ID CONSULT

Should We Consider Giving MMR Earlier?

Parents' concern that children receive too many vaccines too soon can result in delay or avoidance of vaccination, with the measles-mumps-rubella vaccine often being delayed. However, a recent study showed no neurologic harm from on-time receipt of all the recommended vaccines—including MMR—from the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices, and children with on-time receipt of vaccines performed better on select neurologic testing than those delaying vaccine. Another study showed that children lose maternally derived measles antibody protection as early as 1 month of age.

BY CHRISTOPHER J. HARRISON, M.D.

The study by Dr. Michael J. Smith and Dr. Charles R. Woods of the University of Louisville (Ky.) addressed the "too many vaccines too close together" issue. Using publicly available Vaccine Safety Datalink data from a previous study on thimerosal exposure and neuropsychological outcomes, the authors found that getting all recommended vaccines per the ACIP recommended schedule was associated with better—not worse—performance on selected neurologic outcomes at age 7-10 years, even when such factors as socioeconomic status were controlled for (Pediatrics 2010;125:1134-41). Importantly, there were no statistically significant differences favoring the less-vaccinated children. The authors concluded—and, I agree—that these data add reassurance for parents who are concerned that children receive too many vaccines too soon.

In the other study, Belgian investigators measured measles antibodies in mothers and persistence of the maternal antibody transferred to infants (BMJ 2010;340:c1626 [doi:10.1136/bmj.c1626]). They found that the 86 women with antibody from measles vaccine had significantly lower, yet still protective, measles IgG titers, being one-quarter as high as in 120 mothers with antibody from previous measles infection, and that cord blood and initial infant titers correlated with maternal titers.

Of concern is that maternally endowed measles antibody disappeared at a median of 3.8 months in infants of previously measles-infected mothers (only a few infants had antibody at 6 months of age), and at nearly 1 month of age in infants of vaccinated women (none had antibody at 6 months). Thus infants became vulnerable to measles even earlier than previously reported. If maternal antibody is from vaccine, their infants are susceptible for the 9-14 months just prior to the MMR if it is administered at 12-15 months of age.

While waning maternally endowed antibody by 6 months of age is expected for most infections, measles had seemed different. In the 1970s-1980s, MMR was given at 15 months of age. This was because maternal antibody reportedly persisted up to 12 months and prevented a vaccine "take" if the mothers' antibody came from measles infection (J. Pediatr 1977; 91:715-8). A later report showed waning antibody sooner when mothers' immunity came from measles vaccine: no antibody in 71% of 9-month-olds and 95% of 12-month-olds (Pediatrics 1995;96:447-50). This set the stage for the earlier 12-month MMR option. Now we have increasing evidence of even younger age for disappearance of the vaccine-interfering yet protective antibody to measles.

These data also have implications for the infant traveler. Although MMR isn't currently licensed for infants less than 1 year of age, data like these are the rationale for the Redbook recommendation that MMR be given to infants at 6 months of age or older who will be traveling to measles-endemic countries or during measles outbreaks. Of note, this is considered an "invalid" dose and the 12- to 15-month dose is still needed to attend school.

It might surprise some that Switzerland is now a measles-endemic country apparently due to its low 71% measles immunization rate. In fact, the per capita Swiss measles attack rate is similar to Somalia's. This shows that developed countries will have reemergent measles if herd immunity is lost.

I think we can make a case for studying earlier MMR dosing, particularly with measles outbreaks occurring in the United States, and imported cases potentially now coming from developed countries. If herd immunity (greater than 90% immunized) is in place, the infants' gap in measles protection may not be so worrisome. But as MMR immunization rates decline and become particularly low in some pockets in our country, concern increases over potential larger outbreaks. Studies to evaluate MMR at age 9 months could be the first step. If the vaccine were effective, we could narrow the measles-vulnerable window and vaccinate at the 9-month wellness visit. ■

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Probiotic May Benefit Children With Prolonged Diarrhea

VITALS

Major Finding: Overall, 75% of patients randomized to *Lactobacillus* GG returned to normal stool, vs. 70% of those receiving placebo.

