The Epidemiology of Rabies Post-exposure Prophylaxis in Humans, Virginia, 2002-2003

Introduction

Infection with the rabies virus causes disease of the central nervous system (encephalomyelitis) in mammals. Transmission most commonly occurs when saliva containing the virus is passed from an infected animal to an uninfected animal or human through a bite wound.\(^1\) However, various other (rare) routes of transmission have been documented, including contamination of mucous membranes (e.g., eyes, nose, mouth), aerosol transmission, and tissue transplantation.\(^1,2\)

Initial symptoms of rabies in humans are usually nonspecific, consisting of fever, headache, and general malaise. As the disease progresses, neurological symptoms appear and may include insomnia, anxiety, confusion, paralysis, hallucinations, agitation, hypersalivation, difficulty swallowing, and hydrophobia.\(^1\)

Once clinical signs of rabies appear, the disease is nearly always fatal within 2 to 10 days. To date only six documented cases of human survival from clinical rabies have been reported.\(^2\) Fortunately, the disease may be prevented with the timely administration of appropriate biologics following an exposure to a rabid animal.\(^3\)

U.S. Rabies Epidemiology

In 2004, 49 states, the District of Columbia, and Puerto Rico reported 6,844 laboratory-confirmed cases of rabies in animals and eight cases of rabies in humans to the Centers for Disease Control and Prevention (CDC).\(^2\) The overall occurrence of domestic animal and human rabies in the United States...
Virginia Rabies Epidemiology

Rabies is endemic in certain Virginia wildlife and affects domestic animals and, rarely, humans. In Virginia, animals at high risk for acquiring and transmitting rabies include foxes, skunks, raccoons, groundhogs (woodchucks), bats, and bobcats. In potential rabies exposure situations these high risk species are considered rabid unless proven negative by laboratory testing. Animals at low risk for acquiring and transmitting rabies in Virginia include small rodents (e.g., rats, mice, squirrels) and rabbits. These species are not considered a risk for rabies transmission unless their behavior is abnormal or aggressive.5

In 2004, 474 cases of animal rabies were detected in Virginia. Over ninety percent of cases (436 of 474) occurred in wild species (mostly raccoons, skunks, bats, and foxes), while 8% of animal cases occurred in domestic species (cats, dogs, and cattle).

Physicians - How to avoid common rabies PEP errors:

For Persons Not Previously Vaccinated for Rabies

- Give Rabies Immune Globulin (RIG) on day 0; if not available, RIG can be given through the 7th day of treatment. Earlier is better to provide passive protection until an antibody response to the rabies vaccine develops.
- Infiltrate all of the RIG dose (if anatomically possible) around the site of the bite; excess RIG can be given in the gluteal muscles.
- Persons who have not been previously vaccinated for rabies receive five doses of vaccine (days 0, 3, 7, 14, and 28).
- Give rabies vaccine intramuscularly (IM) in the deltoid region; never administer rabies vaccine in the gluteal muscles or at the same site as RIG.

For Persons Who Have Previously Received Rabies Vaccine

- Individuals who have previously completed a pre-exposure prophylaxis or a post-exposure prophylaxis regimen receive two doses of rabies vaccine (days 0 and 3).
- Do not give RIG to persons who have previously completed a rabies vaccination series.

Since 1950, only three human rabies cases have been reported in Virginia.

Rabies Post-exposure Prophylaxis (PEP)

For the prevention of human rabies, two types of rabies immunizing products are available in the United States:
- Rabies vaccines induce an active immune response that includes the production of neutralizing antibodies.
- Rabies immune globulin (RIG) provides immediate passive immunity that persists for only a short period (half-life of approximately 21 days).1

Rabies post-exposure prophylaxis includes wound treatment and rabies vaccination (as part of either a five dose regimen for rabies vaccine-naive persons, or the two-injection regimen for previously vaccinated persons), as well as RIG for vaccine-naive persons. When used appropriately, this approach has proven 100% successful in preventing rabies following exposures.3 However, since PEP is time-consuming, labor intensive, carries the risk of adverse reactions, and represents a significant expense, appropriate clinical decisions based on a careful evaluation of the exposure and the availability of the animal for observation or testing are important. Guidance is available to clinicians through such resources as the Virginia Rabies Control Guidelines (available at www.vdh.virginia.gov/epi/dzee/rabies/index.asp) and through consultation with local health department staff.

