Pathology of the nervous system

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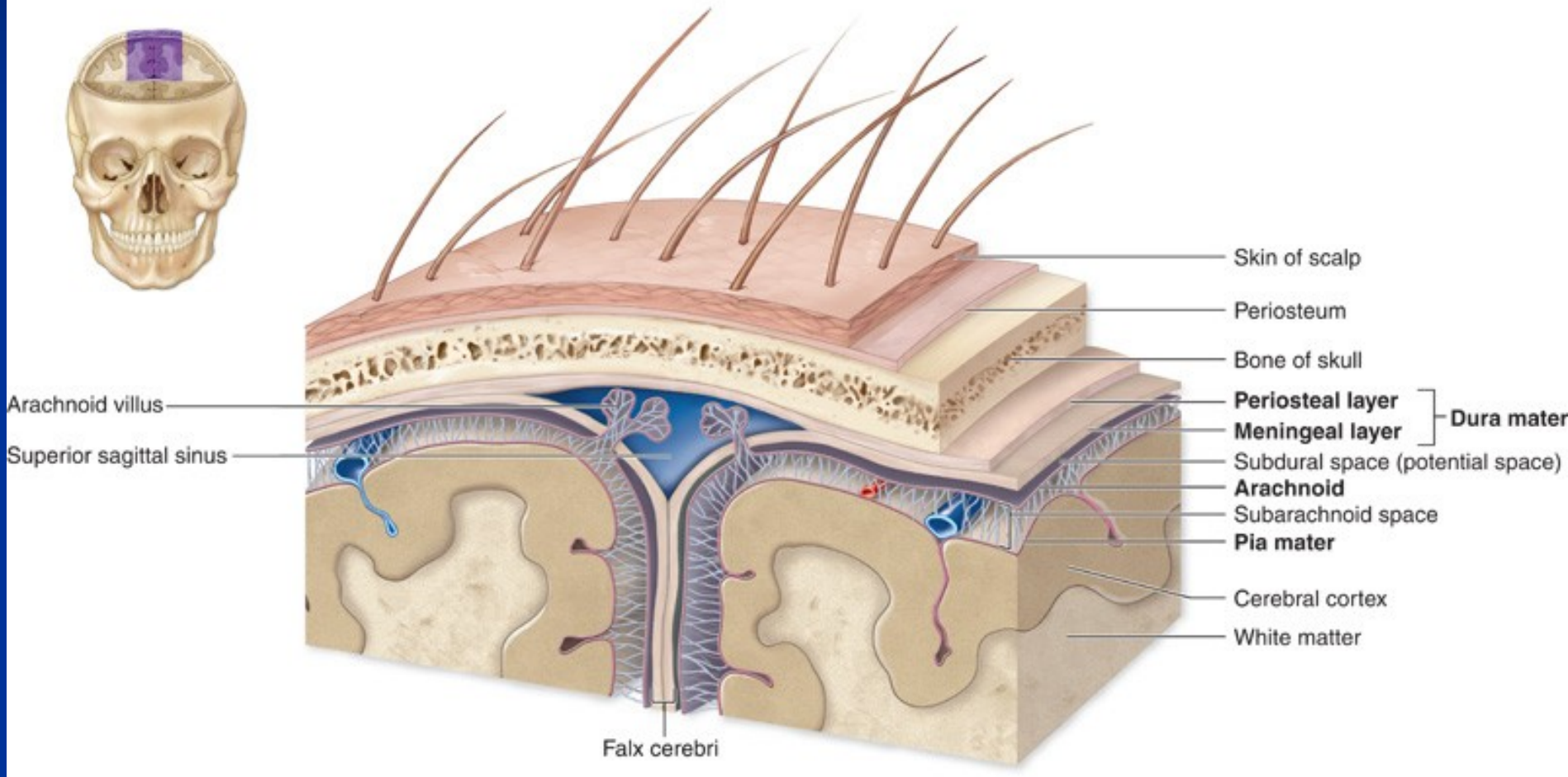
Meninges



CNS trauma

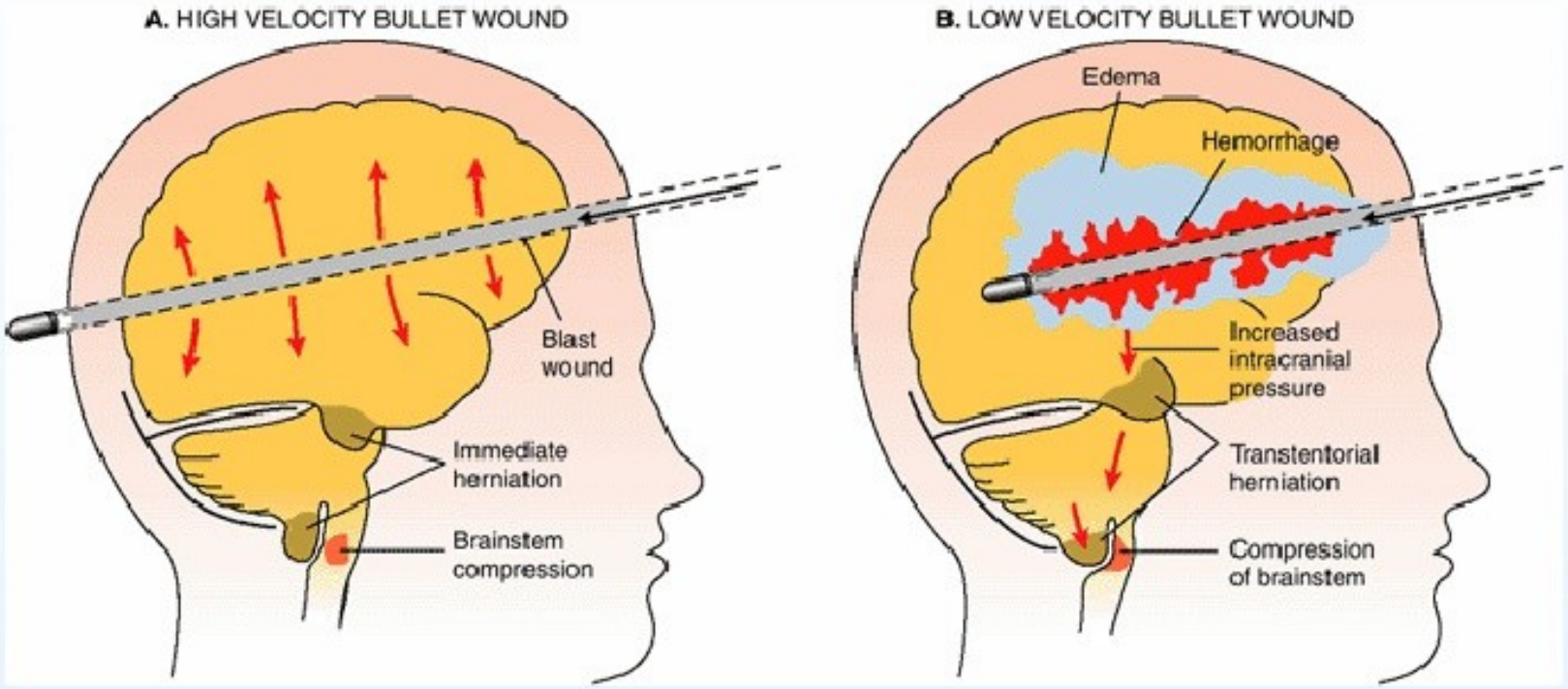
- **Missile** (depressed, penetrating and perforatin injuries)
- **Non-missile injury:**
  - Primary damage (immediate)
  - Secondary damage (after the injury)

- **Primary damage includes:**
  - Focal lesions (contusions and lacerations)
  - Diffuse axonal injury

- **Secondary damage includes:**
  - Intracranial haematomas, herniation, infarction, infections

- **Complications:**
  - epilepsy, persistent vegetative state and post-traumatic dementis

Missile Injury:



The “blast effect” of a high-velocity projectile causes an immediate increase in supratentorial pressure and results in death because of impaction of the cerebellum and medulla into the foramen magnum. A low-velocity projectile increases the pressure at a more gradual rate through hemorrhage and edema.

