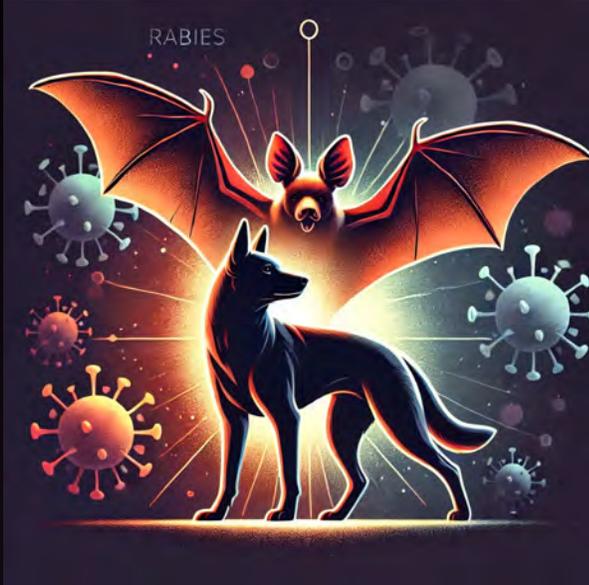


RABIES



ZEYNEP AKKUTAY-YOLDAR,
ASSOCIATE PROFESSOR





Rabies

- Rabies is a zoonotic disease associated with carnivores, such as dogs.
 - The disease is characterized by loss of consciousness, hydrophobia and paralysis.
-

Notifiable

- The virus is excreted in the saliva of infected animals and following infection it moves through the nervous system to attack the brain, causing aggressive behavior which results in the animal biting humans and animals with which it comes into contact and thereby spreading the virus infection.



An image of a rabid dog biting a man. Painting of a rabid dog biting a man. Arabic (Mesopotamian), A.D. 1224; Baghdad school, by Abdallah ibn al-Fadl. (Courtesy of the Smithsonian Institution, Freer Gallery of Art, Washington, D. C.) [Baer, G. M. (2017). The natural history of rabies. Routledge.]

Etiology

- Rhabdoviridae, Lyssavirus
- Bullet-shaped, with short glycoprotein spikes.
- **ANTIGENICITY:** There is one type serologically. Only one type required in vaccine

Etiology

Rabies lyssavirus is an enveloped, negative stranded non segmented RNA virus

Family

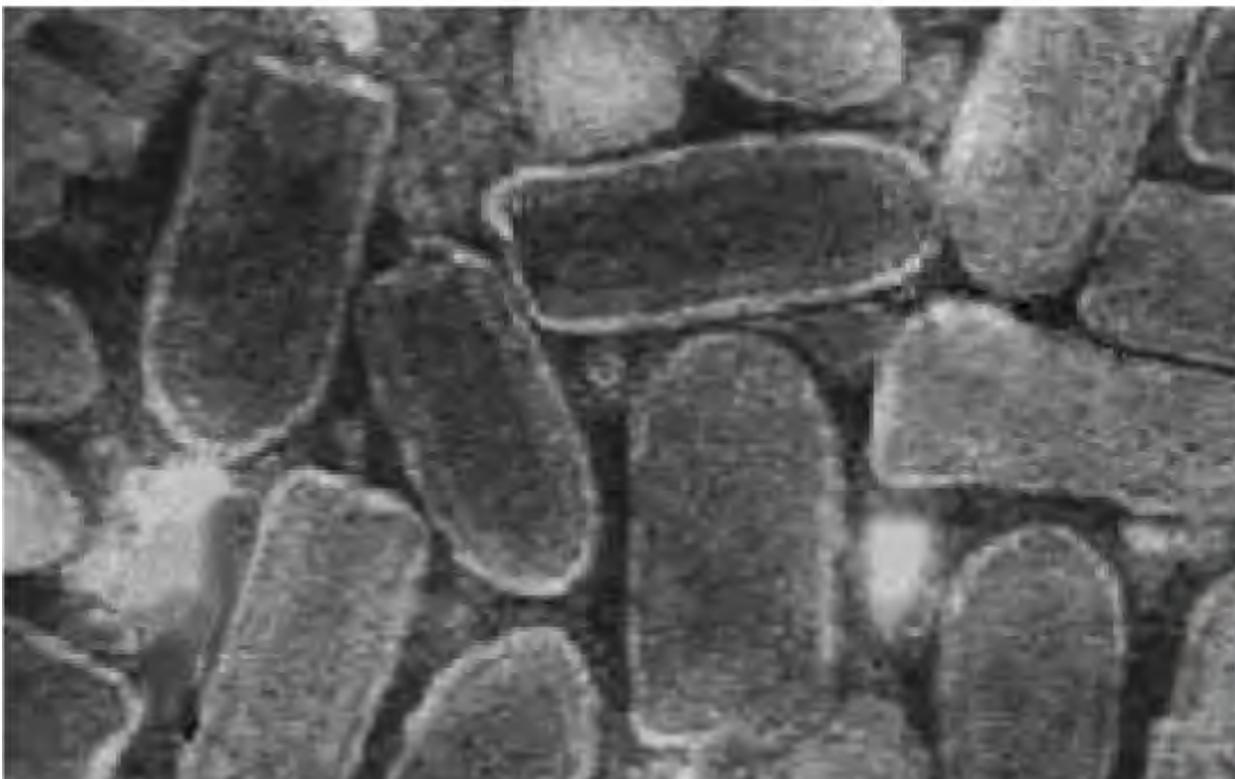
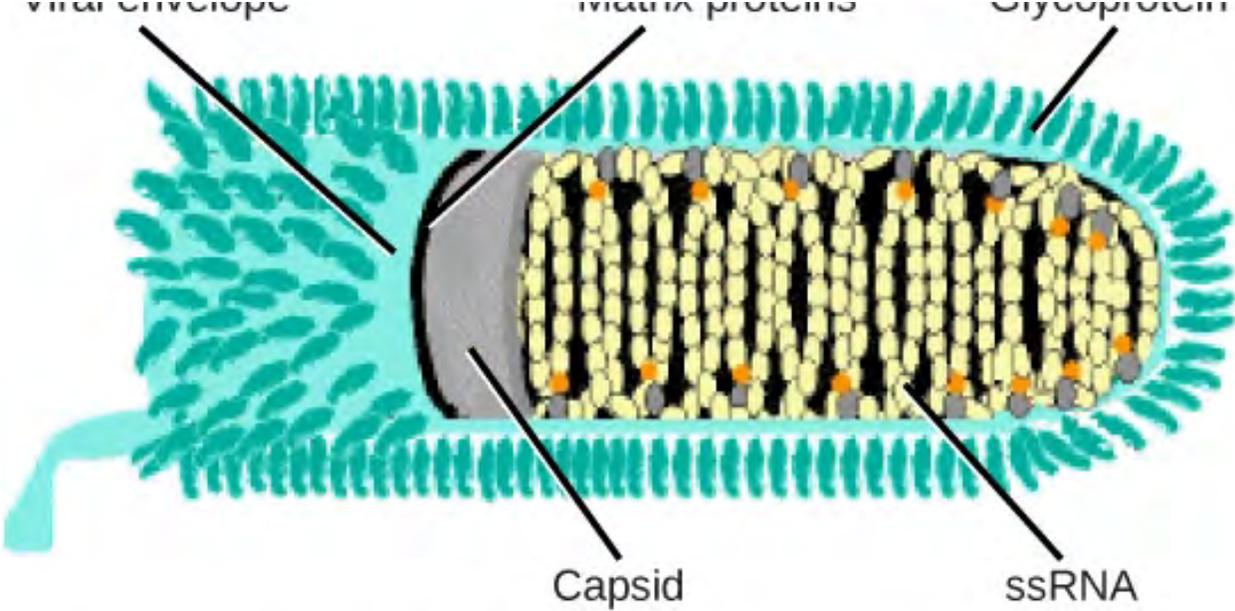
Rhabdoviridae

Genus

Lyssavirus

Species

Rabies lyssavirus



RABIES STILL KILLS



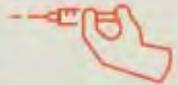


>59,000 people a year 1 person every **9 minutes**



Mostly **children**



AND YET, IT IS 100% PREVENTABLE! 



99% human rabies cases originate from dog bites

NO MORE DEATHS FROM RABIES! VACCINATE DOGS!

