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The New American Academy of Pediatrics Urinary Tract Infection Guideline

This issue of *Pediatrics* includes a long-awaited update¹ of the American Academy of Pediatrics (AAP) 1999 urinary tract infection (UTI) practice parameter.² The new guideline is accompanied by a technical report³ that provides a comprehensive literature review and also a new meta-analysis, for which the authors obtained individual-level data from investigators. The result is an exceptionally evidence-based guideline that differs in important ways from the 1999 guideline and sets a high standard for transparency and scholarship.

The guideline and technical report address a logical sequence of questions that arise clinically, including (1) Which children should have their urine tested? (2) How should the sample be obtained? (3) How should UTIs be treated? (4) What imaging and follow-up are recommended after a diagnosis of UTI? and (5) How should children be followed after a UTI has been diagnosed? I will follow that same sequence in this commentary. I will mention some important areas of agreement and make other suggestions when I believe alternative recommendations are supported by available evidence.

WHICH CHILDREN SHOULD HAVE THEIR URINE TESTED?

Unlike the 1999 practice parameter, which recommended urine testing for all children aged 2 months to 2 years with unexplained fever,² the new guideline recommends selective urine testing based on the prior probability of UTI, which is an important improvement. The guideline and technical report do an admirable job summarizing the main factors that determine that prior probability (summarized in Table 1 in the clinical report). This table will help clinicians estimate whether the probability of UTI is $\geq 1\%$ or $\geq 2\%$, values that the authors suggest are reasonable thresholds for urine testing.

The guideline appropriately states that the threshold probability for urine testing is not known and that “clinicians will choose a threshold depending on factors such as their confidence that contact will be maintained through the illness. . . and comfort with diagnostic uncertainty.” However, the authors assert that this threshold is below 3%, which indicates that it is worth performing urine tests on more than 33 febrile children to identify a single UTI. This is puzzling, because the only study cited to support a specific testing threshold found that 33% of academicians and 54% of practitioners had a urine culture threshold higher than 3%.⁴

An evidence-based urine-testing threshold probability would be based on the risks and costs of urine testing compared with the benefits of diagnosing a UTI. These benefits are not known and probably are not uniform; the younger and sicker an infant is and the longer he or she has been febrile, the greater the likely benefit of diagnosing and treating a UTI. Because acute symptoms of most UTIs seem to resolve un-

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ABBREVIATIONS

AAP—American Academy of Pediatrics

UTI—urinary tract infection

VCUG—voiding cystourethrogram

VUR—vesicoureteral reflux

Opinions expressed in these commentaries are those of the author and not necessarily those of the American Academy of Pediatrics or its Committees.

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eventfully, even without treatment,^{5,6} some of the impetus for diagnosing UTIs rests on the belief that doing so will reduce the risk of renal scarring and associated sequelae.⁷ This belief needs to be proven, and the benefit quantified, if a urine-testing threshold is to be evidence-based. Until then, rather than automatically testing urine on the basis of the risk factors and the 1% or 2% threshold suggested in Table 1, clinicians should continue to individualize. It seems reasonable, for example, to defer urine tests on the large number of febrile infants for whom, if their parents had called for advice, we would have estimated their probability of UTI or other serious illness to be low enough that they could be safely initially watched at home.

A potential source of confusion is that Table 1 lists “absence of another source of infection” as a risk factor, and the technical report indicates that this factor has a likelihood ratio of ~1.4 for UTI. However, the inclusion of this risk factor in the table is inconsistent with the text of the guideline, which directs clinicians to assess the likelihood of UTI in febrile infants with no apparent source for the fever. If children with an apparent source for their fever are included, the use of Table 1 could lead to excessive urine testing (eg, among infants with colds). For example, even using the 2% testing threshold, according to Table 1 all non-black uncircumcised boys younger than 24 months with any fever of any duration, even with an apparent source, would need their urine tested. I doubt that this level of urine testing is necessary or was intended by the authors of the guideline.

