

ID CONSULT

Postvaccination Adverse Events

It's important to keep an open mind when a parent informs you that his or her child has experienced an adverse event following vaccination.

Determining which adverse events are caused by a vaccine and which are mere coincidental associations can be very difficult. As physicians who administer vaccines to children, one of the most important contributions we can make is to report all postimmunization adverse events to the Vaccine Adverse Events Reporting System (<http://vaers.hhs.gov/index>). The VAERS helps authorities spot events that require follow-up with appropriate studies to determine causality. In general, the Centers for Disease Control and Prevention requires an event to occur within 42 days following immunization to be considered biologically plausible.

The best information we have comes from studies that compare population-based rates of a specific event with the postimmunization rates to see if there is a significant difference. Alternatively, case-control studies can identify whether the odds ratio for receipt of a vaccine is increased among cases. Unfortunately, such studies have been done for only a fraction of all reported postvaccination adverse events.

I'd like to highlight a few prominent adverse events that have been reported following immunization. Some, although unusual, have been causally linked to vaccines. Others, particularly certain severe neurologic outcomes, do not appear to be linked although monitoring continues.

► **Thigh swelling and the DTaP vaccine.** This one is fairly well established. Often confused with cellulitis, swelling of the entire arm or leg following receipt of the diphtheria-tetanus-acellular pertussis (DTaP) vaccine is reported in nearly 2% of all children following the fourth dose, with rates and severity increasing with each successive DTaP dose (Pediatr.

Infect. Dis. J. 2008;27:464-5).

However, unlike cellulitis, it is rarely associated with fever or other systemic symptoms, is localized to the vaccinated limb, and usually resolves completely within 48 hours. Although the swelling is likely to occur again with subsequent doses, both the CDC's Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics recommend that the child receive all recommended DTaP doses following appropriate counseling of the parents.

► **Hair loss and the hepatitis B (and other) vaccines.** There have been 60 case reports of hair loss (alopecia) following receipt of vaccines, 46 of them

associated with the hepatitis B vaccine. These included 16 in which the hair grew back but then fell out again after re-vaccination. Nine of the patients reported previous medication allergy (JAMA 1997;278:1176-8). This appears to be a true causal effect, although rare considering the tens of millions of hepatitis B doses given over the last decades. But in a small number of genetically predisposed children – most of them female – there does appear to be biological plausibility because hair loss has recurred with second dose and is further supported by the several case reports of alopecia in chronic active hepatitis B viral infection patients.

► **Idiopathic thrombocytopenic purpura and MMR vaccine.** This link is probably also causal. One study utilizing immunization and hospital admission records demonstrated an absolute risk of one case in every 22,300 doses within 6 weeks of MMR vaccination (Arch. Dis. Child. 2001;84:227-9). Another study, which attempted to control for the effect of viral infections, found a similar idiopathic thrombocytopenic purpura (ITP) risk of about 1 in 30,000 MMR immunizations. That population-based analysis of 506 consecutive pediatric ITP patients also found that the thrombocytopenia dis-

appeared within a month in 74% of patients and lasted longer than 6 months in only 10% (Vaccine 2007;25:1838-40).

► **Myocarditis after vaccination.** Inflammatory myocarditis was reported in 10 of approximately 240,000 military recipients of the smallpox vaccine and in 2 additional civilian cases during the widespread prevent immunization program in 2001. Although it was not definitively linked to the vaccine, ACIP nonetheless recommended that those with heart disease or at risk for it should not receive the vaccine (MMWR 2003;52:282-4).

In children, there have been two reported cases of myocarditis following immunization, one following the hepatitis B vaccine in a previously healthy 12-year-old girl, the other after receipt of meningococcal C conjugate vaccine in a 14-year-old boy. Both showed eosinophilic infiltrates on myocardial biopsies, consistent with an allergic reaction to the vaccine (Pediatr. Infect. Dis. J. 2008;27:831-5). I think the jury is still out on this one. Certainly if you see a case, be sure to report it to VAERS.

