RHABDOVIRUSES

Rabies virus (Lyssavirus):

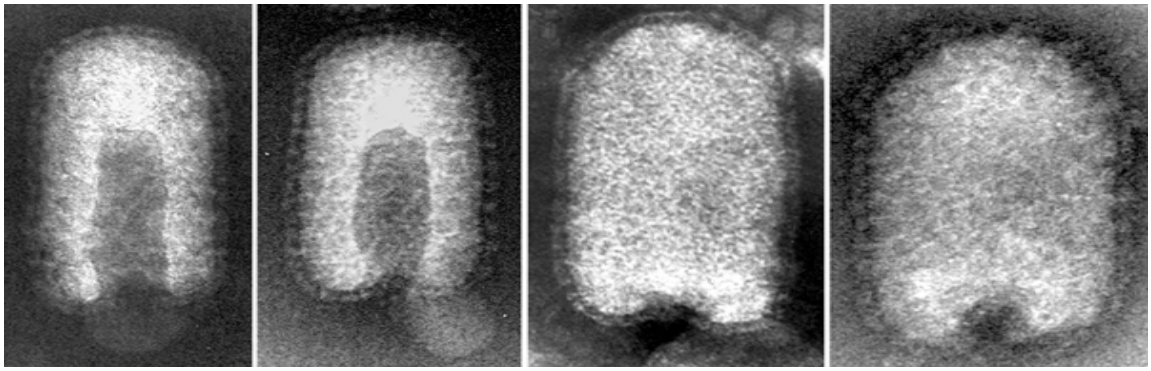
- have a distinctive bullet –like appearance (round on one end and flat on the other end)

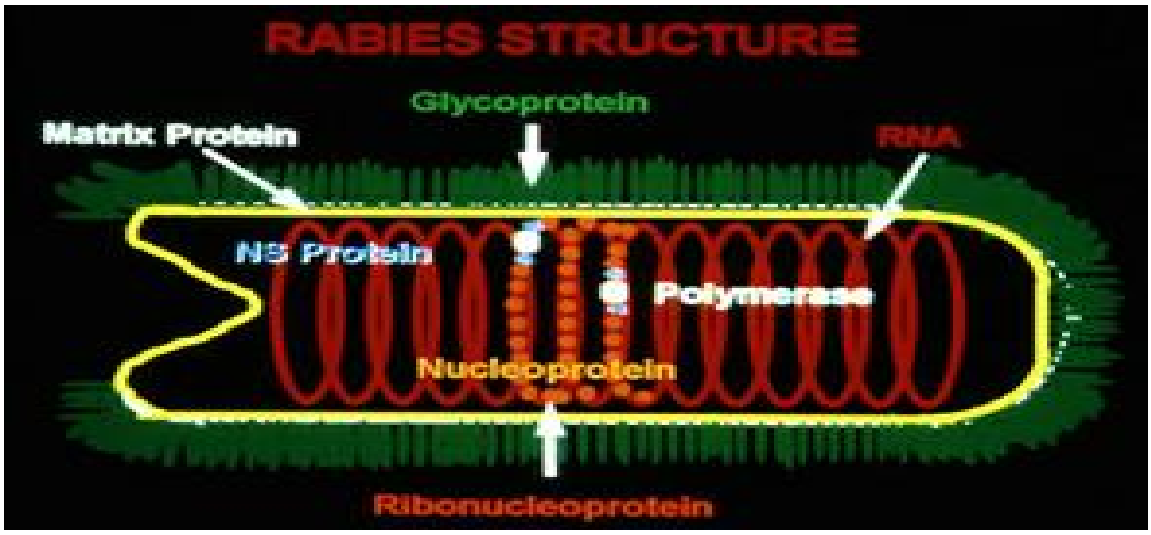
- helical nucleocapsid with spikes that protrude thru the envelope

- family contains approximately 60 different viruses

- only the rabies virus affect humans (rarely, other mammalian lyssaviruses)

- killed by UV irradiation or sunlight





Epidemiology of rabies:

- slow , progressive zoonotic disease characterized by a fatal meningitis
- worldwide distribution in various mammals (skunks, foxes, raccoons, wolves, mongooses, and badger)
- humans become accidental hosts thru dog bites, cat scratches and contact with sylvan animal reservoirs

1.Sylvatic rabies

- rabies in wild animals (bats- vampire bats, skunks, racoons, foxes)
- fruit and herbivorous bats are known to transmit rabies

2. Urban rabies

- rabies in domestic animals (dogs, cats, horses, cattles)

