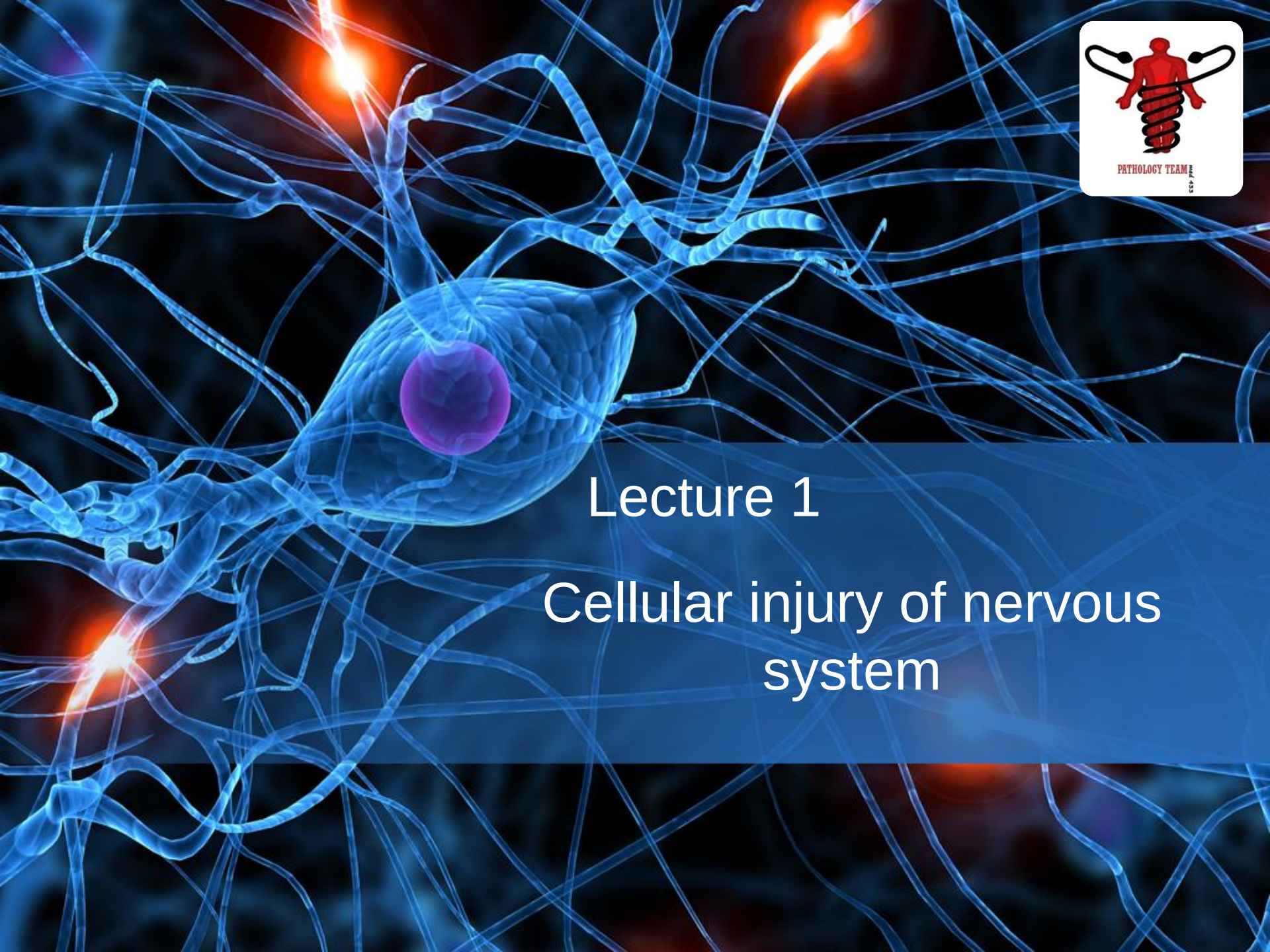
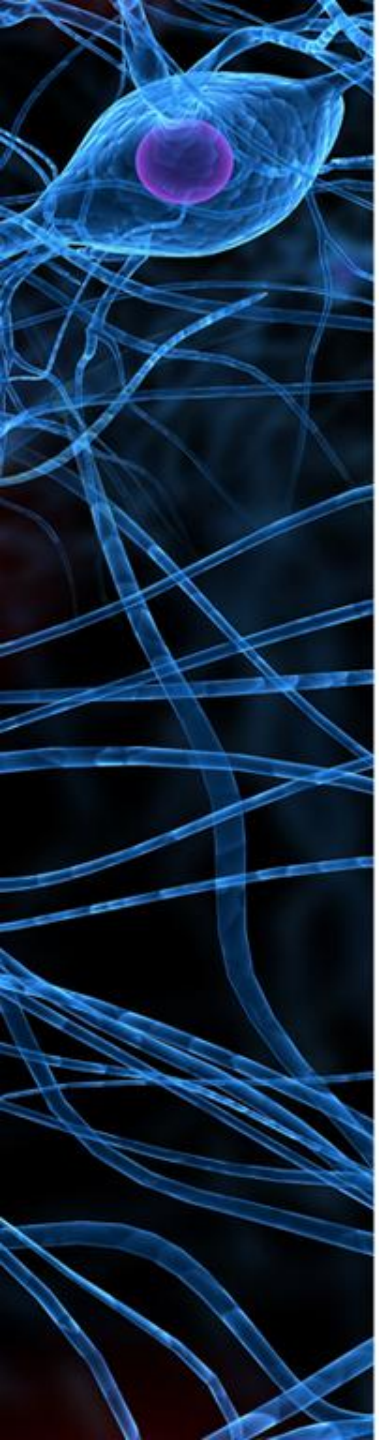