Brain oedema

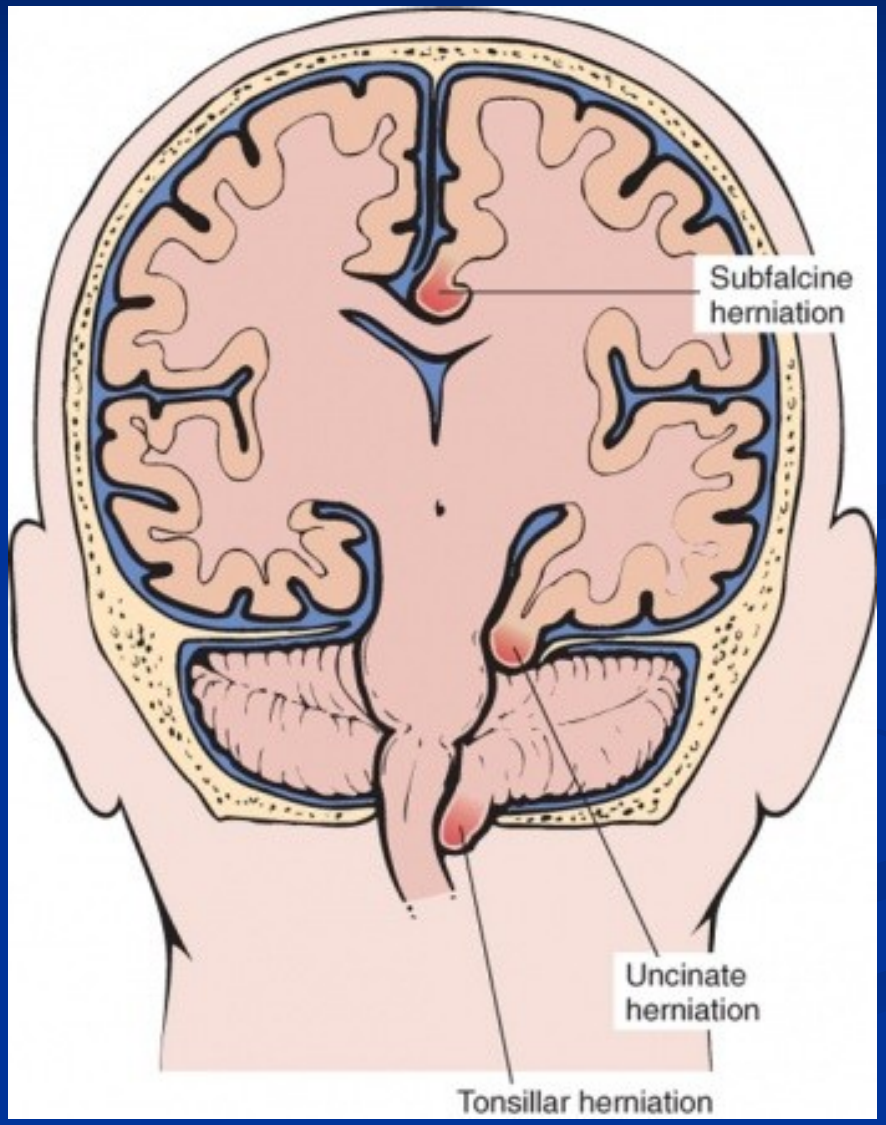
- **Diffuse swelling due to:** vasogenic and cytotoxic reasons
- **Focal swelling due to:** focal lesions (cerebral abscesses, haematomas, intracranial neoplasms
- **Consequences of intracranial space occupying lesions:**

- Raised intracranial pressure
- Intracranial shift and herniation
- Epilepsy
- Hydrocephalus
- Systemic effects

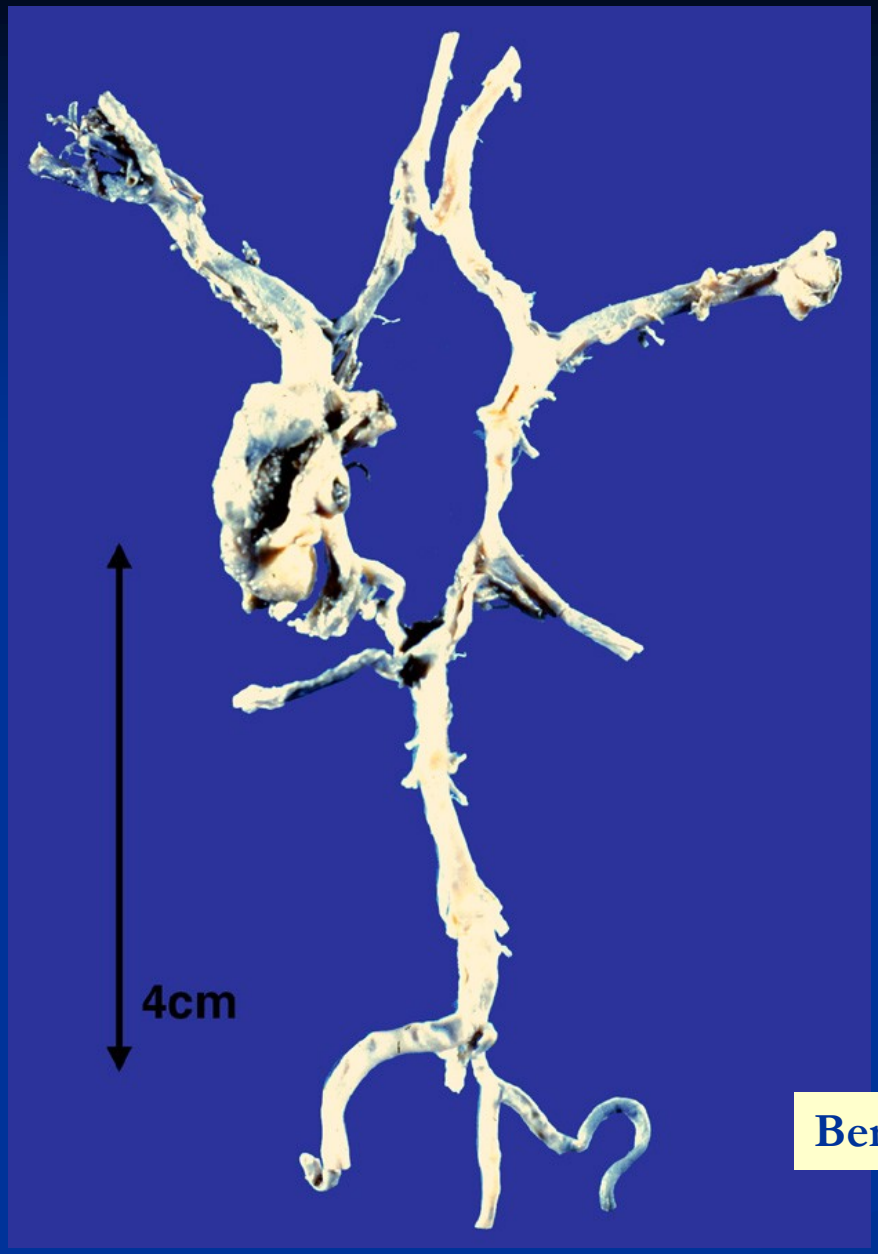
- **Raised intracranial pressure – clinical picture:**

- Papillooedema (optic papilla)
- Nausea and vomiting
- Headache
- Impairment of consciousness

Intracranial herniation



Manifesttion of traumatic intracranial bleeding		
Site	**Mechanism**	**Clinical manifestation**
Extradural space	Skull rupture with arterial rupture	Lucid interval followed by a rapid increase in intracranial pressure
Subdural space	Rupture of venous sinuses or small bridging veins due to torsion force	Acute presentation with a rapid increase in intrcranial pressure. Chronic presentation with personality change, memory loss and confusion, particularly in the elderly
Subarachnoid space	Arterial rupture, berry aneurysm of circle of Willis	Meningeal irritation with a rapid increase in intracranial pressure
Cerebral hemisphere	Cortical contusion Rupture of small intrinsic vessels with intracerebral haematoma	May cause seizures Increased intracranial pressure with focal deficits, usually fatal.

