RABIES VIRUS

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RABIES VIRUS

- Rabies virus belongs to the family: Rhabdoviridae. (Greek: Rhabdos: rod). They can infect a variety of animals and plants
- Worldwide, it is estimated that approximately 55 000 persons die of rabies each year.

Rhabdoviruses

Type	Virus	Distribution	Species infected	Disease
Vesiculovirus	Vesicular stomatitis virus (VSV)	Carribean	Cattle, pigs horse	Acute, self limiting
Lyssavirus	Rabies virus	Worldwide	Many mammals including humans	Slow, progressive
Plant rhabdoviruses				
Other animal rhabdoviruses			Mammals, fish, birds, arthropods	

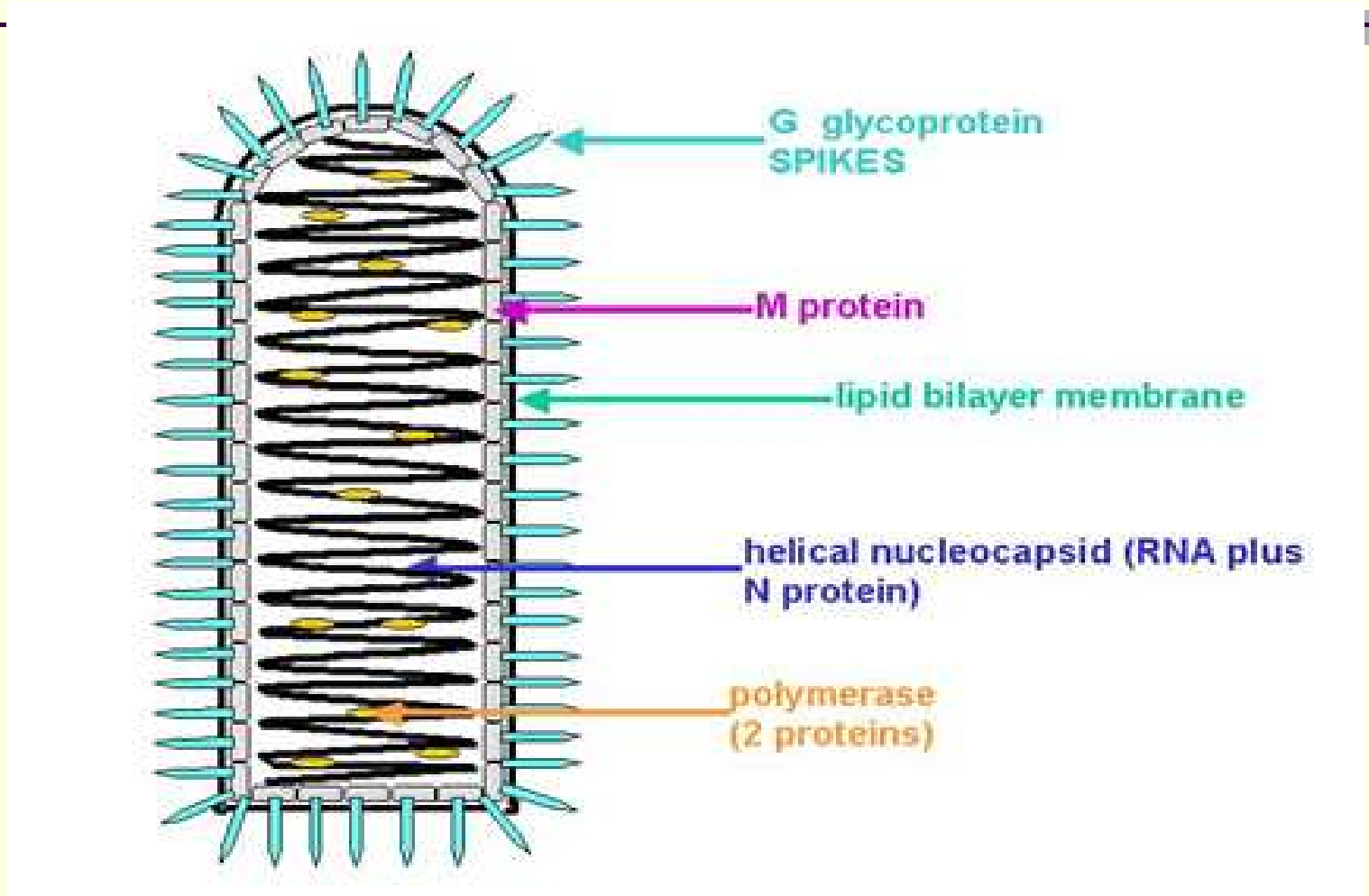
Morphology

- Rhabdoviruses are negative strand RNA viruses; that is they have a single strand of RNA that is anti-sense to the messenger RNA needed to code for viral proteins.
- This means that the RNA cannot code directly for protein synthesis and must be copied to positive strand mRNA. As a result, the virus must carry its own RNA-dependent RNA polymerase.