HOW SHOULD THE SAMPLE BE OBTAINED?

I am glad the new guideline continues to offer the option of obtaining urine for urinalyses noninvasively, but I am

not convinced that the bag urine can never be used for culture. If the urinalysis is used to select urine for culture, the prior probability may sometimes be in a range where the bag culture will be useful. For example, the technical report calculates that “with a prevalence of 5% and specificity of 70%, the positive predictive value of a positive culture obtained by bag would be 15%.” However, with the same 5% pretest probability, a positive nitrite test would raise the probability of UTI to ~75% (using the median sensitivity [58%] and specificity [99%] in the technical report). This is high enough to make the positive culture on bag urine convincing (and perhaps unnecessary).

Although bag urine cultures can lead to errors, catheterized urine cultures are not perfect¹ and urethral catheterization is painful,⁸ frightening,⁹ and risks introducing infection.¹⁰ Fortunately, if other recommendations in the guideline are followed (including the elimination of routine voiding cystourethrograms [VCUGs] and outpatient rather than inpatient antimicrobial therapy; see below), the adverse consequences of falsely positive bag cultures will be markedly attenuated.

HOW SHOULD UTIs BE TREATED?

The guideline recognizes regional variation in antimicrobial susceptibility patterns and appropriately suggests that they dictate the choice of initial treatment. However, I would adjust the choice on the basis of the clinical course rather than on sensitivity testing of the isolated uropathogen, as recommended in the guideline. At the University of California at San Francisco we have the option of a “screening” urine culture, which provides only the colony count and Gram-stain results for positive cultures (eg, “10⁵ Gram-negative rods”). We can later add identification and sensitivities of the organism in the rare instances in which

obtaining them is clinically indicated. Use of screening cultures can lead to considerable savings, because identification of organisms and antimicrobial susceptibility testing are expensive and unnecessary in the majority of cases in which patients are better within 24 hours of starting treatment.

The guideline and technical report cite good evidence that oral antimicrobial treatment is as effective as parenteral treatment and state that the choice of route of administration should be based on “practical considerations.” However, the examples they cite for when parenteral antibiotics are reasonable (eg, toxic appearance and inability to retain oral medications) seem more like clinical than practical considerations. Given equivalent estimates of efficacy and the dramatic differences in cost, the guideline could have more forcefully recommended oral treatment in the absence of clinical contraindications.

WHAT IMAGING IS INDICATED AFTER UTI?

As in the 1999 AAP guideline, the current guideline recommends a renal/bladder ultrasound examination after a first febrile UTI to rule out anatomic abnormalities (particularly obstruction) that warrant further evaluation. Although the yield of this test is low, particularly if there has been a normal third-trimester prenatal ultrasound scan, the estimated 1% to 2% yield of actionable abnormalities was believed to be sufficient to justify this noninvasive test. This may be so, but it is important to note that it is not just the yield of abnormalities but also the evidence of an advantage of early detection and cost-effectiveness that must be considered when deciding whether an ultrasound scan is indicated after the first febrile UTI, and this evidence was not reviewed.

The recommendation most dramatically different from the 1999 guideline

is that a VCUG not be routinely performed after a first febrile UTI. The main reason for this change is the accumulation of evidence casting doubt on the benefit of making a diagnosis of vesicoureteral reflux (VUR). To put these data in historical perspective, operative ureteral reimplantation was standard treatment for VUR until randomized trials found it to be no better than prophylactic antibiotics at preventing renal scarring.^{11–13} Although, as one commentator put it, “It is psychologically difficult to accept results that suggest that time-honored methods that are generally recommended and applied are of no or doubtful value,”¹⁴ ureteral reimplantation was gradually replaced with prophylactic antibiotics as standard treatment for VUR. This was not because of evidence of benefit of antibiotics but because their use was easier and less invasive than ureteral reimplantation. Finally, in the last few years, several randomized trials have investigated the efficacy of prophylactic antibiotics for children with reflux and have found little, if any, benefit.^{1,3} Thus, the risks, costs, and discomfort of the VCUG are hard to justify, because there is no evidence that patients benefit from having their VUR diagnosed.^{15–18}

