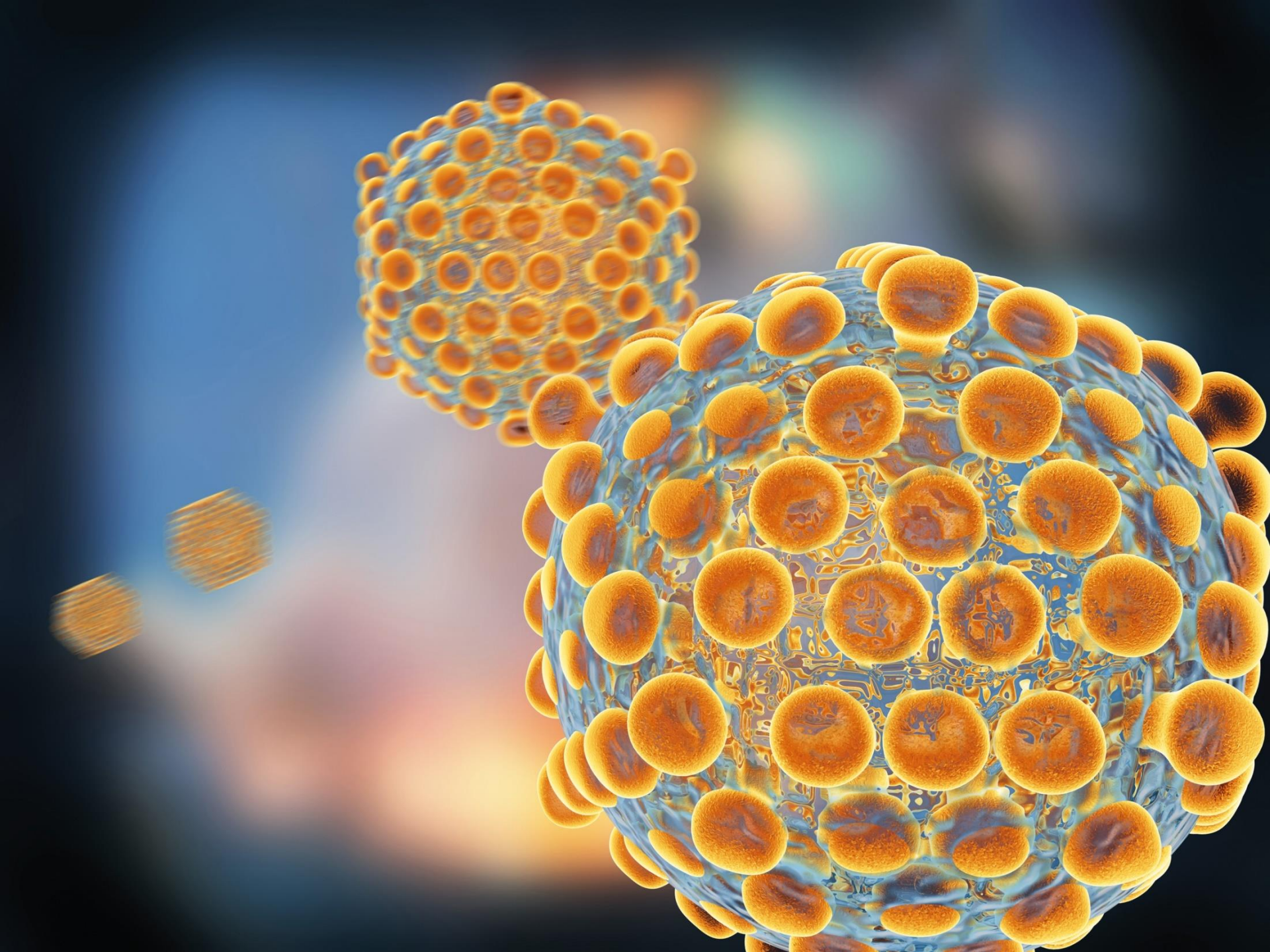
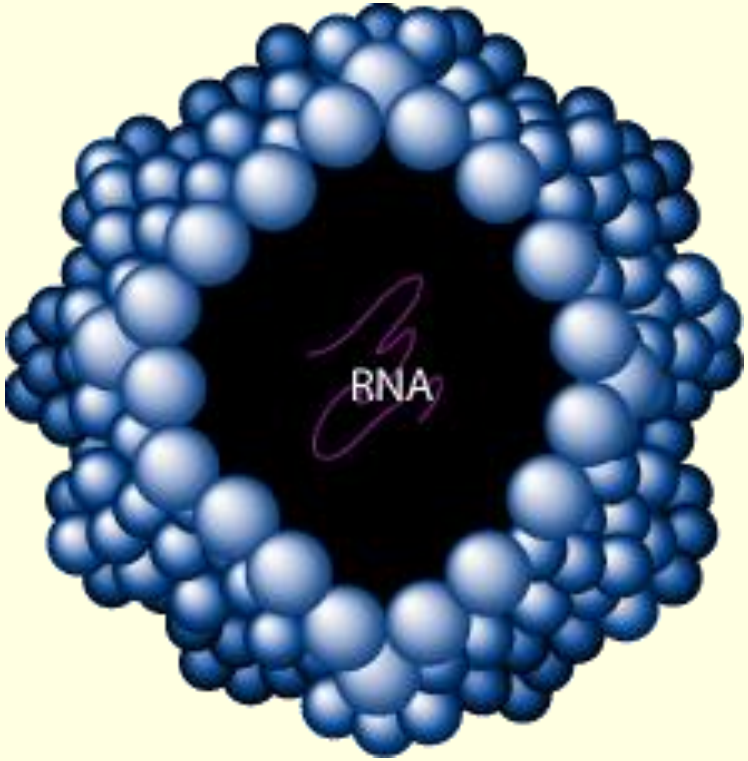


Classification of Enteroviruses

Enteroviruses belong to the ***family Picornaviridae genus Enterovirus.*** From medical point of view important viruses of this group are Polio-, Echo- and Coxsackie- viruses.