Methods

The study design was a descriptive, retrospective chart review of individuals who were reported to have received at least one rabies PEP treatment in Virginia (as part of either a full rabies naïve regimen, or the two-injection regimen for previously vaccinated persons) for an exposure that took place between January 1, 2002, and December 31, 2003. The study received expedited Institutional Review Board (IRB) approval by Virginia Commonwealth University (VCU) and the Virginia Department of Health (VDH).

February 2006
Virginia’s Regulations for Disease Reporting and Control (12VAC5-90-80. Reportable disease list) require that physicians and directors of medical care facilities report rabies post-exposure prophylaxis to the local health department within three days of administration. For 2002, a convenience sample of computerized or paper PEP records from 19 of 35 health districts (54%) were reviewed; for 2003, data from 24 of 35 health districts (69%) were reviewed. Data collected included patient demographics, source animal characteristics, and exposure details. However, not all data were available for every case.

Crude and age-specific PEP incidences were calculated using Microsoft Excel 2002 (Microsoft Corporation). Statistical analysis was performed using the SPSS statistical package version 12.0 for Windows (SPSS Inc, Chicago, IL). Pearson’s chi-square differences in proportions were considered statistically significant at the p<0.05 level.

Appropriateness of PEP administration was analyzed using a stepwise process based on the 2004 Virginia Rabies Control Guidelines PEP Algorithm (Figure 1). The 2004 Virginia Rabies Control Guidelines, containing recommendations that were in effect in 2003, defines a human exposure as:

“Any bite, scratch or other situation where saliva or central nervous system (CNS) tissue of a potentially rabid animal enters an open, fresh wound or comes in contact with a mucous membrane by entering the eye, mouth, or nose.”

In addition, the 1999 Advisory Committee on Immunization Practices (ACIP) recommendations on rabies prevention for exposures to bats were used. Since bat bites are often unrecognized exposures, the ACIP recommendations consider a bat exposure to have occurred following any direct contact with bats or when a bite cannot be ruled out (e.g., discovering a bat in a room with a sleeping person, unattended child, mentally impaired person, intoxicated person, or someone otherwise unable to rule out contact).

Exposures that do not constitute a risk of rabies transmission include exposures to urine, feces, or blood, exposures to CNS material or saliva without mucous membrane or wound contact, touching an animal, or indirect exposures through potentially contaminated fomites (e.g., an animal’s fur that had contact with a potentially rabid animal).

Results

Records from a total of 838 patients who received at least one rabies PEP treatment in 2002 and 2003 were available for review. This represented a total of 73.6% of the 1,139 cases reported to the VDH Division of Zoonotic and Environmental Epidemiology in 2002 and 2003.

Demographic characteristics of the recipients for 2002 and 2003 are shown in Table 1. The estimated incidence of PEP in 2003 was 9.3 PEP/100,000 population/year. The PEP rate for children (persons < 18 years of age) was 10.3 PEP/100,000/year, compared with 7.8 PEP/100,000/year for adults; Figure 2 shows the relative age distribution of persons receiving rabies PEP compared to the age distribution of Virginia’s population. In 2003, the highest rates were in the Northwest (15.1 PEP/100,000/year) and Southwest (12.4 PEP/100,000/year) health planning regions (Figure 3).

Rabies PEP showed a seasonal distribution: numbers increased in the spring and summer months, with the peak in July (Figure 4). Among the 571 animals causing
exposures leading to rabies PEP, the majority (72.2%) were domestic species [mostly cats (50.7%) and dogs (47.8%)]. Wild animals made up the remaining 27.8% of animal exposures leading to rabies PEP, with 41.5% of wild animal exposures from raccoons and 27.0% from bats.

For 2002 and 2003, only 29.5% (175/593) of the animals associated with incidents that could have resulted in rabies transmission were known to have been captured for observation and/or testing; of these, 74.3% (130/175) were positive for rabies.

