**Rabies Exposures in Humans**


Now that warmer weather is here, people will be heading outdoors to work in their gardens, clean their yards, go hiking, and enjoy spring in Virginia. This will bring more people into contact with animals—including animals that may have rabies.

Rabies is a preventable viral disease of mammals most often transmitted through the bite of an infected animal. Although all species of mammals (including humans) are susceptible to rabies virus infection, only a few species are important as reservoirs for the disease.

Of the 542 cases of animal rabies reported in Virginia in 2003, about 90% occurred in wild animals such as raccoons, skunks, bats, and foxes (see Figure 1). Domestic animals (most commonly cats, cattle, and dogs) account for around 10% of the reported rabies cases. However, bites from domestic animals are much more common, and therefore are more likely to result in postexposure prophylaxis.

**Transmission**

The most common mode of rabies virus transmission is through the bite of an infected host (the virus is in the saliva). Non-bite transmission, for example through a scratch from a rabid animal, is very rare.

Other contact, such as petting a rabid animal or contact with the blood, urine or feces (e.g., guano) of a rabid animal does not constitute an exposure and is not an indication for treatment.

**Disease**

Rabies virus infects the central nervous system. The incubation period for rabies may vary from a few days to several years, but is typically 1 to 3 months. The first symptoms of rabies in humans may be a nonspecific flu-like illness—malaïse, fever, or headache, which may last for days. There may be discomfort or paresthesia at the site of exposure (bite), progressing quickly to cerebral dysfunction, confusion, agitation, delirium, abnormal behavior, hallucinations, and insomnia. The acute period of disease typically ends in death after 2-10 days. It is important to have a high index of suspicion for rabies exposure, since there is effective postexposure prophylaxis, but once clinical signs appear the disease is almost always fatal.

**Rabies Vaccine and Immune Globulin**

The rabies vaccine regimen is extremely safe and effective in providing immunity to rabies when used according to directions.

**Preexposure Prophylaxis**

Each year approximately 18,000 people receive rabies preexposure prophylaxis in the U.S. In 2002, 566 courses of preexposure prophylaxis were given in Virginia. Preexposure vaccination does not eliminate the need for additional medical attention after a rabies exposure—but it does simplify therapy by eliminating the need for human rabies immune globulin (HRIG) and by decreasing the number of vaccine doses required for protection. It may also pro-

Additional rabies information for healthcare providers is available at: http://www.cdc.gov/ncidod/dvrd/rabies/Professional/professi.htm
vide protection to persons with unrecognized exposures to rabies.

Preexposure vaccination is recommended for persons in high-risk groups, such as veterinarians and animal handlers. People who work with live rabies virus in research laboratories or vaccine production facilities are at the highest risk of unrecognized exposures. Some international travelers may also need to be considered for preexposure prophylaxis (see the Centers for Disease Control and Prevention’s Yellow Book at http://www.cdc.gov/travel/diseases/rabies.htm).

For vaccinated people at high or frequent risk of exposure, titers should be checked periodically, with booster doses administered as needed. Local health departments can provide the names and addresses of laboratories performing rabies serologic testing. See the Recommendations of the Advisory Committee on Immunization Practices (ACIP) for preexposure vaccination and serology testing protocols.

**Postexposure Care**

Following exposure to a potentially rabid animal, a patient should immediately wash all wounds thoroughly with soap and water, irrigate wounds with a virucidal agent (e.g., povidone-iodine) if possible, and seek medical attention immediately. Healthcare providers should provide tetanus prophylaxis and measures to control bacterial infection as needed. Physicians should then evaluate each possible exposure to rabies for postexposure prophylaxis.

**Postexposure Prophylaxis (PEP) Evaluation**

Approximately 40,000 people receive rabies postexposure prophylaxis in the U.S. each year. In Virginia, 749 courses of postexposure prophylaxis (PEP) were provided in 2002. As a result of effective prevention and treatment, only 3 cases of human rabies have occurred in Virginia since 1953—the most recent case occurred in 2003.

