Universal Flu Shots Will Warrant All Hands on Deck

BY KATE JOHNSON
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TORONTO — Alternative settings, such as schools, should be considered if universal influenza vaccination is recommended for all U.S. school-age children, Dr. Cynthia Rand said in a poster presentation at the annual meeting of the Pediatric Academic Societies

"Kids aged 6-18 years haven't yet had a recommendation for universal influenza vaccination, but we're expecting this recommendation in the flu season of 2008," Dr. Rand of the University of Rochester (N.Y.) said in an interview.

In the study, she calculated that more that 41.5 million extra visits to pediatric offices would be needed annually to meet the increased demand.

Although the emergency department has been suggested as a potential site for universal influenza vaccination (UIV), a related study found the added value of this delivery site would be "modest," at least from a public health perspective, her colleague Christina Albertin, also of the university, reported in another poster.

With data from the 2003-2004 Medical Expenditure Panel Survey (MEPS), Dr. Rand's study calculated the number of well-child and other primary care visits for 4,161 children. From this she estimated the number of extra visits between October and January that would be required for influenza vaccination. It was assumed that children under 9 years would need two visits rather than one visit, if it was their first influenza vaccine.

There are new updated American Academy of Pediatric recommendations that first timers who failed to get their two flu shots should get two for the following year; this would boost the number of visits still further, she commented (Pediatrics 2007;119:846-51).

By focusing specifically on the 6- to 18-year-old age group that is expected to be captured in new UIV guidelines, the study found that for children under 9 years, 33% would need one extra visit and more than 50% would need two—accounting for 16 million additional visits. For 9- to 18-year-old children and teens, 73% would need one extra visit, accounting for more than 25 million additional visits. In total, the 6- to 18-year-old age group would require 41.5 million extra visits to pediatricians during the influenza vaccination period, assuming no missed opportunities for vaccination and that 20% of the population had been vaccinated in a prior season.

'Give vaccines early in time to deliver a second dose before outbreaks occur.'

DR. RAND

Individuals who are black, Asian, uninsured, or living in poverty are more likely to need additional visits, she added. The numbers are overwhelming, underscoring the need for new delivery systems, said Dr. Rand. "School-based systems would require a lot of coordination because school nurses would also be overwhelmed. They would need help from the public health infrastructure."

Emergency departments (EDs) have been discussed as another possible vaccination delivery site, but the benefits of implementing an ED delivery system are unclear, Ms. Albertin said in an interview.

With data from the MEPS (2002-2004), her study analyzed the number of ED visits from a sample of 10,073 children aged 6 months to 18 years between October and December, and calculated how many of them had also had a primary care visit during that period.

"Overall 3.7% of the children had an ED visit, and about half of them had no primary care visit during that time period, and therefore might have benefited from being vaccinated in the ED," she said. Although it's a small percentage of the population, it represents half of the pediatric ED population, suggesting that the benefits of an ED vaccine delivery system may be debatable, she said.

"Of course, EDs are busy places, and vaccination probably won't happen consistently, but is 1.9%—that's the percentage who didn't have a primary care visit—enough to start pushing for vaccination in the ED or not?" she asked.

While many pediatricians have been strong supporters of primary care vaccination, without reliance on the ED, Dr. Rand's study suggests perhaps multiple options will be needed.

In the meantime, "we need to avoid missed opportunities in primary care; give vaccines early in time to deliver a second dose before outbreaks occur; [and] continue vaccinating until the vaccine supply runs out to allow a wider vaccination interval. … Black, Asian, uninsured, and impoverished patients may need focused outreach," she said. ■

EXPERT COMMENTARY

Combination Vaccines: Simpler or More Complex?

Combination vaccines make life easier for our patients. But until the payment and regulatory issues are resolved, the same is not true for us.

