CDC Responds to Rabies Vaccine Supply Concerns

BY MIRIAM E. TUCKER
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ATLANTA — Interim guidelines for use of rabies vaccine have been drafted by an ad hoc working group of the Centers for Disease Control and Prevention to address contingency plans in the event that the current "less than ideal" vaccine supply situation becomes an actual shortage.

At the summer meeting of the CDC's Advisory Committee on Immunization Practices (ACIP), CDC Rabies Program chief Charles E. Rupprecht, VMD, characterized the current rabies vaccine supply situation as being in a "yellow" phase, with "green" being the ability to meet all ACIP recommendations for both pre-exposure and postexposure prophylaxis and red being "critical," where even those in greatest need would not be able to receive the vaccine (MMWR 2008;57[RR03]:1-26).

"Supplies of biologicals used in human rabies prophylaxis are expected to remain less than ideal over the next several years," he said, adding that the CDC, along with the Food and Drug Administration, the Department of Health and Human Services, and national stakeholders "continue to work together toward productive solutions to mitigate current human rabies supply issues."

In June 2007, Sanofi Pasteur Inc. began a planned renovation of its Imovax Rabies vaccine production facility in France to maintain compliance with both FDA and French regulatory requirements. The facility is scheduled to be approved and operational by mid- to late 2009. Prior to suspending production at that facility, the company had established an inventory based on historical levels of sales and projected market demand, Sanofi Pasteur's Dr. David Johnson informed the committee.

After the renovations began, Novartis, the only other supplier of rabies vaccine for the United States (RabAvert), experienced manufacturing problems that prevented them from meeting rabies vaccine supply projections. In early 2008, Novartis announced that it would supply RabAvert for postexposure prophylaxis (PEP) use only. Consequently, in May 2008, Sanofi Pasteur was forced to do the same, as the increase in demand for Imovax began outpacing the company's historical levels of supply.

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Supplies of rabies biologicals are expected to remain less than ideal for several years, CDC Rabies Program chief Dr. Charles E. Rupprecht said.

Those developments, combined with a slight increase in rabies cases—a 5% increase in 2007 over the 6,940 cases reported in 2006—have resulted in the current uneasy situation. "It's been a series of unfortunate concomitant events," Dr. Rupprecht remarked.

A bit of relief is expected in the next few weeks, as Novartis had just received approval for a shipment of a small amount of vaccine prior to the ACIP meeting in late June. The company plans to make a small amount of that supply available for high-priority pre-exposure use, Novartis' Dr. Rajiv De Silva said.

Moreover, Novartis has just broken ground on a new vaccine production facility in Marburg, Germany, which will supply the U.S. market. It is expected to be operational by 2011. In the meantime, "we are working closely with the FDA to implement some interim steps to ensure sufficient production in our existing facility to supply the U.S. market for 2009 and 2010. … Our situation has improved, but we're not out of the woods yet," Dr. De Silva said.

Aside from restricting the vaccine to PEP, other principles outlined in the draft document include centralization of national-state communications, mandatory consultation with knowledgeable public health officials prior to use of the vaccine, and renewed education and outreach for key medical providers regarding what constitutes a true exposure.

In general, PEP should be postponed until animal control can locate and capture the suspect animal for rabies testing and until diagnostic tests are completed, and should be withheld after bites from animals where adequate surveillance exists and there is no documented terrestrial rabies reservoir. Of course, PEP is always instituted if there is a high suspicion of rabies, based in part on animal species, local epidemiology, and the nature of the exposure. Most states have guidelines for the length of time to survey an area and to start diagnostic testing in high-risk situations, Dr. Rupprecht said in a follow-up interview.

If rabies vaccination must be given, options to lessen use during a shortage situation include administering only one booster dose to people previously vaccinated, dropping the fifth (final) dose of the series in a vaccine-naive individual, using alternative schedules, use of an intradermal route, and consideration of using other biologicals.

In general, in the event of any shortage situation, people traveling abroad would be "deprioritized" for pre-exposure vaccine and educated in "bite avoidance." Individuals who will be living overseas can obtain vaccination abroad where safe injection practices are used with an approved cell culture vaccine, Dr. Rupprecht said.

When pre-exposure vaccine becomes available, prioritization will involve "first responders" such as animal control workers, diagnosticians, and veterinary staff.

"We are very cautiously optimistic that, as we speak, supplies will begin to improve to the extent that pre-exposure needs for critical first responders are being met. There are plans afoot to meet the needs of secondary groups at risk in mid-August, such as veterinary schools," Dr. Rupprecht said at the ACIP meeting.

He emphasized that there is no shortage at the moment. "While it may be perceived that there is an alleged shortage, what's being done very strictly now are things that mitigate against the [possibility] of a shortage. There are available supplies such that any folks [who] are truly exposed will be vaccinated and receive rabies immune globulin. We only expect things to improve, based upon information we have at this time." There is currently no supply limitation with rabies immune globulin, although market changes in plasma collection could create an impact beyond 2009, he said. ■

MRSA Spread in Part Due to Stressed Health Care Systems

BY DENISE NAPOLI
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Overcrowding and understaffing of hospitals are two of the major underlying factors driving the spread of methicillin-resistant *Staphylococcus aureus* in this setting, according to a review.

Furthermore, "the economic benefits of downsizing health care systems are likely to have been offset by the increased burden of adverse events, such as MRSA," the authors wrote.

Archie Clements, Ph.D., of the division of epidemiology and social medicine at the University of Queensland (Australia), and his colleagues from the fields of mathematics, statistics, infection surveillance, and medicine, cited 140 studies in their review (Lancet Infect. Dis. 2008; 8:427-34).

They concluded that the direct mechanisms through which hospital-acquired infections are spread—including a decrease in handwashing, less "cohorting" of patients (meaning patients interact with a large number of health care workers), and closer proximity of infected patients to noninfected patients—are themselves caused by a dearth of health care professionals and a surplus of patients.

For instance, in the case of handwashing—a known, simple, and inexpensive method to reduce the spread of MRSA dramatically—overworked health care staff are less likely to wash when indicated, according to several studies cited by the authors. In one, noncompliance was highest in cases of high "intensity of patient care," when there were more than 40 opportunities for handwashing per hour of care, compared with when there were fewer indications per hour (Ann. Intern. Med. 1999;130:126-30).

New admissions for infection, isolation of high-risk patients, and use of more effective hand hygiene products have proved successful.

Additionally, the spread of MRSA within a facility exacerbates overcrowding, as patients' stays are extended, which in turn fuels chronic understaffing. "This contributes to a vicious cycle, where the occurrence of MRSA makes it more difficult to implement effective infection control strategies, leading to subsequent breakdowns in infection control and further increases in the incidence of MRSA," the authors wrote.

The number of patients seeking care, inpatient or otherwise, is not likely to decrease any time soon—an aging population in the developed world means that countries like Australia can anticipate a 70%-130% increase in hospital bed requirements by 2050, according to the review. But there is hope—the authors praised institutions in the Netherlands and Scandinavian countries, for example, for keeping MRSA infection down.

On the level of individual facilities, the researchers cited several studies wherein screening of new admissions for infection, isolation of high-risk patients, and use of more effective hand hygiene products have proved successful.

The authors wrote that they had no conflicts of interest to disclose. ■