PEP is indicated for persons possibly exposed to a rabid animal. Possible exposures include animal bites, or mucous membrane contamination with infectious tissue, such as saliva.

Three questions which help to determine the need for PEP are:

1) Was the person bitten by a possibly rabid animal?

2) Did saliva or central nervous system material from a possibly rabid animal contaminate an open wound or mucous membrane?

3) Was the animal in question a bat?

If the answer to all three is “No,” then no exposure occurred, and PEP is not required. If the answer to at least one question is “Yes,” then exposure to rabies is a possibility.

In addition, the following information is important:

- Whether the animal can be safely captured and observed or tested for rabies; and,

- The type of animal that was involved.

Small rodents (e.g., squirrels, rats, mice, hamsters, guinea pigs, gerbils, and chipmunks) and lagomorphs (e.g., rabbits and hares) have not been known to cause rabies among humans in the U.S. Bites by these animals are usually not consid-
Following a suspected rabies exposure, you must find out:

Is the animal available for observation or testing?

<table>
<thead>
<tr>
<th>Animal type</th>
<th>Evaluation and disposition of animal</th>
<th>PEP recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogs, cats and ferrets</td>
<td>Healthy and available for 10 days observation</td>
<td>Persons should not begin prophylaxis unless animal develops clinical signs of rabies.*</td>
</tr>
<tr>
<td>Rabid or suspected rabid</td>
<td></td>
<td>Immediately vaccinate.</td>
</tr>
<tr>
<td>Unknown (e.g., escaped)</td>
<td></td>
<td>Consult public health officials. Rabies should be considered in the differential diagnosis of any patient who presents with acute progressing encephalopathy of unknown cause.</td>
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<tr>
<td>Skunks, raccoons, foxes and most other carnivores; large rodents (woodchucks and beavers); bats</td>
<td>Regarded as rabid, unless animal proven negative by laboratory tests†</td>
<td>Consider immediate vaccination.</td>
</tr>
<tr>
<td>Livestock, small rodents, lagomorphs (rabbits, hares), and other mammals</td>
<td>Consider individually</td>
<td>Consult public health officials. Bites of squirrels, hamssters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits and hares almost never require antirabies PEP unless the animal is sick or acting abnormally.</td>
</tr>
</tbody>
</table>

*During the 10-day observation period, begin PEP at the first sign of rabies in a dog, cat or ferret that has bitten someone. If the animal exhibits clinical signs of rabies, it should be euthanized immediately and tested.
†The animal should be euthanized and tested as soon as possible. Holding for observation is not recommended. Discontinue vaccine if immunofluorescence test results on the animal are negative.

of others exposed to the source;
• Implementation of appropriate infection control measures;
• Limitation of the number of persons that require PEP;
• Prompt administration of PEP to exposed persons;
• Appropriate counseling and closure with patient’s family and friends; and
• Continued identification of potentially treatable causes if negative results are obtained.

Antemortem testing is done by the Centers for Disease Control and Prevention (CDC). Antemortem brain biopsy for rabies testing is not usually indicated, but if a biopsy has been done to test for other diseases and is negative, the tissue can be tested for rabies as well. Saliva can be tested by virus isolation or reverse transcription followed by polymerase chain reaction (RT-PCR). Serum and spinal fluid can be tested for antibodies to rabies virus. Skin biopsy specimens can be examined for rabies antigen in the cutaneous nerves at the base of hair follicles. Postmortem diagnosis of rabies is made by immunofluorescent staining of viral antigen in touch impressions of brain tissue. Contact your local health department to coordinate testing.

Conclusions

Educating the public on avoiding contact with unknown animals is a critical part of preventing rabies. However exposures continue to occur on a regular basis. Therefore, healthcare providers in Virginia need to evaluate exposures carefully. Although considerations for vaccination can be complicated, healthcare providers can consult their local health department as needed to assist in making an informed assessment.