In January, the Food and Drug Administration's Vaccines and Related Biological Products Advisory Committee endorsed the overall safety and efficacy of Sanofi Pasteur's Pentacel, a combination vaccine containing diphtheria, tetanus toxoid, and acellular pertussis (DTaP), inactivated polio (IPV), and *Haemophilus influenzae* type b (Hib). If approved, that vaccine will compete with GlaxoSmithKline's Pediarix, which contains DTaP, IPV, and hepatitis B antigens.

BY MICHAEL E. PICHICHERO, M.D.

Infants given a dose of hepatitis B (HB) vaccine at birth and then Pentacel at 2, 4, and 6 months of age would not be receiving an extra dose of HB vaccine, as they would with Pediarix. Some see this as an advantage to Pentacel, but my colleagues and I showed that the extra HB dose was not a problem in terms of reactogenicity or immunogenicity, even though it resulted in considerably higher anti-HB levels (Pediatr. Infect. Dis. J. 2002;21:854-9).

Pediarix is now widely used in the public sector through the Vaccines for Children Program. In that setting, it has resulted in improved immunization rates and reduced errors. But the private sector has been slower to adopt Pediarix, and I predict that the same will be true of Pentacel for the same reason: The current lack of appropriate administration fees continues to present a huge barrier to the use of all combination vaccines.

Of course we all want to minimize pain for our patients by reducing the total number of injections we give them at any one visit. However, because most insurers will only pay one administration fee per injection—no matter how many antigens it contains—the loss of income incurred by switching from separate vaccines to combinations is an unacceptable burden for many practitioners.

Here in Rochester, N.Y., for example, physicians charge a $12 administration fee to cover the informed consent process, record keeping, storage, and wastage for each vaccine. The use of either Pediarix or Pentacel (if licensed), results in a loss of $24 per visit per child.

In my mind, it's absolutely wrong to view vaccine "administration" as simply putting a needle into a child's leg. The American Academy of Pediatrics and the vaccine manufacturers have been working to change this system. We can only hope that the anticipated licensure of Pentacel—which has the advantage of fitting better into the current immunization schedule—will add momentum to those efforts.

With even more combination vaccines in the pipeline, the issue of loss of income will need to be resolved.

Another complex problem regarding combination vaccines, this one regulatory, now faces the FDA as it decides whether to follow the advisory panel's advice on licensing Pentacel. At the January hearing, the panel debated a great deal about the importance of a slight diminution in immunogenicity to the vaccine's Hib component in some of Sanofi Pasteur's studies ("FDA Advisory Panel Supports Five-in-One Childhood Vaccine," February 15, 2007, p. 5).

Since 1997, the FDA has required that all components of a vaccine be noninferior to those of the separately administered antigens. The regulation has been widely interpreted to mean that a combination vaccine containing a Hib component must elicit an antibody response of at least 90% of the response to the separate Hib antigen; Pentacel technically did not meet all the criteria with regard to absolute antibody levels.

In contrast, European and Canadian licensing boards have decided that immunologic memory is more important than absolute antibody levels. Thus, a combination vaccine containing Hib conjugate has been licensed in many European countries because it establishes immunologic memory, even though the antibody response is more than 10% lower. Pentacel itself has been licensed in Canada since 1997 and used exclusively there since 1998, with more than 12 million doses distributed. It also is used in several European countries.

In Canada and in Germany, rates of Hib disease have remained very low or nondetectable since Hib-containing combination vaccines were introduced. Seems to me the Europeans got it right.

To resolve this discrepancy in regulatory policy, I think that the FDA needs to look at one more piece of clinical trial data that it is not currently considering: Among vaccine recipients who don't meet the absolute noninferior antibody level, what is the proportion of nonresponders, compared with the proportion whose titers are just beneath the threshold? I'm not worried about the child whose level is at 89%. Thanks to immunologic memory, that child will be protected.

Rather, the important question is whether there is a large proportion with little or no anti-Hib antibody following immunization. Having participated in many of these trials, I can tell you the answer is no. The manufacturers have those data. The FDA needs to start considering them, in order to bring to the market more combination vaccines that could improve the health and well-being of our patients. ■

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