Lecture 1

Cellular injury of nervous system

OBJECTIVES

I. Understand the role of the different constituents of Central nervous system (CNS) cells in the disease status.
II. Understand the “injury” concept.
III. Explain the basic pathological descriptive terms used in CNS cellular injury.
IV. Correlate the different patterns of cellular injury with some important clinical examples.
V. Understand the concept of reaction of neurons, astrocytes and other glial cells to injury.
VI. Recognize the axonal injury in both CNS and Peripheral nervous system as well as the consequences and the pathological findings.



Neuronal Injury in CNS is a number of changes occur in neurons and their processes. Could be detected by H&E stain, within 12 hours of an irreversible hypoxic-ischemic insult (No oxygen and glycogen) .

A) Markers of Neuronal Injury

I. Red Nucleus: fig.1

A cellular pathological sign characterized by:

I. Cell body shrinkage.
II. Nuclear chromatin condensation (**Pyknosis**).
III. Disappearance of Nucleolus.
IV. Loss of Nissl bodies.
V. Eosinophilia (Highly acidophilic cytoplasm).

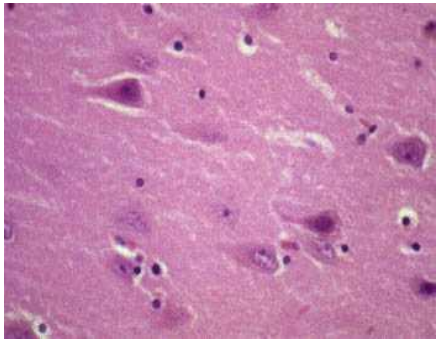


Figure 1

II. Intracellular inclusions: (Typically in infection)

Accumulation of a stainable substance (usually Proteins) inside the affected cell. (E.g. Negri bodies that seen in **Rabies***) fig.2

***Rabies**: viral disease spread to human through bites of infected animals.

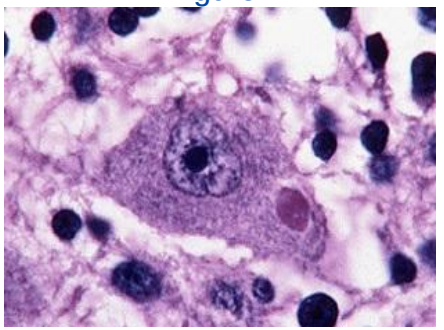


Figure 2

III. Dystrophic neurites*:

Thickening of the processes of the neuronal cell.
Seen in Neurodegenerative diseases. fig.3

