Consider Early Vaccination in Children Who Travel

BY DAMIAN McNAMARA
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MIAMI BEACH, FLA. — Accelerated immunizations for children can optimize disease prevention before international travel, Elizabeth D. Barnett, M.D., said at the annual meeting of the American Society of Tropical Medicine and Hygiene.

Hepatitis A, typhoid fever, yellow fever, Japanese encephalitis, meningococcal infection, and rabies infection are some of the leading concerns for pediatric travelers, according to Dr. Barnett, director of the International Clinic, Maxwell Finland Laboratory for Infectious Diseases, Boston Medical Center.

The good news is that most traveling children have already received vaccines for hepatitis B and pneumococcal disease.

The health and age of the infant or child, the endemic diseases in destination countries, and risk-benefit considerations for each vaccination are all important considerations, she said. For example, efficacy of polysaccharide vaccines will be limited until age 2 years because of impaired T-cell function. In addition, maternal antibodies can impair response to some vaccines in very young infants, such as the measles, mumps, and rubella (MMR) and hepatitis A vaccines. "Balance the lower age limit of the vaccine with risk of disease and vaccine efficacy."

If travel to a measles-endemic area is planned, consider giving MMR beginning at 6 months of age. If the patient is traveling to a region where a polio outbreak is possible, he or she should receive a full course of polio vaccination beforehand.

Dr. Barnett made some specific recommendations:

► **Hepatitis A.** Hepatitis A vaccine should be given 2-4 weeks prior to departure for children traveling to all international destinations except Australia, Canada, Japan, New Zealand, Western Europe, and Scandinavia. Children at least 1 year old can receive the vaccine; the only option for younger travelers is immune globulin. "If the time to departure is short, consider giving immune globulin and vaccine at the same time as MMR or varicella vaccines at different sites," Dr. Barnett said. Immune globulin may impair vaccine activity, so the ideal situation is to give the vaccine first, followed at least 2 weeks later by the immune globulin.

'Balance the lower age limit of the vaccine with risk of disease and vaccine efficacy.'

DR. BARNETT

"The benefit really outweighs the risks with hepatitis A vaccine," Dr. Barnett said.

► **Typhoid.** Vaccination is indicated for, not by length of trip, but by travel to areas where exposure to contaminated food or water is possible. The vaccine's efficacy is limited compared to hepatitis A, Dr. Barnett said. "We generally tell patients the efficacy is 65%-85%."

For infants under 2 years, exposure should be avoided; for ages 2-5 years, limiting exposure and giving a polysaccharide vaccine are recommended; and for children 6 years and older, limiting exposure and giving the parenteral oral polysaccharide vaccine are recommended. Adverse events with the parenteral vaccine include local reactions (7%), headache (1.5%-3%) and fever (0%-1%).

Dr. Barnett said, "In most settings, the benefit for typhoid vaccine is there, limited by incomplete vaccine efficacy."

► **Yellow Fever.** Although the risk is low (0.4 to 4.3 cases per million U.S. travelers to endemic areas) and is only present in Africa and South America, the vaccine is very efficacious, with a single vaccination usually providing lifetime coverage.

"Encephalitis is a rare adverse event following yellow fever vaccine, occurring primarily in infants," Dr. Barnett said. "The vaccine, therefore, is absolutely contraindicated in infants under 6 months."

"The bottom line is, those who are at risk for yellow fever, going to high transmission areas, and who cannot guarantee mosquito protection, should receive yellow fever vaccine unless there are specific contraindications," Dr. Barnett said.

► **Japanese Encephalitis.** There is an effective vaccine, and it is indicated for some travel to higher-risk areas, Dr. Barnett said. "We have to again balance risks and benefits." The risk is greater in rural farming areas, during transmission season, and during outbreaks.

► **Meningococcal Infection.** Sub-Saharan Africa has frequent epidemics and outbreaks. "The overall risk of disease for travelers to sub-Saharan Africa is very low, but the [polysaccharide] vaccine is safe, effective in children over 2, and offers some protection at home," she said. A conjugate vaccine, which can be used in children under 2 years, has recently been approved by the FDA. (See related story below.)

► **Rabies.** Although the benefits of prophylaxis are greatest for travel to high-risk areas and areas far from medical care, and for travel of long duration, "I believe we should be discussing prevention with all families traveling to a destination that is not rabies-free," Dr. Barnett said.

