

# CNS pathology

## Third year medical students

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FRCPath

2017

# LECTURE 1: INTRODUCTION

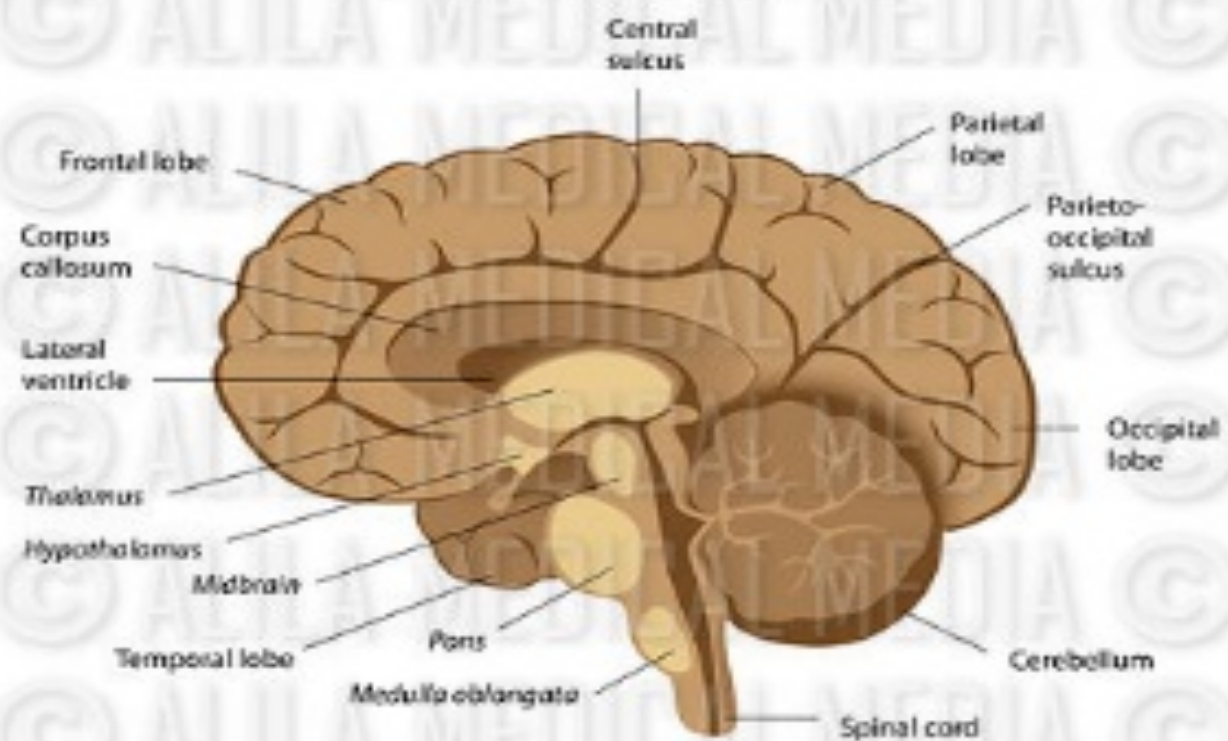
- Don't get lost in the trees that you lose sight of the forest

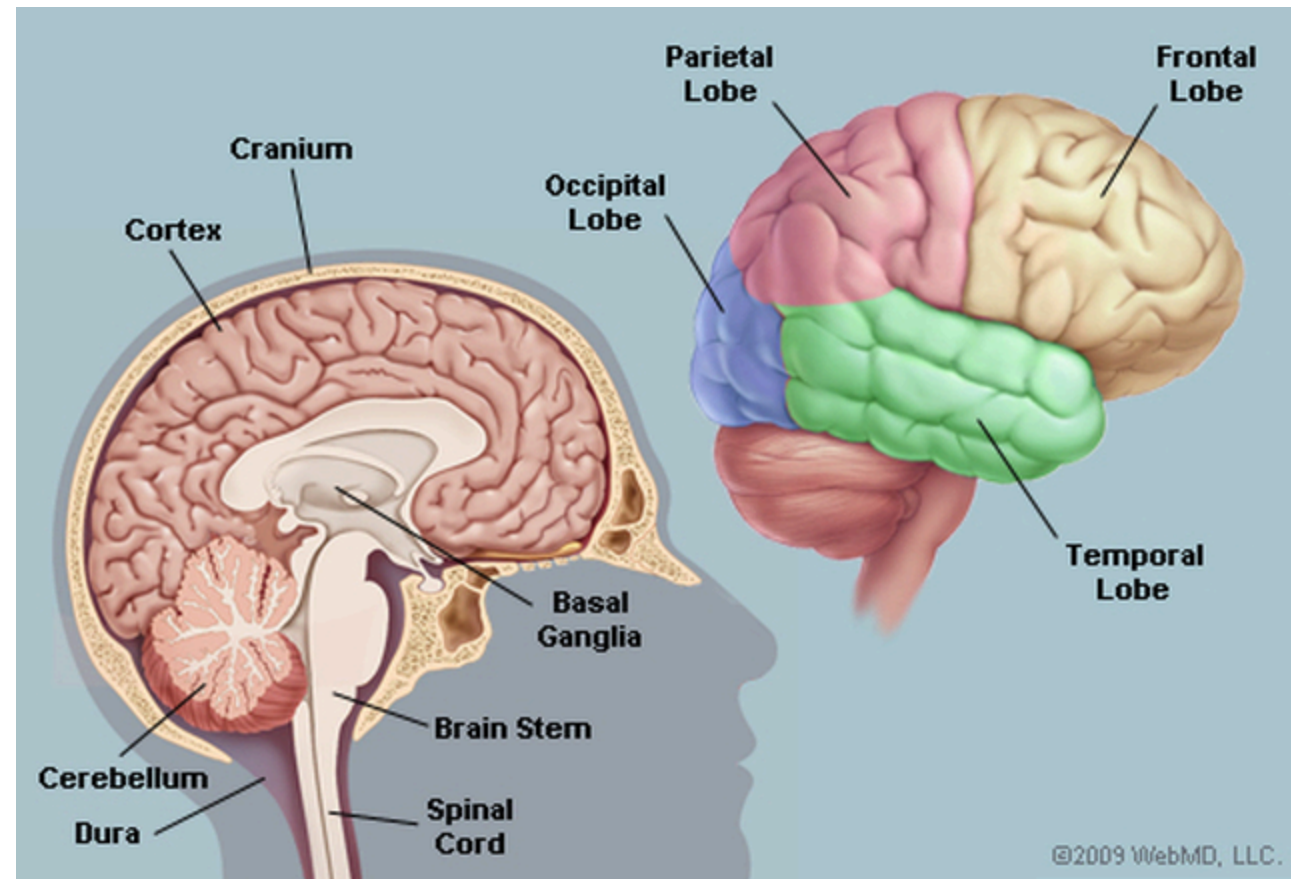


# Intended learning outcomes ILOs

- To know the brain lobes and some of their functions
- To understand the asymmetry between the right and left hemispheres, with examples.
- To know the structure and function of neurons and glial cells
- To understand how neurons and glial cells respond to injury.
- To apply the above knowledge in understanding brain diseases

## Median section of the brain





# Cerebral hemispheres

- Anterior half: for executive function
- Posterior: perception of the environment
- Collections of cells in the depth of the hemisphere deal with motor control(basal ganglia), appropriate attention of sensory perception(thalamus) , emotion and memory (limbic system) and control over body functions (hypothalamus)

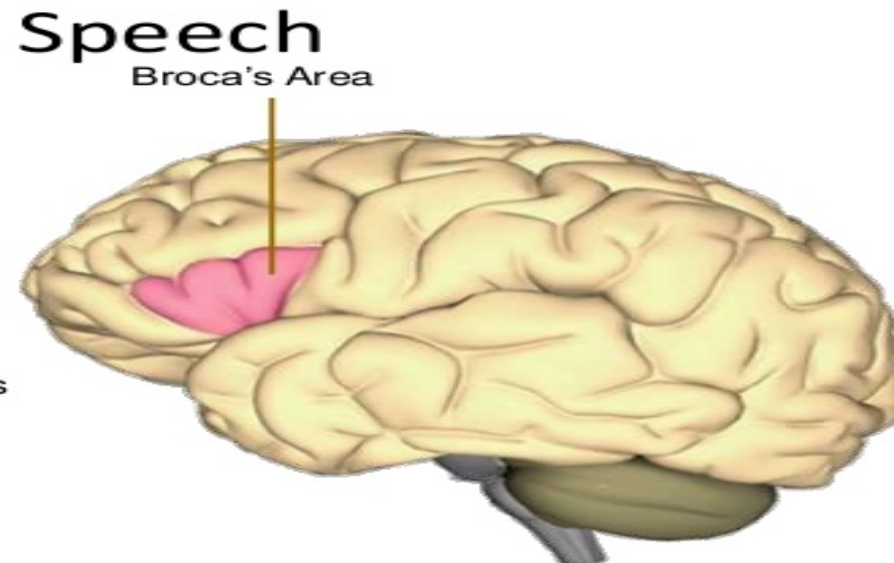
# Cerebral cortex

## 1. frontal lobe

- Contains the primary motor cortex: performs final cortical motor processing
- Broca's area in the left frontal controls **motor** pattern of speech, if damaged = expressive dysphasia

Broca's area is where we formulate speech and the area of the brain that sends motor instructions to the [motor cortex](#).

