



# **Rhabdoviridae**

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# Properties of Rhabdoviruses



**Bullet shape , 75\*180 nm ,  
helical capsid surrounded  
by envelope with glycoprotein  
peplomers**

**Some viruses carry HA which  
agglutinate goose RBCs**

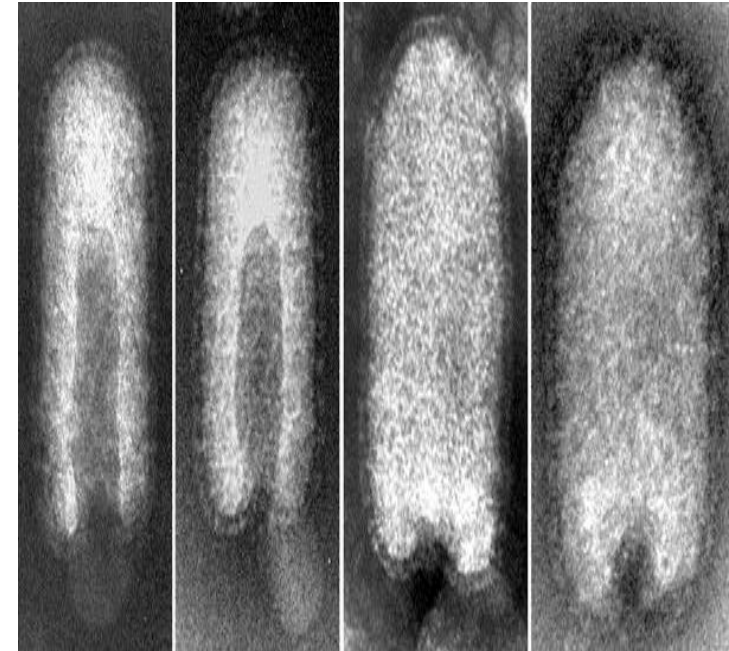
**The family contains 3 genera :**

**G lyssa virus ,**

**G vesiculovirus ,**

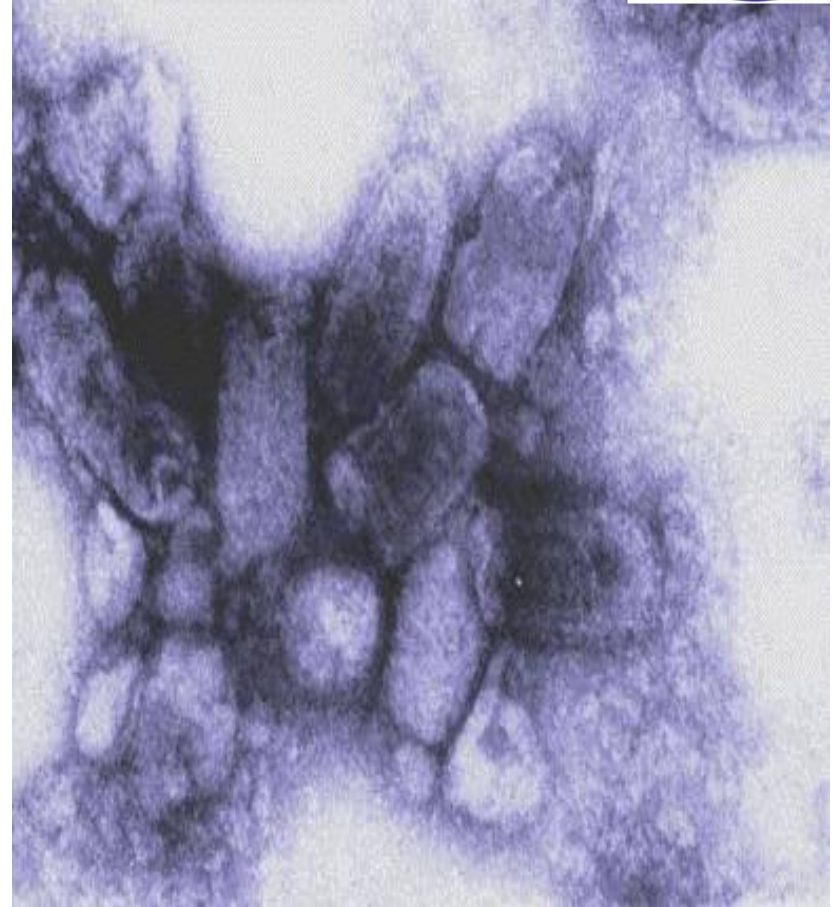
**G ephemerovirus & unnamed  
group contains fish**

**Rhabdoviruses**





**As they enveloped  
,they sensitive to  
ether & chloroform &  
bile salts  
Resist freezing &  
thawing  
Persist in the soil for  
many years at 4-6 C**





# Genera of Rhabdoviruses



- Genus Lyssa virus (neurological)
- Genus Vesiculovirus (epithelial)
- Genus Ephemerovirus (Immune-inflammatory)
- Unclassified group involves fishes Rhabdoviruses



# Genotypes of Lyssa virus



- 1. Classical rabies
- 2. Lagos bat virus
- 3. Mokola virus
- 4. Duvenhage virus
- 5. European bat virus
- 6. European bat virus
- 7. Pteropus Lyssa virus



# Differences between Lyssa viruses of genotype 1

- Monoclonal antibody typing
- Sequencing of PCR products
- Species selection



# Rabies

## Definition

**it is an acute disease of man and animals caused by a specific virus which is usually transmitted through the bite of rabid animals to other animals resulting in a rapidly fatal encephalomyelitis**





# Host affected



**Man and all warm blooded animals including birds are susceptible**







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**Vampire bats ,  
some insects –  
eating bats and  
fruits- eating  
bats may acting  
as natural hosts  
of the virus**

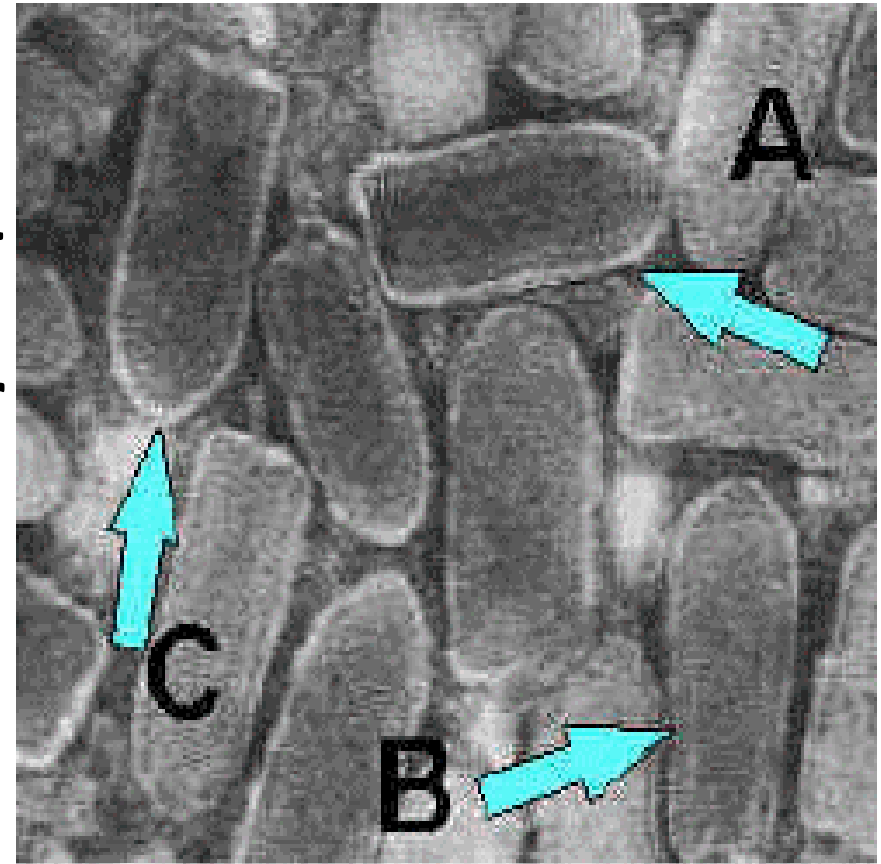




# Virus stability



HA activity occurs at 0-4 C  
& at pH 6.2 with one day  
old chicks or goose RBCs  
Very resistant to autolysis &  
putrefaction remain  
infective in tissues at 4 C for  
2 weeks and for months at  
lower temperature  
Labile at room temperature  
and destroyed after only  
few days



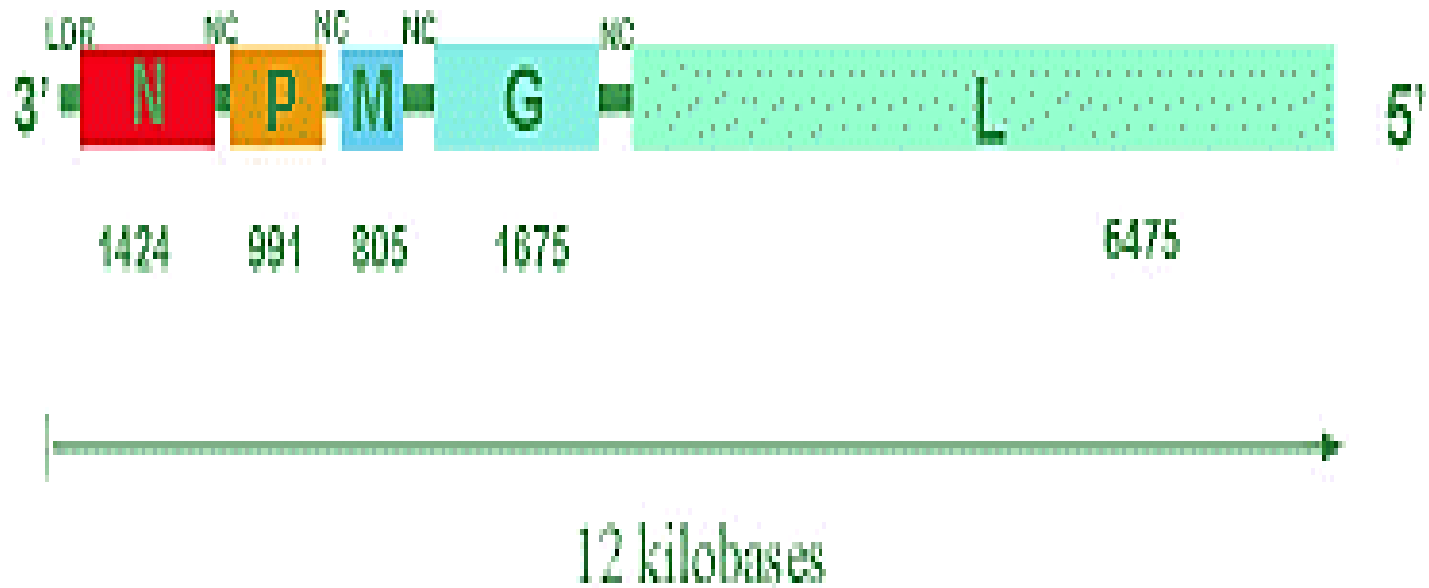


## The virus reduces its infectivity by :

- Repeat freezing & thawing
- exposure to UV rays
- proteolytic enzymes
- acid pH
- chloroform, bile salts , 20% ether
- boiling for two minutes,
- $\beta$ -probiolactone 1/6000 within 2 hours

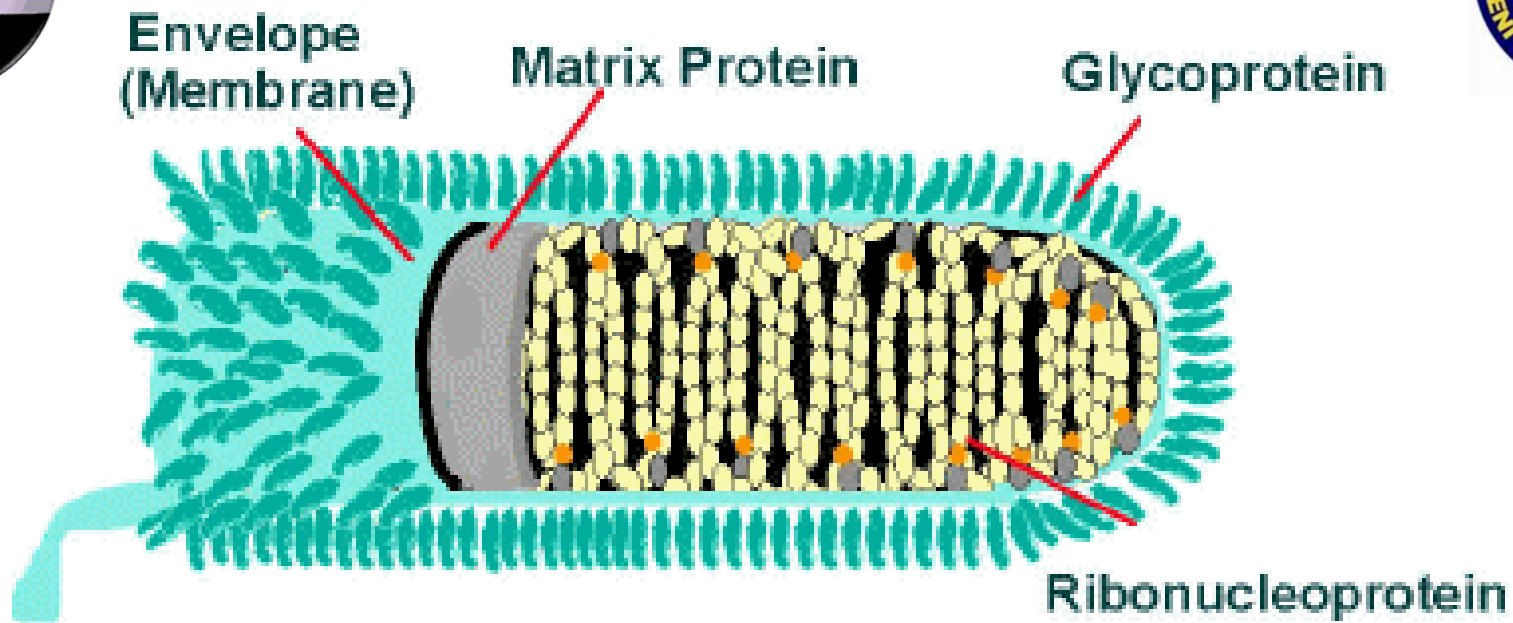


# Rabies Genome

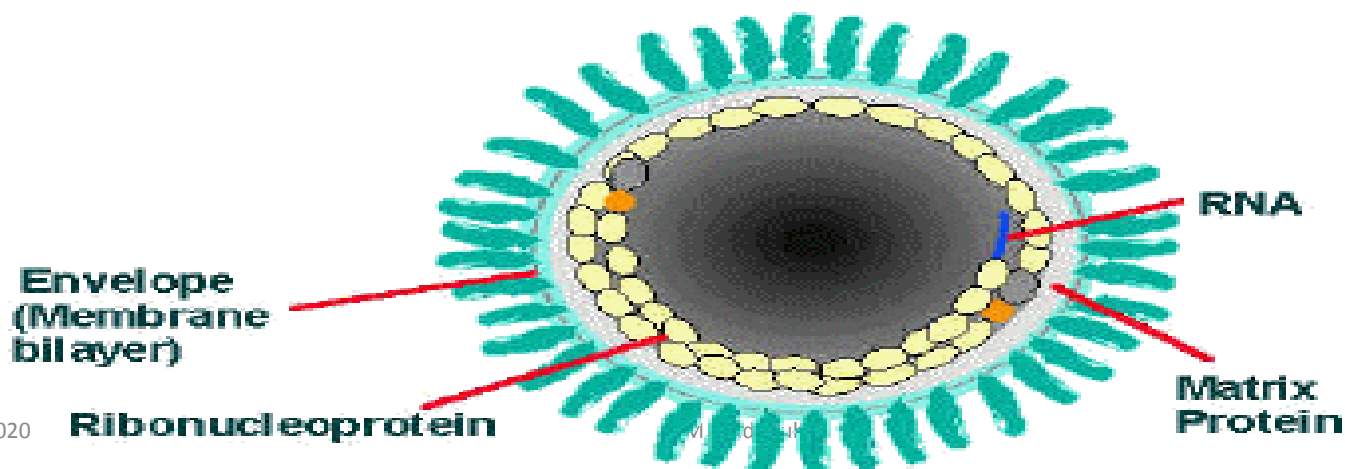




# Viral proteins



## Cross Sectional







# Street and Fixed viruses



**Street virus - natural strains**

**Fixed virus - laboratory strains  
propagated in rabbits - may have  
a less variable incubation period**



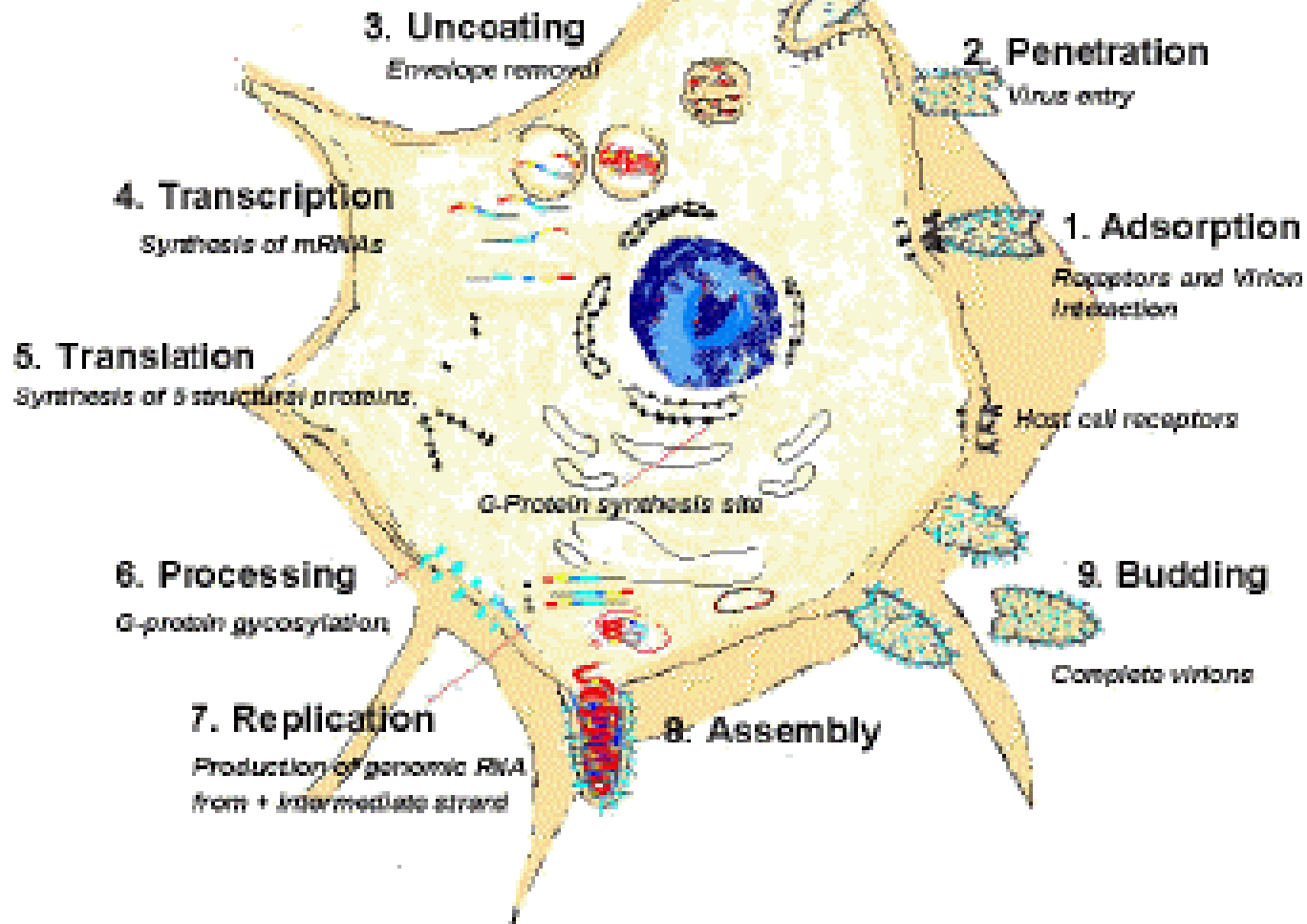
# Differences between street and fixed virus



status	Street virus	Fixed virus
<b>Rate of multiplication</b>	<b>low</b>	<b>rapid</b>
<b>Incubation period</b>	<b>long</b>	<b>Short 4-9 days</b>
<b>Main symptoms</b>	<b>Furious</b>	<b>Paralytic</b>
<b>virulence</b>	<b>decreased</b>	<b>increased</b>
<b>Negri bodies</b>	<b>Very clear</b>	<b>Very small</b>



# Cycle of Infection and Replication





# Transmission







# **Symptoms of rabies in human**



**Incubation period from 2 wks-5 ms (30-60 day average)**

**It is seldom more than 90 days, but a period of 2 years have been recorded**

**Course of the disease 2-6 days ended by death**

**Headache ,loss of appetite, anxiety, insomnia**





• **Infection of the limbic system  
(hypothalamus, hippocampus,)**

– **Restlessness, wandering,**

– **Hypersensitivity to stimulus**

– **Hydrophobia, muscular spasms of  
facial, laryngeal, pharyngeal muscles**

• **Triggered by light, odors, water**

– **Blood in vomit, inability to swallow  
saliva**

– **hyper sexuality**



# **Symptoms in canines**



- (1) The Prodromal stage**
- (2) The furious stage**
- (3) The paralytic or dumb stage**



# Prodromal stage



- Strange in its behavior
- More irritable, alert with a wild staring eyes & dilated pupils, troubled look ,
- Licking at the site of the wound,
- Aimless snapping & barking
- Photophobia







# Furious stage



- Hide in dark places
- Chewing unusual objects(stones,sticks , earth ,clothes
- Changes in barking sound
- Progressive profuse salivation



