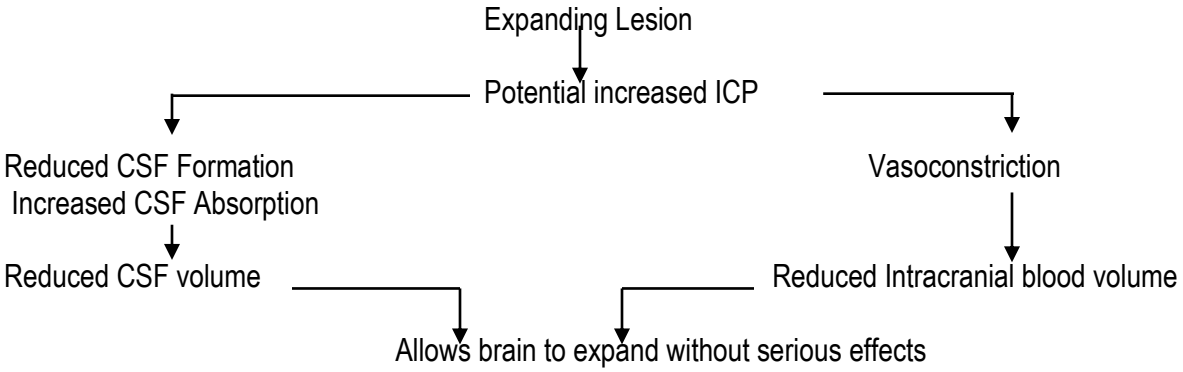
Table 2.1: Stages of ICP

Stage	Intracranial response	Signs/symptoms
1	*Compensatory reduction in CSF and BV; no rise in ICP*	*None*
2	*Compensatory mechanisms exhausted; Slow rise in ICP*	*Drowsy, headache*
3	*Rapid rise ICP; falling cerebral perfusion*	*Deteriorating conscious level; intermittent ↑in BP and bradycardia*
4	*Cerebral vasomotor paralysis; ICP equals mean arterial BP cerebral perfusion ceases*	*Coma; fixed dilated pupils; death*

Stage of Compensation

- Expanding lesion leads to potential increase in ICP which results in vasoconstriction and increased CSF absorption and reduced CSF formation
- Vasoconstriction reduces intracranial blood volume while the changes involving CSF result in reduced CSF volume allowing the brain to expand without serious effects.

Diagram 2:3: Stage of Compensation



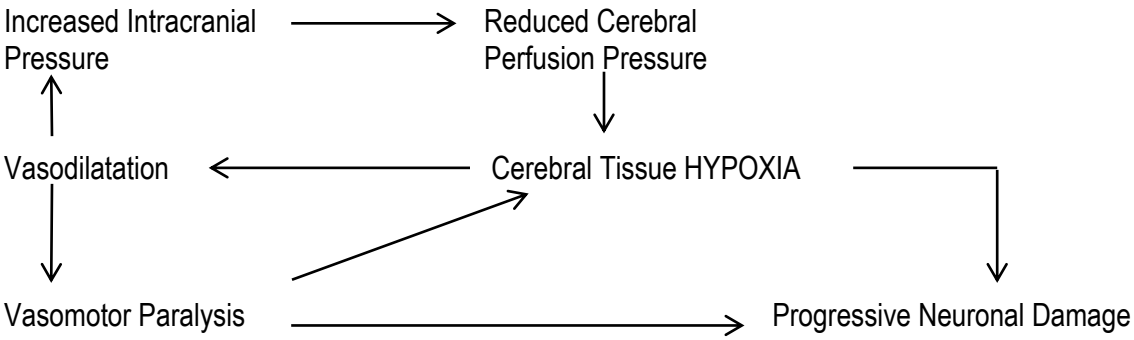
Stage of Partial Compensation

- Compensation reduces the IVC of the circulating blood with no change of tissue perfusion
- Made possible by vasoconstriction that increases the blood pressure
- Systemic arterial blood increases providing the proper brain perfusion

Stage of Decompensation

- There are herniations and distortions of the brain resulting in effects such as: - reduced level of consciousness, dilatation of the pupil ipsilateral to the lesion, papilloedema, bradycardia with raised blood pressure ("Cushing's effect") and Chyne-Stokes respiration

Diagram 2.4: Stage of Decompensation



Vasomotor Paralysis

- There will be a vicious circle due to the higher intracranial pressure there will be a low brain tissue perfusion that leads to hypoxia of brain tissues (and the pCO2 will increase).
- The changes lead to a progressive neuronal injury and a vasomotor paralysis that worsens the hypoxia
- Accumulation of CO_2 in the low perfused tissues disturbs vasoconstriction and leads to a prominent vasodilatation that increases the ICP and brain oedema ensures closing this the pathological ring

Effects of Increased ICP

1. Distortions and dislocations of the brain substance
2. Secondary complications
   a. Vascular damage
      - Compression of central retinal vein causes papilloedema (important clinical sign) and stretching and compression of blood vessels causes haemorrhage and infarction in areas distant to the lesion
   b. Intracranial nerve damage
      - Occulomotor (III) and abducens (VI) nerves are highly vulnerable
      - Vulnerability of cranial nerve VI to damage is due to its long subarachnoid course
   c. Obstruction of the CSF flow - compression of the CSF channels results in obstruction of flow of CSF which in turn aggravates the increased ICP
3. Changes in skull bones - bone erosion and thinning which is visible on X-ray

Clinical Features of ICP

- Include vomiting (projectile), headache, papilloedema, pupillary dilatation, CN VI palsy, nuchal rigidity (neck stiffness, not painful), Cushing's triad (increased pulse pressure, reduced heart rate and irregular respiration – Chyne-Stokes & hyperventilation) and in late advanced stage – bradycardia, hypertension, neurogenic pulmonary oedema

2.2. Cerebral Oedema

- Is accumulation of fluid within the brain substance is a major component of brain swelling
- An important complication of many brain diseases because enlargement of the brain either initiates or aggravates ICP.

Causes

i) Localized conditions e.g. infarcts, local ischaemia, haematomas(secondary to rupture and injury) and tumours
ii) Generalized Conditions e.g. intoxications, metabolic disturbances e.g. hypoglycaemia, generalized hypoxia, severe head injury/trauma and malignant hypertension

Pathogenesis

- Revolves around **cytotoxic** and **vasogenic** mechanisms
  i) Cytotoxic mechanism
     - Early stages - Initiating agent causes cellular membrane injury, disturbance of ion balance of the membrane (Na+ and K+) and the shift of water from the plasma to the interstitium

Diagram 2:5: Pathogenesis of Cerebral Oedema (watery fluid)

Initiating agents → changes in tissues → cytotoxic components

↓

Swollen, damaged cells

↓

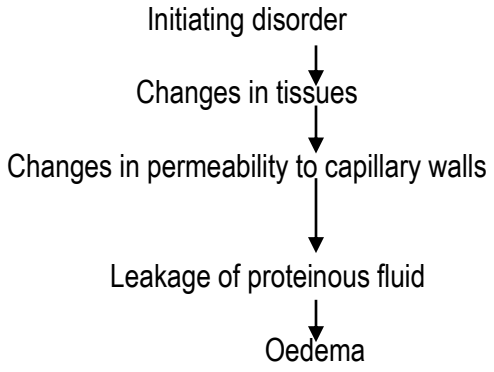
Na+ and K+ leak

↓

Passage of water from plasma to interstitial space

ii) Vasogenic mechanism
- In later stages (2 – 3 days later) capillary wall damage allows shift of plasma proteins to the interstitium with consequent osmotic water binding (shift of water to the interstitium)
- The oedematous fluid has the tendency to spread in the white mate

Diagram 2:6: Pathogenesis of Cerebral Oedema (protein rich fluid)



1. How would you investigate such patients?
2. What history is relevant?

2.3. Ischaemic Brain Damage (Cerebral Ischaemia and Infarction)

Introduction - Blood supply of the CNS

- Arterial supply to the cerebral hemispheres is derived from branches of the circle of Willis
- Spinal cord is supplied with blood derived from the spinal branches of the vertebral, deep cervical, intercostals and lumbar arteries arising from the aorta in a segmental fashion
- These arteries feed into an anterior spinal artery which supplies the anterior 2/3 of the spinal cord and two smaller posterior arteries that supply posterior 1/3 of the spinal cord.
- A period of severe hypoxia of more than 3 – 5 minutes causes irreversible brain damage

Autoregulation

- In an adult the average cerebral blood flow (CBF) is about 50 mls/100 gm/min and the brain normally consumes oxygen at the rate of 3.3 mls/100 mg/min.
- A relatively constant CBF is maintained over a wide range of variations in perfusion pressures by the autoregulation mechanisms.
- Cerebral perfusion pressure (CPP) is the difference between the mean arterial blood pressure (MABP) and the intracranial pressure (ICP) that is MABP - ICP.
- Affected by changes in the cerebrovascular resistance thus when the arterial pressure falls, cerebral arteries dilate and a rise in blood pressure will result in arteriolar constriction
- Fails when the blood pressure falls below 50 mmHg and then the CBF falls rapidly.
- Can be impaired by hypoxia and hypercapnic states, chronic hypertension, head injury, cerebral tumours and stroke

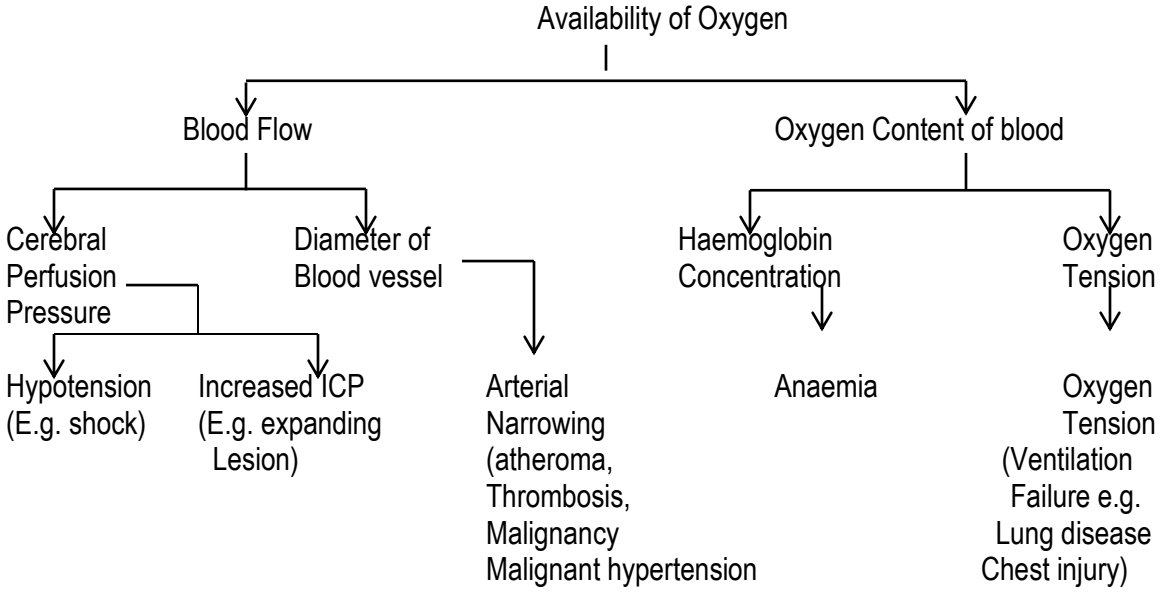
Factors Influencing Availability of Oxygen

i) Availability of oxygen to the brain is proportional to blood flow and blood oxygen content
ii) Blood flow to the brain is determined by cerebral perfusion pressure (CPP) (arterial pressure – intracranial pressure) and diameter of the blood vessels

iii) Cerebral perfusion pressure can be reduced by hypotension (e.g. shock) and increased intracranial pressure (e.g. an expanding lesion)

iv) Oxygen content of blood is determined by haemoglobin concentration and oxygen tension (can be reduced by ventilation failure – lung disease and chest injury).