In 2002 and 2003, 66.7% (559/838) of rabies PEP administered was associated with types of exposures to animals that put the person at risk for rabies transmission. The most common types of such exposures were bite wounds (85.5% of 559 exposures), followed by suspected bat exposures (8.2%), and saliva or a body fluid on a mucous membrane or an open wound (6.3%). The remaining 149 exposures did not indicate a risk of rabies transmission nor a need for rabies PEP according to VDH guidelines. The most common types of these exposures were touching an animal (31.5% of 149 events), secondary exposure through potentially contaminated fomites (26.2%), or a scratch (24.2%) (Figure 5). Data were not available to evaluate the exposure for 130/838 (15.5%) of cases where PEP was provided.

The ability to monitor or test an animal for rabies, as well as the type of exposure, are necessary criteria for appropriate PEP decisions. Overall, when data from 2003 were examined to determine appropriateness of PEP decisions, 22.5% (110/489) of administrations of PEP were determined to be inappropriate; an additional 22.3% of administrations of PEP lacked sufficient data to determine appropriateness. Most inappropriate PEP (87/110, or 79.1%) was determined to be unnecessary because the exposures did not put the person at risk for rabies transmission (e.g., touching an animal, secondary exposure). The remaining 20.9% (23/110) were due to exposures that could result in rabies transmissions (e.g., bites, suspect bat exposures), but where the animals were later determined to be negative for rabies (i.e., the animal was available for testing or observation but PEP was still provided prior to the evaluation of the animal) (Figure 6).

**Discussion**

The estimated incidence of rabies PEP and the temporal pattern of PEP administration in 2003 for Virginia were consistent with a 2005 study of PEP in South Carolina. In Virginia, the majority (66.7%) of PEP provided and reported in 2002 and 2003 was for animal exposures that merited rabies PEP. PEP administration for an exposure that would not transmit rabies virus (e.g., touching an animal, secondary exposure, a scratch, etc.) resulted in the majority (79%) of inappropriate PEP administered. Inappropriate administration of rabies PEP may occur when healthcare professionals are not familiar with the types of exposures that can result in rabies transmission, when patients demand a treatment without an adequate understanding of the risk, or when treatment is initiated but the animal is available for testing or monitoring. Administration of rabies post-exposure prophylaxis is a medical urgency, not a medical emergency.
Therefore, to make appropriate decisions, healthcare professionals should evaluate each possible exposure to rabies and consult with local or state public health officials, when necessary, regarding the need for rabies prophylaxis.1

In 2002 and 2003, a significant proportion (70.5%) of the source animals was not captured or the capture status was unknown. Therefore, if the capture of source animals for testing and/or observation can be improved, a significant amount of rabies PEP may be reduced. While the identification and capture of all animals may not be feasible, healthcare professionals should rapidly notify the local health department of exposures so that animal control officials can be engaged.

Actions that reduce the need for rabies PEP have the potential to save public and private entities significant resources. For example, based on 1998 estimates for PEP treatment, the total direct costs to patients and insurers in Virginia for the 110 cases of inappropriate PEP provided in 2003 was between $144,000 and $489,000 (and represents an underestimate of the true costs).

There were several limitations associated with this study. The data relied on healthcare professional reporting to the local health department. The extent of under-reporting of rabies PEP by healthcare professionals in Virginia is unknown, but failure to report would result in underestimating the extent of PEP usage. Some cases where the administration of rabies PEP was actually appropriate may have been classified as inappropriate due to incomplete documentation of the event by a healthcare professional (e.g., when caring for a young child who can not give a reliable history of exposure). Another limitation was the use of a ‘convenience’ sample, where selected Virginia local health departments were included in the study. This may have produced a selection bias that could affect the study results. Other limitations included the lack of standardized data collection and storage methods by health districts that affect the completeness of records and the comparability of the data. Finally, many health districts in Virginia did not link human and source animal data, limiting the ability to analyze the relationships between exposures and outcomes.

Conclusions

The public’s ability to recognize a potential rabies exposure and the appropriate management of the case by healthcare professionals are critical to maintaining the low rates of human rabies deaths observed in the United States.6 However, appropriate PEP treatment decisions rely not only on correctly assessing an exposure to a rabid or potentially rabid animal, but also on weighing the benefits and costs of treatment if the patient was not truly exposed. Most rabies PEP provided in 2003 in Virginia was appropriate. The majority of inappropriate rabies PEP in Virginia in 2003 was given for exposures that did not represent a true risk of rabies virus transmission. Helmick (1983) found that consultation with health department staff on difficult PEP decisions can significantly reduce inappropriate rabies PEP. In addition, significant inappropriate PEP could be avoided in Virginia if more source animals were captured. Educational strategies for healthcare professionals and public health personnel could also reduce inappropriate PEP administration. Other important actions include:

• Continuing rabies prevention education of the public to emphasize the risk of rabies, and to warn the public not to approach, handle, or feed unfamiliar animals;
• Continuing to promote rabies vaccination of domestic animals, including dogs, cats, and ferrets, and livestock in public settings that may pose a risk of transmission;
• Standardizing data collection methods, linking human and source ani-

(Continued on page 6)
Influenza Activity in Virginia

As of March 3, 2006, for the 2005-2006 influenza season in Virginia the Division of Consolidated Laboratory Services (DCLS) has confirmed 48 cases of influenza A/H3, two cases of influenza A/H1, and one case of influenza B by DFA, RT/PCR, and/or culture. Twenty-four cases were from the southwest, seven from the northwest, nine from the eastern, seven from the central, and four from the northern health planning regions. A commercial laboratory also reported one confirmed case of influenza A by DFA from a central region resident.

For the 2005-2006 influenza season, as of March 3, 2006, six laboratory confirmed outbreaks have been reported. Two have been reported in the southwest, one in the central, and three in the eastern health planning regions.

Information about Virginia’s influenza activity level is available on the VDH website at www.vdh.virginia.gov/epi/flu.htm.

National Influenza Activity

Nationally, as of February 25, 2006, 21 U.S. states (including Virginia) reported widespread influenza activity, 14 states reported regional influenza activity, 10 states reported local influenza activity, and five states reported sporadic influenza activity. The proportion of deaths attributable to pneumonia and influenza in 122 cities monitored by the Centers for Disease Control and Prevention (CDC) has remained below the epidemic threshold. Since October 2, 2005, the CDC has received reports of 15 influenza-associated pediatric deaths; 13 of these deaths occurred during the current influenza season.

The CDC reports that during the week ending February 25, 2006, 439 of 2,066 specimens (21.2%) tested by the World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System (NREVSS) laboratories were positive for influenza viruses. Of these 439 specimens, 134 (31%) were influenza A (H3N2) viruses, 12 (3%) were influenza A (H1N1) viruses, 231 (53%) were influenza A viruses that were not subtyped, and 62 (14%) were influenza B viruses.

Since October 2, 2005, WHO and NREVSS laboratories have tested a total of 79,336 specimens for influenza viruses; 7,256 (9.1%) were positive. Among the 7,256 influenza viruses, 6,853 (94.4%) were influenza A viruses and 403 (5.6%) were influenza B viruses. Three thousand one hundred and five (45.3%) of the 6,853 influenza A viruses have been subtyped: 3,046 (98.1%) were influenza A (H3N2) viruses and 59 (1.9%) were influenza A (H1N1) viruses.

The CDC website at www.cdc.gov/flu/weekly/fluactivity.htm has up-to-date details on influenza surveillance in the U.S.

Composition of the 2006-07 Influenza Vaccine:

Based on recommendations from WHO, the 2006-07 trivalent influenza vaccine for the Northern Hemisphere will contain:

- A/New Caledonia/20/99-like (H1N1)
- A/Wisconsin/67/2005-like (H3N2), an antigenic variant of the current vaccine strain A/California/07/2004; and,

These recommendations were based on antigenic analyses of recently isolated influenza viruses, epidemiologic data, and post-vaccination serologic studies in humans.

Avian Influenza A (H5N1)

The avian influenza A (H5N1) epizootic (animal outbreak) in Asia, Africa, and parts of Europe is not expected to diminish significantly in the short term. It is likely that H5N1 infection among birds has become endemic in certain areas and human infections resulting from direct contact with infected poultry will continue to occur.

As of February 27, 2006, 173 human cases resulting in 93 deaths from avian influenza A (H5N1) have been reported to the World Health Organization since 2003. So far, the spread of H5N1 virus from person-to-person has been rare and has not continued beyond one person. No evidence for genetic re-assortment between human and avian influenza A virus genes has

Flu Corner

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The CDC website at www.cdc.gov/flu/weekly/fluactivity.htm has up-to-date details on influenza surveillance in the U.S.
been found; however, the epizootic continues to pose an important public health threat.

