



BY STEPHEN I. PELTON, M.D.

ID CONSULT

E. coli: Prevention Is Best Cure

The recent outbreaks of *Escherichia coli* O157:H7 linked to spinach and lettuce remind us yet again how limited our tools

are when it comes to treating this infection and its sequelae. Focusing our efforts on prevention is by far the best medicine.

As of Oct. 6, a total of 199 people infected with the outbreak strain of *E. coli* serotype O157:H7 had been reported to the Centers for Disease Control and Prevention from 26 states, including 22 cases in children younger than 5 years of age. Of the total group, 51% were hospitalized and 16% developed hemolytic uremic syndrome (HUS). Twenty-nine percent of children younger than 18 years developed HUS, compared with 8% of adults aged 18-59 years and 14% of those aged 60 years and older, confirming the increased risk for HUS in children and the elderly.

There were three deaths, including a 2-year-old child with HUS whose stool sample contained evidence of the outbreak strain confirmed by "DNA fingerprinting."

About 73,000 infections with *E. coli* O157:H7 occur annually in the United States. Such infections are reportable nationally as well as in most states. In most states, HUS is reportable to departments

of public health as well. The CDC investigates all reported cases to ascertain whether they are outbreak-associated or isolated. Most are the latter. Half of all cases occur between June and September.

Produce was the source in the recent outbreak, but in the past we've seen disease in children associated with undercooked meat, nonpasteurized milk products, and even water. Petting zoos are a major hazard.

During 2004-2005, a total of 173 cases of *E. coli* O157:H7 were reported from outbreaks in Arizona, Florida, and North Carolina. Illnesses primarily affected children who had visited petting zoos at agricultural fairs or festivals. There were 22 cases of HUS, but fortunately no fatalities (MMWR 2005;54:1277-80).

In a study the CDC conducted at a petting zoo, illness was associated with touching or stepping in manure, falling or sitting on the ground, using a pacifier or "sippy" cup, and thumb-sucking. Use of alcohol-based sanitizer was not protective, but reported awareness by the accompanying adults of the risk for disease from contact with livestock was. We should counsel parents about the potential risk and the preventive strategies such as avoidance of manure and of the use of a pacifier or eating while at the petting zoo.

Direct human-to-human contact is a rarer source of *E. coli* infection, but it's important to keep in mind when we see a

child with bloody diarrhea, particularly if that child is in day care.

Unfortunately, we don't have a way to interrupt the progression from colitis to HUS. The role of antibiotics in children with *E. coli* gastrointestinal infection remains controversial. Epidemiologic data have suggested that antibiotics may increase the risk for HUS, perhaps by increased toxin exposure to the kidneys following bacteriolysis in the gut. A meta-analysis of 26 studies conducted between January 1983 and February 2001 did not show a higher risk of HUS due to antibiotic use. However, the authors concluded that a randomized trial of adequate power is needed to conclusively answer the question (JAMA 2002;288:996-1001).

Until then, the potential benefit of antimicrobial therapy in a specific patient presenting with gastroenteritis must be weighed against the potential risk. Stool cultures should be obtained from any child who presents with bloody diarrhea and abdominal pain. If the child is afebrile and otherwise does not appear ill, supportive care is advised. But of course, a child with gastroenteritis who is hypotensive and appears septic requires urgent intervention that may include antimicrobial therapy.

Although we don't know which children with *E. coli*-associated diarrhea will progress to HUS, we do know that certain risk factors, such as young age, long duration of diarrhea, elevated leukocyte count,

and proteinuria, are predictive (Emerg. Infect. Dis. 2005;11:1955-7). Fortunately, there is usually a lag time of several days to a week between the onset of bloody diarrhea and renal failure. If we see the child soon enough, we can intervene with fluid replacement and close monitoring.

At the time of progression to HUS, stool cultures often are negative. The diagnosis is made clinically, on the basis of renal failure and hemolytic anemia, with or without thrombocytopenia. Treatment is supportive: Dialysis has dramatically reduced HUS mortality from about 21% before 1974 to about 4% today.

Intriguing early work is now being done looking at treating HUS with infusion of the human plasma protein serum amyloid P component (J. Infect. Dis. 2006;193:1120-4) and use of specific neutralizing antibodies directed against the A subunit of the toxin (Clin. Microbiol. Rev. 2004; 17:926-41). Clinical use is probably years away, however.

For now, we need to continue to educate our patients about thoroughly cooking meat, washing produce, and exercising caution around farm animals and in petting zoos. ■

DR. PELTON is chief of pediatric infectious disease and also is the coordinator for the Maternal-Child HIV Program at Boston Medical Center. Write to Dr. Pelton at our editorial offices at pdnews@elsevier.com.