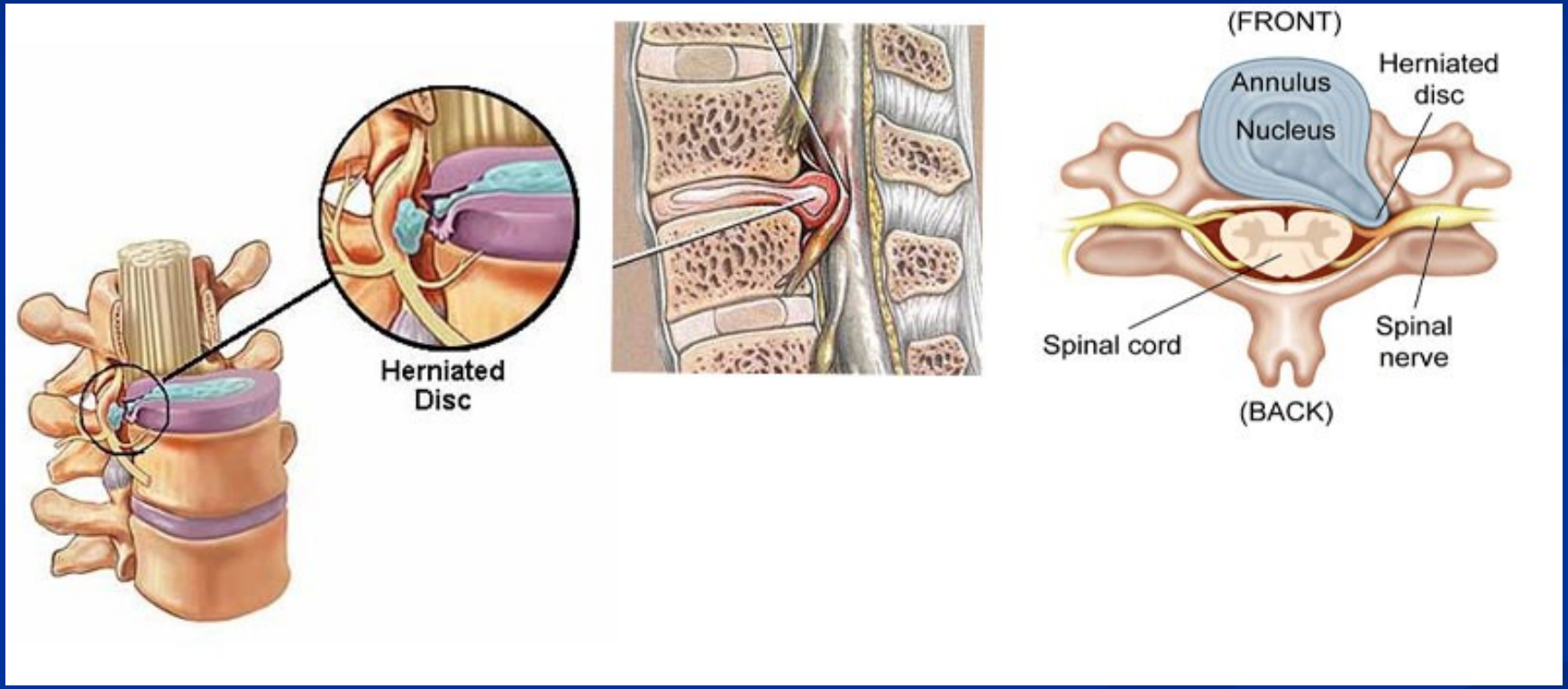


Berry/saccular aneurysm of circle of Willis

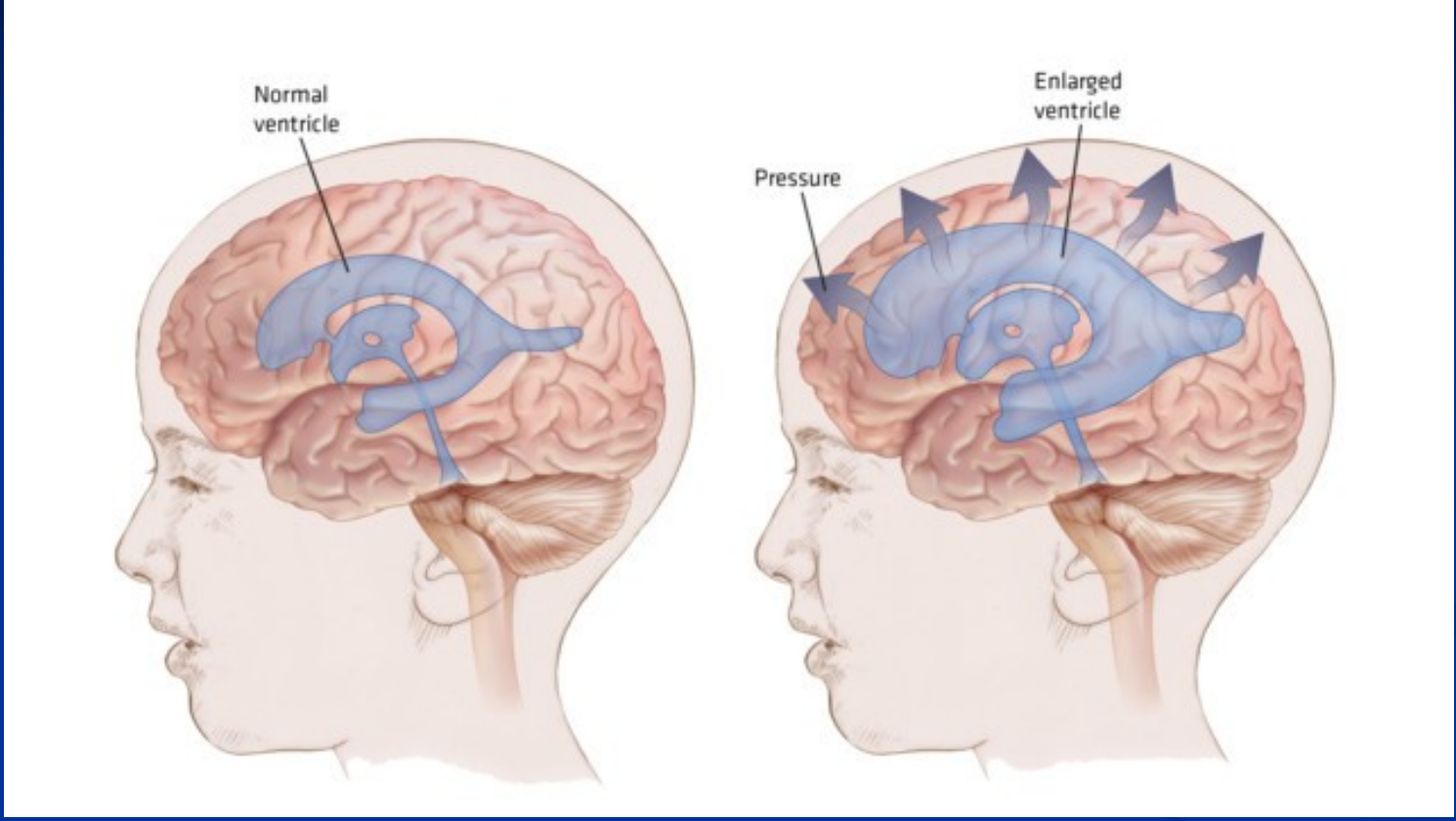
Spinal cord injuries

- **Open injuries due to direct trauma**
- **Closed injuries:**
  - Primary damage: contusions, nerve fiber transection, haemorrhagic necrosis
  - Secondary damage: extradural haematoma, infarction, infection, oedema
- **Complications:**
  - Degeneration of damaged nerve fibres (both ascending and descending)
  - Post traumatic syringomyelia
  - Systemic effects of paraplegia (urinary tract and chest infections, pressure sores and muscle waiting)
- **Spinal cord and nerve root compression:**
  - Intervertebral disc prolapse
  - Neoplasm
  - Skeletal disorders
  - Infections (tbc, abscess)
  - Vascular disorders (arteriovenous malformation, haemorrhage)
  - Trauma

Intervertebral disc prolapse



Hydrocephalus



- Excess of cerebrospinal fluid (CSF) within the intracranial cavity
- Due to obstruction of the CSF pathways (non-communicating, congenital or aquired), impaired CSF absorption, excess CSF production
- Produces irreversible brain damage unless the increased intracranial pressure is relieved by surgical drainage

