

Rabies Post-Exposure Prophylaxis

Introduction

(To be read on a dark and stormy night) Transylvania, 1734: Sleeping peacefully in his bed a man awakens and notices a soreness in his left neck. In the mirror he sees two small puncture wounds just below his mandible, a probable bat bite. Over the next several weeks he begins to thirst for blood and saliva drips from his now fang-like teeth. The light is painful to him so he creeps at night and seeks the soft supple necks of women to feed his sanguinous craving. After biting his victims he morphs back into a bat and flies to his lair where he sleeps in a coffin as one of the living dead. He no longer looks in a mirror as his reflection is not there. The next night he again will resurface and find a new victim that does not protect his or her home with the pungent odor of hanging garlic.

The vampire legend dates back to 13th century or earlier in Europe but the premise that we understand and fear in horror movies likely originated from rabies victims^{1,2}. Fortunately, today rabies is a rare disease but it is still nearly uniformly fatal in humans. Because of this danger between 16,000- 39,000 persons receive post-exposure prophylaxis (PEP) annually in the United States³. Development of symptoms in a patient is the harbinger of an inevitable death making clinical recognition of the disease trivial for the infected individual. Understanding exposure is the most important means of control and treatment to minimize the number of rabies associated human fatalities.

Exposure

Rabies is a viral infection transmitted in the saliva of infected animals. Viral loads are found in saliva and the CSF but not in other body fluids. While wild animal bites are the major transmitter of rabies to humans, domestic animal cases have decreased drastically with vaccine programs. Canine cases have decreased from 4979 cases in 1950 to <250 cases in 1997 but are still high in developing nations. Since 1976 wildlife has accounted for > 85% of animal rabies. From 1980 to 1997, 21 (58% of total) cases of human rabies in the U.S. were attributed to bat variants while a third of cases were acquired outside of the United States³.

The epidemiology of rabies describes two forms: urban rabies, transmitted by domestic animals and sylvatic rabies, transmitted by wild animals (skunks, foxes, raccoons, mongooses, wolves, bats). While over the past two decades the incidence of human rabies in the United States has averaged between 2 and 3 per year, worldwide there are over 30,000 cases annually⁴. The last Minnesotan death from rabies was in Becker County in October of 2000 when a 47 year old man died after a bat bite exposure. This was the first Minnesota case since 1975⁵.

The following 4 factors are essential in deciding whether or not one should be vaccinated.

Type of exposure:

The virus is transmitted only when introduced percutaneously through bite wounds, open cuts on skin, or onto mucous membranes. Therefore only significant bite or non-bite exposure should receive PEP. Bites are any penetration of skin by teeth. Bat bites may be so minor that they go undetected. Non-

bite transmissions are extremely rare but have occurred apparently from aerosolized rabies. Two cases of aerosolized rabies transmission in a laboratory and two cases of aerosolized exposure in caves of free-tailed bats (*Tadarida brasiliensis*) have been reported. The only human-human transmission have been via corneal transplants⁶⁻⁸. Non-laboratory confirmed human-human transmission include a bite and kiss as modes of transmission in Ethiopia. Contamination of open wounds, scratches, abrasions or mucous membranes by saliva or neural tissue from a potentially rabid animal is an exposure. Contact with other body fluids including blood, urine, or feces (e.g. bat guano) is not an exposure. The rabies virus is inactivated by desiccation and UV radiation, thus dry material from a rabid animal can be considered non-infectious³.

Animal rabies epidemiology :

Bats: PEP is appropriate for any bite, scratch or mucous membrane exposure to a bat unless the bat is available for testing and is found to be negative for evidence of rabies. Because bites may be so insignificant, PEP may be appropriate through simple or possible contact. In the 21 bat-associated rabies cases since 1980 only 2 report a definite bite. In other cases either contact occurred but no bite was detected or a bite exposure was suspected as the most likely cause though it was not reported nor detected. For this reason other uncertain contacts such as, a sleeping person awakening with a bat in the room, a bat in the room of a previously unattended child, a mentally disabled person or an intoxicated person, also warrant PEP if the bat is not available for testing. Any bat should be collected with extreme care (see prevention). People should use great caution in picking up a bat which they think they have killed as this often results in bites from a wounded animal, ideally any contact with the bat should be handled by the animal control or other appropriate authorities³.
Wild terrestrial carnivores: Raccoons, skunks, foxes, and coyotes should all be considered potentially infectious and their bites as possible rabies exposures. In Minnesota the overwhelming number of rabies cases in animals are seen among skunks. This number has decreased to under 100 cases annually in the 1990's⁹. With wild animals it is difficult to assess the presence of rabid symptoms clinically. Any animal in this situation should be euthanized immediately and the head submitted for immunofluorescence testing. If none is detected the saliva is presumed clear of virus and the bite victim does not need PEP³.

Other wild animals:

Small rodents and lagomorphs (e.g. rabbits) have never been known to transmit rabies. For this reason PEP is typically not warranted for bite exposure from these animals. Woodchucks have been found to harbor rabies and thus any person bitten by a small rodent or lagomorph should have the local health department consulted before a decision to give PEP is initiated. Any crossbreed of a wild animal with domestic animals should also be considered wild and should be euthanized and examined for rabies in cases of bites³.

