

ID CONSULT

UTI Management Lacks Consensus

The conventional wisdom about urinary tract infections has changed over the years, but we still don't have consensus regarding many of its management issues.

When I was an intern in 1972, it was relatively simple. We would admit a child with a UTI to the hospital, start antimicrobial therapy, do an intravenous pyelogram after a negative urine culture, and keep the child on antibiotics for a month until the follow-up vesicoureterogram (VCUG). But in the 1980s, people began to question the evidence for spending resources on imaging and for promoting antimicrobial resistance when it may not be necessary.

Today we know that UTIs are common in children of all ages, but the main concern is for those in the under-2-year age group, where there is the greatest risk for renal damage that can result from treatment delayed beyond 72 hours of fever. Vesicoureteral reflux is far more common in this age group and tends to remit with increasing age. There is also agreement that evaluation for UTI is essential for any child in that age range who has had unexplained fever for more than 24 hours. Approximately 5% will be positive.

We have data to guide our decisions regarding who is at greatest risk for UTI. It is higher in females than males, with a 2-to-1 ratio in the first year of life and 4:1 in the second. But among boys, those who are uncircumcised have a 15- to 20-fold higher UTI rate than among those who are circumcised.

Since the advent of the 7-valent pneumococcal conjugate vaccine (PCV7), we have seen *Escherichia coli* increase proportionally as a cause of bacteremia as a result of the decline in pneumococcal disease (Arch. Dis. Child. 2009;94:144-7). However, the overall rate of positive urine culture among children aged 3-36 months presenting to the emergency room with fever has not changed with PCV7, remaining at approximately 7%.

There's controversy regarding UTI screening. Urine culture is the standard, with identification of 10 white blood cells per high-powered field in unspun urine on gram stain. However, this is time consuming and requires an expertise that many practitioners have lost since their training.

The presence of leukocyte esterase and nitrites on dipstick has become a widely used screen for children at risk for UTI. They are highly specific for gram-negative UTIs, but not as good for detecting gram-positive organisms.

Dipstick testing works best in ruling out a UTI: If both leukocyte esterase and nitrite tests are negative, the likelihood of a UTI is extremely low. If both are positive in a symptomatic at-risk child, it's an indication to initiate therapy and obtain a culture to confirm the

infection, identify the pathogen, and determine its antimicrobial susceptibility.

While use of the two measures is considered an acceptable, rapid way to screen for UTI, there is a tradeoff. For every 1,000 children with compatible UTI signs and symptoms, these tests will identify greater than 90% of the children with culture-confirmed infection. However, as many as 20% of the children will be treated unnecessarily with antibiotics.

Collecting the urine specimen is another area that lacks consensus. Urine collected in a bag is unreliable in children less than 2 years of age, and it's not certain whether bag collection can be used in older children. Three culture collection strategies are recommended by the American Academy of Pediatrics (AAP) guideline committee report: suprapubic aspiration, catheterized specimen for girls/midstream stream in circumcised boys, or midstream clean void in girls or uncircumcised boys.

Suprapubic aspiration is the standard, but it's more time consuming, difficult, and is associated with more discomfort. It is typically reserved for children less than 6 months of age. On the other hand, a single midstream clean void is just 80%-90% reproducible so some recommend a second specimen to achieve greater (95%) reproducibility.

One area in which I do think the data are clear concerns the duration of therapy. Since approximately 50%-60% of children aged 2 months to 2 years with UTIs also have upper tract infection, there is a far better chance of cure and less chance of recurrence with 7-10 days of antibiotics vs. 3 days or fewer (Pediatr. Infect. Dis. J. 1988;7:316-9).

The most controversial areas in UTI management concern imaging and antimicrobial prophylaxis. Imaging, via sonogram plus either VCUG or radionuclide scan, accomplishes four goals: It localizes the infection (upper vs. lower tract), identifies the presence of reflux, identifies structural abnormalities, and detects renal scarring. But most structural abnormalities are already identified with prenatal ultrasound, and it's not clear whether progression of renal scarring can be prevented with prophylactic antibiotics in children with reflux.

There is recent conflicting evidence regarding the benefit of antimicrobial prophylaxis. In a meta-analysis of eight randomized controlled trials that included 677 children who had recovered from a symptomatic UTI and in whom vesicoureteral reflux had been identified independent of acute infection, there was no difference between those who did and did not receive antimicrobial prophylaxis in recurrence of symptomatic UTI or in the incidence of new or progressive renal scarring (Acta Paediatr. 2009;98:1781-6).

