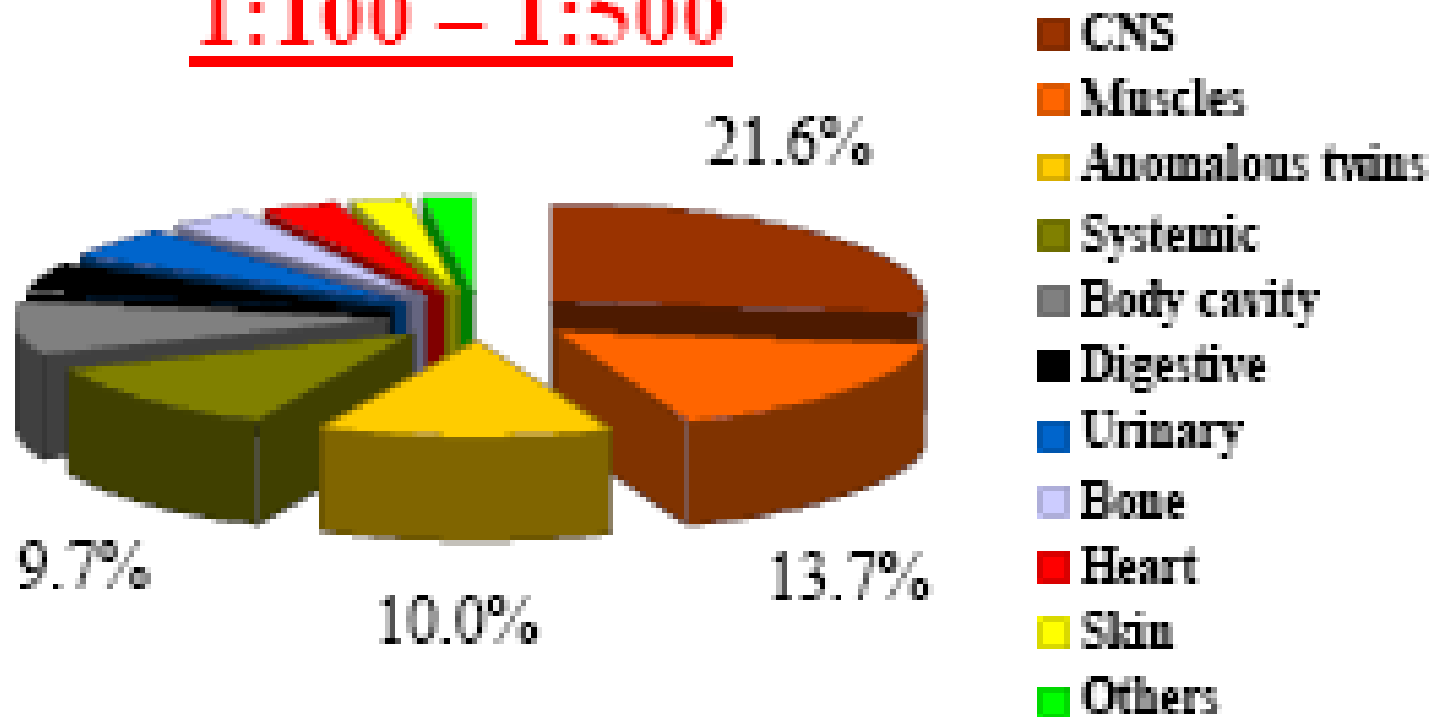
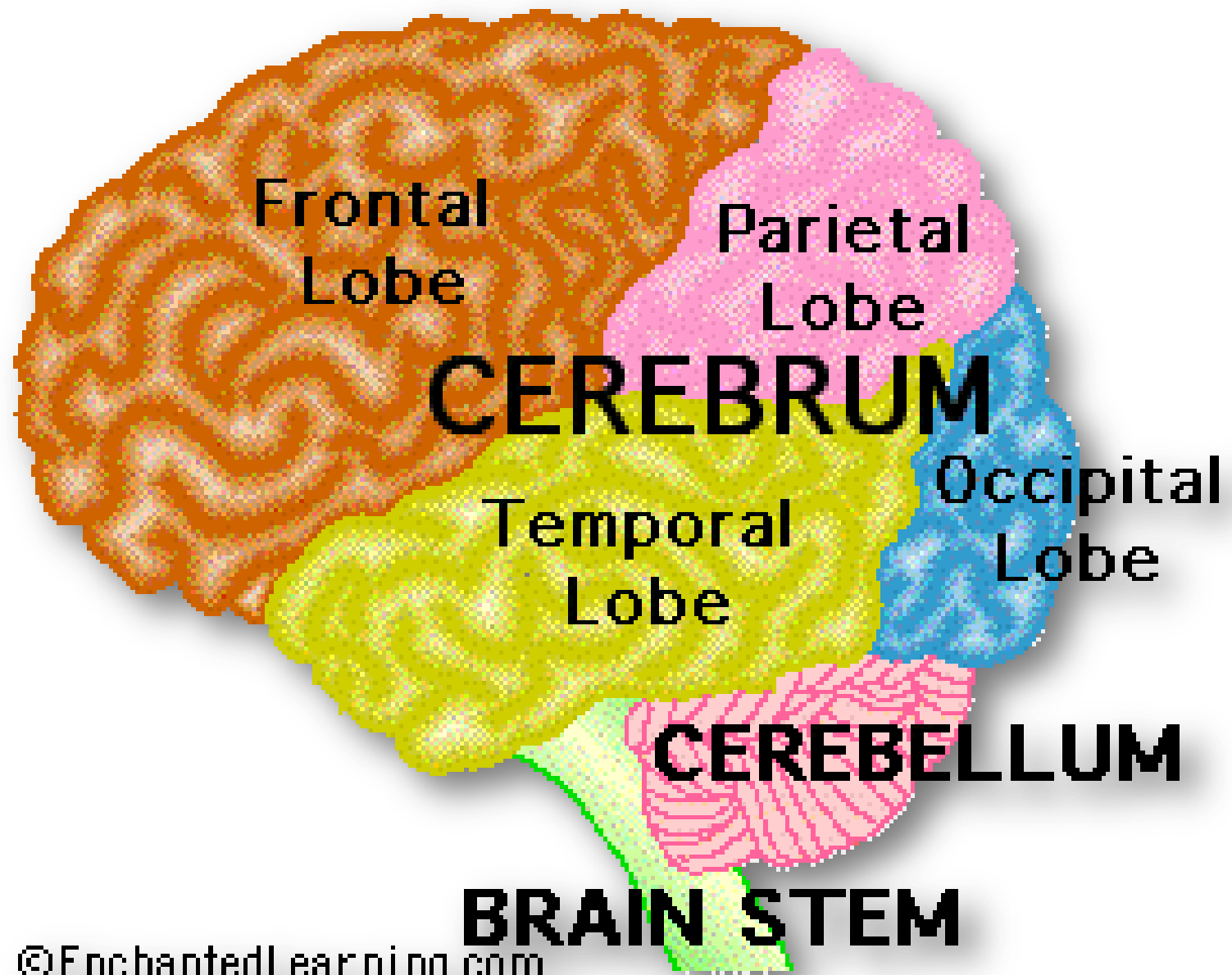


DEVELOPMENTAL MALFORMATIONS OF NERVOUS SYSTEM

Estimated frequency of congenital disorders in cattle

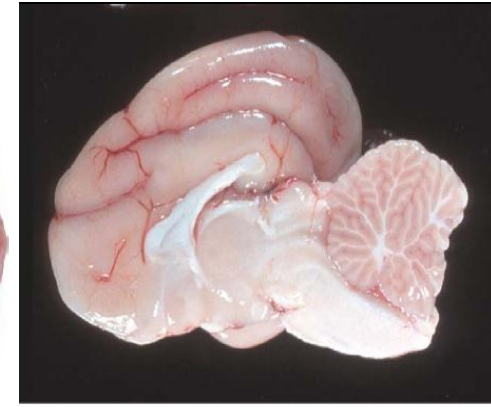
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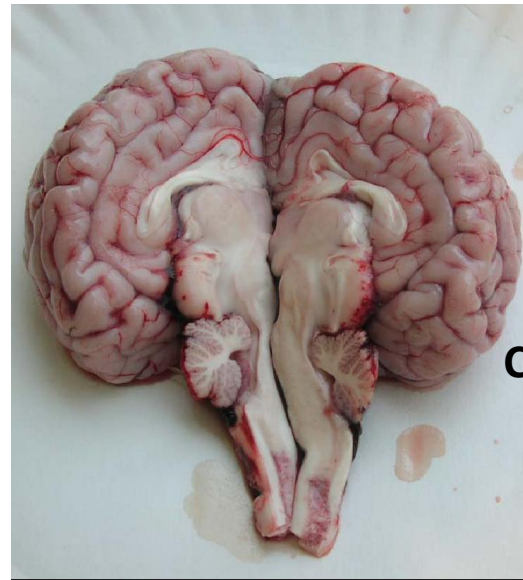


DEVELOPMENTAL MALFORMATIONS OF NERVOUS SYSTEM

- Many noxious agents — developing fetus in the uterus
- During the first trimester
 - **Agensis/Aplasia**
 - **Hypoplasia**
 - **Dysplasia**
- Malformations of the CNS are rather common in domestic animals.
- May be
 - Inherited or
 - Acquired



Normal Cerebellum



Cerebellar Hypoplasia

ANENCEPHALY

- Total absence of the entire brain (**this probably does not occur**).

