Marker	What happens?	Characteristics
CNS		
Red Neuron	Shrinkage of the cell body, pyknosis of the nucleus, disappearance of the nucleolus, loss of Nissl substance, intense eosinophilia of the cytoplasm.	RED NEURON is an early sign of ischemia. Ischemia is irreversible cell injury ends by cell death
Intracellular Inclusions	Nuclear or cytoplasmic aggregates of stainable substances, usually proteins.	Example: Negri bodies in rabies.
Dystrophic neurites	A neurite refers to any projection from the cell body of a neuron	In some neurodegenerative diseases, neuronal processes become thickened and tortuous; these are termed dystrophic neurites.
Axonal		
Axonal Injury	Injured axons undergo swelling (called spheroids) and show disruption of axonal transport.	*Central chromatolysis*
Diffuse Axonal Injury	Wide but often asymmetric distribution of axonal swellings that appears within hours of the injury and may persist for much longer.	Patients who develop coma shortly after trauma, are believed to have white matter damage and diffuse axonal injury.
Peripheral nerve injury		
Axonal Neuropathies	Caused by insults that directly injure the axon.	The entire distal portion of a axon degenerate. (Wallerian degeneration)
Segmental demyelination	Damage to Schwann cells or myelin with relative axonal sparing	Typically occurs in individual myelin internodes randomly

Edema	
Vasogenic Edema	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	An increase in intracellular fluid secondary to neuronal and glial cell membrane injury, as might follow generalized hypoxic-ischemic insult or after exposure to some toxin.

Injury and Repair, What happens?	
Astrocyte	1. The nucleus enlarges and becomes vesicular, and the nucleolus is prominent. 2. *Gemistocytic astrocyte* 3. *Fibrillary astrocytes*
Oligodendrocytes	Exhibit a limited spectrum of specific morphologic changes in response to various injuries.
Ependymal cells	Lining the ventricular system and the central canal. Certain pathogens, particularly cytomegalovirus (CMV), can produce extensive ependymal injury, with typical viral inclusions.
Microglia	○ When these elongated microglia form aggregates at sites of tissue injury, they are termed *microglial nodules.* ○ Similar collections can be found congregating around portions of dying neurons, termed *neuronophagia* (e.g. viral encephalitis).

Tumor	Found in	Affects	Grade	Morphology	Characteristics
Astrocytoma Originates from astrocytes **Fibrillary**	Cerebral hemispheres of adults and the brainstem of children.	4th to 6th decade	Diffuse astrocytoma (II)	▪ Mild to moderate increase in the number of glial cell nuclei ▪ Variable nuclear pleomorphism ▪ Glial fibrillary acidic protein (GFAP)-positive astrocytic cell processes	Static or progress slowly (mean survival of more than 5 yrs).
			Anaplastic astrocytoma (III)	▪ More cellular. ▪ Greater nuclear pleomorphism. ▪ Mitosis.	
			Glioblastoma (IV)	▪ All the features of anaplastic astrocytoma, plus: ▪ ***Necrosis* and/or *vascular or endothelial cell proliferation*** Grim prognosis as the grade increases With treatment, mean survival of 8-10 months.	▪ Most common ▪ **Secondary** glioblastomas share ***p53*** mutations that characterized low-grade gliomas. ▪ **Primary** glioblastomas are characterized by amplification of the epidermal growth factor receptor **(*EGFR*)** gene.
Pilocytic	Cerebellum	Children and young adults	Grade I	• Often cystic, with a mural nodule. • Composed of bipolar cells with long, thin "hair- like" processes that are GFAP-positive. • Rosenthal fibers & hyaline granular bodies are often present. • No necrosis or mitoses	• If it's solid, it's usually well circumscribed. • No mutations in IDH1 and IDH2.
Oligodendr-oglioma	Cerebral hemispheres	Fourth and fifth decades	Well-differentiated (II)	Infiltrative tumors that form gelatinous, gray masses and may show cysts, focal hemorrhage, and calcification. Mitotic activity is hard to detect.	Loss of heterozygosity for chromosomes 1p and 19q
			Anaplastic (III)	A more aggressive subtype with higher cell density, nuclear anaplasia and mitotic activity.	
Ependymoma	Next to the ependyma-lined ventricular system	First two decades of life	• In the fourth ventricle, they are solid or papillary masses extending from the ventricular floor. • Tumor cells may form round or elongated structures (rosettes, canals) that resemble the embryologic ependymal canal, with long, delicate processes extending into a lumen • Anaplastic ependymomas show **increased** cell density, **high** mitotic rates, necrosis and less evident ependymal differentiation		