Submitted by: Suzanne Jenkins, VMD, Director, Division of Zoonotic and Environmental Epidemiology

References:
- MMWR. March 21, 2003 (52(RR05); 1-8.

Table 2. Rabies postexposure prophylaxis schedule

<table>
<thead>
<tr>
<th>Vaccination status</th>
<th>Treatment</th>
<th>Regimen*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not previously vaccinated</td>
<td>Wound cleansing</td>
<td>Immediate thorough cleansing of all wounds with soap and water. If available, use a virucidal agent (e.g., povidone-iodine solution) to irrigate wounds.</td>
</tr>
<tr>
<td></td>
<td>HRIG</td>
<td>Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around the wound(s). If not, any remaining volume should be administered IM at an anatomical site distant from vaccine administration. HRIG should not be administered in the same syringe as vaccine. No more than the recommended dose should be given.</td>
</tr>
<tr>
<td></td>
<td>Vaccine</td>
<td>HDCV, RVA or PCEC 1.0 mL, IM (deltoid area†), on days 0, 3, 7, 14, and 28.</td>
</tr>
<tr>
<td>Previously vaccinated§</td>
<td>Wound cleansing</td>
<td>Immediate thorough cleansing of all wounds with soap and water. If available, use a virucidal agent (e.g., povidone-iodine solution) to irrigate wounds.</td>
</tr>
<tr>
<td></td>
<td>HRIG</td>
<td>HRIG should not be administered.</td>
</tr>
<tr>
<td></td>
<td>Vaccine</td>
<td>HDCV, RVA or PCEC 1.0 mL, IM (deltoid area†), on days 0 and 3.</td>
</tr>
</tbody>
</table>

HDCV=human diploid cell vaccine; PCEC=purified chick embryo cell vaccine; HRIG=rabies immune globulin; RVA=rabies vaccine adsorbed; IM=intramuscular; Day 0=day the first dose of vaccine is administered.

*These regimens are applicable for all age groups, including children.
†The deltid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.
§Any person with a history of preexposure vaccination with HDCV, RVA or PCEC; prior PEP with HDCV, RVA or PCEC; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.
**Temporary Suspension of the Third and Fourth Doses of Pneumococcal Conjugate Vaccine (Prevnar®)**

Effective immediately, all health care providers should temporarily suspend routine use of both the third and fourth doses of 7-valent pneumococcal conjugate vaccine (PCV7) when immunizing healthy children. These recommendations, made by the Centers for Disease Control and Prevention (CDC), in consultation with the American Academy of Family Physicians (AAFP), the American Academy of Pediatrics (AAP), and the Advisory Committee on Immunization Practices (ACIP) will help ensure the most effective use of the limited available doses of vaccine until the manufacturer can restore full production. Children at increased risk of severe disease (e.g., certain health conditions, such as sickle cell anemia or immune system disorders) should continue to receive the full, routine, four-dose series.

Wyeth Vaccines, the sole manufacturer in the United States, markets PCV7 under the trade name Prevnar®. The vaccine is normally recommended for young children in a four-dose schedule: one dose at 2 months, 4 months, and 6 months, and between 12 and 15 months. However, recent PCV7 production problems have resulted in spot shortages that may continue beyond the summer of 2004 and become widespread. CDC had previously recommended that healthcare providers temporarily suspend routine use of the fourth dose. Since that recommendation was issued, PCV7 production has been much lower than expected, resulting in the recommendation to defer the third dose as well. Limiting healthy children to 2 doses of PCV7 will conserve vaccine and permit more children to receive at least 2 doses. In addition, previously unvaccinated healthy children aged 12-23 months need fewer doses for maximum protection and should only receive a single dose while vaccine supplies are limited.

PCV7 is highly effective: the routine 4-dose series has been 97% effective against invasive disease caused by serotypes represented in the vaccine. Data on the long-term efficacy of 3-dose or 2-dose vaccine regimes are limited. Therefore, healthcare providers should consider the diagnosis of invasive pneumococcal disease in incompletely vaccinated children.