Diagram 2.7: Factors Influencing Availability of Oxygen



Causes of Hypoxia

- Cardiac arrest, severe hypotension, respiratory obstruction, brain stem damage, hypoglycaemia, CO poisoning, drug overdose (which drugs?), anaemia and obstruction

Explain how these factors cause cerebral hypoxia

Acute Hypoxic Disorders

- 20% of cardiac output is normally delivered to the brain via **carotid** & **vertebral arteries**
- When the CO falls, an autoregulatory vascular control mechanism normally protects the cerebral blood supply as long as the arterial pressure is kept above 50 mmHg
- Brain cells metabolize glucose aerobically (oxygen present) yielding energy and metabolic products especially lactate
- The brain has no reserves of oxygen or glucose therefore it is necessary to have constant delivery of the two via arterial blood

Ischaemic Brain Damage

- Structural damage arises from ischaemia and results in formation of a cerebral infarct involving necrosis of all tissue elements namely the neurons, neuroglia and blood vessels and severe localized reduction or cessation of blood supply or selective necrosis where only the most susceptible cells (the neurons) are necrosed or hypoxic-ischaemic encephalopathy resulting from generalised cerebral hypoperfusion

Hypoxic-Ischaemic Encephalopathy

- Neurons are highly susceptible to hypoxic damage probably due to the presence of acidic excitatory neurotransmitters called excitotoxins
- Ability of the CNS cells to survive irreversible ischaemic damage is determined by: -
  i) Severity of hypoxic episode
  ii) Presence of pre-existing cerebrovascular disease
  iii) Age of the patient
  iv) Body temperature
- In a normal individual the brain is well perfused up to a systolic pressure of 50 mmHg thus a fall in systolic pressure below this critical value results in rapid fall in cerebral perfusion pressures and eventual ischaemic encephalopathy
- Hypoxic encephalopathy can be followed by post-ischaemic confusional state and complete recovery to a state of coma or persistent vegetative life.

Causes

1) Cardiac arrest
2) Severe hypotension
3) Carbon monoxide intoxication
4) Status epilepticus

Brain Damage due to Cardiac Arrest

- Damage is restricted to selective neural necrosis involving the whole rain tissue
- After more than 12 hours microscopy reveals widespread and severe neuronal necrosis
- There is selective susceptibility for the hippocampus, 3rd, 5th and 6th layers of the cerebral cortex within the sulci of posterior halves of the cerebral hemispheres, basal ganglia and purkinje cells of the cerebellum
- After a few days the dead cells disappear resulting in intense reactive changes in astrocytes, microglia and capillaries
- A similar pathology is seen in carbon monoxide intoxication, status epilepticus and severe hypoglycaemia

Brain Damage due to Hypotension

- Damage is concentred in boundary zones/watersheds between main cerebral and cerebella arterial territories
- Caused by a major and abrupt episode of hypotension followed by a rapid return to normal pressure because such as situation precipitates reduction in arterial pressure causing failure of autoregulation
- Regions furthest from the parent arteries (boundary zones) are affected the most
- Encountered in major operations under general anaesthesia, myocardial infarction and severe haemorrhage.
- Infarcts formed are largest in parieto-occipital regions where territories of anterior, middle and posterior cerebral arteries meet. It mainly involves the basal ganglia and upper 3rd of the putamen.

Carbon Monoxide Poisoning

- Hb has high affinity for carbon monoxide than oxygen hence in states of carbon monoxide poisoning there is reduced oxygen tension in blood which can be made worse by anaemic states resulting in overall reduction in availability of oxygen to the brain cells.

Explain how status epilepticus causes hypoxia

Pathologic Changes

- Pathologic changes depend on duration and severity of hypoxic episode and the length of survival

Table 2.2: Progress of Brain Ischaemia

Duration	Pathological changes
Few hours	• No pathologic changes visible
12 – 24 hours	• No macroscopic changes but microscopic examination reveals early neuronal damage with oesinophilic cytoplasm and pyknotic nuclei (red nucleus)
2 – 7 days	• Focal softening and infarction • The most vulnerable portion is the border zone of cerebral cortex between anterior and middle cerebral arteries where there is formation of parasagittal infarction. Functional zone supplied by major arteries produce border zone or watershed infarcts.

Microscopy

- Dead nerve cells which are replaced by fibrillary gliosis

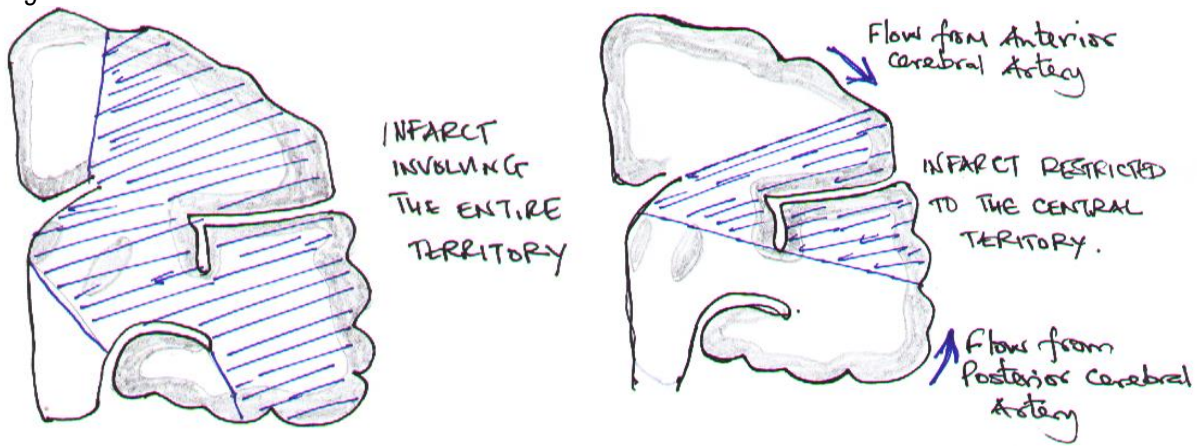
Cerebral Infarction

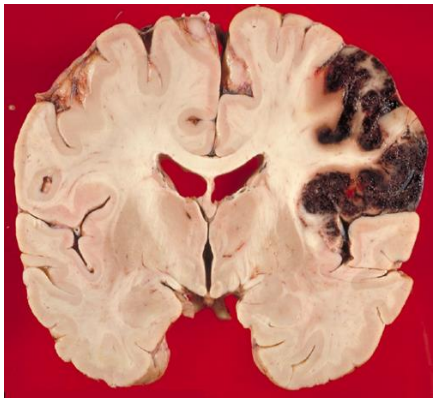
- Is a localized area of tissue necrosis caused by a local arrest or reduction of cerebral blood
- An infarct may range from a small discrete lesion to necrosis of a large part of the brain
- Occur in any part of the brain but commonest site is in the distribution of the middle cerebral artery
- In many cases, cerebral infarction results from a combination of systemic circulatory insufficiency and stenosis of cervical and/or cerebral arteries by atheroma.
- Size and shape of an infarct depends on the extent of anastomotic connections with adjacent arterial branches
- The middle and anterior cerebral arteries have partial anastomoses of their distal branches hence complete occlusion leads to infarct formation
- Small terminal cerebral arteries are end-arteries and their occlusion results in infarction.

Sites

- Cerebral (brain) infarcts can occur in any part of the brain but certain sites are commonly affected depending on development of the precipitating arterial lesions.

Diagram 2.8: Distribution of Cerebral Infarcts





Local Arterial Occlusion

- In local occlusion of arterial blood vessels the internal structures which are supplied by "end" arterial branches are particularly prone to damage
- Cerebral cortex is often protected by the presence of variable degree of anastomoses of other cerebral arteries.

Aetiopathogenesis

1) Arterial occlusion
   a) Embolism
      - Commonly arise from the heart more often from vegetations of infective endocarditis, mural thrombosis in patients with arrhythmias, myocardial infarction and non-thrombotic (bacterial) endocarditis associated with cachexia of advanced chronic disease; open heart surgery; coronary heart surgery using cardiopulmonary by-pass and thrombus formation in ulcerated atheromatous lesions in the aorta and neck arteries
   b) Thrombosis
      - Intracranial arteries, internal carotid and vertebral arteries are affected
      - Commonest intracranial site of thrombotic occlusion is the middle cerebral artery
   c) Atheroma
      - Atheroma of cerebral arteries is associated with atheroma in other parts of the body
      - Atheromatous stenosis usually causes effects when the cross-sectional area of the artery is reduced by up to 90% because below this level blood would still flow if the blood pressure is normal
   d) Vasculitis (arteritis) –
      - Results from infections, sickle cell disease (SCD), syphilitic arteritis or collagen diseases such as polyarteritis nodosa and systemic lupus erythromatosus (SLE) leading to reduced blood supply to target organs.
2) Venous occlusion - less common due to the good communication of cerebral venous drainage.

Causes of venous occlusion

i) Cancer – increases predisposition to thrombosis e.g. superior sagittal sinus thrombosis
ii) Sickle cell disease
iii) Polycytheamia rubra vera
iv) Pregnancy and peurperium
v) Oral contraceptives
vi) Drug addicts using heroin and lysergic acid diethylamide (LSD)
vii) Non-occlusive causes - The non-occlusive causes result from compression of cerebral arteries from outside.

Types of Ischaemic Lesions

- There are 4 main types of ischaemic lesions according to the pathogenesis of reduced blood flow to the brain.
  - i) Large vessel disease
    - Causes regional infarction due to embolism and thrombosis
    - Infarcts correspond to territorial blood supply
  - ii) Small vessel disease
    - Causes microinfarcts (lacunar infarcts)
    - Caused by arteriosclerosis predisposed by hypertension and diabetes
    - Main sites – pons, basal ganglia and internal capsule
  - iii) Venous ischaemia
    - Causes haemorrhagic necrosis
    - Due to thrombosis in main cerebral venous sinus
    - Associated with thrombosis, polycythaemia, or dehydration
  - iv) Global ischaemia
    - Causes widespread neuronal necrosis leading to cortical necrosis
    - Results from reduction in cerebral blood flow as in cardiorespiratory arrest

Evolution of an Infarct

- Within 18 – 24 hours the gross appearances are difficult to see and there is early neuronal damage
- After the first 24 hours there is slight swelling of the brain tissue with blurring of the white-grey matter junction. This is accompanied by early neuronal damage which results in necrosis of neurones with functional loss.
- After a few days there is the necrotic tissue with a visible demarcation line. The necrotic tissue is soft to touch, pale (but may be congested if blood has permeated in – haemorrhagic infarct). During this period, organization of the infarct begins. Macrophages appear and there is capillary sprouting with reduction in oedema.
- After weeks/months, there is demolition and scarring of the infarct resulting information of a cyst with pale of yellowish fluid. There is shrinkage of the scarred area with compensatory dilatation of the ventricles of the brain. The infarct becomes well organized, neurones disappear and there is gliosis with numerous macrophages.

Pathological Changes

- Structural changes in a cerebral infarct depend on the size of the lesion and survival time
- Cerebral infarcts may be pale (anaemic) or haemorrhagic
- Dead tissue is removed by central liquefaction and there is peripheral glial reaction (gliosis) with shrinking of the lesion and thickening leptomeninges to form a cystic infarct
- Cyst is traversed by small blood vessels and glial fibrils.

