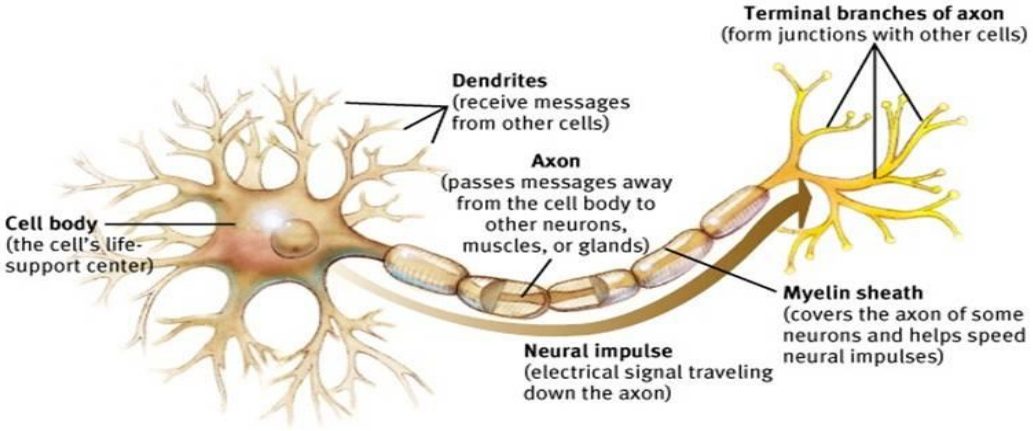
Nervous System

- Nervous system is the chief controlling and coordinating system of the human body.
- It controls and regulates all activities of the body, whether voluntary or involuntary, and adjust the individual to the given surroundings.
- The nervous system is divided into:
    - **Central Nervous System** (**CNS**) – brain and spinal cord.
    - **Peripheral Nervous System** (**PNS**) – cerebrospinal nervous system and peripheral autonomic nervous system.

Neuron Structure

- The **functional and structural unit** of the nervous system
- Specialized to conduct information from one part of the body to another.
- There are many different types of neurons but most have certain structural and functional characteristics in common:
    - **Cell body** (**soma/perikaryon**)
    - **One or more specialized, slender processes** (**axon/dendrites**)
    - **An input region** (**dendrites**)
    - **A secretory (output) region** (**axon terminal**)



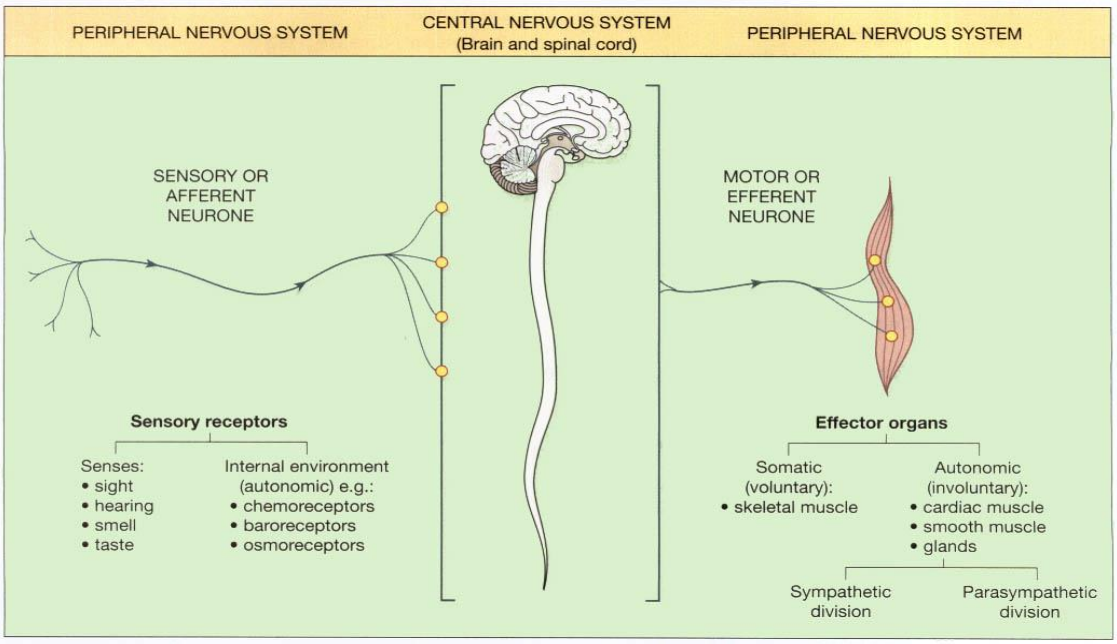


Fig: Functional components of the nervous system.

Synapse and Neurotransmitters

- The **synapse** is an area of functional contact between one neuron and another for purpose of transforming information.
- It is formed between synaptic knob or terminal boutons of axon with dendrites or cell body of another.
- **Neurotransmitters** are chemical substances released at the nerve ending and transmits impulse from nerve to nerve or from nerve to effecter organ.
- E.g.: acetylcholine (ACH), adrenalin (epinephrine), nor-adrenalin (nor-epinephrine), dopamine, histamine, serotonin, gamma aminobutyric acid (GABA).