C. difficile, Other Pathogens Often in ED Stool Samples

BY JOHN R. BELL
Associate Editor

Nearly half of children with diarrhea at one emergency department over a 3-year period had stool samples containing pathogens, including *Clostridium difficile* and Shiga toxin-containing *Escherichia coli*, according to the results of a new study.

Dr. Eileen J. Klein of the University of Washington Children's Hospital and Regional Medical Center, Seattle, and her colleagues conducted a prospective cohort study in which they analyzed stool samples from 1,626 patients discharged with diarrhea, bloody diarrhea, or gastroenteritis at a Seattle emergency department during 1998-2001. Mean patient age was 2.5 years (Clin. Infect. Dis. 2006;43:807-13).

All stool samples underwent bacterial testing, 417 also underwent tests for viruses, and 656 were tested for parasites as well. A total of 372 samples underwent testing for all three types of pathogens and suspected pathogens *C. difficile* and *Blas-tocystis hominis*.

Of those 372 samples, 176 (47%) were positive for at least one pathogen. Of those tested for viral

pathogens, 33% (138 of 417) were positive, and 7% of those tested for bacterial pathogens (118/1,626) were positive (of which 39 contained Shiga toxin-containing *E. coli*, 39 had salmonella, 25 had *Campylobacter* species, 14 had *Shigella* species, and 2 contained *Yersinia enterocolitica*).

For parasites, 7 (1%) of 656 tested samples were positive.

Moreover, 53 samples were positive for candidate pathogens; 7% (46 of 688) of those tested contained *C. difficile*, and 1% (7 of 656 tested) were positive for *B. hominis*.

The investigators also noted which seasons of the year had the greatest incidence of virus- or bacterium-containing stool samples.

For bacteria, winter had the smallest portion of positive samples, 4% vs. 14% for summer. However, the opposite was true for viruses; the summer months had 11% of positive specimens, vs. 53% for winter and 44% for spring.

Dr. Klein and her colleagues noted that they were "unable to develop a model substantially better than physician judgment to identify patients for whom a stool culture would yield positive results." ■

Intussusception Rates With Rotateq Lower Than Expected, CDC Reports

BY MIRIAM E. TUCKER
Senior Writer

ATLANTA — No major safety issues have arisen thus far with the new rotavirus vaccine, Penina Haber said at a meeting of the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.

In fact, rates of intussusception—the complication that resulted in the 1999 withdrawal from the market of the old rotavirus vaccine (Wyeth-Ayerst's RotaShield)—are actually lower with Merck's Rotateq than would be expected in the general population, said Ms. Haber, an epidemiologist with the CDC's Immunization Safety Office.

The CDC is monitoring Rotateq for gastrointestinal-related adverse events as well as any other unexpected problems via the passive Vaccine Adverse Event Reporting System (VAERS). Should any safety "signals" arise, the active surveillance system known as the Vaccine Safety Datalink (VSD), comprising eight large HMOs (covering 3% of the U.S. population), will be utilized to investigate further.

Indeed, the CDC is now using VAERS and VSD to monitor safety for all new vaccines, with researchers from the CDC and the Food and Drug Administration reviewing all reports sent to VAERS on a daily basis, Robert L. Davis, director of the CDC's Immunization Safety Office, said during a joint presentation with Ms. Haber on vaccine safety.

From March 1, 2006, through Oct. 23, 2006, VAERS received a total of 189 adverse event reports following receipt of Rotateq, from a background of 1,786,476 doses distributed as of Sept. 30, 2006. Of the 189 reports, 48% were associated with receipt of Rotateq alone, while the rest were in combination with other vaccines. Children aged 2-3 months accounted for 57% of the reports, while 5% were for children under 2 months of age. (The vaccine is recommended at ages 2, 4, and 6 months). Fifty-five percent of reports were of events occurring within 2 days of vaccination, while another 5% occurred within 7 days.

Among the most frequent adverse events following receipt of Rotateq in children up to 12 months of age were diarrhea (24% vs. 3% following all other vaccines), vomiting (22% vs. 5%), GI hemorrhage (7% vs. 0%), and melena (6% vs. 1%). A total of 30 (16%) of the reports were of serious events, including 6 cases of intussusception. Four occurred after dose 1 and two after the second dose, at an interval of 2-32 days following vaccination.

Calculating from the VSD background intussusception rate of 2.98 per 10,000 person-years, expected cases within a 21-day period would number 30.7. In contrast, just 4 cases were observed within 21 days of Rotateq receipt. Assuming 47% underreporting (Am. J. Epidemiol. 2001;154:1006-12), the number of intussusceptions linked with Rotateq would still be significantly lower than expected, Ms. Haber said. ■