AMYELIA

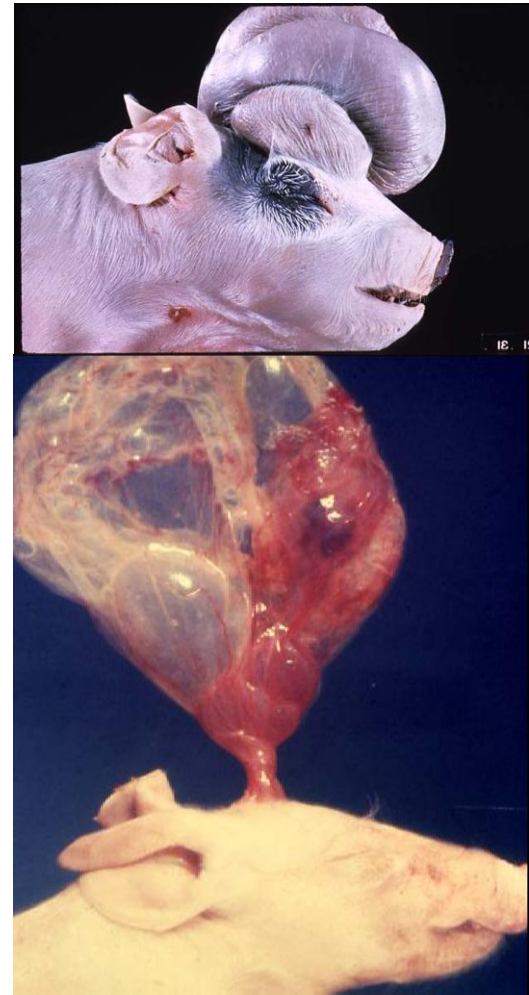
- Total absence of the spinal cord
- Usually occurs in association with anencephaly.

ENCEPHALOCYCE

- Protrusion of the brain (along with the meninges) through a defect in the cranium.
- The skin forms the hernial sac.

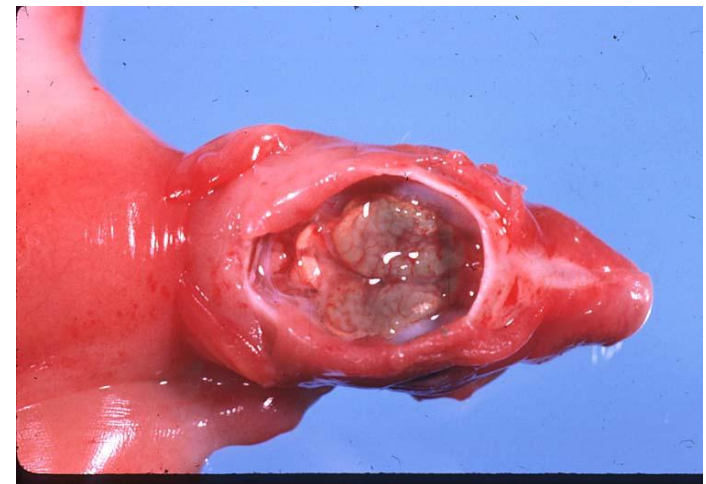
MENINGOCELE

- Protrusion of the meninges through a defect in the cranium.



HYDRANENCEPHALY

- Complete or almost complete absence of the **cerebral hemispheres** in a normal cranium
- The **leptomeninges** form sacs enclosing cerebrospinal fluid
- Hydranencephaly occurs in all species, but it occurs most commonly in **calves** in association with cerebellar hypoplasia
- The defect has been observed in **lambs** of ewes **vaccinated** during pregnancy for **bluetongue**.



SYRINGOMYELIA

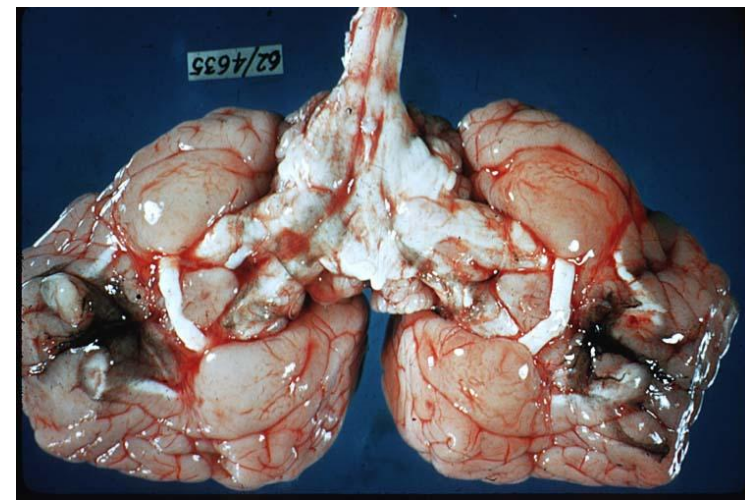
- **Tubular** cavitation of the spinal cord .
- This is a rather **rare** anomaly, except in a breed of dog.

HYDROMYELIA OR SYRINGOHYDROMYELIA

- Simple dilatation of the central canal of the spinal cord
- The cavity is connected with the central canal and lined by **ependymal** cells.
- Causes progressive **ataxia** and **paresis**,
Scoliosis and spinal pain.

DICEPHALUS

- Double brain



HYDROCEPHALUS

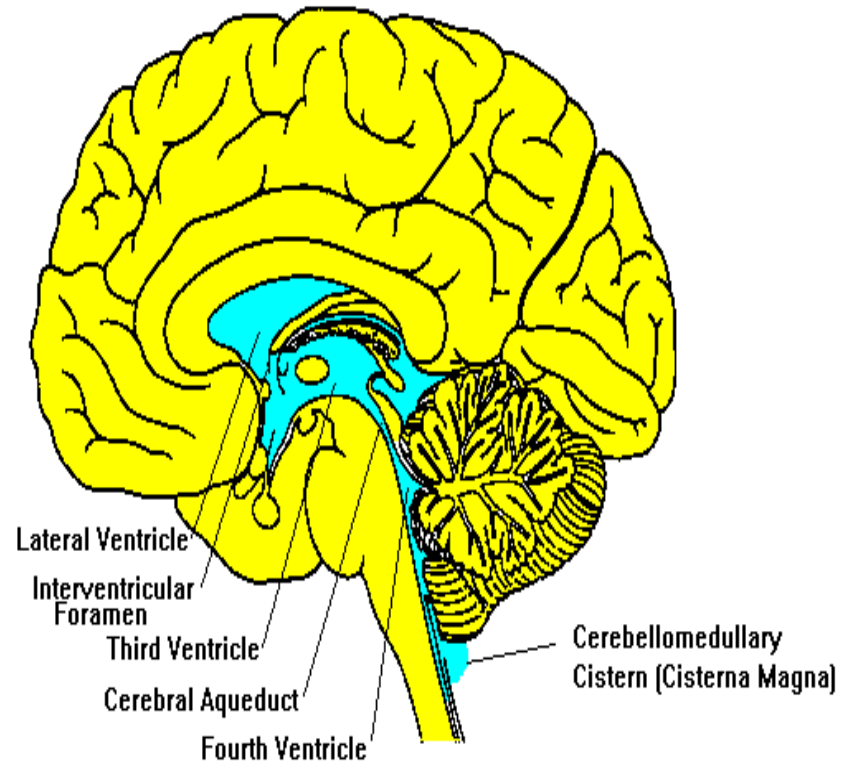
- Abnormal accumulation of **CSF in the cranial cavity**.
- congenital or acquired.
- In **internal** hydrocephalus, the fluid is within the **ventricular** system.
- In **external** hydrocephalus, the fluid is in the **sub-arachnoid** space.
- Congenital hydrocephalus most commonly observed in **pups, foals, calves** and **piglets**
- Acquired hydrocephalus is usually less severe than the congenital defect
- The causes are almost always **obstructive**.
- There is **parenchymal atrophy** affecting chiefly the white matter and the cerebral cortices