<table>
<tr><th>Tumor</th><th>Found in</th><th>Affects</th><th>Grade</th><th>Morphology</th><th>Characteristics</th></tr>
<tr><td rowspan="3">Meningioma</td><td rowspan="3">Meninges</td><td rowspan="3">Adults</td><td>I</td><td>Has many patterns, which are all benign</td><td rowspan="3">Histological types:
Syncytial, Fibroblastic, Transitional (classical), Psammomatous, Secretory</td></tr>
<tr><td>II</td><td>More mitosis</td></tr>
<tr><td>III</td><td>Malignant</td></tr>
<tr><td>Medulloblastoma</td><td>Cerebellum (midline), lateral tumors occur more often in adults.</td><td>children</td><td>IV</td><td>Extremely cellular, with sheets of anaplastic ("small blue") cells.
Small, with little cytoplasm and hyperchromatic nuclei; mitoses are abundant.</td><td>• Neuronal and glial markers may be expressed, but the tumor is often largely undifferentiated.
• Highly malignant.
• Prognosis for untreated patients is dismal; however, it is exquisitely radiosensitive.</td></tr>
<tr><td>Schwannoma</td><td>within the cranial vault in the cerebellopontine angle, 8th</td><td>Schwann cells</td><td>Benign</td><td>• Cellular Antoni A pattern and less cellular Antoni B.
• Axons are largely excluded from the tumor. Thick-walled hyalinized vessels often are present.
• Verocay bodies</td><td>• Type I: Sporadic schwannomas are associated with mutations in the NF2 gene.
• Type II: Bilateral acoustic schwannoma is associated with NF2.</td></tr>
<tr><td>Neurofibroma</td><td colspan="2">Different kinds of cells are involved</td><td>Benign</td><td><table><tr><th>Subtypes</th><th>Characteristic</th></tr><tr><td>Localized cutaneous</td><td>Either as solitary sporadic lesions or as often multiple lesions in the context of (NF1).</td></tr><tr><td>Plexiform</td><td>These tumors are associated with a small but real risk of malignant transformation.</td></tr><tr><td>Diffuse</td><td>Can take the form of large, disfiguring subcutaneous masses.</td></tr></table></td><td>• More haphazard cell growth than schwannoma.
• Cannot be separated from nerve trunk
• These arise sporadically or in association with type 1 neurofibromatosis, rarely malignant.</td></tr>
</table>

Metastatic Tumors

They are tumors from sources outside the CNS. Carcinomas are the most common.

- About half to three-quarters of brain tumors are primary tumors, and the rest are metastatic
- Lung, breast, skin (melanoma), kidney, and gastrointestinal tract are the commonest
- Form sharply demarcated masses with edema.

Demyelinating diseases	*Dysmyelinating diseases*
• Acquired conditions characterized by preferential damage to previously normal myelin • Commonly result from immune-mediated injury • Also viral infection of oligodendrocytes as in progressive multifocal leukoencephalopathy. • Drugs and other toxic agents.	• Myelin is not formed properly or has abnormal turnover kinetics • Associated with mutations affecting the proteins required for formation of normal myelin or in mutations that affect the synthesis or degradation of myelin lipids. • The other general term for these diseases is *leukodystrophy.*

CNS	PNS
Myelinated by oligodendrocytes	**Myelinated by Schwann cells**
Each cell myelinates many axons and forms many internodes	**Each cell myelinates only one axon and forms only one internode**
Do not form neurilemma	**Forms neurilemma**