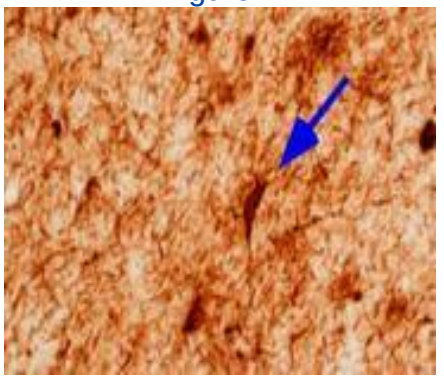
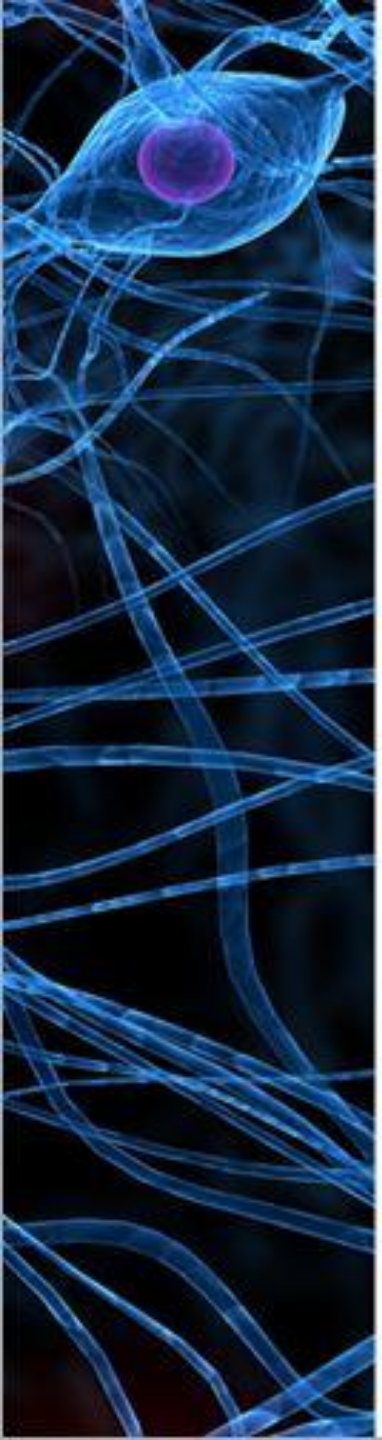


Figure 3

*DON'T BE CONFUSED

Neurite: any projection from the cell body of a neuron (dendrites or axons)

Neuritis: inflammation of one or more nerves.



IV. Axonal Injury:

- Leads to axonal thickening **(Spheroid)** and shows axonal transport disruption fig.1

- Sometimes axonal injury leads to:

A. Cell body enlargement.
B. peripheral nuclear displacement.
C. Enlargement of the nucleolus.
D. Nissl body dispersion **(Chromatolysis):** fig.2

- Seen by staining of **Beta Amyloid Precursor Protein (BAPP),** which is an axonal transport protein, using: **Silver stain / Immunohistochemistry stain.**

