

**Objectives:**

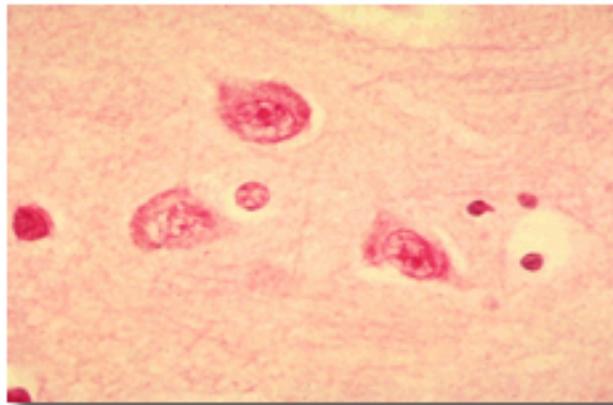
1. For normal neurons, understand structure and function of axons, dendrites and cell bodies.
2. Understand the basic events of synaptic transmission and characteristics of the major neurotransmitters.
3. Know the characteristics of basic pathological reactions of neurons, including necrosis, apoptosis, ischemic cell change, neuronal degeneration, central chromatolysis, neuronal inclusions.
4. Understand characteristics of normal astrocytes, and changes occurring in gliosis.
5. Understand characteristics of normal oligodendrocytes, and general pathological reactions.
6. Understand characteristics of normal ependymal cells.
7. Understand characteristics of normal microglia (CNS representatives of the reticuloendothelial system), and general pathological reactions.

## IA. Neurons - structure/function

### A. Characteristics of normal neurons (review)

#### 1. Structure and Function

The major function of neurons is the transmission of information mostly via chemical mechanisms to other neurons and to target cells such as muscle. The typical neuron consists of a cell body, dendritic processes specialized for receiving information from other neurons, and an axon specialized to conduct impulses away from the cell body. The cytoplasm contains the same organelles found in all cells. Some neurons, especially motor neurons, contain prominent clumps of basophilic granular material known as Nissl bodies, which are composed of rough endoplasmic reticulum and contain many ribosomes. There are three types of neurofibrils: microtubules, neurofilaments, and microfilaments. The neurofibrils function as part of the cellular cytoskeleton and in axonal transport.



**CP 01**

**This image shows three normal neurons in an H&E-stained section. The neurons are the large cells. The two on the right show a large nucleus with a nucleolus.**

#### 2. Synaptic transmission

Calcium influx at voltage-gated ion channels is an important mechanism triggering release of neurotransmitter from synaptic vesicles in the pre-synaptic terminal. The main excitatory transmitter in the CNS is glutamate and the main inhibitory transmitter is GABA. Many other transmitters, including peptides, catecholamines (e.g. dopamine, norepinephrine), serotonin, and acetylcholine, modulate the strength of transmission at excitatory and inhibitory synapses. Postsynaptic receptors may be either ligand-gated ion channels or G-protein linked receptors. Summation of postsynaptic EPSPs and IPSPs at the axon hillock determines if an action potential will be generated.

## **IB. Neurons- pathological changes**

### **B. Neurons - Pathological reactions**

Neurons are more sensitive to injury than other cell types in the CNS. There may be selective vulnerability of groups of neurons to specific types of processes. The following information describes types of neuronal reactions occurring in various disorders. More information will be supplied under specific conditions in which the changes occur.

#### **1. Necrosis**

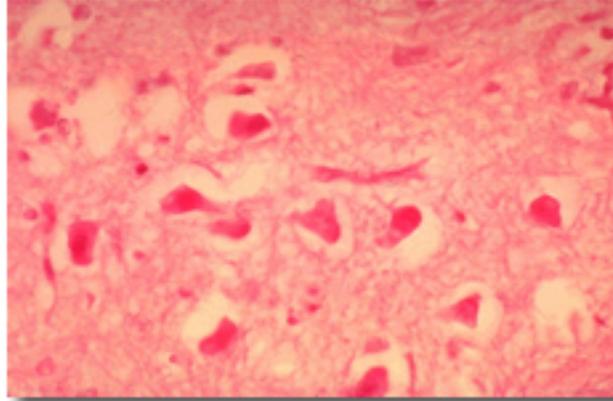
Necrosis refers to a set of morphological changes that follow cell death. The histological appearance is primarily the result of two processes: enzymic digestion of the cell and denaturation of proteins. In the brain, liquefactive necrosis often occurs (rather than coagulative necrosis in which general tissue architecture is preserved in hypoxic death of cells in all tissues except the brain.) Liquefactive necrosis describes dead tissue that appears semi-liquid as a result of dissolution of tissue by the action of hydrolytic enzymes released from lysosomes.

#### **2. Apoptosis**

Apoptosis, a form of programmed cell death, involves different cellular mechanisms than necrosis. Apoptosis is an energy-dependent process designed to switch cells off and eliminate them. Although apoptosis is a physiological process occurring normally during development, it can also be induced by pathological conditions ranging from a lack of growth factor or hormone, to a positive ligand-receptor interaction, to specific injurious agents. The process consists of four major components: (i) signaling pathways; (ii) control and integration mechanisms, in which the Bcl-2 family is important; (iii) an execution phase often involving the caspase family of proteases; (iv) removal of dead cells by phagocytosis.