Injury to Broca's area can cause difficulty in speaking. The individual may know what words he or she wishes to speak, but will be unable to do so.

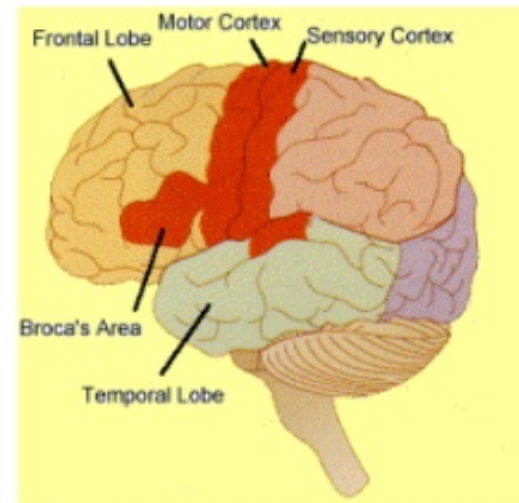


- Prefrontal cortex important for abstract thinking , solving complex problems, high intellectual functions and ambition.

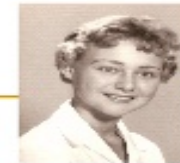


## FRONTAL LOBE

- **Personality**
- **Behavior**
- **Voluntary motor function**
- **Motor speech (Broca's),  
Left side dominant**
- **Intellectual functions, problem solving**
- **Judgment; good/bad, right/wrong**



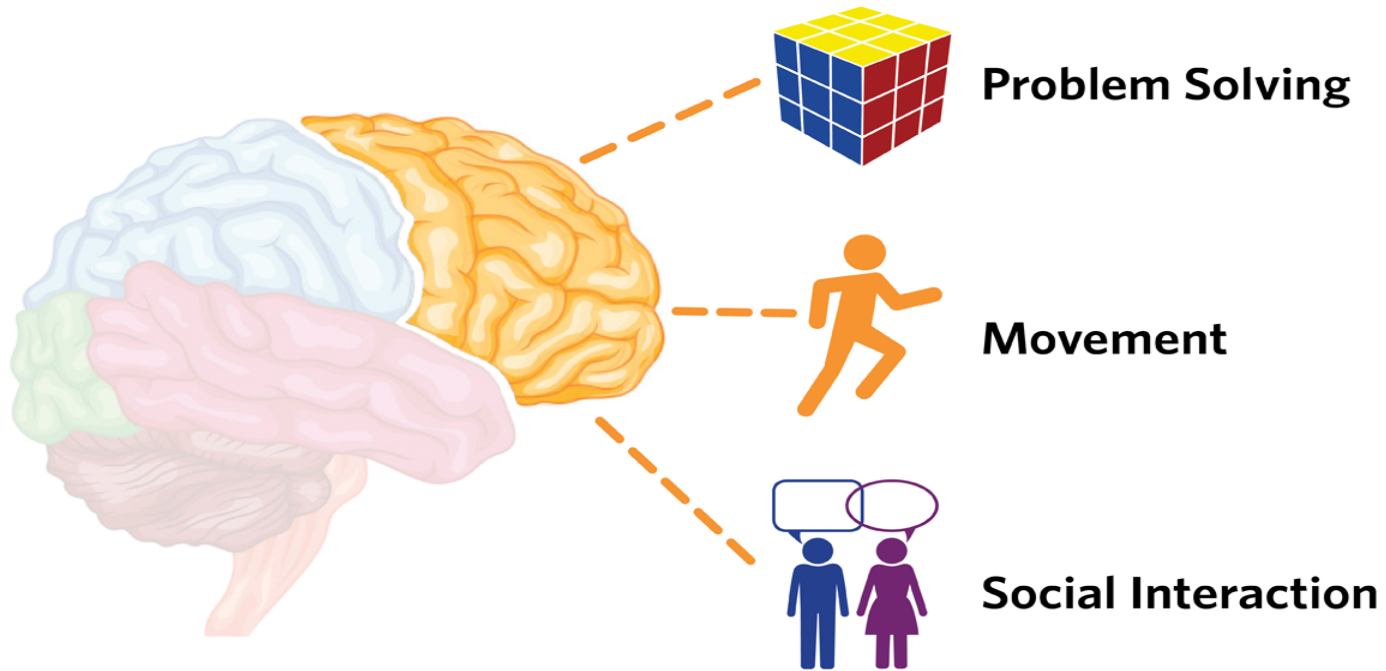
Called the “MOM” portion of the Brain



# Frontal Lobe

The largest of the brain's four main lobes.

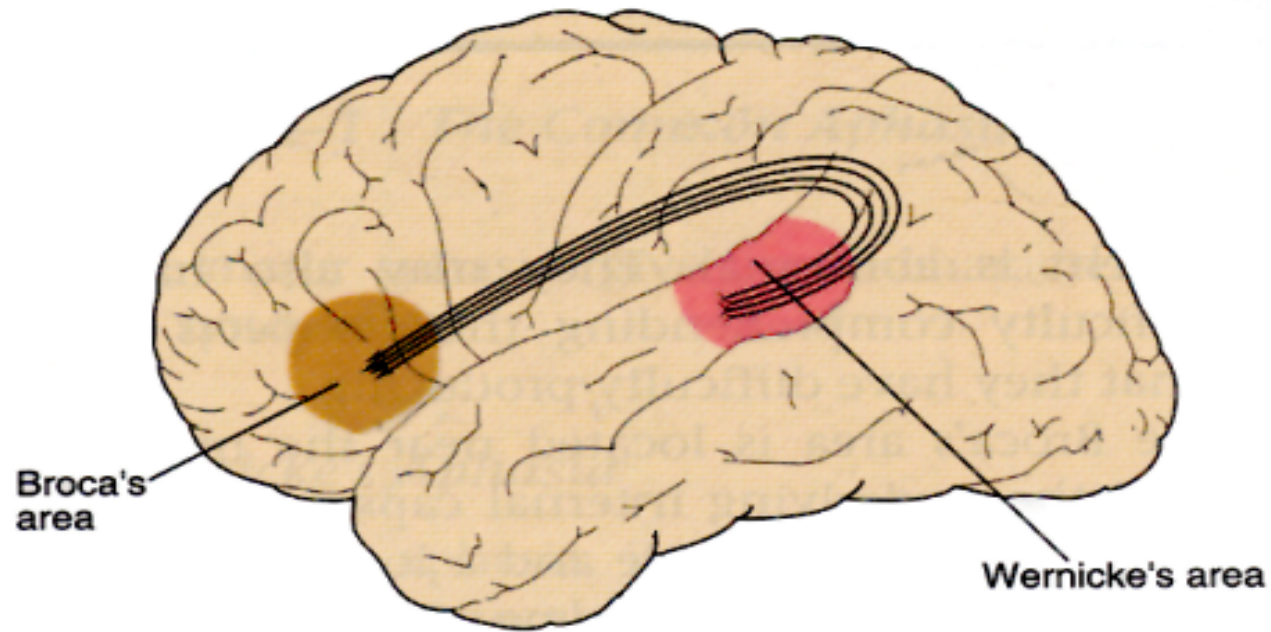
It is the emotional control center and home to personality and decision making abilities.



