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No Vaccine-Autism Link in Feds' Ruling

I would like to clear up some of the confusion surrounding a recent federal government ruling that vaccines might have contributed to autismlike symptoms in a child with underlying mitochondrial disorder. The media have portrayed this as an acknowledgment of a link between vaccines and autism, and that simply isn't the case.

The story broke on the Internet blog of journalist David Kirby, the author of a book promoting the theory that the thimerosal preservative in vaccines is linked with autism. He obtained a copy of the ruling from an unnamed source and posted it on the Internet. The family of the child then spoke publicly about the case at a press briefing sponsored by an autism advocacy group.

The document was evidently issued last November by an official in the Department of Justice who wrote that medical personnel at the Department of Health and Human Services' Division of Vaccine Injury Compensation (DVIC) had reviewed the case and "concluded that compensation is appropriate."

The case involves a 9-year-old girl who, at 18 months of age, received five different vaccines on the same day and in the following months began exhibiting abnormal symptoms deemed to be "regressive encephalopathy with features consistent with an autism spectrum disorder." Subsequent evaluation led to the diagnosis of a previously unrecognized underlying mitochondrial disorder.

At this writing, the federal Health Resources and Services Administration (HRSA), which administers the Vaccine Injury Compensation Program through which this case was reportedly filed, could not confirm any of the information reported because the agency had not yet received written consent from the family to do so.

However, HRSA said in a statement that "HRSA has maintained and continues to maintain the position that vaccines do not cause autism, and has never concluded in any case that autism was caused by vaccination."

But that hasn't stopped the media reports, which have caused a great deal of concern and confusion among the public and the medical community. According to the document, "DVIC has concluded that the facts of this case meet the statutory criteria for demonstrating that the vaccinations [the child] received on July 19, 2000, significantly aggravated an underlying mitochondrial disorder, which predisposed her to deficits in cellular energy metabolism, and manifested as a regressive encephalopathy with features of autism spectrum disorder."

See related editorial on page 24.

First of all, note that this report is not talking about the disorder "autism." Indeed, children with mitochondrial disorders, which produce severe deficits in cellular energy metabolism, often develop regressive encephalopathy and features of autism spectrum disorder such as loss of language skills and impaired motor coordination.

Such manifestations are more likely to occur in those with mitochondrial disorders when there is a physiological stressor such as a viral or bacterial illness. Therefore, it is plausible that receiving five vaccines in 1 day also could provoke the same outcome.

Is that stress equivalent to influenza or a cold? We don't know, but anything that perturbs the balance of energy metabolism in these children is likely to have an adverse impact. Therefore, we could argue that these children *should* be vaccinated to prevent more severe illness.

Note, too, that the ruling does not mention thimerosal, the vaccine ingredient—now removed from nearly all childhood vaccines—that many activists have claimed causes autism.

In February, my colleagues and I published a study in which we showed that the measurement of blood levels of methylmercury from fish used to make nearly all recommendations pertaining to safe levels of mercury exposure were completely inaccurate for risk assessments of children who received vaccines containing thimerosal.

The recommendations in 1999 by the American Academy of Pediatrics and others were based on toxicology data in adults regarding the oral consumption of methylmercury, as would occur from eating fish. Compared with the blood half-life of about 45 days associated with methylmercury from fish consumption, the half-life of intramuscular ethyl mercury from thimerosal in vaccines in infants is substantially shorter, at a mean of 3.7 days with a return to baseline by 30 days post vaccination (Pediatrics 2008;121:e208-14).

Unfortunately, the antivaccine claims are unlikely to abate until more is known about what really does cause autism. Several reports in the literature have documented an association between mitochondrial disorders and similarities to autism spectrum disorders, but none have shown a direct connection.

On the other hand, there is increasing evidence that autism is an inherited disorder. In one interesting example, new data from 751 families with autism participating in the Autism Genetic Resource Exchange point to a novel, recurrent gene microdeletion and a reciprocal microduplication that are associated with substantial susceptibility to autism, and appear to account for approximately 1% of cases (N. Engl. J. Med. 2008;358:667-75).