Morphology Cont..

- The rabies virus is bullet shaped, 180x75 nm, with one end rounded or conical and the other planar or concave.
- The lipoprotein envelop carries knob like spikes, composed of glycoprotein G.
- Two morphological forms : Street virus and Fixed virus.

Structure of Rabies Virus



Pathogenesis

Transmission

- Rabid animals become aggressive and harbor the virus in saliva and thus

transmission is frequently via animal bites. In rare cases, rabies has been transmitted by corneal transplant or transplant of other tissues, or through contact of infected saliva with mucosal membranes or an open wound in the absence of a bite.

Pathogenesis Cont..

Disease

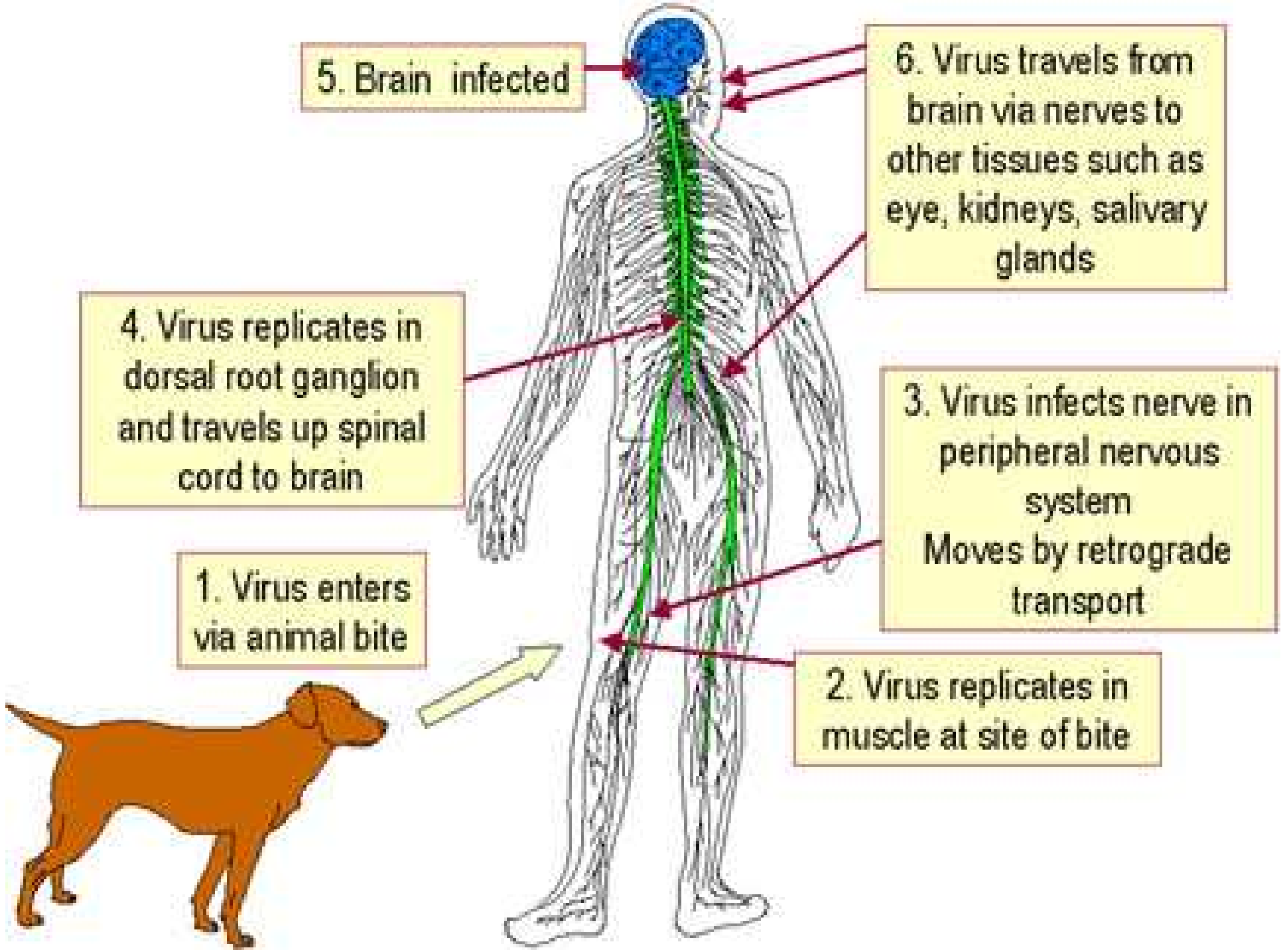
- The virus binds to nerve or muscle cells at the site of the inoculation via nicotinic acetylcholine receptors. Here the virus can remain for a prolonged period of time (up to several months).
- The virus can replicate in muscle cells at the site of the bite with no obvious symptoms. This is the incubation phase.

