Number of Cases Low

Intussusception *from page 1*

er 16 underwent contrast enema reduction.

No intussusceptions have been reported in the 30 days following receipt of the 28,377 doses of RotaTeq administered in six of the eight large managed care organizations that constitute the CDC's Vaccine Safety Datalink (VSD), nor were there any intussusceptions reported among the 1,354 RotaTeq recipients who were followed in Merck's postlicensure surveillance through the second quarter of 2006, Ms. Haber said.

Dr. Patel, who presented a statistical interpretation of the data, said the background rate of intussusception in unvaccinated infants in the VSD was 32.4 per 100,000 infants per year. Another data source, the Healthcare Utilization Project (HCUP), yielded a similar background rate of 37.6 per 100,000 per year.

With use of the VSD background rate, the expected number of intussusceptions within the first 21 days after vaccination would be 52, and within the first week, 17, both greater than the VAERS reports of 17 and 11 cases, respectively.

By comparison, Wyeth-Lederle's RotaShield—the previous rotavirus vaccine that was withdrawn from the market in 1999 because of a proven link to intussusception—had 12 cases of intussusception occurring within 1-7 days after administration among just 1 million doses distributed.

Moreover, the reporting of intussusception was far less with that vaccine because the adverse event was not anticipated at that time. Since the experience with RotaShield, physicians are now on the alert for intussusception with rotavirus vaccine, and are therefore far more likely to report it, Dr. Parashar said.

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Dr. Manish Patel said actual intussusception rates from VAERS were less than expected using the VSD background rate.

On the other hand, the denominator used in making the calculations was the number of doses distributed, which is certainly more than the number actually administered. "The data are reassuring because they tell us that this is not the same thing as RotaShield, but they don't tell us that there's not a risk of smaller magnitude," he noted.

There are several differences between RotaTeq and the old RotaShield vaccine that should give some reassurance. Although both vaccines are human/animal genetic reassortments, the animal component of RotaTeq is bovine whereas RotaShield was rhesus derived. RotaTeq is associated with far lower rates of fever and viral shedding than was RotaShield. "If one of the possible mechanisms of intussusception is active viral replication and inflammation in the intestine, then one could suggest that [RotaTeq] would be less likely to cause that," Dr. Parashar pointed out.

Moreover, the premarketing safety studies for RotaTeq were much larger than were those done with RotaShield, with approximately 70,000 infants followed with RotaTeq, as opposed to about 10,000 with RotaShield. The RotaTeq safety studies were specifically powered to look for intussusception rates on a par with what had occurred with RotaShield.

The ACIP meeting took place the week after Merck had updated the precautions and adverse reactions sections of RotaTeq's label to include postmarketing data on intussusception and hematochezia.

At the same time, the Food and Drug Administration issued a "Public Health Notification" about the 28 intussusception cases that had been reported to VAERS through Jan. 31. That notification was widely reported by the lay media, often in an alarming tone. But the point of the notification was to urge more reporting, not to scare people, Dr. Parashar said.

Indeed, physicians are urged to report all cases of intussusception following receipt of RotaTeq to VAERS at 800-822-7967 or online at www.vaers.hhs.gov.

Merck is also continuing its postmarketing surveillance, and the CDC and FDA will continue to track intussusception rates within the Vaccine Safety Datalink.

Updates will be reported in the CDC's Morbidity and Mortality Weekly Report, Dr. Patel said. ■

Menactra Doesn't Appear to Raise GBS Risk, but Data Are Lacking

BY MIRIAM E. TUCKER
Senior Writer

ATLANTA — Data available thus far suggest that the overall risk for Guillain-Barré syndrome following receipt of the meningococcal conjugate vaccine is not significantly increased, Dr. Robert L. Davis reported at the winter meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

From July 2005 through January 2007, a total of 19 cases of Guillain-Barré syndrome (GBS) occurring within 6 weeks of vaccination with the meningococcal conjugate vaccine (MCV4/Menactra) were reported to the passive Vaccine Adverse Events Reporting System (VAERS). Another four confirmed cases of GBS in 13- to 19-year-olds who had received MCV4 more than 6 weeks prior to onset were not included in further analysis, said Dr. Davis, director of the CDC's Immunization Safety Office. The onset interval for the 19 analyzed cases was 2-33 days following immunization. Seventeen of the 19 were aged 11-19 years old. Information from the eight managed care organizations participating in the Vaccine Safety Datalink (VSD) indicates that approximately 94% of MCV recipients are 11-19 years old, he noted.

In the VSD Rapid Cycle Project from April 2006 through January 2007, there were no cases of GBS reported among vaccine recipients aged 11-19 years old within 6 weeks of vaccination. A total of 0-1 case was expected. However, "not finding any GBS after MCV4 vaccination in 11- to 19-year-olds does not offer substantial reassurance regarding MCV4 safety," Dr. Davis said.

The overall observed reporting rate for GBS after MCV4 vaccination in VAERS, 1.78 per million person-months, was not higher than expected. With two data sources, the VSD and the Healthcare Utilization Project (HCUP), the expected rates of GBS are 1.13 and 1.11 per million person-months, respectively. If these data accurately represent the true magnitude of increased risk after MCV4 vaccination, then there would be an excess of just 0.89 cases per million doses of MCV4 administered, Dr. Davis said.

However, there was a difference in rate ratio when vaccine recipients were divided by age, 11- to 14-year-olds vs. 15- to 19-year-olds: For the younger set, the observed vs. expected is 1.0/4.2, for a rate ratio of 0.25 when controlled for season. In contrast, among the 15- to 19-year-olds, the observed/expected ratio is 16/6.5, for a rate ratio of 2.48, again controlling for season. Seasonality plays a role by age, because the older group is more likely to receive MCV4 prior to school entry whereas the 11- to 14-year-olds are receiving it year-round, Dr. Davis pointed out.

The data are subject to major limitations. On one hand, the passive nature of VAERS means that underreporting is likely, which would raise the risk estimates. On the other hand, there were no surges in GBS cases reported to VAERS after any of the three notices published in the CDC's Morbidity and Mortality Weekly Report, which would be expected if underreporting were marked, he noted.

"Although there appears to be a small increased risk for GBS after MCV4 vaccination in the 15- to 19-year-old age category, the inherent limitations of VAERS require that these findings be viewed with caution," he said.

More data are needed. A larger study led by Harvard Pilgrim is expected to yield data regarding the risk for GBS following MCV4 in approximately 2 years, the length of time necessary to accumulate cases and attain sufficient statistical power.

Physicians should report any case of Guillain-Barré syndrome in a patient following receipt of Menactra to VAERS, at http://vaers.hhs.gov or by calling toll-free at 800-822-7967. ■

FDA Panel Selects 2007-2008 Influenza Vaccine Strains

GAITHERSBURG, MD. — The 2007-2008 trivalent influenza vaccine should retain two strains from the current vaccine and change one strain, a Food and Drug Administration advisory panel voted on Feb. 28.

The Vaccines and Related Biological Products Advisory Committee followed the lead of the World Health Organization, which made its recommendations for a Northern Hemisphere winter vaccine a week earlier. The FDA usually follows its panel's advice.

The decision gives the green light to manufacturers to go ahead with production. It generally takes until July or August for vaccine makers to complete testing, acquire FDA approval, and begin packaging their product. Distribution usually starts in September and ends by Nov. 1.

The WHO recommended keeping the current H3N2 strain, which is the A/Wisconsin/67/2005-like virus. The 2006-2007 flu season had been dominated mostly by influenza A (H1N1) strains, said Nancy J. Cox, Ph.D., director of the Centers for Disease Control and Prevention's influenza division. But in February, it appeared that H3N2 strains were starting to dominate. It wasn't clear yet which of those might be the predominant H3 strain, she said.

Even though panelists were concerned about the emergence of a new H3N2 subtype, 11 of 13 members voted to keep the current H3 strain. "At this point, I feel like we don't have any choice," said Dr. Melinda Wharton, deputy director of the CDC's National Immunization Program and a temporary voting member of the committee. She noted that manufacturers already had started production on the current H3 strain.

Two committee members said they wanted to defer a decision until more surveillance data were available.

The panel voted unanimously to change the current H1N1 strain from A/New Caledonia/20/99-like virus with A/Solomon Islands/3/2006. The WHO had recommended that change. The FDA committee also voted unanimously to retain the current B strain—B/Malaysia/2506/2004-like virus—mirroring the WHO recommendation.

The 2006-2007 season has been fairly mild, said Ms. Cox. As of Feb. 17, widespread flu activity was reported in 24 states, 14 states reported regional activity, 10 reported local activity, and 2 reported sporadic activity. There were 3 pediatric deaths during that week, bringing the total to 15 deaths since the season began Oct. 1, 2006.

—Alicia Ault