Active plaques (During the episode)	Inactive plaques
• There is evidence of ongoing myelin breakdown with abundant macrophages containing myelin debris • Lymphocytes and monocytes are present, mostly as perivascular cuffs. تجمع الخلايا حول الأوعية الدموية • Axons are relatively preserved, although they may be reduced in number.	• When plaques become quiescent[1], the inflammation mostly disappears, leaving behind a little to no myelin. • Instead, astrocytic proliferation and gliosis are prominent

Multiple Sclerosis

Definition	An autoimmune demyelinating disorder characterized by *distinct episodes of neurologic deficits, separated in time.*
Epidemiology	• Most common. • The disease becomes clinically apparent at any age. • Women are affected twice as often as men
Risk Factors	• The risk of developing MS is 15-fold higher when the disease is present in a first-degree relative • The concordance rate for monozygotic twins is approximately 25%, with a much lower rate for dizygotic twins • HLA-DR variants, the DR2 allele being the one that most significantly increases the risk for developing MS
Pathogenesis	MS is believed to be caused by a combination of environmental and genetic factors that result in a **loss of tolerance to self-proteins** → **Antigen presenting cell** comes and activates T-helper (CD4) → T cell cross BBB → Type IV hypersensitivity → **infiltrate** of lymphocytes, macrophages, B Cells and plasma cells produce antibody → **demyelination, axonal loss** and sometimes even leading to **neuronal death.**
Morphology	• MS is a white matter disease. **Luxol Fast Blue** Stain to detect MS • Affected areas show multiple, well circumscribed, slightly depressed, glassy, gray-tan, irregularly shaped lesions, termed plaques. • They occur beside ventricles and they are frequent in the optic nerves and chiasm, brain stem, ascending and descending fiber tracts, cerebellum and spinal cord.
Clinical features	Commonly there are multiple episodes of new symptoms **(relapses)** followed by episodes of recovery **(remissions)**; typically, the recovery is not complete. Charcot classic triad of MS is a SIN: Scanning speech, Intention tremor, Nystagmus **Certain patterns of neurologic symptoms and signs are commonly observed:** • Unilateral visual impairment occurring over the course of a few days is a frequent initial manifestation of MS (due to involvement of the optic nerve "*optic neuritis*") • Involvement of the brain stem produces cranial nerve signs and ataxia, and can disrupt conjugate eye movements • Spinal cord lesions give rise to motor and sensory impairment of trunk and limbs, spasticity, and difficulties with the voluntary control of bladder function.
CSF findings	• It shows mildly elevated protein level with an increased proportion of γ-globulin • In one-third of cases there is moderate pleocytosis. (Increased WBC count in CSF, in the blood it's called Leukocytosis) • When the immunoglobulin is examined further, most MS patients show *oligoclonal bands*, representing antibodies directed against a variety of antigenic targets. • These antibodies constitute a marker for disease activity

Cerebrovascular Accidents

Functional hypoxia, in:	**Ischemia, (*transient* or *permanent*), *in:***
A low partial pressure of oxygen (e.g., high altitude)	A reduction in perfusion pressure, as in hypotension.
Impaired oxygen-carrying capacity (e.g., severe anemia, carbon monoxide poisoning)	Vascular obstruction.
Inhibition of oxygen use by tissue (e.g., cyanide poisoning)	Both

Embolic Stroke	**Sources of emboli include:** ○ Cardiac mural thrombi (frequent). ○ Arteries: often atheromatous plaques within the carotid arteries. ○ Paradoxical emboli, particularly in children with cardiac anomalies. Emboli associated with cardiac surgery or other material (tumor, fat, or air). **The territory of distribution of the middle cerebral arteries is most frequently affected by embolic infarction.** ***Why?*** Because it's an extension of the internal carotid artery and emboli tend to lodge where vessels branch or in areas of stenosis (usually caused by atherosclerosis).
Thrombotic Stroke	○ The **most common** sites of primary thrombosis: ▪ The carotid bifurcation ▪ The origin of the middle cerebral artery ▪ At either end of the basilar artery ○ The majority of thrombotic occlusions causing cerebral infarctions are due to **atherosclerosis** ○ Atherosclerotic stenosis: can develop on top a superimposed thrombosis, accompanied by anterograde extension, fragmentation, and distal embolization. Thrombotic infarction is characteristically an anemic (white) infarct.