Neuroglia

- Within the brain and spinal cord, neurons are **supported** by a **special kind of connective tissue** called **neuroglia**.
- So, they are the **supporting cells of the nervous system**.
- They can be studied as following six types:
    - 4 types are found in CNS
        i. Astrocytes
        ii. Oligodendrocytes
        iii. Microglia
        iv. Ependymal cells
    - 2 types of glia in the PNS
        i. Schwann cells
        ii. Satellite cells
    - It is richly supplied with blood vessels.
- Functions: supporting, insulating, phagocytosis, formation of myelin sheath.

Meninges

- The brain and spinal cord are completely surrounded by three membranes, the *meninges,* lying between the skull and the brain and between the vertebrae and the spinal cord.
- They are:
    - **Dura mater**
    - **Arachnoid mater**
    - **Pia mater**
- The dura and arachnoid maters are separated by a potential space, the *subdural space.* The arachnoid and pia maters are separated by the *subarachnoid space,* containing *cerebrospinal fluid.*

Ventricles of the brain and the cerebrospinal fluid (CSF)

- Within the brain there are four irregular-shaped cavities, or *ventricles*, containing *cerebrospinal fluid (CSF).*
- They are:
    - Right and left lateral ventricles
    - Third ventricle
    - Fourth ventricle.

Cerebrospinal fluid (CSF)

- A modified tissue fluid, formed by choroid plexus of lateral ventricles, 3rd and 4th ventricles of brain.
- Clear, colorless, slightly alkaline fluid contained in the ventricular system of brain and in the sub-arachnoid space around the brain and spinal cord.
- Rate of formation: 0.5 ml/min (720ml/day).
- Volume: remains fairly constant at about 120 ml, which means that absorption keeps pace with secretion.
- Pressure: remains fairly constant at about 10 cmH2O when the individual is lying on his side and about 30 cmH2O when sitting up.
- Specific gravity: 1.005.

Composition:

- Water
- Mineral salts (Na^+, K^+, Ca^{++}, Mg^{++}, $HCO3^{--}$)
- Glucose (40-60 mg/dl)
- Proteins (20-45 mg/dl)
- Chloride (720-750 mg/dl)
- Urea (12 mg/dl)
- Creatinine (1.5 mg/dl)
- Uric acid (1.5 mg/dl)
- Lactic acid (18 mg/dl)
- Cholesterol (0.2 mg/dl)
- Cell count (0-4 cells/mm^3)

Functions of cerebrospinal fluid:

i. It supports and protects the brain and spinal cord.
ii. It maintains a uniform pressure around these delicate structures.
iii. It acts as a cushion and shock absorber between the brain and the cranial bones.
iv. It keeps the brain and spinal cord moist and there may be interchange of substances between CSF and nerve cells, such as nutrients and waste products.

Disorders of the brain

Increased intracranial pressure (ICP)

- This is a very serious complication of many conditions. The cranium forms a rigid cavity enclosing:
    - the brain
    - cerebral blood vessels and blood
    - cerebrospinal fluid (CSF).
- Rising ICP is accompany by bradycardia and hypertension. As it reaches its limit a further small increase in pressure is followed by a sudden and usually serious **reduction in the cerebral blood flow**.
- The result is **hypoxia** and a **rise in CO2 level.** This leads to progressive loss of functioning neurons, which exacerbates bradycardia and hypertension. Further cerebral hypoxia causes *vasomotor paralysis* and *death.*

- The causes of increased ICP include:
    - **Cerebral edema**, accumulation of excess fluid within brain parenchyma.
    - **Hydrocephalus**, the accumulation of excess CSF
    - **Expanding lesions** inside the skull, also known as space-occupying lesions
      -haemorrhage, haematoma
      -tumours (primary or secondary).
- Expanding lesions may occur in the brain or in the meninges and they may damage the brain in various ways.

Effects of increased ICP:

- Displacement of the brain (herniation, i.e., displacement of part of brain from its usual compartment)
- Obstruction of the flow of CSF
- Vascular damage
- Neural damage
- Bone changes (erosion, stretching & thinning)

Cerebral edema

- There is movement of fluid from its normal compartment when edema develops.
- Cerebral edema occurs when there is excess fluid in brain cells and/or in the interstitial spaces, causing increased intracranial pressure.
- ***Vasogenic edema*** occurs when the integrity of the normal blood-brain barrier is disrupted, allowing fluid to shift from the vascular compartment into the extracellular spaces of the brain.
- ***Cytotoxic edema*** is an increase in intracellular fluid secondary to neuronal and glial cell membrane injury.
- It is associated with:
    - traumatic injury
    - haemorrhage
    - infections, abscesses
    - hypoxia
    - local ischaemia, infarcts
    - tumours
    - inflammation of the brain or meninges
    - hypoglycaemia.

Hydrocephalus

- In this condition the volume of CSF is abnormally high (**overproduction**) and is usually accompanied by increased ICP.
- An **obstruction to CSF flow** is the most common cause. Also by **deficient reabsorption of CSF**.
- It is described as *communicating* when there is free flow of CSF from the ventricular system to the subarachnoid space and *non-communicating* when there is not, i.e. there is obstruction in the system of ventricles, foramina or ducts.