► **Acute disseminated encephalomyelitis and vaccination.** These reports have been coming in since the 1970s, for a variety of different vaccines. Examples include Guillain-Barré syndrome (GBS) following the *Haemophilus influenzae B* conjugate vaccine (Eur. J. Pediatr. 1993;152:613-4), central nervous system inflammatory demyelination following hepatitis B vaccination (Neurology 2009;72:2053), and transverse myelitis with oral polio vaccine (J. Paediatr. Child Health 2006;42:155-9).

Without knowing the background rates of these neurologic complications among unvaccinated individuals, it is impossible to ascertain causality. An excellent data analysis conducted by Dr. Steven Black and colleagues provided very helpful estimates of the numbers of specific severe adverse events that would be expected following receipt of the 2009 H1N1 influenza vaccine.

Based on background rates, they determined that within 6 weeks of vaccination there would be 21.5 coincident cases of

GBS per 10 million vaccine recipients, and 86.3 cases of optic neuritis per 10 million female vaccinees. Spontaneous abortions would occur in 16,684 of every 1 million vaccinated pregnant women, and sudden death within 1 hour of any symptom onset in 5.75 of every 10 million people vaccinated (Lancet 2009;374:2115-22).

Another important analysis was conducted by the CDC to determine whether 33 reported cases of GBS in 11- to 19-year-olds within 42 days of receipt of meningococcal conjugate vaccine were causally linked. Background data from the 2000-2004 Healthcare Cost and Utilization project estimated that there would be very close to 36 cases for the entire age cohort, suggesting there was no causal link. However, just 20 cases would be expected among 15- to 19-year-olds, but the actual number was 26.

Although not statistically significant, this difference was enough to merit continued monitoring by the CDC, which advised that children with prior GBS not receive the vaccine (MMWR 2006;55:364-6).

Finally, a population-based case-control study from France investigated cases of acute disseminated encephalomyelitis, optic neuritis, and transverse myelitis in children younger than 16 years of age between 1994 and 2003, using 12 controls per case matched for age, sex, and geographic location. Rates of hepatitis B vaccination were 24% in cases and 27% in controls, for an adjusted odds ratio of 0.74 (Neurology 2009;73:1426-7). One might conclude from this that hepatitis B vaccine is actually protective, but the result was not statistically significant. ■

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CDC Encourages Flu Shots Before the Season Worsens

BY JANUARY W. PAYNE

The Centers for Disease Control and Prevention is warning Americans to get vaccinated against influenza before the season kicks into high gear.

"Don't be fooled by the past few months. Flu is coming," Dr. Anne Schuchat, director of the National Center for Immunization and Respiratory Diseases at the CDC, said at a Dec. 3 media briefing. "And in most years, flu is most active in the winter months." Last season was unusual, she said, because "by this time a year ago, we'd already

seen a tremendous amount" of influenza due to the H1N1 virus. But in a typical season, influenza is most intense between January and March.

"Sharp increases" in influenza activity have been seen in the southeastern United States, Dr. Schuchat said, especially in Georgia and particularly among school-age children.

In the Southeast, where Georgia was the only one of the region's eight districts to report data, 19.3% of outpatient visits for influenza-like illness yielded positive tests for flu virus. The good news, Dr. Schuchat said, is

that the circulating strain appears to be a good match to 'the influenza B strain contained in this year's seasonal flu vaccine. CDC



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DR. SCHUCHAT

regional surveillance data are current for the past 3 weeks.

More than 12,000 people died

from the 2009 H1N1 virus. This year, there has been at least one pediatric death from influenza, she said. Because of the potential for severe illness and death, it is that much more important to encourage people to get this year's seasonal influenza vaccine, which contains strains of the 2009 H1N1 A virus, the H3N2 influenza A virus, and influenza B, officials said.

A CDC telephone survey indicated that some people – but not all – have heeded the

agency's message for everyone with the exception of children under 6 months old to get vaccinated. The agency surveyed approximately 38,000 adults and 9,100 children through the second week of November, and found that about 33% of respondents reported having gotten vaccinated. About two-thirds reported getting vaccinated at a doctor's office, clinic, or hospital; about 16% were vaccinated at a supermarket, retail, or pharmacy clinic; and about 18% were vaccinated at their workplace or school, Dr. Schuchat said. ■