## 2. Temporal lobe

- Important for complex processing of sensory input
- Contains **Wernicke's area** : auditory , visual and somatic associations coalesce in this area.
- If damaged: inability to understand spoken or written language.  
(receptive dysphasia)

There are associations between Broca's and Wernicke's areas



### 3. Parietal lobe

- Contains high order sensory areas
- Contains area for naming objects
- Contains area for processing of visual language= reading

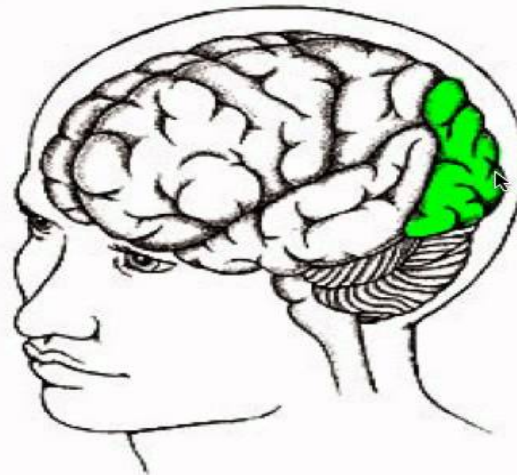
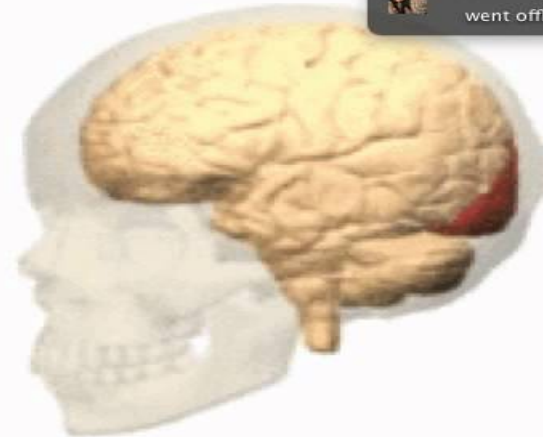
## 4. Occipital lobe: Contains the visual cortex

### *Occipital Lobe*

- Located at rear of brain
- **Involved** in vision
- Select, organise and integrate visual info
- Works with other lobes

#### **Primary Visual Cortex**

- Located at rear of lobe
- Processes information from sensory receptors on retinas
- Left half of each eye sends info to left hemisphere (R-L-L)
- Right half of each eye sends info to right hemisphere (L-R-R)
- Some neurons respond only to certain features



Ashleigh M Sun  
went offline

# Brain asymmetry

## LEFT BRAIN FUNCTIONS

Right side of body control

Number skills

Math/Scientific skills

Analytical

Objectivity

Written language

Spoken language

Logic

Reasoning

## RIGHT BRAIN FUNCTIONS

Left side of body control

3-D shapes

Music/Art awareness

Synthesizing

Subjectivity

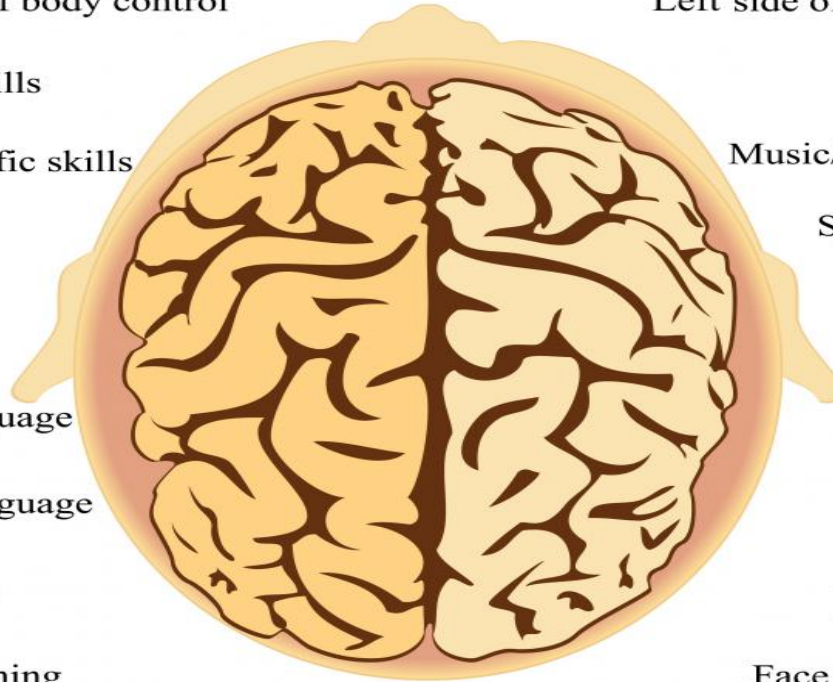
Imagination

Intuition

Creativity

Emotion

Face recognition



wiseGEEK

# Why understanding brain asymmetry is important ?

- Same disease process can have different consequences according to the side affected
- Example: a stroke affecting the Broca's area in the left frontal lobe can result in expressive dysphasia. Similar lesion in the mirror image area in the right side might result in no symptoms at all.



# BRAIN CELLS

- The CNS contains 100 billion **neurons**.
- It also contains 10-50 times this number of **glial cells**.
- 40% of our genes participate in the formation of the CNS.

# neuron

- Is the principal **functional unit** of the CNS.
- They receive and transmit information
- Mature neurons cannot divide: permanent cells
- However, neural progenitors are found in the brain and can divide.....  
??? Expansion of these can help patients with CNS diseases ( this is an area of active research,, we'll come to this later!

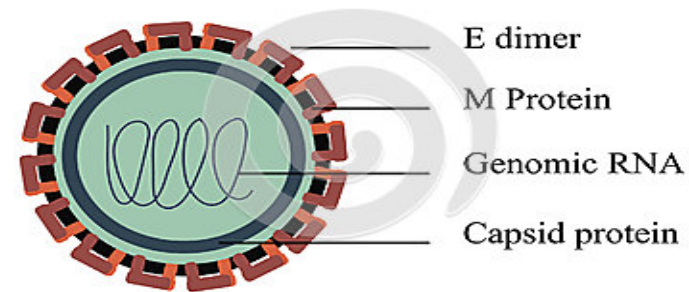
# Neural progenitors

- Neural progenitors are cells that are capable of dividing a **limited** number of times and have the capacity to **differentiate into a restricted repertoire of neuronal and glial cell types.**
- Zika virus infection is associated with microcephaly, probably through infecting neural progenitors causing their death and resulting in decreased brain growth in embryos.