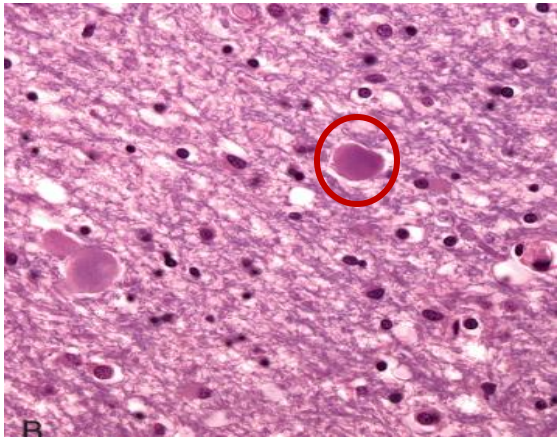


Figure 1

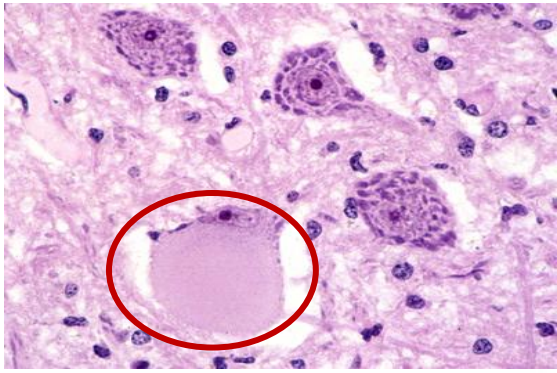


Figure 2

V. Diffuse Axonal Injury:

- It's the reason of coma developed after trauma in 50% of patients**.** Leads to disruption of axonal integrity and function.
- **Caused by**: Sudden movement of one region of brain while other regions are stable.
(E.g. Rapid deceleration during car accidents)
- Characterized by wide asymmetric axonal swellings that appears within hours of the injury.
Seen by: **Sliver / Immunohistochemistry stain** of axonal proteins**.** fig.3

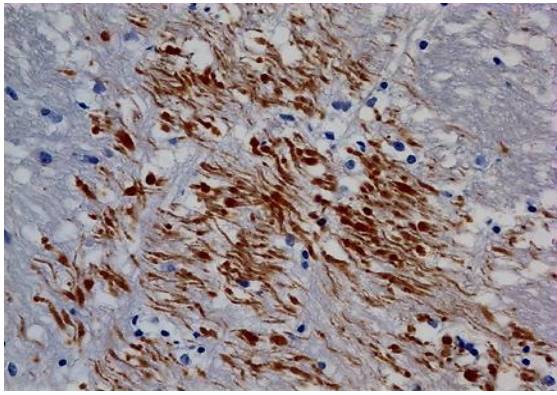


Figure 3

B) Cerebral Edema

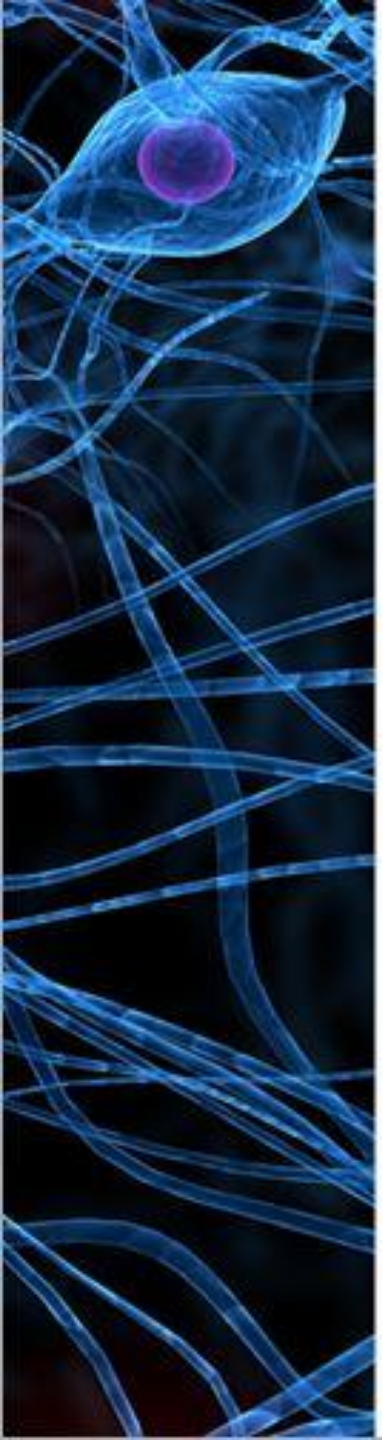
Definition: Fluid accumulation within the brain parenchyma**.**
Two Types which could occur together:

I. Vasogenic: fluid shift from blood vessels into brain ECF after disruption of Blood-Brain Barrier (**BBB**) integrity, which allows the fluid leakage**.** Either localized (e.g. inflammation or tumors increased vascular permeability), or generalized**.**
II. Cytotoxic: increased intracellular fluid due to neuronal or glial cell membrane injury**. Caused by:** generalized hypoxic or ischemic effects or exposure to toxins**.**

C) Glial cells in injuries

I. Astrocytes: Responsible for repair and scar formation in the brain, a process termed ***gliosis***
- When injured happen it**:**
I. Undergoes Hypertrophy and Hyperplasia.
II. Enlarged of the nucleus.
III. Nucleolus becomes large and prominent.
IV. Cytoplasm expands and becomes brightly pink.
V. Emergence of new stout ramifying processes, then it becomes (**Gemistiocytic Astrocyte**), However, it's called (**Fibrillary Astrocyte**) during chronic Gliosis.

Notes:
-There's no fibrosis in brain tissue except some cases which shows little fibroblastic activity like: Penetrating trauma / Abscesses.
- you may see **Rosenthal fibers** (thick, elongated ,bright eosinophilic protein aggregates in astrocyte process) in chronic gliosis and low grade Gliomas (E.g. Pilocytic Astrocytoma)



II. Oligodendrocytes: It may shows some morphological changes when get injured**.**
An important example: viral intracellular inclusion associated with progressive multifocal leukoencephalopathy fig.1 showing homogenous-appearing enlarged nucleus**.**

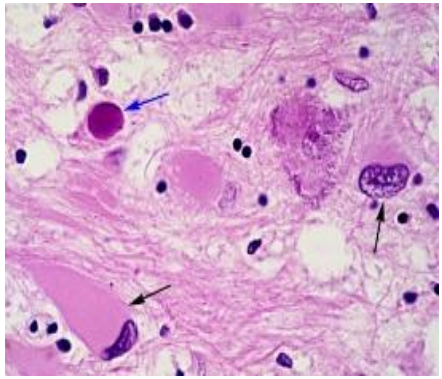


Figure 1

III. Ependymal cells:
They may extensively injured by some pathogens (E.g.**Cytomegalovirus**) showing viral inclusions (intracellular and intra-nucleus inclusions) .

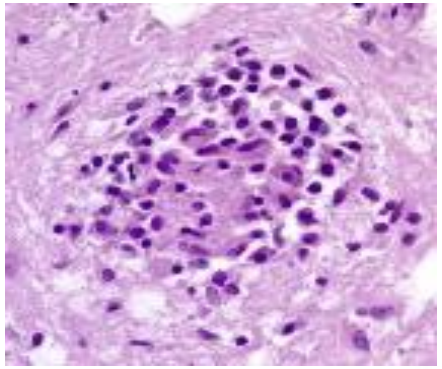


Figure 2

IV. Microglial cells:
They have phagocytic role in CNS**.**
Recognizable in**:**
I. Demyelination.
II. Organizing infarct
III. Hemorrhage
IV. Neuronal Syphilis and other infections while they develop elongated nuclei.