- Enlargement of the head occurs in infancy when ossification of the cranial bones is incomplete but, in spite of this, the ventricles dilate and cause stretching and thinning of the brain.
- After ossification is complete, hydrocephalus leads to a marked increase in ICP and destruction of neural tissue.

Primary hydrocephalus

- caused by obstruction to the flow of CSF and may be communicating or non-communicating.
- caused by malabsorption of CSF by the arachnoid villi.
- *Congenital primary hydrocephalus* is due to malformation of the ventricles, foramina or ducts, usually at a narrow point.
- *Acquired primary* hydrocephalus is caused by lesions that obstruct the circulation of the CSF, usually expanding lesions, e.g. tumours, haematomas or adhesions between arachnoid and pia maters, following meningitis.

Secondary hydrocephalus

- Compensatory increases in the amount of CSF and ventricle capacity occur when there is atrophy of brain tissue, e.g. in dementia and following cerebral infarcts. There may not be a rise in ICP.

Cerebrovascular diseases/accidents (stroke)

Cerebrovascular diseases—the broad category of brain disorders caused by pathologic processes **involving blood vessels**—constitute a major cause of death in the developed world and are the most prevalent cause of neurologic morbidity.

The three main pathogenic mechanisms are (1) **thrombotic occlusion**, (2) **embolic occlusion**, and (3) **vascular rupture**.

Stroke is the clinical designation applied to all of these conditions when symptoms begin acutely.

Predisposing factors include:

- hypertension
- atheroma
- cigarette smoking
- diabetes mellitus.

- Thrombosis and embolism have similar consequences for the brain: **loss of oxygen** and metabolic substrates, resulting in infarction or ischemic injury of regions supplied by the affected vessel.
- Similar injury occurs globally when there is complete **loss of perfusion**, severe **hypoxemia** (e.g., hypovolemic shock), or profound **hypoglycemia**.
- Hemorrhage accompanies rupture of vessels and leads to direct tissue damage as well as secondary ischemic injury.

Hypoxia, Ischemia, and Infarction:

- The brain is a highly oxygen-dependent tissue that requires a continual supply of glucose and oxygen from the blood.
- Cerebral blood flow normally remains stable over a wide range of blood pressure and intracranial pressure because of autoregulation of vascular resistance.
- The brain may be deprived of oxygen by two general mechanisms:

- *Functional hypoxia,* caused by a low partial pressure of oxygen (e.g., high altitude), impaired oxygen-carrying capacity (e.g., severe anemia, carbon monoxide poisoning), or inhibition of oxygen use by tissue (e.g., cyanide poisoning)
- *Ischemia,* either transient or permanent, due to tissue hypoperfusion, which can be caused by hypotension, vascular obstruction, or both

- Finally infarction occurs.

Intracranial Hemorrhage

- Hemorrhages within the brain are associated with (1) **hypertension** and other diseases leading to vascular wall injury, (2) **structural lesions** such as arteriovenous and cavernous malformations, and (3) **tumors**.
- Subarachnoid hemorrhages most commonly are caused by **ruptured aneurysms** but also occur with other vascular malformations.
- Subdural or epidural hemorrhages usually are associated with trauma.

Primary Brain Parenchymal Hemorrhage

- Spontaneous intraparenchymal hemorrhages are most common in mid to late adult life, with a peak incidence at about 60 years of age.
- Most are due to the rupture of a small intraparenchymal vessel.
- Hypertension is the leading underlying cause, and brain hemorrhage accounts for roughly 15% of deaths among persons with chronic hypertension.

Cerebral Amyloid Angiopathy

- Cerebral amyloid angiopathy (CAA) is a disease in which amyloidogenic peptides, typically the same ones found in Alzheimer disease (neurodegenerative disorder), deposit in the walls of medium- and small-caliber meningeal and cortical vessels.
- The amyloid confers a rigid, pipe-like appearance and stains with Congo red.
- Amyloid deposition weakens vessel walls and increases the risk of hemorrhages, which differ in distribution from those associated with hypertension.
- Specifically, CAA-associated hemorrhages often occur in the lobes of the cerebral cortex (*lobar hemorrhages).*

Subarachnoid Hemorrhage and Saccular Aneurysms

The most frequent cause of clinically significant nontraumatic subarachnoid hemorrhage is rupture of a *saccular (berry) aneurysm.*

Hemorrhage into the subarachnoid space also may result from vascular malformation, trauma, rupture of an intracerebral hemorrhage into the ventricular system, hematologic disturbances, and tumors.