Domestic dogs, cats, ferrets: Prevalence of rabies in these animals varies by geographic region and thus recommendations may differ accordingly. Most cases of dog rabies have been along the U.S.-Mexican border while higher rates of rabies among cats was seen in the Eastern U.S. during the epizootic of rabies among raccoons. After any bites these animals should be observed for 10 days. If the animal does not develop illness during that time then it was not infectious during the bite. Any illness should be evaluated by a veterinarian and reported to the local health department, if signs suggestive of rabies are present the animal should be euthanized and its head refrigerated and shipped to a qualified research lab³.

Circumstances of biting incident and vaccination status of exposing animal:

An unprovoked attack by an animal is more likely than a provoked attack to indicate rabies in an animal. A bite during attempted feeding or handling of a healthy animal should be regarded as provoked³.

Geographic area (see “Domestic dogs, cats, ferrets” above):

Prevalence of rabies differs for all species across the United States. Many factors are responsible for these differences. In 1977 the first rabies cases of raccoons were seen in Virginia. There is speculation that the Carter administration, with strong Georgia roots, wanted to continue “coon hunting” while living in Washington. Raccoons were actually transported to forests in Virginia for this purpose and within 2 years of his inaugural address the first case was reported. The epizootic was contained by the Appalachian mountains but now it appears that raccoon rabies has crossed this natural barrier and is spreading westward, currently present in eastern Ohio¹⁰. This epizootic is likely to be responsible for rabies in woodchucks³. In Minnesota skunk cases seem to lie in the counties outside the metro area whereas rabies cases associated with bats seem to center more around the Twin Cities metro area⁹.

Clinical Course

The onset of clinical effects of one infected by rabies is a fatal prognostic sign. The median period of survival after symptom onset is four days with a maximum survival of 20 days. The virus migrates upward from the bite site to attack the CNS of the host causing a fatal encephalomyelitis. Incubation periods vary widely based on a number of factors including brain-bite distance (the virus tracks cephalad through peripheral neurons at a rate of about 3 mm/hr) and range from 7 days to > one year (mean 1-2 months). Rates of infection and mortality are higher with increasing proximity of bite location to the head and face⁴.

Prodromal symptoms occurring in the first 1-4 days include fatigue, fever, headache, and muscle pain. A characteristic symptom suggestive of rabies is tingling or muscle twitching/fasciculations near the site of the bite as the virus multiplies in the sensory nerves from that area within the spinal cord. After the prodromal phase the encephalitic phase begins where many symptoms relate to the legend of the vampire. Confusion, combativeness, hallucinations, and muscle spasms are seen. Excessive sensitivity to light, noise, touch, gentle breeze (aerophobia), and smell (including garlic) with reaction to these stimuli with facial spasm showing bared teeth may occur. The patient will develop hydrophobia, painful, forceful involuntary contractions of upper gastrointestinal, respiratory and diaphragmatic muscles on initiation of swallowing liquids, leading to salivation and the classic “foaming at the mouth”. Autonomic dysfunction may also lead to priapism and ejaculation – contributing to the hypersexuality of the myth. Recoveries from this illness are extremely rare^{1,4}.

Treatment

Every year between 16,000 – 39,000 persons receive PEP. The PEP treatment after a potential rabies exposure constitutes three processes: Wound cleaning, administration of rabies immune globulin, and administration of rabies vaccine. The initiation of immunoglobulin and vaccination against rabies constitute a medical urgency, not emergency. In cases of suspected rabies exposures PEP should begin immediately. With reports of lengthy incubation periods PEP is always indicated no matter how long after a significant exposure provided symptoms of rabies have not developed³.

Treatment of wounds: Immediate and thorough washing with soap and water and a virucidal agent (e.g. povidone-iodine solution) of all bite wounds should be done immediately. Irrigation of the wound with these solutions should be done as thoroughly as possible prior to seeking further medical care. Tetanus prophylaxis and bacterial control measures should be administered as indicated at a health care facility³.

Immunglobulin: Rabies immune globulin (RIG) provides a rapid passive immunity with a half-life of 21 days. It is a solution with antibodies which are meant to bind any rabies virus present. As much of the RIG should be injected around or near the exposure site as anatomically possible. Any remainder RIG should be injected either in the gluteal region or the deltoid opposite the side used for the rabies vaccine. The two RIG products, BayRabTM and Imogam Rabies-HT are an antirabies immunoglobulin (IgG) preparation concentrated from plasma of hyperimmunized human donors. RIG is standardized at a concentration of 150 IU per mL and the recommended dose is 20 IU/kg body weight³.

Patients having received pre-exposure prophylaxis within two years or with known adequate antibody titers should not receive RIG as part of the PEP therapy³.

