

Immunization Efforts Focus on Adolescents

Teenagers increasingly are being recognized as important reservoirs for certain infectious diseases.

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CAMBRIDGE, MASS. — Much of the “action” in the immunization arena is shifting to adolescents, according to Colin Marchant, M.D.

“Adolescent immunizations are a quickly evolving area, as youth in this age group are increasingly being recognized as important reservoirs for certain infectious diseases,” Dr. Marchant said at a pediatric infectious disease meeting sponsored by Boston University School of Medicine, PEDIATRIC NEWS, and FAMILY PRACTICE NEWS.

Until recently, the universal immunization recommendation for the 11- to 12-year preadolescent visit was for a diphtheria-tetanus (DT) booster. Earlier this year, the Center for Disease Control and Prevention’s Advisory Committee on Immunization Practices (ACIP) added the acellular pertussis and the conjugate meningococcal disease vaccines to its list of recommended immunizations for adolescents.

And it is likely that another vaccine—one of the two human papillomavirus vaccines currently wending their way through safety and efficacy trials—will be added to the adolescent immunization roster as soon as the Food and Drug Administration approves them for use, said Dr. Marchant of Boston University.

It is expected that these vaccines will significantly reduce the infection rates of the respective diseases not only among adolescents, but also among infants and immunocompromised individuals in close contact with the adolescents, Dr. Marchant noted.

Acellular Pertussis Vaccine

With respect to pertussis, “adolescent immunization, and in fact adult immunization, is our unfinished business,” said Dr. Marchant, referring to the rise in recent years of pertussis infections.

In 2004, the highest number of U.S. pertussis cases was among individuals 10-18 years of age, with roughly 6,500 cases reported, according to data from the Centers for Disease Control and Prevention. Looking at infection rates across different age groups, “the numbers have remained steady for children ages 1-10, but they increase substantially starting at age 11 and peak around age 15, then start to fall back down,” he said.

“It’s no surprise that kids in the adolescent age range have high rates of infection. They have lower antibody levels because their last pertussis immunization was before their 7th birthday.

“By age 11 or so, the vaccine-related antibody levels will have gone down, leaving these kids vulnerable to infection,” said Dr. Marchant.

Because these children are in such close contact with other children, in school and on sports teams, it’s likely that once they’re exposed to pertussis, they’re going

to get sick, because the infection is so highly contagious, with an airborne spread and from contact with nasal secretions, he said.

The observed rise in antibody levels after age 15 can be attributed to immunity developed through infection.

“We’ve known all along that immunity to pertussis wanes, but it wasn’t until the late ‘80s that we started going around looking for and counting cases of pertussis,” Dr. Marchant stated. With the 1987 introduction of the single-serum blood test to determine pertussis antibody levels, “we began to document cases, and as always, the closer you look, the more you find.”

In 2001, a pertussis outbreak in a youth football team in Arkansas led to 77 documented cases of the disease, forcing a school closure.

Around the same time, 500 cases (median age 13) were documented in a community in Arizona.

In 2003-2004, an outbreak traced to a high school weight room in Wisconsin led to 300 documented cases, primarily among adolescents, but also including some among infants, “who presumably were infected by adolescents or adults and who required hospitalization,” said Dr. Marchant.

These and other outbreaks have led to an increased public awareness of the spread of pertussis infection and have also led to stepped-up efforts to protect adolescents and adults from infection and to minimize the risk of disease transmission to infants, who experience significantly more morbidity and mortality as a result of infection.

In June of this year, with data from large, multicenter trials showing the two tetanus, diphtheria, acellular pertussis vaccines that were recently approved (GlaxoSmithKline’s Boostrix and Sanofi Pasteur’s Adacel) for use in adolescent and adult populations, ACIP recommended that all adolescents get the pertussis-inclusive vaccine instead of the TD-only booster at the 11- to 12-year visit.

In October of this year, the committee further recommended that adults also receive the pertussis vaccine the next time they are due for a booster, said Dr. Marchant.

Conjugate Meningococcal Vaccine

Life-threatening meningococcal disease affects 1,400-2,800 individuals in the United States each year. While the incidence is highest in children younger than 2 years, adolescents and young adults also are at high risk.

According to CDC data, approximately half of all meningococcal infections occur in individuals between 15 and 24 years. “Studies have shown the case fatality rate to be especially high in this age group, but they have also shown the percent preventable to be very high,” said Dr. Marchant.