	Info	Clinical Outcome	Pathology	
Global Cerebral Ischemia	Widespread ischemic/hypoxic injury, common causes: ▪ Cardiac arrest ▪ Severe hypotension or shock	▪ If mild → eventual complete recovery ▪ In severe → widespread neuronal death. ▪ **Persistent vegetative state.** ▪ **"Respirator brain".**	**Gross**	▪ The brain is swollen, with wide gyri and narrowed sulci. ▪ The cut surface shows poor demarcation between gray and white matter.
			Microscopic – Early changes	○ 12 to 24 hours after the insult. ○ Karyorrhexis ○ Red neurons
			Microscopic – Subacute changes	○ 24 hours to 2 weeks. ○ The reaction to tissue damage begins with infiltration by neutrophils. ○ Necrosis of tissue, influx of macrophages, vascular proliferation and reactive gliosis.
			Repair	After 2 weeks. Removal of all necrotic tissue, loss of organized CNS structure and gliosis.
Focal Cerebral Ischemia	Cerebral arterial occlusion	The size, location, and shape of the infarct and the extent of tissue damage that results are determined by modifying variables	**Gross**	▪ First 6 hrs. → Nothing ▪ 48 hrs. → Soft, pale & swollen tissue. ▪ 2-10 days → Gelatinous brain ▪ 10 days-3 weeks → tissue liquefies
			Microscopic	○ First 12 hrs. → Red neurons, both cytotoxic and vasogenic edema, endothelial and glial cells ○ 48 hrs. → Neutrophilic emigration & mononuclear phagocytic cells ○ Phagocytosis and liquefaction proceeds → Astrocytes at the edges of the lesion develop a prominent network of protoplasmic extensions ○ After several months → Astrocytic nuclear and cytoplasmic enlargement recedes
			Appearance	• Parallel ischemic infarction. • Blood extravasation and resorption. • If the person is receiving anticoagulant treatment, may be associated with extensive intracerebral hematomas.

	Info	Clinical Outcome	Pathology
Border zone infarcts	Border zone infarcts are usually seen after hypotensive episodes	A band of necrosis over the cerebral convexity a few centimeters lateral to the interhemispheric fissure	• Wedge-shaped areas of infarction that occur in those regions of the brain and spinal cord that **lie at the most distal fields of arterial perfusion** • In the cerebral hemispheres, the **border zone between the anterior and the middle cerebral artery** distributions is at greatest risk
Intracerebral hemorrhage	Causes severe headache, frequent nausea/vomiting, steady progression of symptoms over 15–20 minutes, and coma.		Hemorrhages within the brain (intracerebral) can occur secondary to: ○ Hypertension (most frequently) ○ Other forms of vascular wall injury (e.g. vasculitis) ○ Arteriovenous malformation ○ An intraparenchymal tumor ○ Hemorrhages associated with the dura (in either subdural or epidural spaces) make up a pattern associated with trauma
Subarachnoid Hemorrhage	• **About 90%** of saccular aneurysms occur in the anterior circulation near major arterial branch points. • Multiple aneurysms exist in 20% to 30% of cases. • The probability of aneurysm rupture increases with the size of the lesion	• Some individuals die with the first rupture. • Recurring bleeding is common in survivors. • The prognosis worsens with each episode of bleeding. • In the early period after a subarachnoid hemorrhage, there is a risk of additional ischemic injury from vasospasm involving other vessels.	• **Rupture** can occur at any time • Blood under arterial pressure is forced into the **subarachnoid space,** and individuals are stricken with sudden, excruciating headache (classically described as "the worst headache I've ever had") and rapidly lose consciousness. ○ **Healing phase of subarachnoid hemorrhage:** • Meningeal fibrosis. • Scarring occurs. They lead to obstruction of CSF flow as well as interruption of the normal pathways of CSF resorption