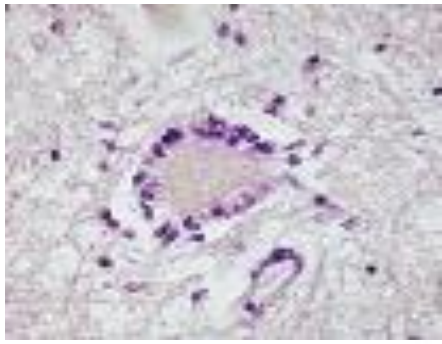


Figure 3

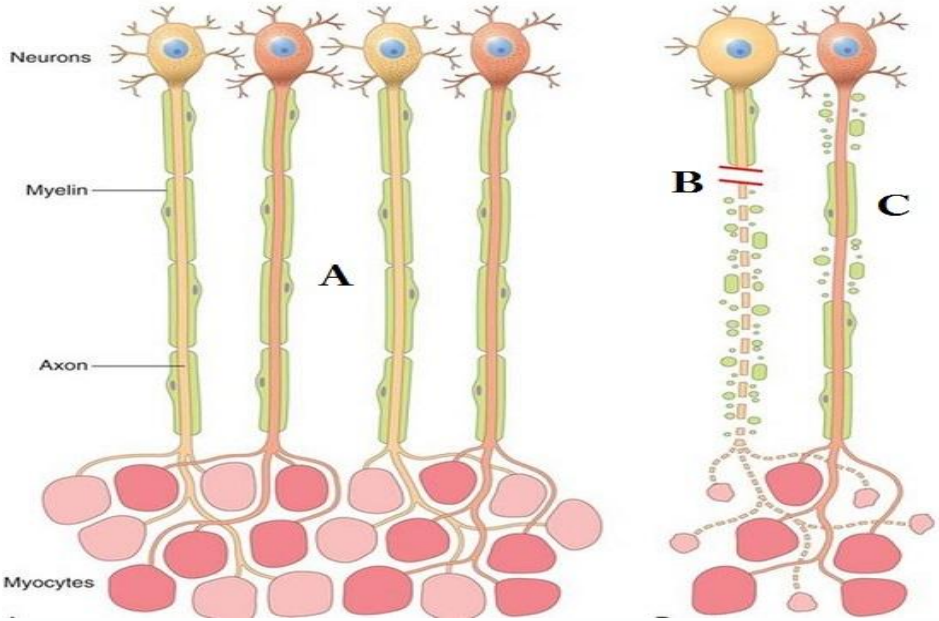
Note: when these elongated microglial cells aggregate around a site of injured tissue they called (**Microglial nodules**)fig.2 but, when they aggregate around portions of dying neurons they called (**Neurophagia**) fig.3**.**
Note: Neurophagia is seen in viral encephalitis**.**

D) Markers of peripheral nerve injury

Classified into:

I. Axonal neuropathies: When the axon directly injured lead to secondary myelin loss (**Wallerien degeneration**).
Could be regenerated: axonal regrowth & subsequent Remyelanation.
Morphological changes: axonal density decrement resulting in reduction in the electrical amplitude.

II. Segmental demyelination: Damage of Schwann cells or myelin, excluding the axon relatively.
Results in abnormal decrease in the conduction velocity.
It occurs in some internodes randomly, that's why it's called **Segmental**.
Morphological changes: Normal axonal density, covered by abnormal thin myelin sheath and short internodes.



A- Normal axons
B- Axonal neuropathies
C- Segmental demyelination

HOMEWORK

Q/ Define Corpora amylacea.
Where and when they are deposited in the CNS?

Amylacea is a Latinate biological word from the Greek *amylon*, which means 'starchy.' It is most commonly used in the medical term *corpora amylacea*.

These are **calcium growths formed from the build-up of protein-laced fluid over time**.

They can range in color from pink to purple to orange, and have a glass-like appearance. They are also usually round in shape. Corpora amylacea, sometimes called **hyaline masses**.

- **Sites** :found in the prostate, **neuroglia**, and pulmonary alveoli.

- **When does it deposit in CNS :**with an **aging of the brain**. because it takes time for significant build-ups of calcium to form. They are **common** in the **brain of elderly dementia patients**.

Challenge Your Self

1. In response to cellular injury, astrocytes undergo:

A. Hyperplasia
B. Hypertrophy
C. Enlargement of nucleus
D. All of the above

2. Which of the following is NOT a marker for red nucleus?

A. Extreme eosinophilia
B. Enlargement of cell body
C. Loss of Nissl substance
D. Disappearance of nucleolus

3. Where we can see Dystrophic neurites?

A. Meningitis
B. Multiple sclerosis
C. Parkinson's disease
D. Gliomas

4. Which of the following cells are responsible for gliosis?

A. Oligodendrocytes
B. Astrocytes
C. Microglial cells
D. Ependymal cells

1- D
2- B
3- C
4- B

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