VIRAL INFECTIONS OF THE NERVOUS SYSTEM

Vascular changes

- ✓ Perivascular cuffing, or accumulation of cells in the adventitia of vessels and in the perivascular Virchow-Robin space (*Infiltrating cells are predominantly lymphocytes)*
- ✓ Hyalinizing or fibrinoid change of the vessel wall (malignant catarrhal fever , equine encephalitis.
- ✓ Endothelial swelling and proliferation (The perivascular cuffs can be large enough to compress the wall of the vessels and the endothelium may be injured such as in classical swine fever and infectious canine hepatitis)

VIRAL INFECTIONS OF THE NERVOUS SYSTEM

- ✓ **Glial reactions:** Diffuse or focal gliosis but is commonly both.
- ✓ **Neuronal degeneration and necrosis**
- ✓ **Demyelination (**as canine distemper, lentivirus leukoencephalitis of goats, and visna)
- ✓ **Meningitis**
- ✓ **Inclusion bodies (**neurons / Rabies, neuroglia, or microglia and other mesenchymal cells. Inclusion bodies in the nervous system are usually acidophilic)

RABIES

- Caused by the species ***Rabies virus*** (RABV), genus ***Lyssavirus***, family ***Rhabdoviridae***.

- Rabies virus has 2 biotypes: "fixed" virus and "street" virus:

✓ Fixed RABV, which is the basis of vaccine strains, is a laboratory biotype, is not secreted in saliva, and does not produce Negri bodies.

✓ Street RABV is the feral biotype, it is tropic for salivary glands and produces Negri bodies.

Pathogenesis of Rabies

It all starts with inoculation of the virus into a wound, which is usually a bite of a rabid animal

After a bite wound,

(1, 2) the rabies virus initially replicates in muscle around the wound bite and then the viral particles invade the local neuromuscular junction and invade neurotendinous spindles and ascend to the CNS (3) and paravertebral ganglia via axoplasmic flow

(can enter peripheral nerves directly), *2*, enters, *3*, and ascends (retrograde axonal transport) the peripheral nerve

Pathogenesis of Rabies

2, enters, *3*, and ascends (retrograde axonal transport) the peripheral nerve,
4, to the dorsal root ganglion,
5, enters the spinal cord,
6, and ascends, *7*, to the brain via ascending and descending nerve fiber tracts, infects brain cells, spreads to salivary glands,
8, and the eye and is excreted in saliva.
After replicating in the central nervous system, centrifugal spread to salivary glands and eye (8)
Andddd virus is secreted through saliva for a few days prior to the appearance of clinical signs.

Pathogenesis of Rabies

There are reported exceptions for transmission by bites, but with a much lesser occurrence frequency .
For example :

Ocular infection
Aerosol infection

Any mammal can become infected with rabies.
The principal reservoir vectors differ according to the region. Bats, skunks, foxes, dogs are examples.
Oral vaccination of wild carnivores, by using vaccine-laden baits, and routine vaccination of dogs have led to almost complete elimination of canine transmitted rabies in developed countries.

- The **clinical course** of rabies is usually acute, from 1-2 days, but can be as long as 10 days.
- The clinical disease in the dog has been divided into three phases: **prodromal, excitatory, and paralytic**.

Furious rabies = the excitatory phase is predominant,

Dumb rabies =excitatory phase is short or absent and the disease progresses quickly to the paralytic phase.

TYPICAL PATHOLOGICAL FINDINGS

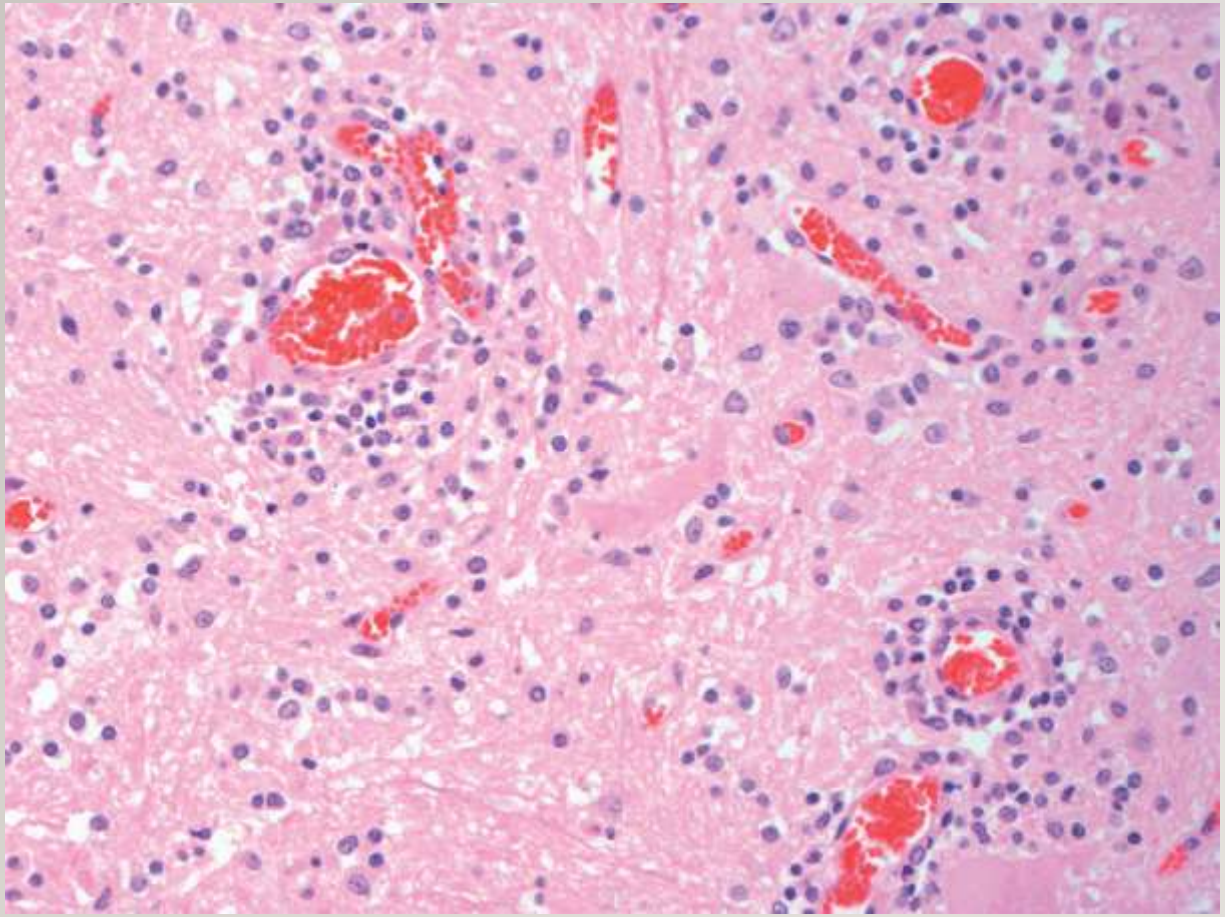
- ✓ **Nonsuppurative encephalomyelitis**
- ✓ **Ganglioneuritis**
- ✓ **Sialoadenitis (parotid adenitis)**