But the 20-center Swedish Reflux Trial

did find benefit. In that study, reflux status was compared in 203 children (128 girls/75 boys) with grade III-IV dilating vesicoureteral reflux who were treated in one of three groups, either with low-dose antibiotic prophylaxis, endoscopic therapy, or with surveillance and antibiotic treatment only for febrile UTI. At 2 years, reflux had improved in all treatment arms, with reflux resolution or downgrading to grades I or II occurring in 39% of the prophylaxis group, 71% with endoscopic treatment, and 47% with surveillance (J. Urol. 2010;184:280-5).

Of concern, however, dilating reflux reappeared after initially being downgraded in 20% of the children who had received endoscopic treatment.

Both antimicrobial treatment and endoscopic therapy reduced the infection recurrence rate among the girls, occurring in 8 of 43 (19%) on prophylaxis and 10 of 43 (23%) with endoscopic therapy, compared with 24 of 42 (57%) on surveillance. In girls, the recurrence rate was associated with persistent reflux after 2 years. However, reflux severity (grade III or IV) at study entry did not predict recurrence (J. Urol. 2010;184:286-91).

Given the conflicting data, it's no surprise that guidelines also differ. The AAP advises ultrasound and VCUG for all children aged 2 months to 2 years, and antimicrobial prophylaxis for all in whom reflux is identified (Pediatrics 103;1999:843-52). In contrast, guidelines from the United Kingdom advise ultrasound only for recurrent or "atypical" UTI, and do not recommend prophylaxis after a first UTI, but only after a recurrence.

Also not surprising, practitioners differ in what they do. In an analysis of Washington State Medicaid data for 780 children diagnosed with UTI during their first year of life, less than half received either timely anatomic imaging (44%) or imaging for reflux (39.5%). Of those who had imaging for reflux, only 51% had adequate antibiotics to maintain antimicrobial prophylaxis between diagnosis and imaging for reflux (Pediatrics 2005;115:1474-8).

I believe there is certainly a role for prophylaxis in a child with recurrent UTI, especially recurrent symptomatic/febrile UTI. But whether there's a role after the first UTI remains uncertain, with conflicting evidence. We might get some answers from an ongoing randomized, placebo-controlled intervention sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (clinicaltrials.gov identifier NCT00405704), for which results are expected in June 2011. ■

DR. PELTON is chief of pediatric infectious disease and also is the coordinator of the maternal-child HIV program at Boston Medical Center. Dr. Pelton said he has received research grants and served as a consultant to GlaxoSmithKline, Pfizer, Novartis, and Intercell.

Risks for Flu Admissions Examined

BY M. ALEXANDER OTTO

FROM THE ANNUAL MEETING OF THE INFECTIOUS DISEASES SOCIETY OF AMERICA

VANCOUVER, B.C. – The risk that a child will be hospitalized with influenza more than doubles if more than half of the household members smoke, maternal age is below 22 years, or household income is below the poverty line.

However, the risk is halved if children are breastfed for 6 months or more, or if caregivers are immunized against the influenza if their children are not, according to Dr. Nila Dharan, who is with New York University's division of infectious diseases.

Dr. Dharan and her colleagues compared the medical and demographic histories of 290 children aged 6-59 months hospitalized with influenza with 1,089 age- and zip code-matched children who were not hospitalized with influenza.

Although most of the risk and protective factors are known, "This study is the largest to date examining the risk of childhood exposure to cigarette smoke and hospitalization for influenza and highlights the importance of reducing children's environmental exposure to smoke, and the need for vaccination of both the child and their household contacts," she said.

Among other findings, children not current with their vaccinations had a greater risk of influenza hospitalization (odds ratio 1.7), highlighting "the benefits of routine childhood vaccinations which may reduce the risk of secondary bacterial infections," Dr. Dharan said at the meeting.

Of all the risk factors, however, preexisting medical conditions were the most significant, including pulmonary and neurologic conditions, but especially hematologic or oncologic ones (OR 12.1).

The study found a statistically significant trend toward greater protection the longer children are breastfed. Breastfeeding for their first year or longer was protective for children aged 2-5 years (OR 0.5); not being breastfed increased the risk of influenza-hospitalization (OR 1.7).

Day care did not increase influenza hospitalization risk (OR 1.1), but being a boy did (OR 1.3).

The study culled information during the 2005-2008 influenza seasons from 10 sites in the Center for Disease Control and Prevention's Emerging Infections Program.

Dr. Dharan said that she has no disclosures. ■