## ****Cellular Pathology of the CNS — Quick Notes****

### ****Principal Cells****

**Neurons**: Functional unit, post-mitotic, irreplaceable after death.

**Glia**: Support cells from neuroectoderm/bone marrow.  
→ Astrocytes, Oligodendrocytes, Microglia, Ependymal cells

**Meningeal & Vascular Cells**

### ****Neuronal Reactions to Injury****

**Acute Injury (Red Neurons)**:  
12–24 hrs after irreversible hypoxia/ischemia.  
📌 Shrinkage, nuclear pyknosis, loss of Nissl substance, eosinophilic cytoplasm.

**Subacute/Chronic Injury (Degeneration)**:  
In progressive diseases (ALS, AD).  
📌 Neuronal loss, reactive gliosis.

**Axonal Reaction (Central Chromatolysis)**:  
📌 Swollen cell body, peripheral nucleus, enlarged nucleolus, Nissl dispersion.

**Neuronal Inclusions**:  
Seen in aging, viral infections, neurodegeneration.

### ****Astrocyte Reaction****

**Gliosis**: Hyperplasia & hypertrophy — key marker of CNS injury.

**Swelling**: In acute insults.

**Rosenthal Fibers**: Eosinophilic inclusions in chronic gliosis.

### ****Microglial Reaction****

**Proliferation**

**Rod Cells**: Neurosyphilis.

**Microglial Nodules**: Around necrosis.

**Neuronophagia**: Around dying neurons.

## 📌 ****Cerebral Edema****

**Vasogenic**: BBB disruption → extracellular fluid.

**Cytotoxic**: Cellular injury → intracellular swelling.

**Morphology**:  
Enlarged brain, flattened gyri, narrowed sulci, compressed ventricles.

## 📌 ****Hydrocephalus****

**Definition**: Excessive CSF in ventricles → ↑ ICP.

**Types**:

**Communicating**: Entire system enlarged.

**Non-communicating**: Blocked ventricular segment.

**Hydrocephalus ex vacuo**: Ventricular expansion due to brain atrophy.

**Before suture closure**: Head enlargement  
**After suture closure**: Ventricular dilation, ↑ICP (no head size change)

## 📌 ****Raised ICP & Brain Herniation****

**Causes**:

Generalized edema

↑ CSF (hydrocephalus)

Mass lesions (tumor, abscess)

**Clinical Signs**:

Papilledema

Nausea & vomiting

Headache

↓ Consciousness

**Types of Herniation**:

**Subfalcine (Cingulate)**: Under falx cerebri → compresses anterior cerebral artery.

**Transtentorial (Uncal)**: Temporal lobe → 3rd nerve palsy (pupil dilation, ocular deficits)

**Tonsillar**: Cerebellar tonsils through foramen magnum → life-threatening (brainstem compression)

✅ **Tip**: Remember **"SVT"** for herniations

**S**ubfalcine

**V** (for vertical → transtentorial)

**T**onsillar

## 📌 ****Bonus Mnemonics****

**Edema Types**: "VC" → Vasogenic, Cytotoxic

**Herniation Danger**:

**Uncal**: 3rd nerve signs

**Tonsillar**: Respiratory/Cardiac arrest

## CNS Malformations, Perinatal Brain Injury & Trauma — Study Notes

### 🧠 Malformations & Developmental Disorders

**Causes:**

Genetic factors

Environmental influences (toxins, infections)

#### 1️⃣ Neural Tube Defects (NTDs)

Failure of neural tube closure or reopening after closure.

Most common CNS malformations, often affecting spinal cord.

**Recurrence risk:** 4–5% in future pregnancies.

**Risk factor:** Folate deficiency in early pregnancy.

**Types:**

**Spina bifida (Spinal dysraphism):**

Occulta: Asymptomatic bony defect

Spina bifida: Severe with meningeal outpouching

**Myelomeningocele:**

CNS tissue extends through vertebral defect (usually lumbosacral)

Motor/sensory deficits, bladder/bowel issues, risk of infection

**Encephalocele:**

Brain tissue herniates through skull defect (often posterior fossa)

