

MICROBIOLOGY

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Number

3

Subject

Poliovirus

Doctor

Ashraf

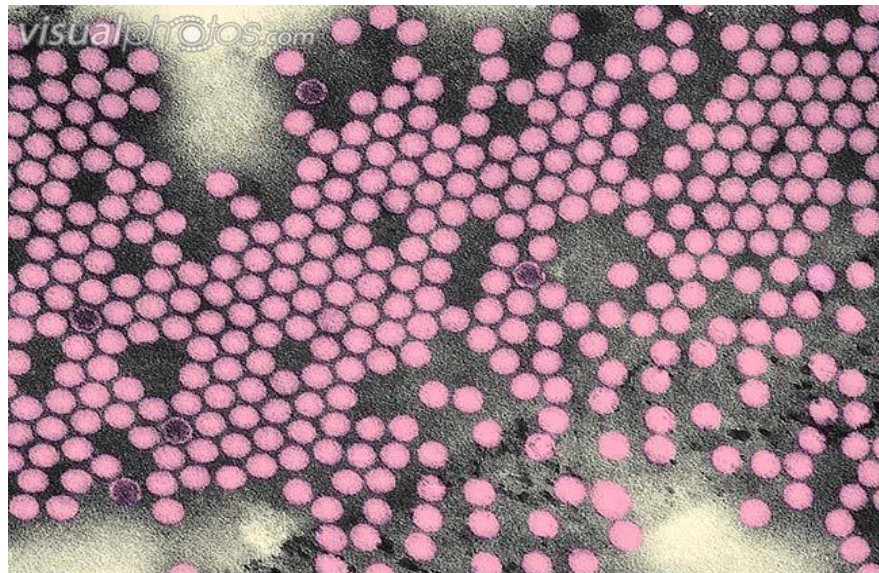
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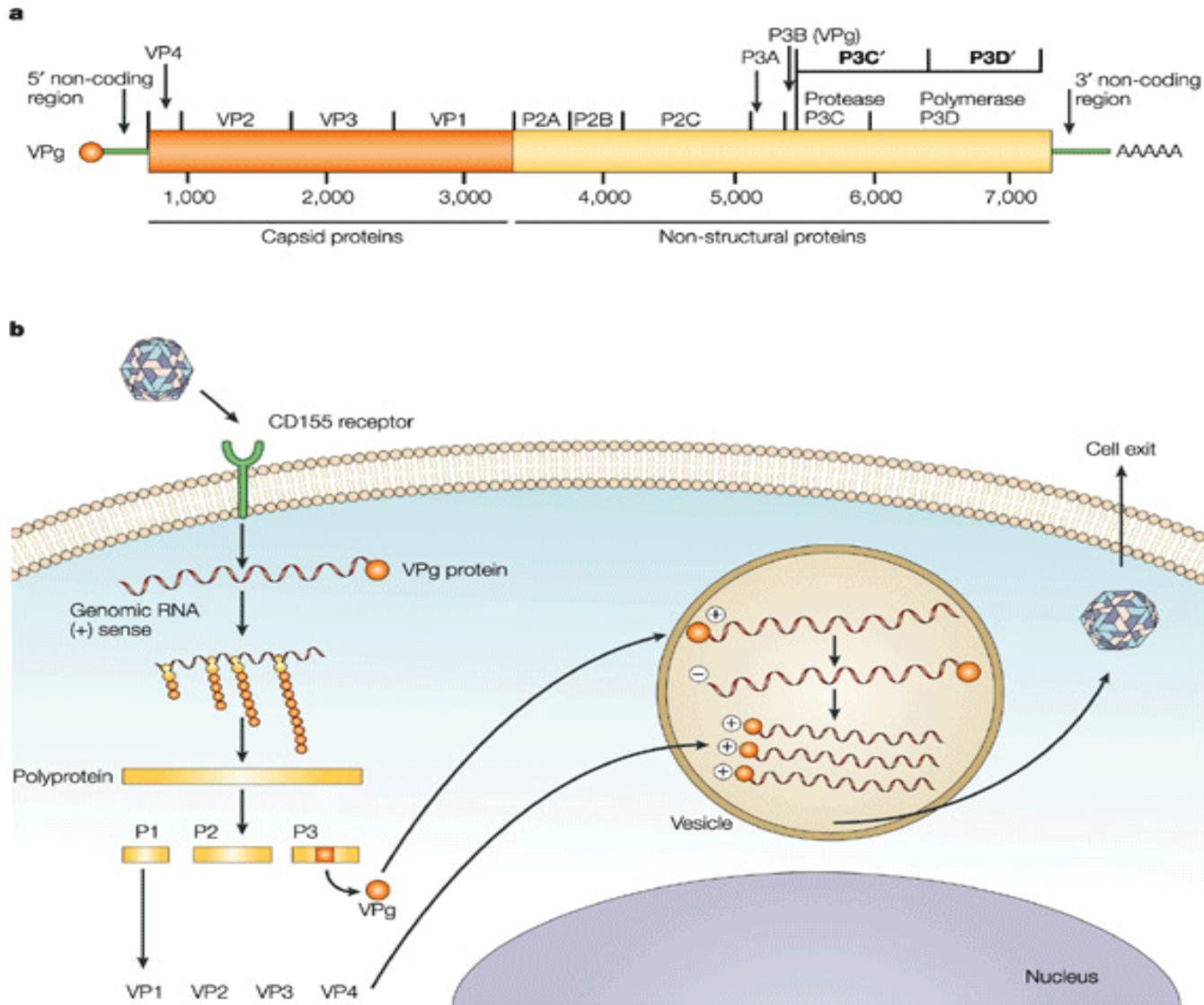
Poliovirus

Poliovirus

- It belongs to the Enteroviruses genus of the picornavirus family which replicate mainly in the gut.
- Single stranded naked RNA virus with icosahedral symmetry
- Capsid has 60 copies each of 4 proteins, VP1, VP2, VP3 and VP4 arranged with icosahedral symmetry around a positive sense genome.
- Stable in acidic pH (3)
- first identified in 1909 by inoculation of specimens into monkeys. The virus was first grown in cell culture in 1949 which became the basis for vaccines.