Children whose third and fourth doses are delayed should receive the missed doses after supplies return to normal. Health care providers should keep track of children who are not able to get all of the recommended doses of the vaccine and then contact those patients when they receive adequate supplies of vaccine. The highest priority for vaccination among children who have been deferred includes those who have received 2 doses or less and who are less than 1 year of age.

CDC will continue to update health care providers on the status of vaccine supplies while the shortage persists. A variety of information, including a fact sheet for parents and current news on the national PCV7 supply is available at the CDC web page (http://www.cdc.gov/nip/news/shortages/default.htm).

Submitted by: Laura Ann Nicolai, Division of Immunization

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**Manufacturer’s Recall of Human Rabies Vaccine**

The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) have been notified that a recent quality-assurance test of IMOVAX® Rabies Vaccine (Aventis Pasteur) found noninactivated Pitman-Moore virus (the attenuated vaccine strain) in a single product lot. IMOVAX® is an inactivated viral vaccine and should not contain live virus. The vaccine lot containing noninactivated virus was not distributed.

As a precautionary measure, Aventis Pasteur initiated a voluntary recall of IMOVAX® vaccine lot numbers X0667-2, X0667-3, W1419-2, and W1419-3. These lots were produced during the same period as the lot containing the noninactivated Pitman-Moore virus, and were distributed in the United States from September 23, 2003 through April 2, 2004. The manufacturer indicated that recalled vaccine had also been distributed internationally. The manufacturer is working with regulatory authorities to determine countries that may have received recalled vaccine. More information about these internationally distributed lots will be posted as it becomes available.

Note that the recalled lots distributed in the United States and internationally had passed all FDA-approved release tests, including testing to confirm the absence of live virus. As a result, any potential risk to those vaccinated with recalled vaccine is likely to be low. To date, no unusual adverse events associated with the recalled vaccine lots have been reported.

However, persons who received vaccine from a recalled lot could theoretically have been exposed to the noninactivated Pitman-Moore vaccine strain of rabies virus. Therefore, healthcare providers should be aware that recommendations are available at www.vaccineshoppe.com for the care of patients who received a vaccination from the recalled lots. Further information about this recall is available from the Aventis Pasteur Medical Information Services Department (800-835-3587).

All clinically significant adverse events following receipt of rabies vaccine should be reported to 1) Aventis Pasteur (800-835-3587) and 2) the Vaccine Adverse Event Reporting System (VAERS) at www.vaers.org, or 800-822-7967. Additional information about rabies and its prevention is available from the CDC (404-639-1050), or at www.cdc.gov/ncidod/dvrd/rabies.
Virginia Department of Health
Public Health Emergency Z-Card

Statewide focus groups, conducted by the Virginia Department of Health (VDH) in early 2003, revealed that many Virginians feel they lack an understanding of public health emergencies (including those related to terrorism) and want to become more knowledgeable. Therefore, VDH is excited to introduce a new tool that will help Virginia residents to be more prepared for public health emergencies. The Public Health Emergency Z-Card is a practical, folded paper product with credit-card sized outer covers and a fold-out insert. The design presents a wealth of information, as well as space to record personal information—all in a durable package that fits easily in a wallet or purse.

The information in the card will help Virginians learn how they can protect themselves during a public health emergency. People should fill in the Z-Card with their personal health and emergency contact information, including the phone numbers of nearby hospitals and local/out-of-town contacts as well as medical information such as blood type, allergies, medical conditions, and current medications.

VDH is partnering with Wal-Mart, Giant, and Safeway to distribute 1.1 million Z-Cards throughout Virginia starting in April 2004. Grocery stores will display the cards at the pharmacy and customer service counters, and Wal-Mart will hand them out at their pharmacies. To ensure that all health districts are covered, cards will also be distributed at Fresh Pride stores throughout the Eastern Shore and the Food Lion in Onley, Virginia.