**Anencephaly:**

Absence of forebrain and calvarium

Occurs by day 28 of gestation

#### 2️⃣ Forebrain Anomalies

Due to abnormal neuron generation/migration

**Megalencephaly:** Abnormally large brain

**Microencephaly:** Small brain — linked with chromosomal anomalies, fetal alcohol syndrome, congenital HIV

#### 3️⃣ Posterior Fossa Anomalies

Affect brainstem/cerebellum

Arnold-Chiari malformation

Chiari type I malformation

Dandy-Walker malformation

Joubert syndrome

#### 4️⃣ Syringomyelia & Hydromyelia

**Hydromyelia:** Central canal dilation

**Syringomyelia:** Fluid-filled cavity in cord

Loss of pain & temperature in upper limbs

### 👶 Perinatal Brain Injury

**Important cause of childhood-onset neurologic disability**

**Cerebral palsy:** Non-progressive motor disorder from prenatal/perinatal insult

**Causes:**

Prematurity

Intraparenchymal hemorrhage

Periventricular leukomalacia

Ischemic lesions (ulegyria, thalamus/basal ganglia injury)

### ⚠️ CNS Trauma

Limited brain repair ability + location of lesion = critical factors

Types:

**Open injury:** Penetrating

**Closed injury:** Blunt trauma

#### 💀 Skull Fractures

**Displaced fracture:** Bone into cranial cavity > thickness of bone

**Basal skull fracture:** Occiput/side impact — CN deficits, orbital/mastoid hematoma, CSF leakage, meningitis risk

#### 🧠 Parenchymal Injuries

**Concussion:**

Temporary LOC, respiratory arrest, reflex loss

Amnesia for event, possible post-concussive symptoms

**Contusion:** Bruising of brain

**Laceration:** Tissue tearing

**Coup:** At impact site  
**Contrecoup:** Opposite to impact

**Diffuse axonal injury:**

Nerve fibers torn by shear forces

Common in coma without contusions

#### 🩸 Traumatic Vascular Injury

**Epidural hematoma:**

Temporal bone fracture tears middle meningeal artery

Lucid interval then rapid deterioration — surgical emergency

**Subdural hematoma:**

Tearing of bridging veins

Symptoms within 48 hrs: headache, confusion, progressive neurological deficits

**Morphology:**

Fresh clot → lysis (~1 week)

Fibroblast ingrowth (~2 weeks)

Hyalinized tissue (1–3 months)

#### 🔄 Sequelae of Brain Trauma

Post-traumatic hydrocephalus

Chronic Traumatic Encephalopathy (CTE)

Post-traumatic epilepsy

Infections

Psychiatric disorders

### 🦴 Spinal Cord Trauma

Often with vertebral displacement

Neurological deficits depend on injury level:

**Thoracic/lower:** Paraplegia

**Cervical:** Quadriplegia

**Above C4:** Respiratory failure

Histology: Similar to brain trauma

## ****Cerebrovascular Disease & CNS Infections — Exam Notes****

## 🧠 ****Cerebrovascular Disease****

### 🔹 Hypoxia, Ischemia & Infarction

**Tissue survival depends on**:

Collateral circulation

Duration of ischemia

Magnitude & rapidity of blood flow reduction

### 🌍 ****Global Cerebral Ischemia****

**Cause:** Generalized ↓ cerebral perfusion (e.g. cardiac arrest, shock, severe hypotension)

**Most vulnerable regions:** Certain neurons & brain areas more prone to hypoxic-ischemic injury

#### Clinical Features:

Influenced by age, ischemia duration, temperature

Deficits range: transient disturbance → brain death

#### Morphology:

**Gross:** Edema, swollen brain, wide gyri, narrow sulci, poor gray-white distinction

**Microscopy:**

Early (12–24 hrs): Red neurons, neutrophil infiltration

Subacute (24 hrs–2 wks): Necrosis, macrophages, vascular proliferation, reactive gliosis

Repair (>2 wks): Gliosis, tissue removal, loss of CNS structure

### 📍 ****Focal Cerebral Ischemia****

**Cause:** Localized ↓/cessation of blood flow (arterial occlusion or hypoperfusion)

**Factors:** Duration, collateral adequacy

#### Causes:

Embolism (cardiac mural thrombi, atheromatous carotids)

In situ thrombosis

Vasculitis

#### Types of Infarcts:

**Hemorrhagic (Red):** Embolic; petechial hemorrhages

**Non-hemorrhagic (Pale):** Thrombotic

#### Clinical:

Deficits reflect anatomic distribution

Rapid onset (minutes → hours)