TRANSMISSION

- primarily affects wild animals
- humans and animals : accidentally infected

1.animal bite – majority

2. via a scratch

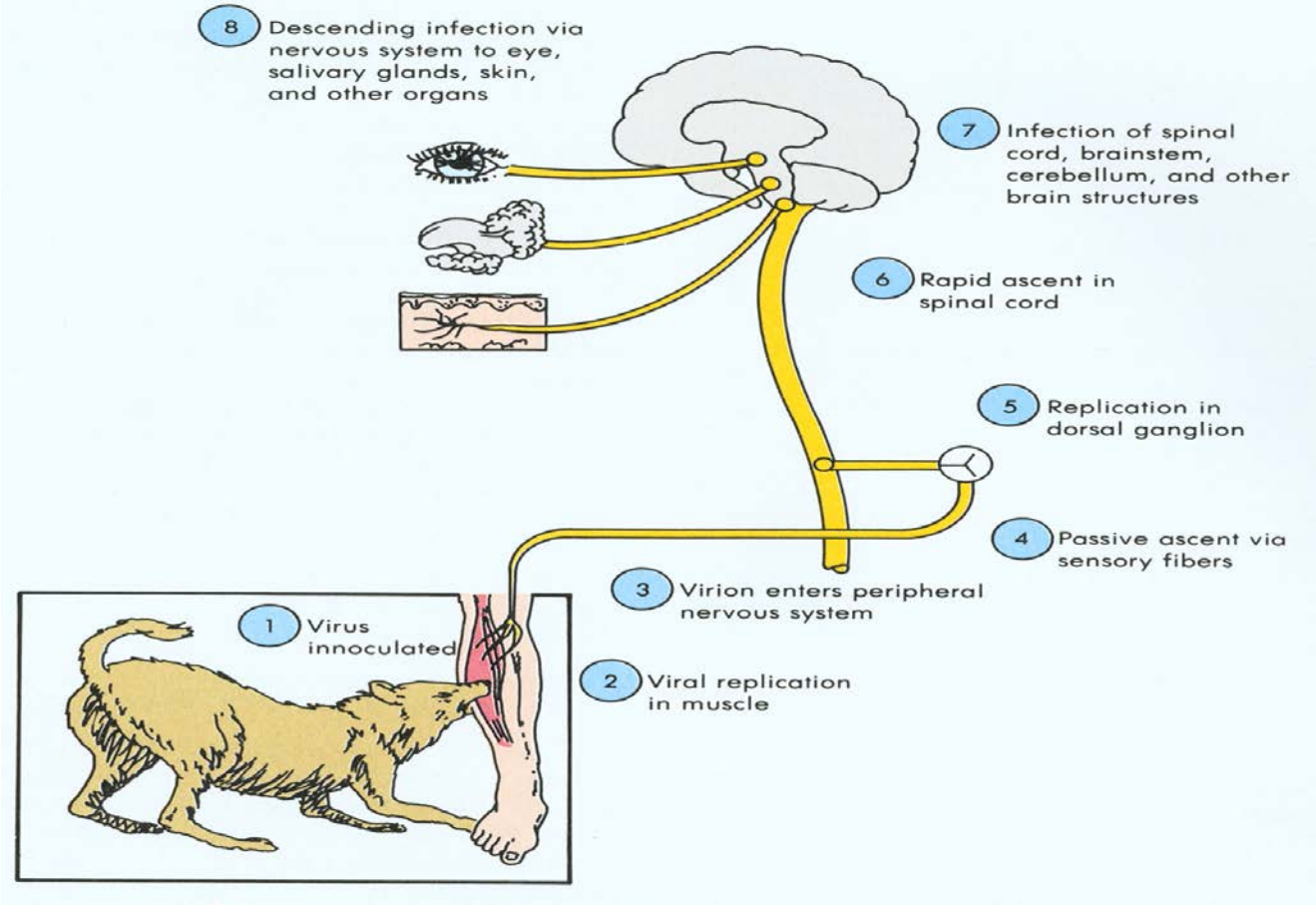
3. inhalation of contaminated aerosolized animal material

4. transplantation of infected tissue (cornea)

5. inoculation through intact mucous membrane

* virus found in saliva of infected animal few days before clinical signs

*** bat infection : latent (bats excrete virus in saliva for months , in South America (source of rabies in cattle)**



Infection and Disease

- begins when an infected animal's saliva enters a puncture site (it may also be inhaled or inoculated orally)

- virus multiplies at the trauma site, up to a week upon transmission

- virus gradually enters sensory nerve endings or neuromuscular junction

and advances toward the sensory ganglia, spinal cord and brain

- virus multiplies throughout the brain with migration to other sites

(eye, heart, skin, and oral cavity)

- viral replicates in the salivary glands and is shed into the saliva

- considered a slow, progressive infection

Clinical phases of Rabies:

<u>Average incubation period</u>: 1-2 months (extremes of 1 week to more than a year)

<u>Incubation period</u> : depends on wound site, its severity, virus concentration in inoculum, host's age, host's immune status: shorter in facial, neck and scalp wounds

due to their proximity to the brain, prodrome begins with fever, anorexia, nausea, vomiting, headache, fatigue, some may have pain, burning, pricking,, tingling sensation at the site of the wound.

