Rabies Virus

Monday, November 3, 2025 12:39 PM

🧬 Properties

Feature	Details
Family	*Rhabdoviridae*
Genus	*Lyssavirus*
Type of Nucleic Acid	Single-stranded RNA (negative polarity)
Genome	Linear RNA associated with RNA-dependent RNA polymerase
Virion RNA Polymerase	Present
Capsid Shape	Bullet-shaped nucleocapsid
Envelope	Present (lipoprotein)
Number of Serotypes	One
Antigenicity	Determined by envelope glycoprotein spikes

💡 *Fun fact:* The bullet shape of the rabies virus is one of the most distinct morphologic features seen under an electron microscope 🔬

Disease Overview

- Disease caused: *Rabies (encephalitis)*
- Characterized by: Inflammation of the brain leading to severe neurological symptoms and, if untreated, death.
- Uniqueness: The only medically important member of the *Rhabdoviridae* family.

Summary of the Replicative Cycle

Attachment & Entry

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Virus binds to acetylcholine receptors on neuronal or muscle cell membranes.

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Penetration by endocytosis and uncoating within the cytoplasm.

Transcription:

Viral RNA-dependent RNA polymerase synthesizes five mRNAs coding for structural proteins.

Genome replication:

Virus-encoded RNA polymerase synthesizes full-length complementary RNA, which acts as a template for new negative-strand genomes.

Assembly:

New genomes associate with nucleoproteins to form nucleocapsids.

Maturation & Release:

Virus acquires its envelope by budding through the cell membrane.

Exam Tip: Remember that replication occurs entirely in the cytoplasm, and the virus carries its own RNA polymerase because of its negative-sense RNA genome.

Transmission & Epidemiology

- Mode of Transmission: Bite of a rabid animal (virus present in saliva).
- Reservoirs:
    - Developed countries: Bats, skunks, raccoons
    - Developing countries: Unimmunized dogs
- Unusual ("non-bite") transmissions:

    - Aerosol exposure to bat secretions in caves
    - Corneal transplants from undiagnosed rabies cases

- Not transmitted by: Rodents or rabbits.

Global Burden:

- <10 human cases per year in the USA (mostly imported).

- ~50,000 deaths annually worldwide, mostly in Asia and Africa.

- USA declared "canine-rabies free" in 2007 due to vaccination programs.

🧬 *Molecular Epidemiology:*

Sequencing of viral RNA helps identify the geographic origin and reservoir host of infection (useful for tracing imported cases).

⚙ Pathogenesis

Sequence of Events:

Site of bite → Local viral replication in muscle → Entry into sensory neurons

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Axonal transport toward CNS (retrograde transport)

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Replication in CNS → Encephalitis develops

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Spread via peripheral nerves to salivary glands and other organs

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Virus secreted in saliva → ready for transmission

Key Points:

- No viremic phase (virus remains within neurons).
- Virus evades immune detection during neuronal transport.
- Negri bodies: Eosinophilic intracytoplasmic inclusions in infected neurons (esp. hippocampus & cerebellum) — pathognomonic for rabies

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Immunity

- Natural infection usually fatal, so immunity post-recovery is rarely studied.
- Antibodies to the envelope glycoprotein are protective and neutralizing, forming the basis of vaccine protection.

Clinical Findings

➢ Incubation Period:

- 2–16 weeks, shorter when bite is closer to the head/neck region.

➢ Prodromal Stage (1–4 days)

- Fever, malaise, fatigue
- Paresthesias or pain at the bite site (important early clue ⚠)

➢ Neurological Phase

Two classic clinical forms:

Form	Features
1. Furious (encephalitic) – *~80% of cases*	Agitation, hyperactivity, hallucinations, seizures, hydrophobia (painful pharyngeal spasms upon attempting to swallow water) 💧
2. Dumb (paralytic)	Flaccid, ascending paralysis without hydrophobia; may resemble Guillain–Barré syndrome.

Outcome:

- Both forms almost always progress to coma and

death, though survival is possible with early intensive supportive care.

 Vaccine & Treatment

Aspect	Details
Vaccine Available	✅ Yes (inactivated human diploid cell vaccine)
Post-Exposure Prophylaxis (PEP)	Wound cleaning → Passive immunization with rabies immunoglobulin → Active immunization with vaccine
Antiviral Therapy	❌ None proven effective
Preventive Measure	Routine vaccination of domestic animals (dogs, cats)

 Summary Table

Parameter	Rabies Virus
Family	*Rhabdoviridae*
Genome	ssRNA, negative sense
Shape	Bullet-shaped

Envelope	Present
Transmission	Bite of infected animal (saliva)
Main Reservoirs	Dogs (developing countries), bats/skunks/raccoons (USA)
Pathognomonic Feature	Negri bodies
Disease Forms	Furious & Dumb
Treatment	Vaccine + Immunoglobulin; no antiviral
Vaccine Availability	Yes

 Laboratory Diagnosis

Purpose:

To confirm the presence of rabies virus in suspected human or animal cases and guide post-exposure management 🧠

1. Diagnosis in Animals

Test/Method	Specimen	Key Findings	Remarks

Fluorescent Antibody (FA) Test	Brain tissue	Bright fluorescence of infected neurons	Most rapid and reliable diagnostic method ⚡
PCR Assay	Brain tissue	Detects viral RNA	Highly sensitive and specific
Histologic Staining (Negri Bodies)	Hippocampal neurons	Eosinophilic intracytoplasmic inclusions	Pathognomonic but may be absent in some cases
Virus Isolation	Brain tissue → cell culture	Virus growth confirmed	Too slow for immediate decisions

🧩 *Exam Tip:* The FA test on brain smears is the gold standard for confirming rabies in animals before deciding on human vaccination.

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2. Diagnosis in Humans

Test/Method	Specimen	Notes
PCR Assay	Saliva, cerebrospinal fluid (CSF), or brain tissue	Rapid and sensitive
Fluorescent Antibody Staining	Skin biopsy from the neck (hairline region)	Detects viral antigen in cutaneous nerve endings
Virus Isolation	Saliva, CSF, brain tissue	Used mainly in reference

		labs
Serology (Antibody Detection)	Serum samples	Rising antibody titer = diagnostic
Negri Bodies	Corneal scrapings or autopsy brain specimens	Classic finding but not always present

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🔍 Flow of Diagnosis (Human)

Suspected exposure

Sample collection (saliva / skin / CSF / corneal scraping)

PCR or FA test for viral antigen detection

If available → Serology for antibody rise

Confirm diagnosis

Treatment

- No specific antiviral therapy is available for rabies once clinical symptoms appear ⃠

- Only supportive treatment (airway management, sedation, ventilatory support) can be given.

- Despite intensive care, prognosis remains poor once encephalitic signs develop.

⚠ *Note:* A few survivors have been reported with experimental therapies (e.g., Milwaukee protocol), but outcomes remain inconsistent.

Prevention

Prevention is the most important and effective approach

since treatment is rarely successful 💉🐾

1. Rabies Vaccine

Type	Description	Notes
Human Diploid Cell Vaccine (HDCV)	Inactivated virus grown in human diploid cells	Preferred vaccine (safe & effective) ✅
Purified Chick Embryo Cell Vaccine (PCECV)	Inactivated virus from chick embryo cells	Acceptable alternative
Duck Embryo Vaccine	Less immunogenic	Not recommended
Nerve Tissue Vaccines	Derived from animal CNS tissue	May cause allergic encephalomyelitis ❌

💡 *Key Concept:* The HDCV is the standard for both pre- and post-exposure immunization.

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2. Approaches to Human Immunization

A. Pre-Exposure Immunization

Used for high-risk individuals such as:

- Veterinarians

- Animal handlers and zookeepers
- Laboratory workers handling rabies virus
- Travelers to endemic regions 🌍

Schedule:

Day 0 → Day 7 → Day 21 or 28

Booster doses are given as needed to maintain antibody titer ≥ 1:5.

B. Post-Exposure Immunization

Given after exposure (e.g., animal bite) — this is life-saving because of the long incubation period ⏳

Steps (Passive-Active Immunization):

Wound cleaning (immediate)

Administer Rabies Immune Globulin (RIG) – provides *passive* immunity

Start Rabies Vaccine (HDCV) – induces *active* immunity

Both given at different sites (to avoid neutralization)

Monitor and observe the animal (if captured) for 10 days

Component	Description	Details
Wound Care	Wash with soap + water (15 min) + disinfectant	Reduces viral load
RIG	Passive antibodies from hyperimmunized humans	Infiltrate as much as possible into wound; remainder IM
Vaccine (HDCV)	Active immunization	5 doses on days 0, 3, 7, 14, 28
Tetanus Prophylaxis	As indicated	Add booster if wound contaminated

🧠 *Remember:*

- Give RIG only once, with the first vaccine dose.
- RIG and vaccine must be administered at different sites.

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3. Decision Factors for Post-Exposure Vaccination

Before starting treatment, assess:

1 Type of Animal: All wild animal bites → vaccinate immediately.

2 Nature of Attack: Provoked vs. unprovoked.

3 Animal's Immunization Status: Is it vaccinated and available for observation?

4 Rabies Prevalence: Is rabies endemic in the area?

5 Public Health Advice: Always consult local authorities.
Hospital Staff Exposure:

Immunization only if significant exposure occurred (e.g., wound with patient's saliva).

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4. Animal Immunization

Animal	Vaccine Used	Schedule
Dogs & Cats	Inactivated rabies vaccine	First dose at 3 months → Booster yearly or every 3 years
Alternative (USA)	Recombinant *canarypox* virus expressing rabies envelope gene	Safe and effective

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Quick Summary

Aspect	Key Point
Gold Standard Diagnosis	Fluorescent antibody test on brain tissue
Pathognomonic Feature	Negri bodies
Treatment	Supportive only
Prevention	HDCV + RIG post-exposure
Pre-Exposure	3 doses (0, 7, 21/28 days)
Post-Exposure	5 doses (0, 3, 7, 14, 28 days) + RIG
Best Animal Control Strategy	Vaccination of domestic animals

Final Takeaway:

Rabies remains one of the most fatal viral infections, yet also one of the most preventable — thanks to effective vaccination and timely post-exposure management