#### **3. Basic histopathologic reactions to injury**

a. Acute neuronal injury / ischemic cell change (eosinophilic/red neurons): Neurons are quickly injured by hypoxia (decreased oxygen supply) or ischemia (regional absence of blood supply). After 6-12 hours morphological changes include acute shrinkage, angularity, and homogeneous eosinophilia of the cytoplasm. The nucleus becomes shrunken, pyknotic and hyperchromatic. These changes are part of the process of cell death. Affected cells are called ischemic neurons or red neurons or eosinophilic neurons.



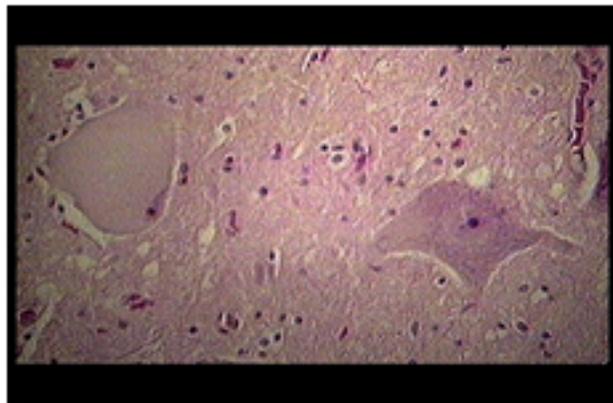
**CP 02**

**This H&E-stained microscopic image illustrates ischemic neurons**

b. “Simple” neuronal atrophy (“degeneration”): There may be neuronal death resulting from a progressive disease process, with cell loss as a characteristic histologic feature.

c. Axonal reaction / central chromatolysis / Wallerian degeneration: When the axon of a neuron is cut or damaged, the axon and its myelin sheath undergo degeneration distal to the lesion (Wallerian degeneration). The sequence of events that takes place in the cell body is known as central chromatolysis or axonal reaction.

- The cell body swells.
- The Nissl bodies disperse and move peripherally.
- The nucleus is displaced peripherally in the cell.
- This is a reparative process associated with increased protein synthesis to facilitate axon regeneration.

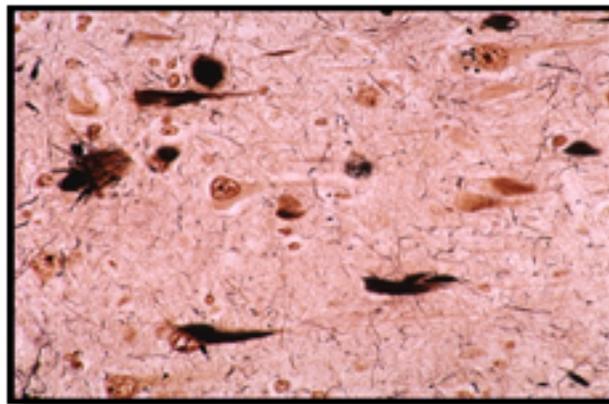


**CP 03**

**The cell on the left is undergoing chromatolysis.**

d. Subcellular alterations in cytoplasm, organelles or cytoskeleton: A wide range of subcellular alterations are recognized.

- Neuronal inclusions may occur as a manifestation of aging. This can involve cytoplasmic accumulation of lipids, proteins and carbohydrates (lipofuscin)
- In many cases of viral encephalitis, inclusion bodies composed of viral particles occur in the cytoplasm or nucleus of infected cells. One example is the Negri body characteristic of rabies.
- In some degenerative diseases, specific types of intraneuronal inclusions characteristically occur. For example, in Parkinson's disease, large spherical intracytoplasmic inclusions called Lewy bodies are found. In Alzheimer's disease, cytoplasmic accumulation of abnormal neurofilaments, called neurofibrillary tangles occurs.
- Neurons may be the site of storage of uncatabolized substances, such as lipids, in a number of inborn errors of metabolism resulting from deficiencies of lysosomal enzymes.



CP 04

## **IIA. Astrocytes - structure/function**

### **A. Characteristics of normal astrocytes**

Astrocytes have many cytoplasmic processes that terminate on blood vessels, neuronal cell bodies, axons and synaptic terminals. Functions of astrocytes include physical and metabolic support for neurons, detoxification, guidance during migration, regulation of energy metabolism, electrical insulation (for unmyelinated axons), transport of blood-borne material to the neuron, and reaction to injury. Axonal end-feet that surround capillaries contribute to formation of the blood-brain barrier. Astrocytes can be identified specifically through immunocytochemical staining for glial fibrillary acidic protein (GFAP).