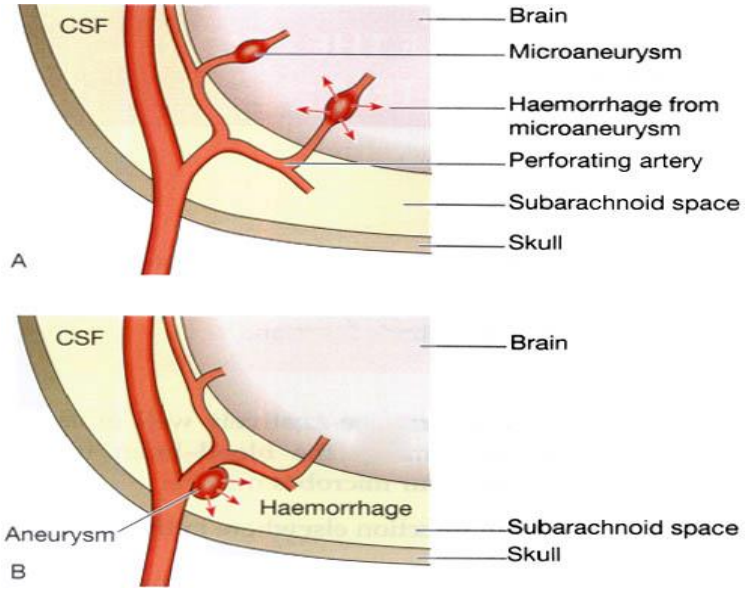


Fig: Types of haemorrhage causing stroke: A. Intracerebral. B. Subarachnoid.

Vascular Malformations

- Vascular malformations of the brain are classified into four principal types based on the nature of the abnormal vessels: *arteriovenous malformations (AVMs), cavernous malformations, capillary telangiectasias, and venous angiomas.*
- *AVMs,* which is a knot of distended blood vessels overlying and compressing the surface of the brain.
- It is the most common of these, affect males twice as frequently as females and most commonly manifest between the ages of 10 and 30 years with seizures, an intracerebral hemorrhage, or a subarachnoid hemorrhage.
- Large AVMs occurring in the newborn period can lead to congestive heart failure because of blood shunting from arteries to veins.
- The risk of bleeding makes AVM the most dangerous type of vascular malformation.

Meningitis

- It is an **inflammation of the meninges**, the protective membrane that surrounds brain and spinal cord.
- Inflammation spreads rapidly throughout CNS because of the circulation of CSF around the brain and spinal cord.
- Infectious meningitis can be broadly divided into:
    - ***acute pyogenic*** (usually bacterial),
    - ***aseptic*** (usually viral), and
    - ***chronic*** (usually tuberculous, spirochetal, or cryptococcal) subtypes.
- Examination of the CSF is often useful in distinguishing between various causes of meningitis.

Pathogenesis:

i. Once the pathogen enters the blood stream, it crosses the blood-brain barrier and initiate an inflammatory response in the meninges.
ii. Independent of the causative agent, inflammation of the subarachnoid space and pia mater occurs.
iii. Since there is little room for expansion within the cranial vault, the inflammation may cause increased ICP.

iv. CSF flows in the subarachnoid space, where inflammatory cellular material from the affected meningeal tissue enters and accumulates, thereby increasing the CSF cell count.
v. Bacterial invasion leads to rapidly increased blood supply to the meninges with massive neutrophil migration.
vi. Meningeal vessels engorged and their permeability increases.
vii. Phagocytic WBCs migrate into the subarachnoid space, forming a purulent exudates that thickens and clouds the CSF and interferes with its flow.
viii. Rapid exudates formation causes further inflammation, impaired CSF flow, and cellular edema cause the intracranial pressure to increase.
ix. Both the pathogenic damage and the ICP may result in brain damage and the life- threatening complications.

Acute Pyogenic Meningitis

Acute pyogenic or acute purulent meningitis is acute infection of the pia-arachnoid and of the CSF enclosed in the subarachnoid space. Since the subarachnoid space is continuous around the brain, spinal cord and the optic nerves, infection spreads immediately to whole of the cerebrospinal meninges as well as to the ventricles.

Etiopathogenesis. The causative organisms vary with age of the patient:

1. *Neisseria meningitidis* causes meningitis in adolescent and young adults and is causative for epidemic meningitis.
2. *Haemophilus influenzae* is commonly responsible for infection in infants and children.
3. *Streptococcus pneumoniae* is causative for infection at extremes of age and following trauma.
4. *Escherichia coli* infection is common in neonates with neural tube defects.
5. *Leptospira* may also cause leptomeningitis (Weil's disease)

Routes of infection:

1. Most commonly by the blood stream.
2. From an adjacent focus of infection.
3. By iatrogenic infection such as introduction of microorganisms at operation or during lumbar puncture.

Acute Lymphocytic (Viral, Aseptic) Meningitis

Acute lymphocytic meningitis is a viral or aseptic meningitis, especially common in children and young adults.
Among the etiologic agents are numerous viruses such as enteroviruses, mumps, echo viruses, coxsackie virus, Epstein-Barr virus, herpes simplex virus-2, arthropode-borne viruses and HIV.
However, evidence of viral infection may not be demonstrable in about a third of cases.

Chronic (Tuberculous and Cryptococcal) Meningitis

There are two principal types of chronic meningitis—one bacterial (tuberculous meningitis) and the other fungal (cryptococcal meningitis).
Both types cause chronic granulomatous reaction and may produce parenchymal lesions.

i. *Tuberculous meningitis* occurs in children and adults through haematogenous spread of infection from tuberculosis elsewhere in the body, or it may simply be a manifestation of miliary tuberculosis.

ii. *Cryptococcal meningitis* develops particularly in debilitated or immunocompromised persons, usually as a result of haematogenous dissemination from a pulmonary lesion. Cryptococcal meningitis is especially an important cause of meningitis in patients with AIDS.