For more information, contact your VDH Regional Public Information Officer.

If your patients ask for more advice about what they can do to help prepare for emergencies, refer them to the VDH website (www.vdh.virginia.gov) or the Virginia Department of Emergency Management website at: http://www.vdem.state.va.us/. In addition, the U.S. Department of Homeland Security has valuable information at: http://www.dhs.gov/dhspublic/.

Flu Corner

Influenza season appears to be over—by March 11, influenza activity had fallen to baseline levels reported in autumn 2003. As of March 1, 2004, the state public health laboratory has reported a total of 88 confirmed cases of influenza type A by direct Fluorescent Antibody (dFA), culture, or both. Laboratory confirmed cases were reported from all regions of the state. A total of five isolates were subtyped as Fujian strain [H3N2]. Therefore, while influenza infections are still occurring, the number of new cases has decreased significantly.

Of note, any remaining doses of influenza vaccine can still be administered until the vaccine expires (June 30, 2004) to avoid wastage. One group that may especially benefit from immunization at this time is children under the age of 9. Previously unvaccinated children younger than 9 years of age have had little exposure to influenza and therefore require two doses of vaccine to produce a satisfactory antibody response. The two doses should be administered ≥ 1 month apart.

Previously unvaccinated children presenting to healthcare providers can receive one dose of influenza vaccine now. In the fall, when vaccine formulated for the 2004-2005 season is available, these vaccinated children will only need to receive one additional dose. Children previously primed by immunization with a related strain of influenza mount a brisk response to a subsequent dose of vaccine. So, vaccinating with the primer dose now will save time and resources in the fall.

2004-2005 Vaccine Formulation

The strains that will be included in the 2004-2005 influenza vaccine formulation are: A/Caldeonia, A/Fujian and B/Shanghai. Most of the disease this past season was caused by the A/Fujian strain. The effectiveness of the vaccine will ultimately be determined by the prevalent strains in the upcoming season, but if the vaccine matches the strains it should be highly effective.
Antibiotic Resistance Education in Virginia

This past year saw Virginia join the national effort to reduce the inappropriate use of antibiotics. The “Get Smart Virginia: Know When Antibiotics Work” campaign kicked off officially in December 2003 with a press conference and the formation of a statewide coalition spearheaded by a unique partnership between the Virginia Department of Health (VDH) and the Medical Society of Virginia Foundation (MSVF). As cold and flu season ends, the Get Smart Virginia program would like to summarize national trends in antibiotic resistance and prescribing and update you on Get Smart Virginia activities.

Resistance and Trends in Pneumococcal Disease

The worldwide increase in resistance of Streptococcus pneumoniae (SP) to penicillin since the early 1990s prompted a concerted effort by the Centers for Disease Control and Prevention (CDC) to address the problem in the US. According to the CDC, by 1997 25% of invasive isolates of SP in the US were partially or fully resistant to penicillin (CDC Active Bacterial Core surveillance). This figure increased each year, reaching 27% in 2000, and decreasing in 2002 to 20%.

The decline in resistance is partially attributed to the introduction of the pneumococcal conjugate vaccine in 2000 by Wyeth Lederle Vaccines. Recommended for all children under the age of two years and for children ages 24-59 months with an increased risk for SP, use of the vaccine led to a decline in the rates of SP in the US. In addition, intensive efforts to promote appropriate antibiotic use parallels the decreasing rates of antibiotic prescriptions in ambulatory settings. Data from the National Ambulatory Medical Care Survey show that the number of antibiotics prescribed in physician offices decreased by 23% with no change in the number of office visits.2

Good News, Bad News

While these results are good news for everyone, they don’t tell the complete story. Between 1991-1999, use of broad-spectrum antibiotics in adults increased from 24% to 48% of antibiotic prescriptions, and in children from 23% to 40% of antibiotic prescriptions.3 This trend warrants concern at a time when rates of macrolide- and fluoroquinolone-resistant pneumococci are on the increase in many parts of the world. CDC recommendations continue to encourage use of targeted agents as first-line therapy even as measures to assess the appropriateness of antibiotic prescribing in children are introduced in the 2004 Health Plan and Employer Data Information Set (HEDIS).