Members of Rhinovirus genus of the family Picornaviridae inhabiting upper respiratory tract have medical importance too.

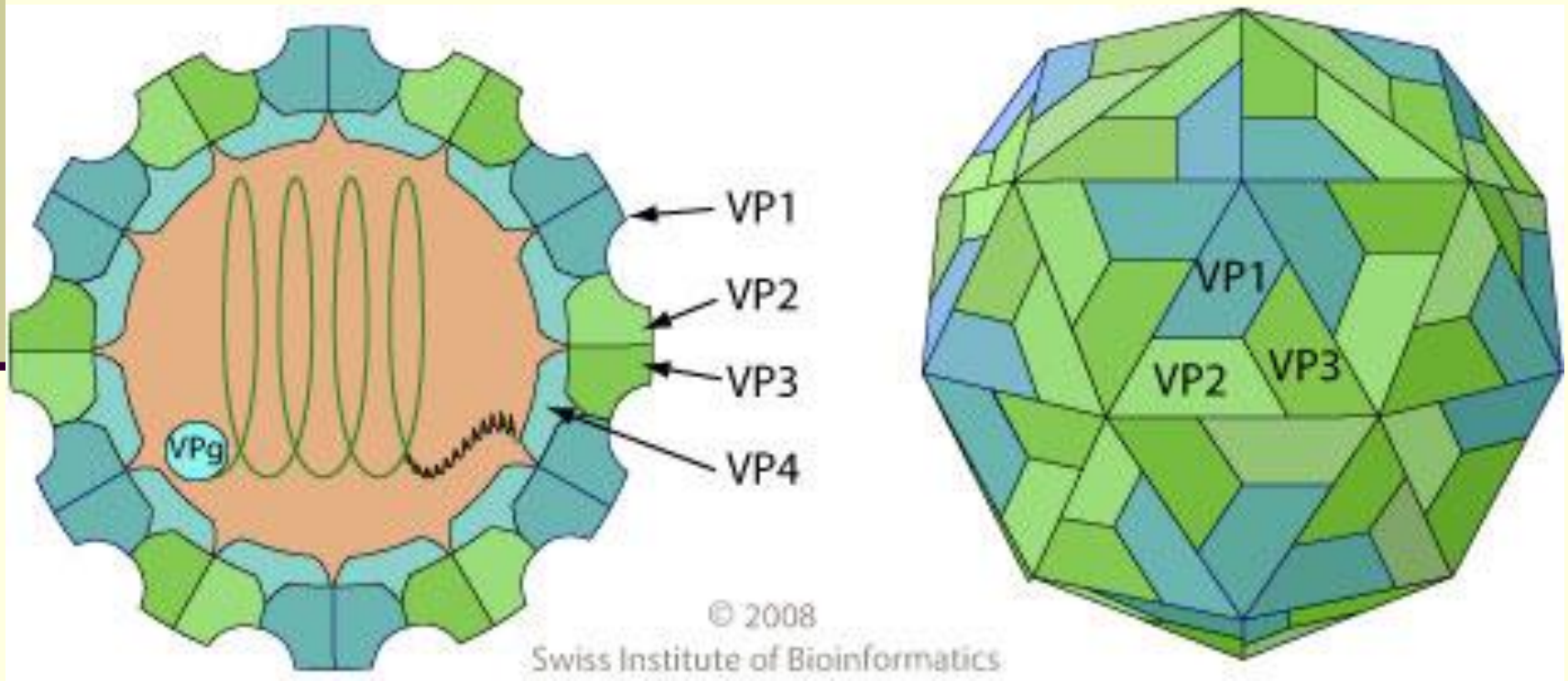


Some properties of Enteroviruses

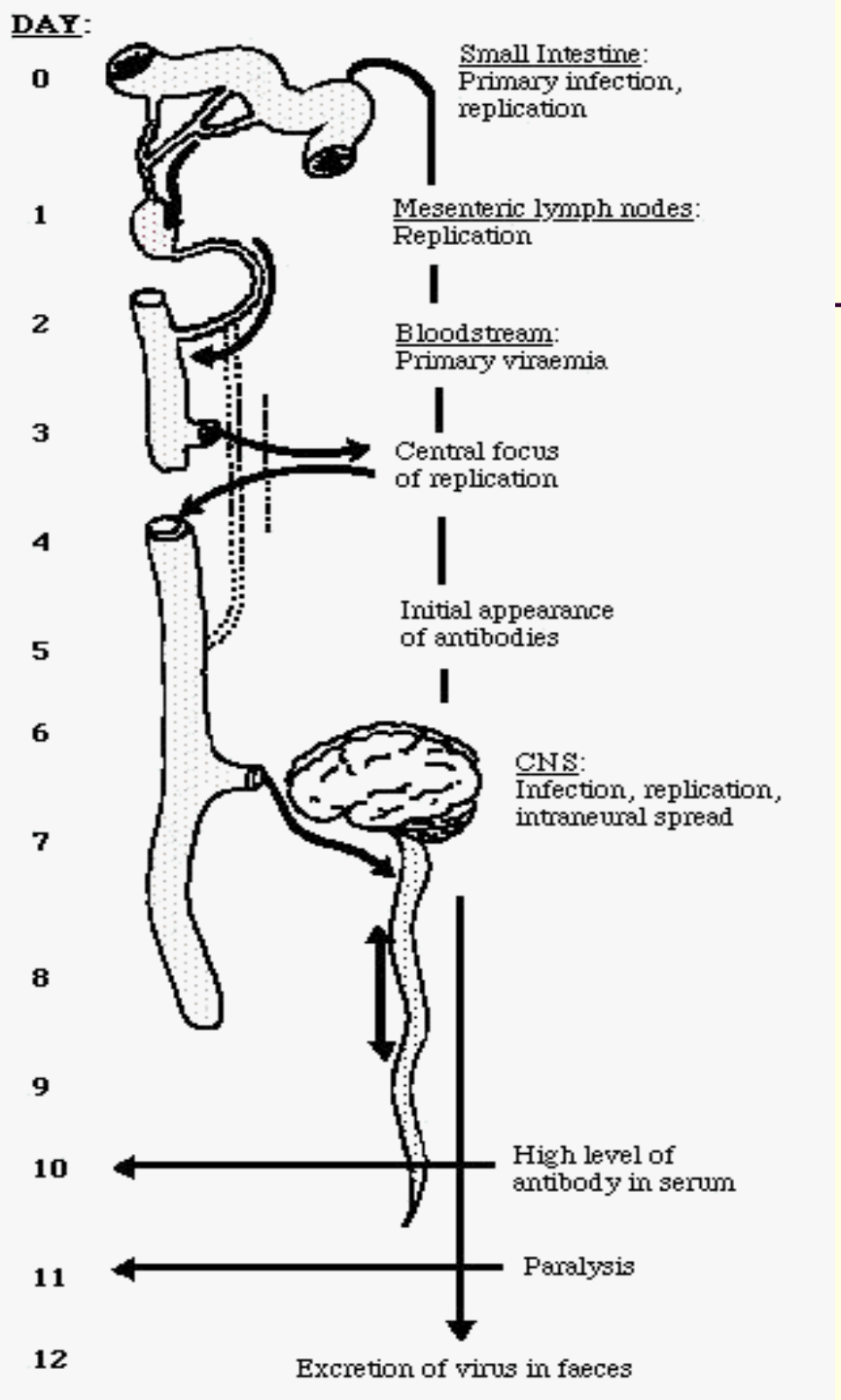
- Size
- Capsid
- Shape
- RNA type
- Acid

- 22-30 nm
- 60 capsomers
- Icosahedral
- Single-stranded,positive-sense
- Stable (pH 3-9)

Non-enveloped, spherical, about 30 nm in diameter, composed of a protein shell surrounding the naked RNA genome. The capsid consists of a densely-packed icosahedral arrangement of 60 protomers, each consisting of 4 polypeptides, VP1, VP2, VP3 and VP4. VP4 is located on the internal side of the capsid.



- Poliovirus is the causative agent of poliomyelitis. Poliovirus strains are classified into three **antigenic types, types 1, 2, 3.** Each type contains **2 type specific antigens, C and D**. C antigen of all types are cross-reactive but D antigens are not. One attack of poliomyelitis gives permanent immunity only against the type causing the infection.
- ***Transmission*** is the fecal-oral route.
- ***Pathogenesis.*** The virus enter the body by ingestion or inhalation and multiplies in limphatic tissue of alimentary canal (from tonsils to Peyer`s patches) entering regional lymph nodes. Then viruses are carried to blood stream from here viruses are taken to spinal cord and brain by passage across the blood-CNS barrier. An alternative pathway may be via entry into motor neurons at peripheral neuromuscular junction. The viruses multiple in the neurons and destroy them with degeneration of Nissle bodies. Lesions are mostly in anterior horn of spinal cord. Sometimes we may find extensive lesions like encephalitis.