HYDROCEPHALUS

Obstructive

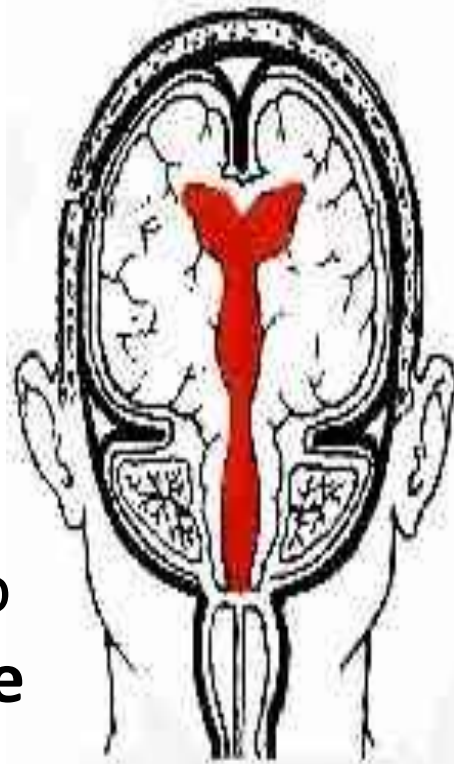
- This type of hydrocephalus results from an **obstruction within the ventricular system** of the brain that prevents CSF from flowing or “communicating” within the brain.
- The most common type is a narrowing of a channel in the brain that **connects two ventricles** together.



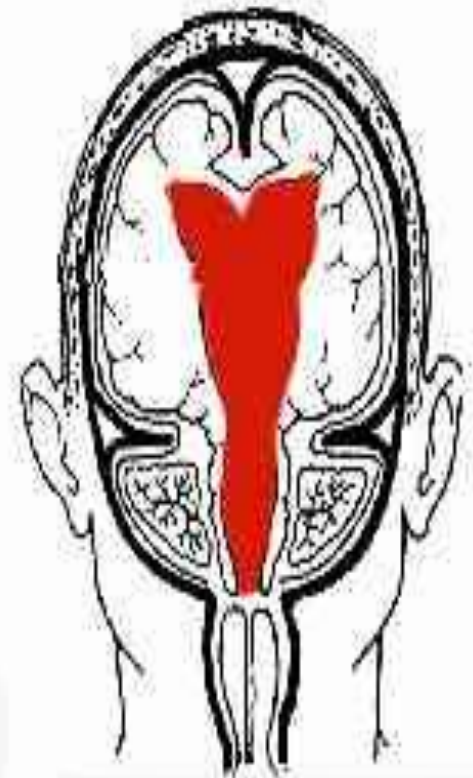
HYDROCEPHALUS

Non-obstructive

- This type results from problems with the **production or absorption** of CSF.
- The most common is caused by bleeding into the **subarachnoid space** in the brain.



Normal ventricles



Enlarged ventricles

Modified from Iyooa Virtual Hospital

SPINA BIFIDA (split spine)

- caused by the incomplete closure of the embryonic neural tube.
- Dysfunction of the tail and anus, incontinence, and sometimes pelvic limb weakness
- The prognosis is poor.
- Spina bifida can also accompany the **sacrocaudal dysgenesis** that is inherited as an autosomal dominant trait in cats.



sacrocaudal dysgenesis

INFLAMMATION OF THE NERVOUS SYSTEM

MENINGITIS (Head Pressing)

inflammation of the protective membranes covering the brain and spinal cord, (meninges).

inflammation of the brain (**encephalitis**)

often are seen simultaneously (**meningoencephalitis**) in the same animal

causes may include: viruses, bacteria or others including drugs.



INFLAMMATION OF THE NERVOUS SYSTEM

ENCEPHALITIS

Inflammatory processes may involve the parenchyma of the brain

MYELITIS

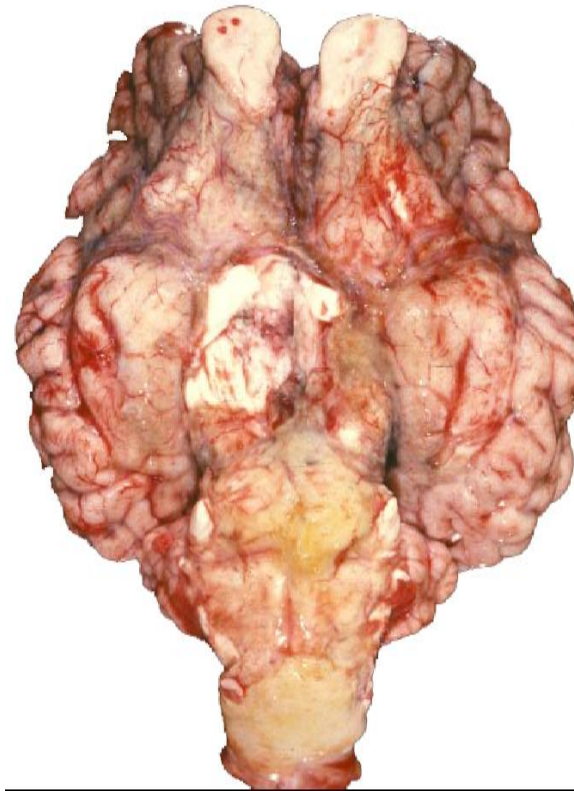
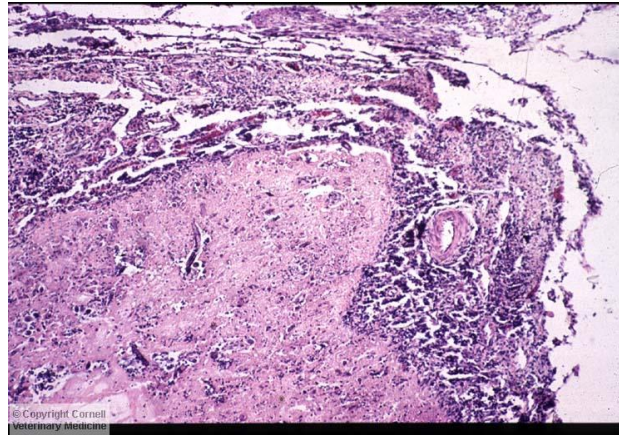
Inflammation of the spinal cord

ENCEPHALOMYELITIS

Inflammation of both brain and spinal cord

ENCEPHALOMENINGITIS

Inflammation of brain and meninges



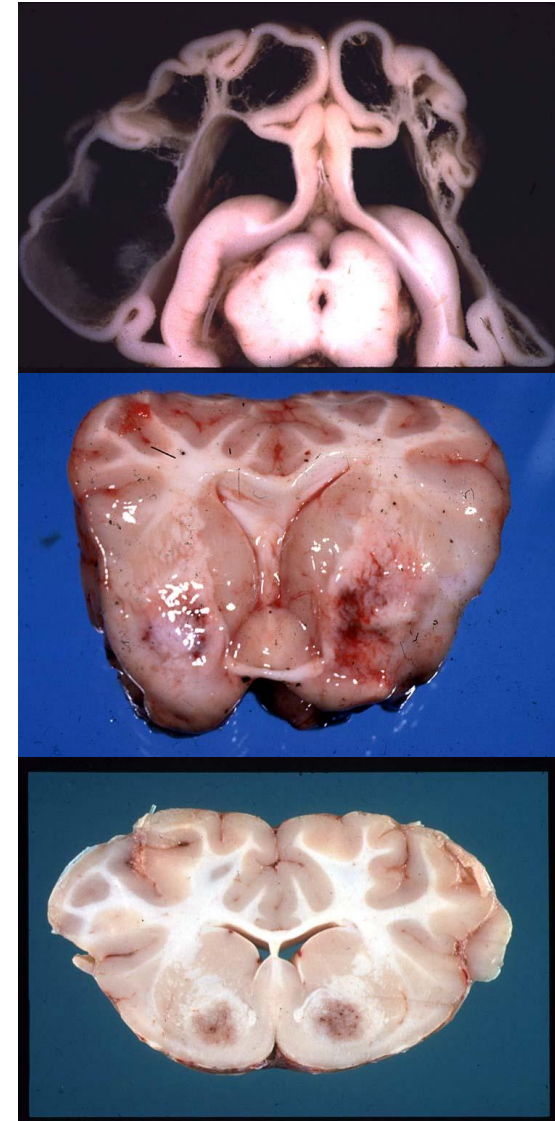
ABSCESSSES OF CNS

- May develop as a result of
 - embolism,
 - by direct implantation or
 - by direct invasion of the brain from an adjacent structure.
- In general, abscesses are more common in white matter than gray matter
- When abscesses are multiple, death is the outcome after a rather short course.