Macroscopy (Gross)

- Large infarct is large, swelling of necrotic tissue & oedema of surrounding brain leads to increased intracranial pressure secondary to an acute expanding intracranial lesion
- After 2 – 3 days the infarct undergoes softening and disintegration

- Macrophages are filled with globules of lipid (lipid phagocytes from breakdown of myelin) are seen around the dead tissue, enlarged astrocytes and early capillary proliferation.
- Dead tissue is removed by central liquefaction and there is peripheral glial reaction (gliosis) with shrinking of the lesion and thickening of leptomeninges to form a cystic infarct. Cyst is traversed by small blood vessels and glial fibrils
- Shrinkage of an infarct in the cerebral hemispheres is usually accompanied by enlargement of the adjacent lateral ventricle

Haemorrhagic Infarct

- Is red and superficially resembles a haematoma (internal architecture does not resemble a haematoma)
- Results from fragmentation of occlusive arterial emboli or venous thrombosis
- Some macrophages will contain haemosiderin and the cyst walls appear brown

Pale Infarct

- Occurs within 6 – 12 hrs and is it difficult to identify the macroscopic features before 24 hrs
- Dead tissue is soft & swollen with a blurring junction between the grey and white matter
- On histology there is ischaemic necrosis of neurons, pallor of myelin staining and polymorphs surrounding the necrotic walls of blood vessels.

2.4. Cerebrovascular Accident (Stroke)

- Is a sudden disturbance of cerebral function of vascular origin (rapid development of signs of focal disturbance of cerebral function of presumed vascular origin that develop over a period of 24 – 48 hours)
- Describes the sudden and dramatic development of focal neurologic deficit which varies from trivial neurological disorder to hemiplegia and coma
- Incidence rises with age (80% of cases occur in patients aged 65 years and above)
- Commonest causes of stroke in descending order of incidence are infarctions (due to thrombosis and embolism) and haemorrhage (spontaneous intracerebral haemorrhage and ruptured intracerebral aneurysm)

Risk Factors

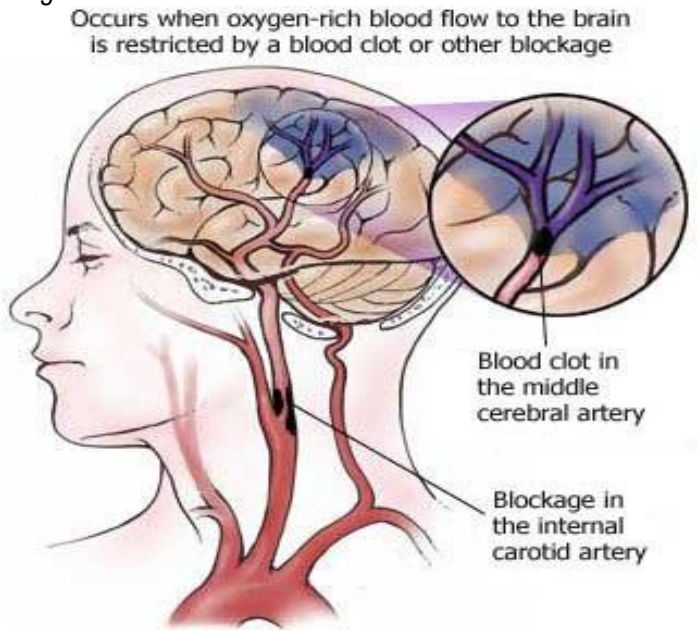
- Atheroma, hypertension, high cholesterol levels/abnormalities in lipid serum, diabetes mellitus, cardiac failure, coronary heart disease, atrial fibrillation, cigarette smoking, obesity, blood disorders e.g. sickle cell, drugs (which drugs?), alcohol consumption, intracranial haemorrhage (hypertension, congenital anomalies, vascular malformations, arteritis and bleeding diatheses)

Ischaemic Stroke

Explain how are these risk factors?

- Account for about 80 percent of strokes
- Occur when arteries to the brain become narrowed or blocked causing ischaemia
- The most common ischemic strokes include:
  i) Thrombotic stroke - thrombus forms in one of the arteries supplying blood to the brain
  ii) Embolic stroke - occurs when an embolus lodges in narrower brain arteries

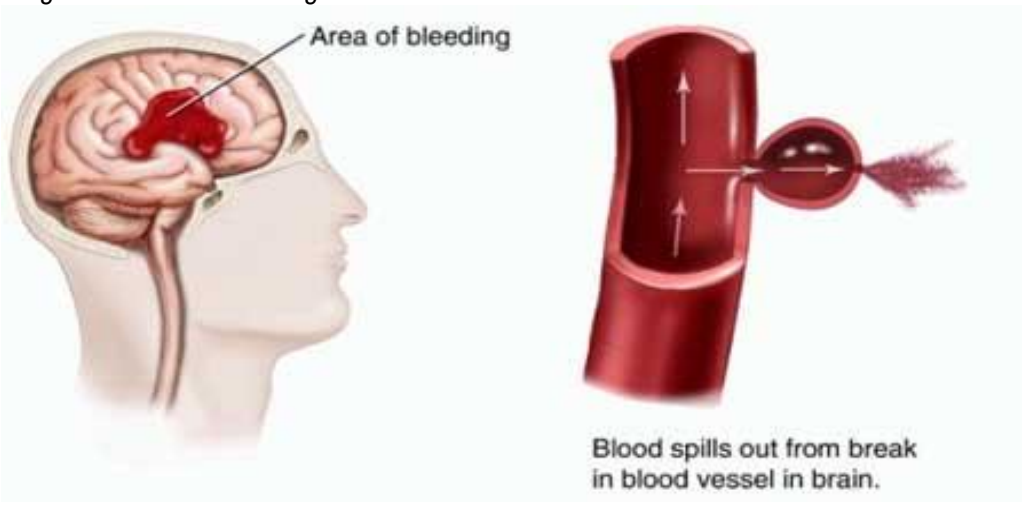
Diagram 2.9: Ischaemic Stroke



Haemorrhagic Stroke

- Occurs when a blood vessel in the brain leaks or ruptures
- Haemorrhages can result from many conditions that affect your blood vessels, including hypertension, aneurysms and arteriovenous malformation

Diagram 2.10: Haemorrhagic Stroke



- Types of haemorrhagic stroke include:
  i) Intracerebral haemorrhage
     - A blood vessel ruptures spilling blood into the surrounding brain tissue, damaging brain cells and brain cells beyond the leak are deprived of blood and damaged
     - Causes include hypertension, trauma, vascular malformations
  ii) Subarachnoid haemorrhage
     - An artery on/or near brain surface ruptures & spills into the subarachnoid space
     - Commonly caused by rupture berry aneurysms in the brain
     - After the haemorrhage, the blood vessels in the brain undergo vasospasm causing brain cell damage by further limiting blood flow.

Effects

- Less common effects of vascular disease include:-
  i) Transient Ischaemic Attack (TIA)
     - TIA is a fully reversible neurological deficit lasting or a few minutes up to 24 hours
     - Usually there is no structural brain damage
     - Completed stroke has permanent brain damage of varying severity
  ii) Vascular headache (migraine, hypertension, and arteritis)
  iii) Local pressure of an aneurysm
  iv) Increased intracranial pressure.

TASK
Discuss the following regarding CVA: -
- Pathophysiology,
- Clinical Features
- Complications,
- Investigations
- Relevant history

Rosier Scale

	Assessment	Score	
		Yes	No
1)	Has there been loss of consciousness or syncope	-1	0
2)	Has there been seizure	-1	0
3)	Is there a new acute onset (or on awakening from sleep) in the following	+1	0
	Asymmetrical facial weakness	+1	0
	Asymmetrical arm weakness	+1	0
	Asymmetrical leg weakness	+1	0
	Speech disturbance	+1	0
	Visual field defects	+1	0
	Patient total score = -2 to +5		
	Stroke is unlikely but not excluded if total score is < 0		

Clinical Features

a) Middle cerebral artery stroke
- Features include contralateral hemiparesis and hypesthesia, ipsilateral hemianopsia
- Gaze preference toward the side of the lesion, agnosia, receptive or expressive aphasia (if the lesion occurs in the dominant hemisphere), neglect, inattention, and extinction of double simultaneous stimulation, with some non-dominant hemisphere lesions
- MCA supplies the upper extremity motor strip, consequently, weakness of the arm and face is usually worse than that of the lower limb

b) Anterior cerebral artery stroke
- Anterior cerebral artery (ACA) occlusions primarily affect frontal lobe function
- Features include dis-inhibition and speech perseveration, primitive reflexes (e.g., grasping, sucking reflexes), altered mental status, impaired judgment, contralateral weakness (greater in legs than arms), contralateral cortical sensory deficits, gait apraxia, urinary incontinence

c) Posterior cerebral artery stroke
- Posterior cerebral artery (PCA) occlusions affect vision and thought
- Features include contralateral homonymous hemianopsia, cortical blindness, visual agnosia, altered mental status and impaired memory

d) Vertebrobasilar artery occlusions

- Cause a wide variety of cranial nerve, cerebellar, and brainstem deficits
- Features include vertigo, nystagmus, diplopia, visual field deficits, dysphagia, dysarthria, facial hypesthesia, syncope, ataxia

2.5. Intracranial (Cerebral) Haemorrhage (ICH)

- Is bleeding into the brain which may be traumatic or spontaneous (no-traumatic)
- Two main types of spontaneous intracranial haemorrhage - intracerebral & subdural haemorrhage
- Results in formation of **intracerebral haematomas (**increase in size rapidly producing a sudden increase in ICP, rapid distortion and herniation of the brain)
- Blood may rupture into the ventricles or through the surface of the brain into the subarachnoid space
- Commonest site is branches of the MCA to basal ganglia and internal capsule
- Clinically, has a sudden onset with headache and loss of consciousness

Sites

- Basal ganglia (40-50%), lobar regions (20-50%), thalamus (10-15%, pons (5-12%), cerebellum (5-10%) and other brainstem sites (1-5%)

Progress

- The onset is usually sudden with headache
- If the BP is high the progress is rapid producing the large haemorrhage which is associated with raised intracranial pressure effects which may lead to death
- Intracerebral bleeding may track irregularly and often reaches the subarachnoid space and ventricles. When bleeding is minimal or limited there is survival with varying residual paralysis
- Usually the final outcome is a cystic space containing yellow-brown fluid walled off by gliosis. The cyst is described as apoplectic cyst.

Risk Factors

i) Modifiable e.g. hypertension, anticoagulant therapy, thrombolytic therapy, high alcohol intake, previous history of stroke and illicit drug use (particularly cocaine)
ii) Non-Modifiable e.g. advanced age, cerebral amyloidosis, coagulopathies, vasculitis, arteriovenous malformations (AVMs) and intracranial neoplasms

Causes

1. Non Traumatic e.g. hypertension, rupture of aneurysms, vascular malformations, haemorrhagic diseases/dyscrasia e.g. acute leukaemia and tumours (haemorrhage into tumours)
2. Traumatic – head injury

Pathophysiology

- Consists of three distinct phases - initial haemorrhage, hematoma expansion and peri-hematoma oedema with disease outcome depending primarily on the latter two phases of progression
  i) Initial haemorrhage
     - Caused by rupture of cerebral arteries influenced by the aforementioned risk factors
  ii) Hematoma expansion,

- Increased ICP disrupts the integrity of the local tissue and the BBB
- Obstructed venous outflow results in local coagulopathy
- In over 1/3 of patients, hematoma expansion is associated with hyperglycemia, hypertension and anticoagulation.

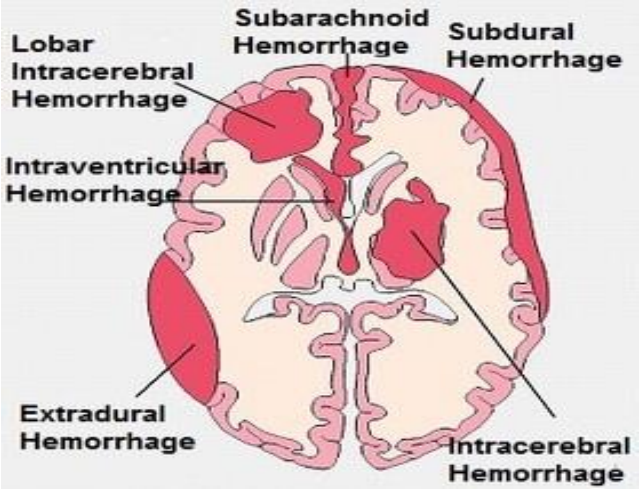
iii) Peri-heameatoma oedema

- Cerebral oedema forms around the hematoma, secondary to inflammation and disruption of the blood-brain barrier
- Primary aetiology for neurological deterioration and develops over days following the initial insult

Types of Intracranial Haemorrhage

- Include intracerebral, intraventricular subarachnoid, subdural and extradural haemorrhage

Diagram 2.11: Types of Intracranial Haemorrhage



Subarachnoid Haemorrhage

- Is spontaneous (non-traumatic) haemorrhage

Causes

- Rupture of a saccular (berry) aneurysm (what are the common sites), rupture of vascular malformations, disease dyscrasias, extension of either intracerebral or intraventricular haemorrhage and idiopathic
- Hypertension is an important contributing factor.