يميل الكلب إلى العزله ويتخير الاماكن المظلمه

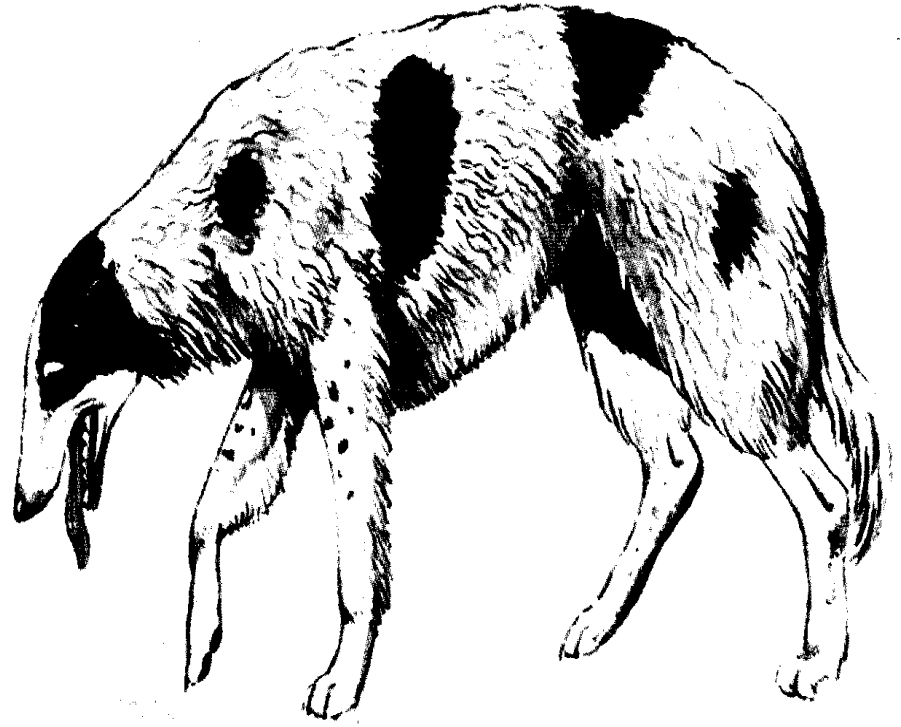


تكسر الاسنان في بعض الحالات





- ❑ Stray long distance from home
- ❑ Walk in a straight line with its head down
- ❑ Bite any movable object



يمشي الكلب مثل الدب وراسه مدلاه لأسفل





# Paralytic (dumb) stage

- Lower jaw paralysis
- The tongue protrudes
- Unable to walk or stand
- Incoordination of movement
- Comatose & die





Furious rabies

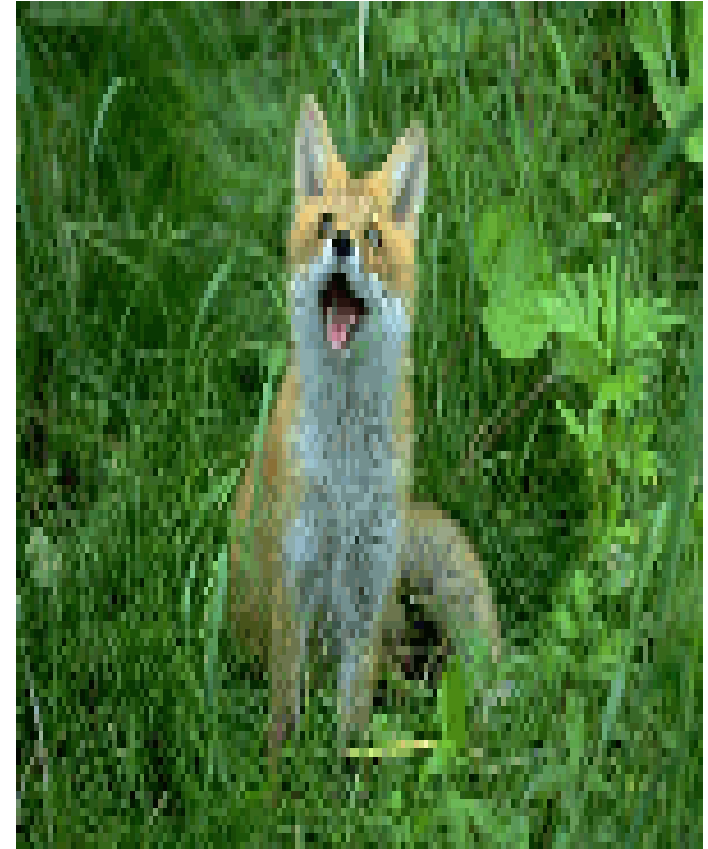


Dumb rabies



# Symptoms in cats

- Mew continually
- More vicious than dogs and attack man & other animals
- Course of the disease 2-4 days







# Symptoms in equines

## A Rabid Horse



- Farm with two cats,& dogs
- Skunk chases dog around the house
- Few weeks later see depressed horse
- Rubs the area of the wound
- Staring eyes & dilated pupils
- Progressive paralysis
- Horse dies
- A few months later another horse die





# **Rabid horse histopathology**



**Multifocal degeneration in trigeminal ganglion**

**Infiltration with mono-nuclear inflammatory cells**

**Neurons contain eosinophilic IC inclusion bodies**

**Cerebellum and mid-brain mono-nuclear inflammatory cells**

**Feds detect rabies virus by IFA**



# Bovine Rabies in Mexico

- 1000 cattle in pasture not vaccinated against rabies
- Vampire bats were found around the farm
- Course of the disease 3-6 days



Vampire Bat (*Desmodus rotundus*)  
©Lynn Chase-Shoemaker





# Bovine Rabies in Mexico

- Vaccination
- Cattle continue to die (84 animals by 13 weeks)
- Bat control

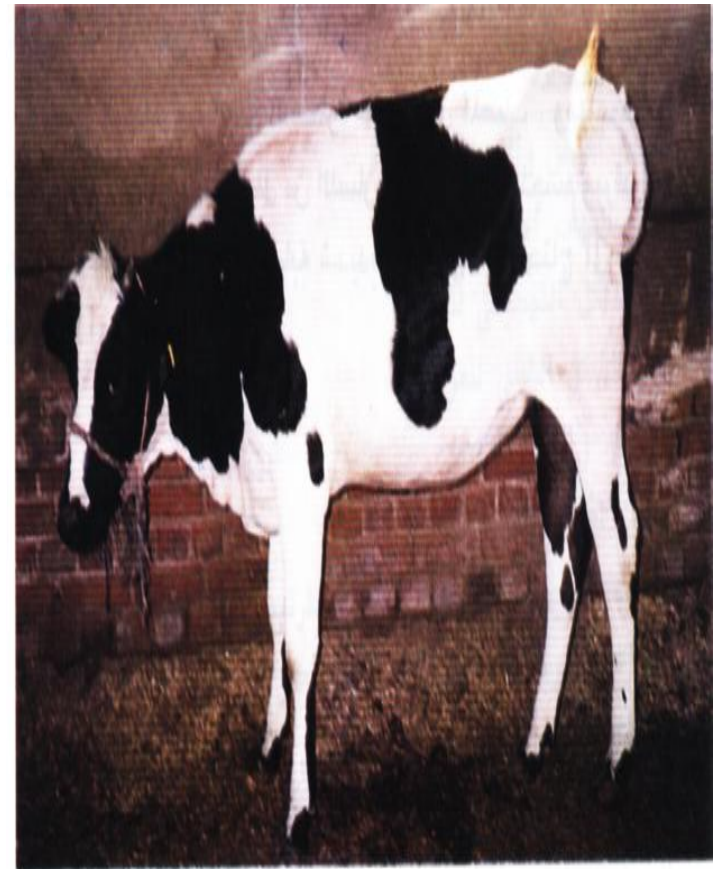


Day and Night House  
Vampire Bat

Photo By  
Joy Spur



- ✓ **Bellow loudly with hard voice**
- ✓ **Biting of udder or genitalia**
- ✓ **Bite or clamber on their stalls as if trying to escape**
- ✓ **Restless, aggressive**
- ✓ **Paralysis of the hind quarters**



