



# Poliovirus and Rabies virus

**Microbiology Lecture 3 PNS Module**

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A 6-year-old boy presents to the pediatric clinic with sudden onset weakness in his legs and difficulty walking. His parents report that he had a fever and mild respiratory symptoms a week ago. On examination, he demonstrates flaccid paralysis in his lower extremities. Suspecting polio virus infection, which of the following statements regarding polio virus is true?

- A) Polio virus is a DNA virus.
- B) The primary mode of transmission of polio virus is through mosquito bites.
- C) Polio virus primarily replicates in the gastrointestinal tract.
- D) The Sabin vaccine is an example of an inactivated polio vaccine.
- E) The majority of polio virus infections result in severe central nervous system symptoms.

هل عندي علاقة بين الpolio and respiratory symptoms

Transmission of enteroviruses through fecal oral and primary replication in oropharynx which is connected to oral and nasal cavity

متى ممكن يعمل النا neurological deficits symptoms

incubation period of polio take 1-2 weeks

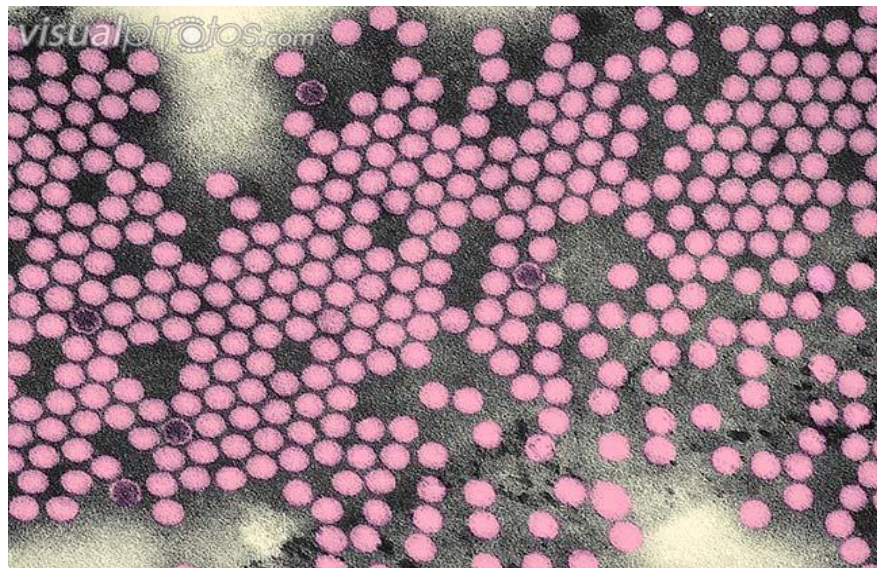
هل في علاقة بين الage and level of paralysis seen in cases of polio infection

a 3 years old and a 30 years old both get infected and progressed to develop paralytic polio, the chance of neurological deficits seen will be less in the 5 yrs old than a 30 yrs old man  
\*so, the 30 old man might develop or end up with (Quadriplegia).  
\*but in the child it might be seen in one of the limbs.