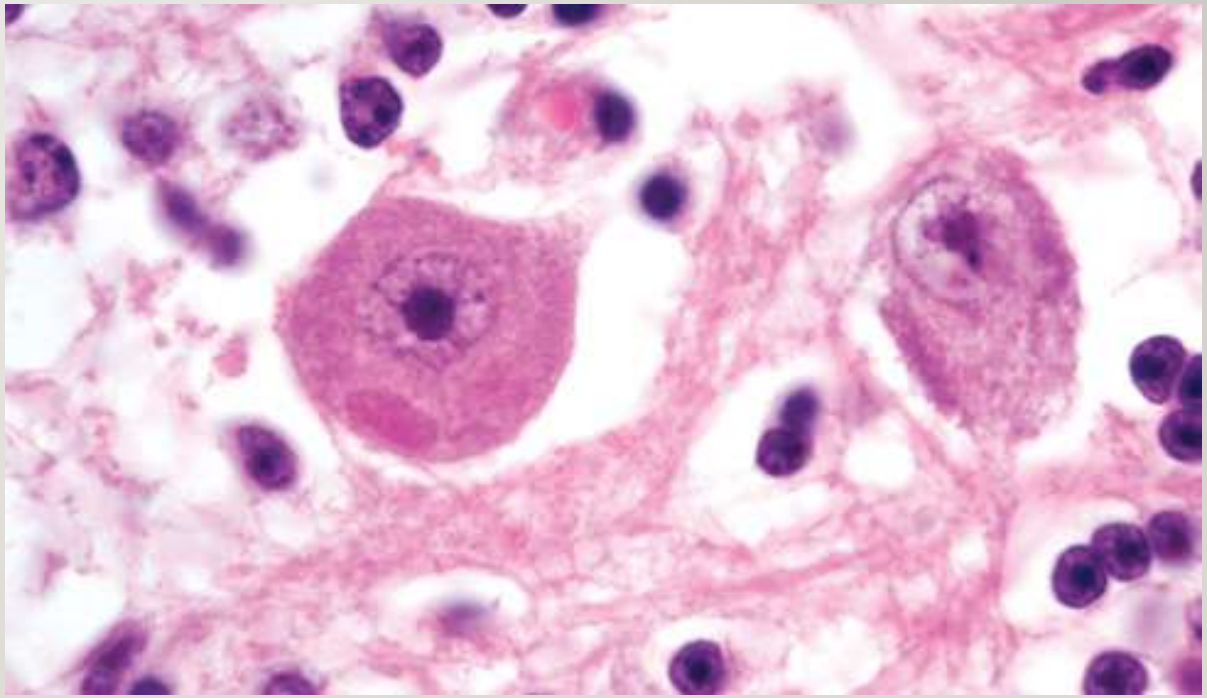
Specific gross lesions are no seen at necropsy

