


NERVOUS SYSTEM (L-2)



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RABIES (Hydrophobia)

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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





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RABIES (Hydrophobia)

AETIOLOGY AND EPIDEMIOLOGY

- Rabies is caused by **lyssavirus** 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.

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- 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



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5

RABIES (Hydrophobia)**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 virus shed into extracellular spaces
 - Then nearby **neuromuscular** and **neurotendinal spindles** are involved
 - It then reaches to **Peripheral nerves**, to **dorsal root ganglia**, to **spinal cord** and **Brain**.



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6

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- 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.



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7

RABIES (Hydrophobia)**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/uneasiness or nervousness,
 - irritability, and hyperexcitability
 - The animal may seek loneliness.
 - Ataxia, altered behavior, and changes in temperament.
 - Uncharacteristic aggressiveness may develop—a normally docile animal may suddenly become vicious.
 - Rabid wild animals may loose their fear of humans,
 - species that are normally nocturnal may be seen wandering during the day.



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8

RABIES (Hydrophobia)

- The clinical course may be divided into 3 phases
 - prodromal,
 - excitative,
 - 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 the 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

**RABIES (Hydrophobia)**

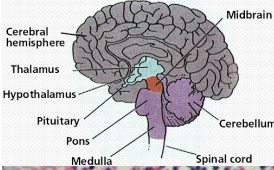
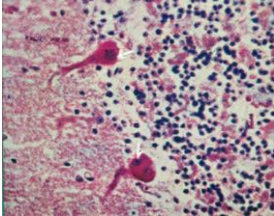
- **Cattle**
 - with furious rabies can be dangerous, attacking and pursuing humans and other animals.
 - Lactation ceases abruptly in dairy cattle.
 - The usual placid expression is replaced by one of alertness.
 - The eyes and ears follow sounds and movement.
 - A common clinical sign is a characteristic 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.

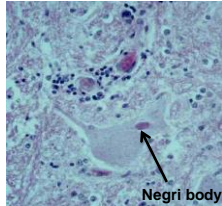
Rabies, cytoplasmic inclusions (arrows) in Purkinje cells, cerebellum of cow.

13

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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,
- Negri bodies are always **intracytoplasmic.**
 - In dog — in the **hippocampus,**
 - In cattle — numerous in the **purkinje cells of the cerebellum.**



14

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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

15

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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

16

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PSEUDORABIES (Mad Itch, Aujeszky Disease)

- Pseudorabies is a viral disease (DNA **herpesvirus 1**) 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.



PSEUDORABIES

- Other studies have demonstrated that the virus can survive
 - for up to **7 hr** in non-chlorinated well water
 - **2 days** in anaerobic lagoon effluent and in green grass, soil, feces, and shelled corn
 - **3 days** in nasal washings on plastic and pelleted hog feed
 - **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.



PSEUDORABIES

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 **padding**) 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**.



PSEUDORABIES

- 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.

• **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, serologic testing.
- Brain, spleen, and lung are the organs of choice for virus isolation.
- ELISA,
- latex agglutination,
- Serum neutralization tests