Gradual improvement over months possible

**Intracranial Hemorrhage**

### 🔸 Intraparenchymal Hemorrhage

**Cause:** Rupture of small vessels

**Types:**

Ganglionic hemorrhages: Basal ganglia & thalamus (mainly hypertensive)

Lobar hemorrhages: Cerebral hemispheres (mainly amyloid angiopathy)

#### Morphology:

Acute: Blood extravasation compresses brain

Chronic: Cavitary destruction with brownish rim

#### Clinical:

Large bleeds: Devastating

Small: May be silent

Gradual hematoma resolution

### 🔸 Subarachnoid Hemorrhage

**Most common cause:** Rupture of berry (saccular) aneurysm

**Sites:** 90% in anterior Circle of Willis

#### Risk Factors:

Genetic (ADPKD, Marfan)

Smoking, hypertension

#### Morphology:

Thin-walled outpouching at arterial branch points

No smooth muscle or intimal elastic lamina in sac

#### Clinical:

Peak incidence: 5th decade, F > M

Classic presentation: Sudden worst headache ever, rapid loss of consciousness

25–50% die on first rupture

Complications: Vasospasm → ischemia, meningeal fibrosis, CSF obstruction

🦠 **Infections of the Nervous System**

### Principal Routes:

Hematogenous (most common)

Direct implantation (trauma, congenital)

Local extension (sinus, tooth, vertebra)

Peripheral nerves (e.g. rabies, herpes zoster)

## 📌 ****Meningitis****

### 🔹 Acute Pyogenic (Bacterial) Meningitis

**Neonates:** E. coli, Group B Strep

**Elderly:** S. pneumoniae, Listeria

**Adolescents/Young adults:** N. meningitidis, S. pneumoniae, H. influenzae

#### Clinical:

Fever, headache, photophobia, neck stiffness, altered consciousness

#### CSF:

Cloudy/purulent

↑ neutrophils (~90,000/mm³)

↑ protein, ↓ glucose

Organisms seen on smear/culture

#### Morphology:

**Gross:** Leptomeningeal exudate

**Microscopy:** Neutrophils in leptomeninges; may extend to brain

#### Complications:

Fatal if untreated

Seizures, cranial nerve palsies (e.g. deafness)