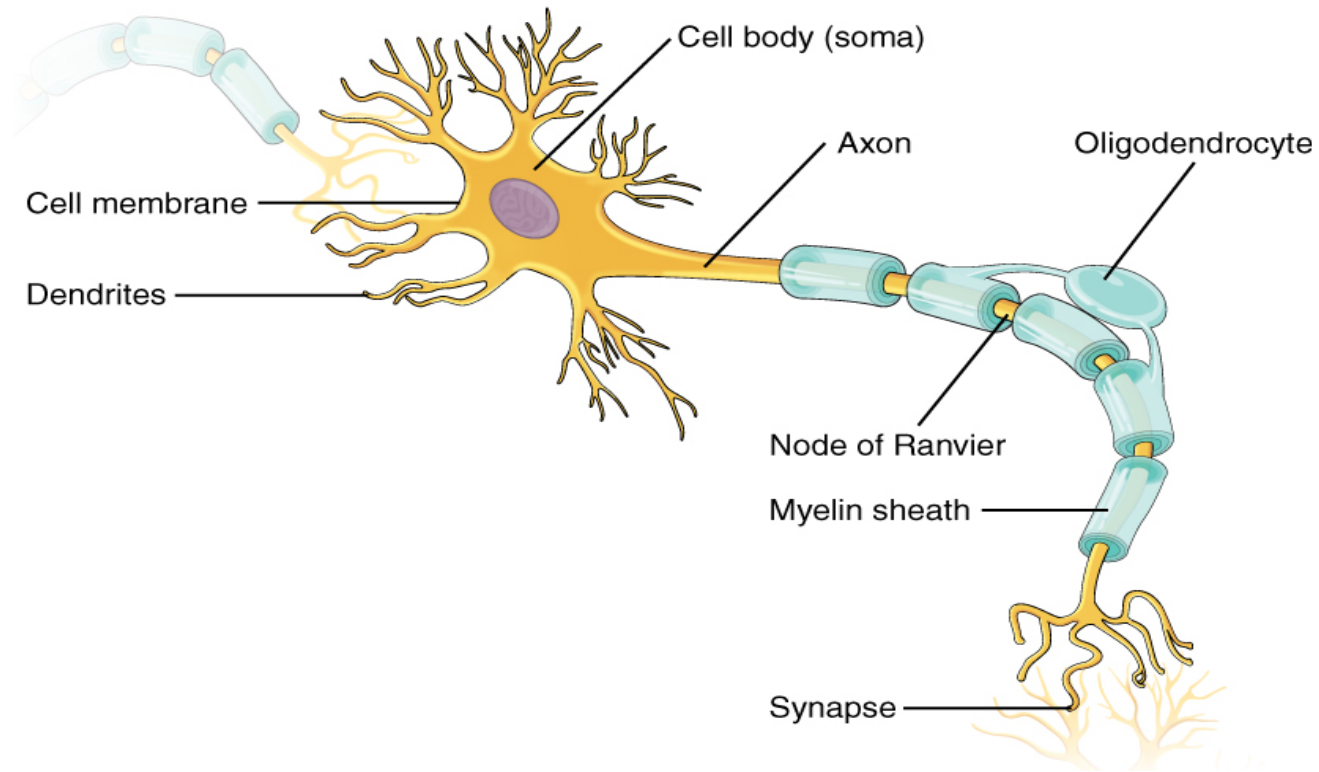
# ZIKA VIRUS

- Based on a systematic review of the literature up to 30 May 2016, WHO has concluded that Zika virus infection during pregnancy is a cause of congenital brain abnormalities, including microcephaly

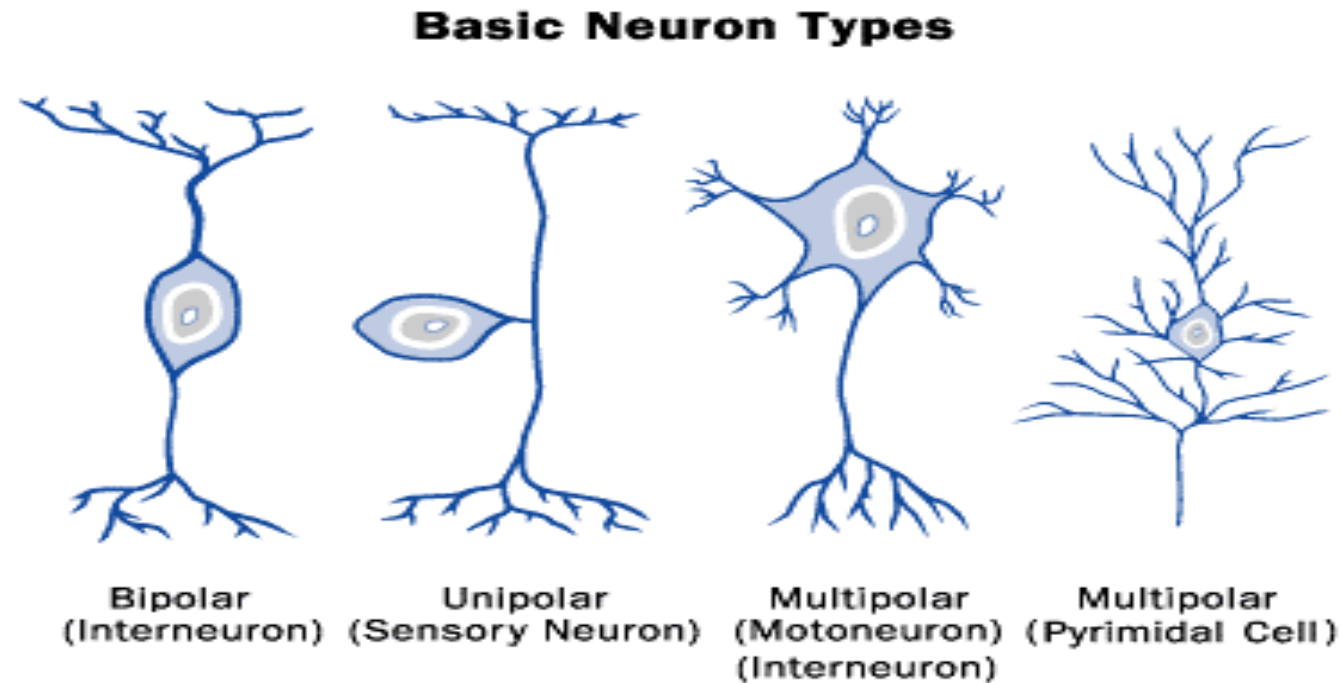
**Structure of Zika virus**



# Basic structure of neurons.



# Neurons come in several shapes!



# GLIAL cells = خَلَايَا دِبْقِيَّة

- Are supportive cells

4 types:

1. Astrocytes
2. Oligodendrocytes
3. Microglial cells
4. Ependymal cells

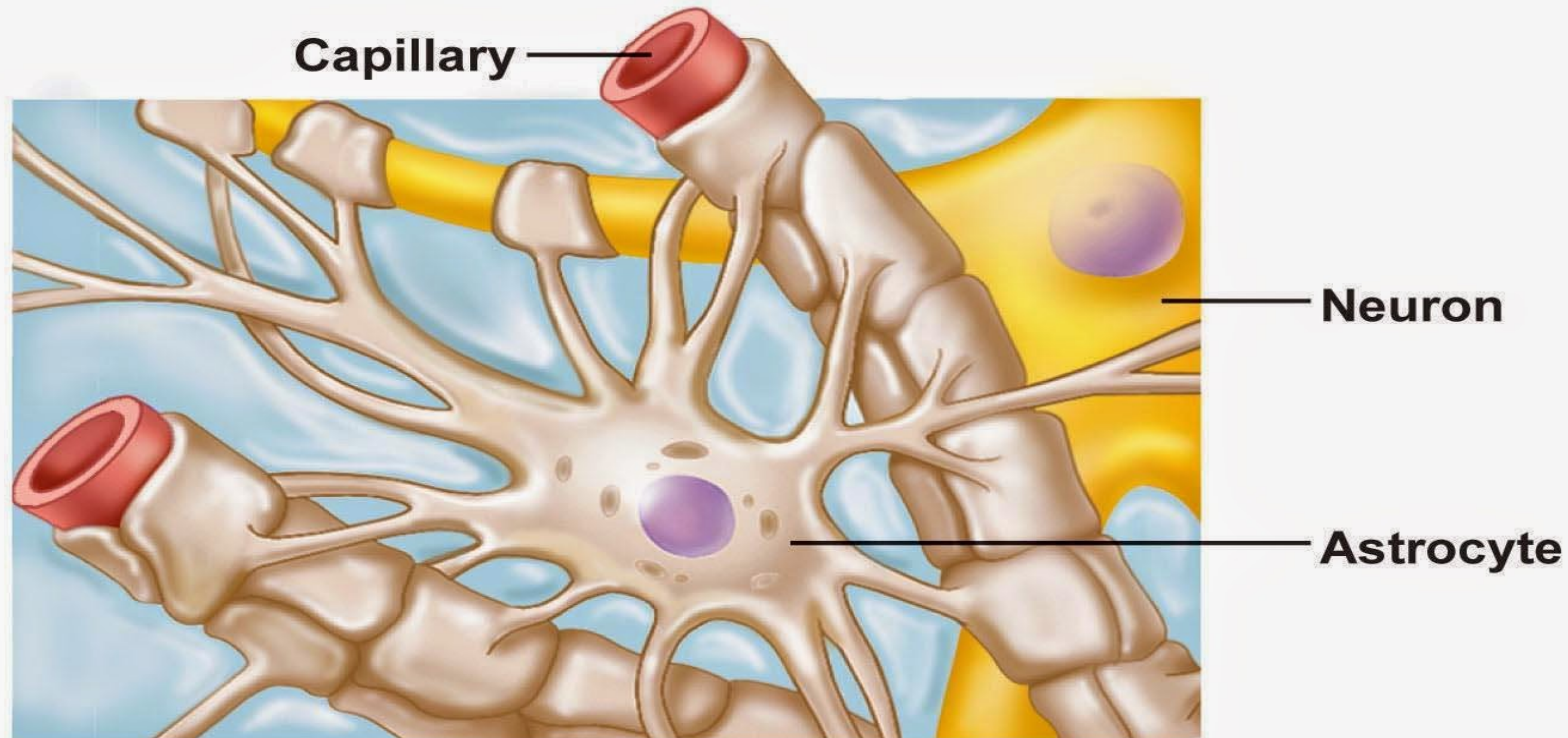
# Astrocytes = خَلايا نَجْمِيَّة

- give structural support to neurons
- control neural biochemical environment.
- Astrocyte processes are associated with the blood vessels to form the blood brain barrier