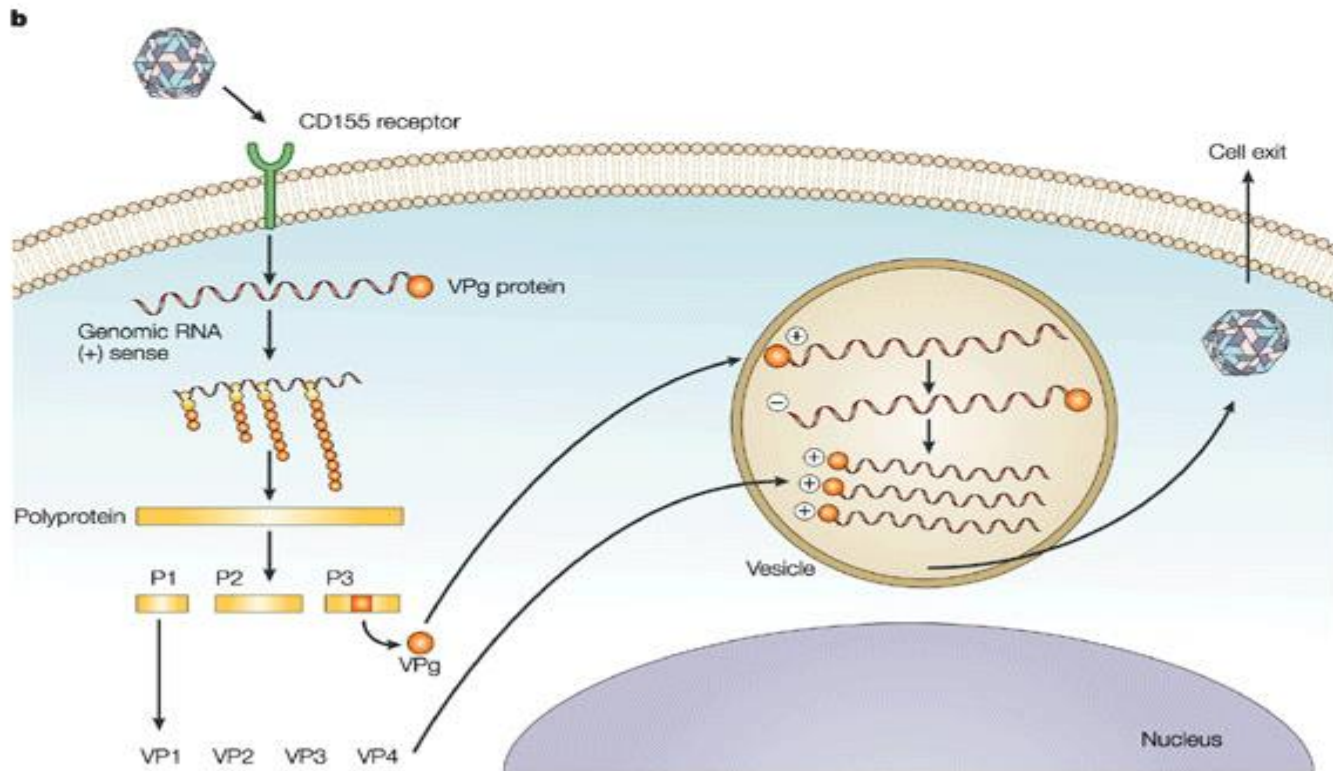
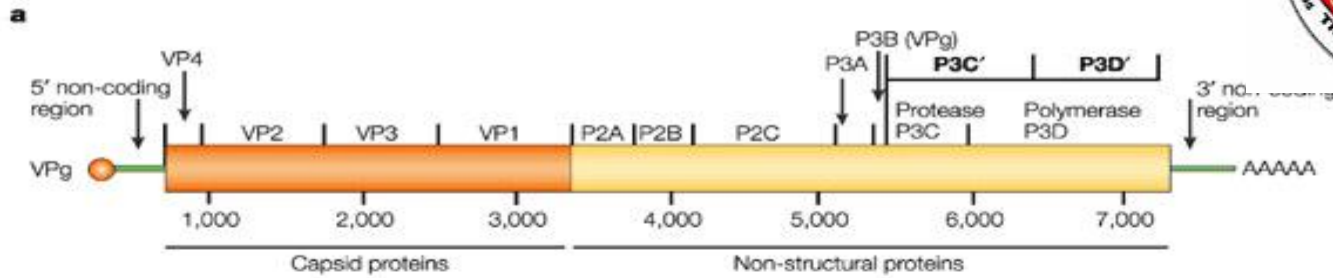
# Poliovirus



- It belongs to the Enteroviruses genus of the Picornavirus family which replicate mainly in the gut.
- Single stranded positive sense, 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. Start in intestinal mucosa then eventually it might reach spinal cord
- 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 viremia.
- 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 non-paralytic 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. (3-4)
- **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.

In paralytic polio ,replicating it leads to leptic infection  
the result it might lead to complete damage or partial  
damage

In partial damage:with physical therapy after (3-4)weeks  
there will be improvement up to 6 month to 1year

In complete damage control: paralysis,not reversible



# 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

The sample from throat,rectal,CSF,blood

- Serology ما ينفع

- 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.
- Two doses 6-8 wks apart, 3<sup>rd</sup> 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**

