

## EXPERT COMMENTARY

## Antibiotic Prophylaxis for UTI Questioned

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 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.



BY CHRISTOPHER J. HARRISON, M.D.

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 simply 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. ■

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## Consider Cat-Scratch Disease in Setting With Fever, Kittens

BY GREG MUIRHEAD  
Contributing Writer

MAUI, HAWAII — "Ask about pets in every febrile patient you see" was one of the take-home messages from Dr. Jay M. Lieberman as he discussed infections you can get from your pets.

And in particular, he said, "Consider cat-scratch disease in any patient with fever of unknown origin who has contact with cats—particularly if they're kittens."

He presented several cases of children with prolonged fevers who remained without a diagnosis, despite extensive evaluations, until the possibility of cat-scratch disease was entertained and a history of contact with kittens was obtained. The diagnosis of cat-scratch disease often can be made from the history and physical examination, and serologies may not be reliable, Dr. Lieberman said at a meeting sponsored by the University Childrens Medical Group and the American Academy of Pediatrics.

Kittens are more likely to cause cat-scratch disease than are older cats. The disease is caused by *Bartonella henselae*, and approximately 40% of cats are bacteremic with the organism, explained Dr. Lieberman, professor of clinical pediatrics at the University of California, Irvine.

Cat-scratch disease is transmitted to humans through scratches, licks, or bites from kittens, less often from older cats, and sometimes from dogs.

A primary papule may be seen 3-12 days after inoculation time, followed 7-60 days (average 12-14 days) later by regional lymphadenopathy that may suppurate or regress over 2-4 months. Lymphadenopathy usually involves the nodes that drain the site of inoculation. Fever



Regional lymphadenopathy, as shown in this 8-year-old patient, can appear 7-60 days after a primary papule.

occurs in half of patients, and malaise, anorexia, and headache also may occur.

The area around the nodes may be noninflamed but can be warm, tender, and erythematous, Dr. Lieberman said at the meeting, which also was sponsored by California Chapter 2 of the AAP. As many as 30% of nodes will suppurate spontaneously.

Atypical presentations of cat-scratch disease included prolonged fever/fever of unknown origin, granulomatous hepatitis, conjunctivitis with preauricular adenopathy (Parinaud's oculoglandular syndrome), encephalopathy/encephalitis, osteomyelitis, and ocular disease.

Although patients may be treated with rifampin or gen-

tamicin or trimethoprim-sulfamethoxazole (TMP/SMZ), or a combination of anti-infectives, Dr. Lieberman does not routinely recommend their use. "In general, we have not treated our patients with antimicrobial therapy," he said. "Most patients do not require specific therapy, and the illness resolves on its own."

One prospective randomized trial of azithromycin vs. placebo found a significantly greater decrease in lymph node size in azithromycin-treated patients at 30 days, but there was no significant difference thereafter (Pediatr. Infect. Dis. J. 1998;17:447-52).

Dr. Lieberman also noted that approximately 5%-15% of dog bites lead to infections, as do 20%-50% of cat bites. *Pasteurella* species, short gram-negative coccobacilli that are part of the normal flora of cats and dogs, are isolated from 75% of infections from cat bites and 50% of infections from dog bites. *Pasteurella* organisms are not susceptible to cephalexin or dicloxacillin, Dr. Lieberman said.

To help prevent infection from bites, wounds should be cleaned, debrided, and closed. Bite wounds should be reevaluated in 1-2 days. When indicated, there may be a need for tetanus and/or rabies prophylaxis.

Antibiotic prophylaxis is indicated for puncture wounds (including all cat bites), bites over tendons, joints, and bone; bites on the face and/or genitals; bites involving an immunocompromised person; and bites that cannot be well cleaned and debrided. Antibiotic prophylaxis, when indicated, may be used for 48-72 hours.

Amoxicillin-clavulanate is the antibiotic of choice for prevention or treatment of animal bite wound infections, he said. Dr. Lieberman disclosed that he is on a speakers' bureau for GlaxoSmithKline. ■