TABLE: CSF Findings in Health and Various Types of Meningitis.

	Feature	Normal	Acute Pyogenic (Bacterial) Meningitis	Acute Lympho-cytic (Viral) Meningitis	Chronic (Tuberculous) Meningitis
1.	*Naked eye appearance*	Clear and colourless	Cloudy or frankly purulent	Clear or slightly turbid	Clear or slightly turbid, forms fibrin coagulum on standing
2.	*CSF pressure*	60-150 mm water	Elevated (above 180 mm water)	Elevated (above 250 mm water)	Elevated (above 300 mm water)
3.	*Cells*	0-4 lymphocytes/µl	10-10,000 neutrophils/µl	10-100 lymphocytes/µl	100-1000 lymphocytes/µl
4.	*Proteins*	15-45 mg/dl	Markedly raised	Raised	Raised
5.	*Glucose*	50-80 mg/dl	Markedly reduced	Normal	Reduced
6.	*Bacteriology*	Sterile	Causative organisms present	Sterile	Tubercle bacilli present

Encephalitis

Encephalitis means inflammation or infection of the brain, usually caused by a virus; it may also be the result of bacterial infection.

It occurs throughout the world and affects all racial groups and ages. Rarely it occurs as a complication of common viral disease such as measles, mumps, glandular fever, or chickenpox.

It may occur with no evidence of infection elsewhere, such as in herpes simplex encephalitis, the most common form seen in Europe and America.

Rabies is another form of viral encephalitis, and the HIV virus which causes AIDS invades the brain to cause another form of encephalitis.

Parenchymal infection of brain is termed encephalitis.

Hence, it may be the result of bacterial, viral, fungal and protozoal infections.

Viral Encephalitis

- A number of viruses can infect the CNS and produce either aseptic meningitis or viral encephalitis, but sometimes combination of both termed meningoencephalitis, is present.
- Most viral infections of the CNS are the end-result of preceding infection in other tissues and organs. There is usually a preceding phase of extraneural viral replication before involvement of the nervous system occurs.
- Most of the viruses reach the nervous system via blood stream before which they enter the body by various routes e.g. infection of the skin and mucous membrane (in herpes simplex and herpes zoster-varicella), by the alimentary tract (in enteroviruses including polio virus), by arthropod bite (in arbovirus), by transplacental infection (in cytomegalovirus), and through body fluids in AIDS (in HIV infection).
- Rabies virus travels along the peripheral nerves to reach the CNS.
- Herpes zoster-varicella is a distinct primary disease (chickenpox) but the virus remains latent for a long time before it gets reactivated to cause herpes zoster.

Pathogenesis:

- Once any of these pathogens enter the body they can spread to the blood stream where they are carried to the nervous system.
- In nervous system, they multiply, cause irritation and inflammation of the brain tissue.
- The brain tissue swells (cerebral edema), which may destroy nerve cells, cause bleeding in the brain (intra-cerebral haemorrhage) and brain damage.

Clinical features:

- Fever and headache
- Brain aberration (i.e., disorientation, neurological deficits, seizures)
- Poor appetite
- Lethargy (sleepiness, decreased alertness and fatigue)
- Malaise
- Nausea and vomiting
- A general sick feeling

In more severe case:

- Severe headache and irritability
- Nausea and vomiting
- Stiff neck
- Change in mental status (confusion, drowsiness, disorientation, delirium, hallucination)
- Convulsion (seizures)
- Problem with walking, speech or hearing or vision.
- Sensitivity to light
- Sudden memory loss, coma.

Poliomyelitis

- This disease is usually caused by *polioviruses* and, occasionally, by other *enteroviruses.*
- Once known as infantile paralysis, this disease is caused by a viral infection involving the brain and spinal cord.
- The infection is spread by food contaminated by infected faecal matter and the initial virus multiplication occurs in the alimentary tract.
- The viruses are then blood-borne to the nervous system and invade anterior horn cells in the spinal cord. Usually there is a mild febrile illness with no indication of nerve damage.
- Irreversible damage to lower motor neurons causes muscle paralysis which, in the limbs, may lead to deformity because of the unopposed tonal contraction of antagonistic muscles.
- Death may occur owing to respiratory paralysis.
- Vaccination programmes have now almost eradicated this disease in developed countries.

Inflammatory/Peripheral Neuropathy

Peripheral neuropathy is the term used for disorders of the peripheral nerves of any cause. It may be polyneuropathy, mononeuropathy and mononeuropathy multiplex.

Polyneuropathy

It is characteristically symmetrical with noticeable sensory features such as tingling, pricking, burning sensation or dysaesthesia in feet and toes.

Motor features in the form of muscle weakness and loss of tendon reflexes may be present.

Involvement of the autonomic nervous system may be associated.

Most cases have origin in acquired metabolic and toxic causes such as thiamine deficiency, diabetes, amyloidosis, autoimmune demyelinating disease (Guillain-Barré syndrome), and administration of toxins and certain therapeutic agents.

Pathologically, polyneuropathy may be the result of axonal degeneration (axonopathy) or segmental demyelination (demyelinating polyneuropathy).

