NERVOUS SYSTEM PATHOLOGY

Prof. Dr. Sevil Atalay Vural

MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM

- **DUPLICATION OF PROSENCEPHALON**
- **MICROENCEPHALY** (**An abnormally small brain**/the diminution affects particularly the cerebrum).
- **CORTICAL DYSPLASIA AND GYRUS MALFORMATIONS**
  - ✓**Neuronal Heterotropia**
  - ✓**MIcrogyrIa (polymicrogyria)**
  - ✓**Ulegyria**
  - ✓**Lissencephaly**
  - ✓**Pachygyria**

MALFORMATIONS OF THE CENTRAL NERVOUS SYSTEM

- **CORTICAL DYSPLASIA AND GYRUS MALFORMATIONS**

✓**Neuronal Heterotropia**

The presence of clusters of nerve cells at a site **where they are normally absent**, such as subcortical white matter

✓**Microgyria (polymicrogyria)**

Convolutions **are small and unusually numerous**, and the normal gyral pattern is lost in affected areas

✓**Ulegyria**

Also a wrinkled appearance of the cortex but arises as a consequence of **scarring** and atrophy in otherwise topographically normal gyri/ it is a result of laminar necrosis of the deep sulcal cortex

- ✓**Lissencephaly (agyria)** Convolutions are almost entirely absent
- ✓**Pachygyria** (**macrogyria)** excessively broad brain convolutions

AGENESIS OF THE CORPUS CALLOSUM

Partial or complete absence (agenesis) of an area of the brain that connects the two cerebral hemispheres.

HOLOPROSENCEPHALIA

Failure of the forebrain to separate normally into 2 discrete cerebral hemispheres.

It includes deformities in the hemispheres and especially aplasias in the bulbus olfactorius and tracts.

Dysplasias are usually associated with facial deformities and are closely related to nervous system findings.

Cyclopia is the most severe of these malformations, and sebocephaly is the mild form

AGENESIS OF THE CORPUS CALLOSUM

Partial or complete absence (agenesis) of an area of the brain that connects the two cerebral hemispheres.

CYSTIC SEPTUM PELLUCIDUM

A cystic fluid filled cavity between the lateral ventricles that varies from a thin slit to a rounder cavity.

This defect is seen together with other defects in fetal infections of Akabane, bluetongue, BVD and border disease viruses.

CYCLOPIA (synophthalmia)

- ✓ **Single large median eye**
- ✓ Failure of division of the optic primordium into paired symmetric optic stalks and vesicles, which therefore results in a single midline globe
- ✓ Ewes ingesting the plant "**veratrum californicum**" on day 14 of gestation give birth to lambs with cyclopia

CEBOCEPHALY (monkey face)

- ✓ Anatomically comparable to cyclopia
- ✓ There are 2 eyes, severely hypoplastic, in separate but approximated orbits.

DYSRAPHIC MALFORMATIONS

- ✓ **ANENCEPHALY** (Absence of brain)
  - **Acrania** (Complete failure of cranial development)
  - **Cranioschisis** (The cranium fails to close completely)
  - **Craniorachischisis** (Both **the brain and spinal cord** fails to close; both anencephaly and spina bifida are present)

- **DYSRAPHIC MALFORMATIONS**

  ✓**CRANIUM BIFIDUM AND RELATED DEFECTS**

  - **Encephalocele** (Protrusion of the brain through a defect in the cranium / **Cranium bifidum**)
  - **Meningocele** (Only fluid-filled meninges protrude)
  - **Meningoencephalocele (**Meningeal and brain tissue protrusion).

HYDROCEPHALUS

- Excessive accumulation of fluid in the cranial cavity

  ✓**Internal Hydocephalus** (The fluid is within the ventricular system)

  ✓**External Hydrocephalus** (The fluid is in the arachnoid space)

  ✓**Communicating Hydrocephalus** (The excess fluid is present in both locations)

- **Cerebrospinal fluid (CSF)** is produced by the ventricular choroid plexuses by means of filtration and secretion.

- The flow of CSF is from the **lateral ventricle** through the **interventricular foramen** to the **third ventricle** and then via the **cerebral aqueduct** to the **fourth ventricle.**
- From here, most of the fluid leaves the ventricular system and passes by way of the **lateral aperture of fourth ventricle** into the **subarachnoid spac**e.