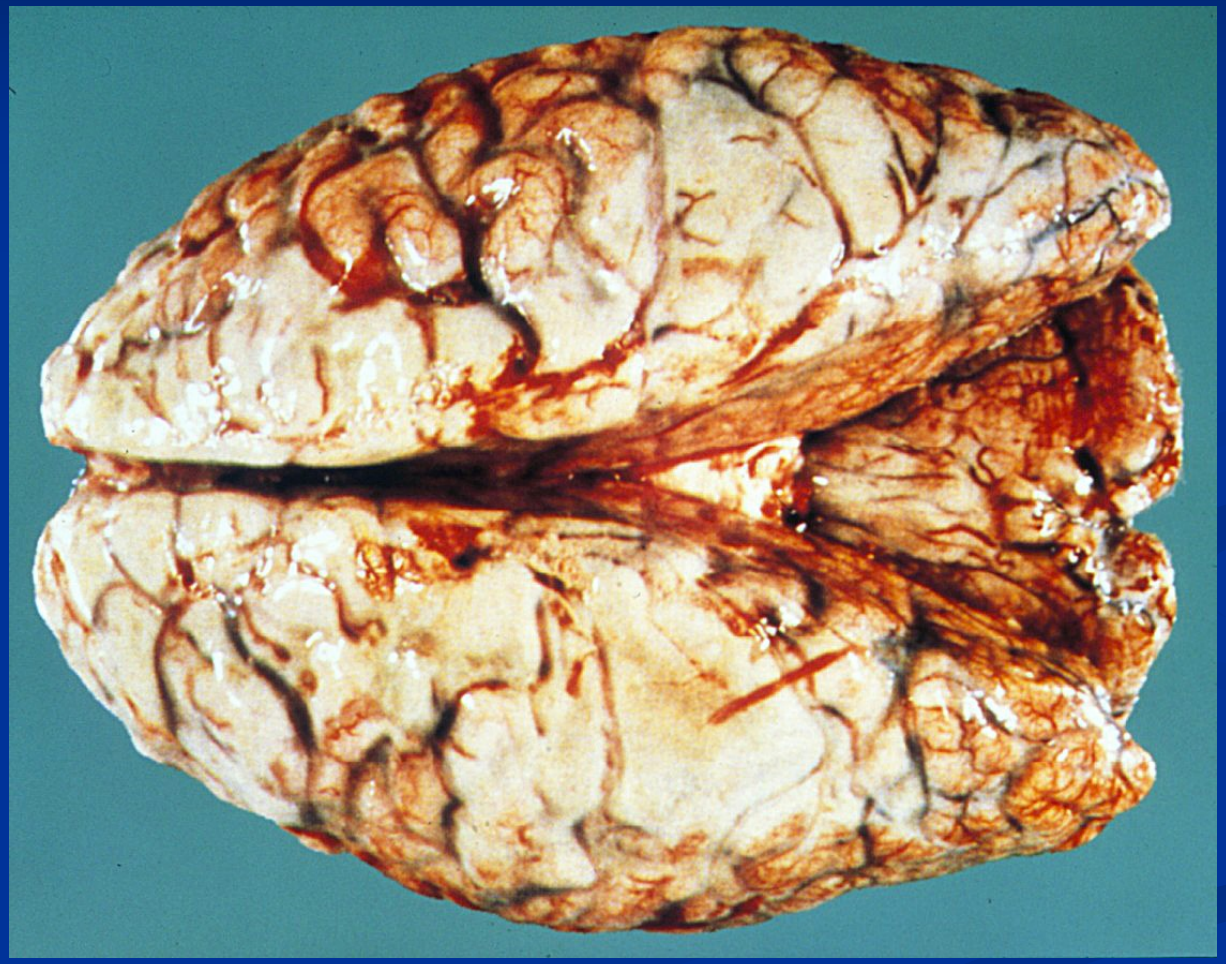
Major causes of stroke				
Cause	**%**	**Clinical presentation**	**Pathogenesis**	**Predisposing factors**
Cerebral infarction	82	Slowly evolving signs and symptoms	Cerebral hypoperfusion (in AS), emblism, thrombosis	Heart disease Hypertension Atheroma Diabetes mellitus
Intracerebral haemorrhage	15	Sudden onset of stroke with raised intracranial pressure	Rupture of arteriole or microaneurysm	Hypertension Vascular malformation
Subarachnoid haemorrhage	3	Saudden headache with meningism	Rupture of saccular/berry aneurysm of circle of Willis	Hypertension Coarctation of the aorta

Hypoxic CNS damage: ischaemia – hypoxia – anoxia

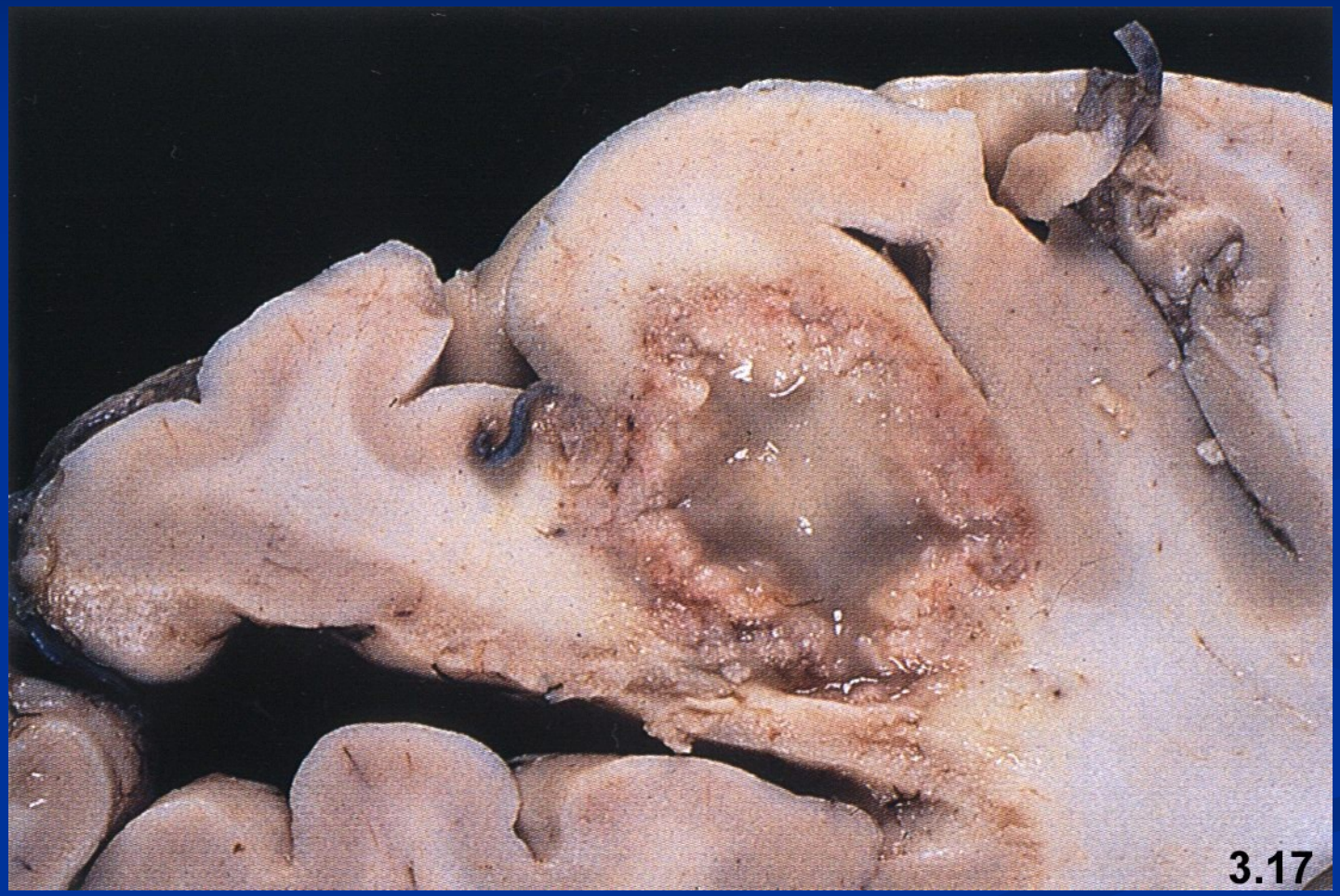
CNS infections: bacterial infection

- Follow the direct spread of infection from the skull, or haematogenous spread
- Leptomeningitis, the most common, in children and in elderly
- Complications: hydrocephalus, cerebral thrombophlebitis, cerebral infarction, abscess, sepsis
- Aetiological agents: *E. coli, Streptococcus agalactiae, Listeria monocytogenes* (in neonates); *Neisseria meningitis* (2-18 years), *Streptococcus pneumoniae* (over 30 years), BK (tuberculous meningitis), *Treponema palllidum* (in syphilis)