Clinical features

Symptoms

- Sudden onset of severe headache (thunderclap headache)
- Neck pain, and nonspecific symptoms
- Nausea and/or vomiting from increased ICP and meningeal irritation
- Symptoms of meningeal irritation, including nuchal rigidity and pain, back pain, and bilateral leg pain, occur Photophobia and visual changes are common.
- Focal neurologic deficits may also occur.
- Sudden loss of consciousness (often is transient) and comatose
- Seizures result from the sudden rise in ICP or direct cortical irritation by blood

Signs

- Mild to moderate blood pressure (BP) elevation, temperature elevation, tachycardia
- Fundoscopy may reveal papilledema.
- Global depression of neurologic - altered level of consciousness and confusional state.
- Motor neurologic deficits
- Seizures may occur.
- Focal neurologic findings - cranial nerve palsies (most frequent is oculomotor nerve palsy with or without ipsilateral mydriasis, which results from rupture of a posterior communicating artery aneurysm and Abducens nerve palsy is usually due to increased ICP rather than a true localizing sign
- Monocular vision loss can be caused by an ophthalmic artery aneurysm compressing the ipsilateral optic nerve
- Hemiparesis results from middle cerebral artery (MCA)
- Aphasia
- Leg monoparesis or paraparesis

Investigations

1) Full blood count—anaemia (SCD), leucocytosis (after a seizure, systemic infection)
2) Coagulation screen—underlying coagulopathy
3) Urea and electrolytes—hyponatraemia is common after subarachnoid haemorrhage due to salt wasting, not inappropriate antidiuretic hormone secretion
4) Serum glucose—hypoglycaemia needs correction, hyperglycaemia is associated with poor outcome after subarachnoid haemorrhage
5) Serum magnesium—hypomagnesaemia is common and associated with poor outcome after subarachnoid haemorrhage
6) Chest radiography—pulmonary oedema, aspiration
7) ECG —cardiac arrhythmia, ST segment changes, myocardial "stunning"
8) CT scan (thin < 3 mm cuts without contrast) - may indicate site of bleed, early complications e.g. hydrocephalus and cerebral oedema, or an alternative diagnosis.
9) Angiography
10) Lumbar Puncture (LP) - check for xanthochromia by spectrophotometry of spun CSF, shielded from light.

Effects/Complications

1. Haemorrhage may be limited to the immediate vicinity but can spread extensively through the subarachnoid space
2. Intracerebral haematoma – blood tracks back to the brain
3. Infarction in the region supplied the affected artery
4. Hydrocephalus
5. Vasospasm
6. Re-bleeding
7. Seizures
8. Cardiac dysfunction

Grading

- Clinical assessment of SAH severity commonly utilizes grading scales
- The 2 clinical scales most often employed are the Hunt and Hess and the World Federation of Neurological Surgeons (WFNS) grading systems. A third, the Fisher scale, classifies SAH based on CT scan appearance and quantification of subarachnoid blood.

World Federation of Neurological Surgeons (WFNS) scale

Grade	Description	Prognosis
Grade 1	Glasgow Coma Score (GCS) of 15, motor deficit absent	
Grade 2	GCS of 13-14, motor deficit absent	
Grade 3	GCS of 13-14, motor deficit present	
Grade 4	GCS of 7-12, motor deficit absent or present	
Grade 5	GCS of 3-6, motor deficit absent or present	

The Fisher scale (CT scan appearance)

Grade	Description
Group 1	No blood detected
Group 2	Diffuse deposition of subarachnoid blood, no clots, and no layers of blood greater <1 mm
Group 3	Localized clots and/or vertical layers of blood 1 mm or greater in thickness
Group 4	Diffuse or no subarachnoid blood, but intracerebral or intraventricular clots are present

The Hunt and Hess grading system

Grade	Description
Grade 0	Unruptured aneurysm
Grade I	Asymptomatic or mild headache and slight nuchal rigidity
Grade Ia	Fixed neurological deficit without acute meningeal/brain reaction
Grade II	Cranial nerve palsy, moderate to severe headache, nuchal rigidity
Grade III	Mild focal deficit, lethargy, or confusion
Grade IV	Stupor, moderate to severe hemiparesis, early decerebrate rigidity
Grade V	Deep coma, decerebrate rigidity, moribund appearance

Lesson 4: HEAD INJURY

Learning Outcomes

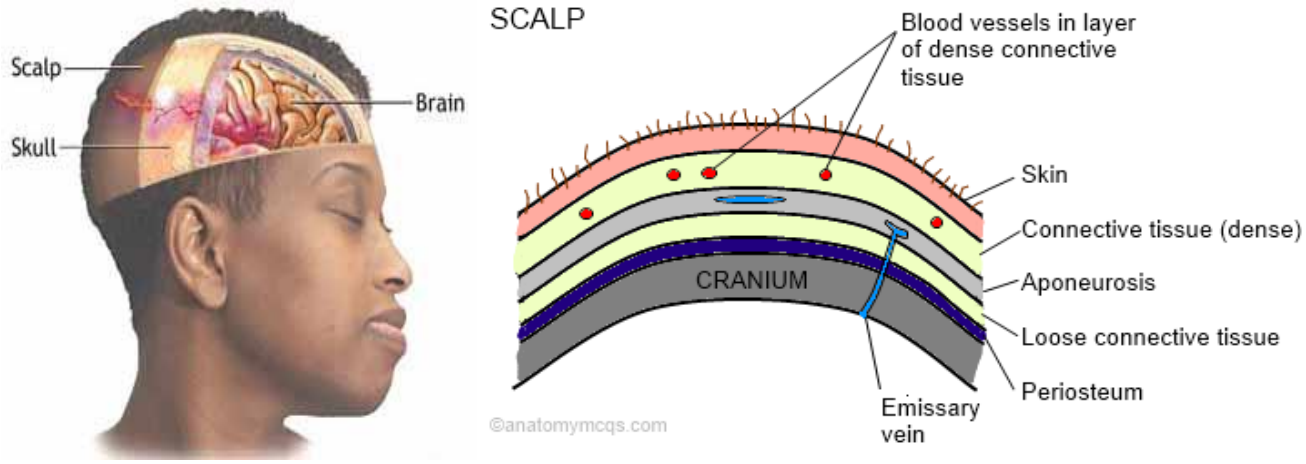
At the end of the lesson the learner should be able to: -

1. Outline causes of head injury
2. Describe mechanisms and the effects of head injury
3. Outline the investigations in head injury and complications of head injury

1.0 INTRODUCTION

- Trauma to the CNS constitutes an important cause of death and permanent disability
- Head injuries of varying severity are common traffic accidents
- Brain damage resulting from a head injury is the most important factor contributing to death or serious incapacity due to trauma
- Important causes of HI are motor vehicle accidents, accidental falls & criminal acts
- Head injury constitutes injury to the scalp, skull and brain

Diagram 3:1: Regions of Head Injury



2.0 CAUSES

1. Road traffic accidents (RTA)/motor vehicle accidents
2. Accidental falls
3. Criminal acts and assault
4. Gunshots
5. Violent shaking

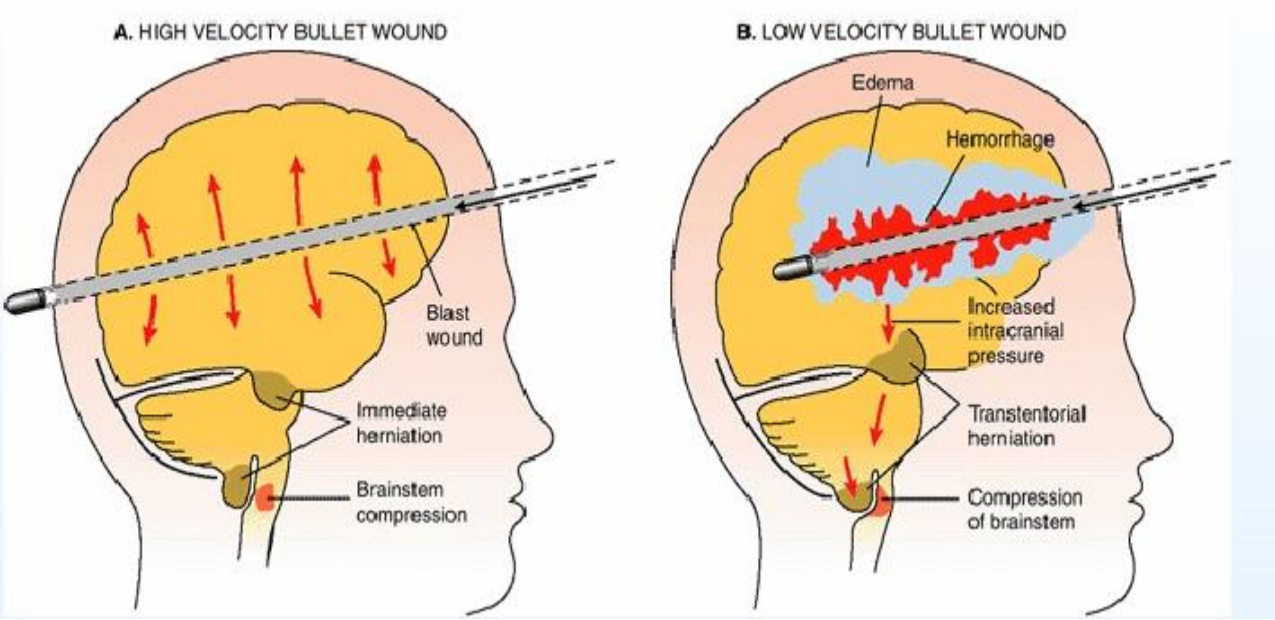
3.0 MECHANISMS OF HEAD INJURY

- Immediate damage is caused by two main mechanisms which overcome the protection of the vulnerable cerebral tissues provided by the skull and CSF "water cushion".
- There are two principal types of head injury
  i) Missile (direct blows to the head) injuries
  ii) Non-missile (involves sudden application of forces) injuries with different mechanisms of brain damage including acceleration, deceleration and rotational forces

3.1. Missile Head Injuries (Open Head Injury)

- Result from direct blows to the head produced by various types of falling or propelled objects
- The objects enter the cranial cavity producing focal brain damage caused by penetration of the skull or brain by an external object such as a bullet.
- Missile injuries can be
  - i) Depressed Injury – skull fracture contusion but no entry to brain.
  - ii) Penetrating Injury – enters but not exit. Infection.
  - iii) Perforating injury – Missile enters and exits, large exit wound, extensive haemorrhage, risk of infection & epilepsy.