Pathogenesis Cont..

- The virus then moves along the nerve axons to the central nervous system using retrograde transport. The virus arrives at the dorsal root ganglia and the spinal cord. From here, spread to the brain occurs.
- A variety of cells in the brain can be infected including in the cerebellum, the Purkinje=s cells and also cells of the hippocampus and pontine nuclei. This is the prodromal phase. Infection of the brain leads to encephalitis and neural degeneration although elsewhere the virus seems to cause little in the way of a cytopathic effect.

Pathogenesis Cont..

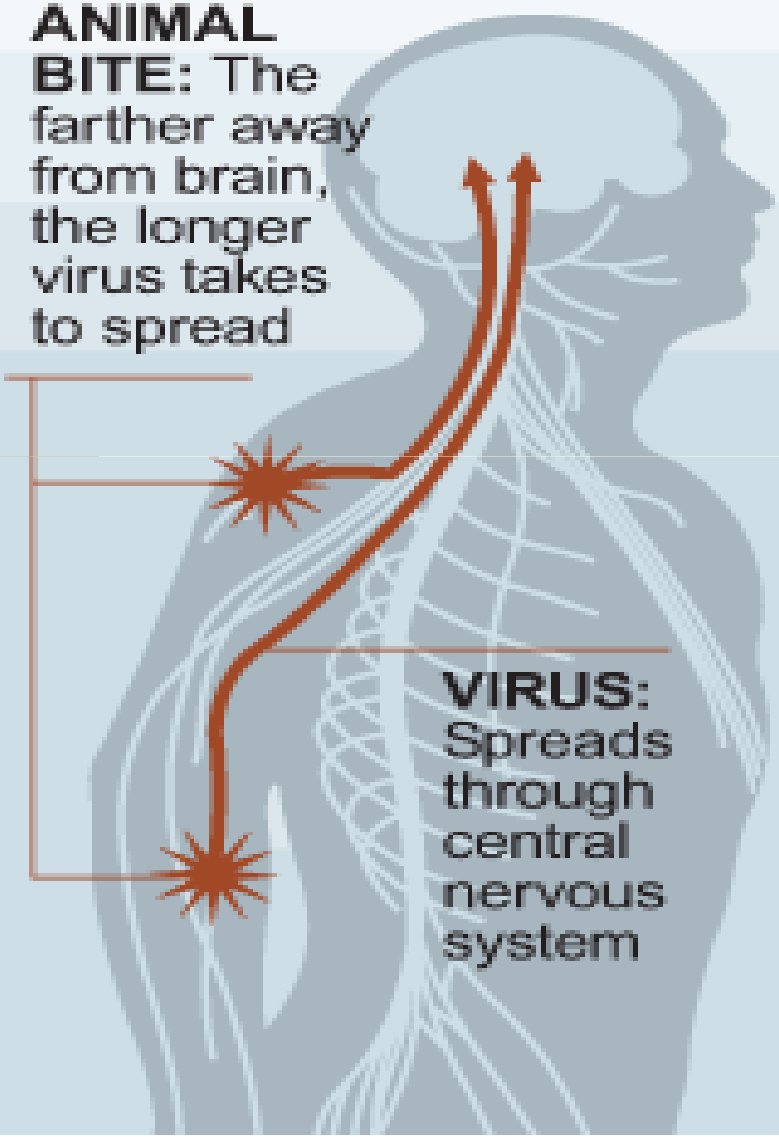
- Involvement of the brain leads to coma and death. This is the neurological phase and during this period, the virus can spread from the central nervous system, via neurons, to the skin, eye and various other sites (adrenals, kidneys, pancreatic acinar cells) and the salivary glands.
- In human Incubation period is 1 to 3 months.