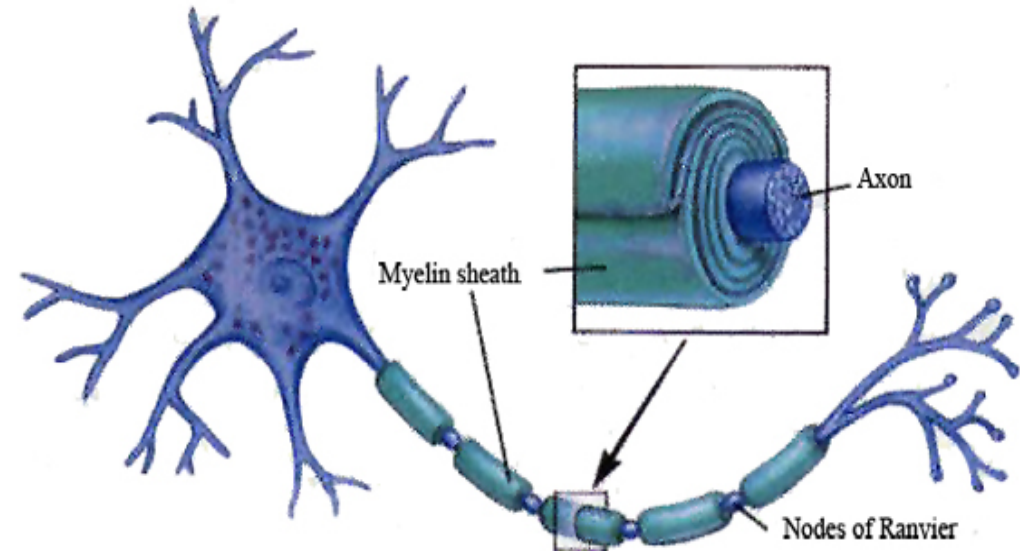
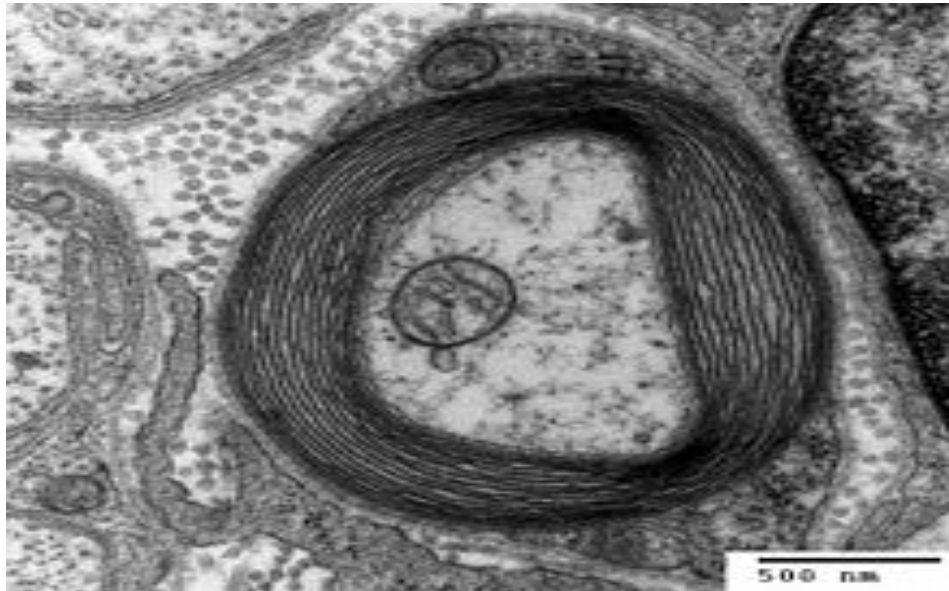
# Astrocytes



**(a) Astrocytes are the most abundant CNS neuroglia.**

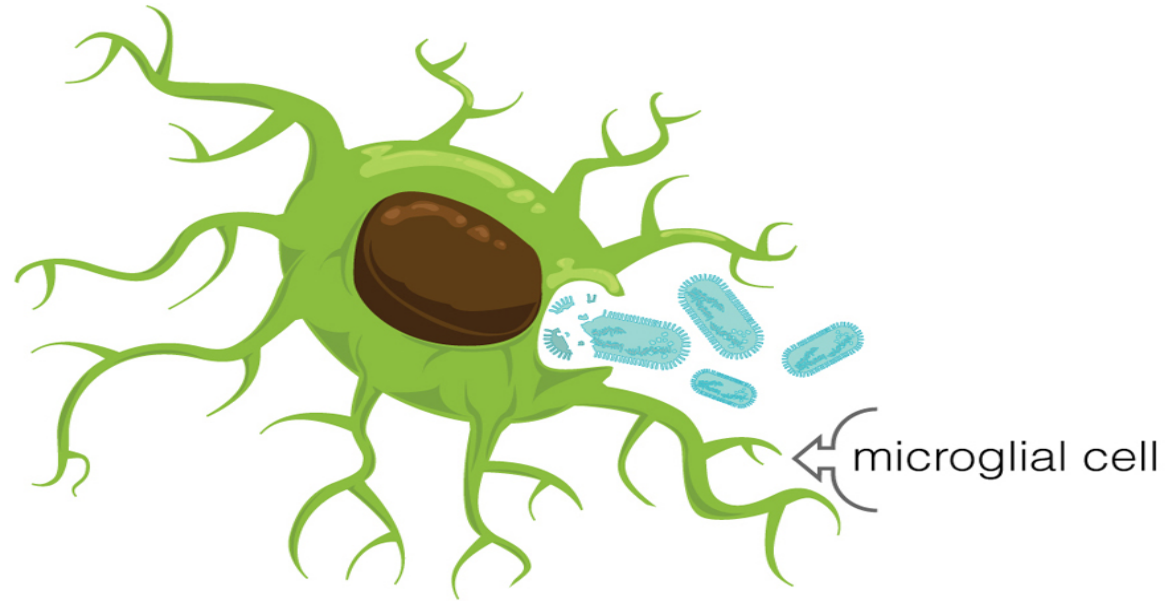
# Oligodendrocytes = دِبْقِيَّةٌ قَلِيلَةٌ التَّغَصُّن [خلية]

- Oligodendrocytes form the myelin sheath which surrounds axons and is important for fast transmission of action potential by salutatory conduction



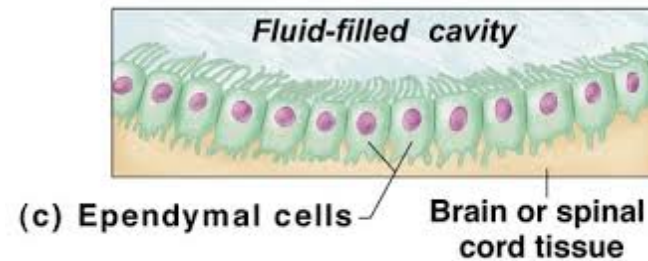
# Microglial cells=الخلايا الدبقية الصغيرة

- Microglia: blood derived macrophages



# Ependymal cells خَلَايَا البِطَانَةِ العَصَبِيَّة =

- They line the ventricle and the spinal cord.



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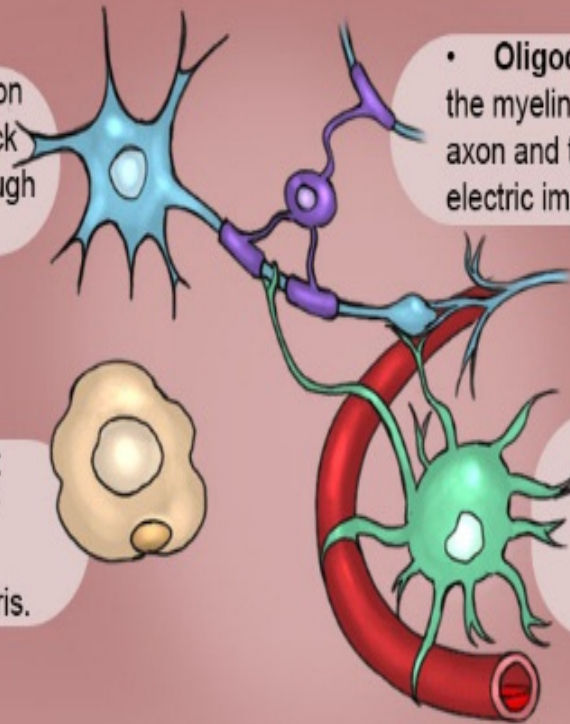
## Cell types in the Central Nervous System

- **Neurons:** They receive information from senses, process it and send back messages to exert an action, all through an electrochemical process.