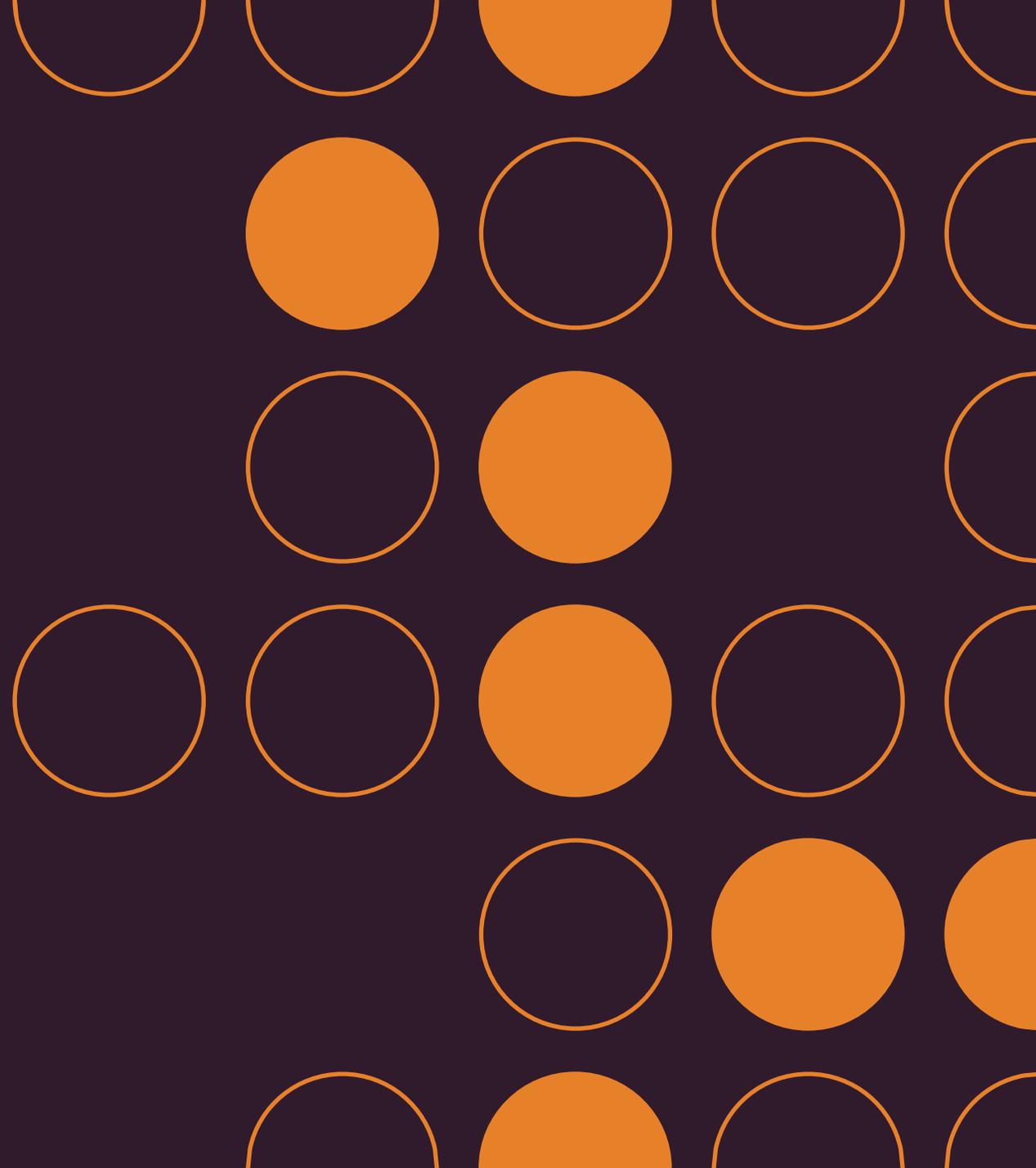

 World Organisation for Animal Health
 Founded as OIE

www.woah.org/rabies



Biotypes

- The pathogenic rabies virus is **STREET VIRUS**
 - **FIX VIRUS** is obtained by passaging the STREET VIRUS in rabbit brain.
 - **FLURY** strain is obtained by ECE passage of pathogenic virus.
-



Biotypes

Street Virus

- Found in saliva
- Causes Negri Bodies
- Pathogen for all mammals
- Incubation period is longer (60-80 days)

Fix Virus

- Does not found in saliva
 - Does not cause Negri Bodies
 - Only pathogen for rabbits
 - Incubation period is shorter (4-6 days)
-

Transmission

Transmitted by bites through infected saliva and by aerosols where high concentrations of virus found. (eg: in caves where there are high concentrations of bats).



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Transmission

- In dogs, virus exists in the saliva and sheds the virus 5 days before the first clinical signs.
- Virus also exists in urine, milk, gaita and blood.

Epidemiology

Australia, Fiji, Finland, Iceland, Ireland,
Japan, New Zealand, Sweden, United
Kingdom

All mammals are
susceptible
including bats

Found throughout
the world but
some countries
are free.



Epidemiology

- Europe - Fox, badger, weasel, stoat.
- Russia and the Middle East – Wolf, dog.
- U.S.A. - Fox, skunk, wildcat]
- Africa, India - Dog
- S. America - Bat - vampire.

Bats are reservoir of different viruses including RABIES

- **Bats** may be persistently viremic and shed virus in saliva.
- They are the only species where rabies is always avirulent.





Epidemiology in Turkey

- Cat, Dog,
- Cattle, Sheep, Goat
- Donkey, Horse,
- Fox, Wolve, Weasel

Animals

In Turkey rabies detected in cattle, donkey, horses, foxes, cats, dogs, and marten.

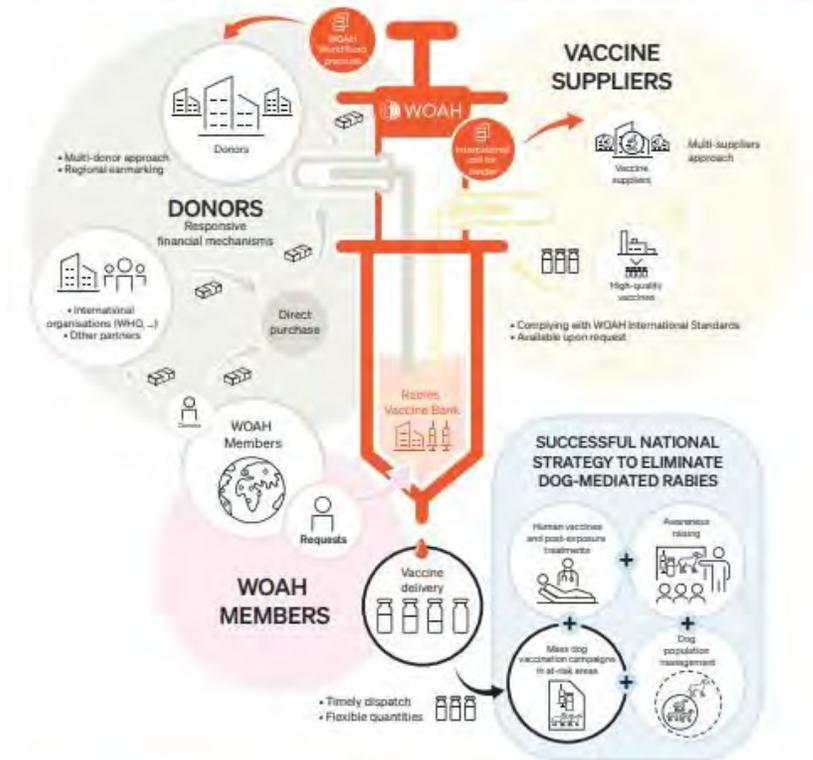


Atıcı, Y. T., 2022. The comparison of full G and N gene sequences from turkish rabies virus field strains. *Virus Research*, 315, 198790. Vos, A., Ün, H., Hampson, K., De Balogh, K., Aylan, O., Freuling, C. M., ... & Johnson, N. (2014). Bovine rabies in Turkey: patterns of infection and implications for costs and control. *Epidemiology & Infection*, 142(9), 1925-1933
Johnson, N., Ün, H., Fooks, A. R., Freuling, C., Müller, T., Aylan, O., & Vos, A. (2010). Rabies epidemiology and control in Turkey: past and present. *Epidemiology & Infection*, 138(3), 305-312.