Purulent meningitis



Brain abscess



CNS infections: viral infections

- Infections spread to the CNS by the haematogenous route or retrograde neural transport

- **Viral meningitis** is a common, self-limiting illness, less severe than bacterial meningitis

- **Viral encephalitis** may result in death or severe disability (virus carried by ticks or mosquitoes)

- **Reactivation of latent viral infection** (e.g. Herpes zoster) may damage the CNS

- *CNS involvement in HIV infection*:

- Cerebral HIV infection (causing progressive dementia)
- Multiple opportunistic infections (e.g. Toxoplasma, fungi)
- Other viral infections (e.g. CMV)
- Primary cerebral lymphoma

CNS infections: viral, fungal and parasitic infections

- **Prion diseases** (prion=pathologic protein) responsible for subacute spongiform encephalopathy, a rare cause of dementia (e.g. Creutzfeldt-Jakob disease and variant CJD („mad cow“ disease)

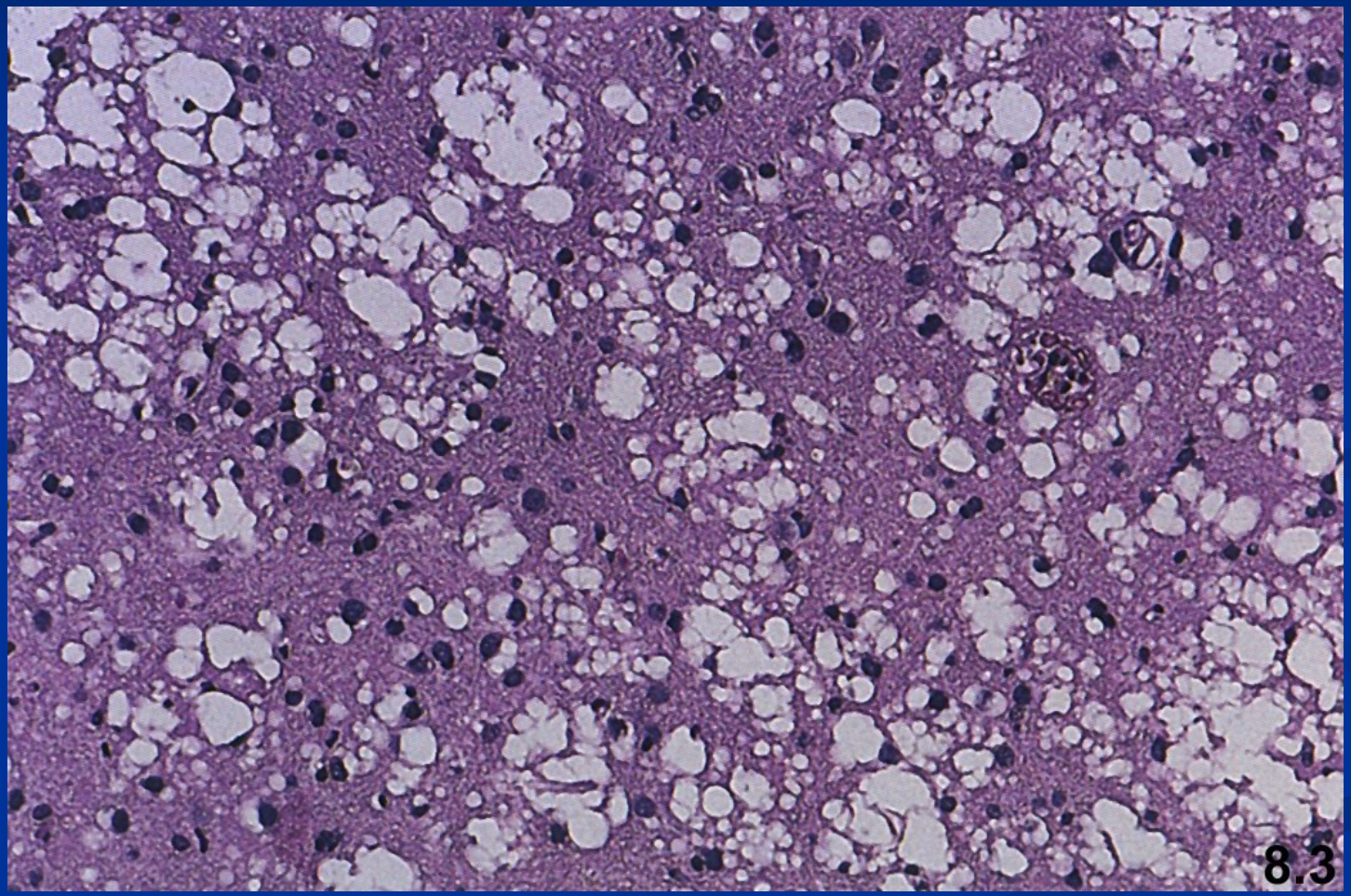
- **Acute disseminated encephalomyelitis**, a demyeliting disorder, may result from virus-induced immune reaction (complications of measles, mumps, rubeola; also following vaccination for smallpox and rabies)

- Antenatal viral infections: CMV and rubella virus resulting in a necrotising encephalomyelitis, developlmenta malformations and microcephaly

- Fungal infections: *Cryptococcus neoformans, Aspergillus fumigatus, Candida albicans,…*
- Parasitic infections: *Toxoplasma gondii, Plasmodium falciparum, Trypanosoma rhodesiense…….*

CNS infections common in immunosuppressed patients!

Subacute spongiform encephalopathy; Creutzfeldt - Jacob, vacuolar transformation of neurons



Demyelinating conditions

- Due to immunological, viral or chemical mechanisms
- Myelin disintegrated, myelin fragments phygocytosed, remyelination does not occur to any significant extent

- **Multiple sclerosis**: commonest demyelinating conditions, v.s. autoimmune, with high incidence in northern countries.
  Clinically:
  - Limb weakness
  - Paraesthesiae
  - Visual abnormalities
  - Diplopia
  - Bladder dysfunctions, vertigo

- Leukodystrophies - inherited disorders of myelin synthesis

Metabolic disorders

- **Hypoglycaemia** (in DM) can result in irreversible neuronal damage and neuronal cell death

- **CNS toxins:**
- methanol, ethanol, metals and industrial chemicals
- drugs (affecting neuronal development (e.g. phenytoin), affecting mature CNS (e.g. vincristin)

- **Deficiency states:** malnutrition, vitamin deficiencies (B1, B12)

- **Inherited metabolic diseases: lysosomal storage diseases** due to deficiences of various lysosomal enzymes (sphingolipidosis, mucopolysacharidosis, glycogenosis, ceroid lipofuscinosis)