5. Brain infected
6. Virus travels from brain via nerves to other tissues such as eye, kidneys, salivary glands
4. Virus replicates in dorsal root ganglion and travels up spinal cord to brain
3. Virus infects nerve in peripheral nervous system
Moves by retrograde transport
1. Virus enters via animal bite
2. Virus replicates in muscle at site of bite

Rabies

How it spreads

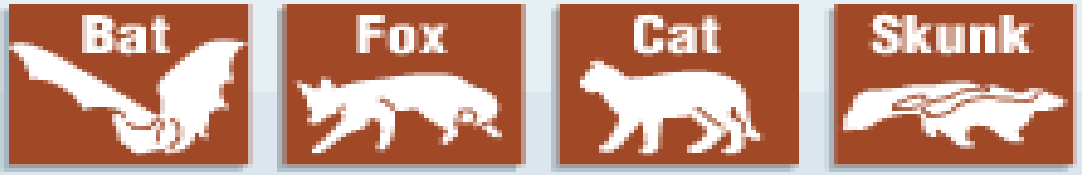
ANIMAL BITE: The farther away from brain, the longer virus takes to spread



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

SOURCE: The World Book Medical Encyclopedia

KRT

Symptoms

- ~~Vaccination, even after exposure, is extremely effective~~ at preventing disease. Without such treatment, rabies is almost invariably fatal (although, see the case report at left).
- During the incubation/prodromal period, symptoms include: pain or itching at the site of the wound, fever, headache and gastrointestinal problems.
- After this period (usually of up to two weeks), CNS infection is apparent. In up to half of patients, hydrophobia is seen. This fear of water is the result of the pain associated with drinking. There are also seizures and hallucinations. In some patients paralysis is the only symptom and this may lead to respiratory failure. Following the neurological phase, the patient becomes comatose.
- Because of the neurological problems including respiratory paralysis, death ensues.

