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Summer Enteroviruses: Avoid Antibiotics

During the summer and early fall, we should be careful about unnecessary antibiotic use in patients who most likely have enteroviral infections.

Nonpolio enterovirus (NPEV) infections are amazingly diverse in their range of clinical manifestations. While most of these infections are self-limited and nonserious, NPEV can turn serious and even fatal in newborns and immunosuppressed individuals. Of course, the diagnosis is easy when we see a child with the classic hand-foot-and-mouth (HFM) blister presentation. But that happens in only a small proportion of cases.

More commonly, we see a child with a high fever, sore throat, a slightly stiff neck, and a very worried mother. Even with a negative strep test, sometimes we retreat to our comfort zone and prescribe amoxicillin. While understandable, we should try to avoid this practice.

In a study my colleagues and I conducted a few years ago, only 8% of 372 children with a clinical diagnosis of systemic NPEV syndrome presented with HFM blisters. More common were stomatitis in 58%, and fever with myalgias and malaise in 28%. Another 3% had pleurodynia, 3% had fever with rash, and 1% had aseptic meningitis. Most patients had four to seven symptoms at the onset of illness and at the time of presentation (Pediatrics 1998;102:1126-34).

To my knowledge, there have been no other published studies since that one on the epidemiology of enteroviral illness in private clinical practice.

Of the 372 index cases, more than half (53%) also had a family member with an NPEV illness, including 51% of the 105 with myalgia/malaise, 20% of the 10 with rash, 57% of the 214 with stomatitis, and 45% of the 11 with pleurodynia. Interestingly, the illness often presented differently in different family members. It was not uncommon, for example, to see one child with HFM, another with just rash and fever, and the mother with malaise and myalgia, but with the identical virus isolated from all three. We were somewhat surprised by this finding.

Also unexpected was the long duration of illness in many instances. While we typically think of a "summer cold" as lasting no more than 2-3 days, in our study the myalgias and malaise lasted a mean of 9.5 days, stomatitis lasted 7 days, HFM 7.2 days, rash 6 days, pleurodynia 8.8 days, and meningitis 6.5 days. Unless we caution our patients about how long these symptoms can linger, we're sure to see them back in our offices, asking for antibiotics.

Unfortunately, efforts that began a decade or so ago to develop rapid-test enterovirus kits for widespread clinical use fell by the wayside for a variety of reasons. Some tertiary medical centers do have polymerase chain reaction–based rapid tests, but their cost is prohibitive for most community hospitals and private physicians' offices.

What I've found most useful in my practice is a simple white blood cell count. Most of these children will have a drop in their WBC count consistent with a viral infection, and an increase in their lymphocytes ("right shift"). During the summer or early fall, a febrile illness—even a high febrile illness—with no specific signs to indicate bacterial disease is most likely caused by an enterovirus.

That knowledge—coupled with a low WBC count and a right shift—should be sufficient in 90% of cases to ensure that you don't need empiric antibiotic therapy, as long as you have good follow-up with the patient.

The exceptions to that are newborns less than 2 months of age and immunosuppressed patients of any age. In those cases, a sepsis work-up is still advised. Indeed, a recent review paper noted that severe NPEV disease develops in a subset of newborns infected in the first 2 weeks of life, consisting of sepsis, meningoencephalitis, myocarditis, pneumonia, hepatitis, and/or coagulopathy. Substantial mortality has been reported, and long-term sequelae may occur among survivors (Paediatr. Drugs 2004;6:1-10).

The National Institute of Allergy and Infectious Diseases had funded an investigation of pleconaril—an agent that inhibits viral attachment to host cell receptors—for use in infants with enteroviral sepsis.

The study was suspended earlier this year, but NIAID is currently in talks with manufacturer Schering-Plough Corp. to restart the trial. ■

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Precollege Rush for Menactra Drove Distribution in First Year

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Despite a recommendation to prioritize 11- to 12-year-olds, distribution of the meningococcal conjugate vaccine was especially high among 18-year-olds and was evenly distributed among 11- to 17-year-olds during its first year on the market, Dr. Gregory Wallace reported at a meeting of the National Vaccine Advisory Committee.