Diagram 3.2: Missile Injuries



- Missile injuries usually cause injury to: -
  - i) Soft tissues of the scalp – laceration and haematoma
  - ii) Skull – facture which is often comminuted with or without depressed fragments
  - iii) Brain - contusion , laceration, haematoma

3.2. Non-Missile Head Injuries (Closed Head Injury)

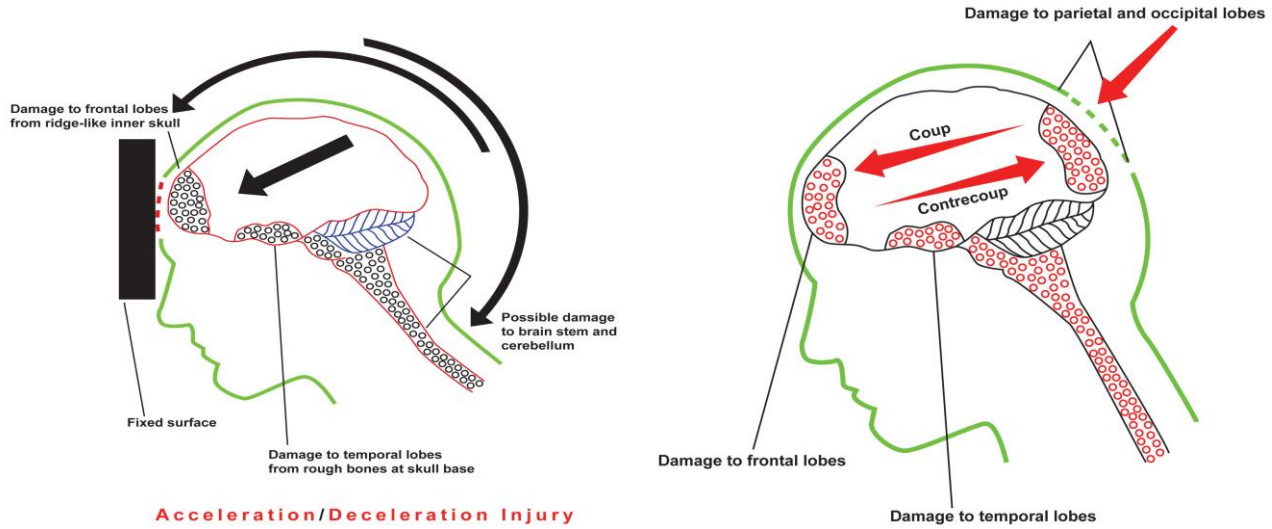
- The head is usually freely movable on the neck so sudden application of force can cause head injury
- Non-missile head injuries involve sudden **deceleration**, **acceleration** and **rotation** of the head which result in movement of the brain within the cranial cavity engendering various shear strains within the brain
- Account for the majority of cases of brain damage
- Rotation of the head in particular causes serious brain injury

Acceleration and deceleration

- In acceleration the skull accelerates rapidly and hits an object resulting in sudden deceleration due to the impact against a hard flat surface
- Sudden acceleration force causes severe distortion and bursting effect which causes linear fractures of both the skull vertex and base

- Acceleration and deceleration forces cause the brain to move forward continuously and it is contused by the rough surface of the middle fossa on the frontal and temporal lobes.
- The contusion affects mainly the gyri sparing the sulci.
- The coup injury on the brain tissue adjacent to the site of force (primary injury) while counter injury occurs on the opposite site (secondary injury)
- During impact to the head, the soft brain crashes back and forth against the inside of the hard skull causing bruising, bleeding, and shearing of the brain

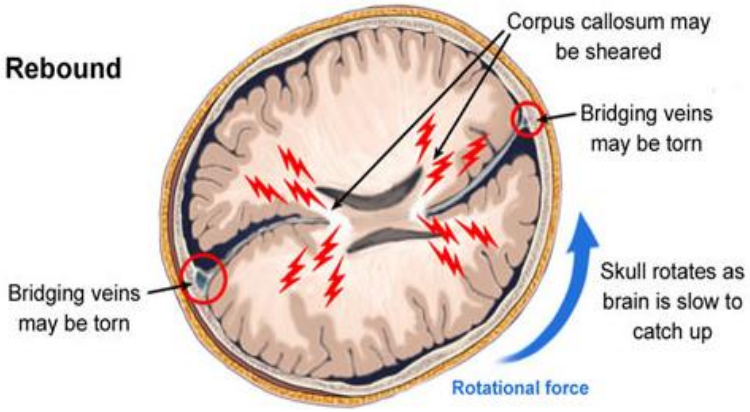
Diagram 3.3: Non-Missile Injuries



Rotation

- Rotary movements of the cerebral hemispheres cause variable diffuse damage to the cerebral tissues (resulting in minute cerebral haemorrhages) and shearing injury to the corpus callosum
- May cause sudden torsion of the midbrain with or without vascular damage a scenario that may prove fatal
- Angular forces cause a shearing injury
- A rotational force is slightly oblique and causes the head to rotate around its point of articulation at the top of the spine as it is hit.
- Because the head is not perfectly round the brain not only spins as a whole but some parts within it spin at different rates. This sets up additional shear forces inside the brain itself. This stress within the brain results in tearing of nerve fibres and tiny veins within the brain. This is called diffuse axonal injury (DAI)

Diagram 3.4: Rotation Injury



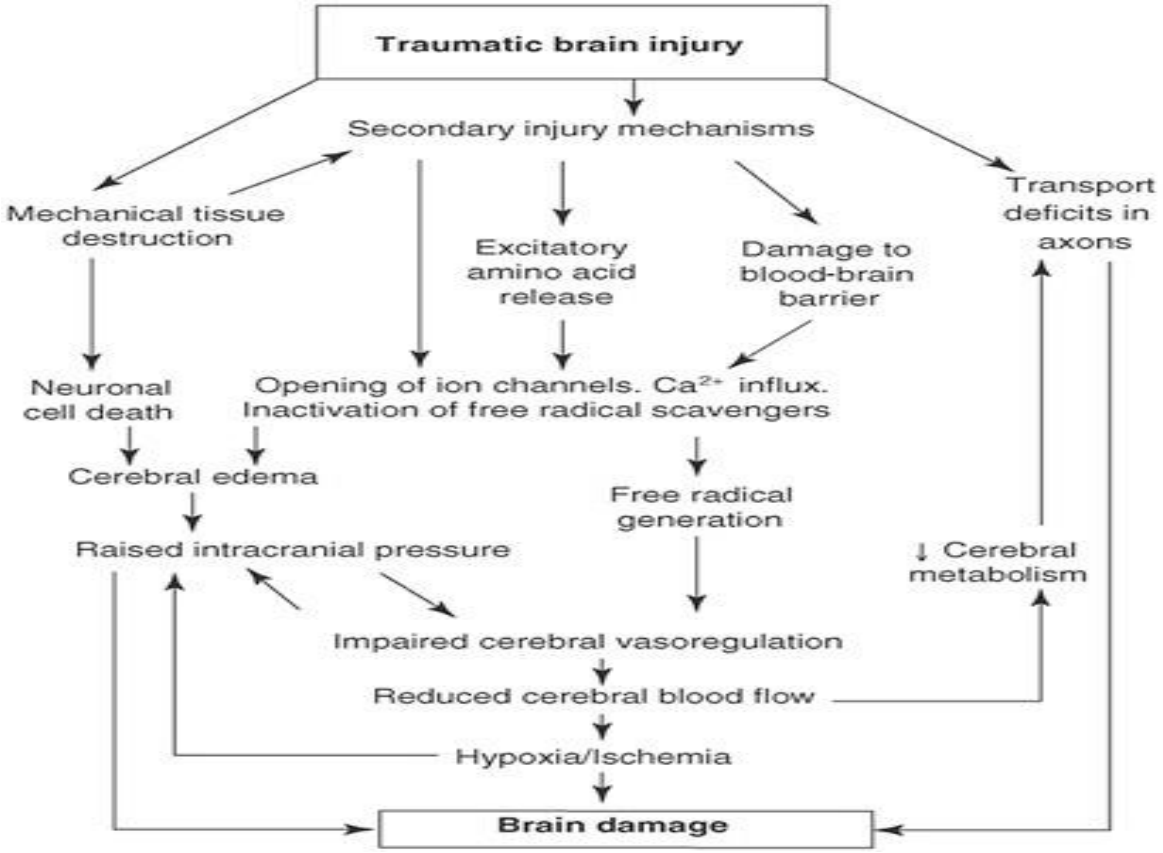
4.0 PATHOGENESIS

i) Focal damage
- Contusion – local injury and haemorrhage
- Healing by gliosis – gross yellow-brown due to haemosiderin

ii) Diffuse axonal injury
- Shearing of neurones resulting in small haemorrhagic lesions in the corpus callosum and dorsolateral quadrant of the brain stem
- Diffuse damage to axons

5.0 PATHOPHYSIOLOGY

Diagram 3.5: Pathophysiology of Brain Injury



6.0 TYPES OF INJURIES

6.1. Primary Damage

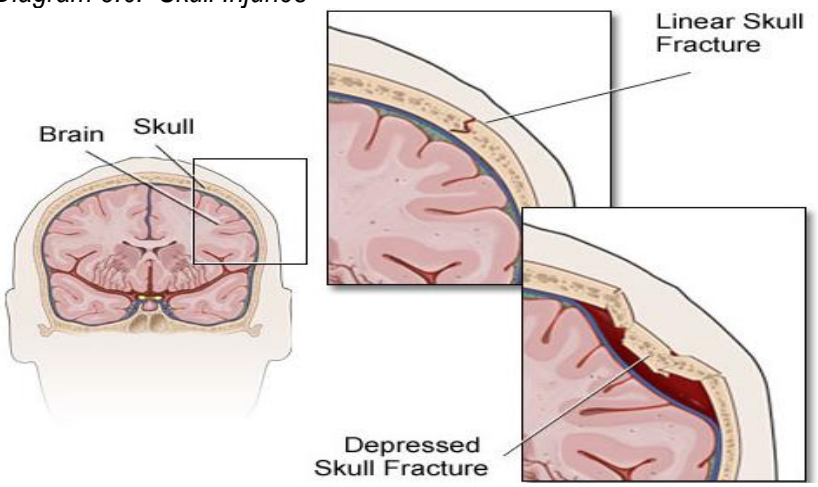
1) Scalp Injuries

- Scalp lacerations are common and result in excessive haemorrhage if not controlled (scalp does not contract easily and the skin rolls or moves with the loose areolar tissue leaving the vessels in the dense fibrous layer being held open)
- Scalp hair is protective because they mat into the wounds assisting haemostasis but likewise mask significant scalp lacerations
- To stop bleeding from the scalp; stitch through all the five layers of the scalp. The scalp's rich vascular supply plays an important role in healing making it a resilient structure.

2) Skull Injuries

- Fractures of the skull can be simple linear fractures, depressed skull fractures (may involve the outer table or both the outer and inner table) and fractures at the base of the skull.

Diagram 3.6: Skull Injuries



3) Brain Damage in Head Injury

- Result in **primary** and **secondary** brain damage
- Primary brain damage occur at the moment of injury e.g. surface contusions, diffuse damage to nerve fibres
- Secondary brain damage occurs sometime after injury – e.g. intracranial haematoma & ICP

a) Primary Brain Damage

- Involves the brain parenchyma - concussion, contusions and lacerations, diffuse axonal injury, traumatic intracerebral haemorrhage and brain swelling (oedema)

i) Concussion

- Is a minor traumatic brain injury caused by closed head injury
- Defined as a complex patho-physiologic process affecting the brain, induced by traumatic biomechanical forces secondary to direct or indirect forces to the head
- Characterized by transient neurological dysfunction and loss of consciousness
- Complete neurological recovery occurs after some hours or days
- No significant morphological change in the brain substance (severe concussion may cause diffuse axonal injury)
- A concussion can cause physical symptoms, cognitive symptoms, behavioural symptoms and emotional symptoms
- Symptoms include nausea, vomiting, headache, double vision or visual disturbance, trouble with bright light or loud noise, feeling sluggish, feeling foggy or groggy, concentration difficulties, memory difficulties, feeling dazed or confused, ringing in ears, difficulty processing information and feeling like your head is spinning

Cognitive symptoms of a concussion

- Feeling mentally foggy
- Problems concentrating
- Problems remembering
- Feeling more slowed down

Emotional symptoms of a concussion

- Irritability
- Sadness
- Feeling more emotional
- Nervousness

Sleep symptoms of a concussion

- Drowsiness
- Sleeping more than usual
- Sleeping less than usual
- Trouble falling asleep

ii) Contusions and Lacerations

- Surface contusions and lacerations are the commonest form of brain damage directly attributed to injury
- Result from direct damage to the brain parenchyma particularly the cerebral hemispheres (most often from blunt trauma)
- Occur at the site of contact particularly if there is a depressed fracture of the skull
- In non-missile head injury they involve the frontal poles, the orbital gyri, temporal poles and the inferior and lateral surfaces of the anterior halves of the temporal lobes (regions are vulnerable because movement of the brain within the skull brings them into forcible contact with bony protuberances of the base of the skull)

Contusions

- Are asymmetrical and may be more severe on the side opposite the point of injury ("countercoup" injury) thus severe frontal contusions occur in association with an impact in the occipital region
- Inner surface of the occipital bone is smooth so an impact on the frontal bone does not produce severe occipital contusions.
- Usually affect crests of gyri but more severe ones extend through the full thickness of the cortex into the adjacent white matter. Such contusions are associated with intracerebral haemorrhage and brain swelling. Old healed contusions are shrunken areas of gliosis
- Gliding contusion is the parasagittal foci of haemorrhage affecting the cortex and adjacent white matter
- Traumatic subarachnoid haemorrhage invariably accompanies cerebral contusions.

