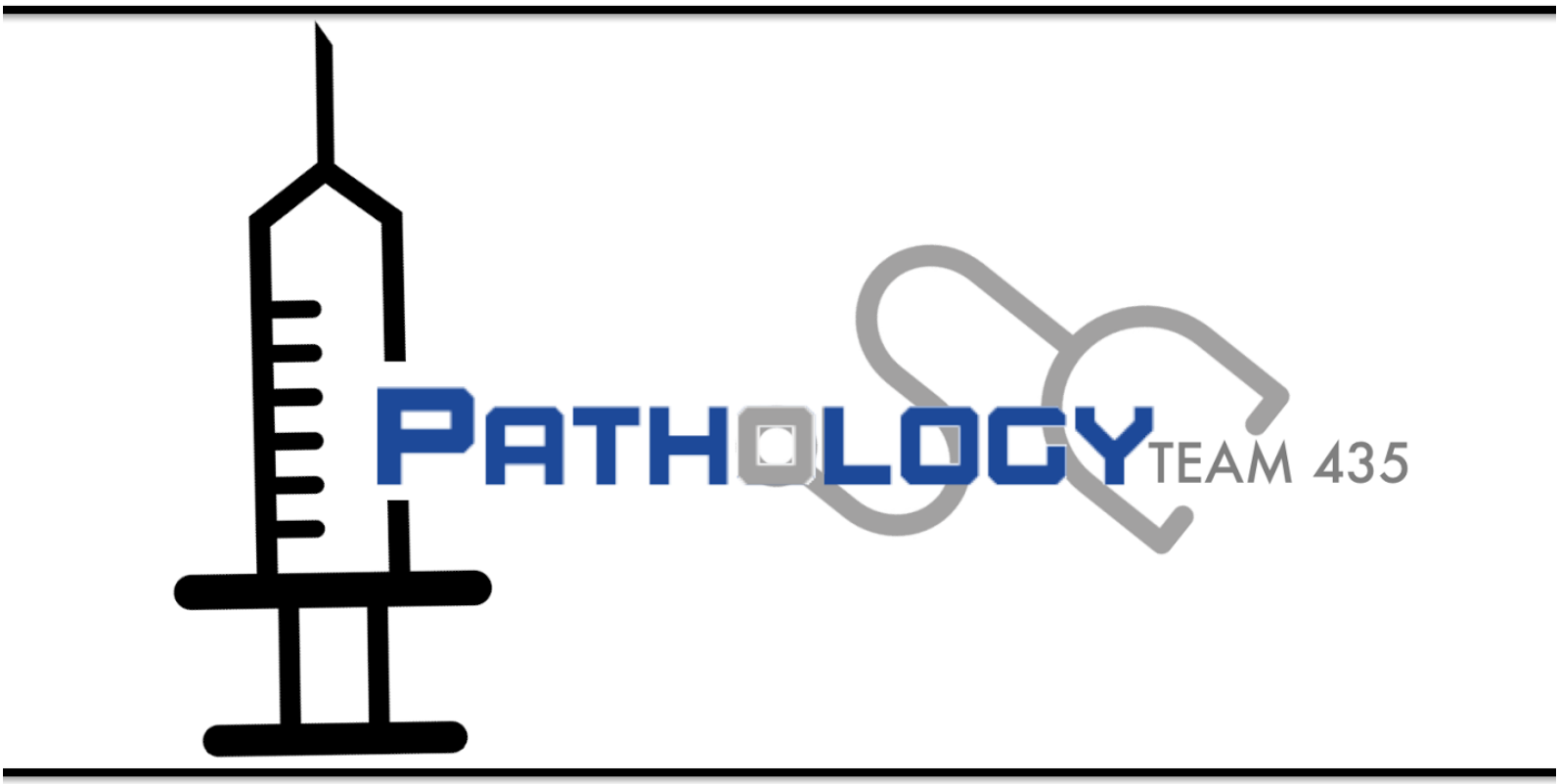
First Four Lectures
Midterm Revision



{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلَّ الجهل طوال حياتهِ }

A Huge Thanks For 434's Team

قام على هذا العمل سارة ناصر الجاسر & مها الربيعة من ٤٣٤،
اذكروهم بدعوة

Cellular Injury of Nervous System

Markers of Neuronal Injury:

1. **Red neurons:** Shrinkage, pyknosis →breakdown of the blood-brain barrier.
2. **Axonal injury:** **Spheroids** (Swelling of the axons) → Chromatolysis (Little chromatin).
    - **Beta amyloid precursor protein (BAPP)** (in diffuse axonal injury that caused by trauma): Immunohistochemistry or silver stain.
    - **Diffuse axonal injury:** characterized by the wide but often asymmetric distribution of axonal swellings.
3. **Intracellular inclusions:** Negri bodies (could be nuclear or cytoplasmic).
4. **Dystrophic neuritis:** ***thickened*** and ***tortuous*** neuronal processes.

Edema:

1. **Vasogenic:** BBB. Related to blood vessels.
2. **Cytotoxic:** Intracellular. Related to cells.

Astrocytes.

- **Gemistocytic =** Active astrocytes.
- **Fibrillary astrocytes =** Long-standing gliosis.
- **Rosenthal fibers:** found in astrocytic processes in chronic gliosis and in some low-grade gliomas (Pilocytic astrocytoma).

- rosenthal fibers are seen mostly in:
  - Child comes with headache, has cystic infratentorial mass → most likely polycystic
- astrocytoma.
  - Adult male comes with abscess and fever, with supratentorial lesions and fibrillary
- astrocytes → reactive gliosis rather than neoplasm.

Oligodendrocytes

- Smudgy homogeneous-appearing enlarged nucleus in **progressive multifocal leukoencephalopathy** & viral inclusions.

Microglia.

- **Bone marrow derived cells.**
- **Neuronophagia:** when they aggregate around portion of dying neurons.
- **Microglial nodules:** when they aggregates at sites of tissue injury.

Ependymal cells.

- **Cytomegalovirus (CMV)**: It can come in all types of cells including Ependymal cells.

Corpora amylacea:

- Small hyaline masses of unknown significance found in the prostate gland, pulmonary alveoli and neuroglia (Astrocytes). Seen in old age.

Markers of peripheral nerve injury:

Axonal neuropathies	Segmental demyelination
Secondary myelin loss (*Wallerian degeneration*)	Damage to Schwann cells or myelin
Decrease in the density of axons	Normal density of axons
Decrease in strength of amplitude of nerve impulses	Slow nerve conduction velocities

Brain Tumors

Epidemiology/Location:

1. **High percentage in children.** (Accounting for 20% of all tumors.)
2. **In childhood** →posterior fossa. (Bottom of the skull)
3. **In adults** →mostly supratentorial. (Forebrain)
4. **Metastasis CNS tumors (secondary) are very common.**

CNS tumors signs & symptoms:

General manifestations:

Seizures, vague symptoms, headaches especially in the morning.

Localized manifestations: According to site of tumor.

REMEMBER: Classification.

Brain tumors are classified with respect to the origins they're arising from:

1. **Cells of the layers covering the CNS** (meningiomas).
2. **Cells intrinsic to the brain** (gliomas, neuronal tumors, choroid plexus tumors).
3. **Other cell populations within the skull** (primary CNS lymphoma, germ-cell tumors).
4. **They may spread from elsewhere in the body** (metastases).