Poliovirus replication



Poliovirus

- The term derives from the Ancient Greek *poliós*, meaning "grey", *myelós* “marrow”, referring to the grey matter of the spinal cord, and the suffix *-itis*, which denotes inflammation. Inflammation of the spinal cord’s grey matter, although a severe infection can extend into the brainstem and even higher structures
- 3 serotypes of poliovirus (1, 2, and 3) but no common antigen.
- *PV1* is the most common form encountered in nature and associated with paralysis, however all three forms are extremely infectious
- Have identical physical properties but only share 36-52% nucleotide homology.
- Humans are the only susceptible hosts.
- Polioviruses are distributed globally. Before the availability of immunization, almost 100% of the population in developing countries were infected before the age of 5.
- The availability of immunization and the poliovirus eradication campaign has eradicated poliovirus in most regions of the world except in the Indian Subcontinent and Africa.

Pathogenesis

- The incubation period is usually 6 - 20 days.
- Infection occurs via the fecal–oral route
- Following ingestion, the virus multiplies in the oropharyngeal and intestinal mucosa.
- Poliovirus divides within gastrointestinal cells for about a week, from where it spreads to the tonsils, the intestinal lymphoid tissue including the M cells of Peyer's patches, and the deep cervical and mesenteric lymph nodes, where it multiplies abundantly. The virus is subsequently absorbed into the bloodstream resulting in a transient viraemia.
- Viremia leads to the development of minor influenza-like symptoms and in a minority of cases the virus may involve the CNS following dissemination.
- In most cases, this causes a self-limiting inflammation of the meninges, the layers of tissue surrounding the brain, which is known as nonparalytic aseptic meningitis

Clinical Manifestations

There are 3 possible outcomes of infection:

- **Subclinical infection (90 - 95%)** - inapparent subclinical infection account for the vast majority of poliovirus infections.
- **Abortive infection (4 - 8%)** - a minor influenza-like illness occurs, recovery occurs within a few days and the diagnosis can only be made by the laboratory. The minor illness may be accompanied by aseptic meningitis
- **Major illness (0.1-1 %)** - the major illness may present 2 - 3 days following the minor illness or without any preceding minor illness. Signs of aseptic meningitis are common. Involvement of the anterior horn cells lead to flaccid paralysis. Involvement of the medulla may lead to respiratory paralysis and death.

Clinical Manifestations

Paralytic polio

- In around 1% of infections, poliovirus spreads along certain nerve fiber pathways, preferentially replicating in and destroying motor neurons within the spinal cord, brain stem, or motor cortex.
- Early symptoms of paralytic polio include high fever, headache, stiffness in the back and neck, asymmetrical weakness of various muscles, difficulty swallowing, muscle pain.
- Paralysis generally develops 1-10 days after early symptoms begin, progresses for 2-3 days, and is usually complete by the time the fever goes away.
- The likelihood of developing paralytic polio increases with age where children under five years of age, paralysis of one leg is most common; in adults, extensive paralysis of the chest and abdomen also affecting all four limbs—quadriplegia—is more likely
- Depending on the site of involvement it can be divided into 3 types:
 - Spinal polio: most common
 - Bulbar polio
 - Bulbospinal polio: paralysis of the diaphragm

Laboratory Diagnosis

- Virus Isolation

- Mainstay of diagnosis of poliovirus infection
- poliovirus can be readily isolated from throat swabs, feces, and rectal swabs. It is rarely isolated from the CSF
- Can be readily grown and identified in **cell culture**
- Requires molecular techniques **PCR** to differentiate between the wild type and the vaccine type because for each reported case of paralytic polio caused by wild poliovirus, an estimated 200 to 3,000 other **contagious asymptomatic carriers** exist

- Serology

- Very rarely used for diagnosis since cell culture is efficient. Occasionally used for immune status screening for immunocompromised individuals.

Prevention (1)

No specific antiviral therapy is available. Treatment of polio often requires long-term rehabilitation, including occupational therapy, physical therapy and sometimes orthopedic surgery.