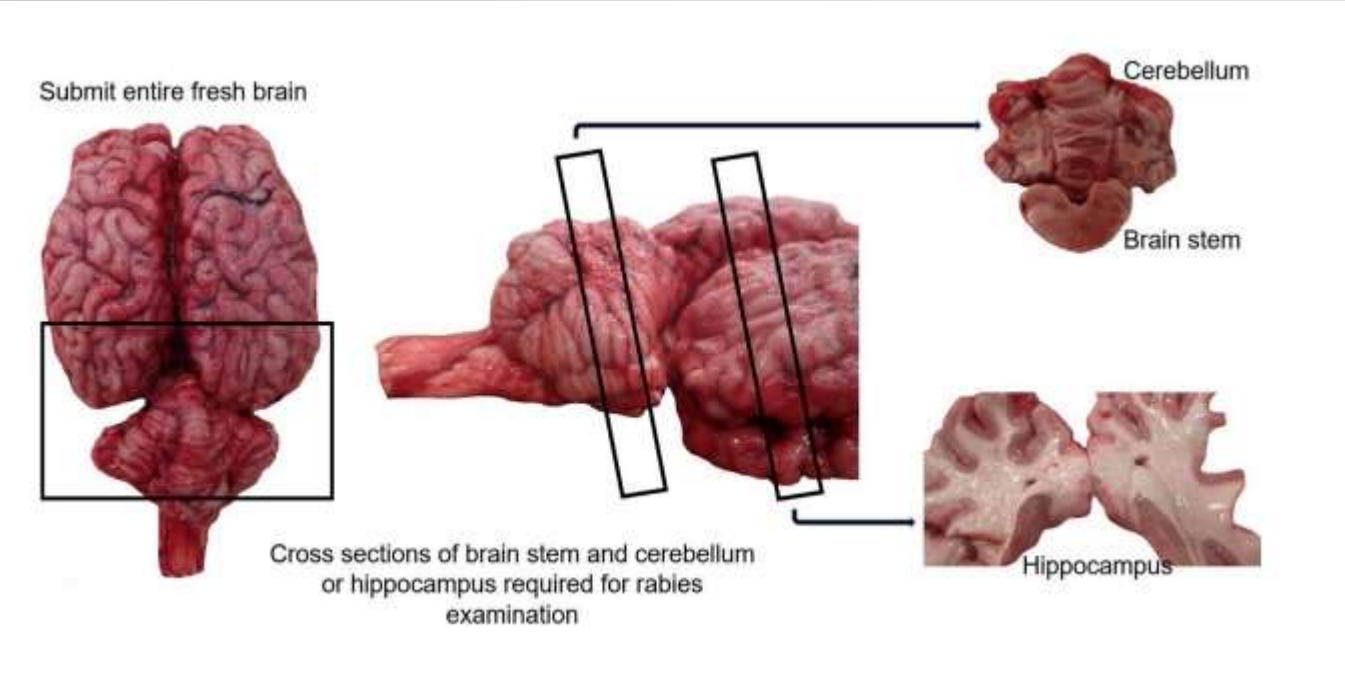
Self-inflicted wounds and foreign bodies in the stomach of a carnivore should raise suspicion.

Histologic lesions of rabies:

- ✓ Perivascular cuffing (composed solely of lymphocytes)
- ✓ Neuronal degeneration
- ✓ Babès' nodules
- ✓ Focal and diffuse gliosis
- ✓ Negri bodies (intracytoplasmic inclusion bodies present in the hippocampus of carnivores and in the Purkinje cells of herbivores).







https://www.vdl.ndsu.edu/sample-submission-guidelines-for-rabies-testing/

Sampling

- Brain stem
  - M. oblongata
- Cerebellum
- Hippocampus
  - Cornu ammonis

- Cerebral cortex

Diagnosis of rabies

- Fluorescent antibody labelling
- Immunohistochemistry performed on paraffin embedded formalin-fixed tissues
- In situ hybridization,
- Electron microscopy,
- PCR-based testing

AUJESZKY'S DISEASE

- Pseudorabies/"Mad itch"
- Not zoonotic
- Pseudorabies is not related to rabies but was named because its clinical signs sometimes resemble those seen with rabies.
- *Suid herpesvirus 1* (SuHV-1)
- Causes **encephalitis** primarily in **pigs**; the disease is sporadic in cattle, dogs, cats, sheep rats and minkes.
- Young, suckling piglets—can die from infection,

Mature pigs — remain persistently infected and act as latent carriers.

- **The signs and course** of pseudorabies in pigs are very variable.
- The mortality rate in nursing pigs and young weaners may be very high.
- In slightly older piglets, incoordination progresses rapidly to paralysis with muscular twitchings, tremors, and convulsion.
- The disease in older pigs is often characterized by fever, rhinitis, and coughing.
- Fetal resorption, mummification, stillbirths, and abortions are reported frequently.

- The CNS is free of **gross lesions.**

✓ Gross lesions in nonneural tissues, include organs of the respiratory system, lymphoid system, digestive tract, and reproductive tract.

✓ Focal tissue necrosis also occurs in the liver, spleen, and adrenal glands, particularly in young suckling pigs.

✓ Evidence of facial pruritus is a common sequela to infection.

Microscopic lesions in pigs :

- Nonsuppurative meningoencephalomyelitis with Trigeminal ganglioneuritis.

- Intranuclear amphophilic inclusion bodies can be present in neurons and astrocytes.

➢ In cattle, sheep, dogs, and cats, the pathogenesis and lesions are comparable to that of pigs.

LOUPING ILL
(OVINE ENCEPHALOMYELITIS)

- Tick-borne viral polioencephalomyelitis of sheep caused by sp
  Louping ill virus (LIV).

- Cattle, horses, goats, deer and human can contract the disease.

- Genus *Flavivirus* of the family *Flaviviridae*.
- Informal name for any virus that is transmitted by arthropod vectors
- *Infection___regional lymph nodes___ viremia____CNS via the hematogenous route.*

Alternatively, the virus may localize indirectly from the blood in nasal structures and enter the brain via the ***olfactory nerves****.*

- *Louping ill is a systemic infection*
- Neurologic signs develop at about day 5 and are characterized by **incoordination, tremors, cerebellar ataxia, and terminal paralysis.**
- There are no gross lesions

Histopathologically :

Acute polioencephalomyelitis

Mild leptomeningitis, neuronal degeneration specially in Purkinje cells, cuffing and focal gliosis in the white matter, poliomyelitis affecting particularly the ventral horns, neutrophils very severe cases.

LENTIVIRAL ENCEPHALOMYELITIS OF SHEEP AND

Genus ***Lentivirus***, family ***Retroviridae***

- Caprine arthritis-encephalitis of goats___***Caprine arthritis encephalitis virus*** (CAEV)
- Visna-maedi disease complex of sheep__***Visna-maedi virus*** (VISNA)

In both natural hosts, *4 clinical and pathologic syndromes are recognized:*

- ✓ **Mastitis**
- ✓ **Arthritis**
- ✓ **Interstitial pneumonia** (maedi, or ovine progressive pneumonia)
- ✓ **Encephalomyelitis** (visna of sheep).