Gliomas: Astrocytomas, Oligodendrogliomas & Ependymomas,

Astrocytomas:

1. **Pilocytic Astrocytoma:** low-grade, in children, contains Rosenthal fibers.
2. **Fibrillary Astrocytoma:** In adults, classified into 3 grades:
   - Diffuse Astrocytoma (GRADE II)
   - Anaplastic Astrocytoma (GRADE III)
   - **Glioblastoma (GRADE IV):** could be primary or progressing from the previous astrocytoma types (secondary.)
     - Secondary glioblastomas share **p53** mutations that characterized low-grade gliomas.
     - Primary glioblastomas → Amplification of the epidermal growth factor receptor (**EGFR**) gene.
     - Histopathological findings: **Pseudopalisading necrosis and/or Vascular proliferation.**

Oligodendroglioma:

- Malignant tumor.

Genetic findings: loss of heterozygosity for **chromosomes 1p and 19q.**

Morphology:

1. Round nuclei often with a cytoplasmic halo. **(Fried egg pattern)**
2. Blood vessels are thin and can form an interlacing pattern. **(Chicken wire pattern**

Ependymoma:

Malignant tumor of ependymal cells in children.

Morphology:

1. Tumor cells may form round or elongated structures (**rosettes, canals**)
2. **Perivascular pseudo-rosettes.**

Meningioma:

- Benign Tumor usually in Adults (women.)
- **PLEASE REMEMBER: The presence of brain invasion → increased risk of recurrence.**

Morphology:

1. Whorled pattern of cell growth.
2. **Psammoma bodies.**

Medulloblastoma:

1. Highly malignant tumor in **children.**
2. It's very **radiosensitive.**

Schwannoma: Benign tumor of Schwann cells.

1. **10%** of **Sporadic schwannomas** are associated with mutations in the **NF2 gene**.
2. **ALL Bilateral acoustic schwannoma** is associated with **NF2. Morphology:**

1. **Cellular Antoni A pattern** and less **cellular Antoni B.**
2. Nuclear-free zones of processes that lie between the regions of nuclear palisading are termed Verocay bodies.

Neurofibroma:

1. Cutaneous (diffuse) neurofibroma in association with type 1 neurofibromatosis (NF1), rarely malignant.
2. Plexiform neurofibroma, mostly arising in individuals with NF1, and associated small real malignant transformation.

	Type 1 Neurofibromatosis	Type 2 Neurofibromatosis
Inheritance	Mutation on chromosome 17 coding for neurofibromin	Mutation on chromosome 22 coding for merlin
Main features	1. Learning disabilities. 2. Seizures. 3. Skeletal abnormalities. 4. Vascular abnormalities with arterial stenoses. 5. Pigmented nodules of the iris (*Lisch nodules*). 6. Pigmented skin lesions (axillary freckling and café au lait spots) in various degrees.	1. Benign tumor 2. Bilateral acoustic neuromas (schwannoma; >90% of cases) 3. CN VIII tumor 4. Sensorineural hearing loss, tinnitus 5. Meningiomas 6. Spinal schwannomas 7. Juvenile cataracts (~80% of cases)

Multiple Sclerosis

- Oligodendrocytes [Multiple axons] Vs. Schwann cells [Only one axon].

Demyelinating diseases	Dysmyelinating diseases
Destruction of normal myelin or oligodendrocyte	Myelin is **not formed** properly

- Multiple sclerosis is autoimmune demyelinating disorder. Attacks myelin.
- **Type IV hypersensitivity.**
- More in women, 20-30 yrs., rare after 30.
- Clinical: Relapsing & remitting.

- **CSF findings:**
    - **Moderate pleocytosis** & **oligoclonal bands.**
    - Mildly elevated protein level
    - Increased proportion of γ-globulin
- We can see plaques usually in **ventricles**.
- **HLA-DR, DR2.**

- **Radiological findings:**
    - **Corpus callosum** will be thinner
    - Periventricular calcification

- **Morphological findings:**

Active plaque	Inactive plaques (quiescent)
● Ongoing myelin breakdown	● **NO** inflammation ● Gliosis are prominent
● **Macrophages** & **Lymphocytes** & monocytes	● Astrocytic proliferation & Decrease oligodendrocytes.
● Axons reduced in number	● No myelin