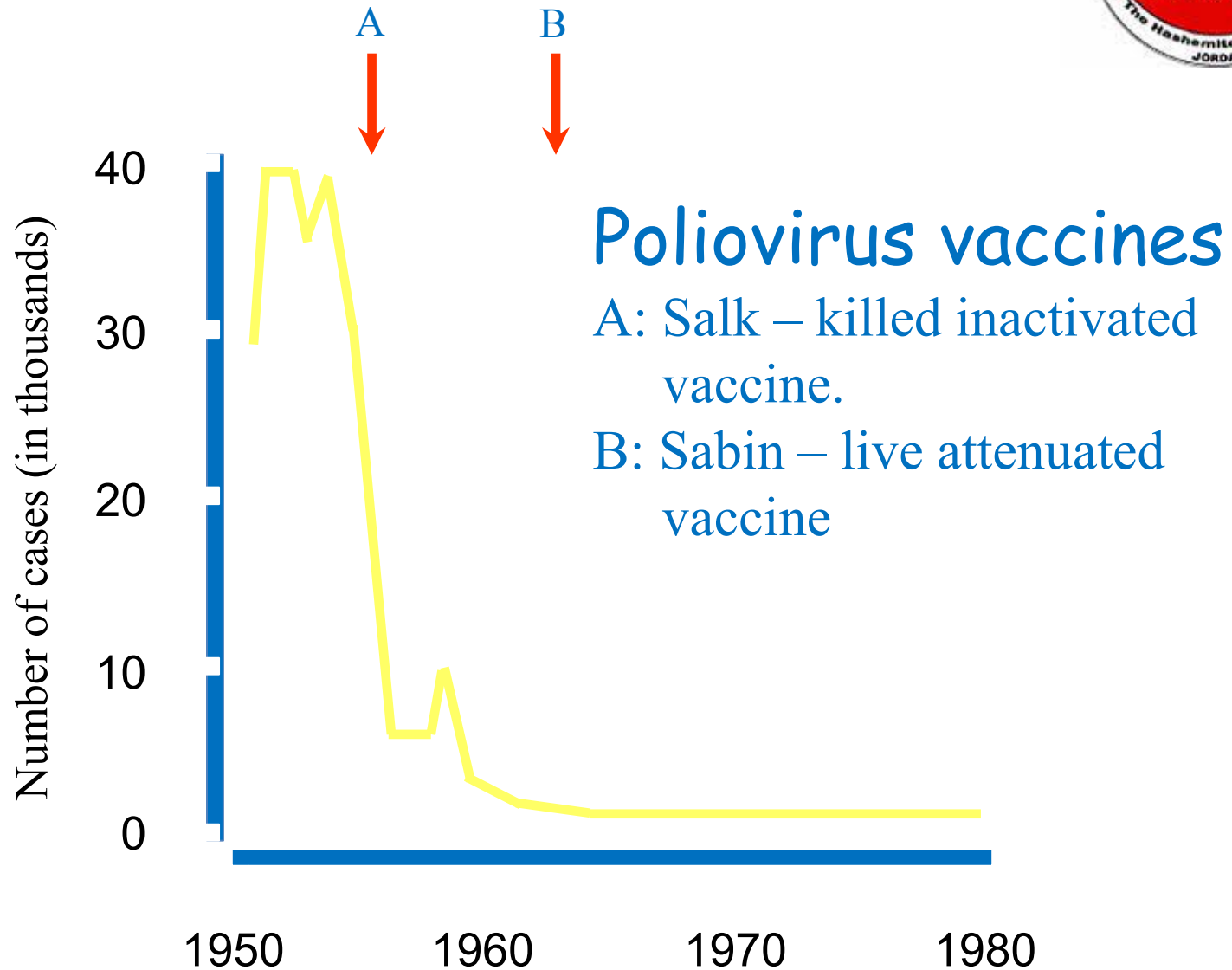
- Consists of live attenuated virus of all 3 serotypes, produced by the repeated passage of the virus through nonhuman cells at subphysiological temperatures
- Two doses 6-8 wks apart, 3<sup>rd</sup> given after 8-12 months; protective 95%
- Produces local immunity through the induction of an IgA response 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

Motherhood & More

أقرب وقت بعد الولادة، يُعطى مطعوم السل (BCG)

بداية الـ 3month

على عمر شهرين (٦١ يوم) يُعطى الطفل الجرعة الأولى من مطعوم شلل الأطفال **IPV** والمطعوم الخماسي الذي يتكون من: المطعوم الثلاثي DPT (الدفثيريا والسعال الديكي والكزاز) + مطعوم المستدئمة النزلية نوع (ب) + مطعوم التهاب الكبد نوع (ب) + الجرعة الأولى من مطعوم الروتافيروس .