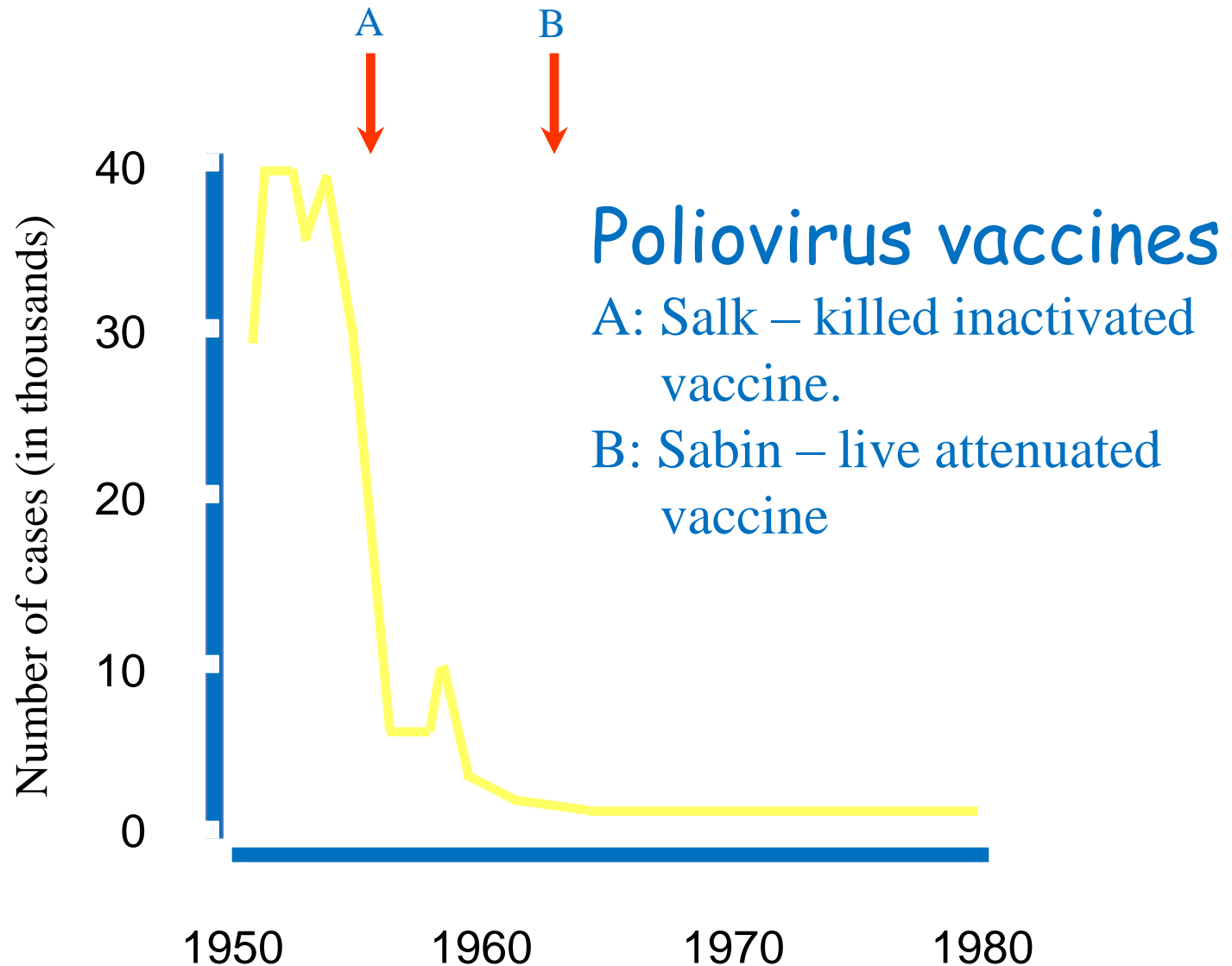
However the disease may be prevented through vaccination. There are two vaccines available.

- **Intramuscular Poliovirus Vaccine (IPV) Salk**
 - consists of formalin inactivated virus of all 3 poliovirus serotypes. Formalin inactivated
 - Two doses 6-8 wks apart, 3rd given after 8-12 months; protective 99%
 - Produces serum antibodies only: does not induce local immunity and thus will not prevent local infection of the gut.
 - However, it will prevent paralytic poliomyelitis since viraemia is essential for the pathogenesis of the disease.
- **Oral Poliovirus Vaccine (OPV) Sabin**
 - Consists of live attenuated virus of all 3 serotypes, produced by the repeated passage of the virus through nonhuman cells at subphysiological temperatures
 - Two doses 6-8 wks apart, 3rd given after 8-12 months; protective 95%
 - Produces local immunity through the induction of an IgA response as well as systemic immunity.
 - Rarely causes paralytic poliomyelitis, around 1 in 2 million doses.

Prevention (2)

- Most countries use OPV because of its ability to induce local immunity and also it is much cheaper to produce than IPV.
- The normal response rate to OPV is close to 95%.
- OPV is used for the WHO poliovirus eradication campaign.
- Because of the slight risk of paralytic poliomyelitis, some Scandinavian countries have reverted to using IPV. Because of the lack of local immunity, small community outbreaks of poliovirus infections have been reported.
- Poliovirus was targeted for eradication by the WHO by the end of year 2000. To this end, an extensive monitoring network had been set up.
- Poliovirus has been eradicated from most regions of the world except the Indian subcontinent and sub-Saharan Africa. It is possible that the WHO target may be achieved.