Laboratory Diagnosis

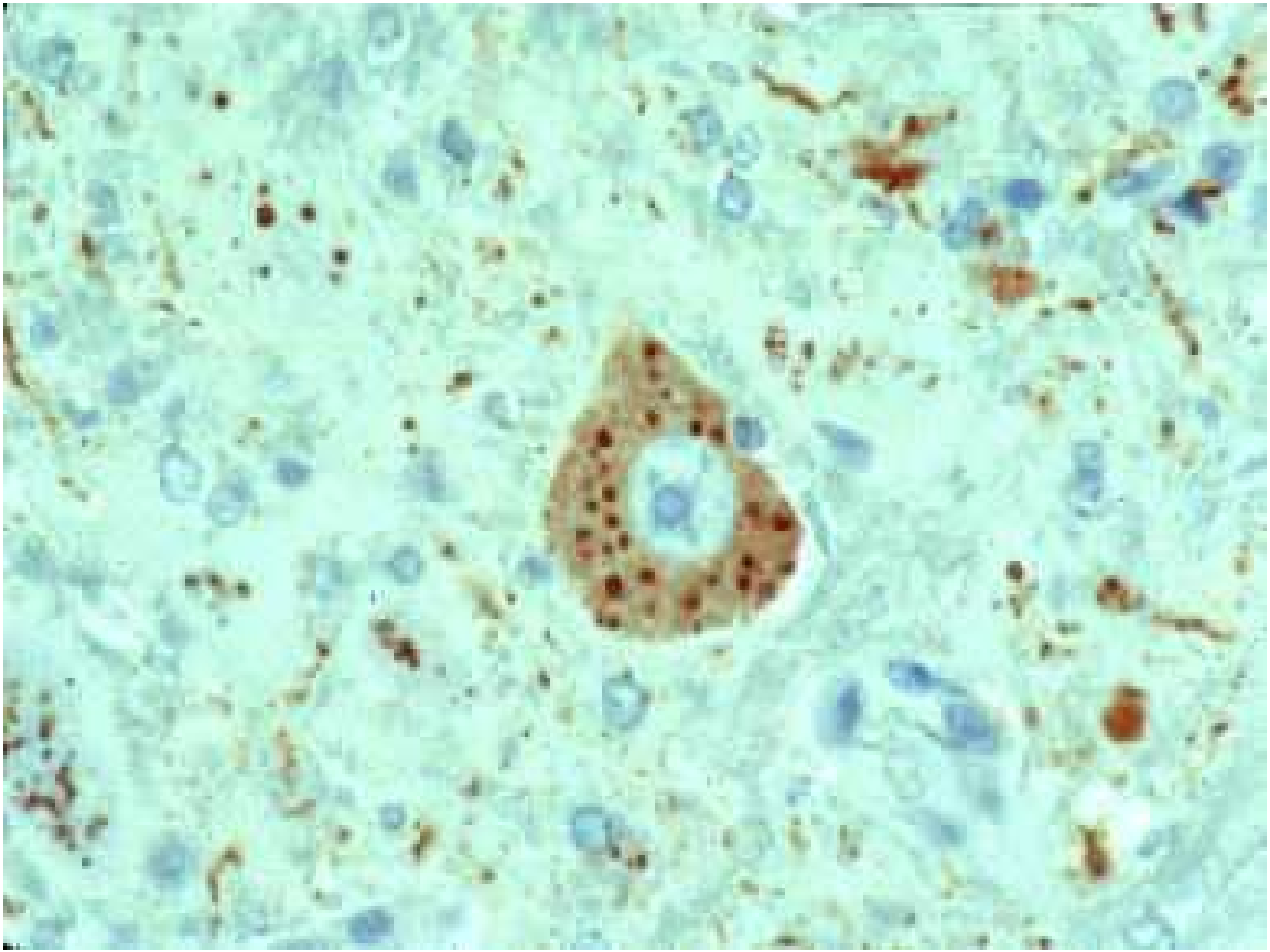
- Serology (neutralizing serum or cerebrospinal fluid antibodies in an unvaccinated person are diagnostic but usually are only detectable late in disease).