على عمر ٣ اشهر (٩١ يوم) يُعطى الطفل الجرعة الثانية - مطعوم شلل الأطفال **OPV+IPV** + المطعوم الخماسي الذي يتكون من: المطعوم الثلاثي DPT (الدفثيريا والسعال الديكي والكزاز) + مطعوم المستدئمة النزلية نوع (ب) + مطعوم التهاب الكبد نوع (ب) + الجرعة الثانية من مطعوم الروتافيروس .

بداية الـ 5month

على عمر ٤ شهور (١٢١ يوم) يُعطى الطفل مطعوم شلل الأطفال الفموي **OPV** + المطعوم الثلاثي DPT (الدفثيريا والسعال الديكي والكزاز) + مطعوم المستدئمة النزلية نوع (ب) + مطعوم التهاب الكبد نوع (ب) على شكل رباعي أو خماسي + الجرعة الثالثة من مطعوم الروتافيروس .

بداية الـ 9month

على عمر ٩ شهور (بداية الشهر العاشر) يُعطى الطفل - مطعوم الحصبة Measles + مطعوم شلل الأطفال الفموي **OPV** + فيتامين أ (١٠٠ الف وحدة دولية).

عند بلوغ الطفل عامه الأول يُعطى الطفل الجرعة الأولى من المطعوم الثلاثي الفيروسي MMR (الحصبة والحصبة الألمانية والنكاف)

Year and 6 month

على عمر ١٨ شهر يُعطى الطفل الجرعة المدعمة من مطعوم شلل الأطفال الفموي **OPV** والمطعوم الثلاثي البكتيري DPT + الجرعة الثانية من مطعوم الثلاثي الفيروسي MMR + فيتامين أ (٢٠٠ الف وحدة دولية).



# 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 partially destroyed, 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



## The Fight to End Polio

COUNTRIES HAVE NEVER STOPPED POLIO

3



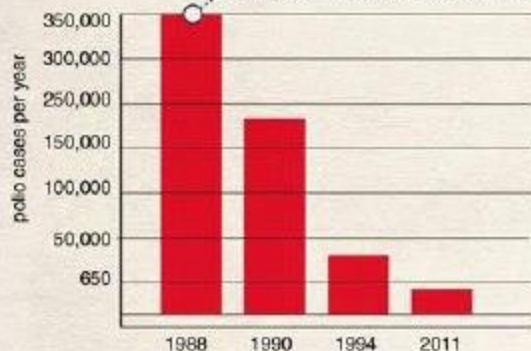
NIGERIA



AFGHANISTAN



PAKISTAN



People that contracted polio in 1988 when the fight to end this disease began.

**\$.60**

60 cents is the cost of protecting one child from polio.

Reaching the final 1% of children is the most difficult because polio still exists in some of the most challenging parts of Africa and Asia.

**99%**

Polio is 99% of the way to being eradicated!

**2.5**  
Billion

Children immunized globally since 1988. That is an average of 3.3 children a second!

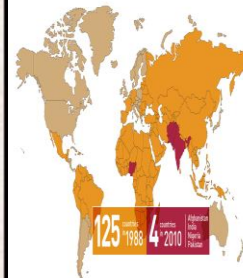
**5**

The majority of children that contract this crippling disease are under the age of 5.

**\$40-\$50**  
Billion

The estimated amount of money polio eradication will save the world over the next 20 years.

After more than 25 years we are "this close" to making history by eradicating polio. With this historic achievement, polio will be only the second human disease in history-after smallpox-to be eradicated worldwide.



**1%**

Learn more about ending polio and take action at [www.endpolionow.org](http://www.endpolionow.org)





# What is Rabies?

- A disease characterized by **sever 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



## RABIES: THE FACTS



### VIRUS TRANSMISSION



Saliva of infected animals



of human cases are caused by **dog bites**

The virus attacks the brain  
Rabies is **fatal** once symptoms appear



### TREATMENT



Thorough washing of the wound with soap, and, vaccine injections can avoid symptoms and **save lives**.