VISNA

- **Main clinical signs:** caudal ataxia and fine trembling of the lips.
- **Chronic multifocal *demyelinating leucoencephalomyelitis.***

Caprine arthritis-encephalitis (CAE)

- Arthritis and encephalitis in kids /fatal
- Synovitis and periarthritis in adults.
- Hindlimb lameness and ataxia with paresis that progresses to paralysis.
- Leucoencephalomyelitis, mastitis, interstitial pneumonia.

CANINE DISTEMPER

- ***Morbillivirus*** (family ***Paramyxoviridae***)
- The infection is systemic, and clinical signs are often referable to the **respiratory**, **gastrointestinal,** and **nervous systems**.
- Ocular disease, **pustular and/or hyperkeratotic cutaneous lesions**, **dental defects**, and **abortion** are other manifestations.

- Neurologic signs in all affected species include convulsions, myoclonus, tremor, disturbances in voluntary movement, circling, hyperesthesia, paralysis, and blindness.

- Lesions characteristically occur in the cerebellum, rostral medullary velum, optic tracts, spinal cord, and surrounding the fourth ventricle, and probably arises from distribution of virus through the cerebrospinal fluid.

- **Microscopically**;

✓Demyelination,

✓Gitter cells,

✓Meningitis,

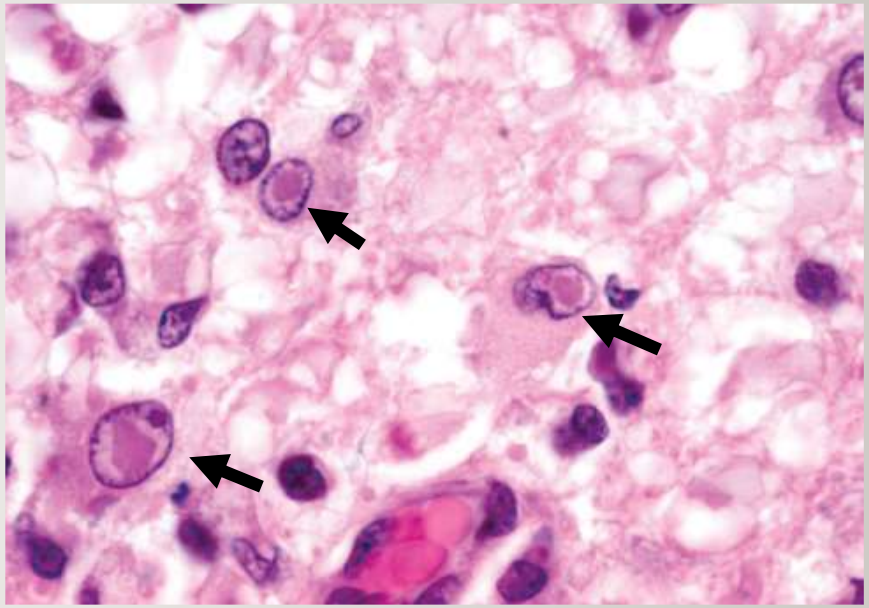
✓Neuronal degeneration,

✓Inclusion bodies (cytoplasmic, nuclear, or both) particularly in astrocytes, but also in ependymal cells and occasionally in neurons,

✓Astrocytic hypertrophy,

✓Microglial proliferation

✓Endothelial proliferation, Perivascular cuffing, vasculitis



Distinct acidophilic *(red)* intranuclear inclusion bodies *(arrows)* are present in astrocytes and some gemistocytes.

Other viral diseases can affect the central nervous system

- Coryza Gangrenosa Bovum
- Infectious canine hepatitis (HCC Hepatitis contagiosa canis)
- *Sporadic Bovine Encephalomyelitis*
- Old dog encephalitis
- Necrotizing meningoencephalitis and necrotizing leukoencephalitis of Pugs and other small-breed dogs
- Granulomatous encephalitis
- Postinfectious encephalomyelitis (*perivenous mononuclear cell infiltration, demyelination)*

PROTOZOAL INFECTIONS

- **Equine protozoal myeloencephalitis**
- **Neosporosis**
- **Toxoplasmosis**
- ***Sarcocystis canis* encephalitis**
- **Sarcocystis-Like ovine encephalomyelitis**
- **Sarcocystis-Like bovine encephalitis**
- *Encephalitozoonosis*