Macroscopy

- Brain tissue at the affected site is haemorrhagic, necrotic and fragmented. The healed lesions appear as shrunken and golden brown (due to haemosiderin pigment on the surface).

iii) Diffuse Axonal Injury

- Shear strains produced by acceleration or deceleration and rotational force tear nerve fibres during injury
- Sudden angular acceleration or deceleration results in widespread axonal shearing in deep white matter of both hemispheres
- Is the most common cause of persistent coma or vegetative state following head injury (occurs in absence of contusions)

Macroscopy
- Small shrunken cystic lesions in corpus callosum and rostral brain stem
- Minimal changes to small multiple haemorrhages are seen
- Enlargement of the ventricular system due to reduced bulk of the white matter.

Microscopy
- Presence of axonal bulbs with extended axo-plasm at the point of injury in all regions of the brain
- Wallerian degeneration in cerebral and cerebellar hemispheres, brain stem and spinal cord.

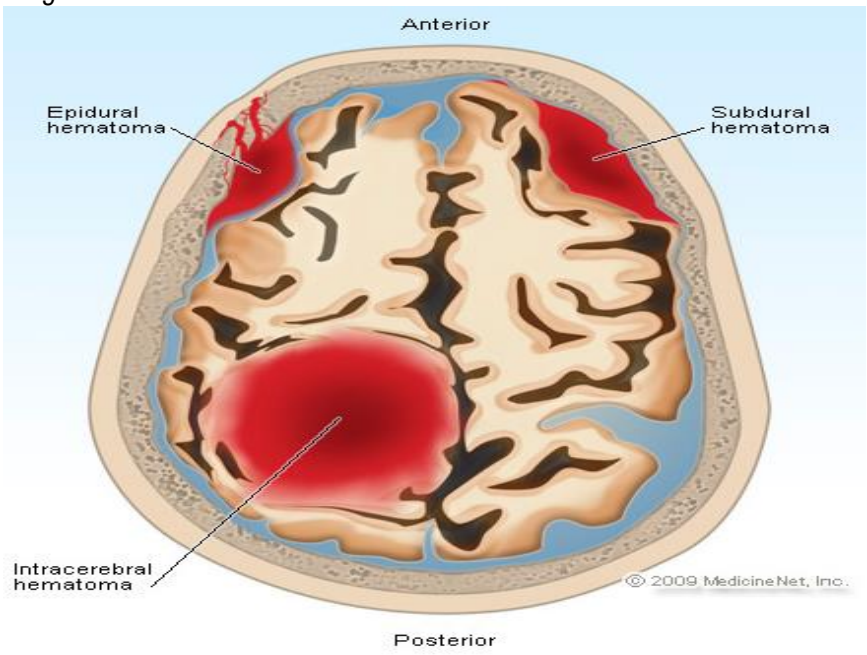
iv) Traumatic Intracerebral Haemorrhage
- Results in tear of parenchymal vessels of the hemispheres causing multiple intracerebral haemorrhages.

v) Brain Swelling
- Localized or diffuse brain swelling results from vascular engorgement due to loss of autoregulation mechanism and an increase in extracellular and intracellular fluid resulting from obscure mechanisms

6.2. Secondary Damage

- Traumatic injuries to the CNS may result in haemorrhage and haematomas
- Intracranial haemorrhage is a frequent complication of head injury and it is the commonest cause of deterioration and death in patients who have been conscious immediately after their injury
- Incidence of haematoma is much higher in patients with fracture of the skull
- Haematomas may be extradural (epidural), subdural or intracerebral.

Diagram 3.7: Haematoma



i) Extradural (Epidural) Haematoma

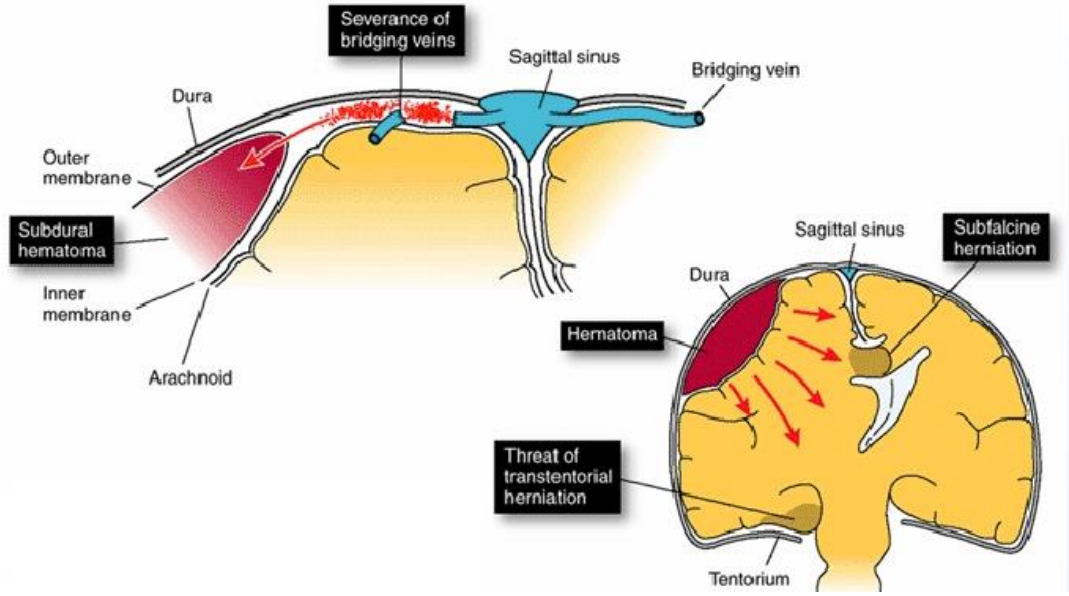
- Formation of blood clot between the dura and the skull due to rupture of a meningeal artery usually the middle cerebral artery following fracture of the skull
- Haematoma expands rapidly due to rapid movement of arterial blood leading to compression of the dura and flattening of the underlying gyri
- Expanding haematoma strips the dura from the skull and forms a large mass that progressively compresses the adjacent brain
- Initial injury may be trivial and the patient has a lucid [1]interval of some hours before developing headache and becoming drowsy
- Progressive enlargement of the haematoma causes increased intracranial pressure which leads to progressive loss of consciousness, coma and death if the haematoma is not drained or evacuated
- Occasionally extradural haematoma occur in frontal and parietal regions or within the posterior fossa.

ii) Subdural Haematoma

- Formation of blood clot between the dura and subarachnoid which results from rupture of veins that cross the convexities of cerebral hemispheres or from haemorrhage into the subdural space from severe contusions
- Blood spreads diffusely throughout the subdural space
- Subdural haematoma may be acute of chronic.

[1] A lucid interval is a period of time that a person with a head injury is conscious (lucid), after being knocked unconscious due to an impact. The interval lasts until they fall unconscious again. Unconsciousness follows, because during the interval, blood builds up on the brain causing extreme pressures on the brain tissue. Ends with these pressures becoming so great that the person loses consciousness

Diagram 3.8: Subdural Haematoma



Acute Subdural Haematoma

- Develops following trauma and consists of clotted blood
- It is of venous origin (symptoms appear slowly) and occurs more often in the fronto-parietal region
- May be large and act as an acute intracranial expanding lesion or be a thin film of blood.
- Swelling of the adjacent cerebral hemispheres with increased ICP
- Some patients experience lucid interval similar to that associated with extradural haematoma

Chronic Subdural Haematoma

- Presents weeks or months after an apparently trivial head injury
- Liquid blood separates the haematoma from underlying brain by a granulation tissue membrane
- Expands very slowly becoming quite large before symptoms appear
- Gradually organized and becomes encapsulated in a fibrous membrane.

iii) Intracerebral Haematoma

- Associated with contusions which affect particularly the frontal and temporal lobes
- Combination of an intracerebral haematoma in constituting with a subdural haematoma through surface contusions is described as burst lobe
- There are also small deeply seated intracerebral haematomas such as the basal ganglia haematomas
- Common in patients with diffuse axonal injury

iv) Increased Intracranial Pressure

- Secondary brain damage due to head injury results in increased intracranial pressure which causes distortion and herniation of the brain
- Ensuing brain swelling also contributes to increased intracranial pressure (swelling occurs around contusions in the ipsilateral hemispheres)

v) Infection

- Results from bacteria entering the skull through a compound fracture of the vault or fracture base of the skull
- Results in meningitis and intracranial abscess which is rare and associated with penetrating injury

7.0 CLINICAL ASPECTS OF HEAD INJURIES

7.1. Brain damage in head injury may be focal or diffuse

- Focal brain damage such as contusions and haematomas are easy to recognize neurologically
- Diffuse brain damage such as axonal injury and ischaemia are hard to detect unless histology studies are undertaken

7.2. Post-Traumatic Amnesia

- Is the period of disturbed consciousness and the interval between injury and return to continuous memory
- Common in diffuse brain damage

7.3. Clinical Severity

i) First Degree - no concussion, bell rung resolution of symptoms within lucid interval
ii) Second Degree - loss consciousness < 15 seconds, no resolution within lucid interval
iii) Third Degree - loss of consciousness > 15 seconds, increasing severity within lucid interval

Severity of Traumatic Brain Injury[8]			
	GCS	PTA	LOC
Mild	13-15	<1 day	0-30 mins
Moderate	9-12	>1 to < 7 days	>30 mins to < 24 hrs
Severe	< 9	> 7 days	> 24 hrs

7.4. Clinical Features

What are the clinical features of head injury?

7.5. Glasgow Coma Scale (GCS)

Glasgow Coma Scale		
Response	Scale	Score
Eye Opening Response	Eyes open spontaneously	4 Points
	Eyes open to verbal command, speech, or shout	3 Points
	Eyes open to pain (not applied to face)	2 Points
	No eye opening	1 Point
Verbal Response	Oriented	5 Points
	Confused conversation, but able to answer questions	4 Points
	Inappropriate responses, words discernible	3 Points
	Incomprehensible sounds or speech	2 Points
	No verbal response	1 Point
Motor Response	Obeys commands for movement	6 Points
	Purposeful movement to painful stimulus	5 Points
	Withdraws from pain	4 Points
	Abnormal (spastic) flexion, decorticate posture	3 Points
	Extensor (rigid) response, decerebrate posture	2 Points
	No motor response	1 Point
Minor Brain Injury = 13-15 points; **Moderate Brain Injury** = 9-12 points; **Severe Brain Injury** = 3-8 points		

PEDIATRIC GLASGOW COMA SCALE (PGCS)				
	> 1 Year		**< 1 Year**	**Score**
EYE OPENING	Spontaneously		Spontaneously	4
	To verbal command		To shout	3
	To pain		To pain	2
	No response		No response	1
MOTOR RESPONSE	Obeys		Spontaneous	6
	Localizes pain		Localizes pain	5
	Flexion-withdrawal		Flexion-withdrawal	4
	Flexion-abnormal (decorticate rigidity)		Flexion-abnormal (decorticate rigidity)	3
	Extension (decerebrate rigidity)		Extension (decerebrate rigidity)	2
	No response		No response	1
	> 5 Years	**2-5 Years**	**0-23 months**	
VERBAL RESPONSE	Oriented	Appropriate words/phrases	Smiles/coos appropriately	5
	Disoriented/confused	Inappropriate words	Cries and is consolable	4
	Inappropriate words	Persistent cries and screams	Persistent inappropriate crying and/or screaming	3
	Incomprehensible sounds	Grunts	Grunts, agitated, and restless	2
	No response	No response	No response	1
TOTAL PEDIATRIC GLASGOW COMA SCORE (3-15):				

8.0 INVESTIGATIONS

1. Skull X-ray (what are the indications?)
2. CT/CAT scan
3. MRI
4. Blood tests
5. LP

State the important parameters in these investigations

- What are components of the Glasgow Coma Scale (GCS?)
- How will you interpret results from the GCS?