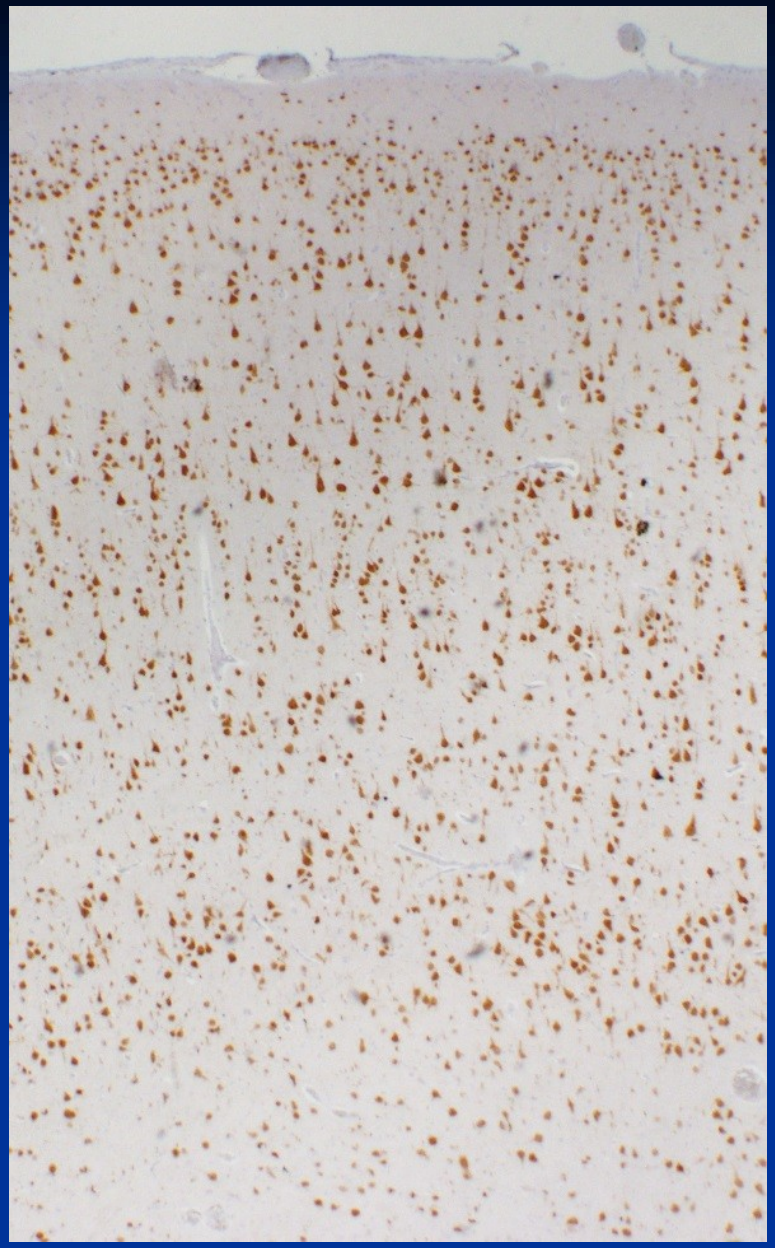
Epilepsy

- Repeated seizures due to paroxysmal neurological dysfunction caused by abnormal discharges from neurones in th brain

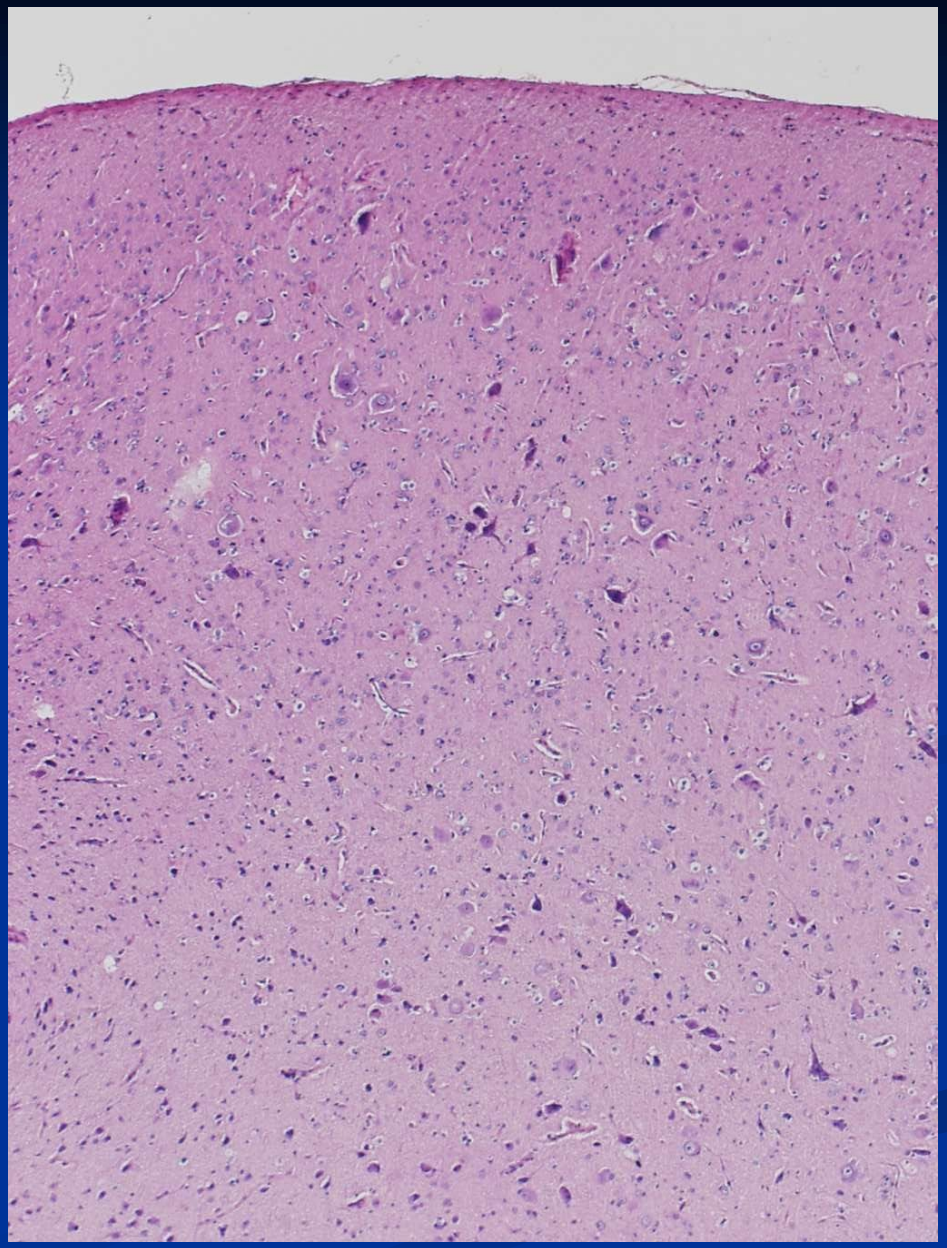
- **Generalised epilepsy:**
  - Synchronous abnormal discharges due to hyperexcitability of membranes
  - Often idiopathic, not associated with structural abnormalities in the brain

- **Focal epilepsy**
  - Associated with structural abnormalities of the cerebral cortex – epileptogenic lesions
  - Malformation of cortical development, tumors, glial scars, vascular abnormalities,….
  - Some cases treated surgically

- **Provoked seizures**
  - Discharges due to acute damage to the brain (head injury, alcohol, metabolic abnormality (e.g. hypoglycaemia)