Incidence of Poliomyelitis



National vaccination program

برنامج التطعيم للأطفال / الأردن

أقرب وقت بعد الولادة، يعطى مطعوم السل (BCG)
على عمر شهرين (٦١ يوم) يعطى الجرعة الأولى من مطعوم التهاب الكبد نوع ب + الجرعة الأولى من المطعوم الخماسي المحسن الذي يتكون من: المطعوم الثلاثي DaPT (الدفتيريا والسعال الديكي اللاخوي والكزاز) + مطعوم المستدمية النزلية نوع ب ومطعوم الشلل المقتول (IPV)
على عمر ٣ شهور (٦١ يوم) يعطى الطفل الجرعة الثانية من مطعوم التهاب الكبد نوع ب + الجرعة الثانية من المطعوم الخماسي المحسن الذي يتكون من: المطعوم الثلاثي DaPT (الدفتيريا والسعال الديكي اللاخوي والكزاز) + مطعوم المستدمية النزلية نوع ب ومطعوم الشلل المقتول (IPV) بالإضافة الى جرعة من مطعوم الشلل الفموي (OPV)
على عمر ٤ شهور (١٢١ يوم) يعطى الطفل الجرعة الثانية من مطعوم التهاب الكبد نوع ب + الجرعة الثالثة من المطعوم الخماسي المحسن الذي يتكون من: المطعوم الثلاثي DaPT (الدفتيريا والسعال الديكي اللاخوي والكزاز) + مطعوم المستدمية النزلية نوع ب ومطعوم الشلل المقتول (IPV) بالإضافة الى جرعة من مطعوم الشلل الفموي (OPV)
على عمر ٩ شهور (بداية الشهر العاشر) يعطى الطفل - مطعوم الحصبة Measles + مطعوم شلل الأطفال الفموي OPV
عند بلوغ الطفل عامه الأول يعطى الطفل الجرعة الأولى من المطعوم الثلاثي الفيروسي MMR (الحصبة والحصبة الألمانية والنكاف)
على عمر ١٨ شهر يعطى الطفل الجرعة المدعمة من مطعوم شلل الأطفال الفموي OPV والمطعوم الثلاثي البكتيري DPT + الجرعة الثانية من مطعوم الثلاثي الفيروسي MMR

Prognosis

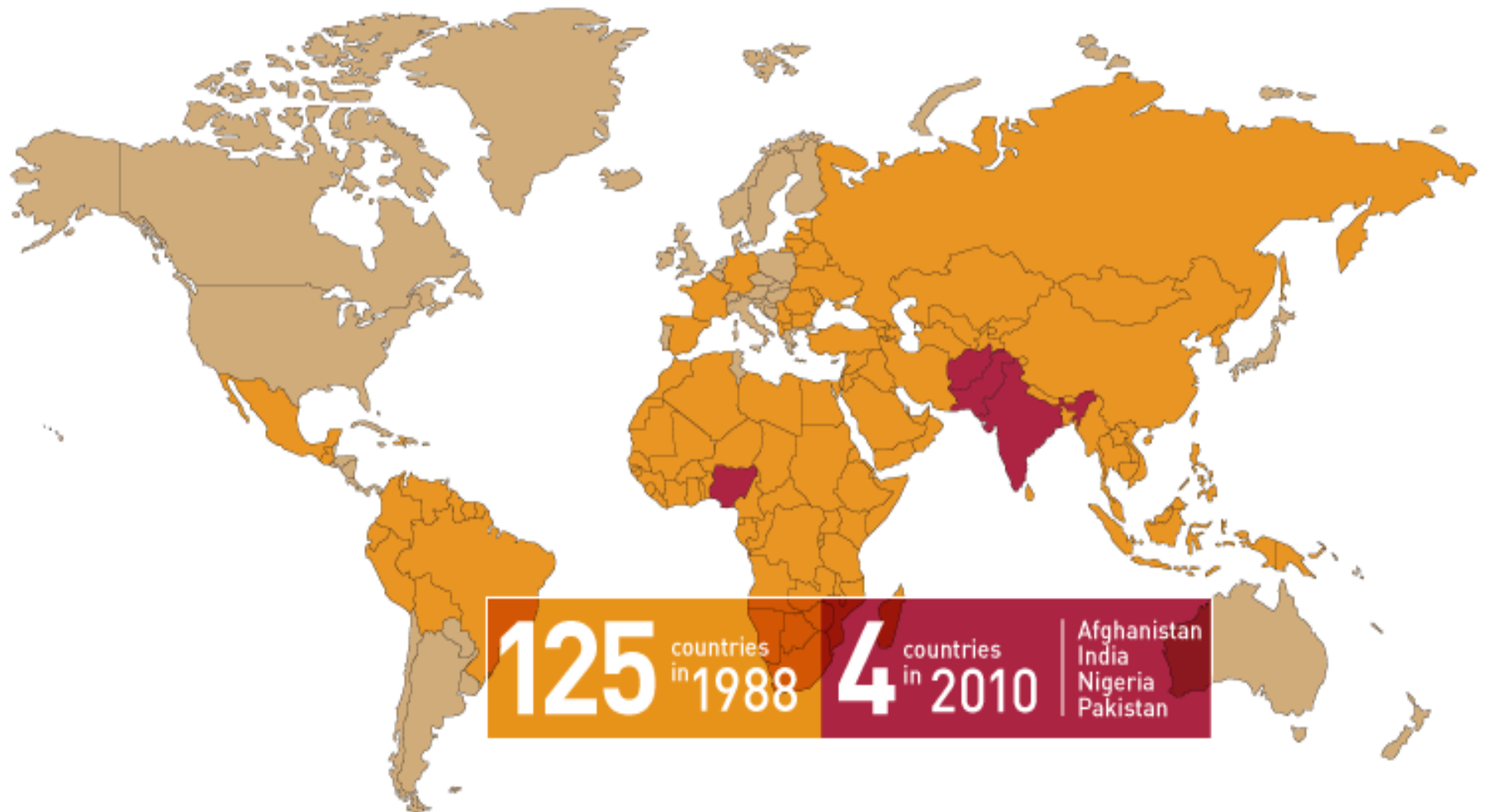
- Patients with abortive polio infections recover completely.
- In those who develop only aseptic meningitis, the symptoms can be expected to persist for two to ten days, followed by complete recovery.
- In cases of spinal polio, if the affected nerve cells are completely destroyed, paralysis will be permanent; cells that are not destroyed, but lose function temporarily, may recover within four to six weeks after onset.
- Half the patients with spinal polio recover fully; one-quarter recover with mild disability, and the remaining quarter are left with severe disability

