Rabies

Introduction

Rabies is a preventable viral disease of mammals most often transmitted through the bite of a rabid animal. The vast majority of rabies cases reported to the Centers for Disease Control and Prevention (CDC) each year occur in wild animals like raccoons, skunks, bats, and foxes. Domestic animals account for less than 10 percent of the reported rabies cases, with cats, cattle, and dogs most often reported rabid.

Rabies virus infects the central nervous system, causing encephalopathy and ultimately death. Early symptoms of rabies in humans are nonspecific, consisting of fever, headache, and general malaise. As the disease progresses, neurological symptoms appear and may include insomnia, anxiety, confusion, slight or partial paralysis, excitation, hallucinations, agitation, hypersalivation, difficulty swallowing, and hydrophobia (fear of water). Death usually occurs within days of the onset of symptoms.

Public health importance of rabies

Over the last 100 years, rabies in the United States has changed dramatically. More than 90 percent of all animal cases reported annually to CDC now occur in wildlife; before 1960 the majority were in domestic animals. The principal rabies hosts today are wild carnivores and bats. The number of rabies-related human deaths in the United States has declined from more than 100 annually at the turn of the century to one or two per year in the1990s. Modern day prophylaxis has proven nearly 100 percent successful. In the United States, human fatalities associated with rabies occur in people who fail to seek medical assistance, usually because they were unaware of their exposure.

The Virus

Natural History

Rabies virus causes an acute encephalitis in all warm-blooded hosts, including humans, and the outcome is almost always fatal. Although all species of mammals are susceptible to rabies virus infection, only a few species are important for as reservoirs for ng the disease in nature. In the United States, several distinct rabies virus variants have been identified in terrestrial mammals, including major terrestrial reservoirs in raccoons, skunks, foxes, and coyotes. In addition to the terrestrial reservoirs for rabies, several species of insectivorous bats also serve as reservoirs for the disease.

Transmission

Transmission of rabies virus usually begins when the infected saliva of a host is passed to an uninfected animal. Various routes of transmission have been documented and include contamination of mucous membranes (i.e., eyes, nose, mouth), aerosol transmission, and corneal transplantations. The most common mode of rabies viral transmission is through the bite and virus-containing saliva of an infected host.

1. Raccoon is bitten by a rabid animal
2. Rabies virus enters the raccoon through infected saliva
3. Rabies virus spreads through the nerves to the spinal cord and brain
4. The virus incubates in raccoon's body for approximately 3-12 weeks. The raccoon has no signs of illness during this time.
5. When it reaches the brain, the virus multiplies rapidly, passes to the salivary glands, and the raccoon begins to show signs of disease.
6. The infected animal usually dies within 7 days of becoming sick.

Following primary infection, the virus undergoes an eclipse phase in which it cannot be easily detected within the host. This phase may last for several days or months. Investigations have shown evidence for direct entry of virus into peripheral nerves at the site of infection, as well as evidence for indirect entry after viral replication in nonnervous tissue (i.e., muscle cells). It is during this time that host immune defenses may play a role in the outcome of viral infection because rabies viral antigens are good simulators of cell-mediated immunity. The uptake of virus into peripheral nerves is important for a progressive infection to occur.

Following uptake into peripheral nerves, rabies virus is transported to the central nervous system (CNS) via retrograde axoplasmic flow. Typically this occurs via sensory and motor nerves involved at the initial site of infection. The incubation period is the time of exposure to onset of clinical signs of disease. The incubation period may vary from a few days to several years, but typically lasts one to three months. Dissemination of virus within the CNS is rapid, with early involvement of limbic system neurons. Active cerebral infection is followed by the passive centrifugal spread of virus to peripheral nerves. The amplification of infection within the CNS occurs through cycles of viral replication and cell-to-cell transfer of progeny virion. Centrifugal spread of virus may lead to the invasion of highly innervated nerve sites of various tissues, including the salivary glands. It is during this period of cerebral infection that classic behavioral changes develop.