**Seek immediate** medical care if bitten.



### FATALITIES

Rabies affects **poor rural communities** mostly in Asia and Africa



Risk to humans of contracting rabies  
HIGH  
MODERATE  
LOW

About **One death** every



**40%**

of the victims are children younger than 15

### HOW TO PREVENT RABIES TRANSMISSION FROM DOGS?



Raise public **awareness**

Learn **dog body language**



**NO DOG BITE = NO RABIES**

### VACCINATING DOGS SAVES HUMAN LIVES

**Rabies is 100% preventable**



Vaccinating **70%** of dogs **breaks rabies transmission cycle** in an area at risk

Every dog owner is concerned



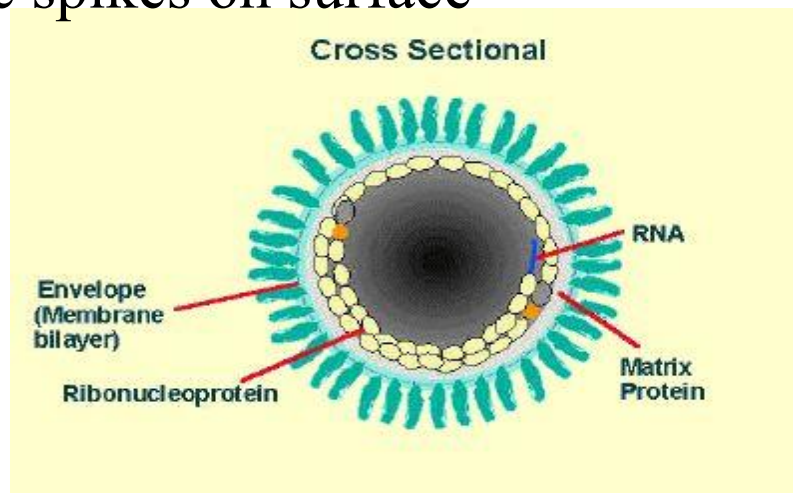
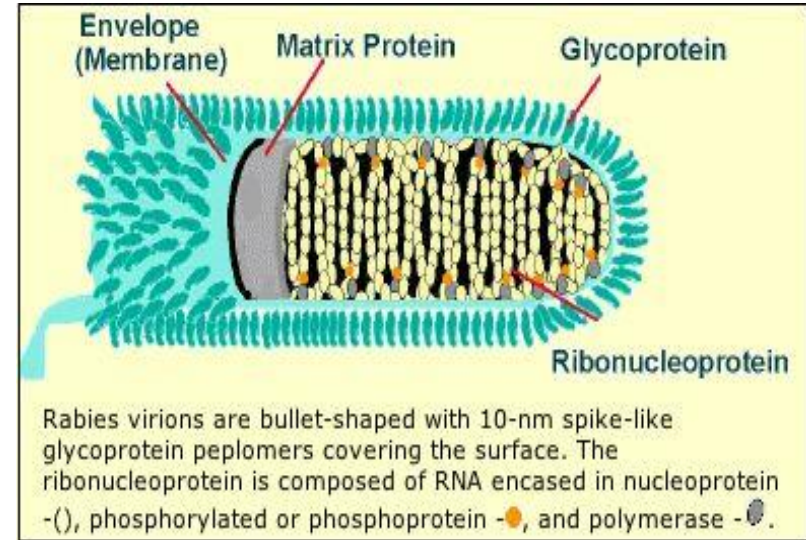
**28 September**