Hypertensive Cerebrovascular Disease

Lacunar infarcts	• Small cavitary infarcts • Most commonly in deep gray matter (basal ganglia and thalamus), internal capsule, deep white matter, and pons • Consist of cavities of tissue loss with scattered lipid-laden macrophages and surrounding gliosis • Depending on their location in the CNS, lacunes can either be clinically silent or cause significant neurologic impairment
Slit hemorrhage	• Rupture of the small-caliber penetrating vessels and the development of small hemorrhages • In time, these hemorrhages resorb, leaving behind a slitlike cavity surrounded by brownish discoloration
Acute hypertensive encephalopathy	A clinicopathologic syndrome: • Diffuse cerebral dysfunction, including headaches, confusion, vomiting, and convulsions, sometimes leading to coma • Does not usually remit spontaneously • May be associated with an edematous brain, with or without transtentorial or tonsillar herniation • Petechiae and fibrinoid necrosis of arterioles in the gray and white matter may be seen microscopically

Vasculitis

- Infectious arteritis of small and large vessels:
  - Previously in association with syphilis and tuberculosis
  - Now more commonly occurs in the setting of immunosuppression and opportunistic infection (such as toxoplasmosis, aspergillosis, and CMV encephalitis)
- **Primary angiitis of the CNS:**
  - An inflammatory disorder that involves multiple small to medium-sized parenchymal and subarachnoid vessels
  - Affected individuals manifest a diffuse encephalopathic clinical picture, often with cognitive dysfunction
  - Improvement occurs with steroid and immunosuppressive treatment

Dementia						
Definition	**Characterized by**	**Causes**				
It is the development of memory impairment and other cognitive deficits with preservation of a normal level of consciousness	○ Memory loss ○ Apraxia ○ Aphasia ○ Agnosia ○ Impaired judgment ○ Delirium	**Primary Neurodegenerative Disease**	**Infections**	**Vascular and traumatic diseases**	**Nutritional diseases**	**Miscellaneous**
		Alzheimer disease	Prion-associated disorders	Multi-infarct dementia	Thiamine deficiency	Brain tumors
		Lewy Body dementia	HIV Encephalopathy	Global hypoxic-ischemic brain injury		Neuronal storage disease
		Huntington disease	Progressive multifocal leukoencephalopathy	Chronic subdural hematoma		Toxic injury

Neuritic plaques	- Focal, spherical collections of dilated, tortuous, silver-staining neuritic processes (dystrophic neurites), often around a central amyloid core. - Plaques can be found in the hippocampus and amygdala as well as in the neocortex. - The amyloid core contains Aβ. - Aβ deposits can also be found that lack any surrounding neuritic reaction, termed diffuse plaques.
Neurofibrillary tangles	Bundles of paired helical filaments visible as basophilic fibrillary structures in the cytoplasm of the neurons that displace or encircle the nucleus, mainly composed of abnormally hyperphosphorylated tau forming paired helical filaments • The presence of Aβ also leads neurons to hyperphosphorylate the microtubule binding protein "tau". • This process also results in neuronal dysfunction and cell death. • Tangles can remain after neurons die. • Commonly found in cortical neurons (pyramidal cells of the hippocampus, amygdala and the basal forebrain) • Tangles are not specific to Alzheimer disease, being found in other degenerative diseases as well.

Alzheimer

Definition

It is the most common cause of dementia in people over the age of 65 (elderly)

Epidemiology

Most cases are sporadic, but At least 5% to 10% are familial

Clinical Features

- Insidious onset, 7-8 decades, Alterations in mood and behavior, Progressive memory impairment
- Later: Severe cortical dysfunction & progressive disorientation, aphasia and apraxia & in 5-10 yrs. they become muted and bedridden.
- Genes associated: ApoE4 & SORL1

Pathology

Accumulation of a peptide **(β amyloid, or Aβ)** result in morphologic changes.

- **Aβ peptide** is derived from a larger membrane protein known as amyloid precursor protein (APP), which is processed in either of two ways:
  1- It can be cleaved by two enzymes, α-secretase and γ-secretase, in a process that prevents formation of Aβ (Normal)
  2- It can be cut by β-site APP-cleaving enzyme and γ-secretase to generate Aβ (Abnormal)
- Generation and accumulation of Aβ occurs slowly with advancing age.
- The presence of Aβ also leads neurons to hyperphosphorylate the microtubule binding protein "tau".
- With this increased level of phosphorylation, **tau redistributes** within the neuron from the axon into dendrites and cell body and aggregates into "tangles".
- This process results in **neuronal dysfunction and cell death.**
- Mutations in APP or in components of γ-secretase [presenilin-1 (PSEN1)] or [presenilin-2 (PSEN2)] lead to early onset familial Alzheimer disease by increasing the rate at which Aβ accumulates.