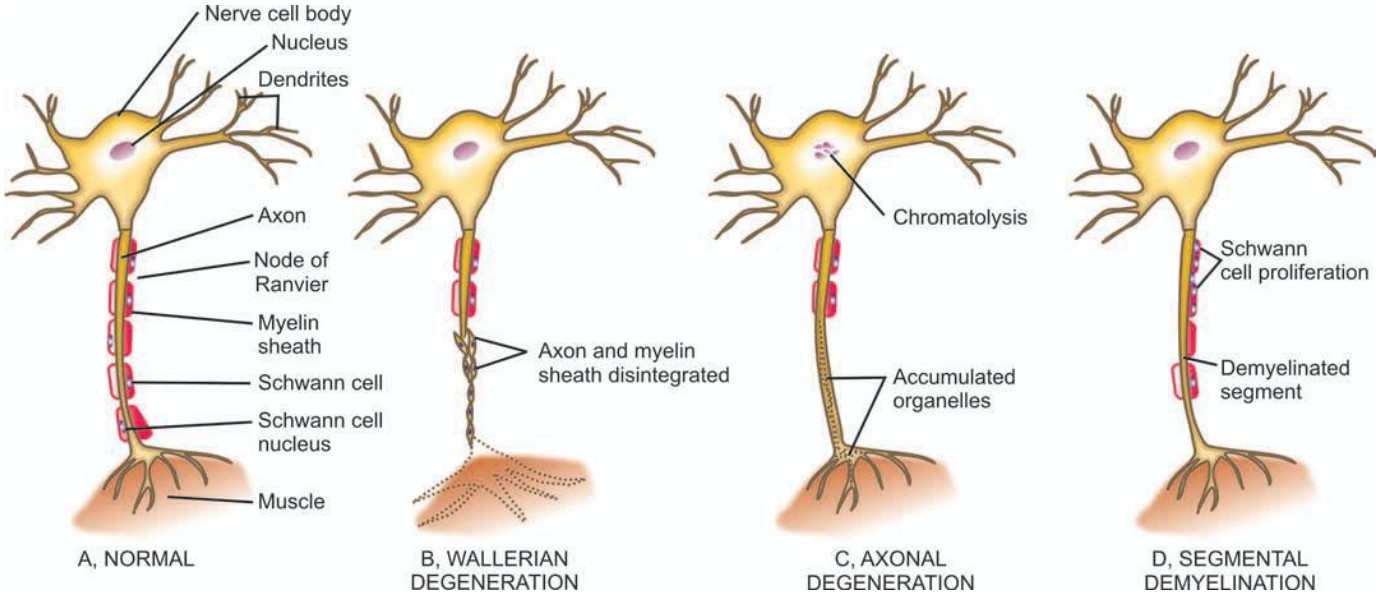


Fig: Pathologic reaction of peripheral nerve to injury

Mononeuropathy multiplex or multifocal neuropathy

- It is defined as simultaneous or sequential multifocal involvement of nerve trunks which are not in continuity.
- The involvement may be partial or complete and may evolve over days or years.
- Multifocal neuropathy represents part of spectrum of chronic acquired demyelinating neuropathy.

Mononeuropathy

- It is focal involvement of a single nerve.
- It is generally the result of local causes such as direct trauma, compression and entrapment.

Brain Tumors / Tumors of CNS

- Tumours of the CNS may originate in the brain or spinal cord (primary tumours), or may spread to the brain from another primary site of cancer (metastatic tumours).
- More than one-quarter of the CNS tumours are secondary metastases arising in patients undergoing treatment for systemic cancer.
- Primary CNS tumours are the second commonest form of cancer in infants and children under the age of 15 years, exceed in frequency only by leukaemia.
- Both benign and malignant CNS tumours are capable of producing neurologic impairment depending upon their site.
- Primary CNS tumours or intracranial tumours include: tumours arising from constituent **cells of the brain** and from the **supporting tissues**.
- Childhood brain tumours arise from more primitive cells (e.g. neuroblastoma, medulloblastoma).
- Among the primary brain tumours,
    - **gliomas** constitute 50-60%,
    - **meningiomas** 25%,
    - **schwannomas** 10% and
    - other primary tumours comprise the remainder.

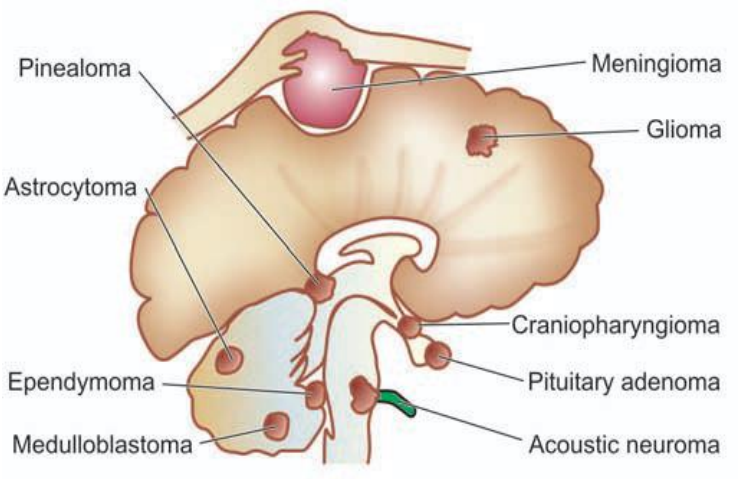


Fig: The anatomic distribution of common intracranial tumours.