It is very important to tell families that additional doses are required after exposure. "We call it pre-exposure prophylaxis, we do not call it a vaccine, because medical care should still be sought if [a person is] bitten," she emphasized. ■

NEW & APPROVED

Menactra, VFEND

BY ELIZABETH MECHCATIE, SENIOR WRITER, AND DAMIAN McNAMARA, MIAMI BUREAU

Menactra
(Meningococcal [Groups A, C, Y, and W-135] Polysaccharide Diphtheria Toxoid Conjugate Vaccine, Sanofi Aventis)

The Food and Drug Administration has approved a conjugate meningococcal vaccine for active immunization of adolescents and adults aged 11-55 years for preventing invasive meningococcal disease caused by *Neisseria meningitidis* serogroups A, C, Y, and W-135 (four of the five serogroups that cause nearly all cases of meningococcal disease worldwide). It is anticipated to have several benefits over Menomune, the currently available polysaccharide meningococcal vaccine that also provides protection against these four serogroups.

► **Recommended Usage:** Single 0.5-mL injection administered intramuscularly.

► **Special Considerations:** Local pain, headache, and fatigue were the most commonly reported adverse reactions in safety studies comparing Menactra and Menomune, with local reactions more common among those who received Menactra.

► **Comment:** Approval was based on safety and immunogenicity data from six studies of more than 10,000 adolescents and adults comparing Menactra and Menomune, which found that immune responses to both vaccines were similar for all four serogroups.

The Centers for Disease Control and Prevention's (CDC's) Advisory Committee on Immunization Practices (ACIP) is expected to approve changes in the recommendations for preventing and controlling meningococcal disease, which will include recommendations on how the new vaccine should be used in populations aged 11 years and older, including children, as well as college students, and adults who travel to endemic areas.

It is anticipated that the immune response to the conjugate vaccine "will be much more durable and will be able to be boosted in subsequent years" if a booster is determined to be necessary, compared with the polysaccharide vaccine, which has a relatively short duration of immunity (thought to be under 4 years) and cannot be boosted, said William Schaffner, M.D., professor and chairman of the department of preventive medicine at Vanderbilt University, Nashville. Herd immunity is another anticipated benefit, since the conjugate vaccine is also effective against nasopharyngeal carriage of the organism, whereas the polysaccharide vaccine has no such impact.

Menactra cannot be expected to completely eliminate meningococcal disease, because it does not cover the group B serotype, which "continues to cause a substantial amount of disease in the United States," said Dr. Schaffner, the Infectious Diseases Society of America liaison to ACIP. The polysaccharide vaccine will continue to be necessary because it is approved down to age 2 years, he noted in an interview. Sanofi Aventis plans to file for approval of Menactra in children aged 2-10 this year; studies in children under age 2 years are underway. Dr. Schaffner stated that he has no conflict of interest.

VFEND
(voriconazole intravenous for injection, tablets, and oral suspension, Pfizer Inc.)

The FDA has approved the extended-spectrum antifungal VFEND in patients aged 12 years and older for treatment of candidemia without neutropenia, as well as for disseminated or deep tissue skin infections and infections of the abdomen, kidney, bladder wall, and wounds from candida.

► **Recommended Dosage:** Recommended oral dosage is 200 mg every 12 hours for patients who weigh more than 40 kg and 100 mg every 12 hours for patients weighing less than 40 kg.

Recommended loading dosage of intravenous VFEND is 6 mg/kg every 12 hours for the first 24 hours, followed by 3-4 mg/kg every 12 hours for maintenance. Treat for at least 14 days following symptom resolution or last positive culture, whichever is longer.

► **Special Considerations:** A relatively common side effect of voriconazole in adults involves visual disturbances, including enhanced visual perception, blurred vision, color vision change, and photophobia. In addition, voriconazole is contraindicated in patients taking CYP3A4 substrates such as terfenadine, cisapride, and quinidine because of potential for prolonged QT syndrome. Clinical trials showed that uncommon but serious hepatic reactions are possible. Liver function tests are recommended before and during treatment.

► **Comment:** A total of 283 nonneutropenic patient participants were randomized to voriconazole and 139 to amphotericin B followed by fluconazole. Efficacy was equivalent at 41% in both groups 12 weeks after end of therapy.

Two other studies included 35 refractory patients with deep tissue candida infections. There was a favorable response in four of seven patients with intraabdominal infections, five of six patients with kidney and bladder wall infections, and three of three patients with deep tissue abscesses or wound infections.

"Voriconazole now represents an approved alternative to other antifungal agents for candida infections," said Joseph W. St. Geme III, M.D., professor of pediatrics and molecular microbiology at Washington University, St. Louis, and director of pediatric infectious diseases at St. Louis Children's Hospital. He has no affiliation with VFEND or Pfizer.

Advantages include availability in both intravenous and oral forms, a favorable safety profile, activity against some strains of candida resistant to other azole agents, and activity against other fungi such as *Aspergillus, Scedosporium*, and *Fusarium*, Dr. St. Geme said. "My experience using voriconazole to treat *Aspergillus* infection has been positive." ■