- **Microglia:** Immune cells that can "eat" the microbes that enter into the CNS. They also clean injured brain areas from cell debris.

- **Oligodendrocytes:** They produce the myelin that covers the neuronal axon and that increase the speed of electric impulses through the axon.

- **Astrocytes:** They take care of the neurons, but also participate in the transmission of messages, cell metabolism and control of blood flow.



# Reaction of neurons to injury

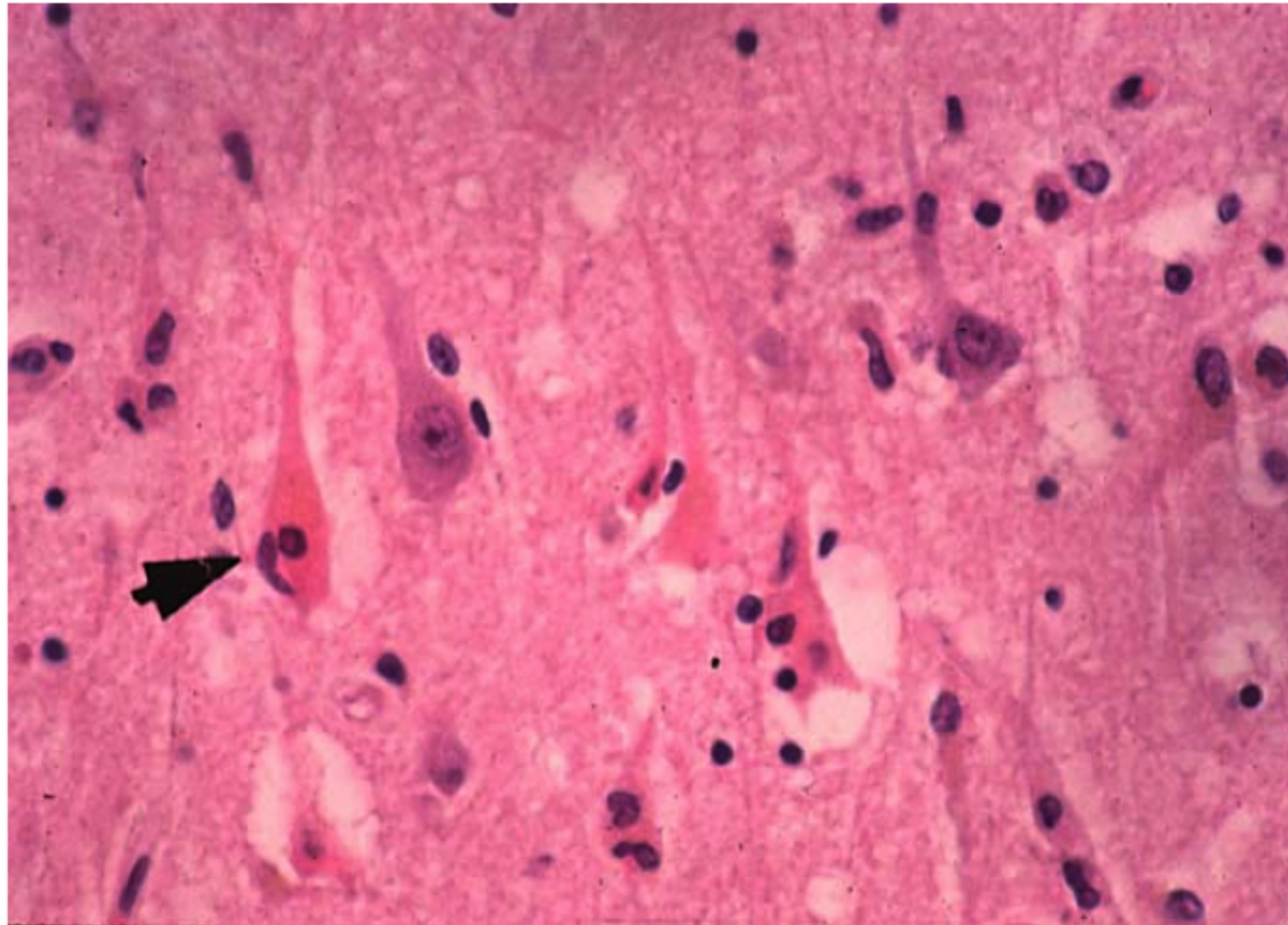
# Reaction of neurons to ACUTE injury

- Acute neuronal injury = red neuron
- Happens due to acute injury due to hypoxia, ischemia
- Is the earliest morphologic manifestation of neuronal cell death
- Appear after 12-24 hours of irreversible injury
- Shrinkage of cell body, pyknosis, disappearance of the nucleolus
- Loss of Nissl substance ( see next slide for definition)
- Intense cytoplasmic eosinophilia

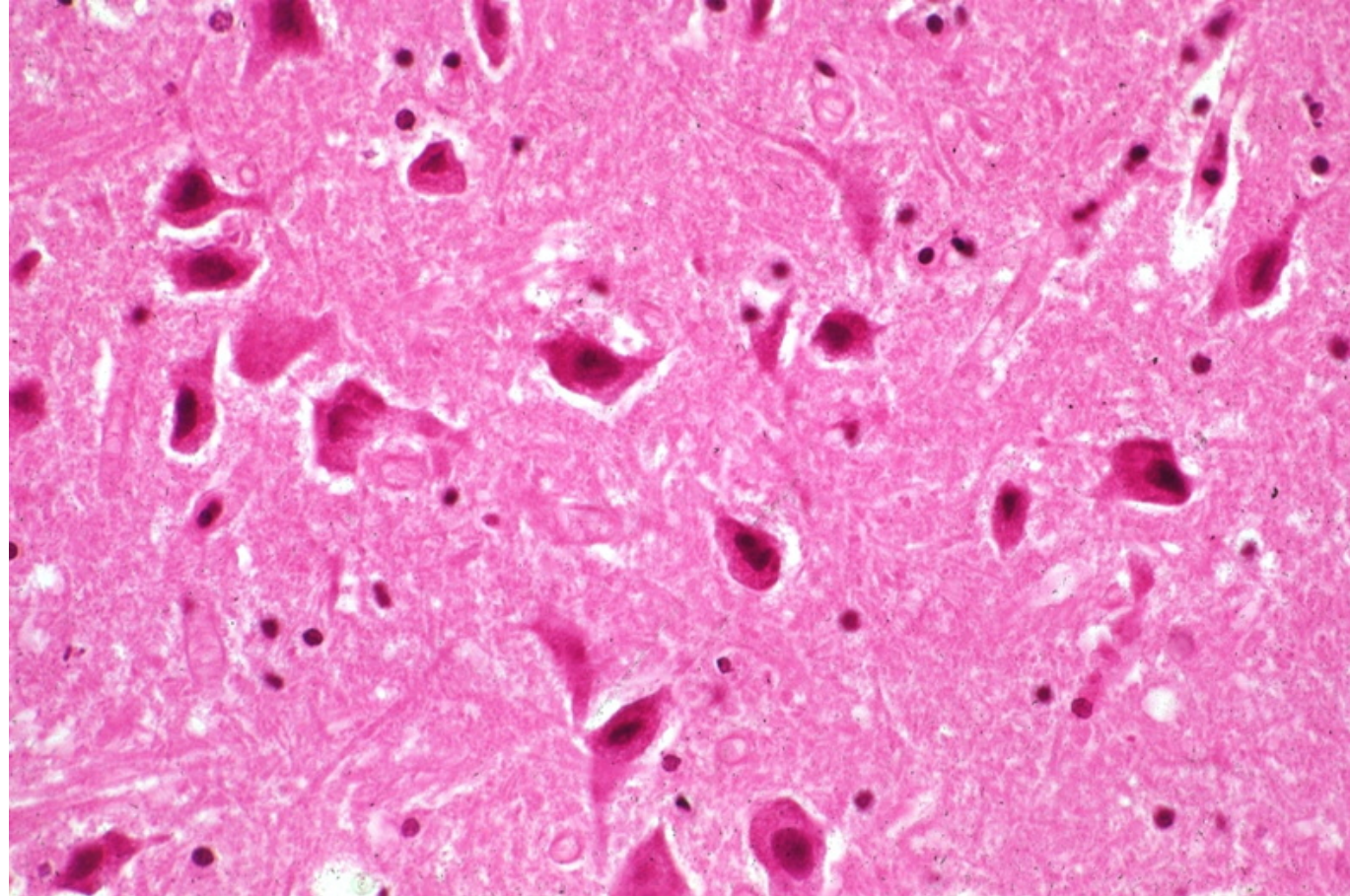
- **Nissl substance:** large granular substance found in neurons. These **granules** are of rough endoplasmic reticulum (RER) with rosettes of free ribosomes, and are the site of protein synthesis.



# Red neurons



# Red neurons



# Subacute and chronic neuronal injury

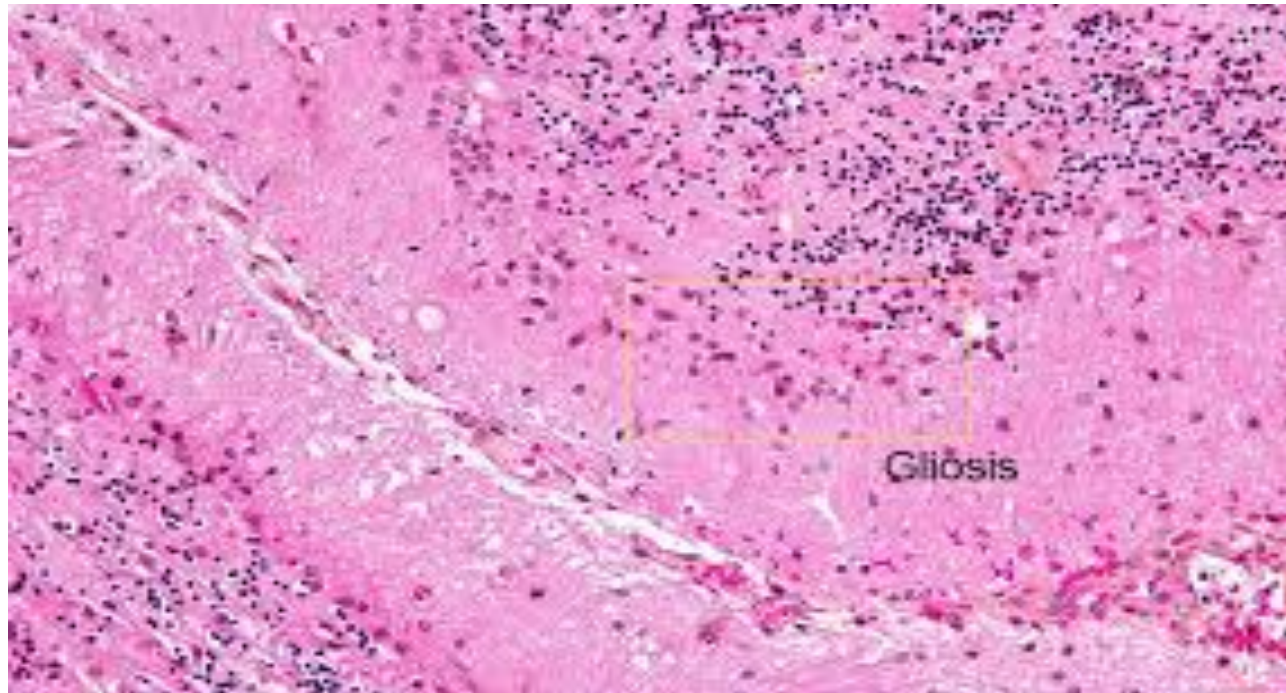
- =degeneration
  - Neuronal death due to progressive disease
  - Example: in Alzheimer
  - Cell loss affecting functionally related neurons ( not necessarily structurally related)
- Neuronal death usually is apoptotic death and is associated with reactive gliosis.

# GLIOSIS

- **Glios**is is a nonspecific reactive change of glial cells in response to damage to CNS. In most cases, **gliosis** involves the **proliferation &/ or hypertrophy of several different types of glial cells**, including astrocytes, microglia, and oligodendrocytes.
- SO: GLIAL CELLS **CAN PROLIFERATE AND DIVIDE** IN RESPONSE TO INJURY.



Gliosis simply means increased glial cells  
think of it as counterpart of fibrosis in the rest of  
the body



# Reaction of astrocytes to injury

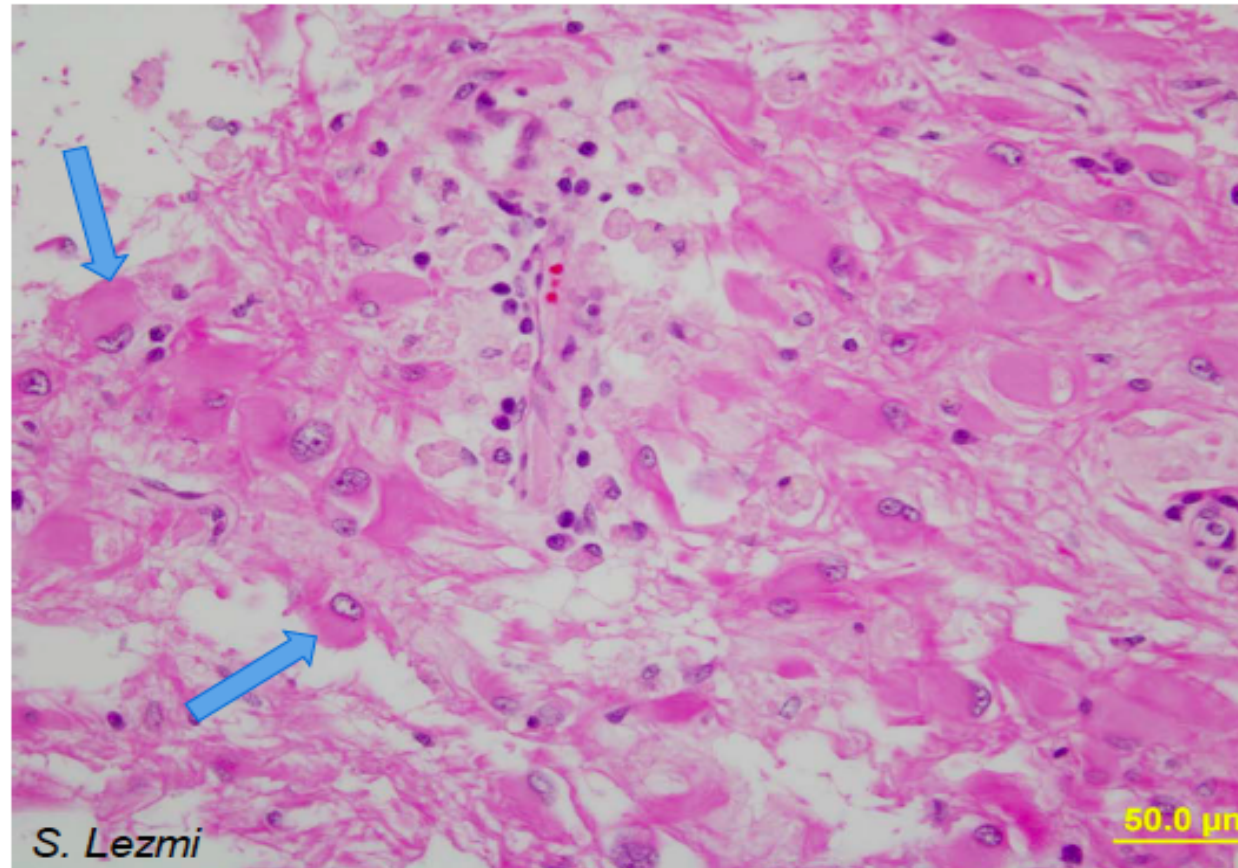
- Astrocytes are the principle cells responsible for repair and scar formation = gliosis
- Reactive astrocytes during repair undergo changes= gemistocytic astrocyte.

# repair

- Astrocytes are the main cells responsible for repair and scar formation (gliosis).
- Injury.. Causes
  1. hypertrophy and hyperplasia in astrocytes.
  2. enlarged nuclei
  3. prominent nucleoli.
  4. increased pink cytoplasm.
  5. increased, ramifying processes

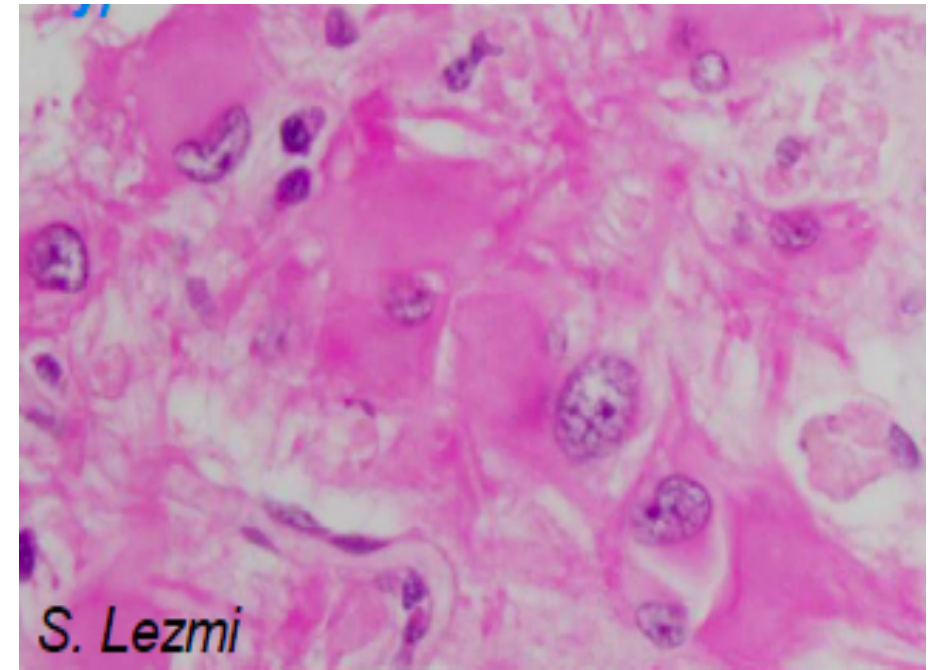
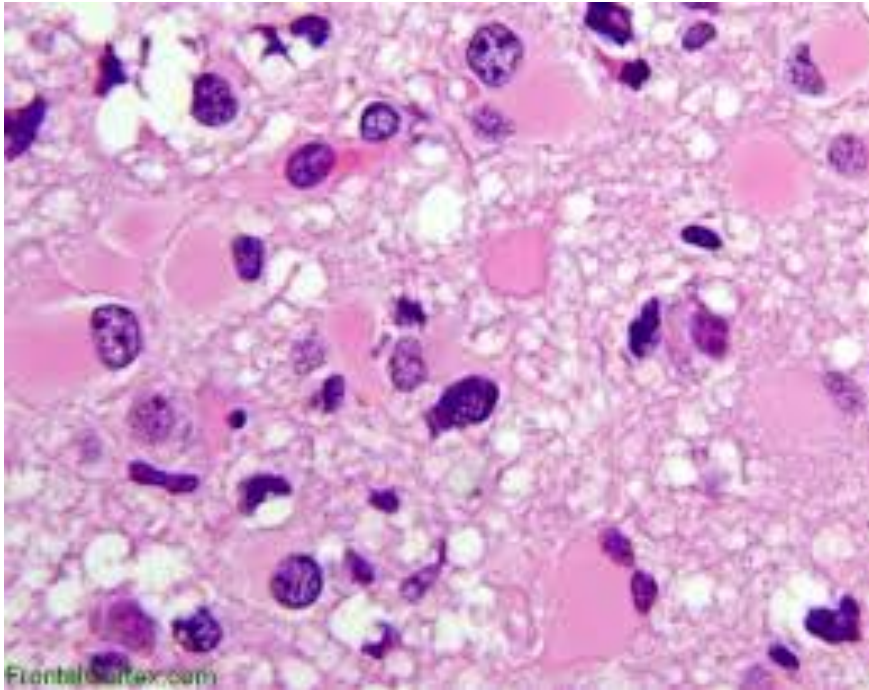
These changes in astrocytes: **gemistocytic astrocyte**.

# gemistocytes





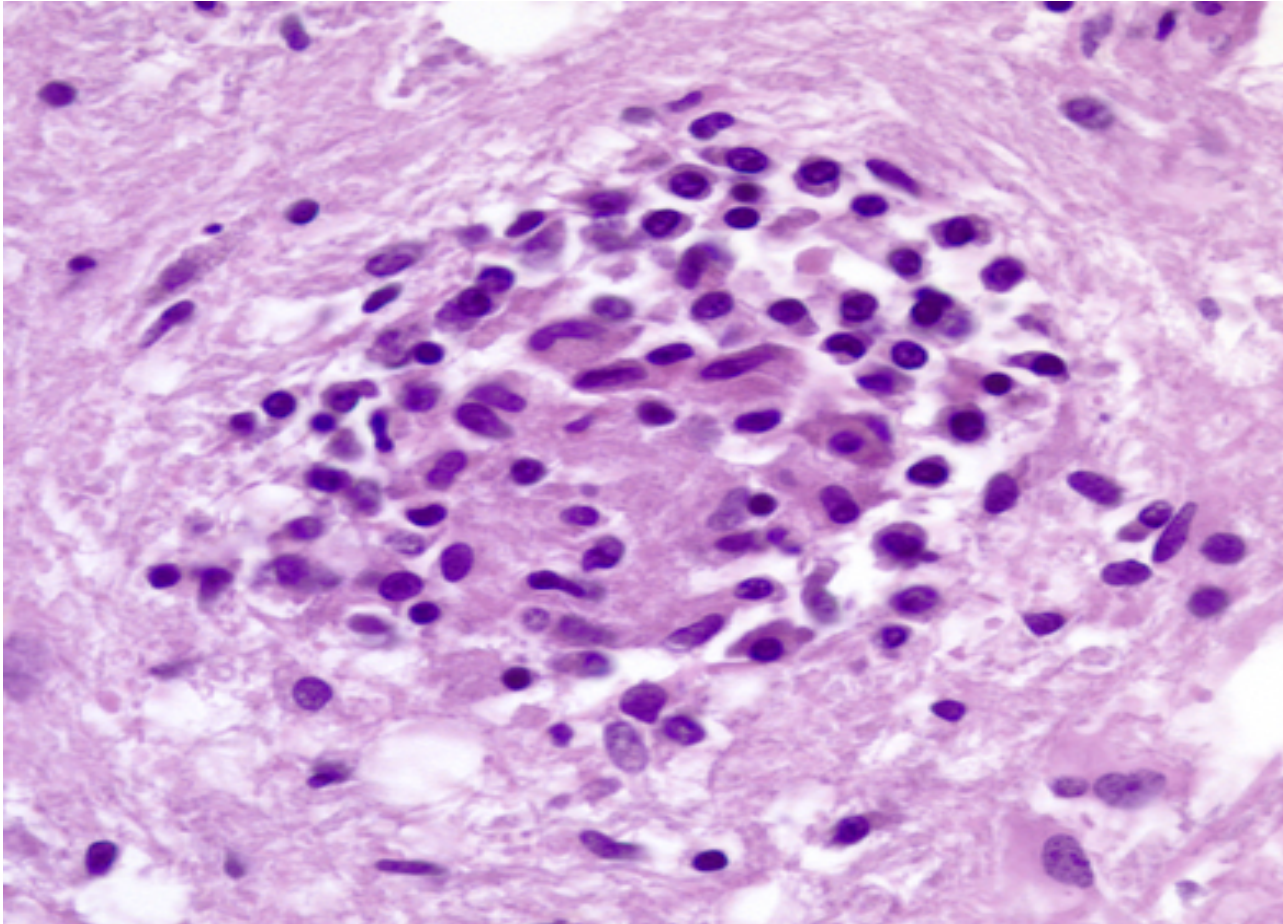
# Gemistocytes



# Reactions of Microglia to Injury

- Microglia are mesoderm-derived phagocytic cells that serve as the resident macrophages of the CNS.
- They respond to injury by (1) proliferating; (2) developing elongated nuclei (*rod cells*) (3) forming aggregates around small foci of tissue necrosis (*microglial nodules*); or (4) congregating around cell bodies of dying neurons (*neuronophagia*).
- In addition to resident microglia, blood-derived macrophages may also be present in inflammatory foci.

# Microglial nodules



# Rod cells