Morphology

Gross	Microscopic
- Atrophy of affected regions. Thin gyri and wider sulci. - Hippocampus and temporal lobes are atrophic. - Compensatory ventricular enlargement	- Plaques (extracellular lesion) - Neurofibrillary tangles (intracellular lesion)

Parkinson

Definition	Motor disturbances that are seen in a number of conditions that share damage to dopaminergic neurons of the substantia nigra or their projection to the striatum
Epidemiology	6-8 decades. Men more than women.
Characterized by	- Diminished facial expression (masked faces). - Stooped posture. - Slowness of voluntary movement. - Rigidity. - "Pill-rolling" tremor. - Festinating gait (progressively shortened, accelerated steps).
Clinical Features	○ Insidious onset, 7-8 decades, Alterations in mood and behavior, Progressive memory impairment ○ Later: Severe cortical dysfunction & progressive disorientation, aphasia and apraxia & in 5-10 yrs. they become muted and bedridden. ○ Genes associated: ApoE4 & SORL1
Pathology	• Mostly sporadic. • α-synuclein mutation causes autosomal dominant Parkinson disease as can gene duplications and triplications. • The diagnostic feature of the disease - the Lewy body - is an inclusion containing α-synuclein. • α-synuclein in the Lewy bodies • Two genetic loci for Parkinson disease: 1- Which involve genes encoding parkin (an E3 ubiquitin ligase) 2- UCHL-1 (an enzyme involved in recovery of ubiquitin from proteins targeted to the proteasome)

Morphology	**Gross**	**Microscopic**
	Pallor of the substantia nigra and locus ceruleus	Loss of the pigmented neurons in these regions. Associated with gliosis. Lewy bodies may be found in some of the remaining neurons

Congenital Malformations & Hydrocephalus

Congenital

Malformations of the brain are more common in the setting of **multiple** birth defects
The timing of an injury will be reflected in the pattern of malformation.

Prenatal or perinatal insults may either cause: Failure of normal CNS development & Tissue destruction

CNS malformation can be caused by Mutations affecting molecules in pathways of neuronal and glial: **Development, migration & connection**

Forebrain

The volume of brain: Abnormally large (***megalencephaly***) Small (***microencephaly***, *more common*)

They can occur in a wide range of clinical settings, including: Chromosome abnormalities ,Fetal alcohol syndrome & (HIV-1) infection acquired in utero

All causes are associated with: ↓ neurons of cerebral cortex & Disruption of neuronal migration and differentiation during development

***Lissencephaly* (*agyria*):** Characterized by an absence of normal gyration and a smooth-surfaced brain

- The cortex is abnormally thickened, single-gene defects, Cortical sulci are absent except, usually, for the Sylvian fissure
- There is a small amount of myelinated white matter between the abnormal cortex and the ventricles.

Neural tube defect

All are characterized by abnormalities involving some combination of neural tissue, meninges, and overlying bone or soft tissues. Collectively, neural tube defects are the most frequent CNS malformations.

Folate deficiency during the initial weeks of gestation is a risk factor. *Diseases associated with Neural Tube defects:*

Myelomeningocele: is an extension of CNS tissue through a defect in the vertebral column. Lumbosacral region, deficits in the lower extremities and problems with bowel and bladder control

Anencephaly: is a malformation of the anterior end of the neural tube, with absence of the brain and top of skull

Encephalocele: is a diverticulum of malformed CNS tissue extending through a defect in the cranium.

Posterior Fossa

The most common malformations in this region of the brain result in either misplaced or absent cerebellum. Associated with hydrocephalus.

