Greater Risk Seen in Older Teens

Guillain-Barré *from page 1*

of the CDC's National Center for Immunization and Respiratory Diseases, suggests that even if the association is real, it is outweighed by the risk of contracting meningococcal disease without the vaccine.

The CDC and the Food and Drug Administration had previously alerted health care providers about a possible association between GBS and the tetravalent meningococcal conjugate vaccine (MCV4), which is marketed as Menactra by Sanofi Pasteur Inc.

Five cases were reported in an October 2005 alert, and three cases in an April 2006 notice. Since then, an additional nine cases have been reported to the Vaccine Adverse Reporting System (VAERS), bringing to 17 the total number of reported cases since the MCV4 vaccine became available in March 2005.

The onset interval for the 17 cases ranged from 2 to 33 days after vaccination, with a mean of 15.7 days, Dr. Davis said.

Further analysis was restricted to the 15 patients aged 11-19 years, because 94% of MCV4 recipients are in that age range (the other 2 patients were aged 30 and 43 years).

A total of 5.9 million doses of MCV4 have been distributed to individuals in that age group.

Compared with the observed GBS rate of 0.2 cases per 100,000 person-months for those vaccinated, data from two separate databases (the Healthcare Cost and Utilization Project and the Vaccine Safety Datalink) both yielded an expected background relative risk for GBS of 0.11 per 100,000 person-months.

"There is evidence for a small increased risk of GBS after MCV4. The timing of neurologic symptoms within 1-5 weeks of vaccination among reported cases is of concern," Dr. Davis said.

He added, "Substantial uncertainty exists regarding the risk estimate, using either the HCUS or VSD background incidence rate." Underreporting is assumed with the VAERS, a passive reporting system, but no surges in GBS reports occurred following either of the previous MMWR notices, he said.

Older teens get the vaccine in the summer before college, which is the season for *Campylobacter jejuni*, a frequent antecedent to GBS.

The increased risk appears confined to older adolescents, with a relative risk of 0.27 per 100,000 person-months among those aged 11-14 years (based on one case out of 2.5 million doses distributed), compared with 2.55 per 100,000 person-months in the 15- to 19-year-old group (14 cases among 3.5 million doses).

Dr. Ban Mishu Allos, an ACIP member from the department of infectious diseases at Vanderbilt University, Nashville, Tenn. noted that many of the older adolescents would likely have received the vaccine prior to the start of college classes during the summer, which happens to be the season for *Campylobacter jejuni* infection, a frequent antecedent to GBS. The younger teens, in contrast, would be more likely to receive the vaccine at other times of the year as well.

No patient had reported diarrheal prodromes, and none of the four individuals tested for campylobacter was positive. However, the infection is often asymptomatic, and the organism would not be detected in stool by the time GBS symptoms appeared, Dr. Allos remarked.

Dr. Cho's analysis compared the health outcomes of vaccination versus no vaccination in the birth cohort of 11-year-olds, which includes 4,076,600 individuals. Among the assumptions were that the risk for GBS lasts 6 weeks after vaccination, and that an 11-year-old has a life expectancy of 67.7 more years.

Parameters included a 5% morbidity rate among adolescents with GBS, which overall carries a favorable prognosis (Lancet 1998;352:635-41).

Meningococcal disease, on the other hand, has a case-fatality rate of 10%. Incidence of disease caused by one of the vaccine's serogroups (A, C, Y, and W-135) is 0.77 per 100,000 unvaccinated individuals, of which the vaccine prevents 93%. With those and other published and unpublished data, Dr. Cho calculated that the vaccine prevents 163 cases of meningococcal disease and 16 deaths due to a vaccine strain for every 3 additional cases of GBS.

These data are subject to many limitations and should be considered preliminary.

But they do suggest that "the period of risk of vaccine-attributable GBS is small and short [compared with] the prolonged benefit of meningococcal disease prevention," Dr. Cho said.

Dr. Michael D. Decker, vice president of scientific affairs at Sanofi Pasteur, said his company is supporting a study to further investigate the issue over a 2-year period in the 11- to 17-year-old population in an HMO database of over 100 million covered lives. "We believe there is enough power to clarify the association," he said in an interview.

The CDC also is continuing to evaluate the issue. ■

Clinicians are requested to report adverse events related to the MCV4 vaccine by going to www.vaers.hhs.gov, sending a fax to 877-721-0366, or calling 800-822-7967.

A Vaccine Information Statement and fact sheet with information on the vaccine and reported GBS cases are available at www.cdc.gov/nip/publications/vis/default.htm, and an updated fact sheet for health care workers is available at www.cdc.gov/nip/vacsafe/concerns/gbs/menactra.htm.