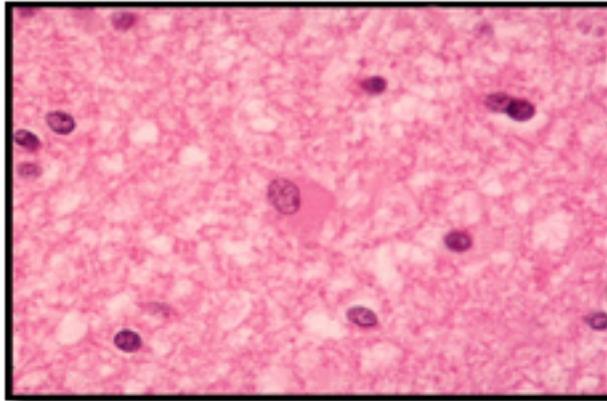
## **IIB. Astrocytes – pathological changes**

### **B. Pathological reactions**

In the brain, repair and glial scar formation is mainly accomplished by gliosis. (Fibrosis and formation of fibrous scar tissue does not generally occur in the brain.) Gliosis involves

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proliferation of astrocytes with formation of many glial processes. Some astrocytes become gemistocytic, i.e. they appear plump or swollen and the cytoplasm is eosinophilic.



**CP 05**

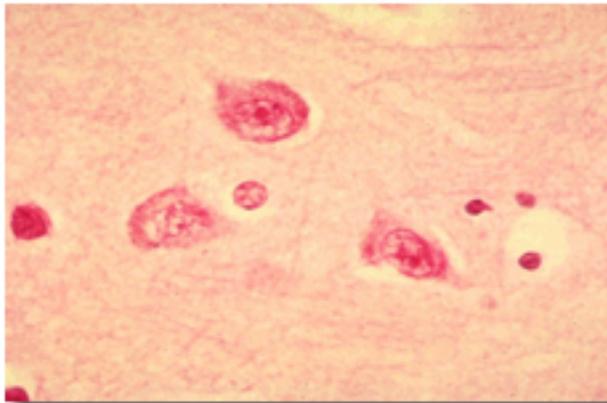
A gemistocytic astrocyte is shown in the center of the image. Note the plump, swollen eosinophilic cytoplasm around a healthy nucleus

### IIIA. Oligodendrocytes - structure/function

#### A. Characteristics of normal oligodendrocytes

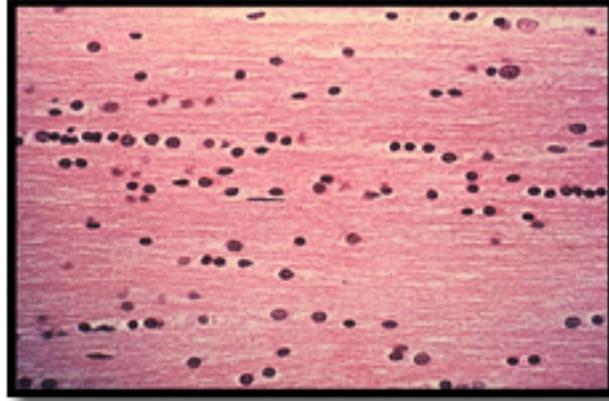
Oligodendrocytes have small amounts of cytoplasm surrounding rounded nuclei, and possess only few short processes. There are two main types:

- satellites around neurons in the gray matter
- myelin-forming cells in the white matter



**CP 06**

Three oligodendrocyte nuclei in the gray matter are shown at the right (small dark nuclei)



### CP 07

**Oligodendrocyte nuclei are seen in the white matter, among myelinated axons. Some of the nuclei in this field are astrocytes.**

There are differences in myelin formation differences in CNS (brain, spinal cord) and in peripheral nervous system (cranial nerves, peripheral nerves).

**oligodendrocytes form myelin in the CNS** and one cell may provide many segments of myelin sheaths.

**Schwann cells form myelin in the peripheral nervous system** and one cell provides only one myelin sheath segment.

### IIIB. Oligodendrocytes – pathological changes

#### B. Pathological reactions

Oligodendrocytes swell in response to almost any type of toxic or metabolic change. Diseases with primary involvement of oligodendrocytes result in disorders of myelin, with demyelination or abnormal myelin formation. The two major groups of diseases affecting oligodendrocytes and myelin are the leukodystrophies, which include inherited disorders of myelin metabolism, and the acquired demyelinating diseases (e.g. multiple sclerosis).

### IV. Ependymal cells

Ependymal cells are cuboidal-columnar ciliated cells that line the ventricles and central canal of the spinal cord. Specialized ependymal cells form part of the choroid plexus, a vascular structure in the ventricles of the brain responsible for the secretion of cerebrospinal fluid.

## V. Microglia

### A. Characteristics of normal microglia

Microglia are mesoderm-derived cells (in contrast to the macroglia -- astrocytes, oligodendrocytes, and ependyma -- which are derived from neuroectoderm). Microglia are the CNS representatives of the reticuloendothelial system. One major function is to serve as a fixed macrophage system.

### B. Pathological reactions

Microglial cells become activated in response to injury and may respond by

- proliferation
- developing elongated nuclei (rod cells)
- forming aggregates around areas of tissue necrosis or dying neurons (neuronophagia, microglial nodule or shrunken)

In addition to microglia, blood-derived macrophages serve as phagocytic cells in the CNS.