Data Source: Double-blind randomized trial of *Lactobacillus* GG in 129 children with acute infectious diarrhea.

Disclosures: Amerifit Brands Inc. provided the study product and placebo, and a small patient incentive. Dr. Nixon disclosed no conflicts of interest.

BY PATRICE WENDLING

FROM THE ANNUAL MEETING OF THE PEDIATRIC ACADEMIC SOCIETIES

VANCOUVER, B.C. — Contrary to prior studies, *Lactobacillus* GG did not significantly affect the overall duration or severity of acute infectious diarrhea, in a double-blind, randomized trial of 129 children presenting in the pediatric emergency department.

Children with longer diarrheal illness however, appeared to respond better to outpatient use of *Lactobacillus* GG (LGG), Dr. Abigail Nixon, a pediatric fellow in training at the Jacobi Medical Center, New York, said at the annual meeting of the Pediatric Academic Societies.

Probiotics have been shown to decrease the duration of infectious diarrhea, although there are no U.S. studies of the use of probiotics to treat infectious diarrhea in the outpatient setting.

The study involved 129 children, aged 6 months to 6 years (mean 25.5 months), presenting to the emergency department (ED) with acute diarrhea, defined as more than two loose stools in the preceding 24 hours (mean 5.3 episodes). Patients were randomized to 10 capsules of dissolvable powder containing LGG or placebo containing inulin, a polysaccharide. Parents administered the powder twice daily for 5 days and recorded in a home diary the number of stools. A blinded researcher called the caregiver daily for 5 days, and recorded the number of stools and the date and time of the first normal stool.

The percentage of children returning to normal stool during the study period was similar among patients randomized to LGG and those receiving placebo, at 75% and 70%, respectively, Dr. Nixon said. There also was no significant difference in the median time to normal stool—60 hours with LGG vs. 74 hours with placebo—or in the number of diarrheal stools during the study—5.0 with LGG vs. 6.5 with placebo.

The lack of a significant benefit from LGG may be caused by the fact that children treated and discharged from the ED are in general not as ill as those who are admitted, Dr. Nixon explained, and therefore it's more difficult to document an effect of the probiotic.

"I think there's a population of children who probably have very mild disease who don't benefit from probiotics because they don't need it; they would have gotten better on their own," she said in an interview. "I think that's why as a group as a whole, we didn't see a meaningful difference." Still, the results support a trend for a benefit of probiotics, she added.

Among patients presenting with more than 2 days of diarrhea, a post hoc subgroup analysis revealed that a significantly higher percentage of the LGG patients returned to normal stool than did placebo-treated patients, 79% vs. 58%.

In addition, LGG patients returned to normal stool almost 24 hours earlier than did their counterparts treated with placebo (51 hours vs. 74 hours), and had half the number of diarrheal stools (3.5 vs. 7). Both differences were statistically significant.

'LGG may have a restorative effect on the intestinal flora' and so, might benefit kids with diarrhea for more than 2 days.

DR. NIXON

After the researchers adjusted for age, children with more than 2 days of diarrhea treated with LGG were twice as likely to return to normal stool as were children in the placebo group.

"LGG may have a restorative effect on the intestinal flora and therefore would preferentially benefit patients presenting with prolonged diarrhea," said Dr. Nixon, who recommends probiotics, either as tablets or fortified yogurt, to her patients in the ED.

She noted that a reduction in the time to resolution of diarrhea might have important public health implications in terms of missed work, lost revenue, and school absenteeism. Diarrhea accounts for about 1.5 million pediatric outpatient visits and more than 200,000 hospitalizations annually in the United States, Dr. Nixon said at the meeting.

Dr. Nixon's study was awarded this year's American Pediatric Association Ludwig-Seidel Award for the best research project in pediatric emergency medicine led by a fellow. ■