Normal cortex



Focal cortical dysplasia

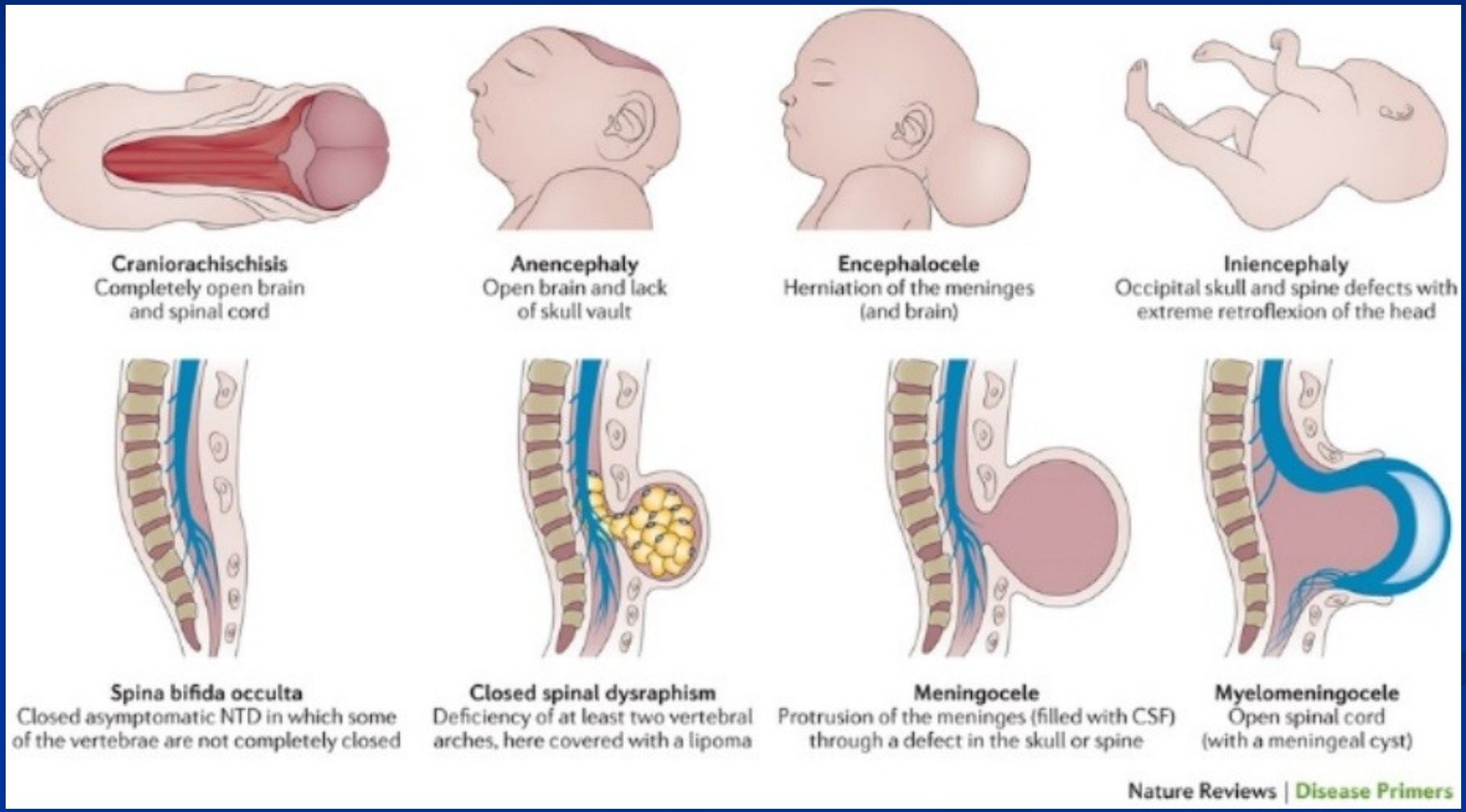
Congenital abnormalities

- **Known causes:**

- Genetic factors (tuberous sclerosis (AD), aqueduct stenosis (X-linked), Down´s syndrome (trisomy 21))
- Maternal infections (e.g. rubella, CMV)
- Irradiation in utero
- Toxic, as in fetal alcohol syndrome
- Dietary factors (e.g. Folic acid deficiency implicated in neural tube defects)
- Metabolic (e.g. Phenylketonuria)

- **Neural tube defects**
- **Posterior fossa malformation**

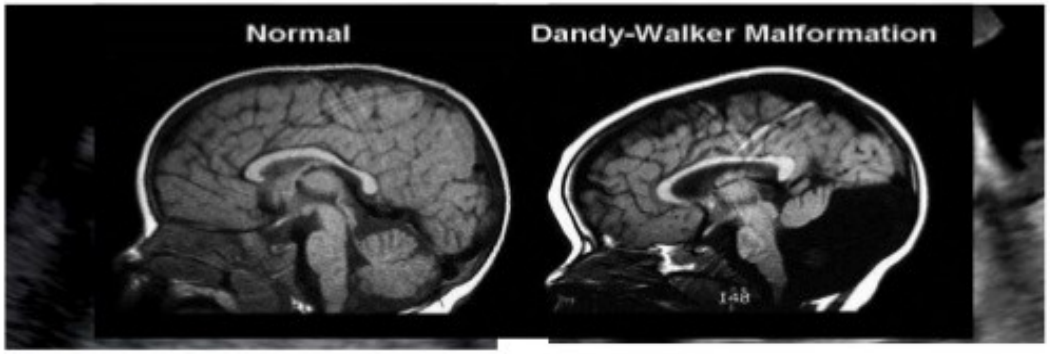
Neural tube defects



Posterior fossa malformations

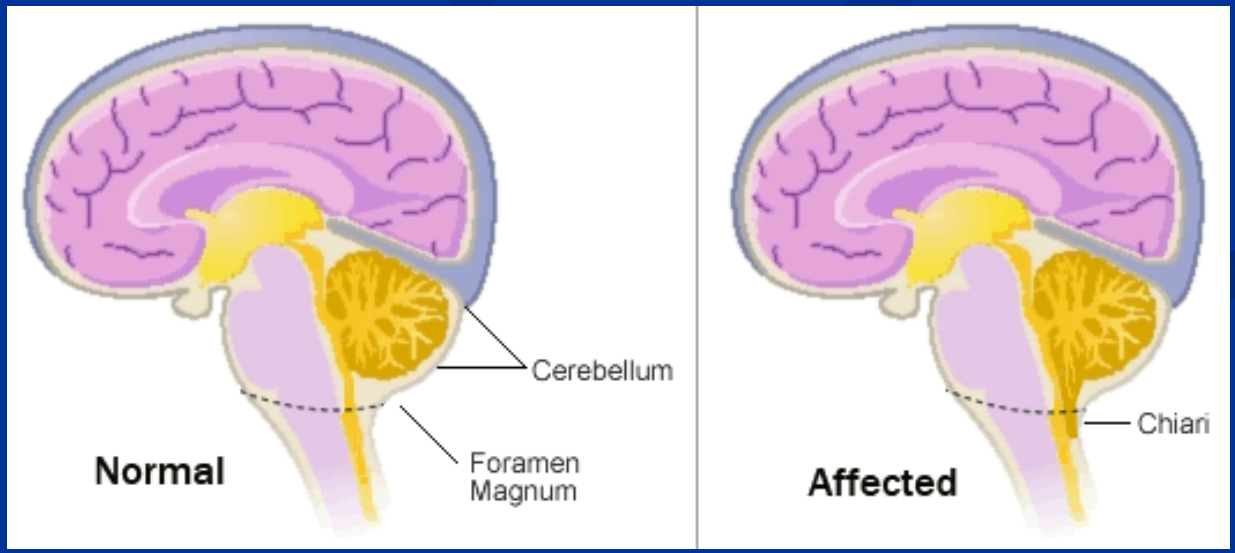
Dandy – Walker malformation

1. Marked cystic dilatation of the 4th ventricle (may fill much of posterior fossa)
2. Hypogenesis or agenesis of the cerebellar vermis
3. Superior displacement of the tentorium and lateral sinuses



Arnold Chiari malformation

1. Involving cerebellum, brainstem, spinal cord
2. Cerebellar tonsils displaced downwards
3. Results in hydrocephalus, communicating
4. Often assoc. with meningomyelocele



Neurodegenerative disorders

- Characterised by progressive loss of neurons in functionally related areas of the CNS
- Aetiologically mostly unknown, some are inherited

- **Motor neuron disease:**

- **Amyotrophic lateral sclerosis**

(both upper and lower motorneurons affected, distal and proximal muscle weakness and wasting spasticity)

- **Progressive muscular atrophy**

(lower motor neuron involvement, weakness an wasting of distal muscles, fasciculations and absent reflexes)