CANINE RABIES VACCINES TO SAVE HUMAN LIVES

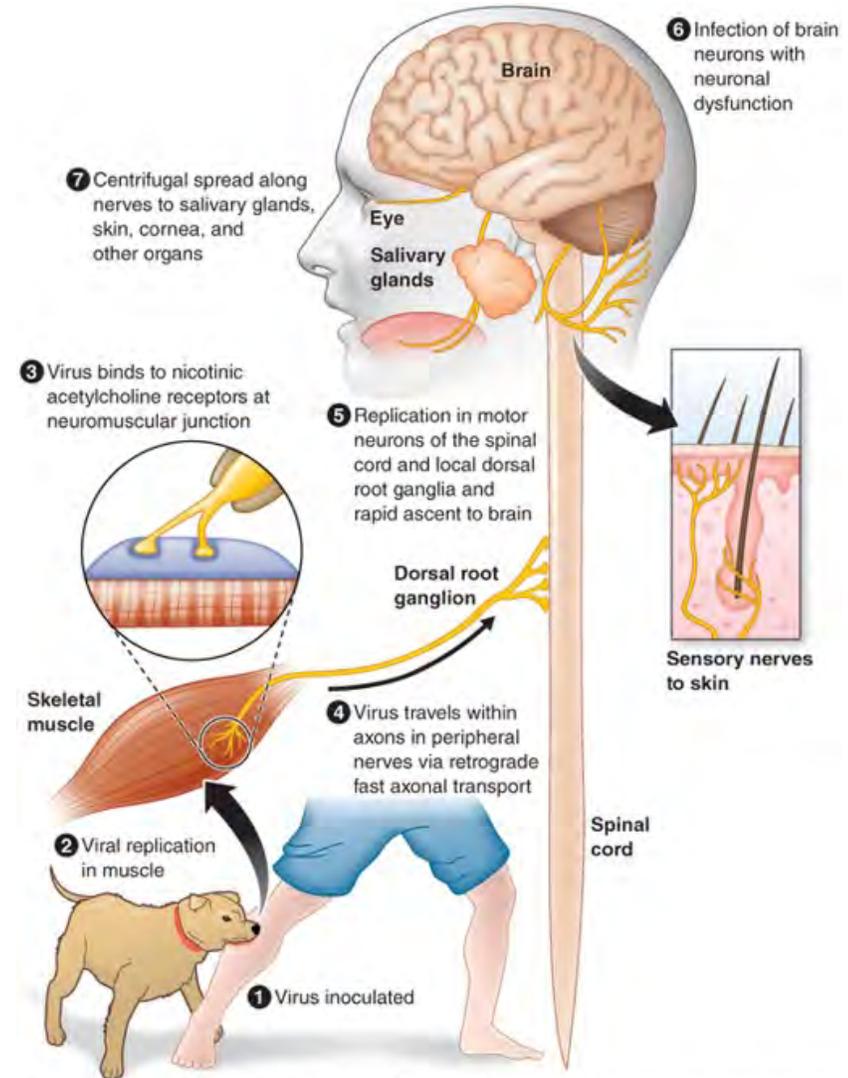
RABIES kills nearly **59,000 PERSONS PER YEAR** with more than **99%** of cases originating from infected **DOG BITES**.

By providing high-quality dog vaccines, our vaccine bank helps countries implement vaccination campaigns and eliminate dog-mediated human rabies.



Pathogenesis

- After inoculation in muscle fibers, virus replicates there and migrates towards brain (centripetal migration).
- It continues to replicate in brain then travels through cranial nerves to reach salivary gland and cornea (centrifugal migration).



5 Virus reaches brain and causes fatal encephalitis.

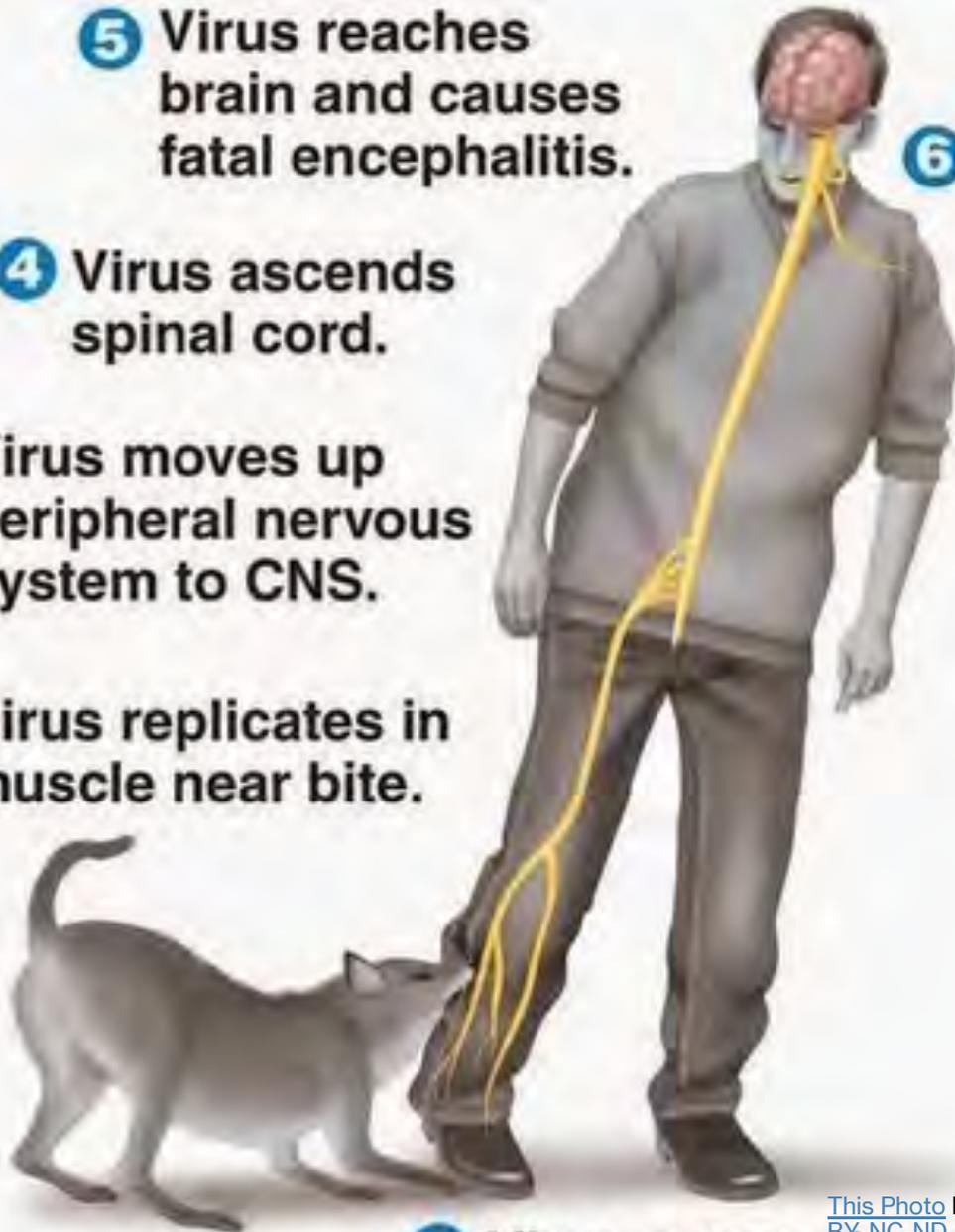
4 Virus ascends spinal cord.

3 Virus moves up peripheral nervous system to CNS.

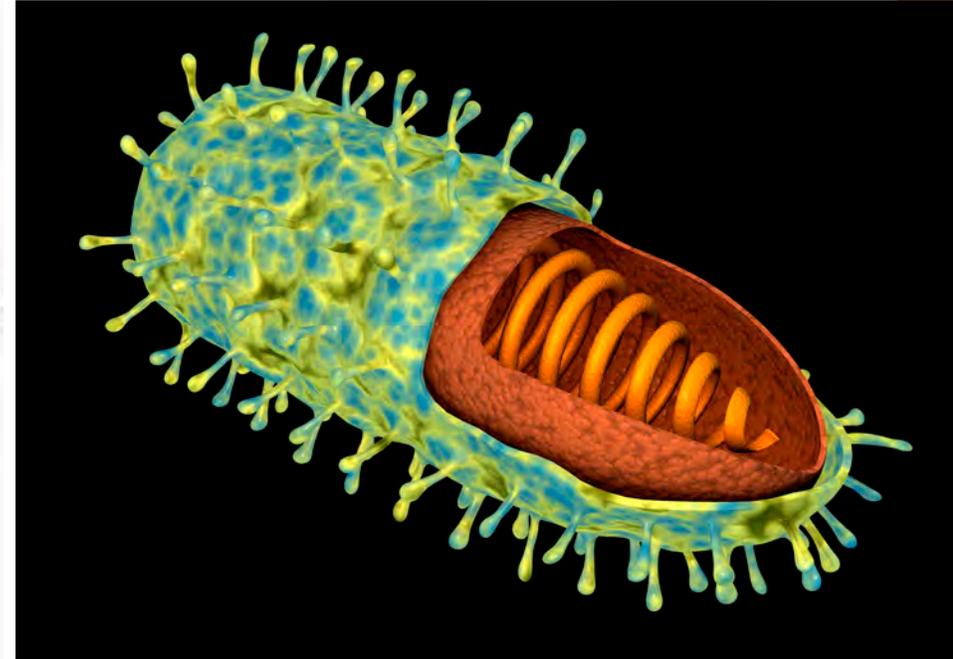
2 Virus replicates in muscle near bite.