Complications: Muscle paresis and paralysis can sometimes result in skeletal deformities, tightening of the joints and movement disability

Polio in children



Current Status of Wild Poliovirus Transmission



What is Rabies?

- A disease characterized by severe neurologic symptoms and signs as a result of an animal bite.
- Progressive excess in motor activity, agitation, hallucination and salivation as a result of virus spread to autonomic nervous system.
- Rabies virus causes an acute encephalitis (inflammation of the brain) in all warm-blooded hosts.
- Rabies is not, in the natural sense, a disease of humans.
- The impact of rabies on public health includes an estimate of the animal population that is affected and the steps involved in preventing transmission of rabies from animals to humans.
- Raccoons, skunks, foxes, coyotes, and several species of insectivorous bats have been identified as reservoirs for the disease.

Pasteur's Contribution

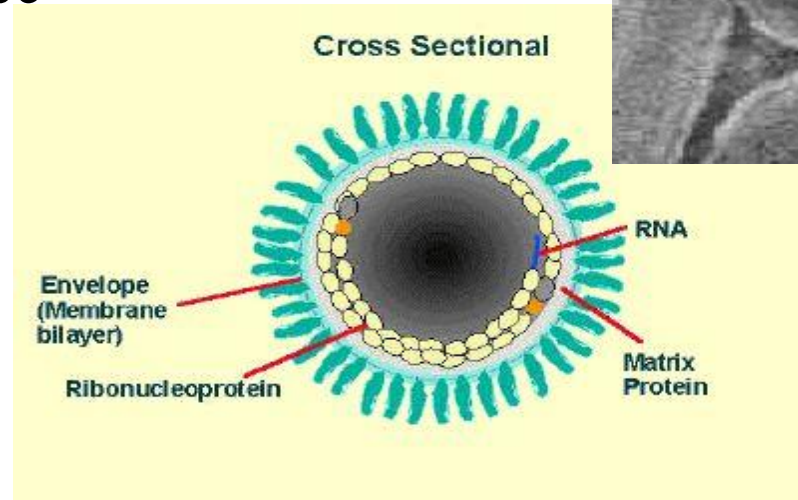
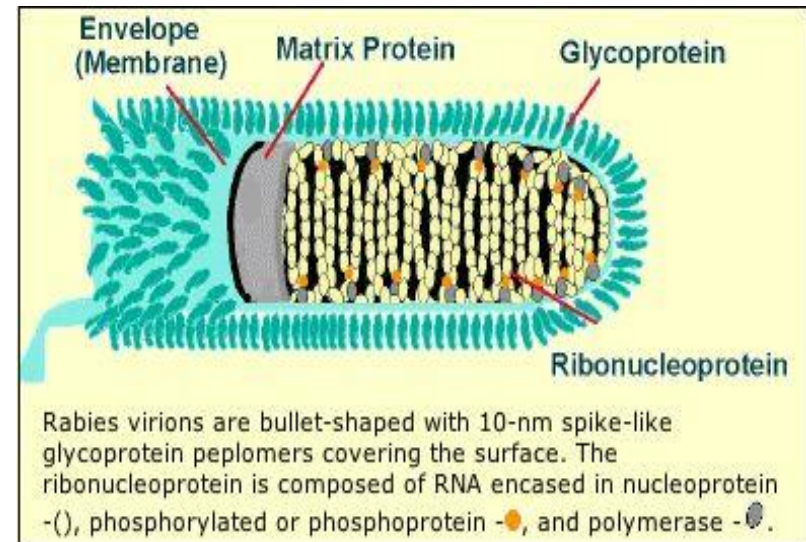
- 1885 he published a method for protecting dogs against rabies
- A dog exposed to rabies was protected by inoculation with an emulsion prepared from the dried spinal cord of a diseased rabbit
- Pasteur had the chance to test this same method on humans when Joseph Meister, a nine-year-old boy who was bitten by a rabid dog was brought to him in July of 1885
- Joseph was injected over several days with the emulsions prepared from animal spinal cord material
- After 2 weeks, Joseph was given an injection of virus that had maximal virulence when tested in a rabbit
- Joseph survived as did thousands of others treated by the same procedure.