Chronic adhesive arachnoiditis → ↓ CSF absorption

### 🔹 Acute Aseptic (Viral) Meningitis

**Cause:** Mostly viruses (Enteroviruses ~80%)

**CSF:**

Lymphocytic pleocytosis

Mild ↑ protein

Normal glucose

#### Morphology:

Clear leptomeninges

Parenchymal edema possible

Lymphocytic infiltrates

### 🔹 Chronic Bacterial Meningoencephalitis

**Causes:** TB, Syphilis (T. pallidum), Lyme (Borrelia)

#### Tuberculous Meningitis:

**Clinical:** Headache, malaise, confusion, vomiting

**CSF:** Mononuclear pleocytosis or mixed, ↑ protein, ↓/normal glucose

**Morphology:**

Diffuse meningoencephalitis

Thick basilar exudate encasing cranial nerves

Obliterative endarteritis

Adhesive arachnoiditis

## 🧠 ****Cerebrovascular Disease****

### ****Hypoxia, Ischemia & Infarction****

**Tissue survival depends on:**

Collateral circulation

Duration of ischemia

Magnitude & rapidity of flow reduction

### ****Global Cerebral Ischemia****

**Cause:** ↓ Cerebral perfusion (cardiac arrest, shock)

**Most vulnerable:** Certain neurons & brain areas

**Morphology:**

**Gross:** Edema, wide gyri, narrow sulci

**Microscopy:**

**Early (12–24 hrs):** Red neurons, neutrophils

**Subacute (24 hrs–2 wks):** Necrosis, macrophages, gliosis

**Repair (>2 wks):** Gliosis, tissue loss

### ****Focal Cerebral Ischemia****

**Cause:** Arterial occlusion/hypoperfusion

**Types:**

**Hemorrhagic (Red):** Embolic

**Non-Hemorrhagic (Pale):** Thrombotic

**Clinical:** Rapid onset; gradual improvement possible

### ****Intracranial Hemorrhage****

**Intraparenchymal:**

**Cause:** Small vessel rupture

**Types:**

**Ganglionic:** HTN (basal ganglia, thalamus)

**Lobar:** Amyloid angiopathy

**Clinical:** Large → severe; small → silent

**Subarachnoid:**

**Cause:** Ruptured berry aneurysm (90% at Circle of Willis)

**Risk:** ADPKD, Marfan, HTN, smoking

**Clinical:** Sudden severe headache; 25–50% die on first rupture

**Complications:** Vasospasm, fibrosis, CSF block

## 🦠 ****CNS Infections****

### ****Routes:**** Hematogenous (commonest), direct, local, peripheral nerves

### ****Meningitis****

**Acute Pyogenic (Bacterial):**

**Neonates:** E. coli, GBS

**Elderly:** S. pneumoniae, Listeria

**Young:** N. meningitidis

**CSF:** ↑ neutrophils, ↑ protein, ↓ glucose

**Acute Aseptic (Viral):**

**Cause:** Enteroviruses (80%)

**CSF:** Lymphocytes, mild ↑ protein, normal glucose

**Chronic Bacterial:**

**Cause:** TB, Syphilis, Lyme

**TB Meningitis CSF:** Mononuclear cells, ↑ protein, ↓/normal glucose

## ⚡ ****Demyelinating Diseases****

**Feature:** Loss of myelin, axons preserved

### ****Multiple Sclerosis (MS)****

**Autoimmune**; relapsing-remitting

**Age:** 20–40 yrs, F>M

**First Signs:** Optic neuritis, limb weakness, bladder dysfunction

**Pathogenesis:** TH1, TH17 cells → macrophages, leukocytes

**Morphology:**

**Gross:** Sclerosis plaques

**Micro:** Active → foamy macrophages, inactive → gliosis

**Course:** Less relapses over time, steady deterioration

### ****Central Pontine Myelinolysis****

**Cause:** Rapid correction of hyponatremia

**Morphology:** Symmetric pontine myelin loss, axons/neurons intact

**Clinical:** Rapid quadriplegia, possible "locked-in" syndrome

## 🧬 ****Neurodegenerative Diseases****

**Common Feature:** Progressive neuron loss, protein aggregates

### ****Alzheimer Disease (AD)****

**Most common dementia** in elderly

**Proteins:** Aβ, tau

**Morphology:**

**Gross:** Cortical atrophy, hydrocephalus ex vacuo

**Micro:** Neuritic plaques, Neurofibrillary tangles, CAA

**Clinical:** Slow decline; final stage: mute, immobile; pneumonia terminal event

### ****Parkinson Disease (PD)****

**Cause:** Dopaminergic neuron loss in substantia nigra

**Morphology:**

**Gross:** Pallor of substantia nigra

**Micro:** Loss of melanin neurons, Lewy bodies

**Clinical:** Hypokinetic movement, tremor, rigidity, festinating gait

### ****Amyotrophic Lateral Sclerosis (ALS)****

**Loss of UMN & LMN** → muscle atrophy

**Morphology:**

**Spinal Cord:** Thin anterior roots, gliosis, Bunina bodies

**Muscle:** Neurogenic atrophy

**CST:** Degeneration, fiber loss

## ****Clinical:**** Asymmetric hand weakness, fasciculations, respiratory failure CNS Tumors — Study Notes

### 📌 General Overview:

**CNS tumors**:

**50–75% are primary**, remainder are metastatic.

**20% of all childhood cancers**.

**70% of childhood CNS tumors** → posterior fossa.

**70% of adult CNS tumors** → cerebral hemispheres above tentorium.

### 📌 Distinct Features:

**Distinction between benign & malignant** less clear than other organs.

**Complete surgical resection** difficult without compromising neurological function.

**Anatomic site can be lethal** regardless of histology.

**Rare metastasis outside CNS**, but spreads via **subarachnoid space**.

## 📌 Major Classes of Primary Brain Tumors:

**Gliomas**

**Neuronal tumors (e.g., ganglion cell tumors)**

**Poorly differentiated tumors (e.g., medulloblastoma)**

**Meningiomas**

## 📌 Gliomas:

Most common primary brain tumors — include:

**Astrocytomas**

**Oligodendrogliomas**

**Ependymomas**

➡️ Arise from progenitor cells differentiating down specific cell lineages.

