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Rabies Vaccine Supply Issue: Facts Are Key

The current limitation of the rabies vaccine supply presents an urgent, but not emergent, situation. In fact, nothing has changed regarding the indications for the vaccine's use. However, the supply issue does underscore the need for judicious use and careful attention to information gathering.

At this time, rabies vaccine is limited to postexposure prophylaxis and is not being given to travelers or individuals with occupational exposure risk. On Oct. 8, the Centers for Disease Control and Prevention announced that Novartis has collaborated with public health and government officials to provide additional supplies of RabAvert vaccine for postexposure prophylaxis without the need for a pass code or other restrictions. (Questions can be directed to Novartis customer service at 1-800-244-7668.)

A pass code is still required to receive Sanofi Pasteur Inc.'s IMOVAX. To obtain IMOVAX rabies vaccine, you must first contact your rabies state health official to conduct a risk assessment for the suspected exposure. (A list of those officials, along with the latest supply updates, is available at www.cdc.gov/rabies.) If the official determines that rabies postexposure prophylaxis is indicated, you will be provided with a pass code to place on the Sanofi Pasteur rabies postexposure form, which must be filled out in its entirety. (To obtain the required form, contact Sanofi Pasteur at 1-800-VACCINE.)

The required form has specific information that should be collected so that an appropriate decision can be made for each patient. Basic information includes details regarding the animal species, the bite circumstances, and local rabies epidemiology. Even when the rabies vaccine supply is back to normal, practitioners will continue to be responsible for obtaining the relevant data that are necessary for making a decision about vaccine.

Children's Mercy Hospital has developed an easy-to-use form that practitioners can utilize now and in the future. Our infectious disease section data analyst, Josh Herigon, helped develop our current form, which can be accessed at http://www.childrensmercy.org/rabiesform.

Parents of children who have had an animal bite are usually highly anxious and need to know that you are collecting all relevant information so that appropriate postexposure prophylaxis occurs in a timely fashion. In cases in which rabies postexposure prophylaxis is not recommended, parents need to understand the rationale for that decision.

Other key concepts include the following:

► Attempts should be made to recover the animal in all cases of exposure or possible exposure. If the animal is in a high-risk category, it should be immediately referred for rabies testing. Domestic animals that are acting normally should be observed, and referred for testing if they begin to exhibit abnormal behavior. Postexposure prophylaxis can be safely delayed for this period of time.

► If the animal can't be recovered, the next step depends upon the information you've gathered. If the animal is in the high-risk category and there was a bite wound, then postexposure prophylaxis—comprising both vaccine and rabies immune globulin—must be initiated.

► On the other hand, bites from low-risk animals that have escaped will rarely require vaccination. Indeed, the animal's ability to escape is a sign of noninfection, because a rabid animal is usually very sick and typically won't be able to make a quick getaway. Knowing whether the attack was provoked or not is also helpful, as a provoked animal is far less likely to be infected than is one that attacks for no apparent reason. Low-risk animals rarely carry rabies, and have never been documented to transmit it to a human in the United States.

► In an intermediate-risk situation, such as a dog bite in which the dog escapes, information such as the local rabies rates, the type and severity of the wound, and whether or not the attack was provoked will help you make the decision regarding whether or not to vaccinate. Again, consult with your local health officials or infectious disease specialist.

► Seeing a bat in the house commonly arouses concern about rabies. In the case of a preverbal child or an impaired (for example, drunk) adult who has no noticeable bite wound but who nevertheless may have been exposed, animal control should be called to capture the animal, and arrangements should be made with the local health department for rabies testing. If the bat cannot be captured, immunization plus rabies immune globulin is necessary. Approximately 5% of bats in the United States are rabid.

► Rabies vaccine is given intramuscularly on days 0, 3, 7, 14, and 28. The same dosage is used for both children and adults, but the injection is given in the deltoid in adults and in the anterolateral thigh in infants and children. Although primary care physicians don't typically administer rabies vaccine, it's important to educate patients about what's in store.

► Wound cleansing is extremely important. Irrigation (except in the case of puncture wounds), tetanus vaccination, antibiotic prophylaxis in appropriate cases, and wound closure when indicated are all essential. Animal studies suggest that wound cleansing reduces the chance of viral transmission.