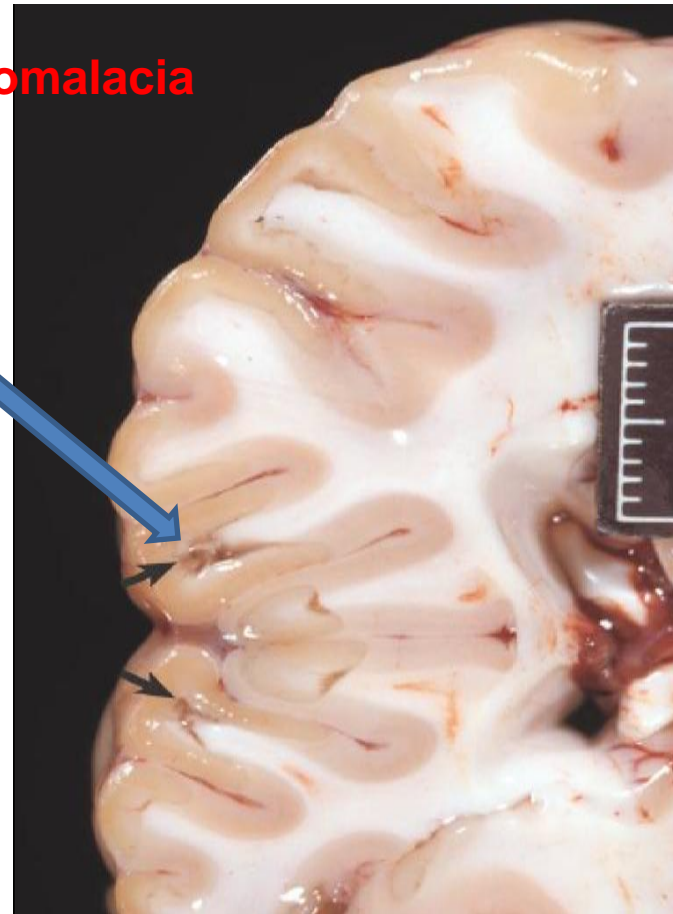
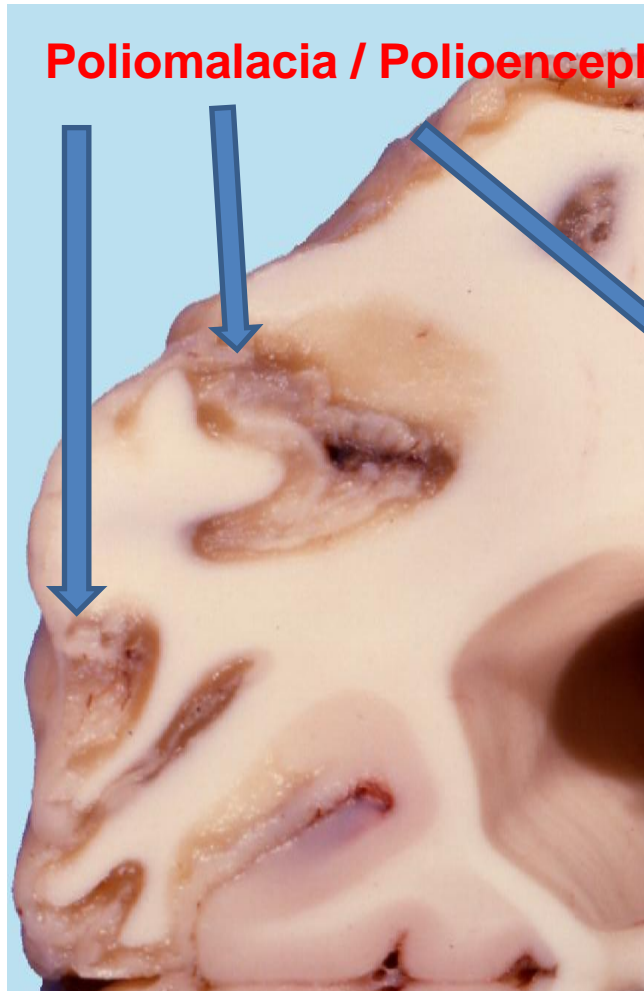


ENCEPHALOMALACIA AND MYELOMALACIA

- Malacia — softening — necrosis of tissue in the CNS.
- Malacia ---- injuries to the CNS (encephalitis, trauma, anoxia, etc.).
- **POLIOMALACIA:** softening of the gray matter
- **LEUKOMALACIA:** Softening of the white matter.



ENCEPHALOMALACIA AND MYELOMALACIA



(Courtesy Dr. R. Storz, College of Veterinary Medicine, Texas A&M University)

LISTERIOSIS (CIRCLING DISEASE)

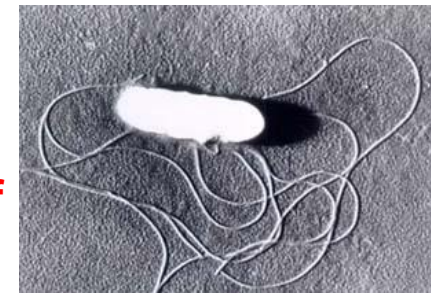
- Sporadic bacterial disease caused by *Listeria monocytogenes*.
- It is most commonly manifested by:
 - Encephalitis or **meningoencephalitis** in adult ruminants,
 - **Septicemia** with focal hepatic necrosis in young ruminants and monogastric animals
 - **Abortion**.
- Recently been recognized as an important **public health problem**.
- Occur in adult sheep with right facial nerve paralysis; drooped right ear, right eye showing no reaction to the flash and atony of right nostril.



LISTERIOSIS (CIRCLING DISEASE)

- The course in sheep and goats is **rapid**, and death may occur in **24-48 hr or 1-4 days**, in cattle from 4-14 days
- The **mortality** may approaches **100%**
- Signs are due to dysfunction of the **third to seventh cranial nerves**.
 - Initially, affected animals are anorectic, depressed, and disoriented.
 - May propels into **corners**, leans against stationary objects, or **circle toward the affected side**, head pressing.
 - **Facial paralysis** with a drooping ear, deviated muzzle, flaccid lip
 - Profuse **salivation**
 - animal circles in one direction only
 - Food often becomes impacted in the cheek
 - Animals fall and unable to rise at last stage
 - Fever, may be **105°F**,
 - **Abortion** — last trimester

**Electronmicrograph of
*L. monocytogenes***



- Bacteria invade **intestinal** mucosa.
 - **D-galactose residues**
- After epithelial cell entry
 - escapes phagosome, multiplies in cytoplasm
 - exocytosis from epithelial cell
 - **Listeriolysin, cytolysin, hemolysin**
 - phagocytosis by MØ, PMN (**internalin protein**)
 - multiplication followed by death of phagocytes, secondary phagocytosis
 - systemic spread

LISTERIOSIS (CIRCLING DISEASE)

- Organism multiplies **intracellularly**, it is largely protected against circulating immune factors such as antibodies and complement
- The effective host response is cell-mediated immunity (**CMI**)
- By means of **CMI, the bacteria spread systemically**
- *Listeria* are able to penetrate the **endothelial layer of the placenta** and thereby infect the fetus
- A peculiar property of *L. monocytogenes* that affects its food-borne transmission is the ability to **multiply at low temperatures**