I suspect we will see more evidence of genetic markers for autism in the future.

In the meantime, I hope that clinicians will view the situation of this particular child as a sad but isolated case. Mitochondrial disorders are extremely rare—I have never seen one in my 20-plus years of practicing general pediatrics. And even among these patients, the benefits of vaccination still likely outweigh the risks.

Thimerosal has now been removed from all childhood vaccines except for multidose influenza vaccines, but the rates of autism have not abated, thus providing very strong epidemiologic evidence that thimerosal did not cause the upswing in autism spectrum disorder diagnoses that began in the 1990s and still continues. The antivaccine folks have begun switching their argument to say that it is multiple vaccines that cause autism and other neurodevelopmental problems by "overwhelming" the immune system.

In an effort to quantitate that, current research is looking at the effect on the immune system when a healthy child becomes colonized with common bacteria such as *Streptococcus pneumoniae*. Thus far, we know that the immune "stress" associated with asymptomatic nasal colonization is quite a bit greater than that of the purified vaccines given to children today.

Infectious diseases are "stressful" to the immune system. Vaccines are not risk free, but they induce far less "stress." We need to inform our patients and their families that while everything has some risk, the real question is risk versus benefit. From that perspective, vaccines are the clear winners.

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Longer Needle, Thigh Site Better for Fifth DTaP Vaccination

BY JOHN R. BELL
Associate Editor

Use of a 25-mm needle was associated with less risk of redness and pain than was use of a 16-mm needle among children receiving their fifth diphtheria-tetanus–acellular pertussis vaccine, according to results from a prospective randomized trial.

The results also suggested that the thigh should be considered as the site for the fifth injection, the investigators reported.

Dr. Lisa A. Jackson of the epidemiology department of the University of Washington, Seattle, and colleagues reported results from 1,315 pediatric patients (median age 54 months) in a study funded by Sanofi-Pasteur Inc.

Most (1,174 patients) received the vaccination in the arm; 141 were injected in the thigh. Among those injected in the arm, there was a significantly greater proportion with any injection-site redness (76%) among the 381 on whom a 16-mm needle was used than there was among the 793 patients on whom the 25-mm needle was used (65%).

Swelling was also significantly less common among patients injected in the arm with the longer versus the shorter needle (reported in 67% and 55%, respectively), as was pain (61% vs. 53%).

Both practices are consistent with guidelines of the American Academy of Pediatrics and the CDC's Advisory Committee on Immunization Practices.

The same trend was seen for each reaction among patients injected in the thigh, but the differences did not reach significance (Pediatrics 2008;121;e646-52).

Relative risks adjusted for age, gender, and body mass index (BMI) showed that the risk for several localized reactions was less when the injection site was the thigh, rather than the arm, especially redness (relative risk 0.63) and swelling (RR 0.53).

"Together these findings suggest that a 16-mm needle should not be used for administration of the fifth DTaP vaccine injections and that vaccination in the thigh is an option that may be considered by parents and providers who would like to decrease the risk of local reactions characterized by redness and swelling," they wrote, adding that these findings are consistent with those of similar studies in the literature.

Both practices are consistent with guidelines from the American Academy of Pediatrics and the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices, they noted.

The investigators cautioned that neither the needle length nor the injection site was randomized, and that the latter factor seemed to correlate with the size of the child.

However, their analyses did control for BMI. "In analyses restricted to children with a BMI of 14.50 to 16.79 kg/m^2 (which represented the majority of children in both the arm and thigh groups) who were vaccinated with a 25-mm needle, reactions characterized by redness were more common in children vaccinated in the arm," they said.

Dr. Jackson has served as a consultant to Sanofi Pasteur in the past and is on the speakers' bureau for Sanofi Pasteur.

She has also received research funding from Wyeth Pharmaceuticals, ID Biomedical Corp., GlaxoSmithKline Inc., and Novartis, and has served as a consultant to Wyeth and Novartis.