Epidemiology

- In 2001, 49 states, the District of Colombia, and Puerto Rico reported 7,437 cases of rabies in animals to the Center of Disease Prevention and Control and no cases in humans were reported.
- Pennsylvania reported the largest number of rabid domestic animals (46) for any state, followed by New York (43)
- The number of rabies-related human deaths in the U.S. has declined from 100 or more each year at the turn of the century to an average of 1-2 each year in the 1990's

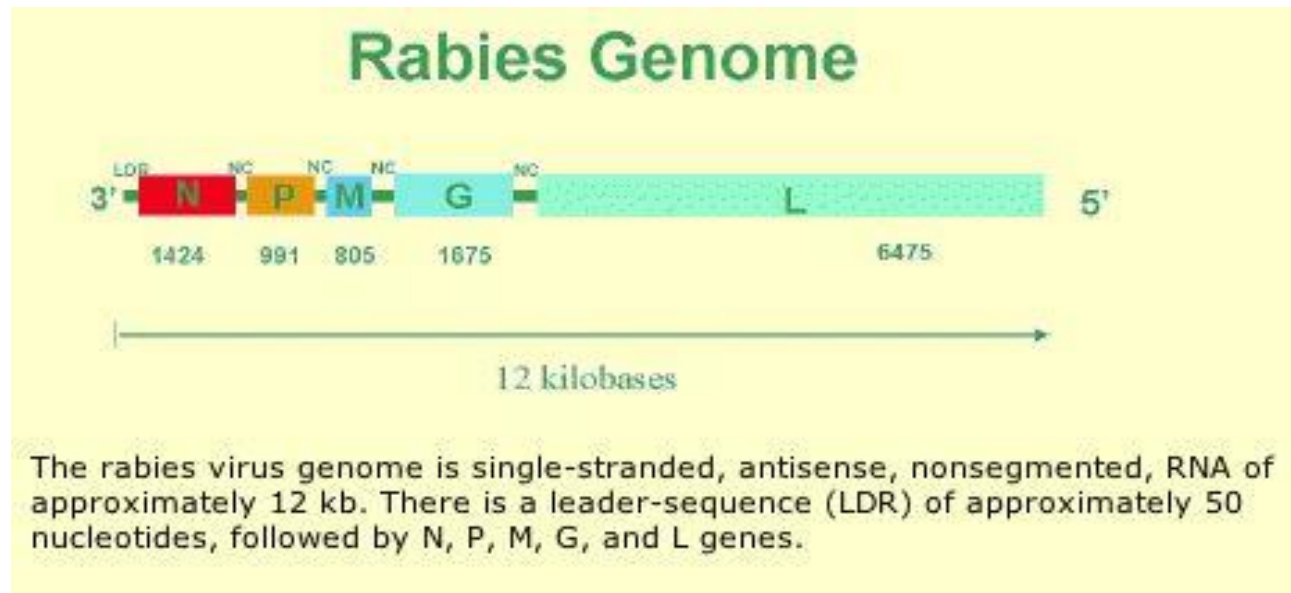
Morphology

- Order- Mononegavirales
- Helical capsid, Nonsegmented genome
- Negative sense, single stranded RNA genome
- “Bullet” shaped- Rhabdovirus
180nm x75nm
- 400 trimeric spikes on surface of virus

