

ID CONSULT

Questioning Antibiotic Prophylaxis for UTI

Emerging evidence suggests that we shouldn't be prescribing prophylactic antibiotics for every child with recurrent urinary tract infection, even when vesicoureteral reflux is present.

Just as the pendulum has swung over the last decade away from universal use of antibiotics with acute otitis media toward selective use of "watchful waiting," data on recurrent urinary tract infection (UTI) suggest that children with lower grades of reflux may not benefit from long-term prophylactic antibiotics. These children may in fact be disadvantaged by prophylaxis's selecting for increased antimicrobial resistance. Therefore, even when we decide to use antimicrobial prophylaxis in selected children with both recurrent UTI plus high-grade vesicoureteral reflux (VUR), we need to consider carefully whether the traditional prophylactic drugs are really the best choice.

The latest evidence comes from a large database study published by Dr. Patrick Conway of the University of Pennsylvania, Philadelphia, and his associates. They retrospectively analyzed the electronic health records of 74,974 children aged 6 years and younger in 27 primary care practices in Delaware, New Jersey, and Pennsylvania over a 5-year period, and identified 666 who had been diagnosed with a first UTI; 611 had at least 24 days of observation. There were 83 with recurrent UTIs, 51 (61%) of which were caused by a resistant pathogen (JAMA 2007;298:179-86).

Significant predictors of recurrence included age 3-4 years (not the toddler in diapers as we might have suspected), white race, and grades 4-5 VUR. Factors that did not affect the risk of recurrent infection included sex, grades 1-3 VUR, and antimicrobial exposure. Because children had

different lengths of follow-up (mean 408 days), time to recurrence was used as the primary outcome measure. Use of antimicrobial prophylaxis had no significant overall effect on time between the initial UTI and the first recurrent UTI, even when the children were stratified by age, race, sex, or VUR grade.

Importantly, despite the lack of effect on time to recurrent UTI, prophylaxis was associated with a 7.5-fold increased likelihood of a resistant pathogen causing the recurrence. In the overall group of 611 children with UTI, trimethoprim-sulfamethoxazole was prescribed for 61%, amoxicillin for 29%, nitrofurantoin for 7%, and other antimicrobials including first-generation cephalosporins for the other 3%. Although the investigators didn't report which antibiotics were used in the 83 children with recurrent UTI, they did note that none of the 9 children who received nitrofurantoin had a recurrence.

This study follows last year's publication of a Cochrane review comprising data for 406 children from five randomized studies in which antibiotic prophylaxis was compared with placebo or no treatment (Cochrane Database Syst. Rev. 2006;3:CD001534).

The results were not conclusive. Antibiotics were found to reduce the risk of repeated positive urine culture (relative risk 0.44), but there was no information about rates of symptomatic recurrent infection or long-term renal sequelae. In one study, nitrofurantoin was more effective than trimethoprim in preventing recurrent UTI over a 6-month period (RR 0.48), but patients were more likely to discontinue nitrofurantoin because of side effects. In another study, cefixime was more effective than nitrofurantoin in preventing

recurrent UTI during the first 6 months (RR 0.74), but adverse reactions were more common with cefixime than with nitrofurantoin (63% vs. 26%).

Historically, the use of antimicrobial prophylaxis in all children with UTIs—in the 1970s—was based on studies that included asymptomatic bacteriuria as well as the more important symptomatic UTIs. The '70s data suggested that prophylaxis prevented recurrent positive urine cultures, many of which were from asymptomatic children. There also were insufficient data to prove that prophylaxis prevented renal scarring or the need for kidney transplantation. People had presumed that asymptomatic bacteriuria was as important as symptomatic UTI in leading to long-term kidney issues, but there was no definitive evidence for this.

Later imaging results indicated that VUR was associated with more frequent UTI, although we still didn't have proof of their association with long-term renal damage. Recent data indicate that lower grades of reflux are not statistically associated with long-term kidney injury or renal scarring, and now we see that the first recurrent UTI occurs just as soon, whether children are on or off prophylaxis. At the same time, we are increasingly concerned about antimicrobial resistance. The drugs typically used for prophylaxis—amoxicillin, trimethoprim-sulfamethoxazole, and first-generation cephalosporins—have become less and less active in vitro against the most common UTI pathogen, *Escherichia coli*.