DAY:
0
1
2
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7
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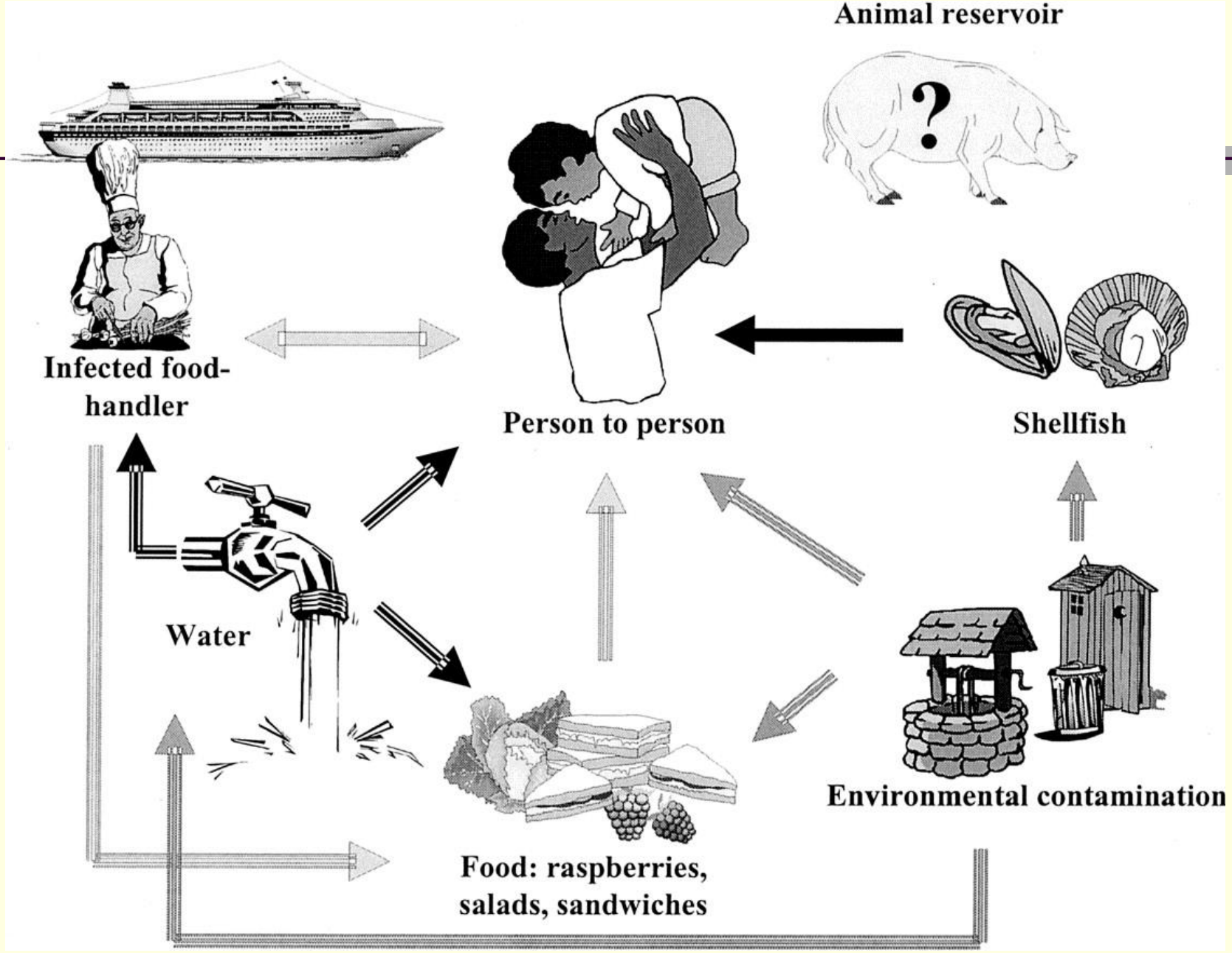
10
11
12
Small Intestine:
Primary infection,
replication
Mesenteric lymph nodes:
Replication
Bloodstream:
Primary viraemia
Central focus
of replication
Initial appearance
of antibodies
CNS:
Infection, replication,
intraneural spread
High level of
antibody in serum
Paralysis
Excretion of virus in faeces


Animal reservoir
?
Infected food-handler
Person to person
Shellfish
Water
Environmental contamination
Food: raspberries, salads, sandwiches

Clinical features

- The incubation period is about 10 days with range from 4 days to 4 weeks. The earliest features associated with phase of viraemia consist of fever, malaise, headache, drowsiness, constipation and sore throat and last for 1 to 5 days.
- Most polio infections **are inapparent** (90-95%). Recovery takes place in a few days.
- In the other cases the following types of disease may occur:
- Aseptic meningitis (**nonparalytic poliomyelitis**) occurs in 1-2% of cases. The patient develops stiffness and pain in back and neck. The illness lasts for 2-10 days. Patient recovers rapidly and recovery is complete.

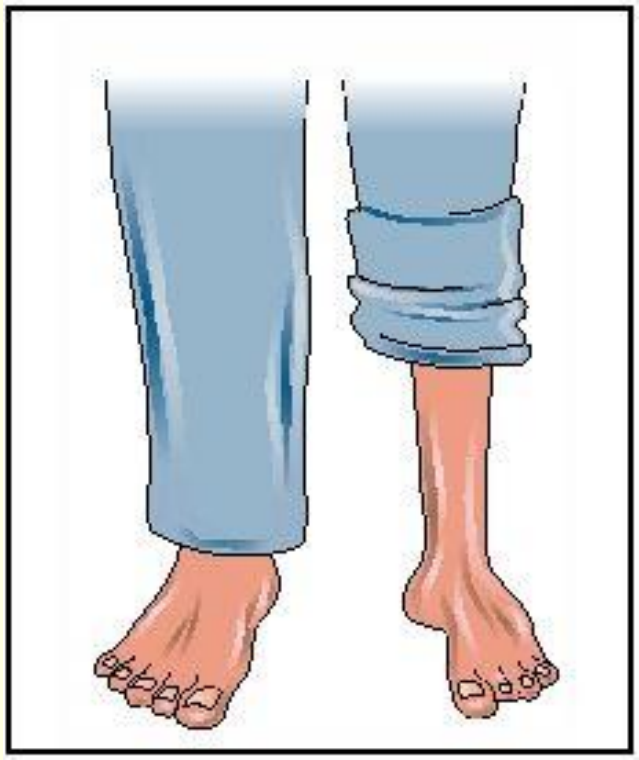
- **Paralytic poliomyelitis** (0,1-2%).