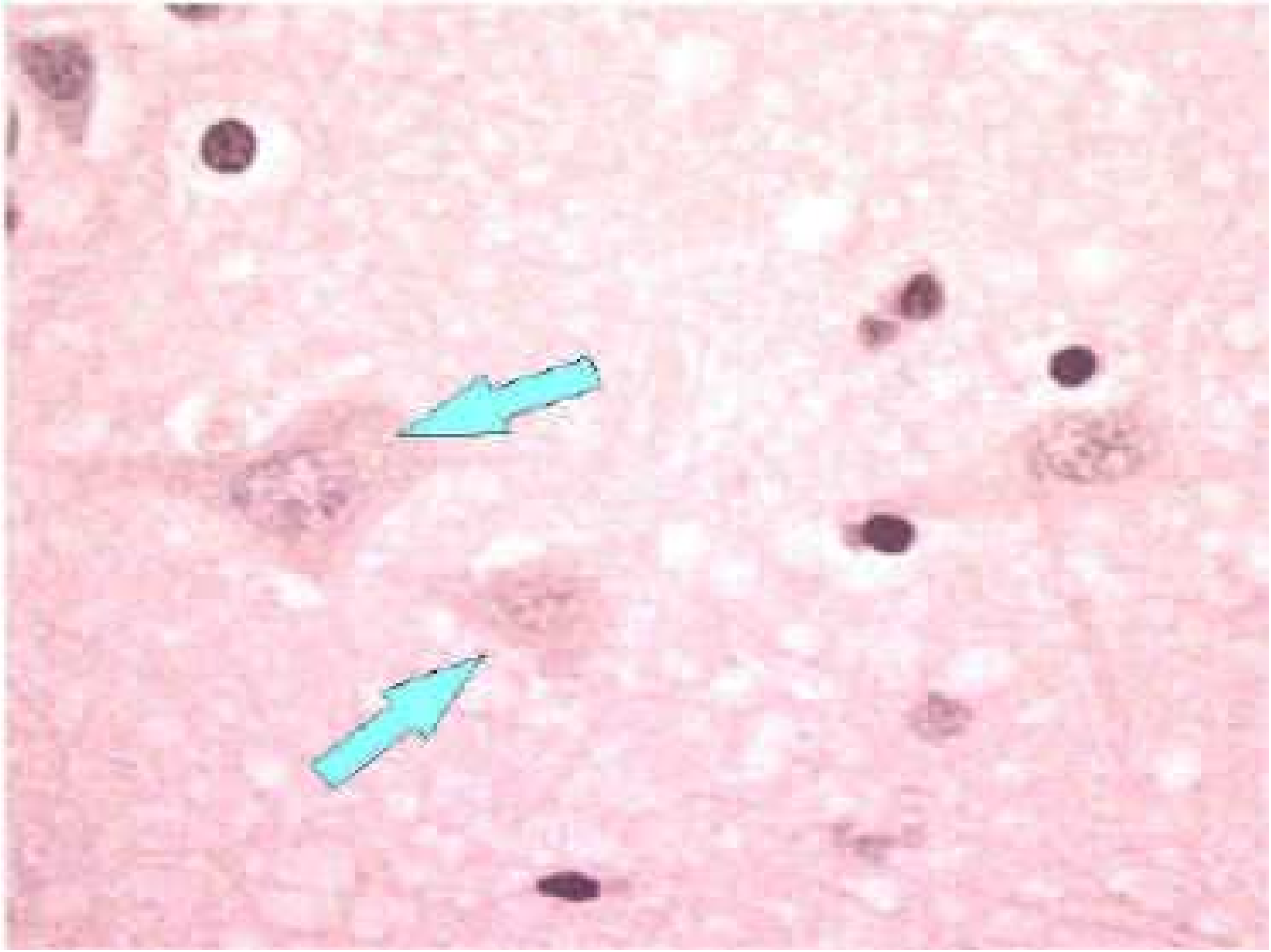
- Immunofluorescence antigen determination using biopsy skin, brain or corneal specimens.). A full thickness nuchal skin biopsy (skin biopsy from the nape of the neck in which the observer looks at the nerves at the base of the hair follicles) or brain biopsy can be examined for rabies antigen using a direct fluorescent antibody test.

Laboratory Diagnosis Cont..

- Saliva may be tested for rabies virus RNA by RT-PCR (reverse transcription-polymerase chain reaction) or by isolation of the virus.

- Histologically very characteristic is the presence of Negri bodies. These are eosinophilic intracytoplasmic inclusions formed by aggregates of nucleocapsids in neurons of about 50 to 80% of infected humans.
- Other tests include the growing of virus in the brains of mice or in culture, after which antigen tests are used to determine the presence of virus. Also anti-rabies antibodies can be detected BUT only very late in the disease. Polymerase chain reaction (PCR) can also be used to detect virus.





PREVENTION AND TREATMENT OF A PERSON WHO MAY HAVE BEEN EXPOSED

- The wound should be immediately and thoroughly washed with soap and water, then treated with 40-70% ethyl alcohol or an antiseptic such as benzyl ammonium chloride.
- If the animal is available, the brain should be examined for rabies virus antigen by fluorescent antibody. (In some cases, if the bite was from a domesticated cat or dog, the animal may be kept under close observation).

Post-exposure prophylaxis

Rabies vaccine.

- This is an inactivated vaccine and is strongly immunogenic. It is grown in human diploid cells or rhesus monkey lung cells and is more potent and has fewer side effects than the vaccine used in the early 1980's.
- A purified chick embryo cell grown vaccine is also available.

Post-exposure prophylaxis Cont..

- ***Human rabies immunoglobulin (HRIG)***. HRIG is prepared from the plasma of hyperimmune donors. Up to half of the recommended dose is infiltrated into the wound area if possible. The remainder is given as an intramuscular injection. A separate syringe and a separate site are used for the HRIG and the vaccine so that the HRIG does not neutralize the vaccine.

TREATMENT

- If symptoms are localized to the site of the bite, aggressive antiviral therapy (vaccine, HRIG, ribavirin, interferon, monoclonal antibodies, etc) may be tried. There is no specific anti-viral treatment once CNS symptoms develop. Intensive supportive care is given.
- Five of the six known survivors of rabies infection received prophylaxis prior to developing clinical symptoms. There has been one documented case of a non-vaccinated survivor of rabies.