The majority of adolescents and young

adults with meningococcal disease are infected with the meningococcal serogroup C, for which vaccine protection is available.

In contrast, infants are generally infected by meningococcal serogroup B, for which there is no vaccine.

Although a polysaccharide meningococcal vaccine (Menomune) has been licensed in the United States since 1978, it was not until the development and FDA licensure of the new quadrivalent conjugate meningococcal vaccine (Menactra) last year that ACIP included it on its list of recommended vaccines for the preadolescent visit.

The conjugate vaccine, approved for use in 11- to 55-year-olds, offers protection against serogroups A, C, Y, and W-135, and it offers improved duration of protection, induction of immunologic memory, booster responses, and reduction in nasopharyngeal bacterial carriage, compared with the polysaccharide vaccine, said Dr. Marchant.

The conjugate vaccine also is recommended for other people at increased risk for meningococcal disease, including college freshmen living in dormitories; microbiologists who are routinely exposed to meningococcal bacteria; U.S. military recruits; individuals traveling to or living in a part of the world where meningococcal disease is common; people who have a damaged spleen or whose spleen has been removed; those with an immune system disorder; and persons who might have been exposed to meningitis during an outbreak.

“We expect the universal immunization recommendation for preadolescents to have a big impact on infection rates,” said Dr. Marchant, noting that universal immunization with the polysaccharide vaccine in the U.S. military significantly reduced meningococcal infections since the immunization policy went into effect, in the early 1970s.

Similarly, a country-wide immunization program with a serogroup C conjugate vaccine in Great Britain (where most of the meningococcal infections among adolescents and young adults have been linked to serogroup C infection) resulted in a significant drop in disease incidence, “suggesting that a conjugate vaccine can control disease,” he said.

An unexpected roadblock to such success with the new conjugate vaccine may be noncompliance with the immunization recommendation resulting from reports of an association with Guillain Barré Syndrome (GBS).

“The immunizations began in the spring of last year, and it came out in September—after 2.8 million doses of the vaccine had been distributed—that there were 6 cases of Guillain Barré that occurred 2-6 weeks post vaccine,” said Dr. Marchant. “While this is more cases than we would like to see, there is not enough evidence to say that this is a cause-and-effect relationship.”

Not only have there not been any further cases reported since that time, there was previous personal or family history of GBS in some of the patients who developed it, further clouding the association, he noted.

“We know that most Guillain Barré is caused by certain infectious agents, but some of these infections are subclinical so we can’t get a nice handle on the cause of the cases that occurred.”

Vaccine recommendations are not being altered by these preliminary reports of GBS, Dr. Marchant stressed. “The fact is, GBS has been reported after every vaccine given some time, somewhere, so these few reports are not enough to sway us from stressing the need for protection from meningococcal disease, which has a much higher attack rate and a much higher mortality rate than Guillain Barré Syndrome,” said Dr. Marchant.

With respect to the potential for GBS, “we’re just going to have to wait and see if it’s out there.”

For families who refuse inoculation for their children because of the GBS reports, “it’s okay to then recommend the polysaccharide vaccine, with the caveat that it doesn’t last as long and may not offer the same protection,” he said.

Human Papillomavirus Vaccine

Although neither of the two human papillomavirus (HPV) vaccines under development—one from GlaxoSmithKline and one from Merck & Co.—have yet to be licensed, infectious disease experts have already begun advocating for their inclusion, upon FDA approval, in the preadolescent immunization lineup.

One of the two vaccines (GlaxoSmithKline’s) targets HPV types 16 and 18, which together are responsible for 70% of all cervical cancers. The other vaccine, from Merck, covers these as well as HPV types 6 and 11, which are responsible for approximately 90% of all anogenital warts. “The interesting thing is that types 6 and 11 also cause some abnormal Pap smears, so a vaccine to fight these virus types should also decrease the number of positive Pap smears and procedures that follow,” said Dr. Marchant.

To date, the safety and efficacy of both products in clinical trials looks good compared to placebo, “and the year 2006 has been bandied about as possibilities for licensure,” Dr. Marchant noted. “The most likely scenario will be that these will be added into the 11- to 12-year visit, although there may be some opposition to this from those on the far right.”

Whether the recommendation, if it comes about, will include males as well as females, is still being considered. “Obviously, males don’t get cervical cancer, but they can spread HPV to females, and they can also be affected by genital warts,” said Dr. Marchant. “However, it’s difficult to show a benefit to immunizing males, in terms of transmission reduction.” ■

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