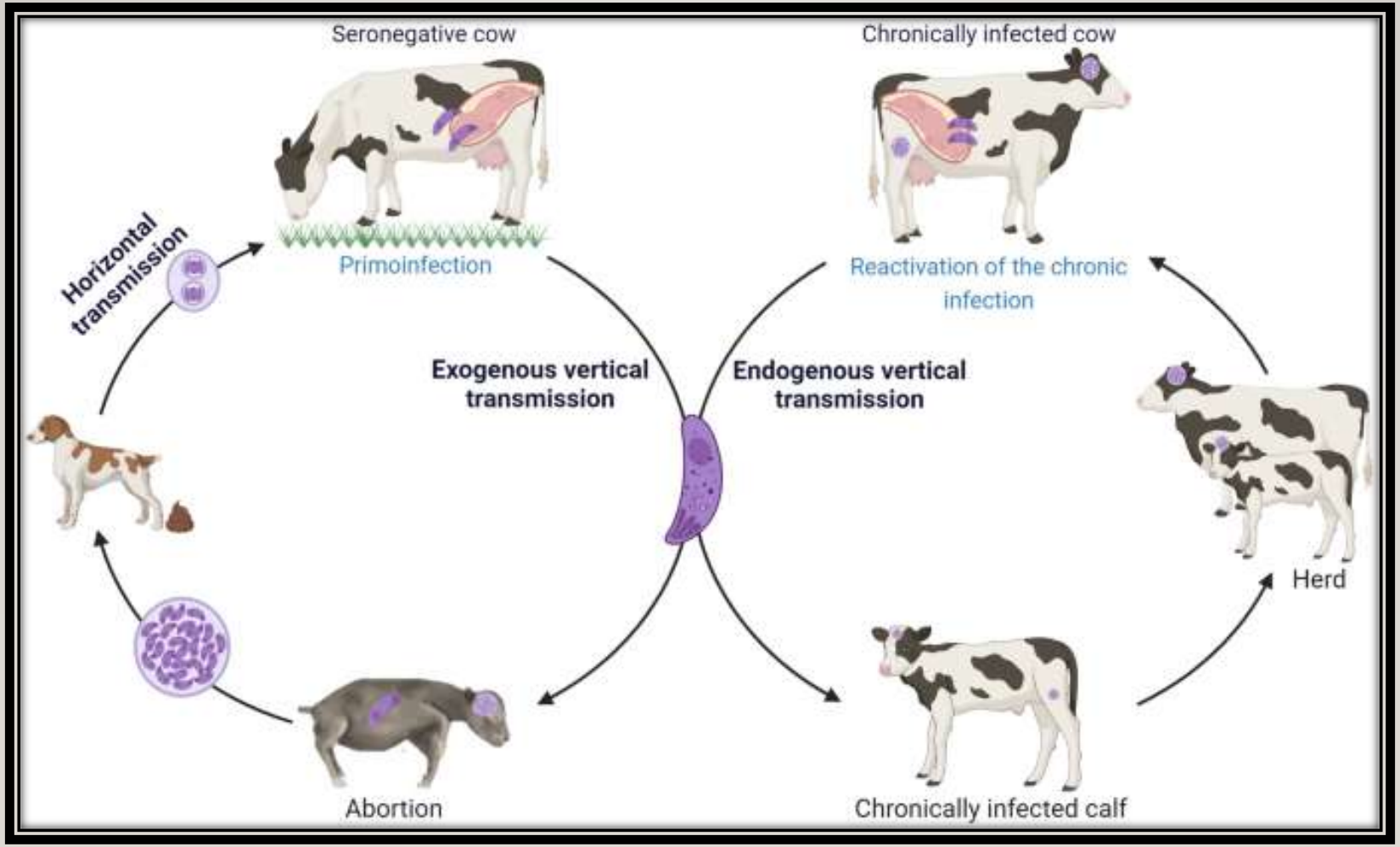
NEOSPOROSIS

Neospora caninum is an apicomplexan coccidian parasite.

Dogs are the primary definitive host, and they are also considered as an intermediate host.

Cattle and other intermediate hosts become infected by ingesting sporulated oocyst-contaminated food, water, or soil.

However, the principal route for infection in cattle is transplacental (vertical) transmission.



https://www.google.com/search?sca_esv=1a93cfe1aa56a321&sxsr

➢ **In cattle** it causes abortion

Extraneural lesions in bovine fetuses include *hepatitis, pancarditis or myocarditis, myositis, and placentitis*.

The most frequent and almost pathognomonic CNS lesion in *bovine fetuses* is the presence of ***multifocal discrete foci of necrosis*** particularly in the brain and to a lesser extent in the cord.

- Neosporosis is a multisystemic infection in the dog

- Infection in adult dogs is usually subclinical.

- Infection in young dogs is severe and characterized pathologically : **Encephalomyelitis**
- **Myositis**
- **Polyradiculoneuritis** and clinically by **hindlimb paresis** that is followed by **paralysis.**

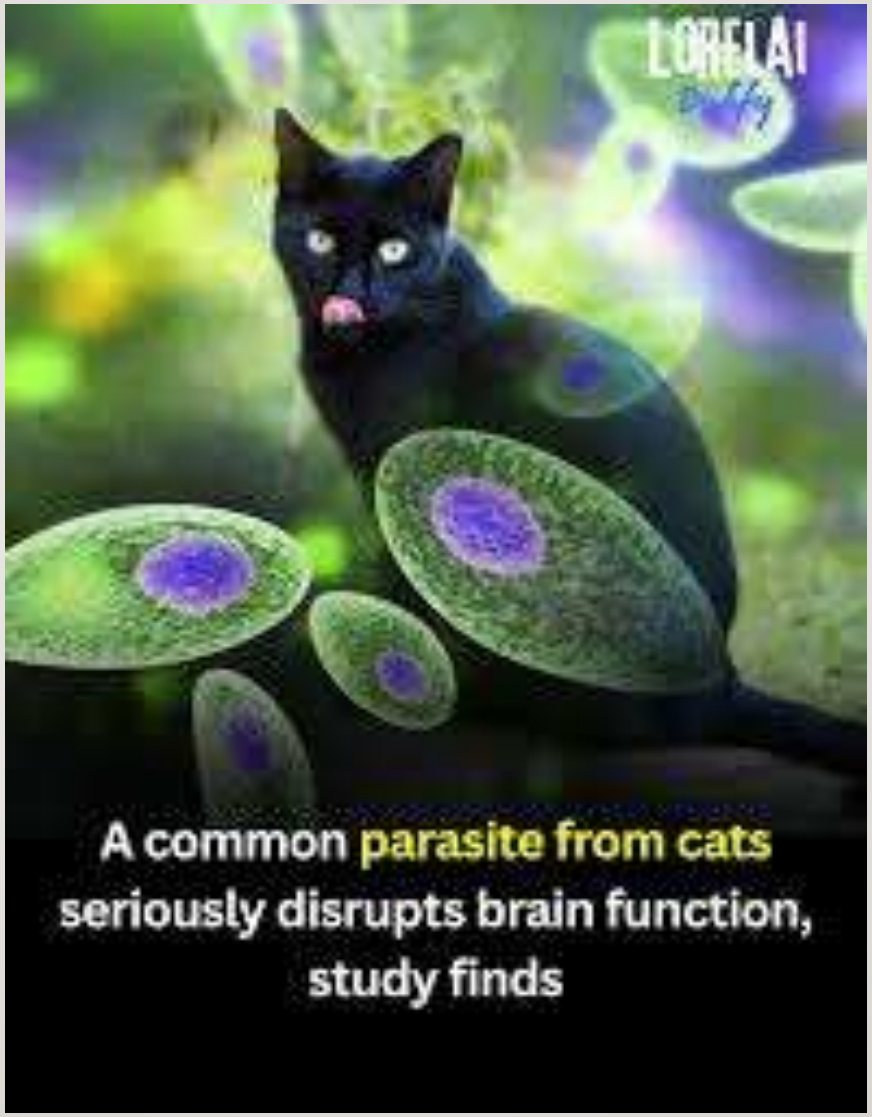
CNS lesions:

- *Necrotizing granulomatous / lymphoplasmacytic / Eosinophilic meningoencephalomyelitis*
- Diffuse gliosis
- Rarely axonal swelling
- Intralesional *N. caninum* tachyzoites and cysts.

TOXOPLASMOSIS

Toxoplasmosis is one of the most common protozoal diseases affecting humans and animals and is caused by ***Toxoplasma gondii.***

Very similar in clinical presentation and pathology to Neosporosis

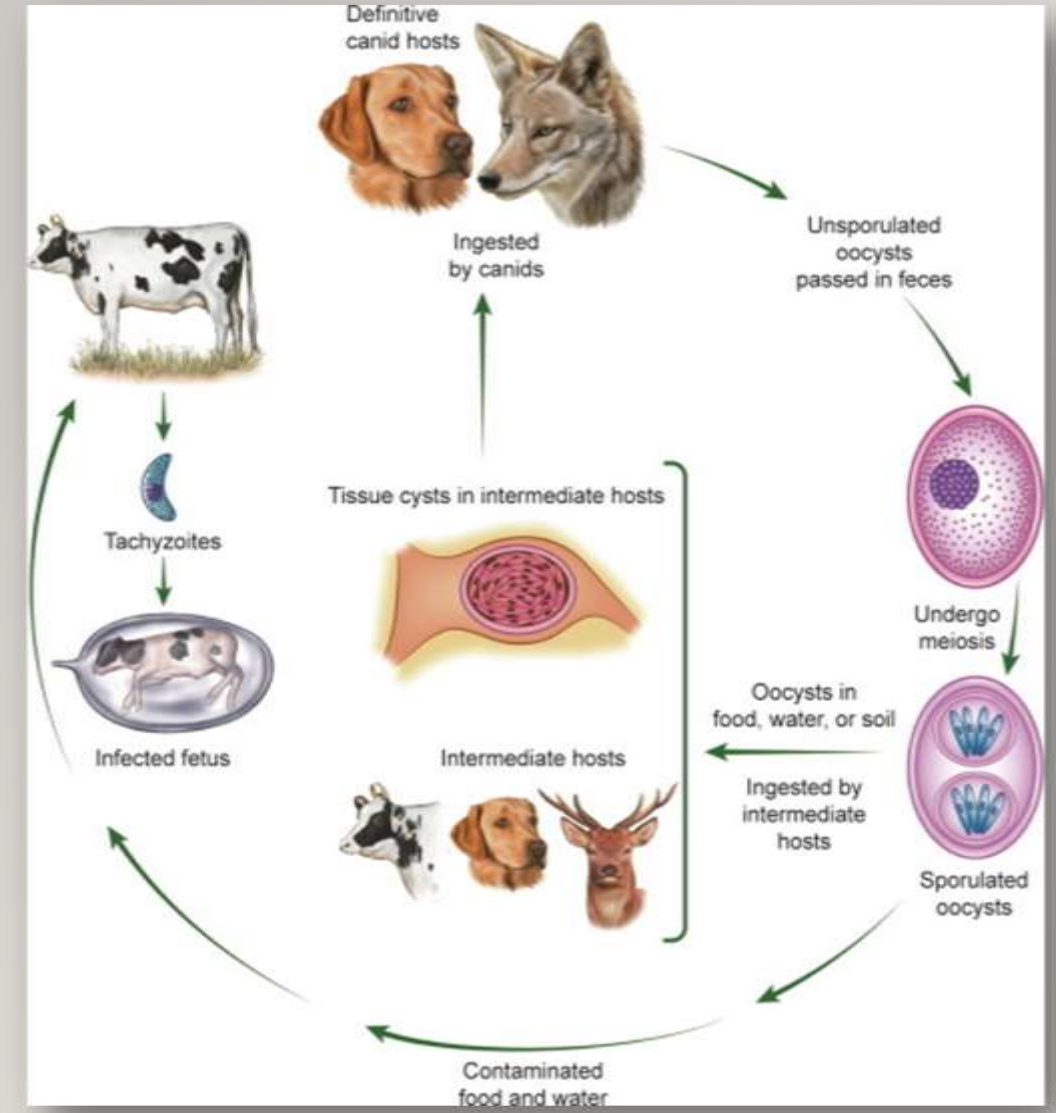


- Felids are the **only definitive host** and they also can act as an intermediate host. Other intermediate hosts include humans and other mammals.