• **World Rabies Day** •

**#rabies**

# Morphology

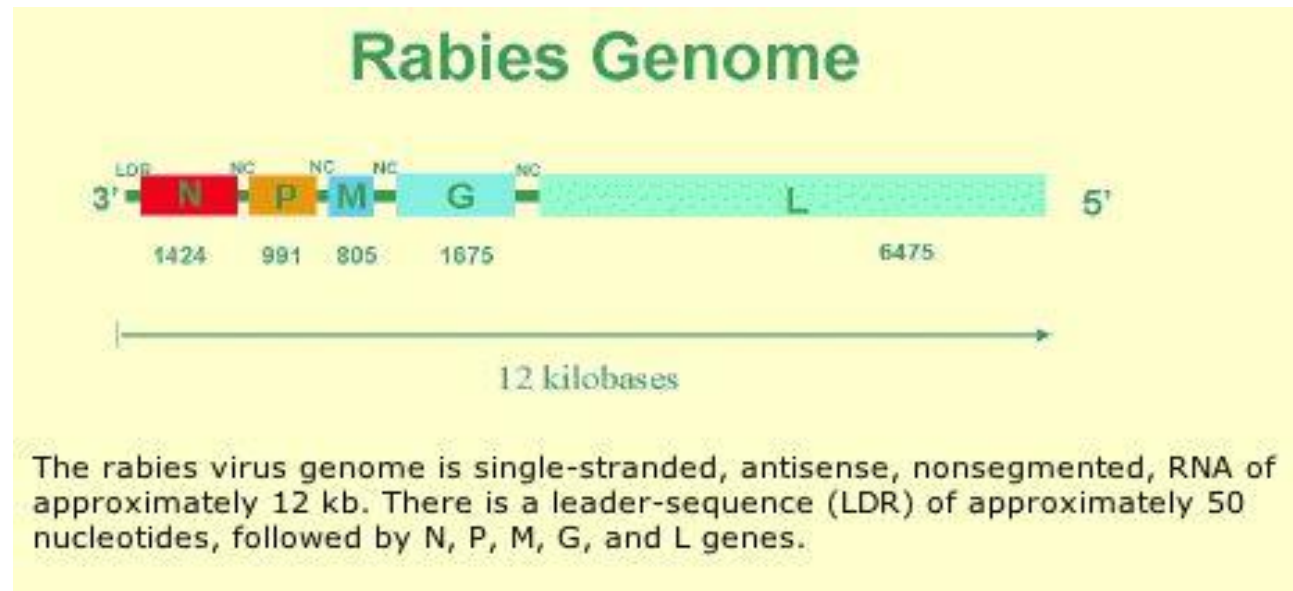
- Order- Mononegavirales
- Helical capsid, Nonsegmented genome
- Negative sense, single stranded RNA genome
- “Bullet” shaped- Rhabdovirus
- 180nm x75nm
- 400 trimeric spikes on surface of virus