► Officials at the CDC anticipate that the rabies vaccine supply will be fully restored in mid-2009, when Sanofi Pasteur's manufacturing facility in France is expected to be reopened. It was the scheduled closing of that facility in June 2007—combined with Novartis' inability to meet the remaining market demand—that resulted in the current supply problems. Hopefully, if we continue to practice judicious use of the vaccine even after the supply is restored, we can prevent a similar situation from reoccurring.

By the way, those of you practicing in Hawaii don't need to worry. Yours is the only U.S. state that has never had a documented case of rabies. ■

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Bacterial Coinfection Often Present in Pediatric Flu Deaths

BY DENISE NAPOLI
Associate Editor

Of the 73 pediatric patients who died of influenza-related causes in the United States during the 2006-2007 flu season, 35% had bacterial coinfection—a fivefold increase over the 2004-2005 season.

Most often, that bacteria was methicillin-resistant *Staphylococcus aureus* (MRSA).

"Physicians should consider treating children with suspected *S. aureus* pneumonia during influenza season with vancomycin or other antibiotics to treat MRSA when [the children] reside in areas where MRSA is prevalent" or when they have additional MRSA risk factors, including underlying conditions or a history of infection, wrote Lyn Finelli, of the National Center for Immunization and Respiratory Diseases, Atlanta, and colleagues (Pediatrics 2008;122;805-11).

Dr. Henry Bernstein, a pediatrician in Lebanon, N.H., and a member of the American Academy of Pediatrics' committee on infectious diseases, agreed.

"It's something that we as practicing pediatricians need to be aware of: When somebody gets the flu, we must evaluate whether in fact it's a typical, routine case of the flu or it's something more, if it's not following the course that we expect."

But the most important lesson from this analysis is to get children vaccinated, Dr. Bernstein said in an interview. "Half of those [deaths] are in kids who could have gotten the flu vaccine, and potentially it could have been prevented. So that's tragic. These aren't just kids who have chronic health conditions. Many of these kids were healthy children. That's a shame," said Dr. Bernstein, who was not involved in the study.

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The researchers defined an influenza season as lasting from Oct. 1 to Sept. 30 of the following year, such that the 2006-2007 season lasted from Oct. 1, 2006, to Sept. 30, 2007. They also defined a child as being fully vaccinated when he or she had received the appropriate number of doses at least 14 days before illness onset.

In the first season looked at, 2004-2005, the rate of bacterial coinfection in the 47 pediatric influenza-related deaths was 6%. By the next season, it was 15%, and by 2006-2007, the rate was 35%. "Overall, *S. aureus* was isolated from a sterile site or endotracheal tube culture in 1 child in 2004-2005, 3 children in 2005-2006, and 22 children in 2006-2007," wrote the authors. Of these 26 infections, 15 were MRSA, 6 were methicillin-susceptible *S. aureus* (MSSA) and 5 were *S. aureus* of unknown susceptibility.

The authors hypothesized that influenza might increase patient vulnerability to bacteria by damaging the epithelial layer of the tracheobronchial tree, "enhancing staphylococcal adherence," or possibly suppressing the "respiratory burst response" and phagocytic activities that occur in a healthy immune system.

Regardless of the mechanism, they conceded that there is likely underreporting of bacterial coinfection in fatal influenza cases in the United States. Indeed, according to the authors, flu-related deaths may themselves be underreported: "Despite the availability … of influenza tests, influenza testing is not currently routinely incorporated into the diagnostic work-up of most children who are seen in primary care of emergency department settings with influenza-like illness."

In all, 166 children in the United States died of influenza-related causes between Oct. 1, 2004, and Sept. 30, 2007. The ages of affected children ranged from 0 to 17 years. The median ages in the three cohorts ranged from 3 to 7 years.

Currently, all children aged 6 months to 18 years should be vaccinated, according to recommendations by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices. Only 5% of those patients for whom vaccination was recommended had received the vaccine.

"Influenza is a serious disease," said Dr. Bernstein. However, "There's no question that influenza is [also] vaccine preventable. You can't die from the flu if you don't get the flu." And as the potential for coinfection with antibiotic-resistant bacteria increases from year to year, the need for vaccination is even more pressing, he said. And not just among patients.

"Health care personnel vaccination rates are somewhere around 50%, at most," he said. "There's certainly room for improvement. Getting a flu vaccine every year ought to become a routine."

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