  A small amount of CSF passes into the **central canal of the spinal cord** from the **fourth ventricle**.

- A disturbance of cerebrospinal fluid (CSF) **formation, flow, or absorption,** leads to **excessive accumulation of CSF** within the cerebral ventricles and/or subarachnoid spaces, resulting in ventricular dilation and increased intracranial pressure.

Depending on the aetiology, hydrocephalus is classified into congenital and acquired forms;

✓Congenital Hydrocephalus

- Most common in toy and brachycephalic breed dogs, calves and foals
- The causes include genetic factors, developmental anomalies, intrauterine or prenatal infections, dietary deficiency of vitamin A,
- **If** hydrocephalus develops in infancy *before closure of the cranial sutures*, the head enlarges.

Note the symmetrically enlarged and dome-shaped calvaria. The bone of the calvaria is thinned and distorted from pressure from the expanding brain during gestation.

✓Acquired Hydrocephalus

- The causes are almost always obstructive;
- Causes of obstruction include compression by cerebral abscesses and neoplasms, and blockages by infectious/inflammatory disease resulting in a ventriculitis and, uncommonly, by cholesteatomas in the choroid plexus of the lateral ventricles of the horse.

✓Physiologic Hydrocephalus

Hydrocephalus is "physiologic" in the early fetus when the hemispheres are largely thin-walled vesicles

HYDRANENCEPHALY and PORENCEPHALY

The formation of fluid filled cavities in the brain, termed **porencephaly** (small cavities) and **hydranencephaly** (large cavities), usually occurs **in utero during gestation.**

HYDRANENCEPHALY

- Complete or almost complete absence of the cerebral hemispheres, leaving only membranous sacs filled with CSF and enclosed by leptomeninges.

- The cavitation results from **destruction of immature neuroblasts** whose loss prevents normal development **as a result of faulty or aberrant neuroblast migration.**

- **The cranial cavity is always complete**, in contrast to hydrocephalus

- Hydranencephaly occurs in all species but is more common in calves and lambs.

- Viral causes of hydranencephaly: **Akabane virus, Bluetongue virus, Bovine viral diarrhea virus, Border disease virus,** etc….

CEREBELLAR DEFECTS

- ✓**Cerebellar Hypoplasia (**The size of the cerebellum is reduced)
- ✓**Cerebellar Abiotrophia** (Premature or accelerated degeneration of fully formed cerebellar neurons)
- ✓**Hereditary Striatonigral & Cerebelo-Oliver Degeneration**
- ✓**Hereditary Convulsion and Ataxia of cattle**
- ✓**Gomen Disease**

CEREBELLAR DEFECTS

- **Cerebellar Hypoplasia**

(The size of the cerebellum is reduced)

- One of the most common nervous system defects
- Inherited in Shorthorn cattle, Arabian horses, Arabian horse crosses, Gotland ponies and some dog breeds
- Seen in pups born from pigs treated with organicphosphorus drugs during pregnancy
- In kids and lambs at microscopic level due to copper deficiency.
- Most cerebellar hypoplasias have a viral etiology (Feline parvovirus, BVD virus, border disease virus, and swine cholera virus)

CEREBELLAR DEFECTS

- ✓ **Cerebellar Abiotrophia** (Premature or accelerated degeneration of fully formed cerebellar neurons)
- ✓ In lambs, dogs, Holstein calves and piglets. In lambs, the cerebellum is macroscopically normal in size and appearance.
- ✓ Histological changes are in Purkinje cells in the median lobe. Degeneration and loss of these cells creates empty basket areas
- ✓ At the onset of degeneration, Purkinje cells are shrunken and hyperchromatic, pale in color and contain vacuoles. It then melts and disappears. In their place, gaps remain between the granular and molecular layer.

INTRAUTERINE VIRAL CAUSES OF DEVELOPMENTAL DEFECTS OF THE CENTRAL NERVOUS SYSTEM

- AKABANE VIRUS INFECTION
- CHUZAN VIRUS INFECTION
- CACHE VALLEY VIRUS INFECTION
- BLUE TONGUE VIRUS INFECTION
- RIFT VALLEY FEVER AND VESSEL BRON DISEASES
- BOVINE VIRAL DIARRHEA
- BORDER DISEASE
- HOG CHOLERA
- FELINE PARVOVIRUS INFECTION

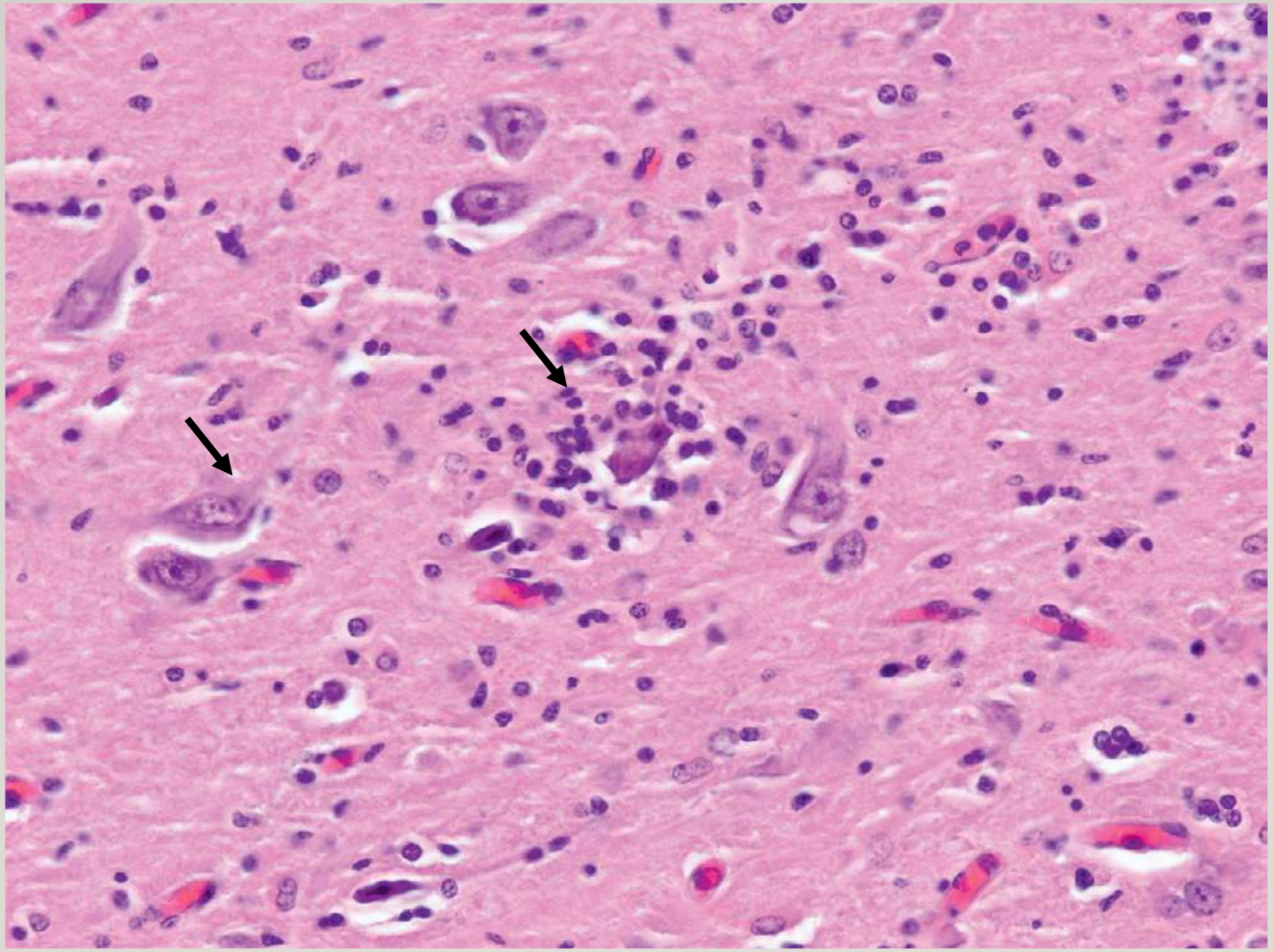
CYTOPATHOLOGY OF NEURONS

- **Nuclear margination** (The neuronal nucleus is usually single and centrally located, and its margination can indicate nonspecific degeneration).
- **Chromatolysis** (Chromatolysis is **about clearing of Nissl granules in the perikaryon**. It is **peripheric** when we have clearing of the periphery of the soma, with Nissl granules persisting around the nucleus. And its **central** when Nissl granules clear from the central region of the cell body.)

✓ **Central chromatolysis**

✓ **Peripheral chromatolysis**

- **Neuronal atrophy** (Loss of cytoplasmic bulk and reduction in size)
- **Liquefactive necrosis**
- **Satellitosis** (gathering of phagocytes around the neuron) **and neuronophagia** (phagocytosis of dead neurons by macrophages)



Perineuronal satellitosis. Glial cells and lymphocytes encircle a necrotic neuron (black arrow). Normal intact neurons are depicted with white arrows in all images.

CYTOPATHOLOGY OF NEURONS

- Ischemic necrosis
- Chronic neuronal injury
- Vacuolar degeneration
- Storage of pigments and other materials
- Siderotic pigmentation of neurons
- Viral inclusion bodies
- Nonviral eosinophilic cytoplasmic inclusion bodies
- Lafora bodies

WALLERIAN DEGENERATION

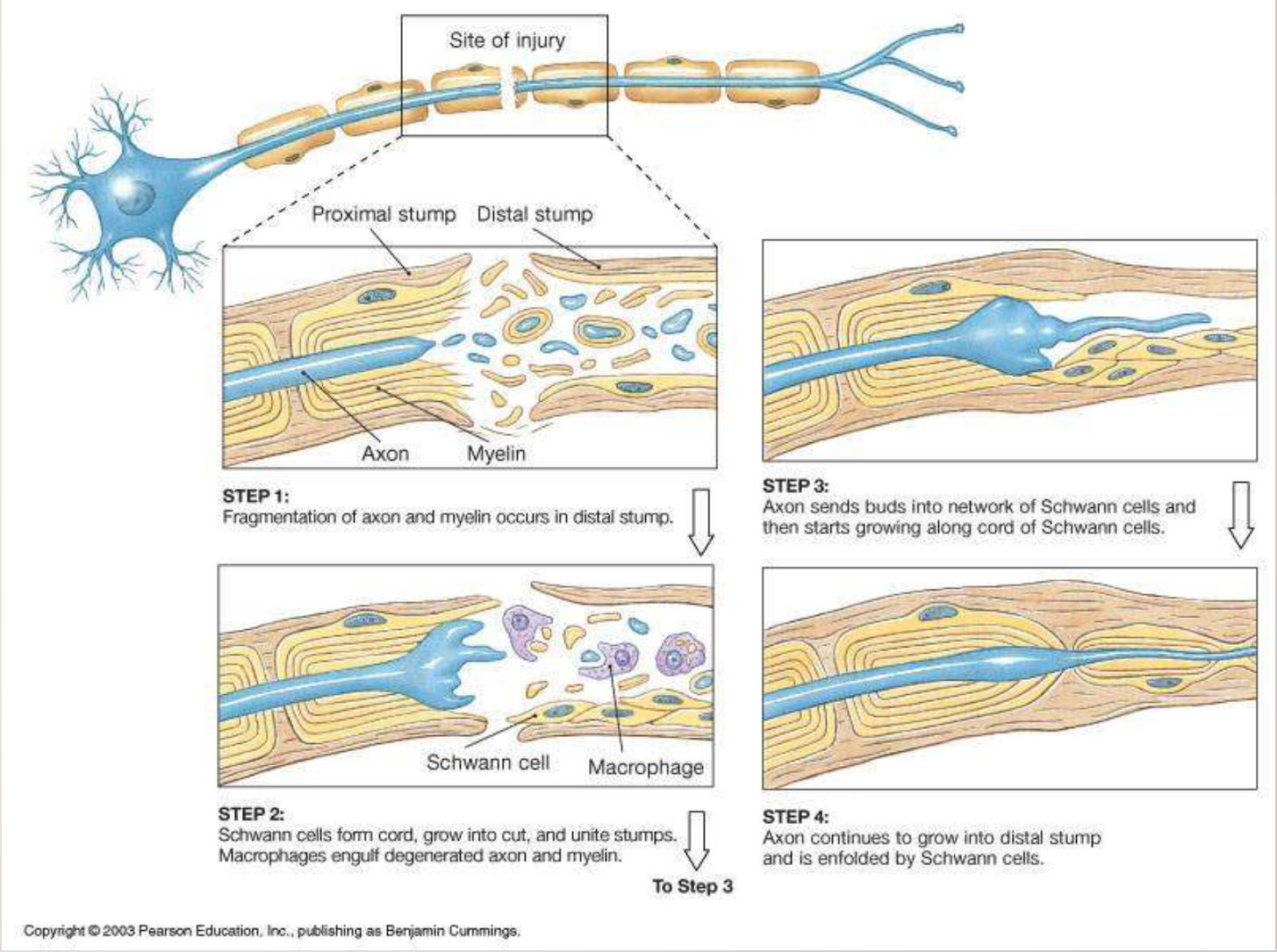
Wallerian degeneration denotes the changes that follow acute focal injury to a myelinated axon.

- First, Focal eosinophilic swellings occur, often containing accumulations of degenerate organelles, and then fragmentation happens.
- The myelin itself condenses into aggregates and fragments and, together with remaining axonal debris, becomes the target of invading macrophages.
- Some of the myelin debris is phagocytosed by Schwann cells themselves, and they begin to proliferate. As the debris is cleared away, proliferating Schwann cells form bands along the myelinated axons.

- Similar Wallerian changes occur at the opposite end of injured axon.

If conditions are favorable at the site of injury, sprouts from the axonal stump will reach to their correct destinations along the Schwann cell bands .

- Finally, a new axon arise and is remyelinated by Schwann cells.



MYELINOPATHIES

- **Hypomyelinogenesis** (a process in which there is underdevelopment of myelin)
- **Dysmyelination** (the formation of biochemically defective myelin)
- **Demyelination** (degeneration and loss of myelin already formed)

MYELINOPATHIES

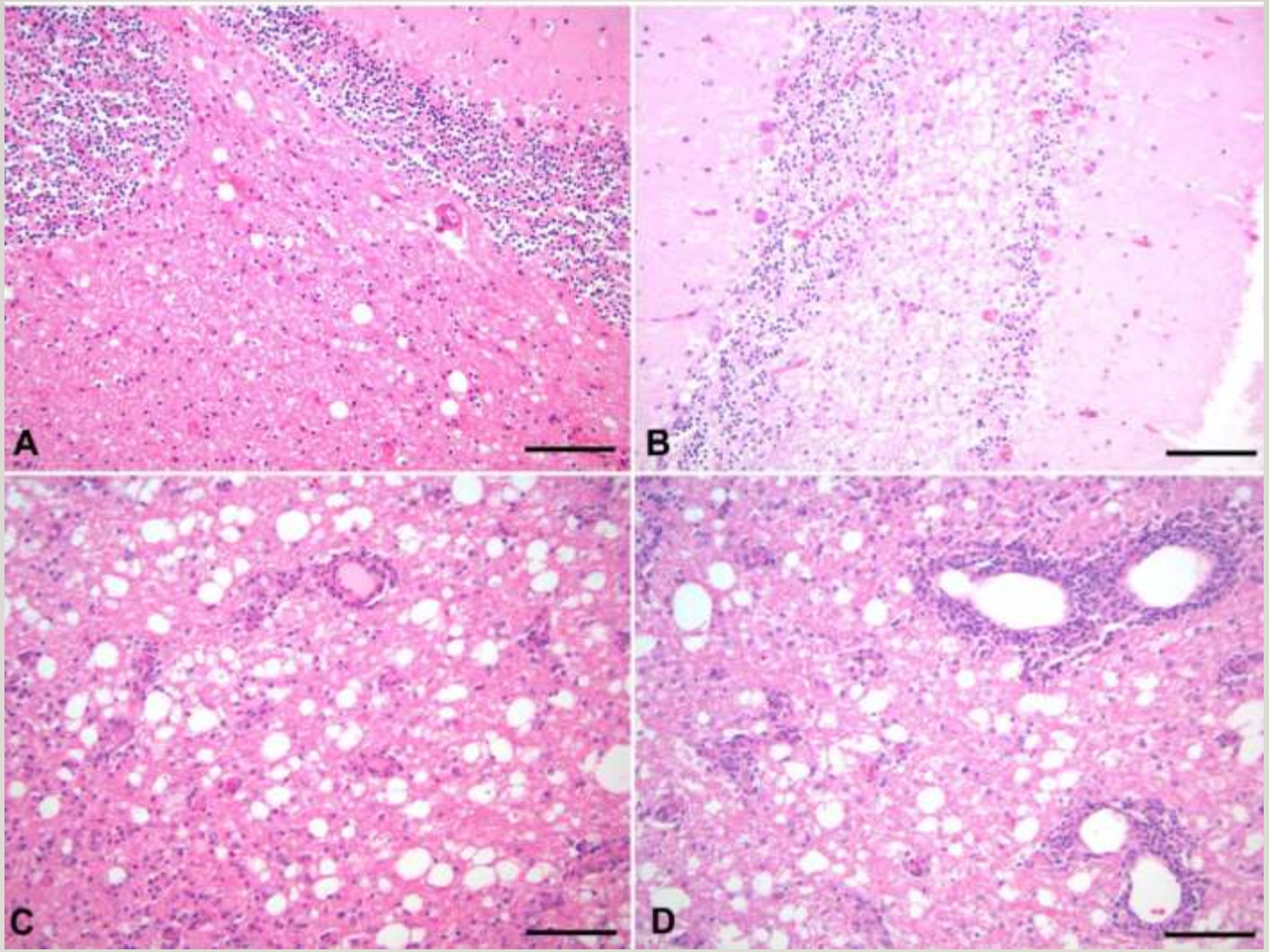
- **Demyelination** (degeneration and loss of myelin already formed)

  Primary demyelination (exp, multiple sclerosis in humans

  Although the axon and nerve cell are intact, the myelin sheath degenerates in B12 avitaminosis and hypersensitivity reactions.

  Secondary demyelination (exp, Waller degeneration)

  Demyelination follows axon degeneration as the axon is destroyed by anoxia, ischemia, infectious agents and toxins.


A
B
C
D

MYELINOPATHIES

- **Intramyelinic edema (Status spongiosus)**

Spongy degeneration or Status spongiosus is a group of diseases of young animals characterized by a motheaten appearance (referred to here as status spongiosus) that primarily occurs in the white matter of the CNS but also extends into the gray matter.

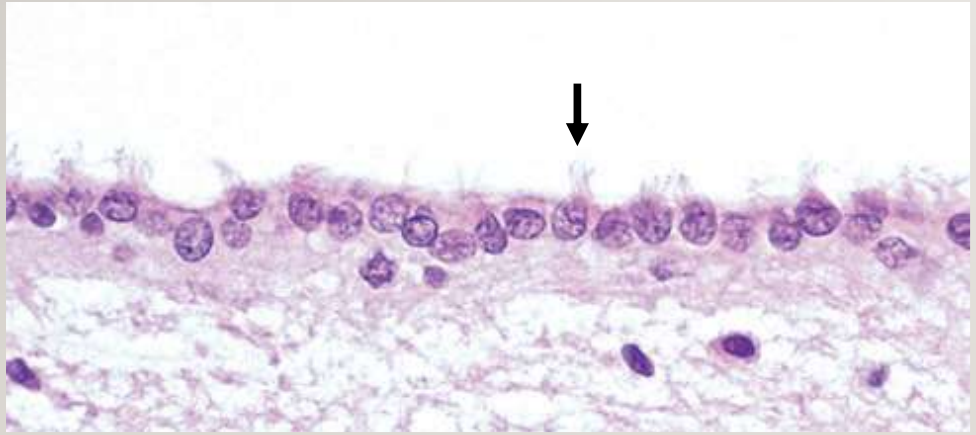
NEUROGLIAL CELLS

Neuroectoderma

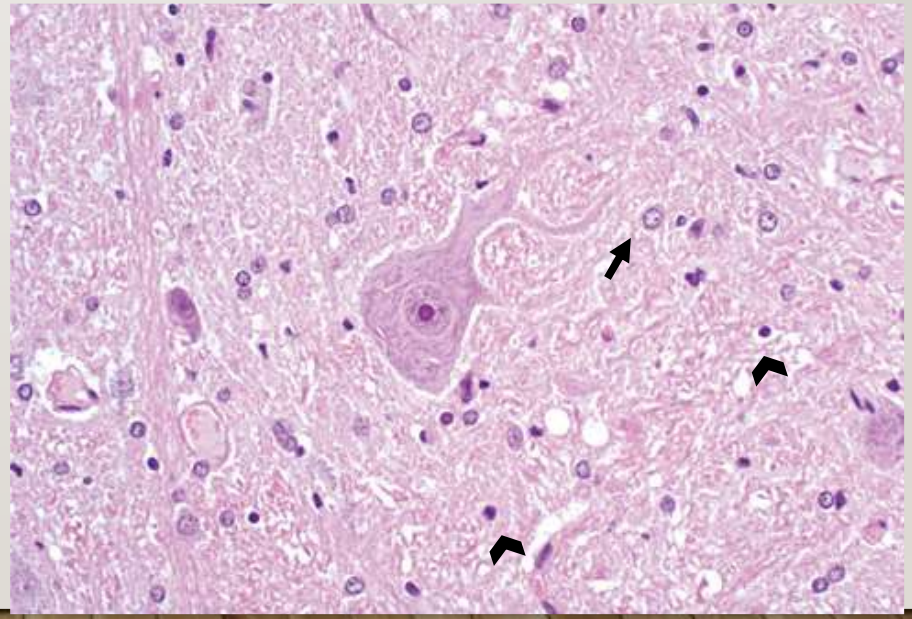
- Astrocyte
- Oligodendroglia
- Ependymal cells

Mesodermal

- Microglia



Ependymal cells are ciliated and assist with the flow of cerebrospinal fluid (CSF) through the ventricular system.



A neuronal cell body and its processes at the center, Astrocytes (arrows) and Oligodendroglial cells (arrowheads)

Increased Intracranial Pressure Cerebral Swelling, and Edema

✓ **Generalized edema**

Acquired hydrocephalus

Vitamin A deficiency

Viral encephalitides

Acute bacterial toxemias (clostridial enterotoxemia)

Chemical intoxications (lead and organomercurial poisoning)

✓ **Localized edema**

Neoplasms

Inflammations

Parasitic cysts

Trauma

(space-occupying lesions of the meninges that cause pressure on the

- **Vasogenic edema, or tissue swelling:**
  - ✓ The most common type of edema in the central nervous system.
  - ✓ Common complication of traumatic, inflammatory, neoplastic, and haemorrhagic lesions of the nervous system.
  - ✓ Injury to vascular endothelium and leakage of plasma constituents into the perivascular extracellular space, particularly that of the white matter

- **Cytotoxic edema, or cell swelling:**
  - ✓ The accumulation of fluid intracellularly in neurons, astrocytes, oligodendroglia, and endothelial cells (called hydropic degeneration in other cells of the body) as a result of altered cellular metabolism, often caused by ischemia.

- **Interstitial (Hydrostatic) edema** is characterized by the accumulation of fluid in the extracellular space of the brain because of elevated ventricular hydrostatic pressure.

  As for interstitial cerebral edema results from the outflow of cerebrospinal fluid from the intraventricular space to the interstitial areas of the brain

  Hydrocephalus → **Interstitial edema** that affects the central white matter

  Hydromyelia and syringomyelia → **Interstitial edema** that affects the spinal cord

LESIONS OF BLOOD VESSELS AND CIRCULATORY DISTURBANCES

The blood supply to the brain is derived from the **internal carotid** and **vertebral arteries**

Circulatory disturbances

Ischemic lesions	Hemorrhagic lesions	Microcirculatory lesions
Arteriosclerotic changes	Spontaneous hemorrhages	Diapedesis of red cells
Hyaline necrosis	Isolated hemorrhages or hematomas	Leakage of plasma
Amyloid degeneration	Epidural/subdural meningeal hemorrhages	
Cerebrospinal vasculitis		
Thrombosis and embolism		
Result = arterial venous infarcts		

Disturbances in the cerebrospinal vasculature with impaired blood flow may be ischemic (**obstructive lesions**

Degenerative vascular disease of **arteriosclerotic type** is not of great importance in animal diseases.

Hyaline necrosis in meningeal vessels, which is observed in swine.

Amyloid degeneration of meningeal and intracerebral vessels occurs in aged dogs.

Cerebrospinal vasculitis occurs in infectious diseases, genetic disorders, presumed autoimmune diseases, and neoplastic diseases of many animal species.

Thrombosis and embolism in the cerebrospinal arterioles is very seldom observed in animals (arterial venous infarcts)

Hemorrhages in the central nervous system (CNS) may be traumatic or spontaneous. Isolated hemorrhages or hematomas are quite rare in animals. They may result from vascular malformations (hamartomas) or tumors (cavernous hemangiomas). Meningeal hemorrhages, both epidural and subdural, are common in lambs and calves that have required obstetric assistance.

Microcirculatory lesions A range of changes affecting the microcirculation in the nervous system may not produce ischemia or hemorrhage.