The rationale for the recommendation was to help establish an adolescent vaccine visit, and was not generated because of an increased disease risk among 11- to 12-year-olds, explained Dr. Wallace, chief of the Vaccine Supply and Assurance Branch at the Centers for Disease Control and Prevention.

The vaccine is also recommended for adolescents entering high school who have not been previously vaccinated, as well as for college freshmen living in dorms.

Demand for the meningococcal conjugate vaccine (MCV4), marketed as Menactra, was high starting in June 2005 after the publication and promotion of the vaccination recommendations by the CDC's Advisory Committee on Immunization Practices, the American Academy of Pediatrics, and the American Academy of Family Physicians.

The demand was initially highest for 18-year-olds, and the peak months were June and July 2005. The high demand then decreased during the fall of 2005, as did patients' and parents' concerns about the vaccine supply.

The overall vaccine distribution rate from March 2005 to March 2006 was approximately 10% for 11- to 17-year-olds, but nearly 16% among 18-year-olds, based on physicians' billing-claims data provided by the vaccine's manufacturer, Sanofi Pasteur USA.

To handle the anticipated summer rush among 18-year-olds this year, CDC recommends that physicians defer the vaccination of 11- to 12-year-olds.

About 4.2 million doses were distributed between March 2005 and March 2006. Although the manufacturer projects that 6 million doses will be available for 2006-2007, the amount currently available for the summer months of 2006 is approximately the same as last year, Dr. Wallace said.

Sanofi Pasteur expects the demand for the vaccine to exceed supply this summer. To handle the anticipated summer rush among 18-year-olds, the CDC and other organizations have recommended that physicians defer the vaccination of 11- to 12-year-olds until further notice from the manufacturer that the shortage has been resolved. The current supply projections should be sufficient to cover adolescents entering high school, dorm-dwelling college freshmen, and other high-risk groups, including military recruits and travelers to areas where the risk of meningococcal disease is high. For periodic vaccine supply updates, visit www.cdc.gov/nip/news/shortages/default.htm. ■

Company Halts Enrollment in Pediatric Studies of Telithromycin

BY ALICIA AULT
Associate Editor, Practice Trends

The Food and Drug Administration has determined that the antibiotic telithromycin (Ketek) may be associated with serious liver injury and liver failure, and has been linked to four deaths and one liver transplant. The drug's maker, Sanofi-Aventis, has upgraded a caution in the drug's label on the potential for liver injury to a bolded warning that serious hepatic injury has been "observed during or immediately after treatment." Injury has progressed rapidly after just a few doses, according to the company.

Ketek has not received a black box warning, and both the FDA and Sanofi say the drug's benefits outweigh its risks.

"We are advising both patients taking Ketek and their doctors to be on the alert for signs and symptoms of liver problems," Dr. Steven Galson, director of the FDA's Center for Drug Evaluation and Research, said in a statement.

However, the drug maker has stopped enrollment in five pediatric trials investigating use of Ketek in acute otitis media, community-acquired pneumonia, and tonsillitis in children 6 months to 18 years old.

The new warning is based partly on an FDA analysis that found that Ketek may be associated with 12 cases of liver failure and 4 deaths since its approval in 2004. "We're engaged in ongoing discussions with the FDA regarding a detailed medical evaluation of hepatic events reported in connection with Ketek use," said Sanofi spokeswoman Melissa Feltmann.

Ketek is currently approved for use in adults to treat community-acquired pneumonia, sinusitis, and acute exacerbation of chronic bronchitis.

Emmy Tsui, also a Sanofi spokeswoman, said therapy will continue according to protocol in children already enrolled in the five pediatric trials, but that Sanofi would not enroll any new trial participants until it was certain that its development program "remains consistent with the current thinking of the FDA regarding the structure and design of antibiotic drug development in pediatrics."

The Senate Finance Committee has been investigating Ketek's approval, as well as a postmarketing safety study that was later found to be fraudulent.

Committee chairman CharlesGrassley (R-Iowa) said that he has been stonewalled by the FDA in his attempts to meet with the agency's special agent who investigated the fraud. In mid-June, he visited the Department of Health and Human Services headquarters to demand such a meeting.

"Based on the runaround that's gone on, I smell a cover-up," Sen. Grassley said in a statement issued after his HHS foray. ■