Updated information for travelers about avian influenza A (H5N1) is available at the CDC Travelers’ Health Web site (www.cdc.gov/travel/). Some recommendations for travelers to affected areas include:

- Avoid all direct contact with poultry, including touching well-appearing, sick, or dead chickens and ducks. Avoid places such as poultry farms and bird markets where live poultry are raised or kept, and avoid handling surfaces contaminated with poultry feces or secretions.
- Practice careful and frequent handwashing with soap and water. Waterless alcohol-based hand gels may be used when soap is not available and hands are not visibly soiled.
- Cook all foods from poultry, including eggs and poultry blood, thoroughly. Egg yolks should not be runny or liquid.

If a traveler to an affected area develops a fever associated with cough, sore throat, or trouble breathing during their travel or within a 10-day period after leaving an affected area, they should consult a healthcare professional. Before visiting a healthcare setting, the traveler should inform the healthcare professional of: 1) symptoms, 2) where they traveled, and 3) if they had direct contact with poultry or close contact with a severely ill person. Healthcare providers should place any suspected cases of human avian influenza A (H5N1) infection in appropriate isolation precautions and contact their local health department for guidance.

Updated information on the avian influenza A (H5N1) situation is available from the CDC at www.cdc.gov/flu/avian/outbreaks/current.htm, and from the WHO at www.who.int/csr/disease/avian_influenza/en/.

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**Pesticide-Related Illness Reporting**

The Office of Pesticide Services within the Virginia Department of Agriculture & Consumer Services (VDACS) is charged with managing the U.S. Environmental Protection Agency’s Worker Protection Standard (WPS) in Virginia. The WPS program is responsible for ensuring the health and safety of all agricultural workers who use pesticides and workers who operate in pesticide-treated fields.

A critical component of the program is accurate and timely information about pesticide-related illness. This information can help VDACS gauge how well the WPS protects workers and identify ways to more effectively allocate limited resources to the areas of greatest need.

VDACS would like to remind Virginia’s medical community that, as required by the Virginia Board of Health’s *Regulations for Disease Reporting and Control* (12VAC5-90-80), physicians and directors of medical care facilities must report cases of toxic-substance related illness (including those related to pesticide exposures) to their local health department. This information is then provided to VDACS through the Office of Epidemiology at the Virginia Department of Health.

For further information on reporting requirements and procedures related to toxic substances, please contact your local health department, or Lala Wilson at the Office of Epidemiology at (804) 864-8184. If you have any questions, concerns, or comments about the Worker Protection Standard, contact Doug Edwards at the Office of Pesticide Services at (804) 786-4845, or by e-mail at douglas.edwards@vdacs.virginia.gov.
Total Cases Reported, January 2006

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Total Cases Reported Statewide, January

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An Outbreak of Invasive Group A Streptococcal Infection in an Assisted Living Facility

**Background:** In March, 2005, an outbreak of invasive Group A streptococcal (GAS) infections was identified in an assisted living facility in Roanoke County, Virginia.

**Methods:** Intensive case finding efforts were initiated, including obtaining throat cultures from all non-ill residents and staff to identify asymptomatic carriers. Employees also were asked to complete a one page questionnaire about respiratory illness in themselves and in household members. Environmental health staff and a nurse epidemiologist from the Office of Epidemiology conducted inspections of the facility.

**Results:** Five laboratory-confirmed cases of invasive GAS were identified among approximately 160 residents. All cases had septicemia with group A streptococci isolated from blood cultures. Two of the five cases had necrotizing fasciitis resulting in an amputation. There were two deaths. Five asymptomatic residents were identified with positive throat cultures. Eight of 58 (14%) staff throat cultures were positive for GAS.

Following the environmental health and nurse epidemiologist's inspection, recommendations were made for improving handwashing, using personal protective equipment, and training staff. Laboratory results showed that 16/18 isolates (5 cases, 5 asymptomatic residents, 8 asymptomatic staff) had an indistinguishable pulsed field gel electrophoresis pattern. The two isolates that did not match the outbreak strain did not match each other.

**Conclusions:** GAS outbreaks have been reported in nursing homes and in the community at large; however, this was Virginia's first reported GAS outbreak in an assisted living facility. Although the exact cause of the outbreak was undetermined, the results of the actions taken to control the outbreak demonstrate that effective control strategies can halt the transmission of infection.

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