1 Virus enters tissue from saliva of biting animal.

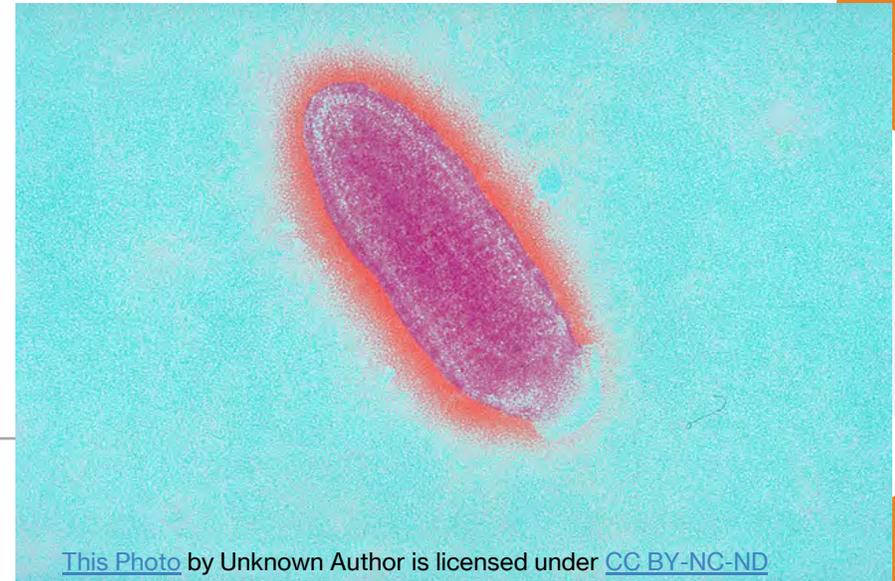
6 Virus enters salivary glands and other organs of victim.



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Pathogenesis

Incubation period is variable and can be long:

10 days to 12 months (even 7 years) but usually less than 3 months;

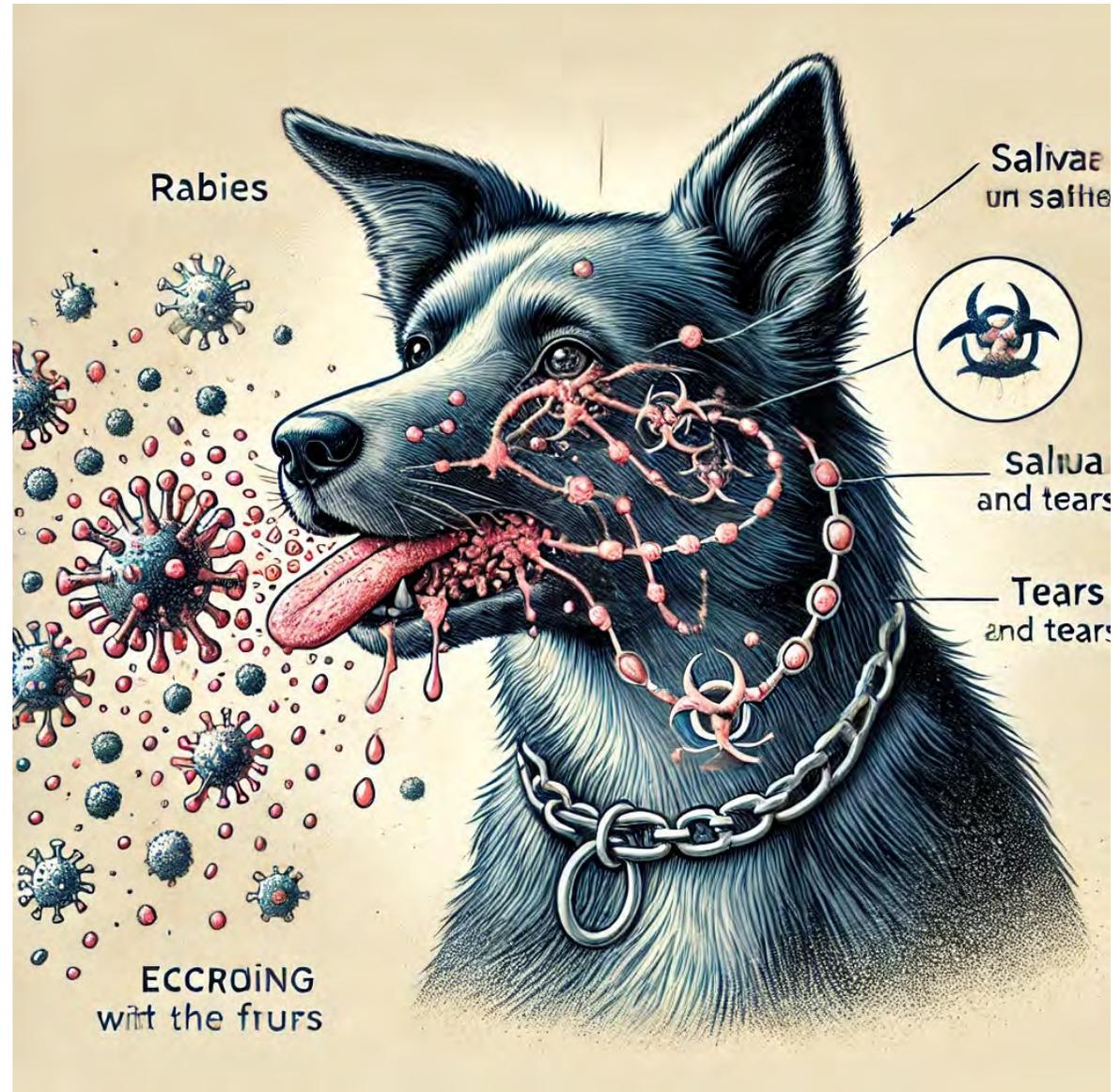
Distance of the bite is important.

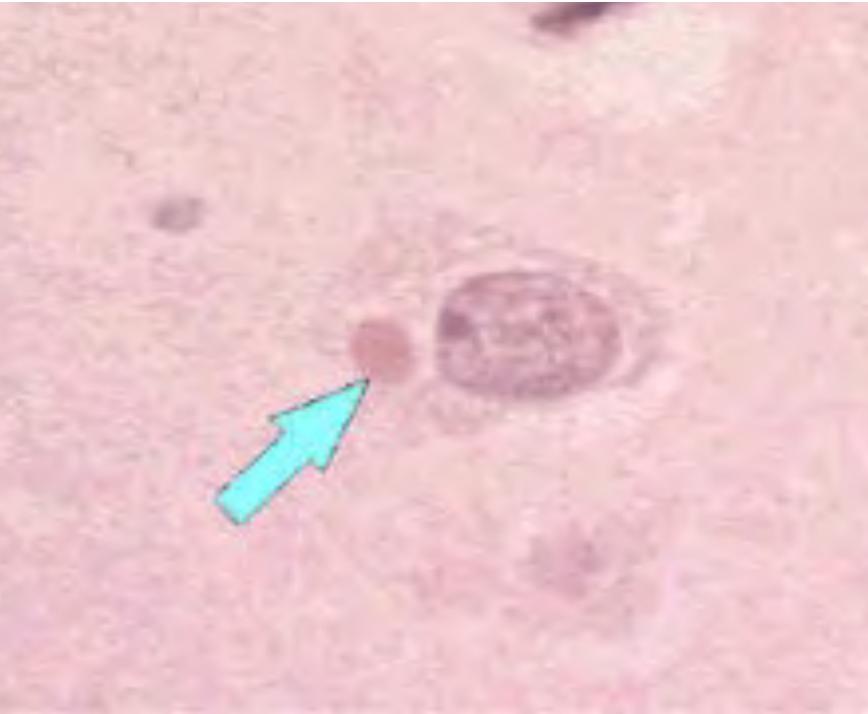
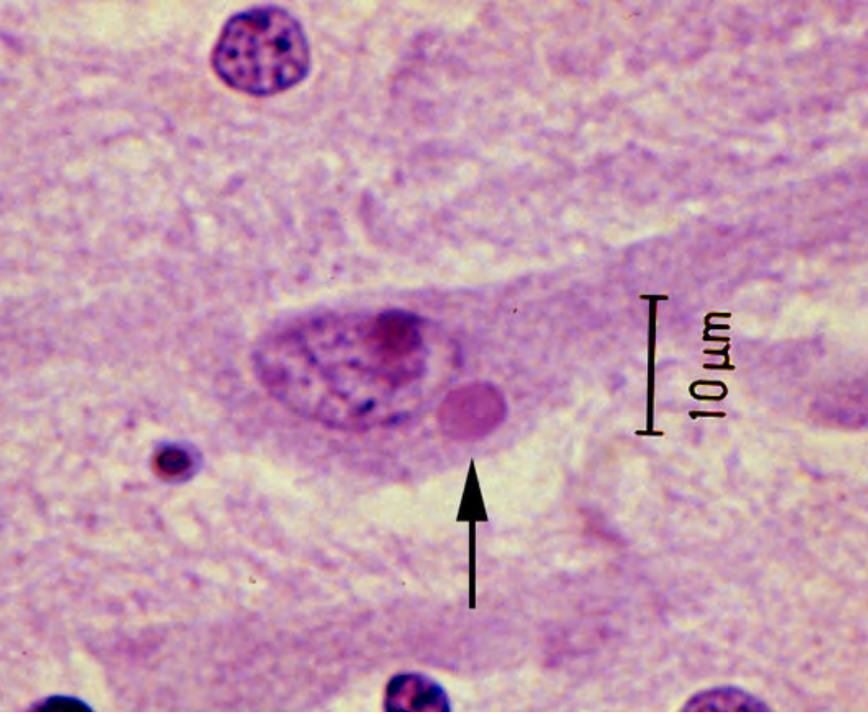
Primary replication occurs in the muscle fibres then gains access to the nerve fibres where the virus travels towards the brain (centripetal migration)