  - Spinal poliomyelitis is characterized by flaccid paralysis because the disease process involves motor neurons. The paralysis is ussually asymmetrical. The proximal muscles are more likely to be involved than the distal muscles, and the lower extremities are involved more often than upper extremities. The paralyzed muscles eventually become atrophic as a result of a lack of motor innervation.

  - Bulbar poliomyelitis involves the base of the brain and is a much more serious condition than spinal poliomyelitis. The involvement of cranial nerves and the respiratory and circulatory centers in the medulla compromises vital functions, particularly the control of respiratory muscles. Bulbar poliomyelitis is more common in adults.

  - Bulbospinal poliomyelitis. In bulbospinal poliomyelitis the prognosis is very poor.

- In its most severe form, polio causes paralysis of the muscles of the legs, arms, and respiratory system. All muscle tone is lost in the affected limb, and the muscle becomes flaccid and begins to atrophy, as shown in the illustration above.

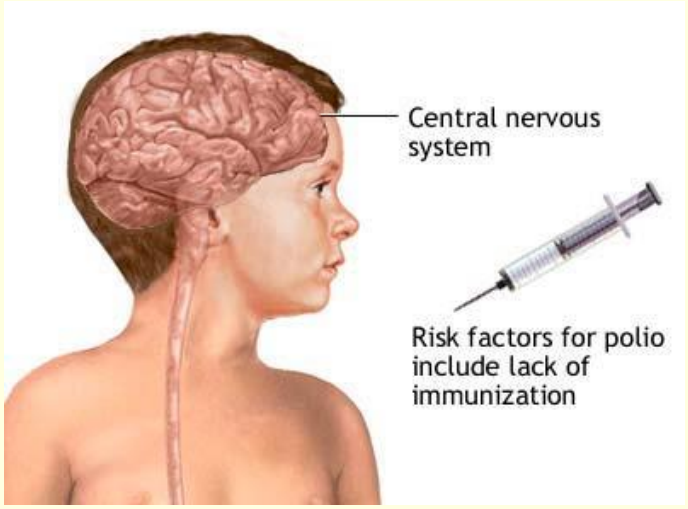


- Encephalitis as a result of poliovirus infection is rare, but carries a grave prognosis.
- Postpolio syndrome. 20-30% of individuals who experienced a paralytic episode of polio in their youth experience fatigue, muscle pain, weakness, and atrophy 25-35 years later. The recurrence seems to be associated with further denervation of previously affected groups. The cause for this denervation is unknown.

- ***Laboratory diagnosis*** is made by isolation of viruses from throat (first 3 days) and faeces (1 - 2 weeks). After processing specimen is inoculated into tissue culture. The poliovirus is cultivated in human and simian cell lines. CPE is observed in 2-3 days. Identification of virus is done by neutralization test with standard sera of 3 types.
- Virus can be detected in stool by electron microscopy as well as by immune electron microscopy.
- Serology. Paired serum specimens are tested for neutralising and complement fixing antibodies.

Prophylaxis

- Live oral attenuated polio vaccine (OPV) [Sabin`s vaccine]
- Killed polio vaccine (Inactivated Polio vaccine, IPV) [Salk`s vaccine]