9.0 COMPLICATIONS

1. **Immediate complications**
   a) Scalp laceration
   b) Scalp haemorrhages and haematoma
   c) Skull fractures
   d) Brain damage – contusion, laceration, haematoma
   e) CSF rhinorrhoea and otorrhoea

2. **Delayed complications**

   a. Haemorrhages - extradural haemorrhage, subdural haemorrhage, intracerebral haematomas
   b. Cerebral oedema – increased ICP and cerebral hypoxia
   c. External leakage of CSF and blood from the ear and nose may complicate fractures of the skull base. This may be a potential route of entry of infection
   d. Local infect ion – compound fractures and lead to development of meningitis
   e. Meningitis
   f. Brain abscess
   g. Cranial nerve injury
   h. Post traumatic encephalopathy

3. **Late Complications**

   a. Hydrocephalus
   b. Epilepsy
      - Head injury is an important cause of epilepsy with the risk being highest in severe missile head injury as well as episodes of ischaemic brain damage
      - 10% of patients with head injury develop fits in the first week of injury (early epilepsy) or more delayed for 2 – 3 months (late epilepsy)
      - Predisposing factors to epilepsy are depressed skull fracture and intracranial haematoma
      - Fits are likely to reoccur in patients in patients with early epilepsy
      - With penetrating head injuries the incidence of epilepsy increases to 45%.
   c. Amnesia
   d. Chronic subdural haematoma
      - A thick layer of fluid and partially clotted blood that gradually accumulates between the dura and arachnoid membranes which exhibit considerable reactive thickening

Lesson 4: INFECTIONS OF THE NERVOUS SYSTEM – BACTERIAL

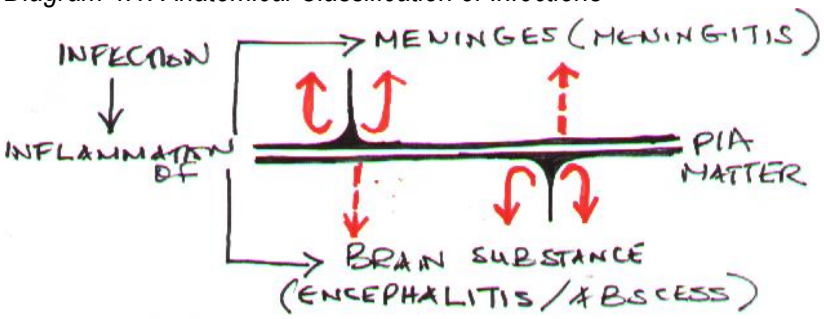
Learning Outcomes

1. Describe the routes of infections of the nervous system
2. Describe the causes, pathogenesis, pathophysiology, pathology, features, investigations and complications of infections of the nervous system
3. Investigate infections of the nervous system

1.0. INTRODUCTION

- The brain and spinal cord are relatively well protected from bacteria but once the microorganisms gain access the infection may spread rapidly by way of the CSF pathways
- Many organisms which are relatively non-pathogenic elsewhere in the body can cause serious and fatal infections of the nervous system
- Diffuse inflammation of the meninges is called **meningitis** while that of the brain parenchyma is called **encephalitis**.
- Anatomically infections of the nervous system fall into two main groups which remain separated due to the intervention of the **pial barrier**.
- The forms of infections of the nervous system include: -
  - i) Myelitis – diffuse inflammation of the spinal cord parenchyma
  - ii) Encephalitis – diffuse inflammation of the cerebral parenchyma
  - iii) Meningitis – diffuse inflammation of the meninges (leptomeningitis and meningomeningitis)
  - iv) Meningoencephalitis – diffuse inflammation of the brain and leptomeningitis
  - v) Cerebritis and cerebral abscess (focal inflammation of the brain)

Diagram 4:1: Anatomical Classification of Infections



2.0. ROUTES OF INFECTION

1. Vascular spread (Via blood stream) – this is the most common route
   - Spread via arterial route from another focus (most common mode of infection)
   - Retrograde venous route
   - Lodgement of septic emboli in the brain

2. Direct extension from adjacent structures
   a) Direct implantation - follows skull fractures, defects in the bony and meningeal coverings of the nervous system
   b) Local extension - from contagious focus such as otitis media and frontal or mastoid sinusitis may occur. Infection from the middle ear spreads to the bone and then penetrates the dura. The infection usually

remains localized only spreading to the adjacent brain causing a brain abscess; occasionally it becomes widespread causing meningitis or may result in infected thrombosis of the lateral sinus.

3. Ascending neural route (Along nerve) - Certain viruses such as herpes simplex, herpes zoster and rabies spread along cranial and peripheral nerves and ascend to the central nervous system.

3.0. ENCEPHALITIS

- Is the parenchymal infection of the brain
- May be as a result of bacterial, viral, fungal and protozoal infections

3.1. Bacterial Encephalitis

- Is usually secondary to involvement of the meninges rather than a primary bacterial parenchymal infection resulting in cerebritis which progresses to form brain abscess
- Tuberculosis and syphilis can primarily involve the brain parenchyma.

3.2. Viral Encephalitis

- A number of viruses can infect the CNS and produce aseptic meningitis or viral encephalitis or occasionally a combination of the two – meningoencephalitis
- Occurs as an end-result of preceding infection in other tissues and organs
- There is usually a preceding phase of extraneural viral replication before nervous system involvement
- Causal virus can be isolated from the brain tissue on biopsy or autopsy but rarely from the CSF
- Most viruses reach the nervous system via blood stream after entry into the body via various routes such as skin (herpes simplex, herpes varicella zoster), alimentary tract (enteroviruses e.g. polio), arthropod bite (arbovirus), transplacental (cytomegalovirus, HIV), intimate contact in AIDS (HIV). Rabies viruses travel along the peripheral nerves
- All these viruses cause acute viral encephalitis. Slow viral diseases such as Kuru and Creutzfeldt-Jakob disease (CJD) have a long latent period and the disease develops slowly producing sub-acute sclerosis panencephalitis and progressive multifocal leucoencephalopathy

Pathological Changes

Microscopy and Histology

- Presence of lymphocytes, plasma cells and macrophages in the subarachnoid space which appear as cuffs around blood vessels within the brain
- Diffuse hyperplasia of microglia with formation of rod cells and small clusters of microglia
- Tissue destruction in some areas which show astrocytosis and lipid-containing macrophages
- Central chromatolysis, necrosis of neurones and neuronophagia
- Necrosis ranges from selective neuronal necrosis as in polio to frank infarction of grey and white matter e.g. herpes simplex encephalitis

3.3. HIV Encephalopathy (AIDS Dementia Complex)

- Brain is affected in more than 50% of individuals with AIDS
- Involves common opportunistic diseases such as toxoplasmosis, cryptococcis and cytomegalovirus encephalitis

- AIDS dementia is poorly understood but the principal structural feature is microglial hyperplasia and presence of multinucleated macrophage-type cells
- HIV encephalopathy or AIDS dementia complex is a group of central nervous system manifestations with the major clinical feature being dementia
- Dementia is a fall in the cognitive ability of the individual. It develops in 25% cases of AIDS.

Histology

- Changes seen in subcortical area of the brain and consist of gliosis, multinucleate giant cell encephalitis and vacoular myelopathy.

3.4. Fungal and Protozoal Encephalitis

- Fungal diseases of the CNS usually develop by blood stream from systemic mycoses elsewhere in the body
- Are particularly common in immunocompromised individuals e.g. AIDS, lymphomas and other cancers
- It involves *Candida albicans*, *Mucor*, Aspergillus *fumigatus*, *Cryptococcus neoformans*, *Histoplasma capsulatum* and *Blastomyces dermatitidis*.
- Produce three patterns of disease - fungal chronic meningitis, vasculitis and encephalitis
- Protozoal diseases e.g. malaria, toxoplasmosis, amoebiasis and trypanosomiasis can affect the CNS

4.0. MENINGITIS

4.1. Introduction

- Is inflammation of the coverings of the brain (meninges)
- Meningitis involving the dura is called patchymeningitis while that involving the pia and arachnoid is called leptomeningitis
- Leptomeningitis is the most common and unless stated, meningitis would mean leptomeningitis

Pachymeningitis

- Is practically invariably an extension of the inflammation from the bones of the skull resulting from chronic suppurative otitis media or from a compound fracture of the skull
- Suppuration occurs between the bone and the dura resulting in formation an **extradural abscess**
- Further spread of the infection may penetrate the dura and the pus can spread widely over the cerebral hemispheres to form a **subdural abscess**
- Other effects of patchymeningitis are localized or generalized leptomeningitis and cerebral abscess.

Leptomeningitis

- Is commonly called meningitis and is usually the result of infection but occasionally chemical meningitis and carcinomatous meningitis may occur
- Infectious meningitis is broadly classified into three types namely: -
  i) Acute pyogenic meningitis
  ii) Viral or aseptic meningitis (acute lymphocytic)
  iii) Chronic meningitis (bacterial or fungal)

4.2. Causes of Meningitis

1. Bacterial - *Neisseria meningitidis, Streptococcus pneumoniae* , *Staphylococcus aureus* (70%), *Streptococci* group B, Gram Negative Bacilli - *Haemophilus infleunzae* and *Escherichia coli*, *Myocobacterium tuberculosis* and *Trepanoma pallidum*
2. Viral - Enteroviruses – ECHO and Coxsackie, Mumps, *Herpes simplex,* HIV, EBV
3. Fungal - *Cryptococcus neoformans* , Candida

4.3. Acute Pyogenic (Suppurative) Meningitis

- Is acute infection of the pia-arachnoid meninges and the subarachnoid space
- Since the subarachnoid space is continuous around the spinal cord and the optic nerves, the infection spreads immediately to the whole of the cerebrospinal meninges and to the ventricles.

Causative Organisms

1. *Neisseria meningitidis* – causes meningitis in adolescents and young adults and it is responsible for epidemics.
2. *Streptococcus pneumonia* – causes infection at extremes of age and following trauma
3. *Haemophilus influenzae* – infants and children (common)
4. *Escherichia coli* – common cause in neonates and infants

Mode of Infection

1. Blood stream
   - Most cases of meningitis are haematogenous origin
   - In meningococcal meningitis the infection is spread by droplet infection from nasopharyngeal carriers
   - The meningococci pass to the meninges by the blood stream
   - Meningococcal meningitis occurs in epidemics
   - It is favoured by poor hygienic conditions
   - In epidemics, fatal cases of meningococcal septicaemia occur but there may be no enough time for meningitis to develop. Other features of meningococcal meningitis include haemorrhagic rash and spontaneous haemorrhage into the adrenal glands (Waterhouse-Frideichsen syndrome)
2. Spread from an adjacent focus of infection
   - Local spread from infection in the bones or after compound fracture of the skull
3. Iatrogenic infection - Organisms can be introduced at operation or during lumbar puncture.