Christine Kilgore contributed to this report.

Menactra Supply Restored; Resume Routine Vaccination

Atlanta — Supply problems with the tetravalent meningococcal conjugate vaccine have been resolved, and routine vaccination of 11- to 12-year-olds should be resumed.

That recommendation from the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices was discussed at the committee's fall meeting and published the following week (MMWR 2006;55:1177).

The supply problem was announced in May of 2006, with Sanofi Pasteur's estimation that demand for Menactra would outpace the supply at least through the summer.

At that time, the CDC, in consultation with the American Academy of Pediatrics, the American Academy of Family Physicians, the American College Health Association, and the Society for Adolescent Medicine, recommended deferral of routine use of the vaccine in 11- to 12-year-olds (MMWR 2006;55:567-8).

Vaccination with MCV4 was to continue in other high-risk groups, including adolescents at high school entry who have not previously received the meningococcal conjugate vaccine, college freshmen living in dormitories, and other individuals—such as military recruits, travelers to endemic areas, microbiologists routinely exposed to *Neisseria meningitidis*, and certain immunocompromised individuals—who are at high risk for meningococcal disease.

More than 6 million doses of Menactra had been distributed by the end of September, according to the CDC.

Now, an additional 3.5-4.5 million doses are projected to be distributed through March of 2007, enough to allow a return to routine immunization of 11- to 12-year-olds and continuation in all the other recommended groups, said Dr. Gregory S. Wallace, chief of the CDC's Vaccine Supply and Assurance Branch.

—Miriam E. Tucker

Anticoagulation for Pediatric Stroke Not Associated With Hemorrhage

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

Pittsburgh — Anticoagulant therapy is appropriate for children with arterial ischemic stroke, since the rate of intracranial hemorrhage in treated patients is low, Dr. Adam Kirton said in a poster presented at the annual meeting of the Child Neurology Society.

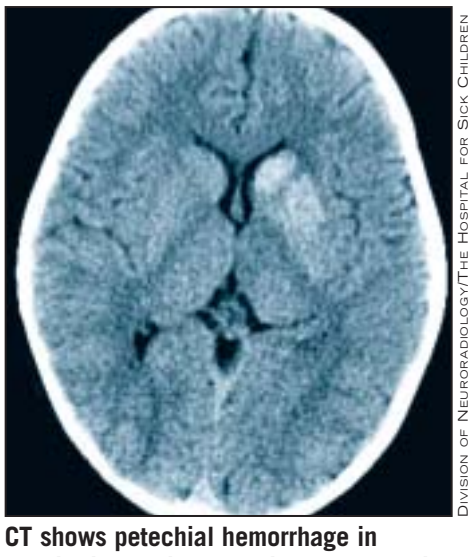
"Our study suggests that intracranial hemorrhage in children with arterial stroke treated with anticoagulation is infrequent and usually very mild in severity," Dr. Kirton said in an interview.

"The findings add important safety data to support current consensus guidelines recommending the use of anticoagulation in children with stroke."

His study, carried out in collaboration with the thrombosis program at the Hospital for Sick Children in Toronto, included 126 children younger than 18 years who were treated with anticoagulation therapy for acute arterial ischemic stroke.

Sixteen patients (13%) experienced intracranial hemorrhage, said Dr. Kirton, of the Children's Stroke Program at the Hospital for Sick Children in Toronto. All of the bleeds occurred within 24 days of the stroke diagnosis, with a mean time to bleed of 11 days (range 2-24 days). "This suggests a fixed period of vulnerability," Dr. Kirton said.

Most of the bleeds (10) were asymptomatic. In the six symptomatic bleeds, symptoms were irritability (three), headache and vomiting (one), loss of consciousness (one), and dysarthria (one).



Division of Neuroradiology/The Hospital for Sick Children

CT shows petechial hemorrhage in arterial ischemic stroke in basal ganglia.

Treatment regimens in patients with bleeding included low-molecular-weight heparin (five patients); unfractionated heparin (four); warfarin alone (one); warfarin plus low-molecular-weight heparin (two); warfarin plus unfractionated heparin (two); low-molecular-weight heparin plus aspirin (one); and unfractionated heparin plus aspirin (one).

Three of the children with bleeds died—two from cardiac causes and one who had preexisting promyelocytic leukemia.

Congenital heart disease significantly increased the risk of an intracranial bleed on anticoagulant therapy.

Bleeds occurred in 26% of the 38 children with congenital heart disease, but in only 7% of those without it.

A larger study of intracranial bleeding in pediatric stroke comparing treated with untreated patients will help confirm the spontaneous occurrence of bleeding and further support the safety of this important therapy. ■