Comparison of Polio Vaccines

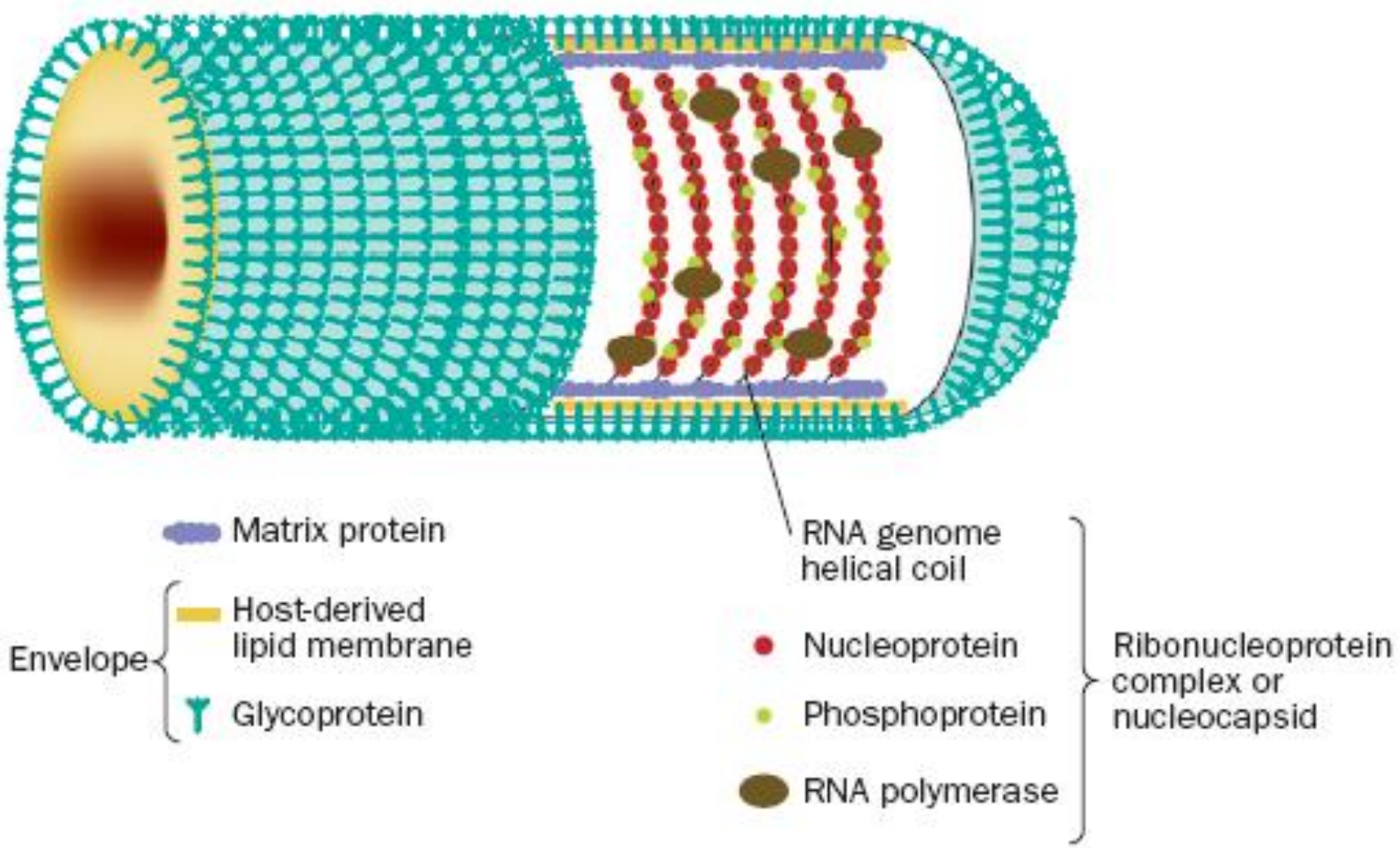
Characteristic	Sabin`s Vaccine	Salk`s Vaccine
Immunizing agent	Live, attenuated virus	Killed virus
Administration route	Oral	Parenteral
Immunity	Mucosal (Ig A) and systemic	Systemic
Induction of herd immunity	Yes	No
Reversion to virulent form	Possible,but very rare	No

Morphology of Rabies virus

- *Classification.* Rabies virus belong to the family Phabdoviridae genus Lyssa virus.
- The rabies virion is bullet-shaped and approximately 180x75 nm. Its core is a single negative strand of non-segmented RNA, associated with a nucleoprotein (N), a phosphoprotein (NS), and an RNA polymerase (L) to form a helical ribonucleoprotein complex (RNP). The enveloping membrane consists of inner matrix protein (M) covered by a coat of glycoprotein (G) and host-derived lipid. This G molecule bears numerous spikes, 10 nm long, and its composition determines viral virulence.
- Virus isolated from naturally infected animals is known as “street” virus. Repeated intracerebral passage in rabbits produces “fixed” virus with a shortened incubation period and reduced pathogenecity for other species. This is used for vaccine production.

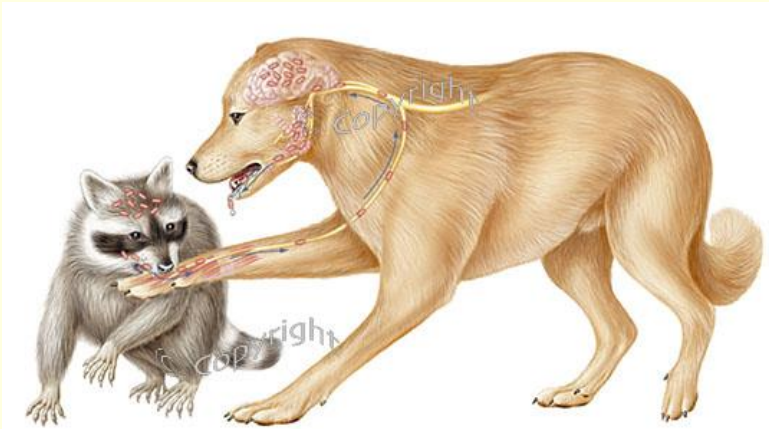
The internal ribonucleoprotein (RNP) core of the rabies virion consists of a negative-sense genome RNA encapsidated by nucleoprotein, polymerase cofactor phosphoprotein, and the virion-associated RNA polymerase. The RNP core is covered in matrix protein and surrounded by a lipid-bilayer envelope (Warrell et al. 2004).