Pathological Changes

- Whole subarachnoid space contains purulent exudates (more pronounced in the sulci and around the brain base cisternae)

Macroscopy

- Accumulation of pus in the intracranial and spinal subarachnoid spaces (CSF becomes turbid or frankly purulent)
- Pus is thickest within the sulci and the cisterns at the base of the brain
- Little involvement of the underlying cortex
- Ventricles are involved and contain turbid CSF with pus or fibrin on the ventricular wall and choroid plexus

- Purulent material and exudates may interfere with CSF flow resulting in mild obstructive hydrocephalus

Microscopy

- Numerous polymorphonuclear neutrophils are seen in the subarachnoid space and meninges especially around blood vessels
- There are causative bacteria on Gram stain.

Clinical Features

- Features of meningitis; fever; severe headache. Vomiting; drowsiness; occasionally convulsions, Stupor, Coma

Diagnosis

1. History and physical examination
2. CSF examination
   a) Turbid or distinctly purulent
   b) Increased CSF pressure
   c) Cell count – polymorphonulcear leucocytosis (1000 – 10 000/ul)
   d) Increased CSF proteins (> 50 mg/dl)
   e) Reduced CSF glucose concentration (< 40 mg/dl) or absent
   f) Bacteriologic examination – Gram stain and CSF culture

Investigations

1. Lumbar puncture – CSF findings
2. Blood cultures
3. Blood sugars
4. Chest X-Ray
5. Skull X-ray
6. CT scan

What are the complications of pyogenic meningitis?

4.4. Acute Lymphocytic (Viral/Aseptic) Meningitis

- Commonest form of meningitis and the disease is usually mild and only the meninges are involved, recovery is usually complete
- Causative agents include mumps virus, Echo virus, Coxsackie virus, Epstein Barr virus (EBV) and Herpes simplex type II virus. Is a common and less severe acute infection of the CNS frequently caused by entero viruses or mumps virus and has complete recovery and is self-limiting.

Mode of Infection

- Blood stream (haematogenous) when there is viraemia after primary replication of viruses in lymphoid tissue
- Viruses can enter the body by various routes e.g. infections of the skin or mucous membranes (herpes simplex), by alimentary tract (enteroviruses) or by the bites of an arthropod (arbo viruses)
- Few viruses reach the nervous system by travelling along peripheral nerves (rabies virus)
- The symptoms occur late when the viraemia is subsiding and circulating antibodies increasing (suggests that brain damage is due to immunological reaction to antigens in the nervous system).

Pathology

- Infiltration of the subarachnoid space by lymphocytes, plasma cells and macrophages.

Clinical Features

- Meningitic syndrome – triad of headache, neck stiffness and fever; photophobia;malaise; Kerning's sign positive; progressive drowsiness; lateralizing signs and cranial nerve palsies (venous sinus thrombosis , severe cerebral oedema, cerebral abscess and encephalitis); papilloedema

Diagnosis

1. Clinical features
2. CSF examination
   - Clear or slightly turbid
   - Slightly increased CSF pressure
   - Increased cell count - lymphocytes and monocytes (10 – 100 cell/ul), occasionally plasma cells
   - Protein – normal or slightly increased
   - Normal glucose
   - CSF is bacteriologically sterile

Differential Diagnosis

1. Subarachnoid haemorrhage
2. Migraine
3. Cerebral malaria
4. Brain abscess

How will you differentiate these diagnoses?

4.5. Chronic Meningitis

- Two principal types of chronic meningitis – one bacterial (tuberculous meningitis) and the other fungal (cryptococcal meningitis) which cause chronic granulomatous reaction and produce parenchymal lesions. Without treatment TB meningitis is always fatal.

TB Meningitis

- Is always secondary to disease elsewhere in the body
- Occurs in children and adults through haematogenous spread of infection from other sites in the body or may be a manifestation of miliary tuberculosis
- In every rare occasion it may spread directly from tuberculosis of a vertebral body

Pathological Changes

Macroscopy

- Subarachnoid space contains thick/gelatinous or caseous exudates which is abundant in the basal cisterns, the sulci and around the spinal cord
- Small tubercles measuring 1 – 2 mm in diameter can be seen in the pia-arachnoid adjacent to the cortical blood vessels
- The exudates obstructs CSF flow causing hydrocephalus

Microscopy

- Exudate shows acute and chronic inflammatory cells and Langerhan's giant cells or granulomas with or without caesation necrosis. The exudate is fibrinocaseous, diffusely permeated by lymphocytes, plasma cells and macrophages.
- Bacilli may be demonstrated
- Later there is dense fibrinous adhesions in the subarachnoid space
- There is obliterative endoarteritis which leads to reduced lumen of the affected arteries causing resulting in small infarcts in the brain or in cranial nerve roots. This results in focal neurological signs.

Diagnosis

1. Clinical features - Symptoms – headache, confusion malaise, vomiting
2. CSF examination
    - Increased CSF pressure
    - Clear but more often slightly turbid and may form a fibrin web on standing
    - Increased cell count – lymphocytes and macrophages
    - Increased protein content
    - Reduced blood glucose
    - Centrifugal deposits of CSF for ZN stain and culture

Tuberculoma

- Is an encapsulated caseous mass which is a common cause of intracranial expanding lesions that cause increased intracranial pressure
- In adults it affects mainly the cerebral hemispheres but in children it affects the cerebellum
- Composed of a core caseous material surrounded by a broad brand of tubercles and Langerhan's giant cells.

Syphilis

- Lesions in syphilis may be in the form of syphilitic meningitis in secondary syphilis

Cryptococcal Meningitis

- Is caused by *Cryptococcus neoformans* develops particularly in debilitated or immunocompromised persons usually as a result of haematogenous dissemination from a pulmonary lesion
- It is especially an important cause of meningitis in patients with AIDS
- Cryptococcal meningitis presents as sub-acute meningitis.

Pathological Changes

Macroscopy

- The exudate in the subarachmoid space is scanty, translucent and gelatinous and contains masses of encapsulated cryptococci.
- Flask-shaped cysts filled with cryptococci are found in superficial layers of the cortex.

Microscopy

- Cellular infiltration by lymphocytes, plasma cells and occasionally granuloma and abundant characteristic capsulated cryptococci.

Differential Diagnosis

1. Intracranial mass (SOL)
2. Epilepsy
3. Focal signs

5.0. TB MENINGITIS

6.0. OTHER BACTERIAL INFECTIONS

6.1. Brain Abscess (Pyogenic Brain Abscess)

- Result from direct spread of infection from an adjacent infection or by haematogenous dissemination
- Abscesses are often multiple and frequently involve the parietal lobes and cerebellum
- The infection may originate from any part of the body but primarily so from the lungs (bronchioectasis)
- Individuals with congenital cyanotic heart disease (CHD) are particularly susceptible to brain abscesses
- Multiple abscesses occur in staphylococcal pyaemia and microabscesses may complicate bacterial endocarditis.

Causative Organisms

- Anaerobic Streptococci; Staphylococci; Bacteroids; Diphtheroids; Coliforms; Yeasts and fungi

Routes of Infection

- Brain abscesses may arise by one of the following routes: -
  i) Direct implantation of organisms - E.g. following compound fractures of the skull
  ii) Direct spread of infection from the adjacent bone e.g. chronic suppurative otitis media, mastoiditis and sinuisitis.
    - Bone is eroded by chronic osteititis with the production of extradural and subdural abscesses. Bacteria then spread into the brain
    - Diffuse bacterial meningitis is curtailed by local adhesions in the subarachnoid space. Infection from the middle ear spreads upwards through the tegmen tympani to the temporal lobe. Infection spreading from the mastoid antrum leads to abscess formation in the cerebellum.
  iii) Haematogenous spread
    - Spreads from primary infection in the heart e.g. acute bacterial endocarditis and from lungs e.g. bronchiectasis

Pathological Changes

Macroscopy (Gross)

- Abscess becomes localized by a pyogenic membrane which becomes a well-defined capsule made of connective tissue, new capillaries, enlarged astrocytes and macrophages
- Localized area of inflammatory necrosis
- Adjacent brain tissue has oedema and gliosis

Microscopy

- Liquefaction necrosis in the centre of the abscess containing pus (thick, greenish-yellow) with a foul odour due to mixed bacterial flora
- Surrounded by acute inflammatory cells, chronic inflammatory cells (macrophages and plasma cells)
- Surrounding tissues have oedema and neovascularization
- There is septic thrombosis of vessels, fibrous encapsulation and a zone of gliosis
- CSF and overlying meninges show features of acute and chronic inflammation

Clinical Features

- The features of abscess include fever, headache, vomiting, seizures and focal neurological deficits depending on location of site
- Brain abscess in common in cerebral hemispheres and less frequent in the cerebellum and basal ganglia.

> - What do you understand by the term focal neurological deficits?
> - What investigations are significant?
> - What are the complications?

Outcome

1. Remain latent but usually enlarges resulting in increased intracranial pressure
2. May become multilocular
3. Gradual spread
   a) Rupture into a ventricle or into the subarachnoid space causing meningitis
   b) Cause surrounding oedema leading to increased intracranial pressure
4. Healing with scarring leading to functional loss or disturbance (including epilepsy)

6.2. Syphilis

- *Trepanoma pallidum* gains access to the CNS early in the secondary stage of the disease
- Patients rarely show features of a transient meningoencephalitis
- Lesions in syphilis may be in the form of neurosyphilis of third stage which presents in two principal forms of tertiary neurosyphilis and quaternary (parenchymatous) neurosyphilis
- Syphilitic meningitis is chronic meningitis with distinctive perivascular inflammatory reaction
- Neurosyphilis is suggested by CSF WBC count >10 cells/mm^3 (10 x 10^6 cells/L), CSF protein >50 mg/dL (0.50 g/L) and a positive CSF VDRL or RPR test.

Tertiary Neurosyphilis

- Takes form of sub-acute meningitis where lymphocytes and plasma cells are seen in the subarachnoid space
- Perivascular arteritis results in meningovascular syphilis while obliterative endoarteritis result in focal ischaemic lesions in the brain, cranial and spinal nerve roots
- Gummas occur in meninges especially over the convexity of the cerebral hemispheres or over the cerebellum
- There is necrosis, a periarteritis and infiltration by lymphocytes and plasma cells.

Parenchymatous Neurosyphilis

- Occurs after as long as 20 years after the primary infection and presents in two forms of General Paralysis of the Insane (GPI) and tabes dorsalis

Tabes Dorsalis (Locomotor ataxia)

- Results from selective slow progressive degeneration of the posterior spinal nerve roots immediately proximal to the posterior root ganglia and the posterior columns of the spinal cord
- There is selective involvement of the fibres responsible for pain, temperature and proprioception
- Posterior nerve roots become grey and shrunken and the spinal cord becomes reduced in size particularly in the antero-posterior diameter due to demyelination and shrinkage of posterior columns (due to Wallerian degeneration)
- Affects the lumbosacral nerve roots but occasionally cervical nerves (cervical tabes) which are most severely affected producing loss of coordination of muscles and joints resulting in locomotor ataxia
- There is loss of pain sense and Argyll-Robertson pupils which react to accommodation but not to light.

General Paralysis of the Insane (GPI)

- GPI is sub-acute encephalitis characterized clinically by progressive dementia
- Results from diffuse parenchymal involvement with widespread lesions in the nervous system
- There are widespread lesions in the brain
- Abnormalities include: -
    i) Perivascular cuffing of vessels within the CNS by lymphocytes and plasma cells.
    ii) Similar inflammatory response in subarachnoid space
    iii) Cerebral atrophy leads to small rounded gyri and widened sulci
    iv) Enlarged ventricles and granular ependymitis

Clinical Features

- Personality change, memory impairment, altered mood, confusion, seizures, tremor and Argyll-Robertson pupils[2]

Investigations

1) VDRL
2) Khan Test
3) CSF –Increased cells (lymphocytes), increased proteins, increased IgG
4) Positive Wassermann reaction
5) Treponemal enzyme immune assay (EIA)
6) T. pallidum particle agglutination assay (TPPA)
7) T. pallidum haemagglutination assay (TPHA)
8) Fluorescent antibody absorption (FTA-ABS)
9) Imunocapture assay (ICA)

[2]