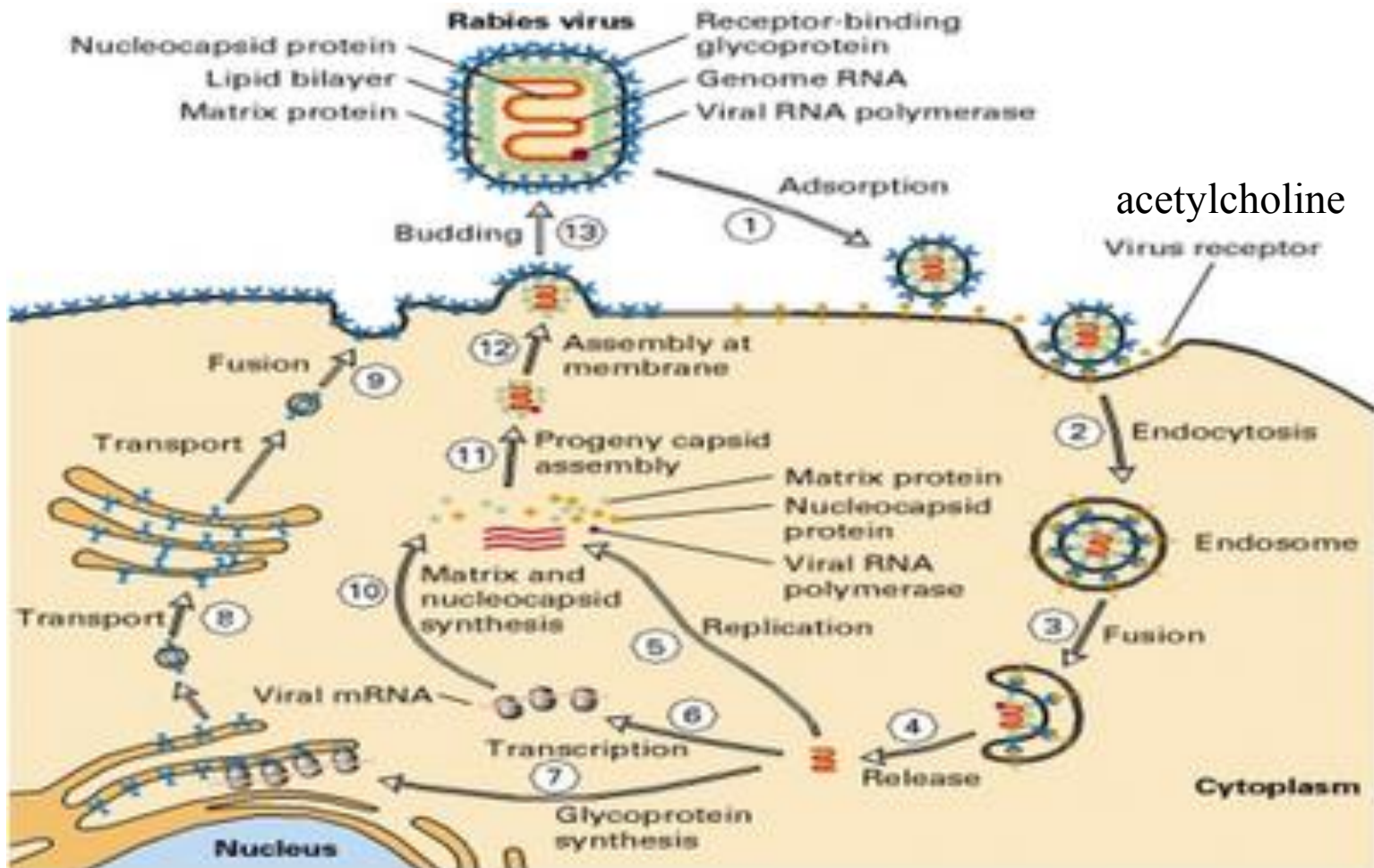


# Physiology

- 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

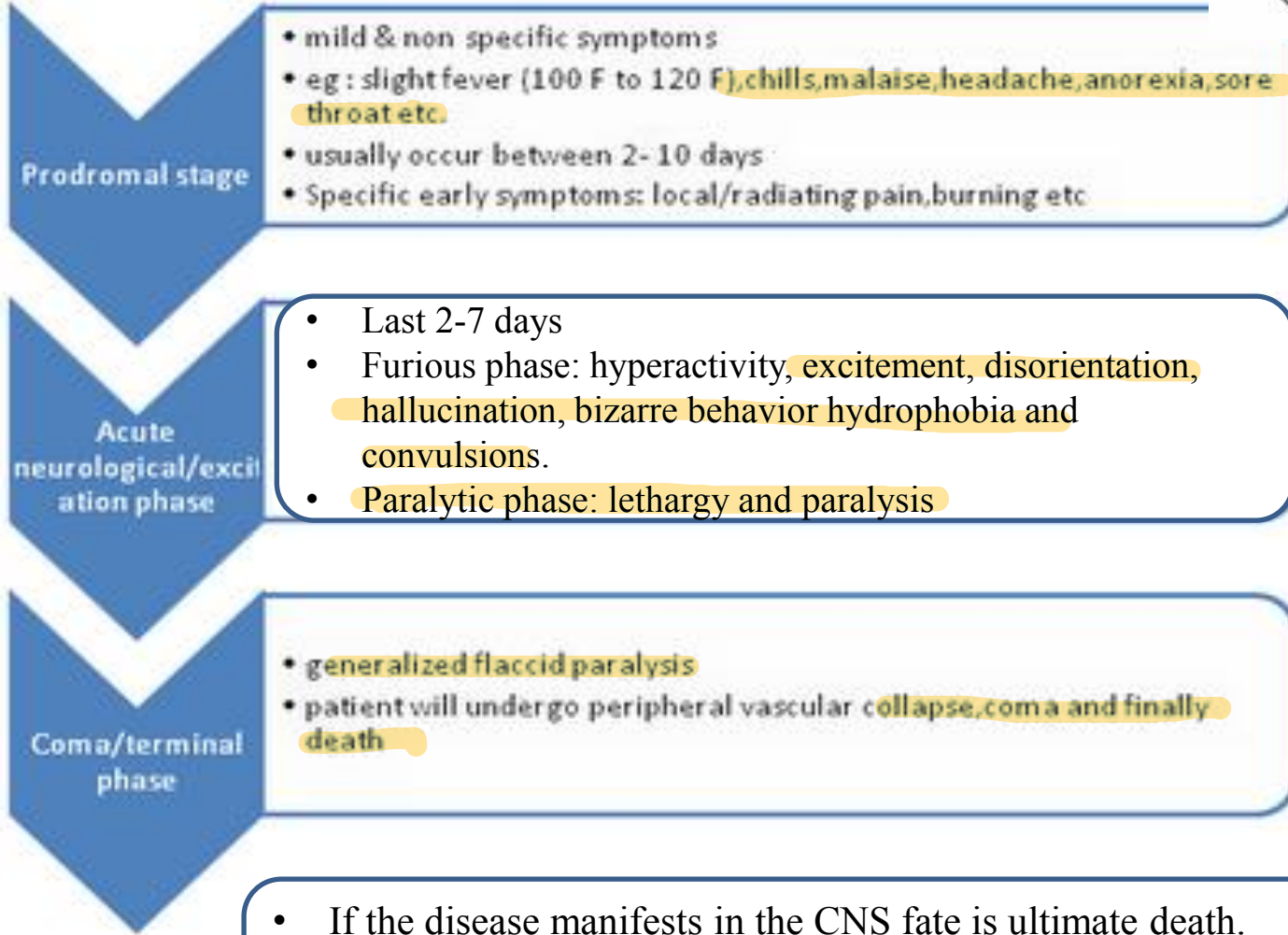
- Infection of new host via saliva
- Death of host
- Wild rabid animals may infect domestic animals/people
  - Cattle, horses, pigs, dogs, cats
  - Humans
- Rabid domestic animals may infect humans