- **Progressive bulbar pulsy**

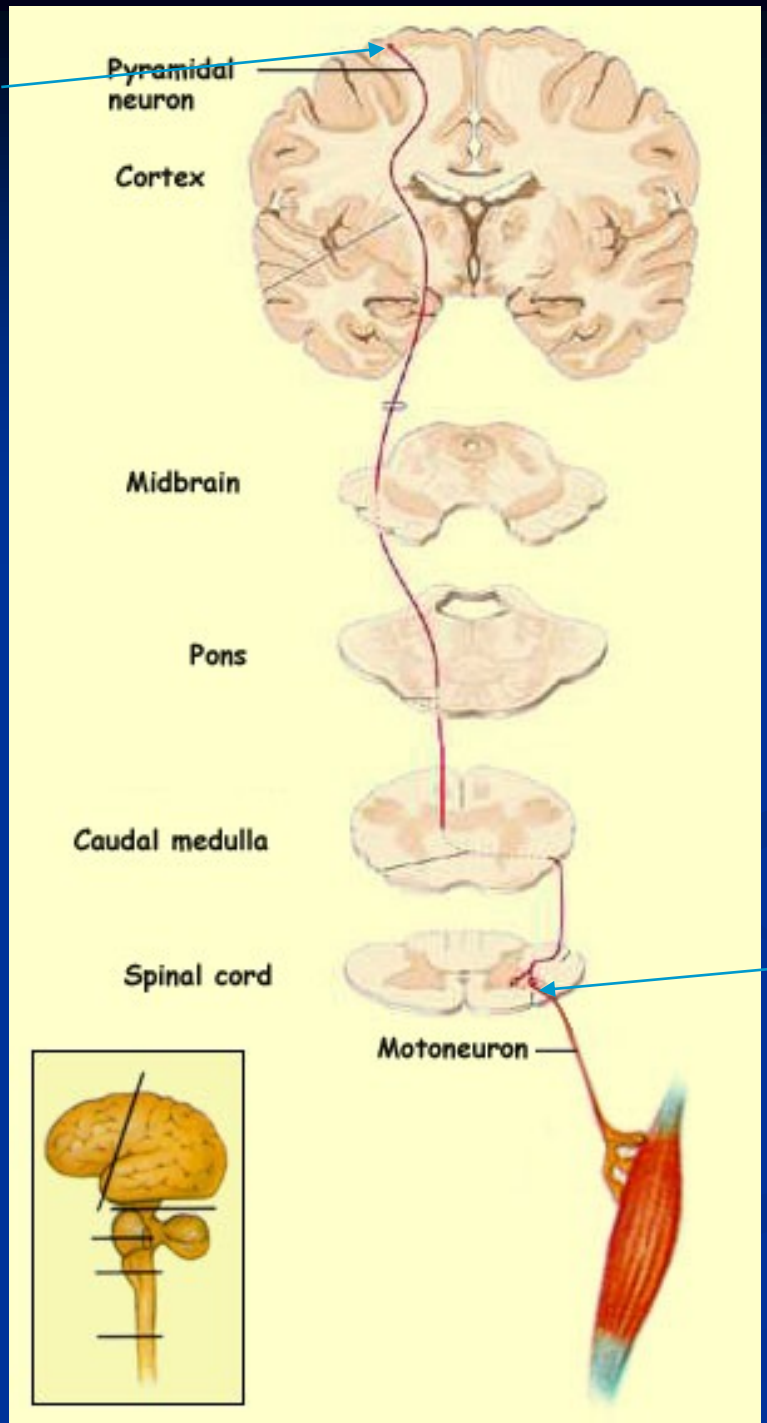
(cranial nerves involvement results in weakness of the tongue, palate, pharyngeal muscles)

- **Parkinson´s disease**

- tremor, bradykinesis, rigidity; manifestation between 45-60 years
- caused by progressive loss of pigmented neurones in substantia nigra resulting in relative dopamin deficiency

Motor neuron tract

Upper motoneuron



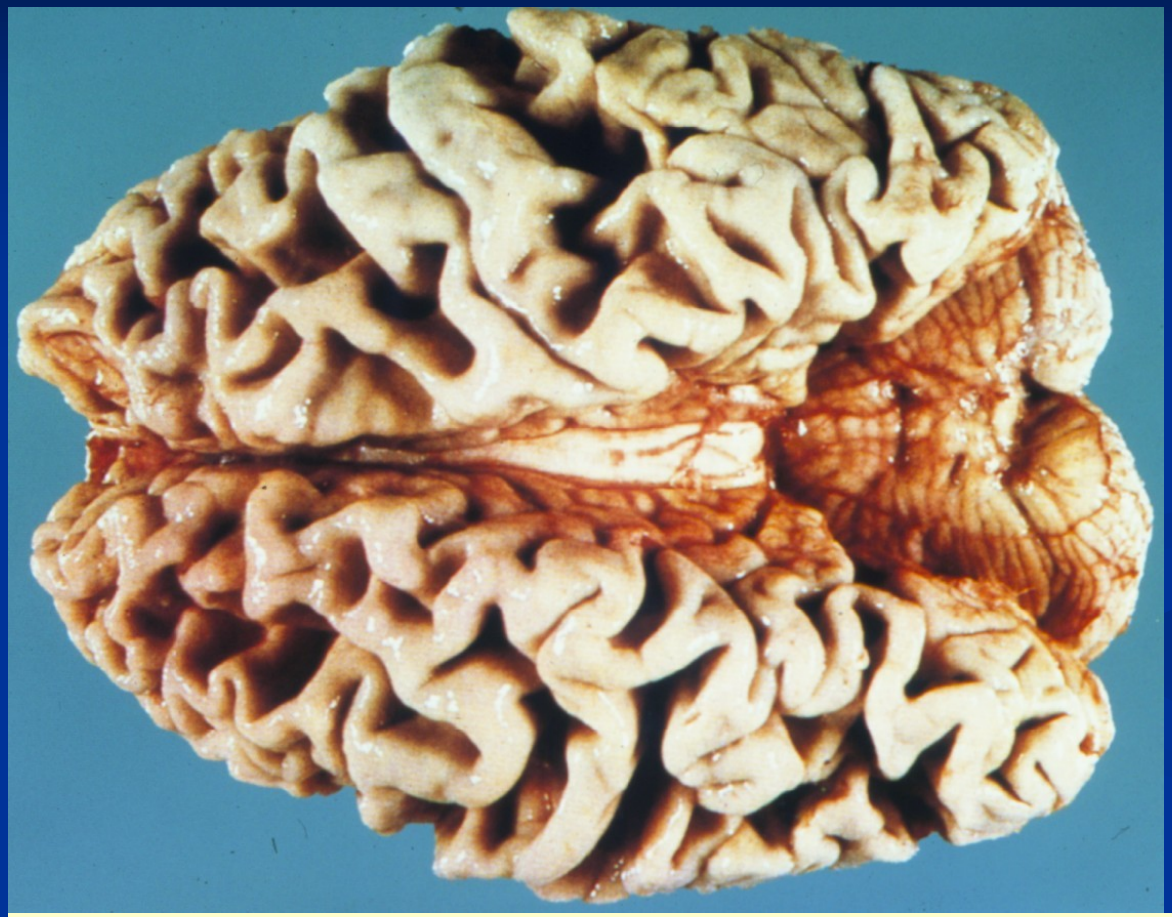
Lower motoneuron

Dementia

- **Acquired global impairment of intellect, reason and personality without impairment of consciousness**

- **Disorders resulting in dementia:**
- Primary neurodegenerative diseases
  - **Alzheimer´s d.**
  - **Pick´s d.** (frontotemporal dementia)
  - **Huntington´s d.** (AD, choreiformic movements, jerking dementia)
- Cerebrovascular disease (e.g. multinffarct dementia)
- Infections (e.g. CJD, syphilis, HIV)
- Space occupying diseases (e.g. neoplasms, haematomas)
- Hydrocephalus
- Drugs and toxins
- Metabolic disorders (e.g. hypothyreoidism, hypoparathyreoidism, hepatic failure,..)
- Vitamin deficiences (e.g. B1, B12)
- Paraneoplastic syndromes (e.g. limbic encephalitis)

Brain atrophy – Alzheimer disease



- Sporadic and familiar cases
- Cortical atrophy
- Amyloid angiopathy, neurochemical abnormalities, neuronal loss, amyloid plaques and tangles

Cell of origin	Tumor
Glial cells	Astrocytoma (both low grade and high grade) Oligodendroglioma (both low grade and high grade) Glioblastoma (Ependymoma)
Primitive neuroectodermal cells	Medulloblastoma (CNS; central nervous system, cerebellum) Neuroblastoma (PNS; peripheral nervous system, adrenals) Retinoblastoma …..*all mentioned are pediatric tumors*
Arachnoidal cells	Meningioma
Nerve sheath cells	Schwannoma, neurofibroma Malignant schwannoma, neurofibrosarcoma
ANS; autonomous nervous system	Paragangliomas, chemodectomas, pheochromocytoma

+ secondary, metastatic tumors

CNS tumors

- **Clinicopathological features:**
- **CNS tumors do not metastasise to othe organs**
  - (only infiltration of adjacent tissues and spreading through
  - CSF pathways)
- **Local effects**
  - Signs related to the site of the tumor
  - e.g. epilepsy with a temporal lobe tumor, paraplegis in spinal cord tumor
- **Mass effects**
  - Signs and symptoms of space occupying lesions
  - Vasogenic oedema around CNS tumor
  - Herniation
  - Hydrocephalus in posterior fossa tumor

Peripheral neuropathy: peripheral nerve disorders

- **Mononeuropathy**
  - a single nerve involved
  - e.g. carpal tunnel syndrome

- **Mononeuritis multiplex**
  - Several isolated nerves involved
  - e.g. polyarteritis nodosa, sarcoidosis

- **Polyneuropathy:** multiple nerve involvement
- Mainly motor: e.g. Guillain-Barre sy (autoimmune polyradiculoneuritis)
- Mainly sensory: carcinomatous neuropathy
- Sensorimotor: e.g. alcoholism
- Autonomic: e.g. diabetes

Thank you for your attention….