### 📍 Astrocytomas:

#### Types:

**Diffusely infiltrating astrocytomas**

**Pilocytic astrocytomas**

#### Grades:

WHO Grade I to IV

Can occur from infancy to old age, anywhere along the neuroaxis.

### 🔸 Infiltrating Astrocytomas:

**80% of adult primary brain tumors.**

**Common in cerebral hemispheres, ages 40–60.**

**Types (by aggressiveness):**

**Well-differentiated astrocytoma (Grade II)**

**Anaplastic astrocytoma (Grade III)**

**Glioblastoma (Grade IV)**

**Clinical Course:**

Well-differentiated: 5–10 years survival.

Glioblastoma: highly aggressive, ~12 months median survival.

**Morphology:**

**Gross:** Infiltrative, ill-defined, blurring landmarks.  
Glioblastomas show necrosis & hemorrhage.

**Microscopy:** Pleomorphism, mitosis, necrosis with pseudo-palisading, microvascular proliferation.

### 🔸 Pilocytic Astrocytoma:

**Relatively benign (WHO Grade I)**

**Children/young adults**

Common in **cerebellum**, also 3rd ventricle walls, optic nerves.

**Morphology:**

**Gross:** Cystic mass with enhancing mural nodule.

**Microscopy:** “Piloid” hair-like processes, cystic areas, Rosenthal fibers, eosinophilic granular bodies.

## 📌 Oligodendrogliomas:

**5–15% of gliomas**

**Adults, 40–50 years**

Less aggressive than astrocytomas; **more chemo-responsive**

**Morphology:**

**Gross:** Well-circumscribed, gelatinous, gray, with cysts, hemorrhage, calcification.

**Microscopy:**

Round nuclei with perinuclear halo (**fried egg appearance**).

Satellitosis (clustering around neurons/vessels).

Branching capillaries (**chicken-wire vasculature**).

## 📌 Ependymomas:

**Arise adjacent to ependyma-lined ventricles/central canal**

**Children:** Near 4th ventricle

**Adults:** Spinal cord (common in **NF2** patients)

**Morphology:**

**Gross:** Solid/papillary masses from 4th ventricle floor.

**Microscopy:**

Ovoid nuclei with cytoplasmic processes.

**Pseudorosettes:** Around vessels

**True rosettes:** Around lumen

## 📌 Neuronal Tumors:

More common in young adults

Often cause **seizures**

**Types:**

**Gangliogliomas**

**Dysembryoplastic neuroepithelial tumor**

**Central neurocytoma**

### 🔸 Gangliogliomas:

Most common neuronal tumor

Mixture of mature neuronal + glial cells

**Temporal lobe** predilection, often cystic

Neoplastic ganglion cells irregularly clustered; random neurites; binucleate forms seen

Glial part resembles low-grade astrocytoma

## 📌 Poorly Differentiated Neoplasms:

### 🔸 Medulloblastoma:

**20% of pediatric brain tumors**

**Exclusively cerebellar**

Composed of **primitive undifferentiated cells**

WHO Grade IV

**Morphology:**

**Small round cell tumor**

May form **Homer-Wright rosettes** (cells around central fibrillar core)

**Complications:**

**Noncommunicating hydrocephalus**

**Gait abnormalities**

**CSF dissemination with drop metastases to spinal cord**

## 📌 Meningiomas:

**Predominantly benign in adults**

Female predominance (express **progesterone receptors**)

Arise from **meningothelial cells of arachnoid**

Increased frequency in **NF2**

**Locations:**  
Cranial vault, spinal cord.

**Morphology:**

**Gross:** Firm, dural-based, well-demarcated tumors  
May invade skull/soft tissue. Brain invasion rare.

**Microscopy:**

Common patterns: **whorls of meningothelial cells**, **psammoma bodies**

**Atypical** and **anaplastic variants** exist.

## 📌 Metastatic Tumors:

**25–50% of intracranial tumors in hospitalized patients**

**Common primaries:**  
Lung, breast, melanoma, kidney, GI tract (80%)

**Notable points:**

**Choriocarcinoma:** high brain metastasis likelihood

**Prostate adenocarcinoma:** rarely metastasizes to brain

**Morphology:**

**Intraparenchymal metastases**: Sharply demarcated masses at **gray-white junction**, surrounded by edema.

**Microscopy:** Well-defined tumor-brain boundary, nodules with central necrosis, reactive gliosis.