Arnold-Chiari malformation (Chiari type II malformation):

A small posterior fossa, A misshapen midline cerebellum, Downward extension of vermis through the foramen magnum, Hydrocephalus & A lumbar myelomeningocele

Hydrocephalus

An abnormal accumulation of C S F in the ventricles, which in turn may lead to an increased intracranial pressure (ICP).

- When hydrocephalus develops in infancy before closure of the cranial sutures → enlargement of the head
- When Hydrocephalus develops after fusion of the sutures → expansion of the ventricles and increased intracranial pressure, without a change in head circumference.

Types of hydrocephalus:

- **Noncommunicating hydrocephalus:** An obstacle to the flow of CSF leads to enlargement of a portion of the ventricles
- **Communicating hydrocephalus:** All of the ventricular system is enlarged; here the cause is most often reduced resorption of CSF.

What can causes hydrocephalus? 1- **Hypersecretion of CSF**. 2- **Obstructive hydrocephalus** 3- **Defective filtration of CSF**

Meningitis

Epidural and subdural infections	Epidural abscess, commonly associated with osteomyelitis, arises from an adjacent focus of infection, such as sinusitis or a surgical procedure. Infections of the skull or air sinuses may also spread to the subdural space, producing subdural empyema.

Acute pyogenic meningitis

CSF Findings	○ Cloudy or frankly purulent CSF. ○ ↑ Protein level & ↓ glucose content. ○ Bacteria may be seen on a Gram stained smear.
Clinical Features	○ Meningeal irritation signs and neurologic impairment: Headache, photophobia, irritability, clouding of consciousness and neck stiffness. ○ Can be fatal. ○ Antimicrobial agents markedly reduce its mortality
Complications	○ Phlebitis → venous occlusion → hemorrhagic infarction of the underlying brain. ○ Leptomeningeal fibrosis→ hydrocephalus. ○ Septicemia → hemorrhagic infarction of the adrenal glands and cutaneous petechiae ○ Focal cerebritis & seizures. ○ Cerebral abscess. ○ Cognitive deficit. ○ Deafness.

Aseptic Meningitis

CSF Findings	○ ↑ Lymphocytes ○ Protein elevation is only moderate ○ Glucose content is normal
Clinical Features	○ The clinical course is usually self-limiting, and most often is treated symptomatically. ○ Viral meningitis carries a better prognosis than bacterial meningitis. ○ Mortality is low. ○ Symptoms resolve after 1 month with supportive care.
Morphology	○ Most commonly the pathogen is **an enterovirus.** ○ Macroscopic characteristic is brain swelling (seen sometimes) ○ On microscopic examination, there is either no recognizable abnormality or a mild to moderate infiltration of **the leptomeninges** with **lymphocytes.**

Tuberculous Meningitis (Chronic)

CSF Findings	○ Moderate increase in cellularity of the CSF (pleocytosis) made up of mononuclear cells, or a mixture of polymorphonuclear and mononuclear cells. ○ ↑ Protein level ○ The glucose content typically is moderately reduced or normal.
Clinical Features	Generalized signs and symptoms of headache, malaise, mental confusion, and vomiting.
Morphology	○ Mycobacterium tuberculosis also may result in **Tuberculoma** which is a well-circumscribed intraparenchymal mass. ○ Rupture of tuberculoma into subarachnoid space results in **tuberculous meningitis.** ○ Always occurs after hematogenous dissemination of organism from **primary pulmonary infection.** ○ On microscopic examination, there is usually a **central core of caseous necrosis** surrounded by a typical tuberculous **granulomatous** reaction.

Brain Abscess

CSF Findings	○ Contains only scanty cells. ○ ↑ protein. ○ Normal level of glucose.
Clinical Features	○ Most common on cerebral hemispheres ○ Present clinically with progressive focal neurologic deficits in addition to the general signs of raised intracranial pressure
Complications	○ Herniation (Diffuse cerebral edema carries a risk of fatal herniations). ○ Rupture of abscess into subarachnoid space or ventricle.
Morphology	○ **Streptococci and staphylococci** are the most common organisms identified in non-immunosuppressed populations. ○ Liquefactive necrosis. ○ The surrounding brain is **edematous**, congested & contains reactive astrocytes & perivascular inflammatory cells.