Where it replicates followed by "centrifugal" migration down the cranial nerves replicating in the salivary gland and cornea.

Pathogenesis

- Virus excretion in saliva and tears.
- Virus may be shed before classical symptoms.
- Obvious clinical signs develop after salivary excretion of virus.





Pathogenesis in the brain

- No gross signs
 - Negri bodies (%50 of clini
 - Neuronal degeneration (apoptosis)
 - Infiltration by mononuclear cells
-

Clinical Signs

Furious



Fear of water



Hypersensitivity to sound



Hypersensitivity to light



Aggressiveness



Convulsions



Excessive salivation and sweating



Insomnia

Paralytic



Depression



Lethargy



Increased blood pressure



Tachycardia



Confusion



Hallucination



Paralysis

Clinical Signs

- Nonspecific prodromal signs may be seen during the early stage of rabies.
 - They can include malaise, fever or headache, as well as discomfort, pain, pruritus or other sensory alterations at the site of virus entry.
-



- After several days,
 - anxiety,
 - confusion and
 - agitation may appear,
 - and progress to insomnia,
 - abnormal behavior,
 - hypersensitivity to light and sound,
 - delirium,
 - hallucinations,
 - slight or partial paralysis,
 - hypersalivation,
 - difficulty swallowing,
 - pharyngeal spasms upon exposure to liquids,
 - convulsions and
 - other neurological signs.



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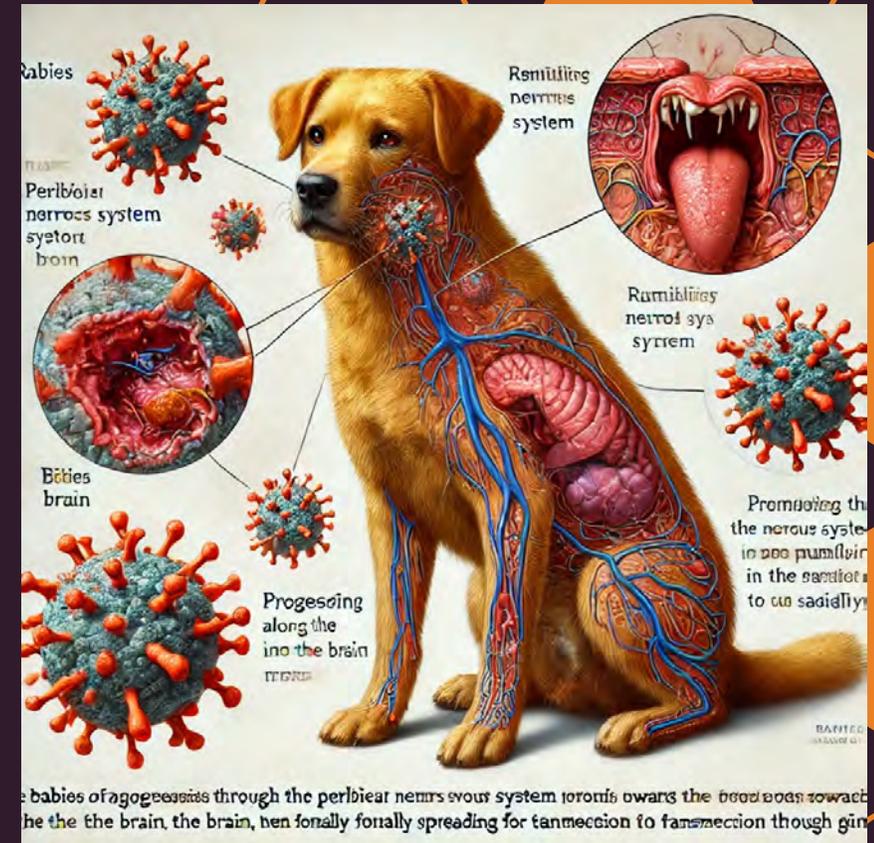


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There are two forms of the disease

1-Furious (fatal) rabies

- Animals may be anxious, highly excitable and/or aggressive.
- Animals with this form of rabies may demonstrate sudden behavior changes, and attack without provocation.
- As the disease progresses, muscular weakness, incoordination and seizures are common. Death results from progressive paralysis.



2-Dumb Rabies (Paralytic)

- **Animals** with this form of rabies may be depressed or unusually docile. The animal will often have paralysis, generally of the face, throat and neck, causing abnormal facial expressions, salivate and inability to swallow. Paralysis first affects the hind legs. The paralysis progresses rapidly to the whole body with subsequent coma and death.
- **In humans**, early signs can include fever or headache. As the disease progresses, symptoms may include confusion, depression, sleepiness, agitation or paralysis of the face, throat and neck. Death generally results from progressive paralysis.



Diagnosis

1-Seller's staining Method:

Rabies suspects specimens are stained
Searching negri body.

2-Fluorescent Antibody Method; (GOLD STANDARD)

Direct antigen detection. Used routinely.

3-Histopathological method:

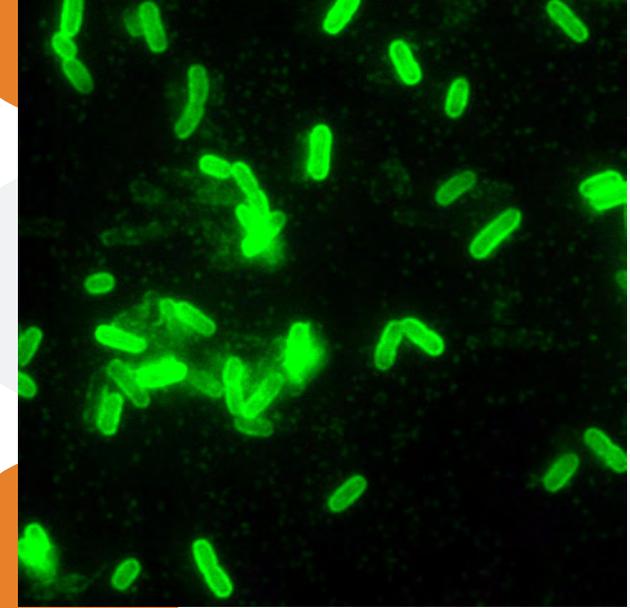
Searching for Negri bodies. (not any more)

4-Experimental Animals

Inoculation to mice, IF and search for Negri
bodies.