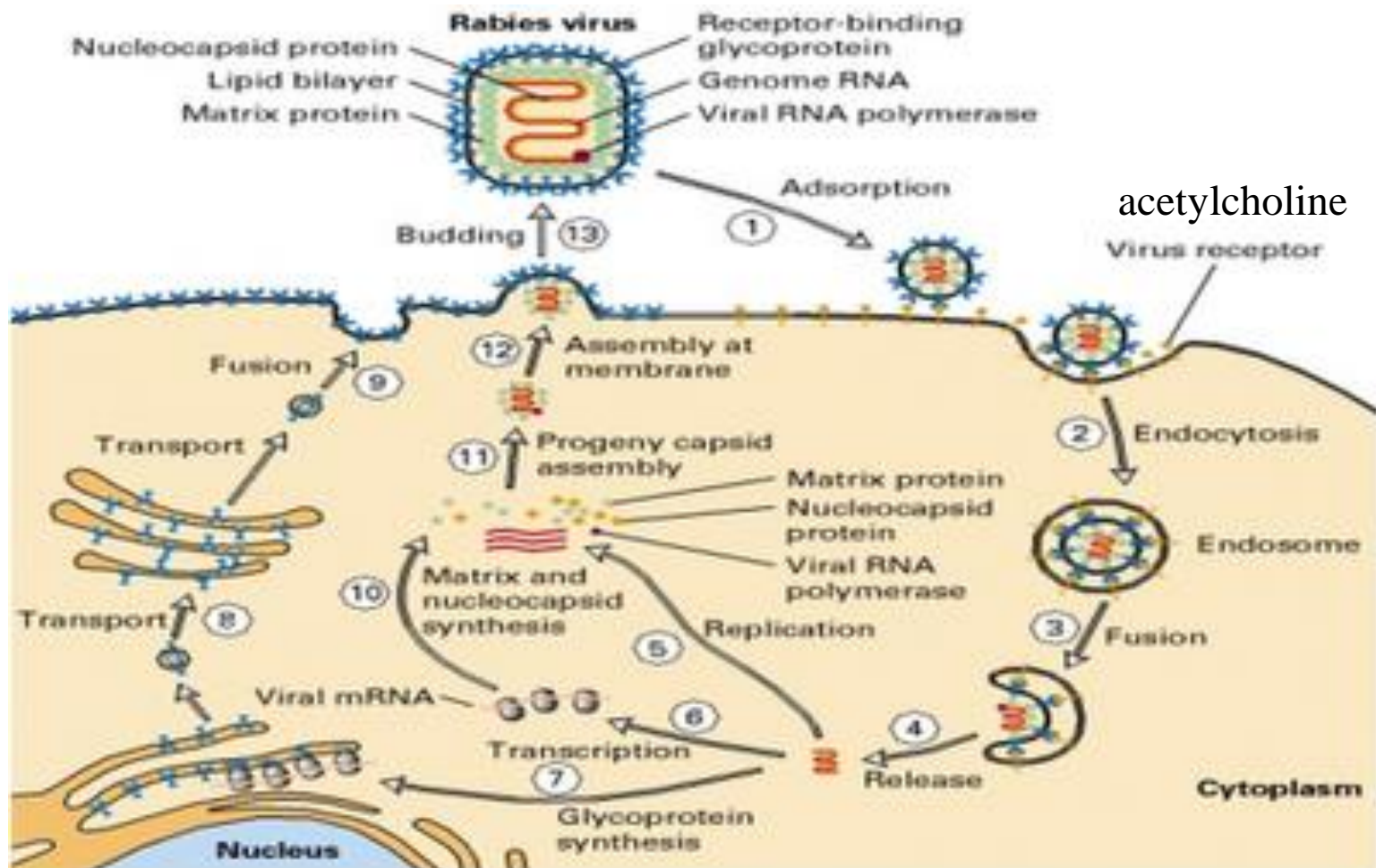


Physiology

- Genome encodes 5 proteins:
 - Nucleoprotein- encases RNA
 - Phosphoprotein- associated with ribonuceoprotein core
 - Matrix protein- central protein of rhabdovirus assembly
 - Glycoprotein- forms 400 trimeric spikes
 - Polymerase- transcribes genomic strand of rabies RNA



Rabies virus replication



Epidemiology

- Rabies exist in two epizootic forms
 - Urban: unimmunized dogs or cats
 - Sylvatic: skunks, foxes and raccoons and bats
- Transmitted through animal scratches, bites or inhalation of bat dropping in caves.

Pathogenesis

- Rabies virus replicate in striated muscle tissue at the site of inoculation.
- Immunization at this stage will prevent viral migration to neural tissues.
- Absent immunity: virus enter peripheral nervous system at neuromuscular junction then spread to the CNS (replicate in gray matter).
- pass across autonomic nerves to reach salivary glands, adrenal medulla, kidneys and lungs.
- Infected tissue: infiltration by lymphocytes and plasma cells and nerve cell destruction.