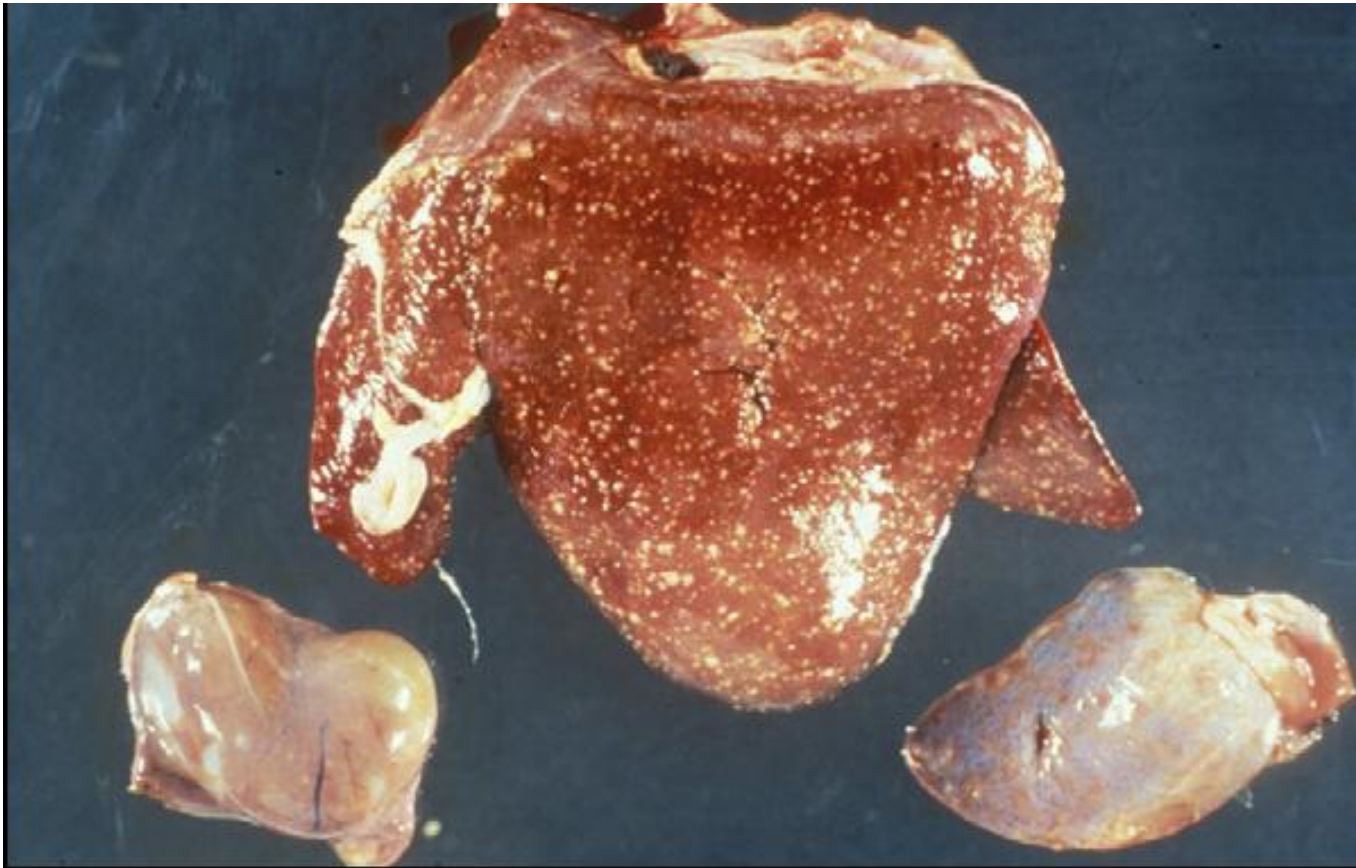


Gross lesions

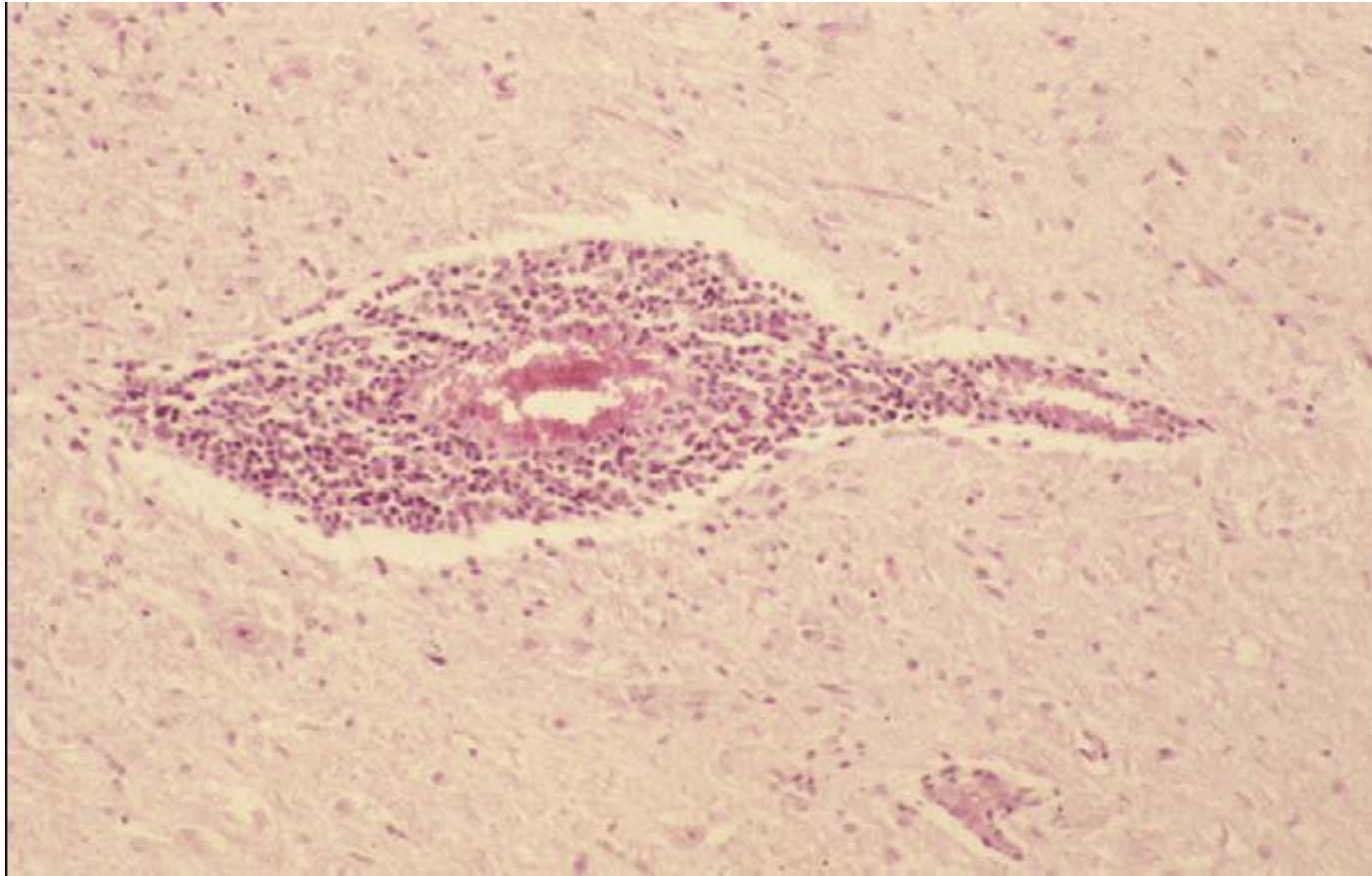
- **Usually not observed in the brain**; however, occasionally grayish foci of **malacia** may be found in cross-sections of the **medulla**.
- Lesions are most severe in the **medulla** and **pons**.
- Congestion of **meningeal** vessels and **cloudiness of CSF**
- **Visceral lesions** occur as multiple foci of **necrosis in the liver, spleen, endocardium, myocardium** and in the aborted fetus.
- In animals which abort, there is **placentitis** and **endometritis**.

Microscopically,

- The primary lesion is circumscribed collections of mononuclear cells, with or without neutrophils, around blood vessels
- Well-defined **micro-abscesses** may occur (are characteristic of the disease) , but they are most common in sheep.

LISTERIOSIS (CIRCLING DISEASE)

Post-mortem findings in a two-day-old lamb with septicaemia caused by listeriosis; presence of micro-abscesses on the heart, the liver and the kidneys.

LISTERIOSIS (CIRCLING DISEASE)

Histopathological findings in the brain of a sheep caused by listeriosis; encephalitis with perivascular cuffing with lymphocytes.

LISTERIOSIS (CIRCLING DISEASE)**Diagnosis**

- **CSF** has an increased **protein concentration** (0.6-2.0 g/L [normal 0.3 g/L])
- Isolation and identification of *L. monocytogenes*

Differential Diagnosis

- Nervous form of Ketosis
- Brain abscess
- Rabies
- Ear infection
- Pseudorabies
- Viral encephalitis

Disinfection

- Is susceptible to 1% sodium hypochlorite, 70% ethanol or glutaraldehyde.
- It can also be killed by moist heat (121°C for 15 min) or dry heat (160-170°C for 1 hour).