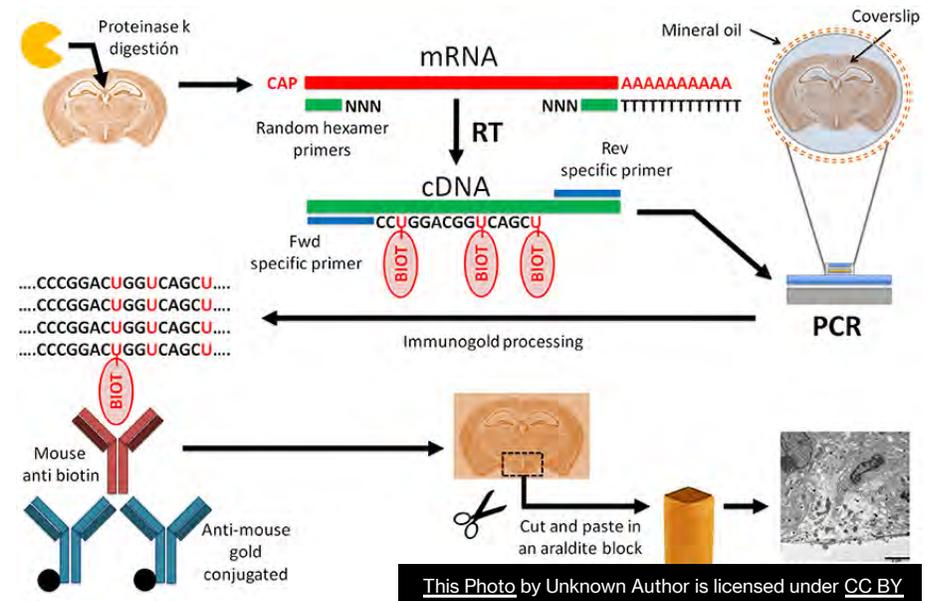
Currently, Cell culture are using.

5-Electron microscopy



Diagnosis

- Molecular methods,
 - RT-PCR and other amplification techniques, are playing an important role but are not recommended currently for routine post-mortem diagnosis of rabies if brain tissue is available, when the FAT should be used.



Prevention and Control

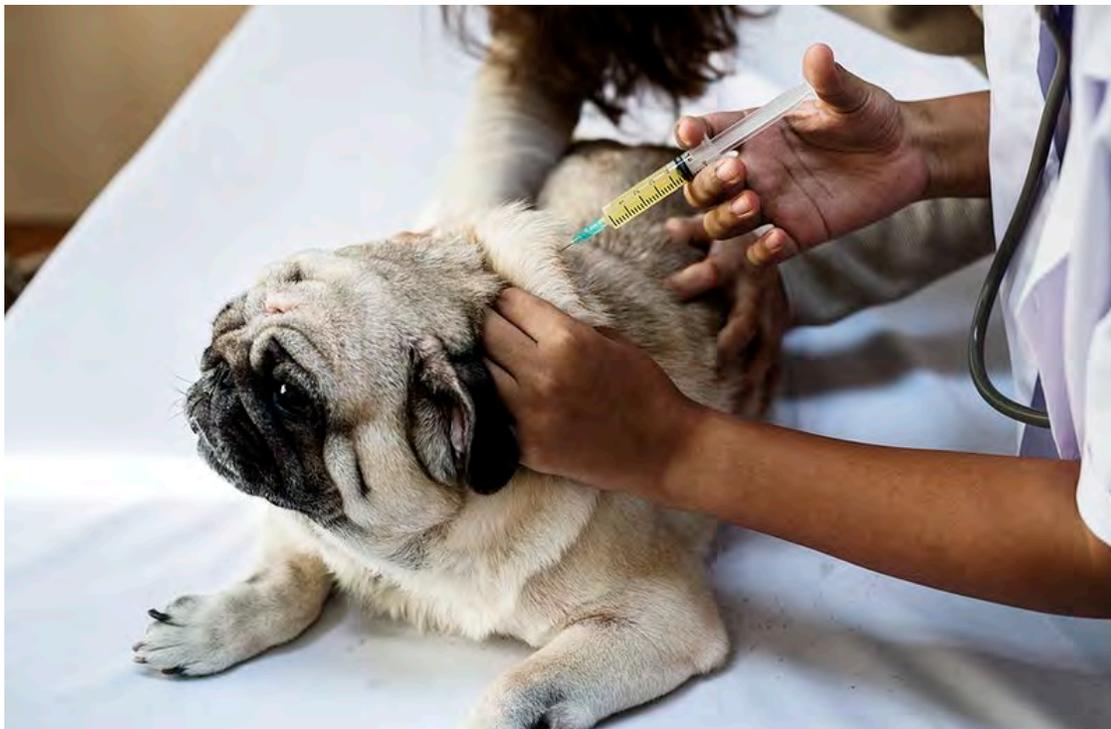
Unfortunately, there is no
treatment of rabies.

no.

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Prevention and Control

- The animals with suspected rabies held in quarantine for 10 days.
- Animals with rabies die within a maximum of 10 days from the first appearance of rabies symptoms.



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Vaccination is most efficient way for prevention.



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Oral and parenteral vaccination is possible for wildlife. The best way to protect against wildlife animals is through oral immunization regimens.

In pet animals: Apply first Rabies vaccine at 3 months old, then repeat annually.

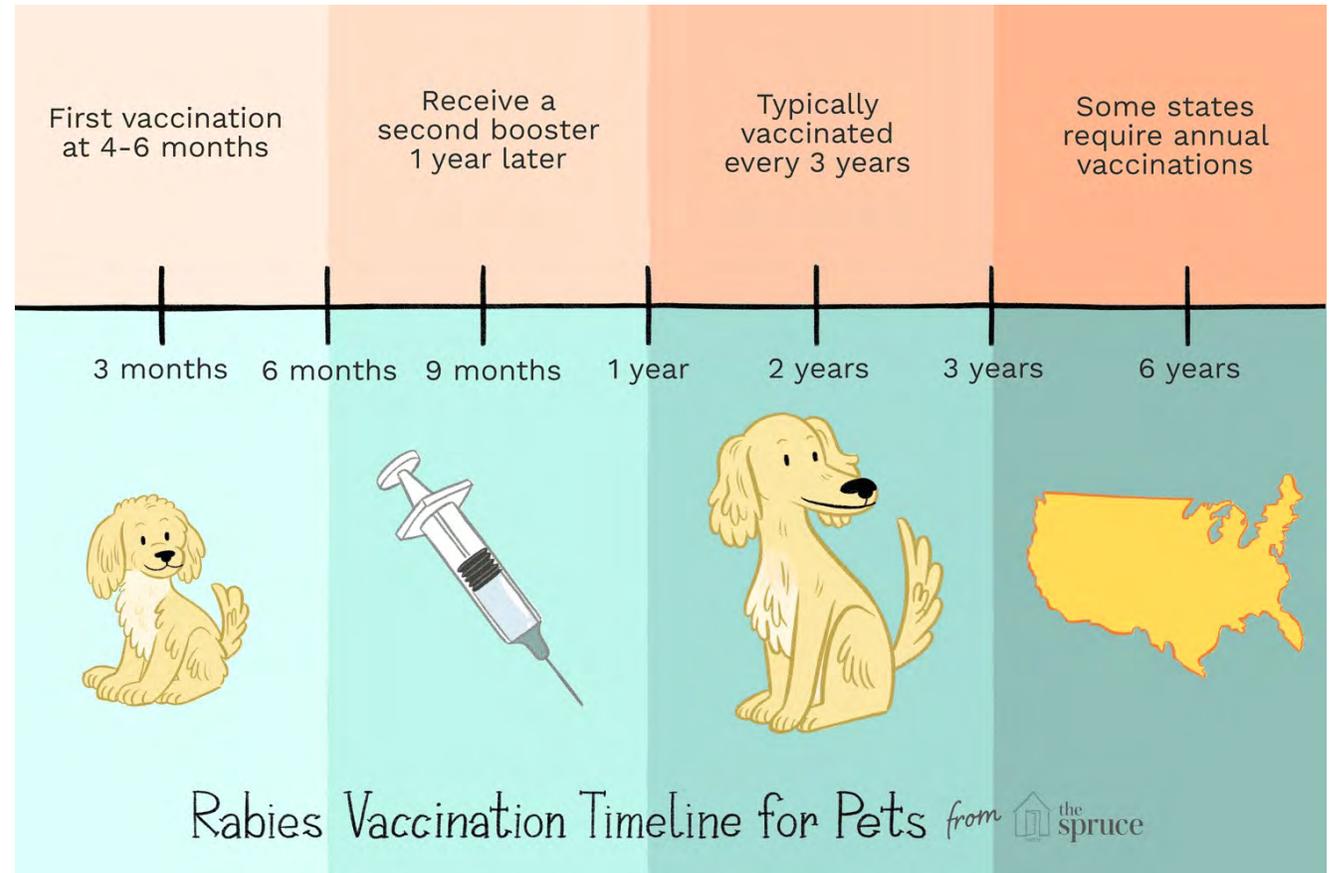
For humans: 4 dose Rabies vaccination after bitten; 0th, 3rd and 7th day and then 1 other dose between 14th and 28th day.