Classification of Intracranial /Brain Tumours

I. TUMOURS OF NEUROGLIA (GLIOMAS)

1. **Astrocytoma**
2. Oligodendroglioma
3. Ependymoma
4. Choroid plexus papilloma

II. TUMOURS OF NEURONS

1. **Neuroblastoma** (common malignant tumour of embryonic nerve cells, children under 5 years of age)
2. Ganglioneuroblastoma
3. Ganglioneuroma

III. TUMOURS OF NEURONS AND NEUROGLIA

1. Ganglioglioma

IV. POORLY-DIFFERENTIATED AND EMBRYONAL TUMOURS

1. Medulloblastoma
2. Neuroblastoma
3. Primitive neuroectodermal tumour (highly malignant small round cell tumour, age of 5 and 20 yrs)

V. TUMOURS OF MENINGES

1. Meningioma
2. Meningeal sarcoma

VI. NERVE SHEATH TUMOURS

1. **Schwannoma** (neurilemmoma)
2. **Neurofibroma**
3. Malignant nerve sheath tumour

VII. OTHER PRIMARY INTRAPARENCHYMAL TUMOURS

1. Haemangioblastoma
2. Primary CNS lymphoma
3. Germ cell tumours

VIII. MISCELLANEOUS TUMOURS

1. Malignant melanoma
2. Craniopharyngioma
3. Pineal cell tumours
4. Pituitary tumours

IX. TUMOUR-LIKE LESIONS

1. epidermal cyst, dermoid cyst, colloid cyst

X. METASTATIC TUMOURS

GLIOMAS

- The term glioma is used for all tumours arising from neuroglia, or more precisely, from neuroectodermal epithelial tissue.
- Gliomas are the most common of the primary CNS tumours and collectively account for >40% of all intracranial tumours.
- They include tumours arising:
    - *from astrocytes (*astrocytomas and glioblastoma multiforme);
    - *from oligodendrocytes (*oligodendroglioma*);*
    - *from ependyma (*ependymoma); and
    - *from choroid plexus (*choroid plexus papilloma*).*
    - Gliomas may be well-differentiated or poorly-differentiated.
- Gliomas are disseminated to other parts of the CNS by CSF but they rarely ever metastasise beyond the CNS.

Astrocytomas

- Astrocytomas are the most common type of gliomas. In general, they are found in the late middle life with a peak in 6th decade of life.
- They occur predominantly in the cerebral hemispheres, and occasionally in the spinal cord.
- In children and young adults, pilocytic astrocytomas arise in the optic nerves, cerebellum and brainstem.
- Astrocytomas have tendency to progress from low grade to higher grades of anaplasia. Low-grade astrocytomas evolve slowly over several years whereas higher grades (anaplastic astrocytoma and glioblastoma multiforme) bring about rapid clinical deterioration of the patient.
- The diagnosis of various types of astrocytomas can be generally made by routine H & E morphology, immunohistochemical staining with glial fibrillary protein (GFAP) or by electron microscopic demonstration of glial filaments can be done.

Pilocytic Astrocytoma

- Pilocytic astrocytomas are relatively benign tumors, typically affecting children and young adults.
- Most commonly ventricle, the optic pathways, spinal cord, and occasionally the cerebral hemispheres.
- There is often a cyst associated with the tumor, and symptomatic recurrence from incompletely resected lesions is often associated with cyst enlargement, rather than growth of the solid component.
- Tumors that involve the hypothalamus are especially problematic because they cannot be resected completely.

Diffuse Astrocytoma:

- Diffuse astrocytomas account for about 80% of adult gliomas.
- They are most frequent in the fourth through the sixth decades of life.
- They usually are found in the cerebral hemispheres.
- The most common presenting signs and symptoms are seizures, headaches, and focal neurologic deficits related to the anatomic site of involvement.
- On the basis of histologic features, they are stratified into four groups:
    - diffuse astrocytoma (grade I), *low-grade tumour having good prognosis*

- well-differentiated astrocytoma (grade II), *well-differentiated with fibrillary background of astrocytic processes*
- anaplastic astrocytoma (grade III), *features of anaplasia such as hypercellularity, pleomorphism, nuclear hyperchromatism and mitoses.*
- glioblastoma multiforme (grade IV) *most aggressive with foci of haemorrhages and necrosis.*

Nerve Sheath Tumours

- Tumours of the peripheral nerves are commonly **benign** and include **schwannoma** (neurilemmoma) and **neurofibroma**.
- Both of them arise from **Schwann cells** but neurofibroma contains large amount of **collagen**.
- Rarely, may lead to malignant peripheral nerve sheath tumour.

Schwannomas (Neurilemmomas)

- Schwannomas or neurilemmomas arise from cranial and spinal nerve roots.
- An *acoustic schwannoma* or *acoustic neuroma* is an intracranial schwannoma located within the internal auditory canal originating from vestibular portion of the acoustic nerve.
- *Intraspinal schwannomas* are found as intradural tumours in the thoracic region.
- In the peripheral nerves, they occur as solitary nodule on any sheathed sensory, motor, or autonomic nerve.
- Occur in Von Recklinghausen's disease *(inherited disease, neurofibromatosis, tumours along the course of nerves beneath the skin).*
- Schwannomas are tumours of adults.