تضطرب وترفع رؤوسها وتخفضها وتكثر من هز ذبواها



# **Bovine Rabies in Mexico**

## **(..cont)**

- Calf develops neurological signs - Post-mortem exam - unremarkable
- Brain submitted to Mexico City
- Three other animals become sick:
- Febrile, photophobic, drooling, decreased cutaneous sensitivity,
- Incoordination - euthanized



# **Bovine Rabies in Mexico (...cont)**

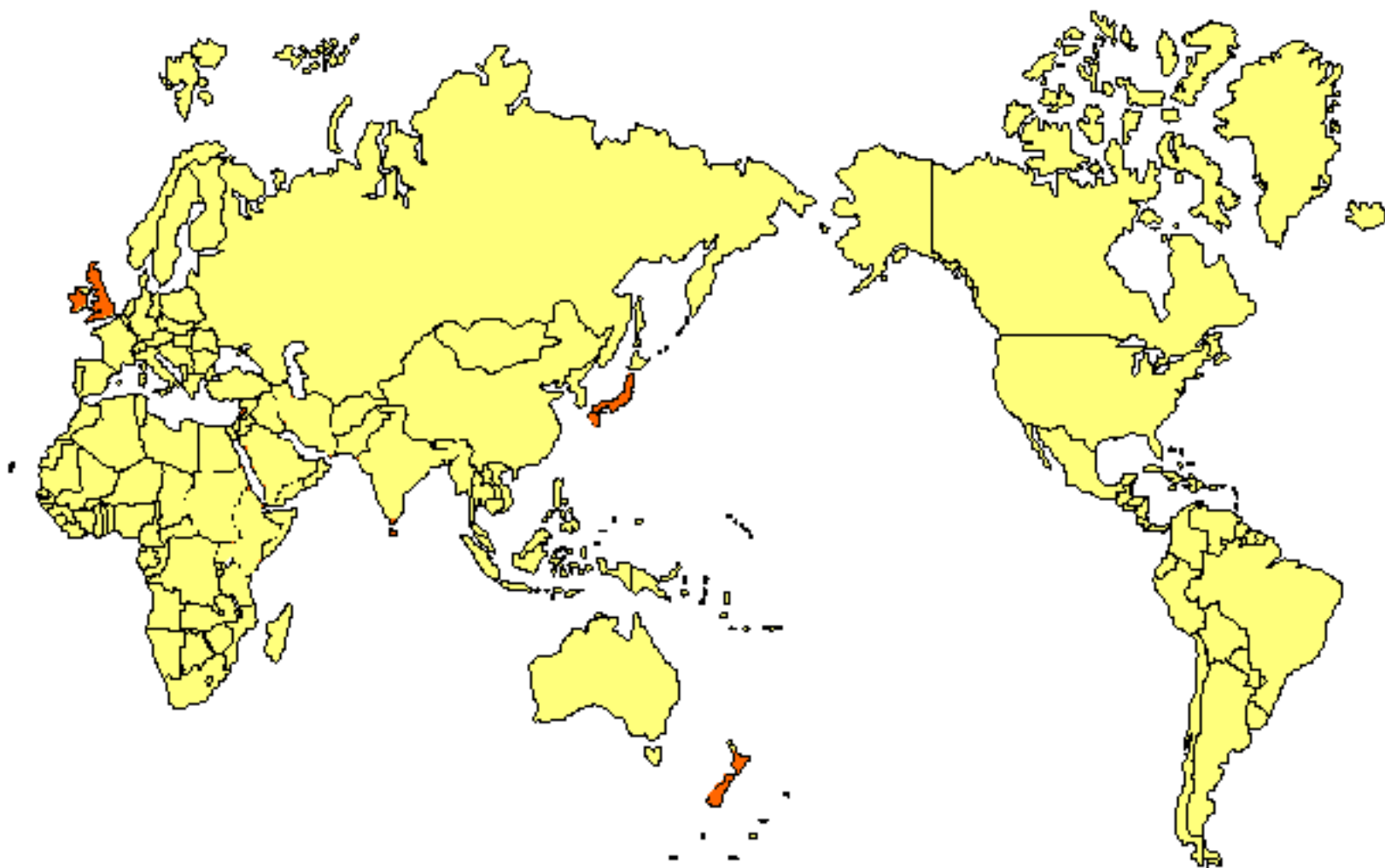
- **Non-suppurative encephalitis, Negri bodies**
- **Rabies virus confirmed by FAT (LCN), immunohistochemistry (WCVM)**
- **Virus serotype-1, vampire strain**



# Symptoms in sheep & goats

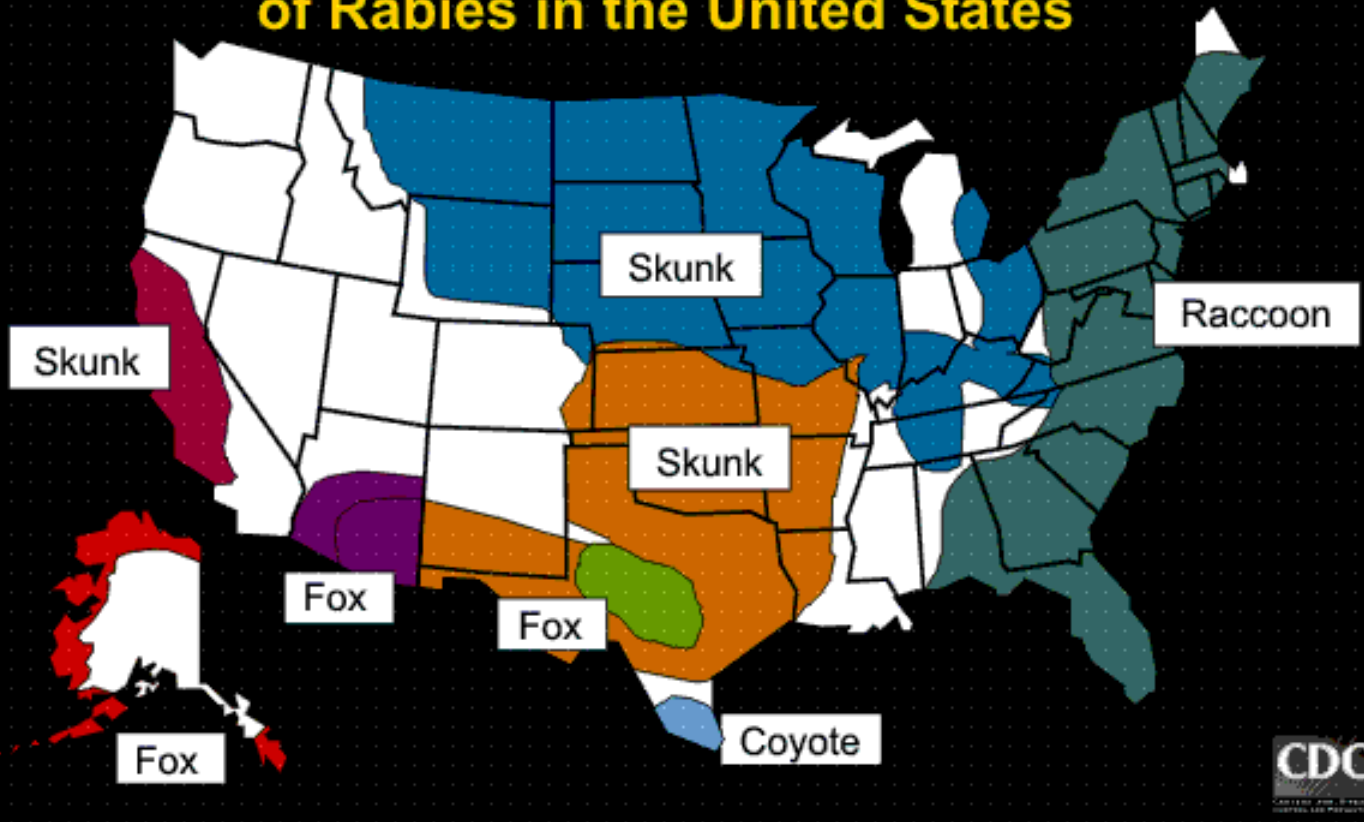
- Like that of cattle
- Increase sexual desire
- Continually mounting each other