Vaccine: Rabies vaccine activates an immune response producing antibodies against the virus. This response occurs in 7-10 days and should persist for > 2 years. The rabies vaccine comes in three approved forms in the United States: Human Diploid Cell Vaccine (HDCV), Rabies Vaccine Adsorbed (RVA), and Purified Chick Embryo Cell Vaccine (PCEC). These are typically administered as 1 cc IM injections into the deltoid and are preparations of inactivated virus. The vaccine should not be administered on the same extremity as any RIG as it would then be bound by the immunglobulin and not elicit an immune response. The vaccine is given as a series of five injections on days 0, 3, 7, 14, and 28. The first dose should be given as soon as possible on the same day as the RIG is administered³.

Patients who have received a pre-exposure prophylaxis will only require two doses of PEP vaccine on days 0 and 3.

Systemic prophylactic treatments often cause local discomfort or redness but serious adverse effects including Guillan-Barre syndrome are extremely rare. Symptoms such as headache, nausea, abdominal pain, muscle aches, and dizziness have been infrequently reported. Local pain and low-grade fever may follow injection of rabies immune globulin⁴.

Prevention

Pre exposure vaccine should be offered to people in high risk occupations including veterinarians, animal handlers, and certain laboratory workers. People traveling to certain areas outside the United States may also consider the vaccine along with others who may come into contact with potentially rabid animals (e.g. cavers). Advantages of pre-exposure prophylaxis are that the RIG step is eliminated. It allows for a shorter vaccine treatment in the post-exposure scenario and may allow for delayed treatment if it is not readily available (e.g. in some foreign countries). The vaccine is given in 3 IM or ID doses on days 0, 7 and 21 or 28. Antimalarials appear to interfere with the HDCV vaccine and for this reason pre-exposure prophylaxis should be given at least one month before any antimalarial therapy is started. Antibody titers generally do not require checking unless the individual is immunosuppressed³.

All domestic animals should be vaccinated and protected from wild animals. Stray animals should be reported and domestic animals should be spayed or neutered to control the pet population.

Wild animals should be enjoyed from afar. If a bat is found flying inside a home all people should be removed from the room where the bat is and any windows to the outside should be opened while any doors or windows leading to other areas of the house should be closed. The bat should fly out on its own. If it does not, a bat may be removed safely, however, if there is any question of exposure, leave the bat alone and call animal control or a wildlife conservation agency for assistance. If professional assistance is unavailable, use precautions to capture the bat safely. You will need leather work gloves (put them on), a small box or coffee can, a piece of cardboard, and tape. When the bat lands, approach it slowly and place a box or coffee can over it. Slide the cardboard under the container to trap the bat inside. Tape the cardboard to the container securely. Contact your health department or animal control authority to make arrangements for rabies testing¹¹. Contact your health provider immediately if you think there was any chance you may have been bitten during the removal attempt.

Conclusion

Though still a rare disease, rabies, the inspiration of vampire legends, has a nearly 100% mortality rate. The virus is transmitted through saliva and neural tissue. The most important guide to treatment is knowing the details of the exposure including the type of exposure, type of animal, circumstances surrounding the exposure, and geographic area. All bat exposures involving the possibility of a bite and bites from larger mammals such as raccoons and wolves are significant and require PEP. When PEP is necessary it includes washing the wound and injections with RIG and rabies vaccine separated anatomically. Pre-exposure prophylaxis may be indicated for some professions or people traveling abroad. These therapies have been 100% effective in the United States in the past 20 years when given before any initiation of symptoms.

Questions regarding any possible rabies exposures should be directed to the following:
Acute Disease Epidemiology Section
Telephone (612) 676-5414

-- Michael Connelly, MD, MPH

References

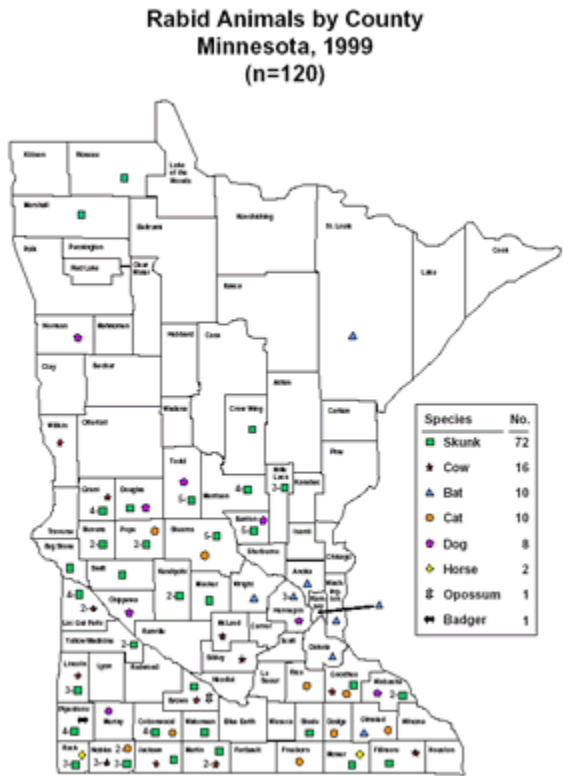
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Minnesota Poison Control System, Hennepin County Medical Center