Vaccination

- <https://www.regentstreetclinic.co.uk/rabies-vaccine/>



While some rabies vaccinations are licensed for one year, others are labeled for three years.



Two approaches in Europe

1. Vaccination of domestic animals with inactivated or live attenuated vaccines

2a. Control of the wildlife reservoir: population density of reservoir species reduced by gassing & shooting

2b. Vaccination of wildlife. Has been effective in reducing the prevalence of rabies but as a consequence the fox population is increasing! Vaccines are either attenuated virus or a recombinant vaccinia vaccine. Fed in bait. A successful strategy in Europe.



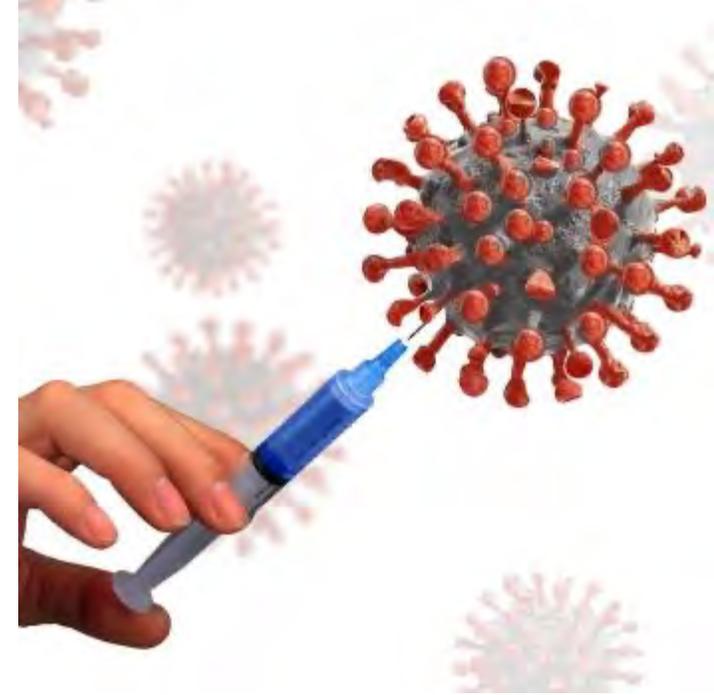
Kelev & Semple vaccines replaced by modern rabies vaccines



The Flury Vaccine

The rabies virus Flury strain (isolated from a girl who died of rabies in Macon, GA, USA) was adapted to 1-day-old chicks in 1940.

Many effective vaccines, such as modified live virus, recombinant, and inactivated types, are available for use throughout the world.



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Tissue Culture Vaccines

Vaccinations made from inactivated tissue cultures are very successful at stopping the spread of rabies.

Primary Hamster Kidney Cells: The first tissue culture vaccine was derived from virus grown in primary hamster kidney cells.

Human Diploid Cells: It is the second tissue culture vaccine.

Vero Cell Line Rabies Vaccine: Vero cells are a continuous cell line derived from the kidney cells of African green monkeys

Vaccinations should be done at 3 months, boost at 1 year, every three years after that (in high risk areas may require annual vaccinations)

Cattle and horses - vaccinate annually

1885: Pasteur *et al.* developed a method to prevent human rabies



1900s–1960s: Fermi, Semple and Fuenzalida/Palacios rabies vaccine

1885: Roux maintained a live portion of the medullary plates of an embryonic chicken *in vitro* for several days

1907: Harrison cultivated nerve fibers *in vitro*

1931: Goodpasture infected chicken embryos with varicella virus



1950s–1960s: Chicken and duck embryo-derived rabies tissue vaccines

1949: Enders *et al.* grew polio virus in primary monkey cells



1960s–1980s: Rabies vaccines in PHKC, bovine and dog kidney cells, PDEC and PCEC vaccines

1951: Gey developed the HeLa cell line

1961: Hayflick *et al.* developed the human diploid cell strain WI-38



1974: HDCV rabies vaccine (WI-38, MRC-5) licensed, recommended by the WHO as the gold standard

1962: Yasumura and Kawakata developed the vero cell line

1985: PVRV licensed using Vero cells

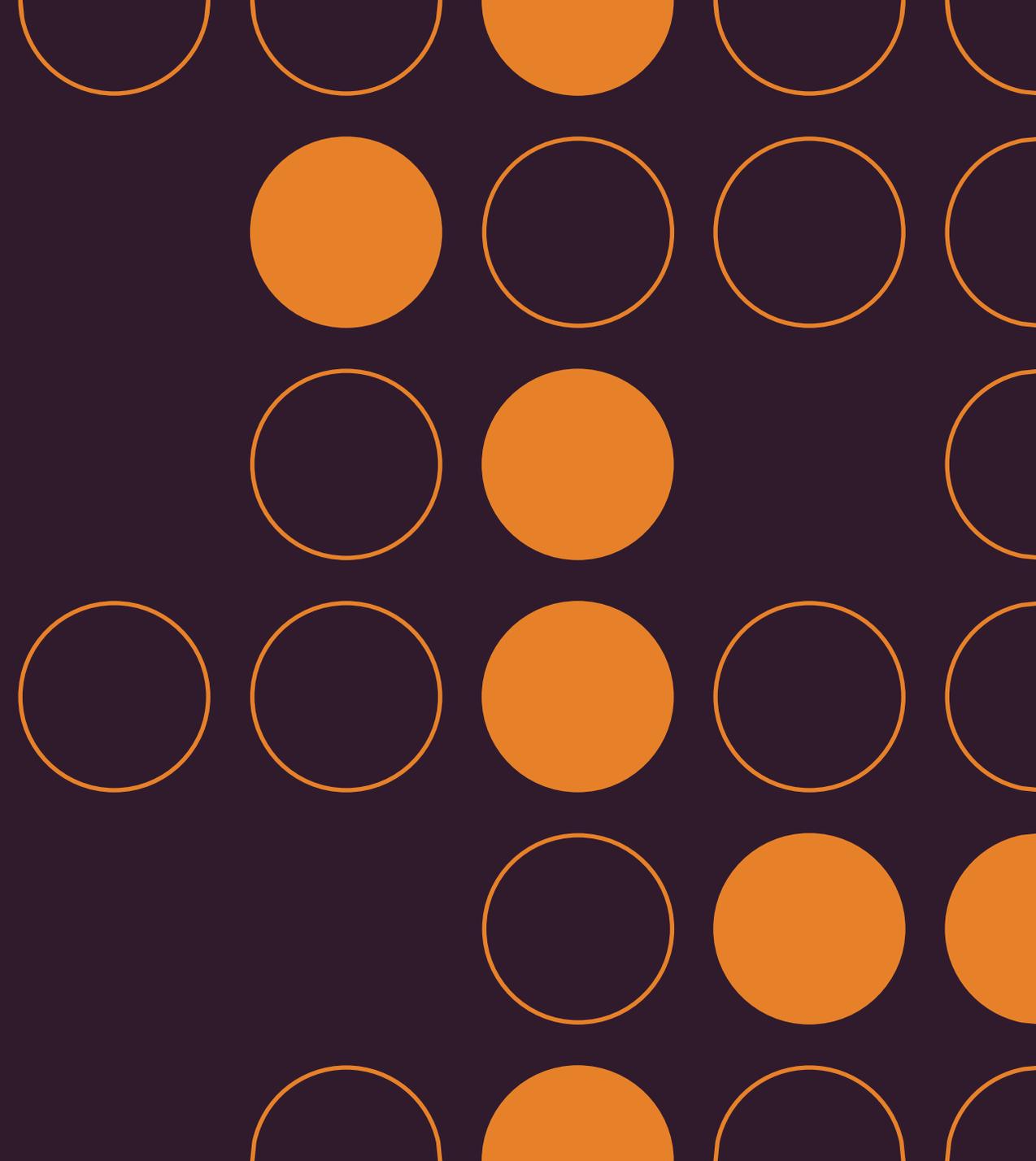
Wu, Xianfu & Smith, Todd & Rupprecht, Charles. (2011). From brain passage to cell adaptation: The road of human rabies vaccine development. *Expert review of vaccines*. 10. 1597-608. 10.1586/erv.11.140.