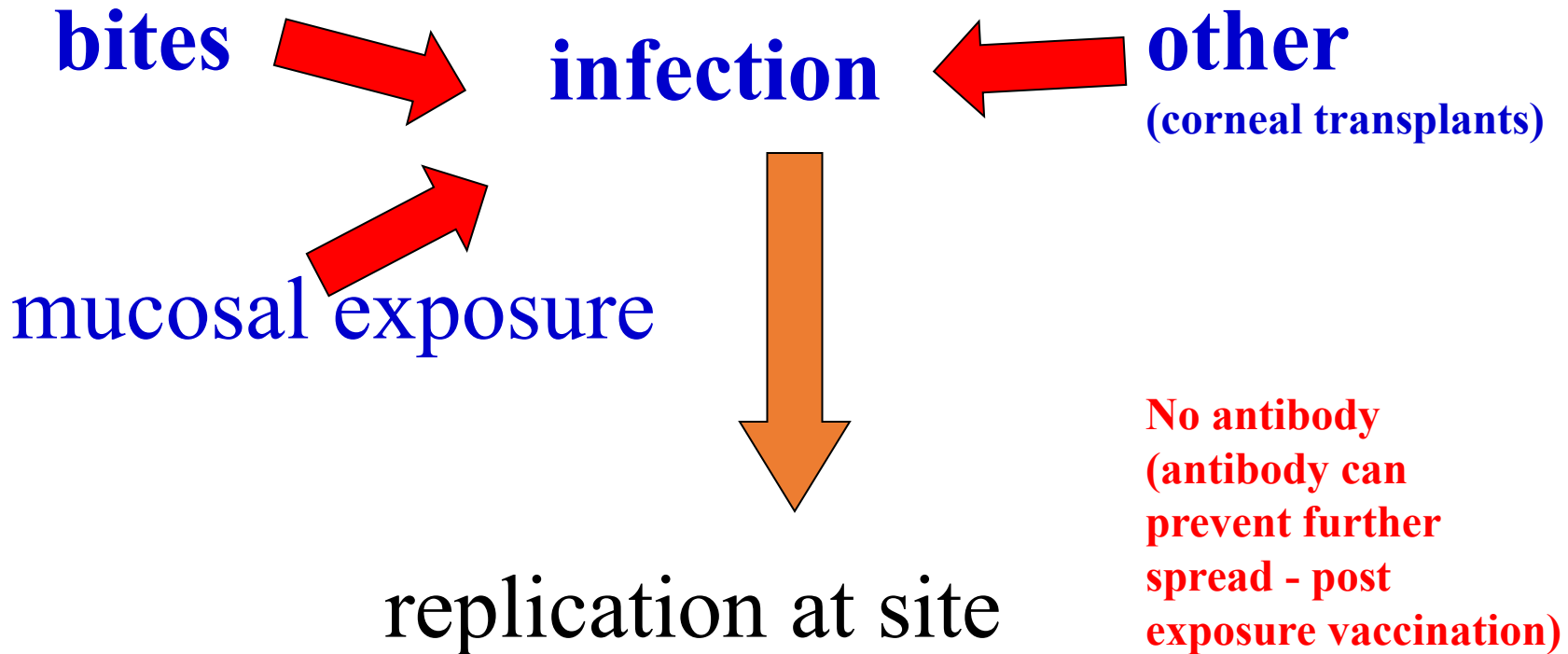


## Distribution of Major Terrestrial Reservoirs of Rabies in the United States





# Pathogenesis: infection and incubation period



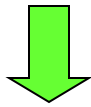
**Incubation period 14-90 days (7 years!)**



# Pathogenesis: Spread to the brain, clinical signs



infection of neurons



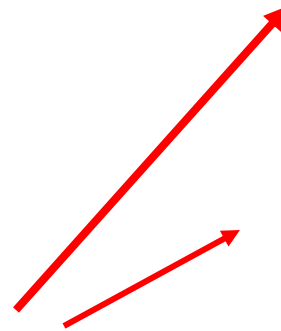
centripetal spread to neurons in spinal cord, spread to brain



centrifugal spread to sal. glands, skin

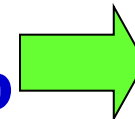


clinical signs



**Furious** (limbic System)

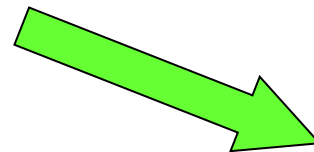
**Dumb** (neocortex)



**death**



2-3 days



**Virus shedding**



# Pathogenesis: in the brain

- No gross signs
- Negri bodies
- Neuronal degeneration (apoptosis)
- Infiltration by mononuclear cells





# Diagnosis

- (1) Clinical symptoms
- (2) Laboratory diagnosis



# Laboratory diagnosis

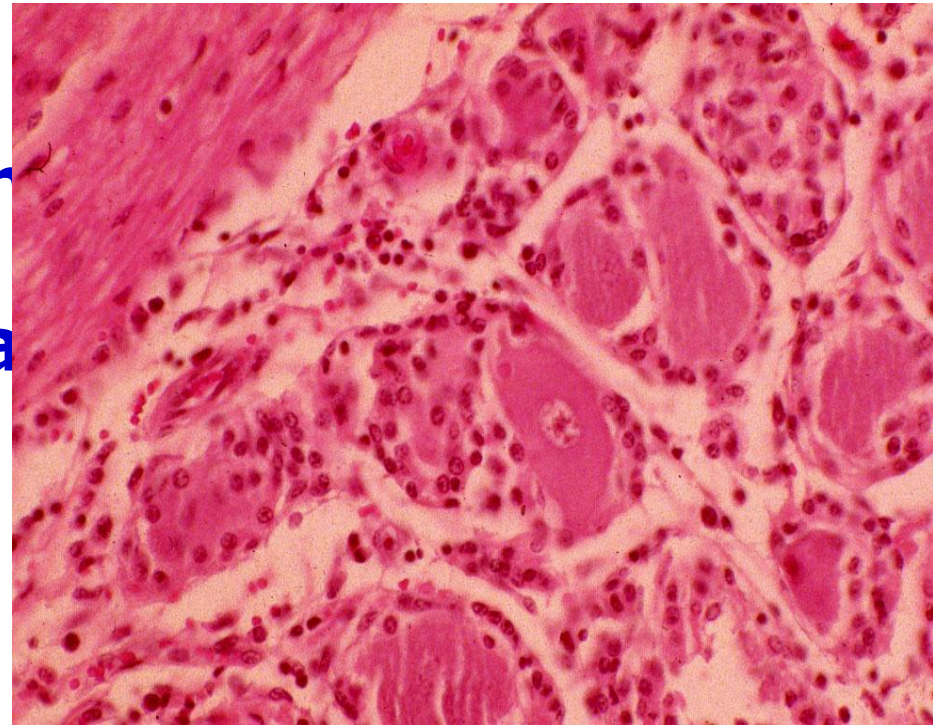


- (1) Microscopically examination**
- (2) animal inoculation**
- (3) IFA**
- (4) Molecular diagnosis**



