

# New Data Find No Link Between Menactra, GBS

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 sug-



**Interim data from a study of 4.5 million 11- to 18-year-olds also failed to find a tie between MCV4 and GBS.**

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gested a small increased risk for Guillain-Barré syndrome after receipt of MCV4 (Menactra). 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. 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 that provides data from 8.8 million members annually.

Between April 2006 and February 2009, 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 after 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.

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, 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.

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

# HPV Vaccine May Not Increase Guillain-Barré Syndrome Risk

BY KERRI WACHTER

The human papillomavirus vaccine does not appear to increase the risk of developing Guillain-Barré syndrome, despite isolated reports of the condition following vaccination, a study shows.

"I found that there's some overlap between the incidence of Guillain-Barré in the general population and Guillain-Barré after vaccination with Gardasil," Dr. Nizar Souayah said in an interview. However, he and his colleagues have not found Guillain-Barré to occur more often among those who have received the HPV vaccine than among people in the general population.

Dr. Souayah will present the study at the American Academy of Neurology annual meeting in Seattle, April 25–May 2. The data were released early.

The Food and Drug Administration approved the vaccine in 2006 for use in girls and women aged 9-26 years to prevent infection against HPV strains 16 and 18, which cause most cervical cancers, and strains 6 and 11, which are responsible for most genital warts in the United States. Since the approval of Gardasil, more than 16 million doses have been given. There have been isolated reports of Guillain-Barré syndrome (GBS) after receiving the vaccine.

Dr. Souayah and his colleagues used data from the Vaccine Adverse Event Reporting System, which is a cooperative program for vaccine safety of the Centers for Disease Control and Prevention and the FDA.

The system is a postmarketing safety surveillance program that collects information about adverse events that occur after the administration of U.S. licensed vaccines. ■

Dr. Souayah searched the database using the key words: "Guillain," "Barré," "Guillain-Barré syndrome," "numbness," and "tingling." He identified roughly 350 patients, then reviewed the data for each of these patients and characterized them as highly likely to have GBS, highly unlikely to have GBS, and unclear. He and his colleagues included in this analysis only those patients considered to be highly likely to have GBS.

They found 36 reported cases of GBS after vaccination with the HPV vaccine between 2006 and 2008. The mean age was 17 years. The estimated incidence of GBS after vaccination is 7 cases per million vaccinations. In comparison, the estimated incidence for the general population is 4-10 cases per million individuals.

"The most striking data [are] that most of the [GBS] cases occurred within 6 weeks of vaccination," said Dr. Souayah, of the departments of neurology and neurosciences at the University of Medicine and Dentistry of New Jersey, Newark. The onset of GBS occurred within 6 weeks of vaccination in 75% of the individuals for whom the vaccination date was known.

"Our results show that Guillain-Barré is not occurring more often after HPV vaccination than it does in the general population. However, the fact that most of these cases occurred within 6 weeks of vaccination does warrant careful monitoring for any additional cases and continued analysis," he said in a statement.

He urged caution in interpreting the results. The database may not contain all cases of GBS after administration of the HPV vaccine; alternatively, the database might contain cases that were not confirmed. "I would like to emphasize that we need more research," he said. ■

# 'Definitive' Study: VZV Shot Not Tied to Ischemic Stroke

BY JEFF EVANS

Vaccination with live, attenuated varicella zoster virus was not associated with an increased risk of ischemic stroke in pediatric patients in the year after they received their vaccination, a retrospective, population-based study of children registered in the Vaccine Safety DataLink shows.

The study is the first to systematically examine the association between varicella zoster virus (VZV) vaccination and ischemic stroke. In previous studies, infection with the wild-type VZV has been associated with ischemic stroke in adults after herpes zoster ophthalmicus and in children after primary infection with the virus (chickenpox). Suspicion of an association between varicella vaccination and ischemic stroke initially arose because of case reports of children with signs and symptoms of ischemic strokes who had been vaccinated with live, attenuated VZV.

In the study of about 3.25 million children who were members of eight medical care organizations that participate in the Centers for Disease Control and Prevention's Vaccine Safety DataLink project, strokes were diagnosed in a significantly lower percentage of children who received at least one varicella vaccination than in those who did not receive the vaccine (0.003% vs. 0.008%), James G. Donahue, D.V.M., Ph.D., of the Marshfield (Wis.) Clinic Research Foundation and his colleagues reported (Pediatrics 2009;123:e228-34).

Although unvaccinated children had a significantly older mean age than did vaccinated children (7.9 years vs. 1.9 years), because the vaccine was not widely distributed until the late 1990s, adjustment for age did not alter the results of the analysis.

Dr. David Kimberlin, a member of the American Academy of Pediatrics Committee on Infectious Diseases who

specializes in varicella, called the study "definitive." The results show that "using the varicella vaccine can save lives and morbidity among survivors who would have gotten chickenpox, anyway."

The study "really shows the power of the Vaccine Safety DataLink. It is a phenomenal means by which complications of vaccinations can be assessed, and in this case, ruled out," Dr. Kimberlin of the division of pediatric infectious diseases at the University of Alabama, Birmingham, said in an interview. He was not involved in the study.

The study included children older than 11 months but younger than 18 years, excluding those diagnosed with infantile cerebral palsy or those who were diagnosed before 11 months of age with stroke, hemiplegia, or hemiparesis. The investigators said that they analyzed the 12 months after vaccination because "reports have suggested that the incidence of stroke rarely exceeds 1 year after VZV infection." ■

Within the study period of 1991-2004, the investigators identified 39 children with an inpatient diagnosis of ischemic stroke out of roughly 1.14 million children in the cohort who had received at least one varicella vaccination, compared with 164 diagnoses of stroke in unvaccinated children.

There was no evidence of temporal clustering of the 39 patients who had strokes after vaccination. The risk of stroke was not significantly elevated at any point in time during the 12-month period after vaccination.

The study was funded entirely by the Centers for Disease Control and Prevention.

Three of the investigators reported that they served as a consultant to or received research support from Merck Pharmaceuticals. One of these investigators also has received research support from Novartis, GlaxoSmithKline, Sanofi Pasteur, and MedImmune. ■