Breakthroughs in vaccine substrates and their influence on rabies vaccine development. HDCV: Human diploid cell vaccine; PCEC: Purified chicken embryo cell; PDEC: Purified duck embryo cell; PHKC: Primary hamster kidney cell; PVRV: Purified Vero cell rabies vaccine.

Product Name	Produced by	Marketed by	For use in	(mL)	Vaccination	Recommended	Inoculation
A) MONOVALENT (Inactivated)							
TRIMUNE	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	Dogs	1	3 mos	1 yr later & triennially	IM ⁵
			Cats	1	3 mos	1 yr later & triennially	IM
ANNUMUNE	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	Dogs	1	3 mos	Annually	IM
			Cats	1	3 mos	Annually	IM
DEFENSOR 1	Pfizer, Inc. License No. 189	Pfizer, Inc.	Dogs	1	3 mos	Annually	IM or SC [¶]
			Cats	1	3 mos	Annually	SC
DEFENSOR 3	Pfizer, Inc. License No. 189	Pfizer, Inc.	Dogs	1	3 mos	1 yr later & triennially	IM or SC
			Cats	1	3 mos	1 yr later & triennially	SC
			Sheep	2	3 mos	Annually	IM
			Cattle	2	3 mos	Annually	IM
RABDOMUN	Pfizer, Inc. License No. 189	Schering-Plough	Dogs	1	3 mos	1 yr later & triennially	IM or SC
			Cats	1	3 mos	1 yr later & triennially	SC
			Sheep	2	3 mos	Annually	IM
			Cattle	2	3 mos	Annually	IM
RABDOMUN 1	Pfizer, Inc. License No. 189	Schering-Plough	Dogs	1	3 mos	Annually	IM or SC
			Cats	1	3 mos	Annually	SC
RABVAC 1	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	Dogs	1	3 mos	Annually	IM or SC
			Cats	1	3 mos	Annually	IM or SC
RABVAC 3	Fort Dodge Animal Health License No. 112	Fort Dodge Animal Health	Dogs	1	3 mos	1 yr later & triennially	IM or SC
			Cats	1	3 mos	1 yr later & triennially	IM or SC
			Horses	2	3 mos	Annually	IM
PRORAB-1	Intervet, Inc. License No. 286	Intervet, Inc.	Dogs	1	3 mos	Annually	IM or SC
			Cats	1	3 mos	Annually	IM or SC
			Sheep	2	3 mos	Annually	IM
PRORAB-3F	Intervet, Inc. License No. 286	Intervet, Inc.	Cats	1	3 mos	1 yr later & triennially	IM or SC
IMRAB 3	Merial, Inc. License No. 298	Merial, Inc.	Dogs	1	3 mos	1 yr later & triennially	IM or SC
			Cats	1	3 mos	1 yr later & triennially	IM or SC
			Sheep	2	3 mos	1 yr later & triennially	IM or SC
			Cattle	2	3 mos	Annually	IM or SC
			Horses	2	3 mos	Annually	IM or SC
			Ferrets	1	3 mos	Annually	SC
IMBAR	Merial, Inc.	Merial, Inc.	Cattle	2	3 mos	Annually	IM or SC

Rabies in Humans

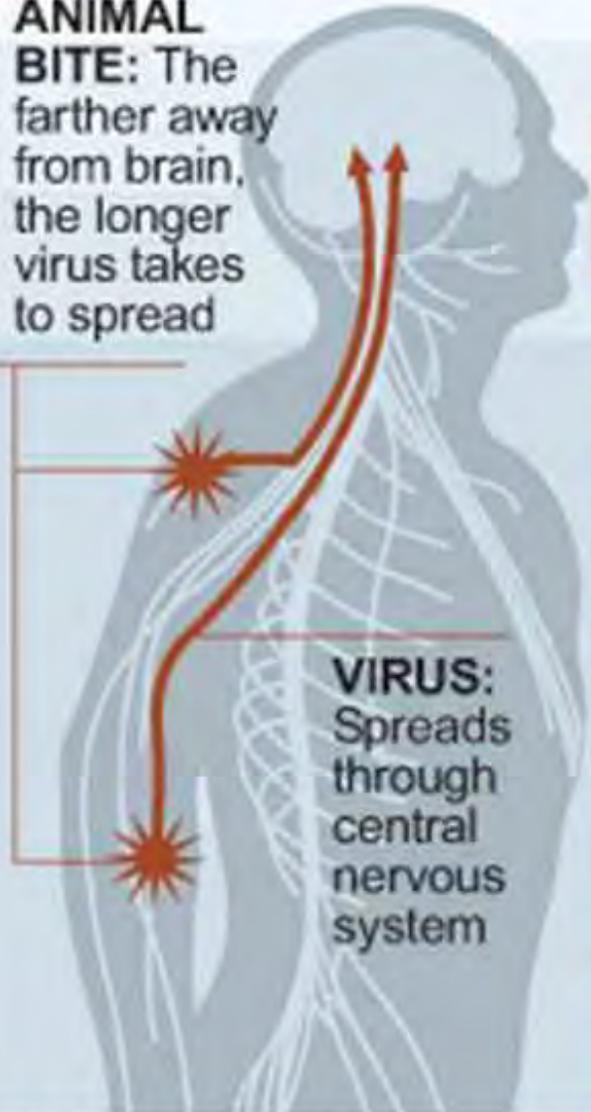
- Incubation period lasts 30-90 days.
 - The first symptoms are pruritus, burning, and pain.
 - Larynx and Pharynx spasm results in Hydrophobia, Aerophobia, Photophobia and Strong Salivation
-



Rabies

How it spreads

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



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 vaccine

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

Foaming at mouth after drinking: Produced by spasms in throat

- Wound treatment is applied to people bitten by animals suspected of rabies.
- The wound should be washed with soapy warm water and disinfected with Alcohol and Iodine.
- NO Stitches.

DON'Ts AND DOs

DON'T



Magical , religious practices do not help (e.g. witchcraft, turmeric powder etc.)



AT HOME or CLINIC



Wash the wound thoroughly with plenty of water and soap



AT CLINIC



Cat II & III



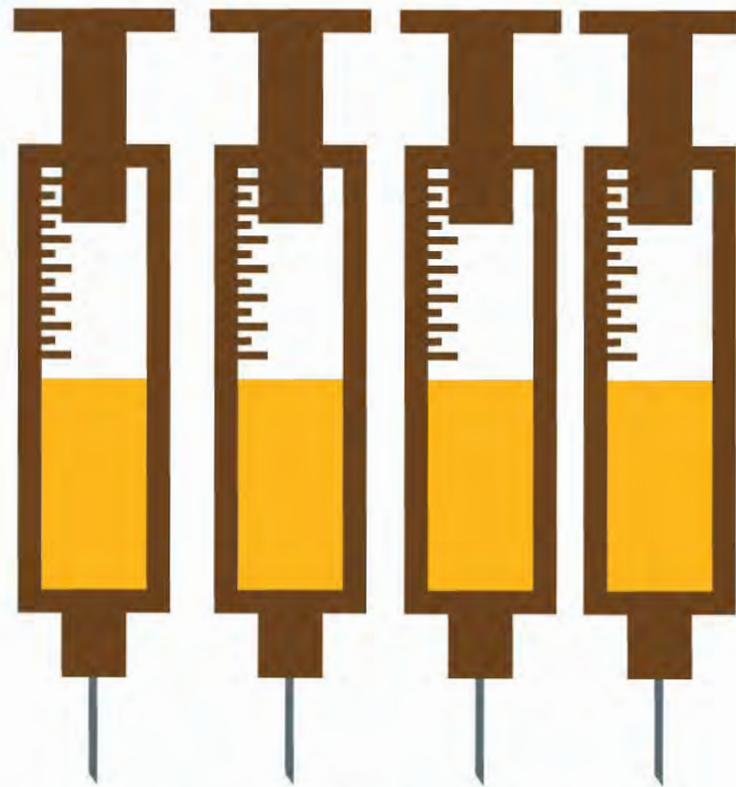
A person who is exposed and has never been vaccinated against rabies

- Should get 4 doses of rabies vaccine. The person should also get another shot called rabies immune globulin (RIG).
 - A person who has been previously vaccinated should get 2 doses of rabies vaccine and does not need Rabies Immune Globulin.
-



**VACCINATE
WITH
ONE**

**TREAT
WITH
FOUR**



www.RabiesFreeAfrica.org

RABIES

INFOGRAPHICS

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Dogs are infected with rabies.

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Source



Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam.



Treatment

Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam.

Symptoms



Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam.

First Aid



Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam.