Rabies

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Rabies is a viral encephalitis transmitted by the saliva of infected bats and certain other infected mammals. Symptoms include depression and fever, followed by agitation, excessive salivation, and hydrophobia. Diagnosis is by serologic tests or biopsy. Vaccination is indicated for people at high risk of exposure. Postexposure prophylaxis involves wound care and passive and active immunoprophylaxis and, if promptly and meticulously executed, almost always prevents human rabies. Otherwise, the disorder is almost universally fatal. Treatment is supportive.

Rabies causes > 55,000 human deaths worldwide annually, mostly in Latin America, Africa, and Asia, where canine rabies is endemic. In the US, vaccination of domestic animals has reduced rabies cases in people to < 3/yr, mostly transmitted by infected bats. Infected raccoons, skunks, and foxes can also transmit rabies.

Rabid animals transmit the infection through their saliva, usually by biting. Rarely, the virus can enter through a skin abrasion or across mucous membranes of the eyes, nose, or mouth. The virus travels from the site of entry via peripheral nerves to the spinal cord (or to the brain stem when the face is bitten), then to the brain. It then spreads from the CNS via peripheral nerves to other parts of the body. Involvement of the salivary glands and oral mucosa is responsible for transmissibility.

Symptoms and Signs

Pain or paresthesias may develop at the site of the bite. Rapidity of progression depends on the viral inoculum and proximity of the wound to the brain. The incubation period averages 1 to 2 mo but may be > 1 yr.

Initial symptoms are nonspecific: fever, headache, and malaise. Within days, encephalitis (furious rabies; in 80%) or paralysis (dumb rabies; in 20%) develops. Encephalitis causes restlessness, confusion, agitation, bizarre behavior, hallucinations, and insomnia. Salivation is excessive, and attempts to drink cause painful spasms of the laryngeal and pharyngeal muscles (hydrophobia). In the paralytic form, ascending paralysis and quadriplegia develop without delirium and hydrophobia.

Diagnosis
• Skin biopsy
• Sometimes PCR testing of fluid or tissue samples

Rabies is suspected in patients with encephalitis or ascending paralysis and a history of an animal bite or exposure to bats; bat bites may be superficial and overlooked.

Direct fluorescence antibody testing of a biopsy specimen of skin from the nape of the neck is the diagnostic test of choice. Diagnosis can also be made by PCR of CSF, saliva, or tissue. Specimens tested for rabies antibodies include serum and CSF. CT, MRI, and EEG are normal or show nonspecific changes.

**Treatment**

• Supportive care

Treatment is only supportive and includes heavy sedation (eg, with ketamine and midazolam) and comfort measures. Death usually occurs 3 to 10 days after symptoms begin. Few patients have survived; many received immunoprophylaxis before onset of symptoms. There is evidence that giving rabies vaccine and immune globulin after clinical rabies develops may cause more rapid deterioration.

Experimental therapies with ribavirin, amantadine, interferon-alfa, and other drugs are sometimes tried in desperation (see Care of Rabies protocol).

**Prevention**

Rabid animals can often be recognized by their strange behavior; they may be agitated and vicious, weak, or paralyzed and may show no fear of people. Nocturnal animals (eg, bats, skunks, raccoons) may be out during the day. Bats may make unusual noises and have difficulty flying. An animal suspected of having rabies should not be approached. Local health authorities should be contacted to remove the animal.

**Preexposure**

Human diploid cell rabies vaccine (HDCV) is safe and recommended for preexposure prophylaxis for people at risk, including veterinarians, animal handlers, spelunkers, workers who handle the virus, and travelers to endemic areas. A total of three 1-mL doses are given IM, one each on days 0, 7, and between day 21 and 28.

**Postexposure**

Exposure is considered to be a bite that breaks the skin or any contact between mucous membrane or broken skin and animal saliva. If exposure occurs, prompt, meticulously executed prophylaxis almost always prevents human rabies. The wound is cleansed immediately and thoroughly with soap and water or benzalkonium chloride. Deep puncture wounds are flushed with soapy water using moderate pressure. Wounds are usually left open.
Postexposure prophylaxis (PEP) with rabies vaccine and rabies immune globulin (RIG) is given depending on the biting animal and circumstances (see Table: Rabies Postexposure Prophylaxis). PEP is begun, and the animal's brain is tested for virus. Local or state health departments or the Centers for Disease Control and Prevention usually conduct testing and can advise on other treatment issues.
<table>
<thead>
<tr>
<th>Animal Type</th>
<th>Evaluation and Disposition of Animal</th>
<th>Postexposure Prophylaxis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skunks, raccoons, bats,† foxes, and most other carnivores</td>
<td>Regarded as rabid unless proved negative by laboratory tests‡</td>
<td>Consider immediate vaccination and rabies immune globulin.</td>
</tr>
<tr>
<td>Dogs, cats, and ferrets</td>
<td>Healthy and available for 10 days of observation</td>
<td>Do not begin immunoprophylaxis unless animal develops symptoms of rabies.§</td>
</tr>
<tr>
<td>Unknown (escaped)</td>
<td></td>
<td>Consult public health officials.¶</td>
</tr>
<tr>
<td>Rabid or suspected rabid</td>
<td></td>
<td>Vaccinate immediately.</td>
</tr>
<tr>
<td>Livestock, small rodents (eg, squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice), lagomorphs (rabbits, hares), large rodents (eg, woodchucks, beavers), and other mammals</td>
<td>Considered individually</td>
<td>Consult public health officials.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Immunoprophylaxis is almost never required for bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, or lagomorphs.</td>
</tr>
</tbody>
</table>

*Clean all bites immediately with soap and water.

†Because detecting bat bites is difficult, vaccination is indicated if a bite is reasonably likely, as when a person awakens with a bat in the room or a young child is found with a bat.

‡The animal should be euthanized and tested as soon as possible. Holding for observation is not recommended. Vaccine is stopped if rabies immunofluorescence tests of the animal are negative.

§If the animal remains healthy during the 10-day observation period, it was not infective at the time of the bite. However, treatment with rabies immune globulin (RIG) and human diploid cell rabies vaccine (HDCV) is begun at the first sign of rabies in a dog, cat, or ferret that has bitten someone. A symptomatic animal should be immediately euthanized and tested.

¶If expert consultation is not available locally and rabies is possible, immediate vaccination should be considered.

For PEP, RIG 20 IU/kg is infiltrated around the wound for passive immunization; if injection volume is too much for distal areas (eg, fingers, nose), some RIG may be given IM. This treatment is accompanied by HDCV for active immunization. HDCV is given in a series of four 1-mL IM injections (deltoid area is preferred), beginning on the day of exposure (day 0), in a limb other than the one used for RIG. Subsequent injections occur on days 3, 7, and 14; immunosuppressed patients receive a 5th dose on day 28. Rarely, a serious systemic or neuroparalytic reaction occurs; then, completion of vaccination is weighed against the patient’s risk of developing rabies. Rabies antibody titer is measured to help assess risk of stopping vaccination.

PEP for a person previously vaccinated against rabies includes 1-mL IM injections of HDCV on days 0 and 3 but no RIG.

**Key Points**

- Worldwide, rabies still causes tens of thousands of deaths yearly, mostly in Latin America, Africa, and Asia, where canine rabies is endemic.

- In the US, rabies kills only a few people yearly; it is usually transmitted by bats, but possibly by racoons, skunks, or foxes.

- Pain and/or paresthesias at the bite site are followed by encephalitis (causing restlessness and agitation) or by ascending paralysis.

- Biopsy neck skin or do PCR of saliva, CSF, or tissue if patients have unexplained encephalitis or ascending paralysis.

- Treat patients supportively.

- Before exposure, give the rabies vaccine to people at risk (eg, veterinarians, animal handlers, spelunkers, workers who handle the virus, travelers to endemic areas).

- After exposure, thoroughly clean and debride wounds, then give the rabies vaccine and rabies immune globulin.

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- Brain Abscess
- Encephalitis
- Rabies
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- Progressive Multifocal Leukoencephalopathy (PML)
- Intracranial Epidural Abscess and Subdural Empyema