Forms of Rabies:

1.Furious form – agitation, disorientation, seizures, and twitching

- spasms in the neck and pharyngeal muscles lead to severe pain on swallowing

(even the sight of liquids can bring about *hydrophobia*) - the patient is fully coherent and alert

2. Dumb form – patient is paralyzed, disoriented and stuporous

***Both forms eventually lead to coma and death from cardiac or respiratory arrest.**

***<u>Only 3 patients have recovered from rabies with minimal Residua</u>**

Diagnosis

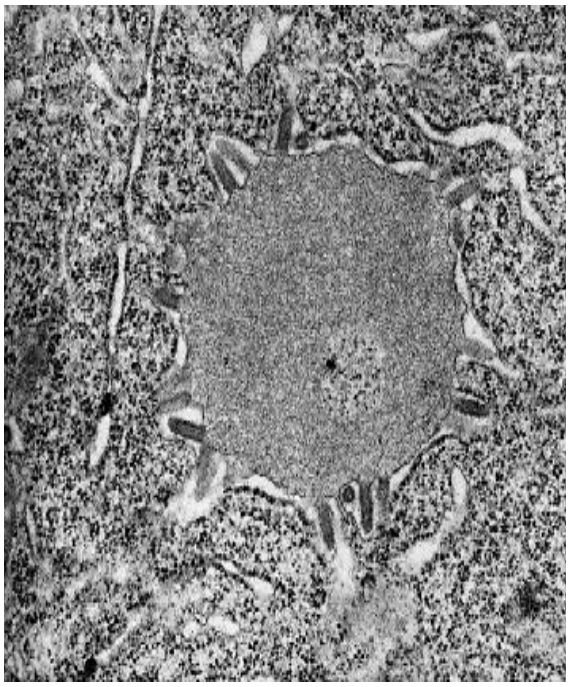
- when symptoms appear after a rabid animal attack→ the diagnosis is readily made

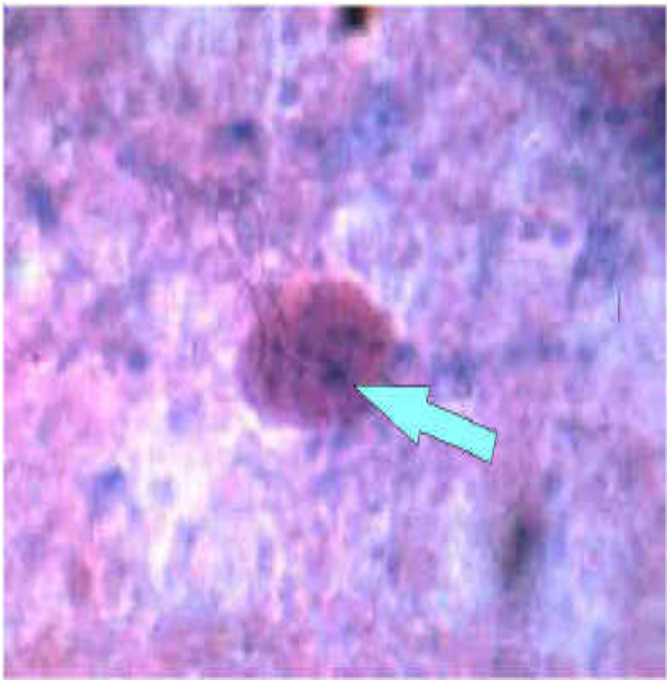
- often the diagnosis is made at autopsy, - the laboratory criteria most diagnostic of rabies are :

1. intracelllular inclusions (Negri bodies)

2. identification, isolation of rabies virus in saliva or brain tissue

3. demonstration of rabies virus antigens in brain, serum , CSF





Section of brain showing rabies viruses. Rabies virus infected - Negri body - note dark blue basophilic granules (Sellers stain)

Rabies Prevention and Control:

Measures that effectively prevent and limit rabies are:

1. Postexposure vaccination

2. Animal control

- 3 IM injections of HDCV (human diploid cell vaccine) are recommended

- **for high risk groups (veterinarians, animal handlers, lab personnel, and travelers to endemic areas) other control measures such as vaccination of domestic animals, elimination of strays, strict animal quarantine have reduced the virus reservoir**

- **A new genetically engineered vaccine made with a vaccinia virus that carries the gene for rabies virus surface antigen**

Postexposure Prophylaxis:

1. A wild animal especially a skunk, raccoon, fox, or coyote that bites without provocation is considered to be rabid and treatment is commenced

2.If the animal is captured, brain samples, and other tissues are examined for verification of rabies

3. In an apparently healthy dog or cat they are quarantined for

10 days for observation

4. Following an animal bite the wound should be scrupulously washed with soap or detergent and water, followed by debridement and application of an antiseptic that inactivates the virus (alcohol or peroxide)

5. Combination of passive and active postexposure immunization is very effective: wound is infused with human rabies immunoglobulin (HRIG) to impede spread of virus , also injected IM-a full course of (HDCV) is given simultaneously

Slow infections in human

- **VIRUSES**
  - **SV40-like viruses (PML)**
  - **measles virus (SSPE)**
  - **rubella virus (PRP)**
- **ATYPICAL AGENTS (prion)**
  - **Kuru, Creutzfeld-Jakob disease (CJD),(new) variant CJD disease (vCJD=nvCJD)**
- **TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHIES (TSEs, TRANSMISSIBLE CEREBRAL AMYLOIDOSES, PRION DISEASES)**
- **human :**
  - **Kuru ,Creutzfeldt-Jakob disease (CJD), Gerstmann-Straussler-Scheinker syndrome (GSS) ,fatal familial insomnia (FFI), variant CJD ('human BSE')**
- **animal**
  - **scrapie (sheep and goats), bovine spongiform encephalopathy (BSE),**
  - **transmissible mink encephalopathy, etc**
  - **Progressive multifocal leukoencephalopathy**
- **Polyoma virus family, SV40-like (JC virus etc)**
- **progressive, usually fatal, associated with immune suppression**
  - **- HAART(high activity anti-retrov. Treatment) may prolong life in AIDS patients but little effect on PML incidence, typically non inflammatory but**

can get an inflammatory response in the brain after HAART treatment (immune reconstitution inflammatory syndrome)

- **demyelination (oligodendrocytes infected)**
- **Progressive multifocal leukoencephalopathy: reactivation of latent infection**
- **70-80% population are seropositive associated with immunosuppression**

BK virus (polyoma)

- **Associated with urinary tract infections in immunosuppression**
- **Possibly contributory factor in prostate cancer???**

MEASLES VIRUS

- **paramyxovirus family (morbillivirus genus)**
- **sub-acute sclerosing panencephalitis(SSPE)**
- **inflammatory disease to defective virus established~1-10 yrs after initial infection, early infection with measles is a risk factor**
- **rare complication of measles (7-70 cases per 1,000,000 cases measles)**
- **vaccine protects against SSPE**

RUBELLA VIRUS: togavirus family (rubrivirus genus) inflammatory disease

- **progressive rubella panencephalitis(PRP) may start years after initial infection congenital / very early infections,it is very rare**

transmissible subacute spongiform encephalopathies

transmissible cerebral amyloidoses, prion diseases(Atypical agent)

- SIMILAR TO VIRUSES: Small, filterable, need host cells

no machinery for energy generation or protein synthesis

- **DIFFERENT FROM VIRUSES**
  - **no detectable virions in infected tissues**
  - **no detectable virions in purified infectious material**
  - **if nucleic acid is present, very small, Highly resistant to inactivation**
- **RESISTANT TO OR ONLY PARTIALLY INACTIVATED BY:**
  - **formaldehyde ,ethanol, glutaraldehyde,ultraviolet and ionizing irradiation**
  - **non-ionic detergents**
  - **INACTIVATED BY:**
  - **autoclaving (121C for one hour) (> standard), 5% sodium hypochlorite**
  - **sodium hydroxide, proteases, urea, other protein denaturants**

IMMUNE RESPONSE

- **no inflammatory response, no interferon induction, no antibody response**

  no cell-mediated response

DIAGNOSIS

- **CLINICAL PICTURE, EEG, MRI (vCJD), USUALLY CONFIRMED by POST-MORTEM**
  - **NOW HAVE ANTIBODIES RAISED IN RECOMBINANT MICE: can be used on biopsy of brain (or peripheral lymphoid tissue in vCJD)**

CONCEPT QUESTIONS

- Is the rabies virus morphology distinctive ?

- **-Define: rabies**
- **- Mention the epidemiologic feature of rabies virus.**
- **- What is sylvanic rabies, and whatis urban rabies ?**
- **- What are the of rabies virus transmission ?**
- **-Describe infection and disease development of rabies.**
- **- Mention the cliniocal phases of rabies .**
- **- Enumerate the forms of rabies .**
- **-Mention the lab. Criteria most diagnostic to rabies.**
- **- Define negri bodies.**
- **- What are the measures that effectively prevent rabies?**
- **- What are thew postexposure prophylaxis ?**