Until we get more definitive data, I think that we can be more selective in deciding which patients with a first UTI should receive antimicrobial prophylaxis without exposing these children to extra risks. My personal bias is to limit prophylaxis to those in whom imaging shows either grade 4 or 5 VUR or other obstructive anatomic abnormalities. For children with lower grades of reflux, I would sim-

ply observe them for a recurrence pattern, keeping in mind that some may show more frequent recurrences than expected. This subset might need urologic referral to look for more subtle problems that can benefit from intervention. Given what we know about the risk of antimicrobial resistance, my advice would be to avoid 365 days per year of antibiotic exposure (prophylaxis) with low-grade VUR unless there were more than three UTI recurrences per year.

For children with high degrees of reflux (4 and 5), in vitro resistance data and hints from recent studies suggest that nitrofurantoin may currently be our best bet for prophylaxis. The micronized formulation (Macrobid) appears to have the fewest gastrointestinal side effects, so I'd use it as a first choice.

If patients don't tolerate nitrofurantoin, we should look at local resistance patterns, or perhaps a first-generation cephalosporin might be the next best choice. It's possible that broader-spectrum antimicrobials may work well in certain patients, but we don't have enough data on the prevalence of mechanisms of resistance, and tendencies to induce resistance, to comfortably use them empirically.

And, of course, we need to remember that when we do decide to prescribe long-term daily antibiotics, we can't assume for a minute that adherence will be complete. As the old saying goes, "Two-thirds of patients take two-thirds of the antibiotic two-thirds of the days prescribed." One thing for which we have definitive proof is that nobody takes a drug every single day. ■

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BY CHRISTOPHER J. HARRISON, M.D.

Community-Acquired MRSA, Spider Bites Present Similarly

BY JANE SALODOF MACNEIL
Senior Editor

PHOENIX — When a child presents with what looks like a spider bite, but the family can't find a spider, Dr. Lawrence F. Eichenfield considers community-acquired methicillin-resistant *Staphylococcus aureus*.

"Most pediatric cases we see are not in wrestlers or football players. They are in families that have problems with MRSA, so the epidemiology has changed," he told clinicians at a clinical dermatology conference sponsored by Medicis.

Spider bite–appearing lesions are a classic presentation of MRSA, according to Dr. Eichenfield, chief of pediatric and adolescent dermatology at Rady Children's Hospital–San Diego and professor of pediatrics and medicine at the University of California, San Diego. If the child's lesion looks like a spider bite, he recommended asking whether any-



one in the family has a history of abscesses or recurrent folliculitis.

Draining abscesses is usually more effective than using antibiotics when patients have community-acquired MRSA, Dr. Eichenfield said. He cited a recent study that found 57% of emergency department patients received the wrong antibiotics for skin and soft-tissue infections caused by community-acquired MRSA (N. Engl. J. Med. 2006;355:666-74). Many busy physicians don't want to take the time to drain an abscess, he said, but "study after study shows it [drainage] is way more effective."

DR. EICHENFIELD

Warm soaks and drainage often are sufficient, he said, but warned that lesions greater than 5 cm present a higher risk. "Many times we use antibiotics concurrently, but drainage is really the key," he said.

The lesion always should be cultured, Dr. Eichenfield said. Community-acquired MRSA has different patterns of susceptibility to antibiotics than does hospital-acquired MRSA.



A MRSA abscess, like this one on a patient's hip, often can resemble a spider bite.

Community-acquired MRSA skin infections are being seen in neonates, though less frequently than in older children. He cited a study of 89 infants, mostly boys, who were less than 30 days old and had *S. aureus* infections. Among these, 77 infections involved skin and soft tissue, and 61 were methicillin resistant. Mothers of 13 infants with MRSA had a history of skin infections (Pediatrics 2006;118:874-81). ■