The National Committee for Quality Assurance has developed standardized measures to monitor inappropriate antibiotic utilization and to encourage quality improvement. Appropriate Treatment of Children With Upper Respiratory Infections tracks the rate of antibiotic prescriptions for children between 3 months and 18 years of age who were diagnosed with URI. Appropriate Testing for Children with Pharyngitis promotes the proper diagnosis of strep throat by measuring the rate of children between 2 and 18 years of age who were diagnosed with pharyngitis, tested for Group A streptococcus, and prescribed an antibiotic.

Virginia’s Efforts

The primary focus of Get Smart Virginia is consumer education and awareness. The campaign centers around three key messages to prevent misuse:

- Antibiotics don’t cure viral infections;
- Take antibiotics exactly as prescribed by your doctor and always finish the medicine; and
- Don’t save your antibiotics for another illness or share your medicine with others.

In the fall of 2003, posters and brochures about appropriate antibiotic use were developed and made available to a variety of community organizations. A website for childcare providers, schools, consumers and clinicians can be accessed for additional information and resources at: http://www.vdh.virginia.gov/epi/getsmart/index.asp. Interventions currently in development for the 2004 cold and flu season will include:

- a public relations campaign;
- clinic-based patient education; and
- community outreach activities.

To assess consumer knowledge and use of antibiotics, questions about antibiotic resistance were added for 2004 to the Behavioral Risk Factor Surveillance System, a year-round annual survey of adults living in a household with a telephone. Results will be available in Spring 2005.

Facilitated by the VDH/MSVF partnership, a Physician Advisory Group is providing guidance and leadership in developing and distributing materials for clinicians to support their efforts to discourage patient demands for antibiotics. A variety of patient education interventions are being considered and include cold care kits, posters and brochures, viral illness “prescription” sheets, posters and brochures. Contact Melissa King (804-353-2721) at the MSVF for more information or to provide input. Posters and brochures are available by calling 804-864-8106.

Submitted by: Kate Grant, Project Director, Get Smart Virginia

References:
### Cases of Selected Notifiable Diseases Reported in Virginia*

<table>
<thead>
<tr>
<th>Disease</th>
<th>State</th>
<th>NW</th>
<th>N</th>
<th>SW</th>
<th>C</th>
<th>E</th>
<th>This Year</th>
<th>Last Year</th>
<th>5 Yr Avg</th>
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<td>Syphilis, Early§</td>
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<td>0</td>
<td>8</td>
<td>25</td>
<td>39</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>12</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>12</td>
<td>23</td>
<td>19</td>
</tr>
</tbody>
</table>

*Total Cases Reported, February 2004*

*Total Cases Reported Statewide, January - February*

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Localities Reporting Animal Rabies This Month: Albemarle 1 raccoon; Amelia 1 raccoon; Augusta 1 skunk; Charles City 1 fox; Chesterfield 1 raccoon; Culpeper 1 raccoon, 1 skunk; Cumberland 1 raccoon; Fairfax 1 fox, 1 groundhog, 7 raccoons; Frederick 1 raccoon, 1 skunk; Fredericksburg 1 raccoon; Henrico 1 raccoon; Isle of Wight 1 raccoon; Loudoun 1 raccoon, 1 skunk; Madison 1 raccoon; Newport News 2 raccoons; Northampton 1 raccoon; Rockingham 2 cows, 1 raccoon; Spotsylvania 1 fox; York 1 raccoon.

Toxic Substance-related Illnesses: Arsenic Exposure 1; Cadmium Exposure 1; Lead Exposure 3.

*Data for 2004 are provisional. †Elevated blood lead levels ≥ 10µg/dL.

§Includes primary, secondary, and early latent.