No Apparent Tie Between MCV4, Guillain-Barré

Despite reassuring new data, the jury is still out on potential link.

BY MIRIAM E. TUCKER

ATLANTA — The jury is still out regarding a potential link between the quadrivalent meningococcal conjugate vaccine and Guillain-Barré syndrome, but new data from the Centers for Disease Control and Prevention provide some reassurance in favor of the vaccine's safety.

In October 2006, the CDC published findings from the Vaccine Adverse Event Reporting System (VAERS) that suggested a small increased risk for Guillain-Barré syndrome following receipt of MCV4 (Menactra), Dr. Angela Calugar said at a meeting of the CDC's Advisory Committee on Immunization Practices.

The VAERS data had shown that the observed rate of GBS within 42 days after receipt of MCV4 was not elevated among 11- to 19-year-olds overall (33 observed cases vs. 36 expected from background rates), but the rate of GBS did appear to be elevated among adolescents aged 15-19 (26 vs. 20 cases). However, that difference still did not reach statistical significance, said Dr. Calugar of the CDC's Immunization Safety Office.

Since VAERS is a passive reporting system that is used only to generate a "signal" of a possible problem, the CDC undertook an investigation using the Vaccine Safety Datalink (VSD), a collaboration between the agency and eight managed care organizations that provide data from 8.8 million members annually, approximately 3% of the U.S. population.

Between April 2006 and February 2009, a total of 642,493 doses of MCV4 were administered in the eight VSD sites.

Among those, five cases of GBS were reported to have occurred in 42 days or less following vaccination. Of those, one had onset of symptoms on day 0, and was therefore out of the "risk window." Another had pre-existing GBS, and two others were found on further investigation to have diagnoses that were not GBS. The fifth case was still pending medical review at the time of Dr. Calugar's presentation.

But even if that case does turn out to be GBS, one case is the expected background number for the population during the study time period, she noted.

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"These are some very reassuring data," Dr. Carol J. Baker said of interim study findings on the subject.

Still the CDC remains vigilant, and is continuing to monitor for GBS reports following receipt of MCV4 vaccine through both VAERS and VSD, she said.

Dr. Carol J. Baker, chair of the ACIP meningococcal working group, added that interim data from a study at Harvard Medical School/Harvard Pilgrim Health Care also have thus far failed to find a link between MCV4 and GBS.

That study population included 4.5 million 11- to 18-year-olds, of whom 8% had received MCV4 through May 2007.

Of 240 potential GBS cases identified in claims, just 100 had sufficient information to determine claim status, and 29 met the primary study end point definition. None had received MCV4—or any other vaccination—within 42 days.

"These are very reassuring data," said Dr. Baker, professor of pediatrics, molecular virology, and microbiology and head of pediatric infectious diseases at Baylor College of Medicine, Houston.

"The Harvard Pilgrim analysis has been completed. I am fairly certain we will have these data in June, and I hope that this will put to rest the GBS safety issue," she said in an interview following the meeting.

This has implications because in December 2007, the CDC recommended that a history of GBS be considered a "precaution" to administering MCV4 (MMWR 2007;56:1265-6).

The package label, meanwhile, was updated to list such a history as a "contraindication," Dr. Calugar said.

Dr. Baker stated that she had no disclosures to make. ■

Other Meningococcal Vaccination Issues

The meningococcal working group will present ACIP with information on the duration of protection of MCV4 and the introduction of a second meningococcal conjugate vaccine later this year, Dr. Baker said.

When Sanofi Pasteur's Menactra was recommended in 2005 for use in 11- to 12-year-olds as part of the adolescent vaccination visit, it was assumed that the vaccine would protect for at least 10 years, including the high-risk college years. However, "there were no data then and the 5-year data [now] suggest that 10 years may not be realistic. We hope to have more data in June," Dr. Baker said in an interview after the meeting.

The current recommendation for revaccination with the meningococcal polysaccharide vaccine is 3-5 years, and a revaccination recommendation may be necessary for MCV4 as well. "Meningococcal conjugate vaccines are unlikely to provide lifelong protection," she said during the meeting.

Later this year ACIP also is expected to hear immunogenicity data for a new quadrivalent meningococcal conjugate vaccine, Novartis's Menveo, which is expected to be licensed in the summer of 2009. Its composition is different from that of Menactra, and it is not known yet whether or how that might impact duration or degree of protection, Dr. Baker said in the interview.

Vaccine to More Contacts

HepA *from page 1*

In one instance, a 10-month-old nonjaundiced adoptee was the source of infection for 12 other nontraveling contacts, including 6 household members and 2 extended family members.

The proportion of hepatitis A–infected individuals who are asymptomatic is 70% among children younger than aged 6 years, compared with 20%-50% of infected children aged 6-17 years. The ACIP considered recommending vaccination of contacts of only those adoptees younger than 6 years, but ultimately voted to include contacts of adoptees in all age groups.

Countries of origin of international adoptees have shifted over the years. South Korea predominated in 1990, while Russia and China became more frequent sources of adopted children around 2000. Guatemala now has surpassed China, although the two each account for a little over 20%.

However, nearly all of the foreign countries from which Americans adopt children are endemic for hepatitis A, Dr. Chaves noted.

By statistical estimation, the risk of hepatitis A infection is approximately 106 per 100,000 close contacts of international adoptees in the United States, compared with the actual annual incidence of 1.2/100,000 in 2006 in the general population, Dr. Chaves said. ■

ACIP Updates Vaccine Storage Guidelines

BY MIRIAM E. TUCKER

ATLANTA — Clarifications to existing vaccine guidelines aimed at ensuring appropriate vaccine storage temperatures were approved by the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

The new language will be added to the "storage and handling" section of the committee's revised General Recommendations on Immunization, which were last published in 2006 (MMWR 2006;55[RR15]:1-48). The document is directed to providers who give many different vaccines on a daily basis, Dr. Andrew Kroger said at ACIP's winter meeting.

According to the current statement, "Refrigerators without freezers and stand-alone freezers (either manual defrost or automatic defrost) usually perform best at maintaining the precise temperatures required for vaccine storage, and such single-purpose units sold for home use are less expensive alternatives to medical specialty equipment." The new statement will add "and are preferable to combination units" to the end of that sentence.

The committee also approved language stating that new units may need 2 or more days of operation to establish a stable operating temperature after being set up, and that vaccine should not be stored in the unit until the appropriate temperature has stabilized.

Other language was "weakened" somewhat from the current statement with reference to situations in which a temperature problem can't be resolved, such as when the unit is unplugged or the door left open. The current statement advises that in such instances "a plan should be developed to transfer vaccine to a predesignated alternative emergency storage site." The new statement simply says that such a transfer "might be necessary."

The rationale for that change is that in certain environments, it might actually be dangerous for staff to enter. Moreover, external temperature monitoring may reduce the need for staff to enter the environment and open the door, and vaccine stability is enhanced if the door is not opened, noted Dr. Kroger of the CDC's immunization services division. ■