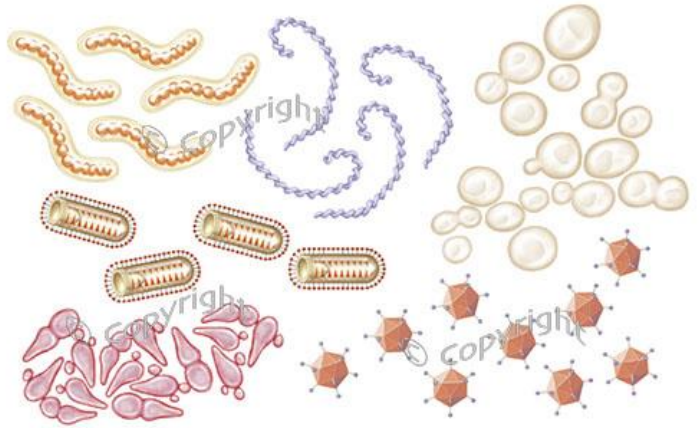
Permission to use figure pending.



Epidemiology of Rabies

Rabies is a zoonosis that remains endemic in most parts of the world. Rabies is a natural infection of dogs, foxes, wolves, skunks, cats and bats.
Fox, vampire bats and dogs are important maintenance hosts. Humans are occasionally infected by wild mammals, but domestic dogs and cats, the principal vectors in the urban phase of rabies, are responsible for more than 90% of human cases worldwide.

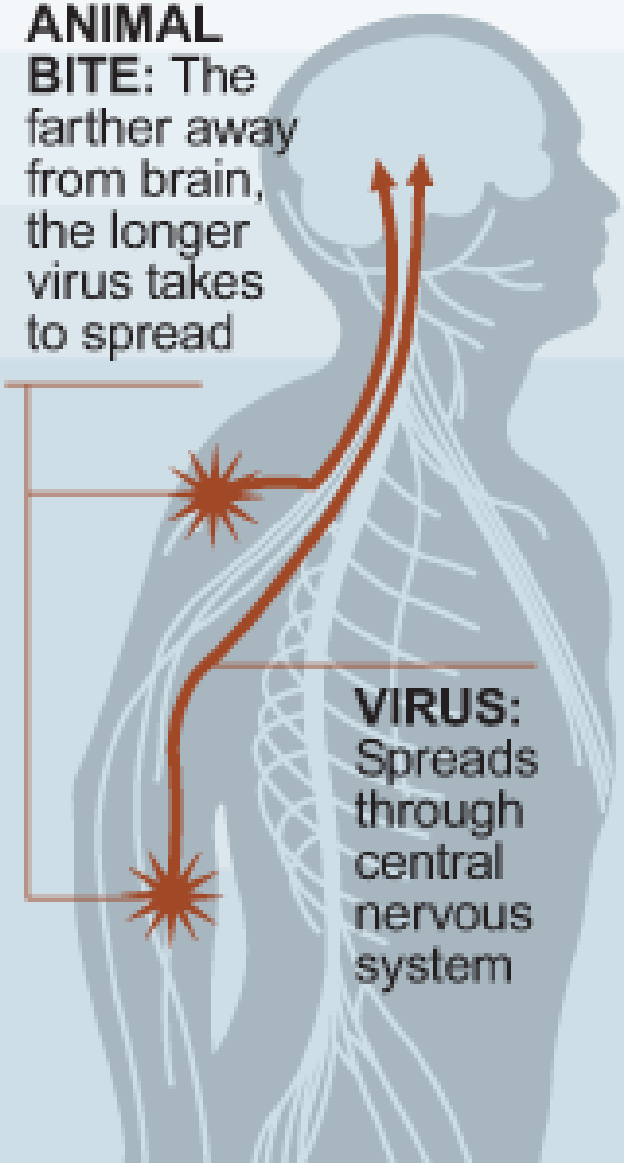




Rabies

How it spreads

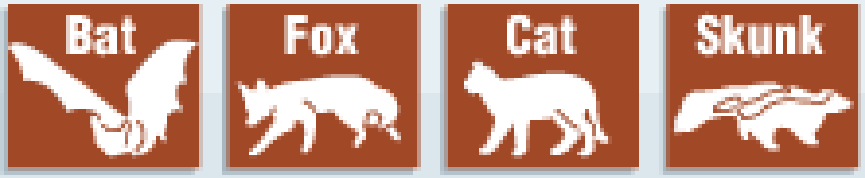
ANIMAL BITE: The farther away from brain, the longer virus takes to spread



VIRUS: Spreads through central nervous system

Common carriers of rabies

Infected animals: Show no fear for humans; act very agitated



Dog: Another common rabies source

Symptoms in humans

- Fever, depression
- Agitation
- Painful spasms followed by excessive saliva
- Death within a week without vacine

Treatment: Hospitalization, immune globulin injections, anti-rabies vaccine

Foaming at mouth after drinking: Produced by spasms in throat

In Western Europe, 86% of all isolates of rabies are from foxes. Cyclical epizootics of rabies, such as the current fox epizootic in Europe, result from an uncontrolled increase in the population of the key reservoir species.