# Clinical stages of rabies virus infection



These days depends on site of bite from dates to months

اي شخص عنده bite animals تعطيه مطعوم  
does 4 يعني (14-7-3-0)



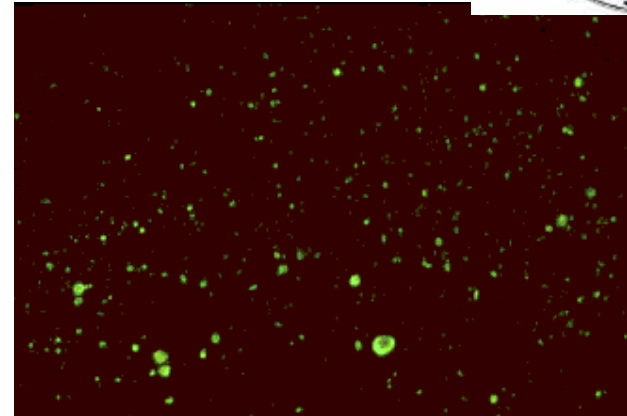
- If the disease manifests in the CNS fate is ultimate death.
- Combination of excess salivation and difficulty swallowing produce the fearful picture “foaming at the mouth”
- Median survival after onset of symptoms is 4-20 days.

# Rabies Diagnosis in animals

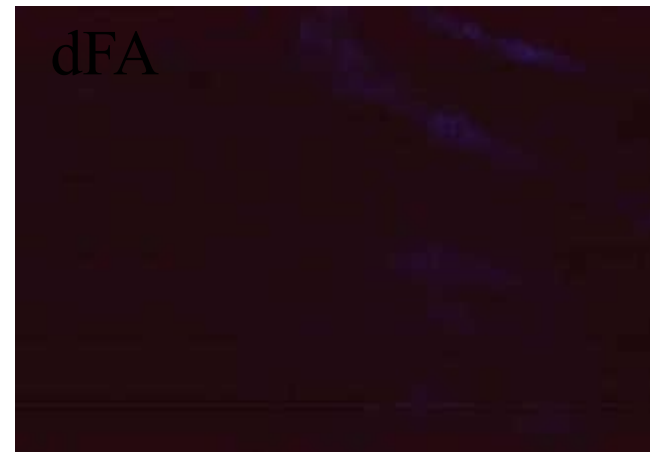


- The direct fluorescent antibody test (dFA) is the test most frequently used to diagnose rabies. Biopsy from nape of the neck in live patients.
- The dFA test is based on the fact that infected animals have rabies virus proteins (antigen) present in their tissues.

ناخذ دماغ الحيوان ونعمل عليه  $Ab$  fluorescent  
ممکن نشوف وقتها ال  
 $Ab$  bind to  $Ag$  وما بنعمله للإنسان  
إلا اذ مات



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**  
For diagnostic



# Prevention

- Rabies Vaccine: A killed virus vaccine (Human Diploid Cell Vaccine, HDCV) grown in human fibroblasts is available for safe use in humans.
- less expensive purified chicken embryo cell vaccines (CCEEV) and purified Vero cell rabies vaccines are now available
- 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.