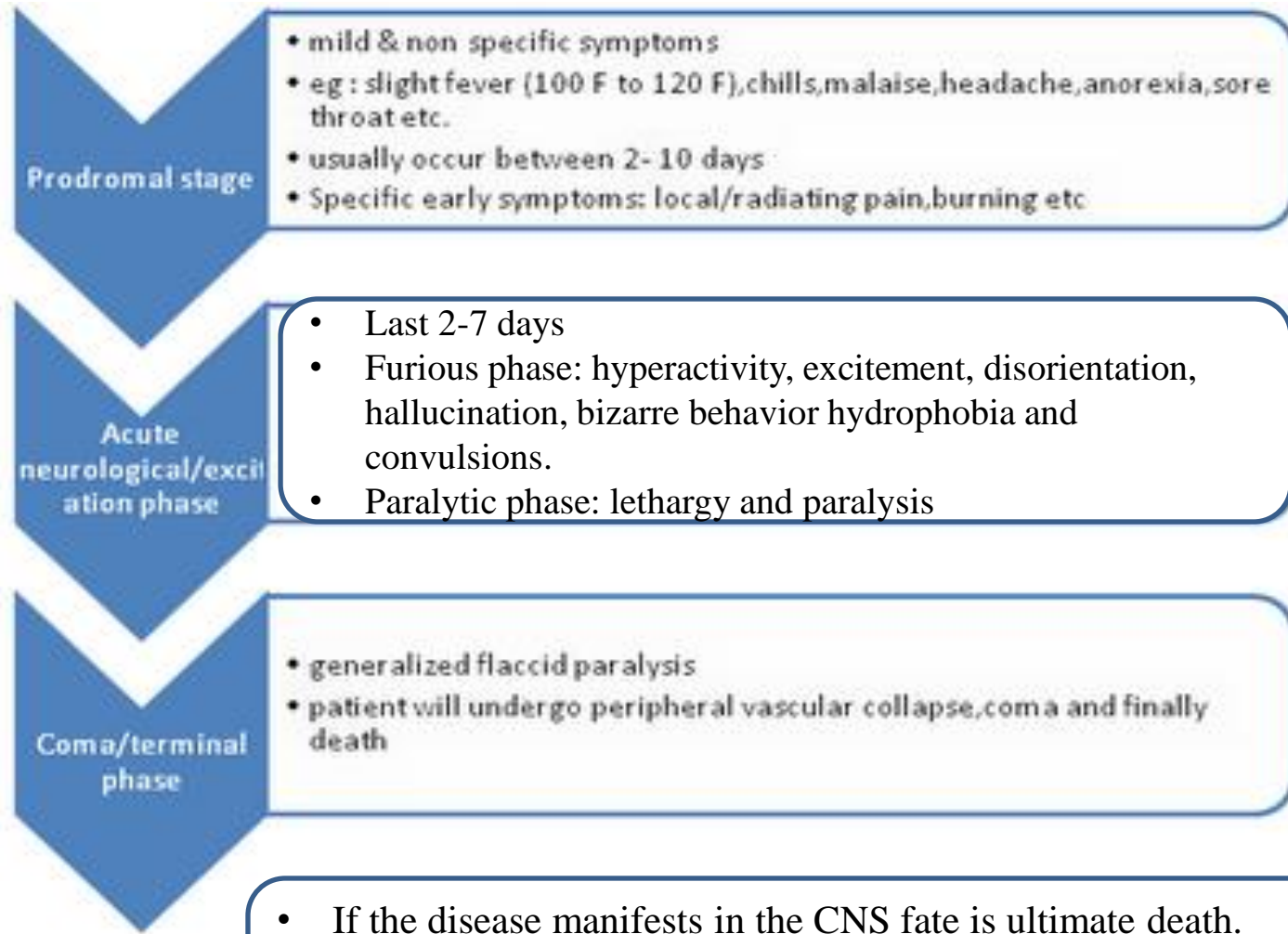
Pathogenicity

- Defined by encephalitis and myelitis
- Perivascular infiltration throughout entire central nervous system
- Causes cytoplasmic eosinophilic inclusion bodies (Negri bodies) in neuronal cells
- Long incubation period 10 days – 1yr
- Several factors may affect outcome of rabies exposure.
 - Dose: amount of virus, amount of tissue involved
 - Route: bite, scratch or inhalation of droppings
 - Location of exposure: distance traveled to CNS
 - Individual host factors: immunity

Discharge and Intermediate Hosts

- Infection of new host via saliva
- Death of host
- Wild rabid animals may infect domestic animals/people
 - Cattle, horses, pigs, dogs, cats
 - Humans
- Rabid domestic animals may infect humans

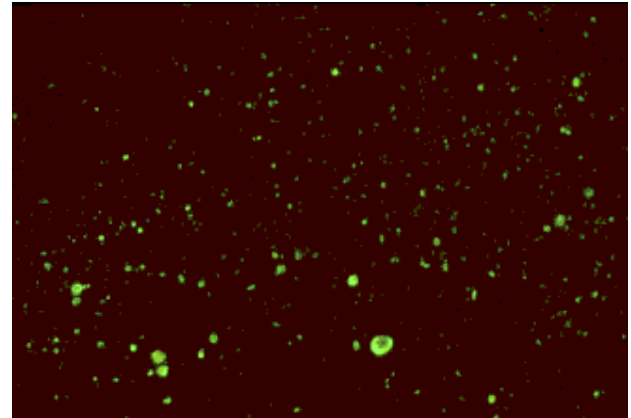
Clinical stages of rabies virus infection



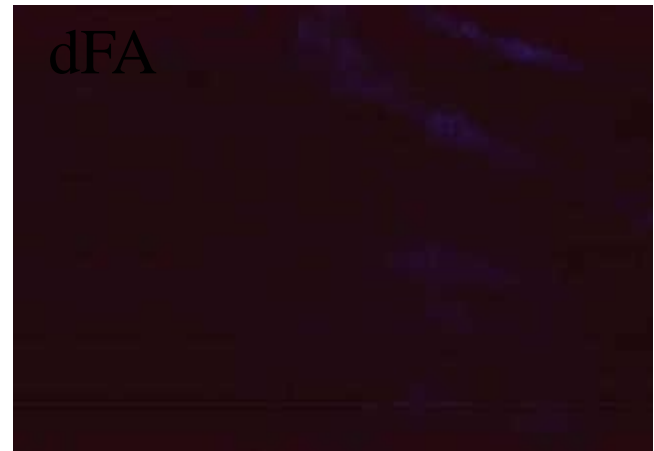
- If the disease manifests in the CNS fate is ultimate death.
- Combination of excess salivation and difficulty swallowing produce the fearful picture “foaming at the mouth”
- Median survival after onset of symptoms is 4-20 days.

Rabies Diagnosis in animals

- The direct fluorescent antibody test (dFA) is the test most frequently used to diagnose rabies. Biopsy from nape of the neck in live patients.
- The dFA test is based on the fact that infected animals have rabies virus proteins (antigen) present in their tissues.



Positive



Negative dFA

Rabies Diagnosis in humans

- Saliva can be tested by virus isolation or reverse transcription by polymerase chain reaction (RT-PCR).
- Serum and spinal fluid are tested for antibodies to rabies virus.
- Skin biopsy specimens are examined for rabies antigen in the cutaneous nerves at the base of hair follicles.
- Brain biopsy NEGRI BODY

Methods of Cure

- Rabies Vaccine: A killed virus vaccine (Human Diploid Cell Vaccine, HDCV) grown in human fibroblasts is available for safe use in humans.
- The unusually long incubation period of the virus permits the effective use of active immunization with vaccine post-exposure.
- If rabies has not been diagnosed and the victim is not treated with a vaccine and the clinical disease manifests, it is nearly always fatal, and treatment is typically supportive.

Control and Prevention

- Pre-exposure prophylaxis vaccination
- 3 doses: 0, 7, 21 (days)
- Post-exposure treatment
- If you are exposed to a possible rabid animal:
 - Wash wound with soap and water
 - Seek medical attention immediately
 - Rabies immunoglobulin
 - Vaccine 4 doses: 0, 3, 7, 14 (days)
 - If previously vaccinated should be given 2 doses: 0 and 3 and no need for immunoglobulin

Control of Rabies

- **Urban** - canine rabies accounts for more than 99% of all human rabies. Control measures against canine rabies include;
 - stray dog control.
 - Vaccination of dogs
 - quarantine of imported animals
- **Wildlife** - this is much more difficult to control than canine rabies. However, there are on-going trials in Europe where bait containing rabies vaccine is given to foxes. Success had been reported in Switzerland.