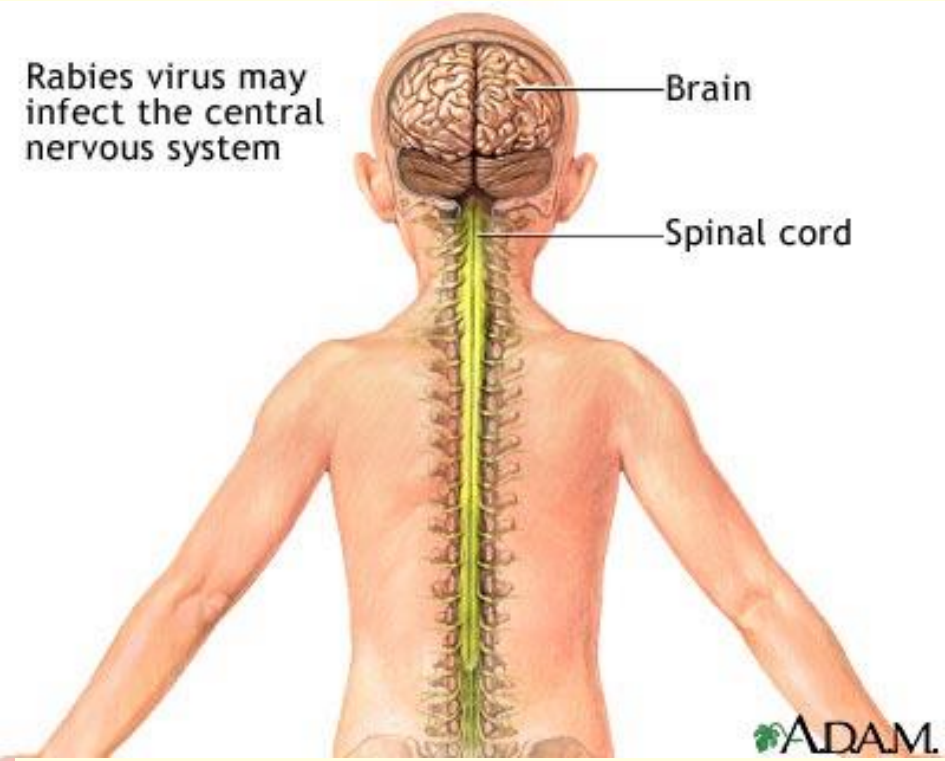
Incidence of human rabies. In 1992, in India the estimated mortality was 30000, and in Bangladesh it was 2000. In the same year in Nepal, 200 deaths, in Sri Lanka 112 deaths, in Pakistan 6500 deaths were reported. In Columbia almost 2% of autopsies showed evidence of rabies.

Pathogenesis and clinical features of Rabies

- Virus penetrate broken skin and intact mucosae. Humans are usually infected when virus-laden saliva is inoculated through the skin by the bite of a rabid mammal. Inhalation of rabies virus may be an important method of transmission among cave-dwelling bats. In Texas, two men died of rabies after visiting caves inhabited by millions of Mexican free-tailed bats, many of which were rabid. They inhaled an aerosol created by the bats infected nasal secretions. The saliva, respiratory secretions, tears and urine of rabies patients contain virus.

- *Incubation period* varies from 1-3 months, sometimes may be short (10 days) particularly in children and with wounds on face and neck.
- Rabies virus may replicate locally in muscle cells or attach directly to the motor or sensory nerve endings. Rabies virus travels centripetally within the axoplasm. A current hypothesis is that the virus travels in an incomplete form, perhaps as naked ribonucleoprotein complexes, at this stage. On reaching the central nervous system, there is massive viral replication on membranes within neurones and direct transmission of virus from cell to cell occurs across synaptic junctions.The virus spreads widely from brain along the nerve trunks to salivary glands and other tissues.

Rabies


Rabies virus may infect the central nervous system
Brain
Spinal cord
A.D.A.M.


Brain inflammation
Virus transmitted by infected saliva through bite or wound
A.D.A.M.

- *Clinical features.* In many patients, the first symptom is itching, pain or paraesthesia at the site of the healed bite wound. Non-specific prodromal symptoms include fever, chills, malaise, headache, photophobia, myalgia, anxiety, depression, irritability. After a prodromal period, infected person develops characteristic fear of water (hydrophobia). Attempts at drinking provokes violent contraction of diaphragm and inspiratory muscles. Thereafter, mere sight, sound or even mention of water precipitates distressing muscular spasm. About one-third of the patients will die during a hydrophobic spasm in the first few days. The rest lapse into coma and generalized flaccid paralysis, and rarely survive for more than a week without intensive care.

Laboratory diagnosis

- A suspect rabid animal that might have infected a patient should be killed and the brain examined without delay. Rabies antigen can be detected within a few hours by a direct immunofluorescent antibody test on acetone-fixed, brain impression smears or using a rapid enzyme immunodiagnosis kit if a fluorescent microscope is not available. Virus isolation takes up to 3 week by introcerebral inoculation of mice. In men, rabies can be confirmed early in the illness by demonstration of viral antigen by immunofluorescence in nerve twiglets in skin biopsies. The polymerase chain reaction is used too. During the first week of illness virus may be isolated fom saliva, brain, CSF, and rarely urine. Rabies antibodies are not usually detectable in serum or CSF before the eighth day of illness in unvaccinated patients.

Prophylaxis of Rabies

- Pre-exposure prophylaxis is necessary for person who handle potentially infected animals.
- Post-exposure prophylaxis. When the risk of rabies is great, individuals should be given post-exposure prophylaxis by hyperimmune serum and vaccine.
- Vaccines are of two categories - neural (Semple vaccine, Betaproiolactone (BPL) vaccine) and non-neural (Human diploid cell strain vaccine (HDCV), Purified chick embryo cell vaccine (PCECV)).
- Because of some risks with neural vaccine, nonneural vaccines are being used increasingly.