The recommendation not to perform a VCUG after the first UTI is consistent with a guideline published by the

United Kingdom’s National Institute for Health and Clinical Excellence (NICE).¹⁹ However, unlike the AAP, the NICE does not recommend that VCUGs be performed routinely for recurrent UTIs in infants older than 6 months, which makes sense; the arguments against VCUGs after a first UTI still hold after a second UTI. The AAP recommendation to perform a VCUG after the second UTI is based on the increasing likelihood of detecting higher grades of reflux in children with recurrent UTIs and the belief that detecting grade V reflux is beneficial. However, the guideline appropriately recognizes that grade V reflux is rare and that the benefits of diagnosing it are still in some doubt. Therefore, the guideline suggests that parent preferences be considered in making these imaging decisions.

HOW SHOULD CHILDREN BE FOLLOWED AFTER A UTI HAS BEEN DIAGNOSED?

The guideline recommends that parents or guardians of children with confirmed UTI “seek prompt (ideally within 48 hours) medical evaluation for future febrile illnesses to ensure that recurrent infections can be detected and treated promptly.” As pointed out in the guideline, parents will ultimately make the judgment to seek medical care, and there is room for judgment here. After-hours or weekend visits would not generally be required for in-

fants who appear well, and the necessity and urgency of the visit would be expected to increase with the discomfort of the child, the height and duration of the fever, the absence of an alternative source, and the number of previous UTIs.

It should be noted that the guideline does not recommend prophylactic antibiotics to prevent UTI recurrences. This was a good decision; meta-analyses^{3,20} have revealed no significant reduction in symptomatic UTI from such prophylaxis regardless of whether VUR was present. Even in the study that showed a benefit,²¹ the absolute risk reduction for symptomatic UTI over the 1-year follow-up period was only ~6%, and there was no reduction in hospitalizations for UTI or in renal scarring. Thus, as one colleague put it, if UTI prophylaxis worked, it would offer the opportunity to “treat 16 children with antibiotics for a year to prevent treating one child with antibiotics for a week.” (A. R. Schroeder, MD, written communication, June 24, 2011).

CONCLUSIONS

I salute the authors of the new AAP UTI guideline and the accompanying technical report. Both publications represent a significant advance that should be helpful to clinicians and families dealing with this common problem.

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HEALTH AND HEALING THROUGH A GREEN THUMB: *While the summer is coming to an end, there is still ample time to get outside, enjoy the warm weather, and work in the garden. While gardening can yield flowers and produce, using your green thumb may improve your overall health. According to CNN.com (Health: July 8, 2011), gardening has been linked to decreased stress and depression, slowed dementia progression, and improved nutrient intake. Researchers in the Netherlands found that compared to those who read a book, individuals who garden after a stress-inducing task reported having better moods and show decreased cortisol levels. In addition, Norwegian researchers report that the novelty of gardening is powerful enough to decrease depressive symptoms in those with mood disorders. Research from the University of Colorado at Boulder adds that gardening leads to increased serotonin levels, likely contributing to the mood improvements in depressed individuals. Gardening, however, does more than just improve mood. It is a unique and easy-to-maintain form of exercise. Current research indicates that the mix of physical and mental exercise gardening provides may lower a person's risk of developing dementia. And, lastly, growing your own fruits and vegetables is linked to an increase in nutrient intake. So, what is keeping us all from taking advantage of these gardening benefits? Time pressures, the limited availability of yard space, and the expenses that go along with maintaining the yard and garden may make it difficult to engage in this hobby. However, with all of the benefits, it might be worthwhile to make getting outside and planting a priority!*

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