

Virology

Lec (10)

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Teaching Objectives:

1. Define Rabdoviridae.
2. Know general characteristic of Rabdoviridae.
3. Recognize the mechanism of entry, replication and pathogenesis.
4. List factors effecting of infection
5. Know methods of diagnosis, treatment and prevention.

Rabdoviridae

The name of these viruses is derived from the Greek word rhabdos, which means a rod. The virions of some rhabdoviruses, especially those infecting plants, are in the shape of rods with rounded ends, while others, especially those infecting animals, are bullet shaped. Rabdoviridae are very widely distributed in nature, infecting vertebrates, invertebrates and plants. Rabies is the only medically important species

Important properties of Rhabdoviruses

- Important Properties, It has single-stranded RNA negative polarity (12kb), Virion contains an RNA- dependant RNA Polymerase.
- Enclosed within Bullet-shaped capsid surrounded by
- Have lipoprotein envelop with spike (G-protein).
- Rabies consist of 5 type of protein **NP** (nucleoprotein), 2 polymerase [phosphoprotein (**p**), and large protein (**L**)], non glycosylated Matrix protein (**M1** and **M2**) and single surface glycoprotein (**G**).
- Rabies virus has a single antigenic type.
- It has broad host range; it can infect all mammals.
- Rabies is killed rapidly by exposure to ultraviolet radiation or sunlight by heat (1 hour at 50 °C). By lipid solvents, detergents and extremes of Ph.
- Can storage at 4°C for weeks and at -70°C for years, it is inactivated by CO₂

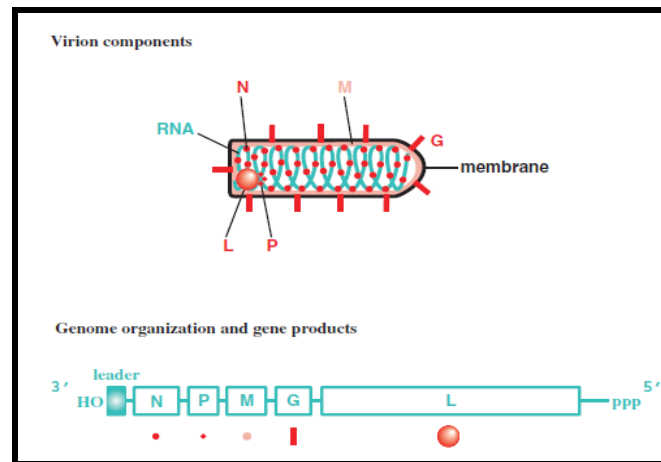


Figure (1): Rhabdovirus virion and genome organization. The genome has a leader sequence and the genes for five structural proteins, the genes are separated by short intergenic sequences.

Mode of transmission:

- Bite of a rabid animals
- Inhalation of aerosols of bat secretion containing rabies virus.
- Organ transplantation such as corneas taken from undiagnosed patients who died of rabies.

Summary of replicative Cycle:

Rabies virus attaches to cells via its glycoprotein spike, the acetylcholine receptor may serve as a cellular receptor for rabies virus. The single-stranded RNA genome is transcribed by the virion-associated RNA polymerase to five mRNA species. The monocistronic mRNAs code for five virion proteins, nucleocapid (N), polymerase protein (P, L), matrix (M), and glycoprotein (G). The genome RNA is a template for complementary positive-sense RNA, which is responsible for the generation of negative-sense progeny RNA. The same viral proteins serve as polymerase for viral RNA replication as well as for transcription. The newly replicated genome RNA associated with viral transcriptase and nucleoprotein to form RNP core in cytoplasm. The particles acquire an envelope by budding through the plasma membrane. The viral matrix protein forms a layer on the inner side of the envelope, whereas the viral glycol protein is on the outer layer and forms the spikes.

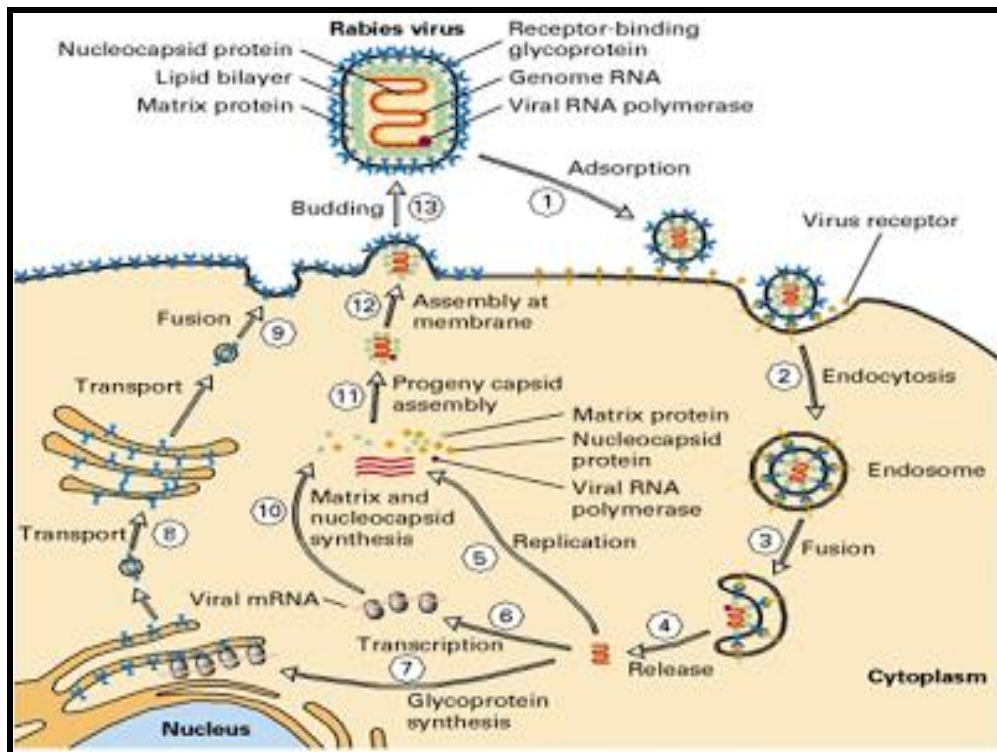


Figure (2): Replication cycle of Rabies virus

Pathogenesis:

The virus multiplies locally at the bite site (muscle or connective tissue), then virus enters peripheral nerves at neuromuscular junctions and spreads up the nerves to central nervous system, it multiplies in the central nervous system. Within CNS, encephalitis develops, with death of neurons and demyelination. Infected neurons contain eosinophilic cytoplasmic inclusion called a Negri body, which is important in laboratory diagnosis of rabies. Then spread through peripheral nerves to the salivary glands, it enters the saliva to be transmitted by bite, and other tissues such as pancreas, kidney, heart and cornea. There is no viremic stage

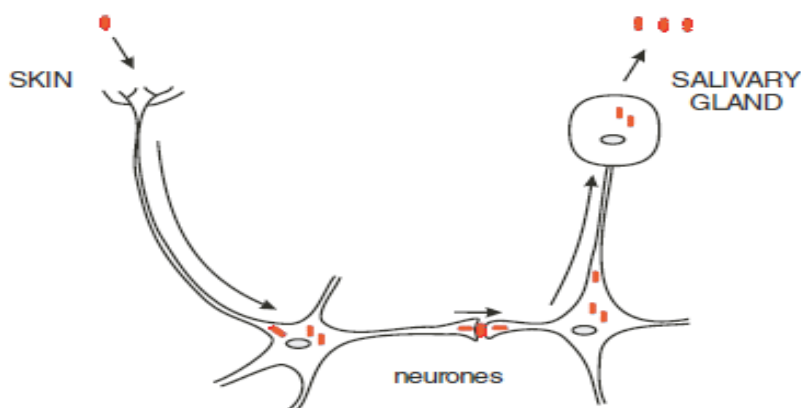


Figure (3):

Rabies virus infection of the animal body, after entering the body through damaged skin a virion

infected a neurone via the nerve endings and is transported to the cell body , where virus replicate takes place. The infection spreads to other neurons and to salivary gland cells, which shed virions into the saliva.

Clinical Findings:

The incubation period varies, according to the location of the bite, from as short as 2 weeks to 16 weeks or longer. It is shorter when the bites are sustained on the head rather than on the leg, because the virus has a shorter distance to travel to reach the CNS.

The clinical spectrum can be divided into three phases.

- 1- Prodromal phase. During this phase many nonspecific symptoms occur of patients such as fever, headache, malaise, anorexia, photophobic, sore throat, nausea, vomiting and changes in sensation at the bite site. This phase lasting 2-10 days.
- 2- Acute neurologic phase. Within a few days, nervous system dysfunction such as nervousness, apprehension, hallucination and bizarre behavior. A general sign over activity is observed such as confusion; lethargy, lacrimation, pupillary dilation and increased salivation develop. Most notable is the painful spasm of the throat muscles on swallowing. This results in hydrophobia, an aversion to swallowing water because it is so painful. This phase which lasts 2-7 days.
- 3- Coma phase. Within several days, the disease progresses to seizures, paralysis and coma. Death almost invariably ensues, but with the advent of life support systems a few individuals have survived.

Susceptibility to infection

1. Host age
2. Genetic background
3. Immune state
4. Viral strain
5. Dose of inoculum
6. Extent of damage(location)
7. Distance of bit from CNS (location of bit)

Laboratory diagnosis:

- 1- Isolation of the virus from saliva, spinal fluid and brain tissue then inoculated intracerebrally into suckling mice, infection in mice results in encephalitis and death. The central nervous system of the inoculated animal is examined for Negri bodies.
- 2- Serological test for detection of antibody's titer in serum patients, IgM in the early stage and IgG in the late stages.
- 3- In human, diagnosis can be made by fluorescent Ab staining of a biopsy specimen taken from the skin.
- 4- Rapid diagnosis of infection in the animal is usually made by examination of brain tissue by using fluorescent antibody to rabies virus or histologic staining of Negri bodies.

Treatment and Prevention:

- 1- No antiviral therapy, only supportive treatment.
 - 2- There are low approaches to prevent rabies in humans:
 - Preexposure: immunization with rabies vaccine should be given to individuals in high-risk group, such as veterinarians, zoo keepers. **Preexposure** immunization consists of three doses given on day 0, 7, and 21 or 28. Booster doses are given as needed to maintain an Ab titer of 1:5.
 - The rabies vaccine, which is killed virus vaccine, is the only vaccine that is routinely used postexposure, e.g., after the person has been exposed to the virus via animal bite. The long incubation period allows the virus in the vaccine sufficient time to induce protective immunity.
 - **Postexposure** immunization involves the use of both the vaccine and human rabies immune globulin plus immediate cleaning of the wound. This is an example of passive-active immunization.
 - Tetanus immunization should also be considered.
- Immunization should be done at different site to prevent neutralization of the virus in the vaccine by the Ab in the rabies immune globulin.
- 3- **Rabies antibody.** Rabies immune globulin, Human (HRIG) prepared from the plasma of hyperimmunized humans, and antirabies serum, equine usually prepared from horses hyperimmunized it has been used in countries where HRIG is not available.