# Histopathologic evidence of rabies

1. Mononuclear infiltration
2. Perivascular cuffing of lymphocytes or polymorphonuclear cells
3. Lymphocytic foci
4. Babes nodules consisting of glial cells
5. Negri bodies

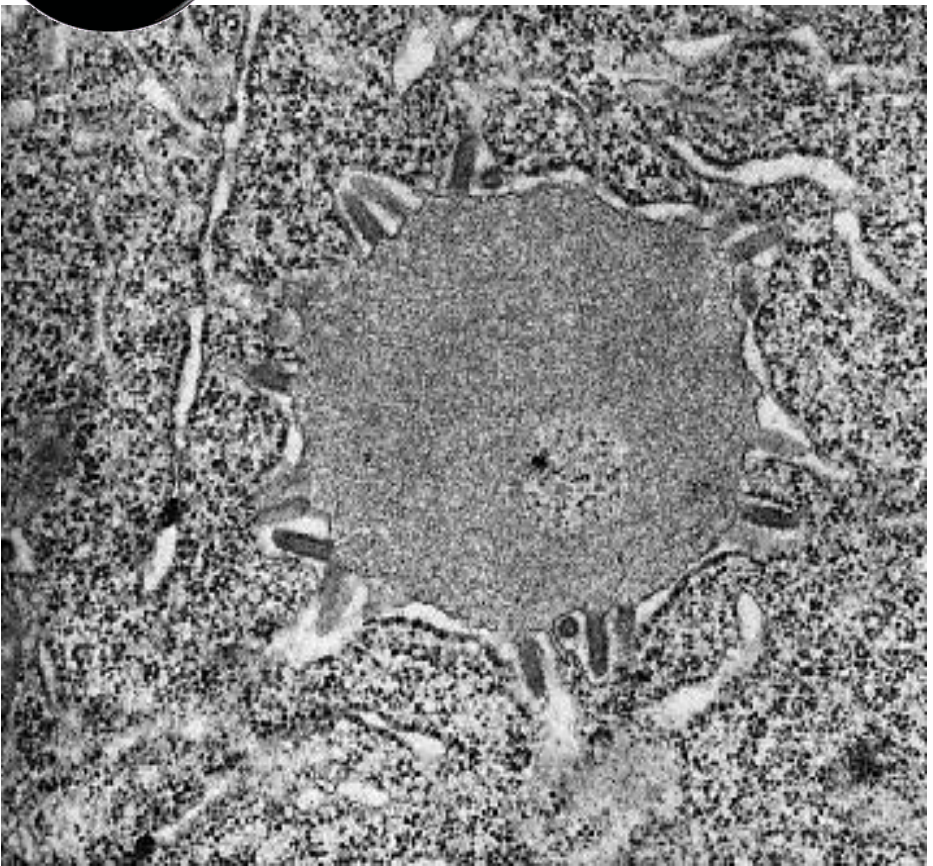


Negri body in a neuron cell in the trigeminal nerve ganglion

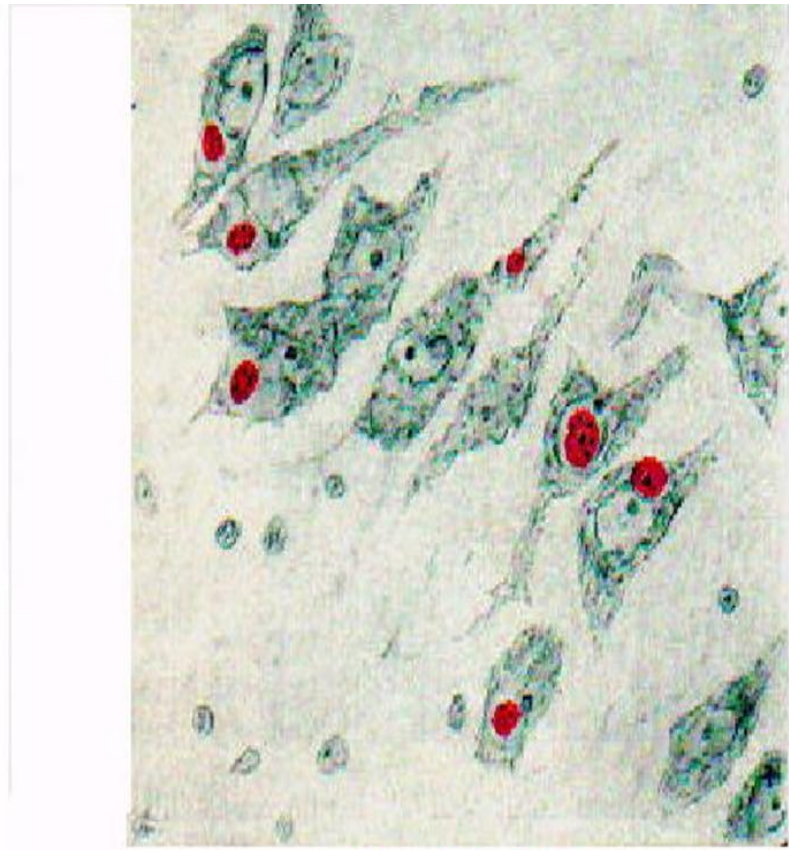




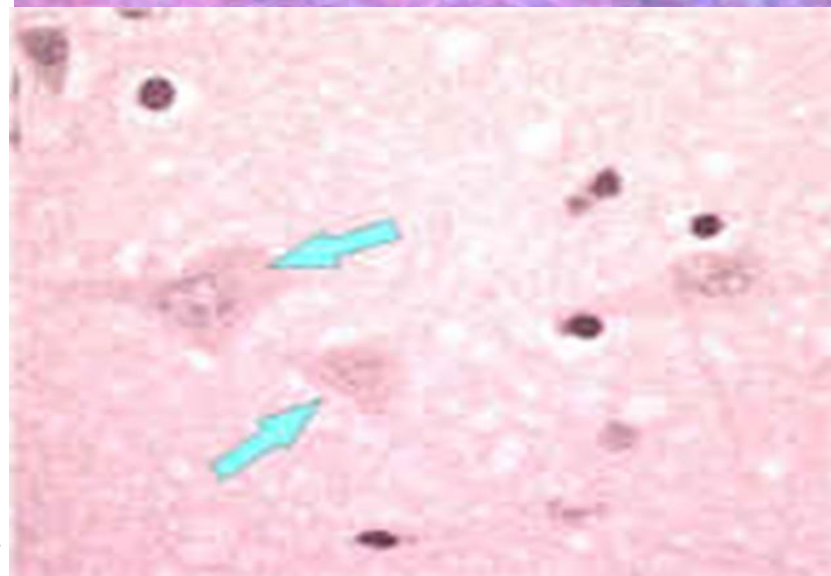
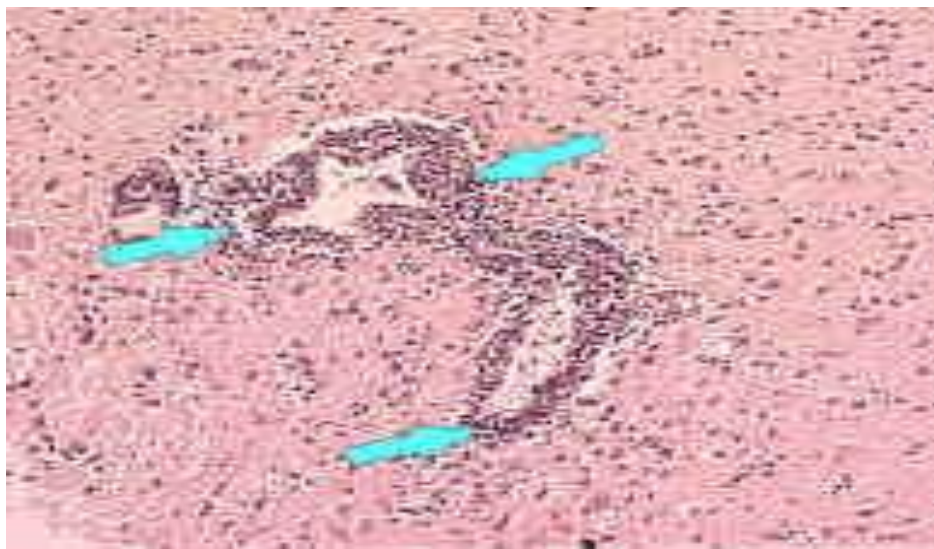
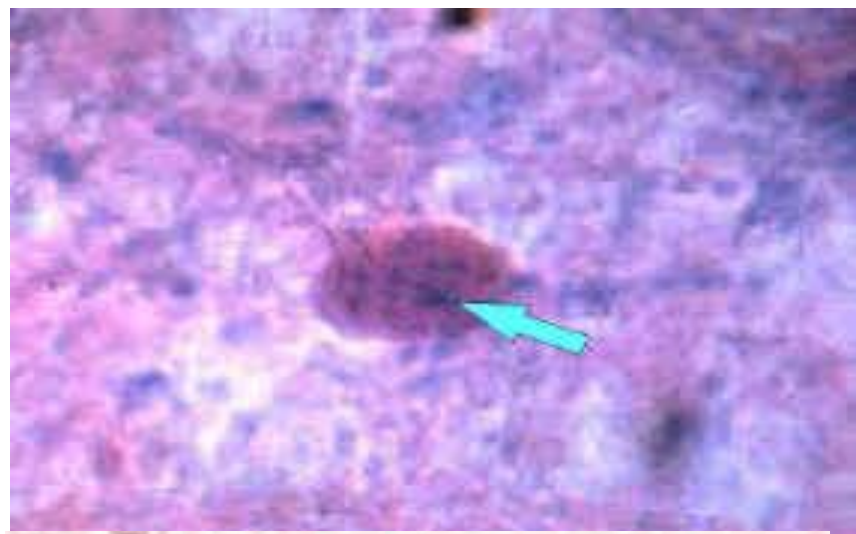
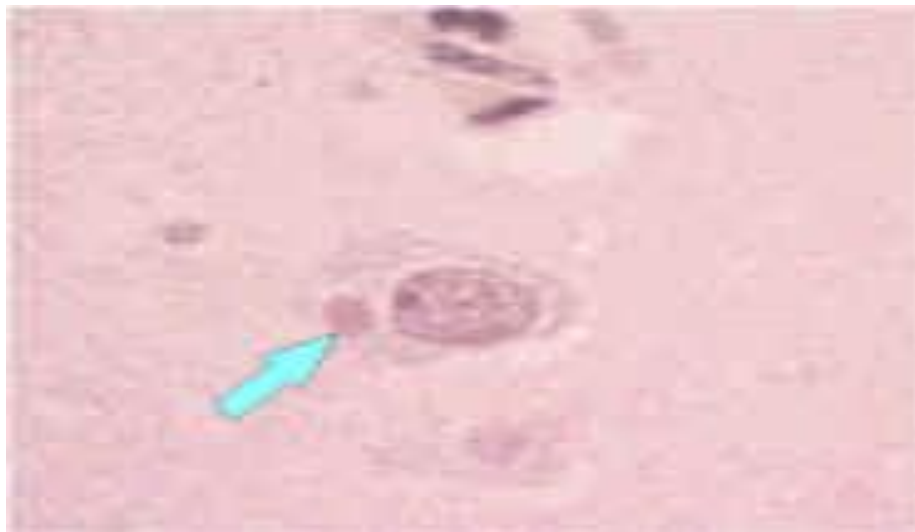
# Negri Bodies



An electron micrograph of a Negri body with budding virus particles



**Negri Bodies**  
Intracytoplasmic inclusion bodies in the neurons of Ammon's horn in rabies (dog)



July





# **Animal inoculation**

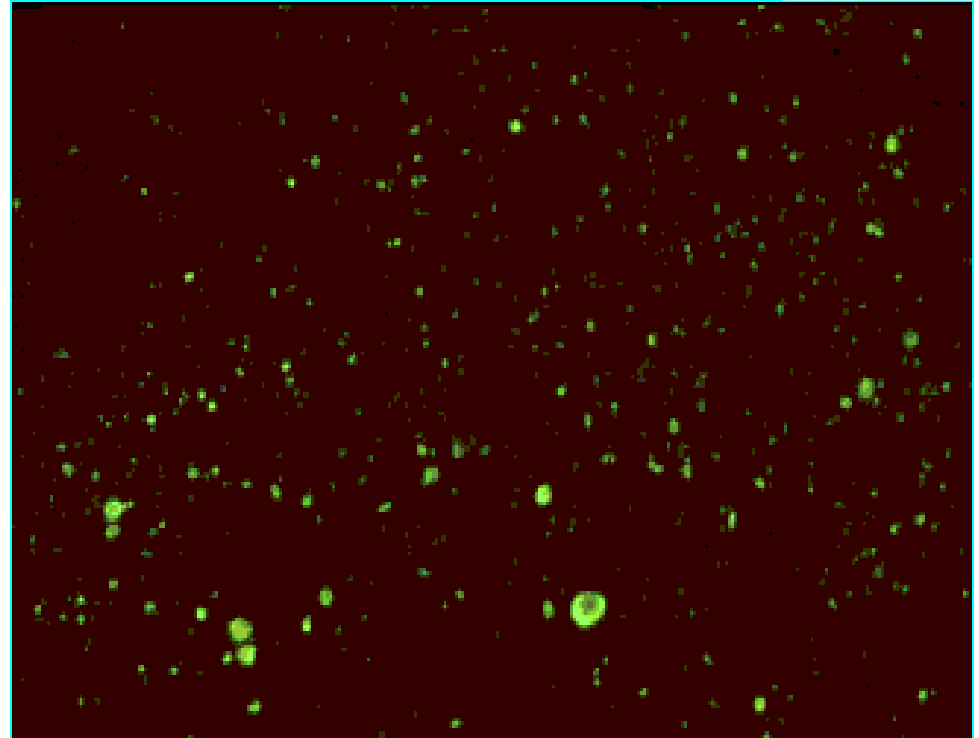
- \* 3-6 weeks old mice inoculated with brain suspensions of rabied animal**
- \* Inoculated mice observed for 3 weeks**
- \* Negative result :no symptoms**
- \* Positive result: tremors,Incoordination of gait, paralysis**
- \* Death after 24 hours of inoculation non specific due to trauma of the brain**



# IFA



**Normal brain tissue ,not showing any fluorescence granules**



**Rabied brain tissue showed fluorescence granules**



# vaccines



- Veterinarians and humans at risk
- Vaccine taken after biting (according to the site of bite) & or injection of anti rabies HIS 1-7 days (after 24 hours of HIS)
- Three types of vaccines are available
  - live attenuated
  - inactivated
  - vectored vaccines



# Vaccines (inactivated vaccines)

- Pecks vaccine(1955) on EDE;  $\beta$ -probiolactone
- Rabguard TC
  - Dogs, cats, cattle, horses, sheep
- Rabvac 3
  - Dogs, cats, horses
- Vaccinate at 3 months, boost at 1year, every three years after that (in high risk areas may require annual vaccinations)
- Cattle and horses - vaccinate annually



# **Live attenuated vaccines**

## **HEP; LEP Flury strain vaccines**





# Vaccines for control in wild-life

- Modified live rabies virus vaccine
- Vectored (vaccinia or canary-pox virus)vaccine