RABIES (Hydrophobia)



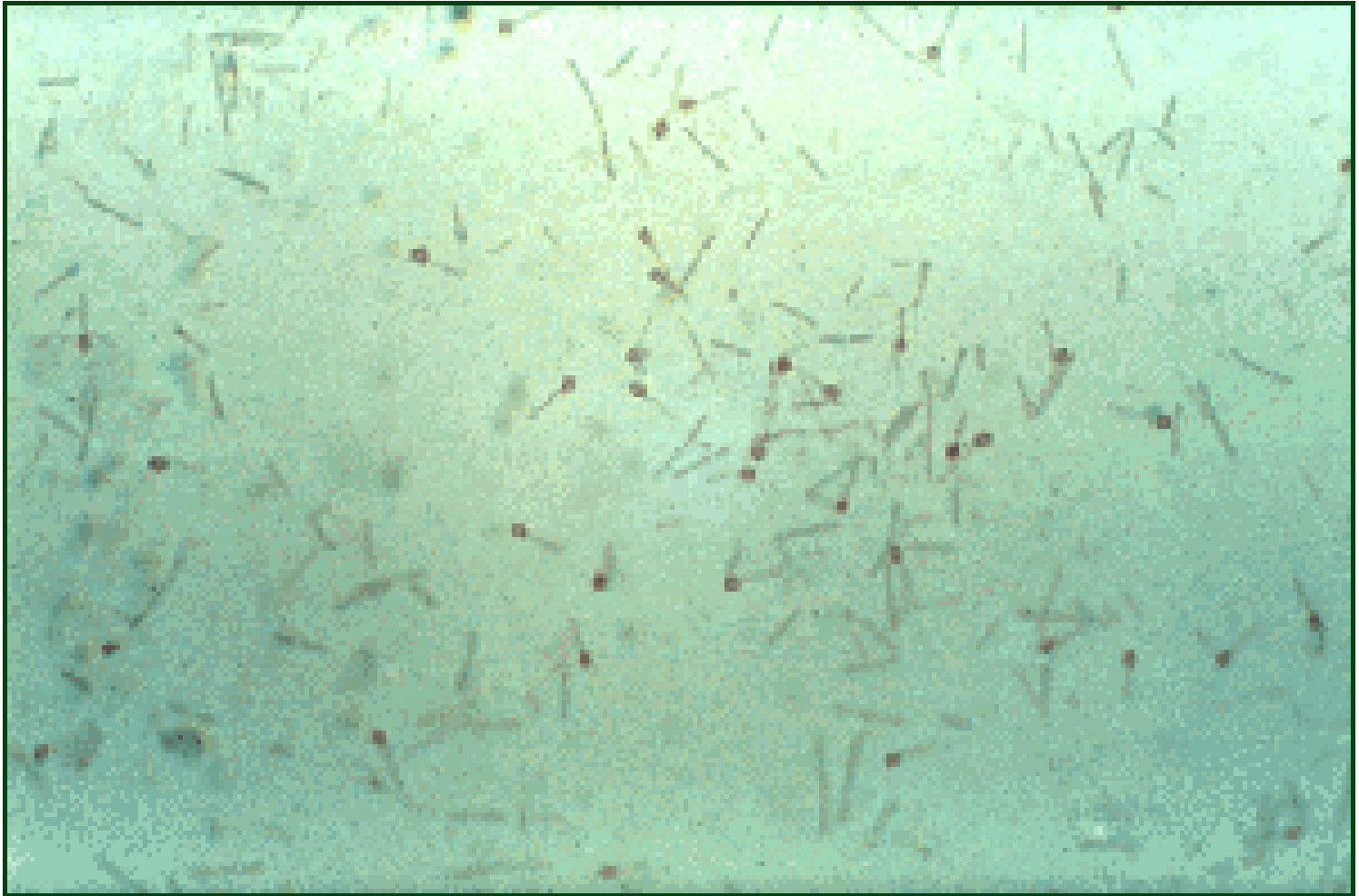
RABIES (Hydrophobia)

- An acute infectious disease of mammals, especially carnivores and bats, characterized by CNS pathology leading to paralysis and death.
- Important Zoonotic Disease
- It is invariably fatal once clinical signs appear
- The virus is usually present in the saliva of infected animals and is transmitted by their bite
- Disease is most common in carnivores such as dogs, wolves, and foxes

TETANUS

- The disease is produced by the **toxin** of ***Clostridium tetani*** characterized by hyperaesthesia, tetany and convulsions.
- Spores can survive many years and are resistant to most disinfectants.
- Present in soil, especially soil containing mammalian faeces.
- Temperature above 115°C for 20 minutes – spores are destroyed
- Disease results when spores enter the body, usually following a wound and the provision of an anaerobic environment in the tissues.
- Disease is Known since days of Hippocrates





Courtesy : Google Image on tetanus

- Gram +, spore forming, drumstick rods - anaerobic and motile
- Multiple antigenic types - some with reduced virulence
- Toxins - **Tetanolysin** and **Tetanospasmin** (most important)
- Reported case in man following pecking by a hen.
- Solipeds and man are highly susceptible. Next are sheep, cattle and swine.
- Disease is rare in the dog and cat.
- Extremely rare in poultry.

PATHOPHYSIOLOGY

- **spores enter the body**, usually following a wound and the provision of an anaerobic environment in the tissues.
- Spores **vegetate, produce their toxin** -- affinity for nervous tissue
- Transported within nerve **axons to the CNS**.
- The **BACTERIA DO NOT MOVE** from the site of original infection.

PATHOPHYSIOLOGY

- Tetanus usually occurs **sporadically – occasional outbreaks**
- Outbreaks – about 1 week after **marking**
- May affect **1-5% of lambs**, rarely more.
- Enter wounds castration and tail docking
 but also shearing, dehorning,
 after lambing.
- Lambs under 6 months old -- most commonly affected.
- Older animals often have natural protective antibodies

CLINICAL SIGNS

- Muscular stiffness, spasms and tremors,
- prolapse of the nictitating membrane.
- Hyperaesthetic, -- noise or touch precipitates tetany.
- On walking -- stiff-legged and turn without flexing their spines.
- Ultimately, they cannot walk and lie in lateral recumbency with legs out stiffly and head extended back.
- Rectal temperature is raised by muscular activity.

DIAGNOSIS

- Clinical signs are usually diagnostic
- The history and presence of a recent wound.



COENURUS CEREBRALIS INFECTION

(Gid, Sturdy)

- Coenurosis is a disease of the brain and spinal cord caused by the intermediate stage of *Taenia multiceps* (**tape worm**) which inhabits the intestine of dogs, cats and wild carnivores.
- Clinical disease occurs in **sheep** and rarely in **cattle**.

Life cycle

- **Eggs** expelled with **dog feces** are ingested by the intermediate host (sheep).
- **Larvae** hatch in the **intestine** and pass with the **blood stream** towards **different organs**.
- Larvae which reach the **brain and spinal cord** grow to the **coenurus stage**.
- *Coenurus cerebralis* - mature in the **brain and spinal cord**.

Clinical Findings

- During migration of larval stage
 - Blindness
 - Muscular tremor and in-coordination
 - Excitability and collapse
- Infection with the fully developed larval stage
 - Salivation
 - Wild expressions
 - Crazy running and convulsion
 - Deviation of eye and head
 - Dullness
 - Incomplete mastication
 - Head pressing
 - Incomplete paralysis and, in spinal cord involvement, inability to rise



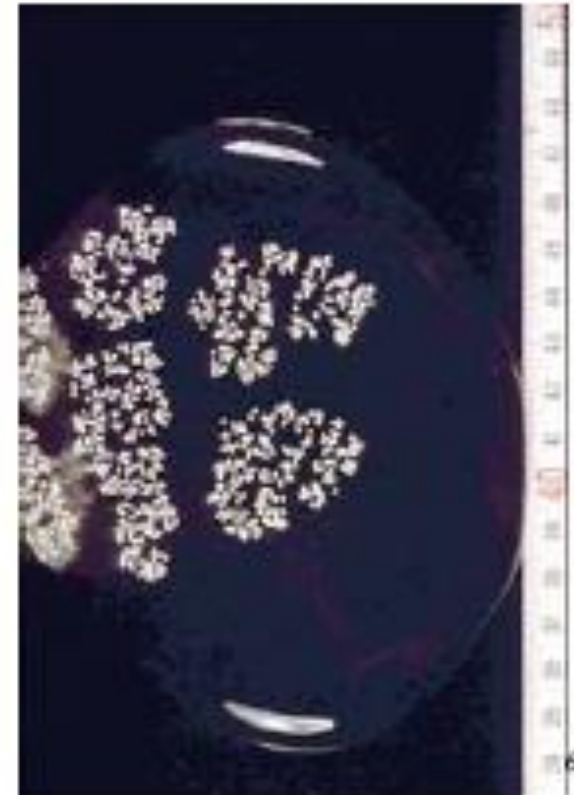
Postmortem findings

- Thin walled **cyst in the brain**
- Lesion in the **lumbar region** and rarely, in the cervical area of the **spine**

Gid – *Coenuris cerebralis*

Diagnosis

- Clinical Signs
- Postmortem findings



LOUPING ILL

(Ovine Encephalomyelitis, Infectious Encephalomyelitis of Sheep, Trembling-ill)

- Acute tick-transmitted (*Ixodes ricinus*) viral disease primarily of CNS infecting **sheep**, characterized by
 - **biphasic fever 107°F** (second rise occur 5th day of first signs)
 - depression,
 - ataxia,
 - muscular in-coordination,
 - tremors,
 - posterior paralysis,
 - coma, and death.

Etiology and Transmission

- Caused by a neurotropic **single-strand RNA virus** — *Flavivirus*
- Louping-ill is **endemic in rough upland areas in Scotland, Northern England, Wales and Ireland.**
- A disease of sheep very closely related to LI has been reported in Bulgaria, Turkey, Spain and Norway.
- **Incubation period — 6 to 18 days.**

Clinical Signs

- sheep are often **hypersensitive** to noise and touch and will go into convulsive spasms if disturbed.
- Affected animals exhibit **head-pressing, paraplegia, convulsions, opisthotonos** and **coma.**
- In many cases, death supervenes after a clinical course ranging from **7 to 12 days.**
- Animals that survive never regain full health and display residual central nervous system deficits of variable severity.

- lambs born of immune dams are passively protected in their first year of life but then become susceptible.
- **Mortality** rates as high as **60% in young stock**
 - in mature sheep is usually low unless they have recently been moved from a non-LI endemic area into an area in which the disease is endemic.
- the **prevalence** of infection may be as high as **60%**,
- the case fatality rate is low and uncommonly exceeds **15%**.

Lesions

- With the exception of **congestion of meningeal vessels**, there is no pathognomonic gross lesion.

Diagnosis

- signs of central nervous system disturbance
- history of tick-infested pastures
- Heparinized blood — during the first 3 to 4 days after the onset of fever
- virus isolation
- RT-PCR
- ELISA

Differential Diagnosis

- scrapie, pregnancy toxemia, hypocalcemia, tetanus, listeriosis, tick pyemia, rabies, hydatid disease, and various plant poisons.
- in cattle must be differentiated from MCF, listeriosis, pseudorabies, BSE, rabies, hypomagnesemia, hypocalcemia, acute lead poisoning, and certain plant poisons.

AETIOLOGY AND EPIDEMIOLOGY

- Rabies is caused by lyssaviruses of Rhabdovirus family
- Rabies in man results from the **BITE of a rabid dog, wolf, fox etc. ?**
- Carnivores — cattle, horses, and sheep — seldom spread it further.
- Insectivorous and frugivorous bats — harbor the virus
- **Canine rabies** predominates in Africa, Asia, Latin America, and the Middle East.
- **Bat rabies** is distributed throughout the USA and Central and South America.
- In **Europe, red fox** rabies predominates.



AETIOLOGY AND EPIDEMIOLOGY

- No cat-to-cat transmission of rabies has been recorded, and no feline rabies virus variant is known.
- However, cats are the most commonly reported rabid domestic animal in the USA.
- Virus is present in the saliva of rabid cats

Hog



Shunk



Fox



Racoon



PATHOPHYSIOLOGY

Travel of virus from an inoculation site to the CNS

- Virus injected into muscle mostly by bite of rabid animal
 - The incubation period is prolonged and variable
 - Most cases in dogs develop within **21-80 days** after exposure, but it may be shorter or as long as **6 years**
 - Replicate in **muscle cells**, then virions shed into extracellular spaces
 - Then nearby **neuromuscular** and **neurotendinal spindles** are involved
 - It then reaches to **Peripheral nerves**
 - Then to **dorsal root ganglia**
 - Then to **spinal cord** and **Brain**.

PATHOPHYSIOLOGY

- Replication of virus occur in most neuronal cells of the CNS and eventually spread centrifugally to involve neuronal cells throughout the body.
- Virus reaches sites such as
 - **taste buds** in the mouth and **olfactory cells** in the nose,
 - where replication is intense – increasing the chances for the spread of virus in **saliva** or **nasal secretions**
- Haematogenous spread does not occur
- The aerosol transmission has also been documented.

CLINICAL SIGNS

- Typical signs of CNS disturbance, with minor variations among species
- The signs, are acute **behavioral changes** and unexplained **progressive paralysis**.
- Behavioral changes may include
 - sudden anorexia,
 - signs of apprehension or nervousness,
 - irritability, and hyperexcitability
 - The animal may seek loneliness.
 - Ataxia, altered behavior, and changes in temperament are apparent.
 - Uncharacteristic aggressiveness may develop—a normally docile animal may suddenly become vicious.
 - Rabid wild animals may lose their fear of humans,
 - species that are normally nocturnal may be seen wandering during the day.

RABIES (Hydrophobia)

- The clinical course may be divided into 3 phases
 - prodromal,
 - excitative, and
 - paralytic/end stage.
- However, this division is of limited practical value because of the variability of signs and the irregular lengths of the phases.
- The prodromal period may last ~1-3 days, animals show only vague CNS signs.
- The disease progresses rapidly after the onset of paralysis, and death is virtually certain.
- Some animals die rapidly without marked clinical signs.

RABIES (Hydrophobia)

- The clinical symptoms usually appear in one of two forms:
 - the "**DUMB**" and
 - the "**FURIOUS**"
- In the "**FURIOUS**" form (mad-dog syndrome)
 - Biting and slashing at any moving object
 - Furious champing of the jaws – excessive salivation,
 - Saliva streams from the mouth or is churned into foam which may adhere to the lips and face
 - Attack human subjects.
 - The posture and expression is one of alertness and anxiety, with pupils dilated.
 - They commonly swallow foreign objects, e.g., feces, straw, sticks, and stones.
 - As the disease progresses, muscular in-coordination and seizures are common.

RABIES (Hydrophobia)

- In the **DUMB form**
 - This is the first manifest by paralysis of the throat and masseter muscles
 - often with profuse salivation and inability to swallow.
 - Dropping of the lower jaw is common in dogs.
 - These animals may not be vicious and rarely attempt to bite.
 - The paralysis progresses rapidly to all parts of the body, coma and death follow in a few hours.
 - **Paralysis may follow either the "furious" or "dumb" stage of the disease**
- **Death — within 10 days**
- Some animals and people **may recover** from rabies infection

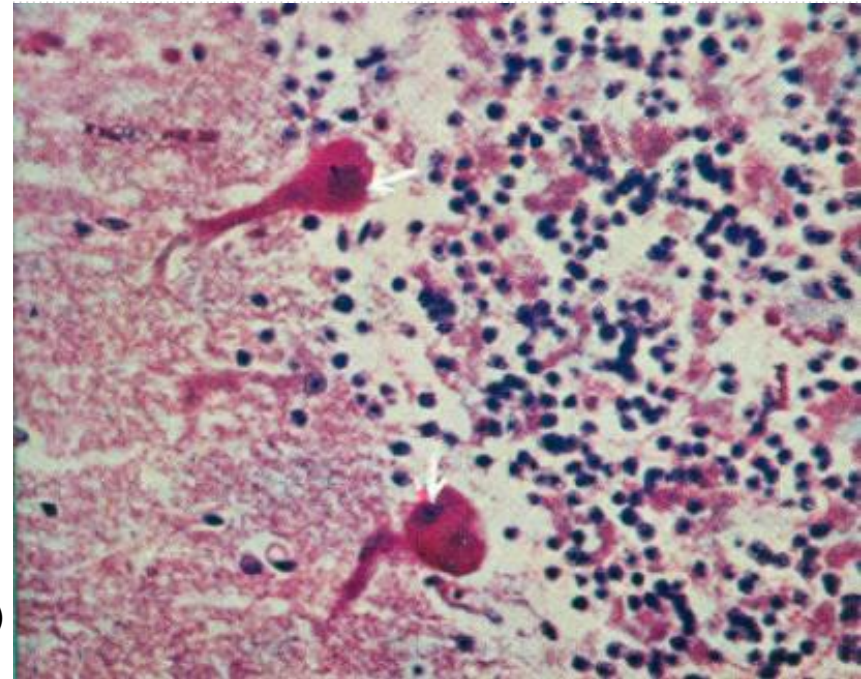
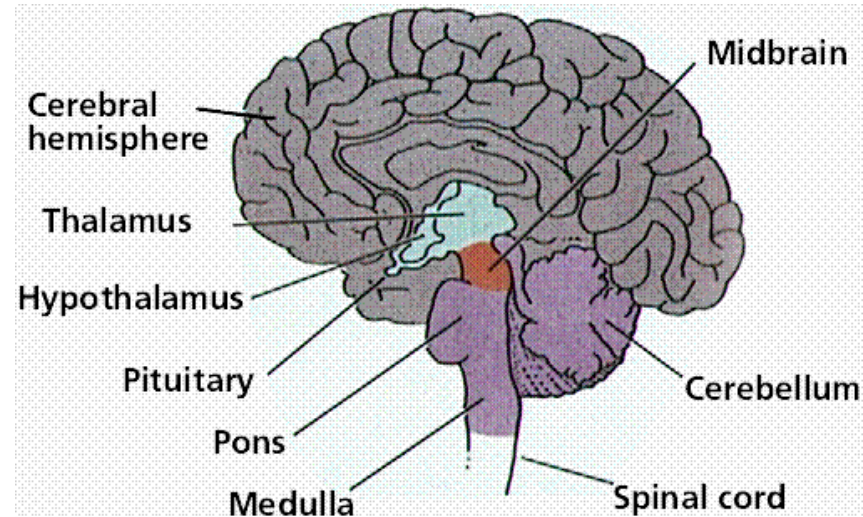
- Cattle
 - with furious rabies can be dangerous, attacking and pursuing humans and other animals.
 - Lactation ceases abruptly in dairy cattle.
 - The usual placid expression is replaced by one of alertness.
 - The eyes and ears follow sounds and movement.
 - A common clinical sign is a characteristic abnormal bellowing, which may continue intermittently until shortly before death.

RABIES (Hydrophobia)

LESIONS

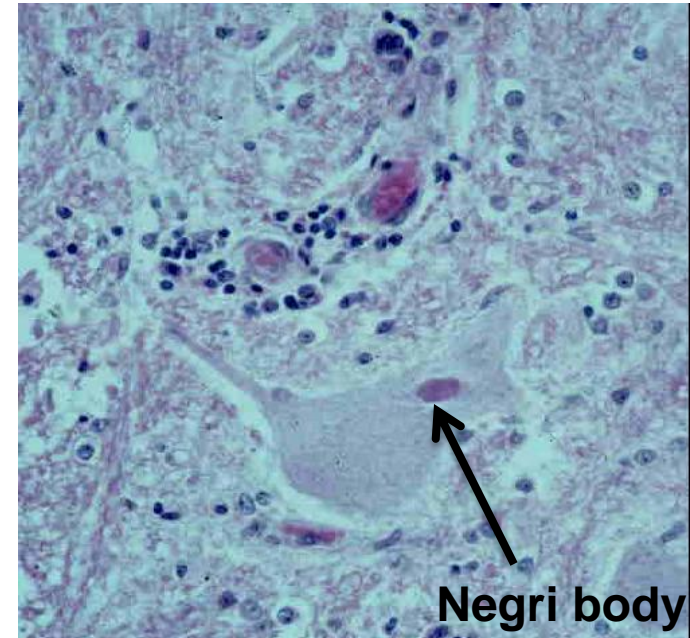
- May be **undetectable** or **early necrosis** of neurons with specific **cytoplasmic inclusion bodies** in the affected nerve cells
- In some cases diffuse encephalitis is demonstrated by **perivascular cuffing**, **nodules**, and **necrosis**
- Site — **Brain stem**, the **hippocampus**, and the **gasserian ganglia**.
- May be mild infiltration of lymphocytes and plasma cells, and encroachment of proliferating glial cells "**Babes nodules**" upon the neurons.

Rabies, cytoplasmic inclusions (arrows) in Purkinje cells, cerebellum of cow.



RABIES (Hydrophobia)

- Spherical cytoplasmic inclusion bodies with clear hallow around — called **Negri bodies**.
 - Negri bodies are **not always present** in rabies, and certain strains of rabies virus do not produce inclusion bodies, indicating that Negri bodies are not necessary for viral replication
- Negri bodies are always **intracytoplasmic**.
 - In dog — in the **hippocampus**,
 - In cattle — numerous in the **purkinje cells** of the **cerebellum**.



DIAGNOSIS

- Signs and symptoms
- Demonstration of typical Negri bodies — in **30%** of cases may be **no Negri bodies**.
- Animal (mouse) inoculations.
 - Following intra-cerebral inoculation, newborn mice usually succumb within 14 days, but should be examined daily for at least four weeks before the test is considered negative.
- Isolation in tissue culture
- FAT — fluorescent antibody technique

DIFFERENTIAL DIAGNOSIS

- Canine hepatitis
- Toxoplasmosis
- Distemper in dogs
- *Oestrus ovis infestation in sheep and*
- Listeriosis in sheep and cattle
- Differentiation of canine hepatitis and canine distemper are of considerable importance, since inclusion bodies may occur in both of these diseases.
 - Both are also much more common in dogs than is rabies

PSEUDORABIES (Mad Itch, Aujeszky Disease)

- Pseudorabies is a viral disease (DNA herpesvirus) **that occurs in a number of animal species but primarily in swine.**
- In **cattle the disease is nearly always fatal.**
- Swine are the natural host and principal reservoir.

Epidemiology

- The virus can be transmitted via **nose-to-nose** or **fecal-oral** contact.
- Indirect transmission commonly occurs via inhalation of aerosolized virus.
- Data from England indicate that virus may travel via aerosols for up **to 2 km** in certain weather conditions.

- Other studies have demonstrated that the virus can survive
 - for up to 7 hr in non-chlorinated well water;
 - for 2 days in anaerobic lagoon effluent and in green grass, soil, feces, and shelled corn;
 - for 3 days in nasal washings on plastic and pelleted hog feed;
 - for 4 days in straw bedding.
- The virus is enveloped and, therefore, is inactivated by drying, sunlight, and high temperatures ($\geq 37^{\circ}\text{C}$).
- Dead-end hosts, such as dogs, cats, or wild animals, can transmit the virus between farms, but these animals survive only 2-3 days after becoming infected.

Clinical Findings And Pathogenesis

- Young swine are highly susceptible, and losses may reach 100% in piglets <7 days old.
- In general, signs of CNS disease (e.g., tremors and paddling) are seen.
- A generalized febrile response (41-42°C), anorexia, and weight loss are seen in infected pigs of all ages.
- Mortality can be very low (1-2%) in grower and finisher pigs but may reach 50% in nursery pigs.
- Sneezing and dyspnea are frequently seen, and CNS involvement is reported occasionally.

- After natural infection, the primary site of viral replication is nasal, pharyngeal, or tonsillar epithelium.
- The virus spreads via the **lymphatics** to regional lymph nodes, where replication continues.
- Virus also spreads via **nervous** tissue to the brain, where it replicates, preferentially in **neurons of the pons and medulla**.
- In addition, virus has been isolated from alveolar macrophages, bronchial epithelium, spleen, lymph nodes, embryos, and luteal cells.
- Viral **excretion** begins **~2-5 days after infection**, and virus can be recovered from nasal secretions, tonsillar epithelium, vaginal and preputial secretions, milk, or urine for >2 wk.
- A latent state, in which virus is harbored in the trigeminal ganglia, may exist.

Lesions:

- **Gross lesions** are often undetectable.
 - Serous **rhinitis**, necrotic tonsillitis, or hemorrhagic pulmonary lymph nodes may be seen.
 - **Pulmonary** edema, as well as pneumonic lesions of secondary bacterial pathogens may be present.
 - Necrotic foci (2-3 mm in diameter) may be scattered throughout the **liver**.
 - Such lesions are typically found in young (<7 days old) piglets.

Lesions:

- **Microscopically**

- **Non-suppurative meningoencephalitis** is a characteristic lesion in gray and white matter.
- **Mononuclear perivascular cuffing** and neuronal necrosis may be present.
- The meninges are thickened as a result of mononuclear cell infiltration.
- **Necrotic tonsillitis** with the presence of **intranuclear inclusion bodies**, as well as necrotic bronchitis, bronchiolitis, and alveolitis are commonly seen.
- **Focal areas of necrosis** are often found in the liver, spleen, lymph nodes, and adrenal glands of macerated fetuses.

Diagnosis:

- Gross and microscopic lesions,
- virus isolation, fluorescent antibody testing, and serologic testing.
- Brain, spleen, and lung are the organs of choice for virus isolation.
- ELISA, latex agglutination, Serum neutralization tests