➢ **Grossly,** a schwannoma is an encapsulated, solid, sometimes cystic, tumour that produces eccentric or unusual enlargement of the nerve root from where it arises.

❖ **Microscopically,** the tumour is composed of fibrocellular bundles forming whorled pattern.

❖ There are areas of dense and compact cellularity ***(Antoni A pattern)*** alternating with loose acellular areas ***(Antoni B pattern)***. Areas of Antoni A pattern show palisaded nuclei called ***Verocay bodies***.

❖ Nerve fibers are usually found stretched over the capsule but not within the tumour.

❖ Areas of degeneration contain haemosiderin and lipid-laden macrophages.

❖ Schwann cells characteristically express S-100 protein. A schwannoma rarely ever becomes malignant.

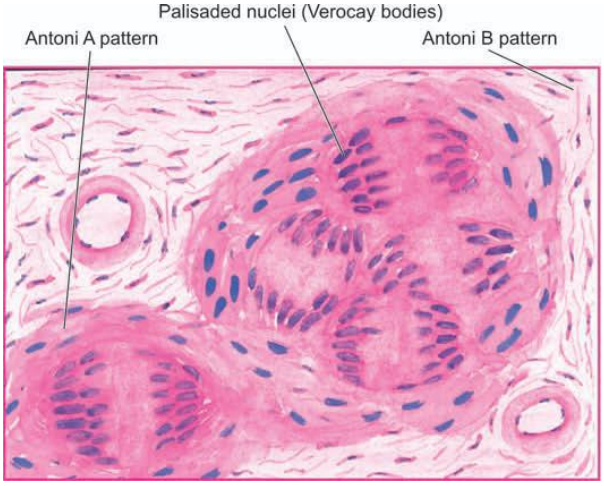


Fig: Schwannoma (neurilemmoma), showing whorls of densely cellular (Antoni A) and loosely cellular (Antoni B) areas with characteristic nuclear palisading (Verocay bodies).

Neurofibromas and Von Recklinghausen's Disease

- Neurofibromas may occur as solitary, fusiform or spindle-shaped cutaneous tumour of a single nerve.
- Solitary neurofibroma is a tumour of adults and multiple neurofibromas or neurofibromatosis is a hereditary disorder with autosomal dominant inheritance.
- Neurofibromatosis type 1 is a genetic disorder having mutation in chromosome 17 while type 2 has mutation in chromosome 22.
- Solitary neurofibroma is generally asymptomatic and patients with Von Recklinghausen's disease have a triad of features:
    - Multiple cutaneous neurofibromas.
    - Numerous pigmented skin lesions.
    - Pigmented iris hamartomas (overgrowth of mature tissue).

➢ ***Grossly,*** neurofibroma is an unencapsulated tumour producing fusiform enlargement of the affected nerve.

➢ Neurofibromatosis in Von Recklinghausen's disease is characterised by numerous nodules of varying size.

➢ Neurofibromatosis may involve a group of nerves or may occur as multiple, oval and irregular swellings along the length of a nerve (plexiform neurofibroma).

❖ **Microscopically,** a neurofibroma is composed of interlacing bundles of delicate and elongated spindle shaped cells having wavy nuclei.

❖ The cellular area is separated by loose collagen and mucoid material. Residual nerve fibres (neurites) may be demonstrable.

❖ Histologic appearance of Antoni B pattern of schwannoma may be seen in neurofibroma and cause diagnostic difficulty.

❖ Immunohistochemically, neurofibroma is positive for epithelial membrane antigen (EMA) and some tumours express S-100 protein as schwannomas do.

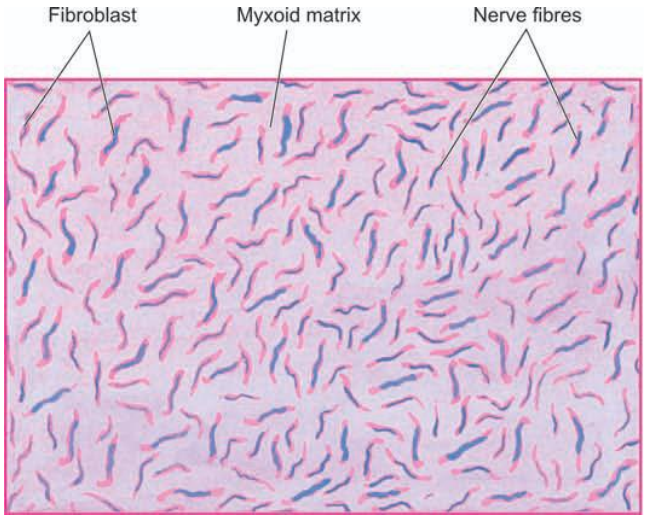


Fig: Neurofibroma, showing interlacing bundles of spindle-shaped cells separated by mucoid matrix. The cells have wavy nuclei and a residual nerve fibre (neurite) is also identified.