Signs and symptoms

The first symptoms of rabies in people may be nonspecific flu-like signs - malaise, fever, or headache, which may last for days. There may be discomfort or paresthesia at the site of exposure (bite), progressing within days to symptoms of cerebral dysfunction, anxiety, confusion, agitation, progressing to delirium, abnormal behavior, hallucinations, and insomnia. The acute period of disease typically ends after two to 10 days (6). Once clinical signs of rabies appear, the disease is nearly always fatal, and treatment is typically supportive. Disease prevention is entirely prophylactic and includes passive

antibody (immune globulin) and vaccine. Non-lethal exceptions are extremely rare, with only six documented cases of human survival from clinical rabies, but each included a history of either pre- or postexposure prophylaxis.

Rabies diagnosis in animals

The direct fluorescent antibody test (dFA) is most frequently used to diagnose rabies. This test can be performed on brain tissue of animals suspected of being rabid.

Rabies diagnosis in humans

Several tests are necessary to confirm or ruleout rabies in a human intra-vitam (while living). No single test can be used to ruleout rabies in humans with certainty. Tests are performed on samples of serum, spinal fluid, skin biopsies from the nape of the neck, and saliva. Routinely, serum and spinal fluid are tested for antibodies to rabies virus. The skin biopsy specimen is examined by dFA for the presence of rabies antigen in cutaneous nerves at the base of hair follicles. Saliva maybe tested by virus isolation or nested reverse transcription polymerase chain reaction (RT-PCR) methods.

Rabies vaccine and immune globulin

There is no treatment for rabies after symptoms of the disease appear. However, two decades ago scientists developed an extremely effective new rabies vaccine regimen that provides immunity to rabies when administered after an exposure (postexposure prophylaxis) or for protection before an exposure occurs (preexposure prophylaxis). Although rabies among humans is rare in the United States, every year an estimated 18,000 people receive rabies preexposure prophylaxis and an additional 40,000 receive postexposure prophylaxis.

Preexposure prophylaxis

Preexposure vaccination is recommended for persons in high-risk groups, such as veterinarians, animal handlers, and certain laboratory workers. Other persons whose activities bring them into frequent contact with rabies virus or potentially rabid bats, raccoons, skunks, cats, dogs, or other species at risk of having rabies should also be considered for preexposure prophylaxis. In addition, international travelers likely to come in contact with animals in areas of enzootic dog rabies which lack immediate access to appropriate medical care, including biologics, should be considered for preexposure prophylaxis. (For more information about preexposure prophylaxis, see Human Rabies Prevention - United States, 1999 Recommendations of the Immunization Practices Advisory Committee (ACIP).)

People who work with live rabies virus in research laboratories or vaccine production facilities are at the highest risk of inapparent exposures. Such persons should have a serum (blood) sample tested for antibody every 6 months and receive booster vaccine, when necessary. Routine preexposure prophylaxis for other situations may generally not be indicated.

Administration of rabies PEP is a medical urgency, not a medical emergency. Physicians should evaluate each possible exposure to rabies and as necessary consult with local or state public health officials regarding the need for rabies prophylaxis.

What to do after a possible exposure

If you are exposed to a potentially rabid animal, wash the wound thoroughly with soap and water, and seek medical attention immediately. A health care provider will care for the wound and will assess the risk for rabies exposure. The following information will help your health care provider assess your risk:

- the geographic location of the incident
- the type of animal that was involved
- how the exposure occurred (provoked or unprovoked)
- the vaccination status of animal
- whether the animal can be safely captured and tested for rabies

Steps taken by the health care practitioner will depend on the circumstances of the bite. Your health care practitioner should consult state or local health departments, veterinarians, or animal control officers to make an informed assessment of the incident and to request assistance. The important factor is that you seek care promptly after you are bitten by any animal.