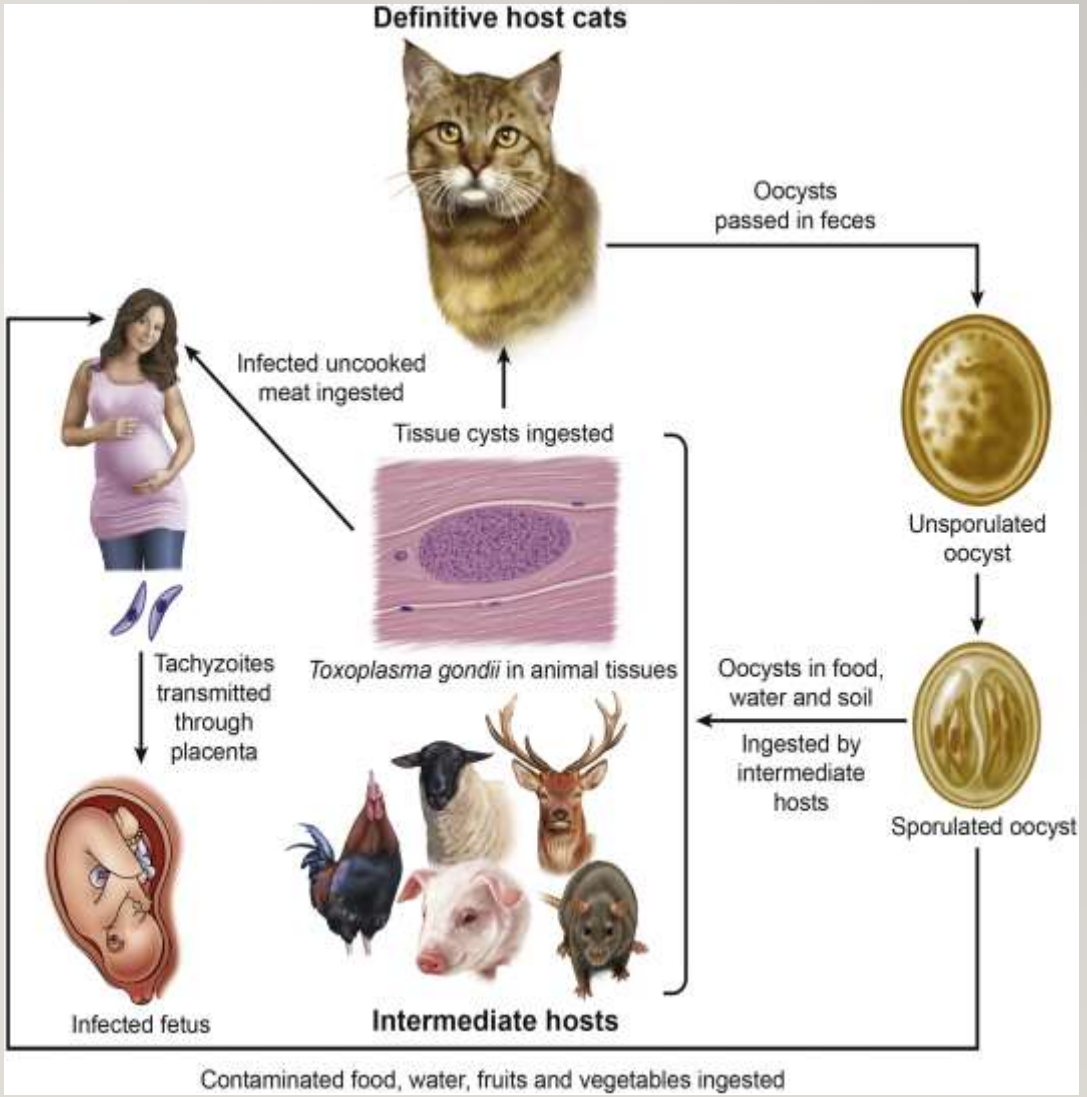
Felids become infected by ingestion of tissues contaminated with tissue cysts, and shed oocysts in their feces.

Human and other intermediate hosts, including felids, can become infected by ingesting sporulated oocyst-contaminated food, water, or soil.

Transplacental transmission is important in cats, goats, and sheep

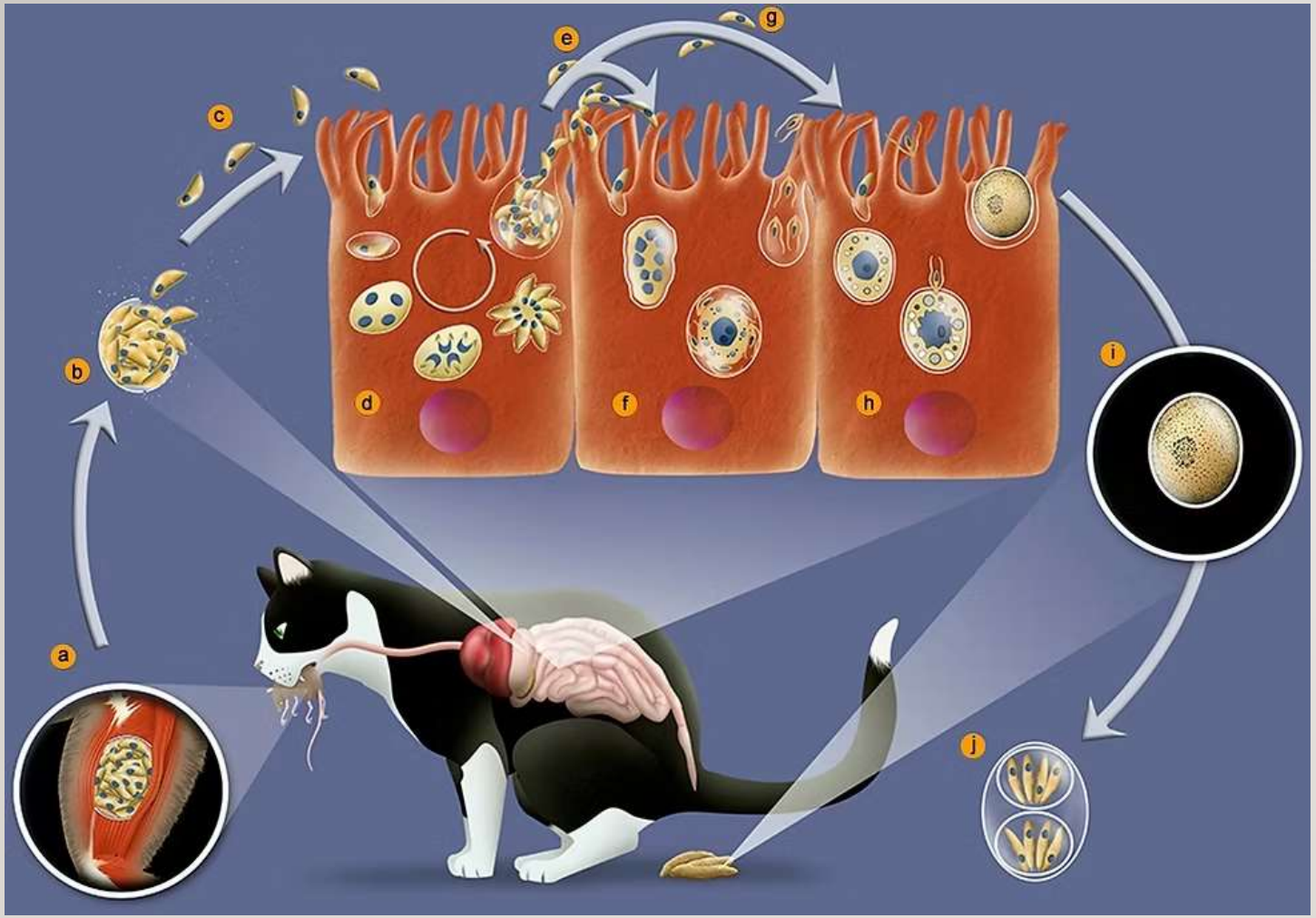


Life cycle of *Neospora caninum.*



Life cycle of *Toxoplasma gondii.*

Neosporosis, Toxoplasmosis, and Sarcocystosis in Ruminants
David S. Lindsay, J.P. Dubey, 2020



https://www.google.com/search?q=toxoplasmosis&sca_esv

a. Ingestion of prey containing tissue cysts.
b. The cyst wall is digested in the stomach and intestines, liberating bradyzoites.
c. Bradyzoites invade epitelial cells of the intestine.
d. In the enterocytes bradyzoites divide by schizogony giving rise to merozoites.
e. Merozoites differentiate into microgamonts, or macrogametes (f).
g. Fertilization gives rise to an unsporulated oocyst excreted with cat feces (h).
i. Sporulation occurs and generates two sporocysts with four sporozoites each (j).

Where is it Found?


Contaminated Meat


Contaminated Water


Contaminated Surfaces


Contaminated Cat Feces

What Does it Infect?


Lungs


Brain


Heart


Eyes

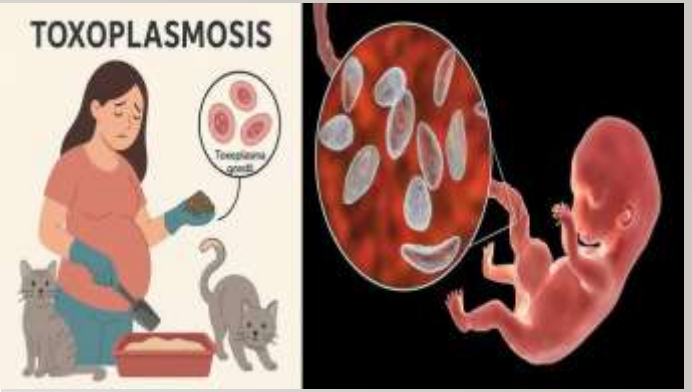
How Does it Spread?


Eating Meat


Drinking Water


Touching Surfaces


Touching Cat Feces



Improper handling of cat litter

https://ultraviolet.com/toxoplasma-gondii-inactivated-uv-light/

- Nervous system lesions including polyradiculoneuritis, are identical to those described for neosporosis; however, the tissue cyst has a **thinner Wall** (<0.5 μm), is 5-70 μm in size, and contains **several bradyzoites** 0.7-1.5 μm. Tachyzoites are 2-6 μm in size.

- The encephalitic form of toxoplasmosis is most likely to occur in immunosuppressed dog and cats or kittens.

NEOPLASTIC DISEASES OF THE NERVOUS SYSTEM

- Tumors of the meninges
  - Meningiomas

Meningotheliomatous or epithelioid meningioma
Psammomatous meningioma
Fibroblastic meningioma
Angiomatous or angioblastic meningiomas
Microcystic meningioma
Chordoid meningioma
Papillary meningiomas
Anaplastic (malignant) meningiomas
Granular cell meningiomas

- Meningeal sarcomatosis

NEOPLASTIC DISEASES OF THE NERVOUS SYSTEM

- Tumors of neuroepithelial tissue

Astrocytoma

Oligodendroglioma

Oligoastrocytoma (mixed glial tumor)

Ependymoma

Choroid plexus tumors

Neuronal and mixed neuronal-glial tumors

Embryonal tumors

Pineal tumors

NEOPLASTIC DISEASES OF THE NERVOUS SYSTEM

- Hematopoietic tumors
- Tumors of the sellar region
- Metastatic tumors
- Tumors of the peripheral nervous system

Peripheral nerve sheath tumors

Peripheral neuroblastic tumors

Paraganglioma

REFERENCES

- Cantile C, Youssef S (2017). Nervous system. In: *Pathologic Basis of Veterinary Disease*, 6th Ed., Ed.: Zachary JF, Elsevier, St. Louis, Missouri. s.: 251-406.

- Miller A, Zachary JF (2016). Nervous system. In: *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals*, 6th Ed., Ed.: Grant Maxie M, Elsevier, St. Louis, Missouri. s.: 806-906