Section on Urology Response to New Guidelines for the Diagnosis and Management of UTI

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This commentary provides a summarized response regarding the newly published American Academy of Pediatrics Guidelines on urinary tract infection (UTI) diagnosis and evaluation from the Section on Urology of the American Academy of Pediatrics. Although the section supports some aspects of the guidelines, the new recommendation not to perform a voiding cystourethrogram (VCUG) after a first febrile UTI is not supported. The section expresses significant concern that the recommendation is based on a flawed interpretation of limited data and that this stands to potentially harm significant numbers of children because of delayed diagnosis of harmful urinary tract conditions.

The Section of Urology of the American Academy of Pediatrics enthusiastically supports many aspects of the new Guideline on UTI evaluation and management. Specifically, when faced with a febrile sick child (aged 2 months to 2 years), UTI should be considered a significant cause and a urine culture be obtained by urethral catheterization or suprapubic aspiration. Bag urine cultures are not recommended. Antibiotic therapy should not be started without a urine culture. The presence of ≥50 000 CFU/mL is now considered to be diagnostic of UTI, and oral or parenteral antibiotic therapy, tailored to bacterial sensitivity and clinical efficacy, is adequate initial therapy.

Under the 1999 Guideline, after a culture-proven febrile UTI, the recommended workup included a renal and bladder ultrasound (RBUS) and a VCUG. The new Guidelines recommend that an RBUS be performed but that a VCUG not be done if the RBUS is normal. This represents a paradigm shift in the evaluation of children with a febrile UTI. We agree that an ultrasound should be performed in a child after a febrile UTI; we do not agree that a VCUG should not be routinely performed. The recommendation is based on several recent studies comparing antibiotic prophylaxis with no prophylaxis in children with vesicoureteral reflux (VUR), with the conclusion that it is not worth making the diagnosis of VUR. We believe that these conclusions are premature and represent a misinterpretation of the data presented.

The studies cited are concerning in several ways. The Guidelines stress repeatedly that proper urine samples be obtained by urethral catheterization or suprapubic aspiration to accurately diagnose a UTI. Yet the articles cited depend heavily on data from bag specimens. The circumcision status for boys is unaccounted for; this is important because of the well-known relationship between febrile UTI and being uncircumcised in boys <1 year of age. It is not unexpected that uncircumcised boys in these cohorts would have UTIs, whether or not they were on prophylaxis. In addition, bagged specimens are particularly inaccurate in these boys. There is no

ABBREVIATIONS

RBUS—renal and bladder ultrasound
UTI—urinary tract infection
VCUG—voiding cystourethrogram
VUR—vesicoureteral reflux

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acknowledgment of the role of bladder and bowel habits in most of these studies nor in the Guidelines, yet this has significant impact on VUR outcomes. These studies also lack statistical power to make the determination that antibiotic prophylaxis or non-treatment was better, especially when comparing individuals with different grades of reflux. Compliance with antibiotic prophylaxis was only assessed in 1 study and then only in those who had recurrent UTI. Renal scarring cannot be determined by ultrasound, dimercapto succinic acid (DMSA) scans can detect scarring, but in 3 of the studies, they were not routinely performed.

The meta-analytic combination of the data in these studies raises concerns regarding the validity of the conclusions as well. The individual studies (see Fig 3 in the Guidelines) actually show a small trend toward antibiotic prophylaxis efficacy. The Swedish Reflux Trial, for example, showed that antibiotic prophylaxis significantly decreased the recurrent febrile UTI rates in girls with grade III or IV VUR. In addition, new renal damage due to infection seen on renal scan was 3 times greater in the nontreatment group than the prophylaxis group. When combined, however, the overall effect disappears possibly reflecting an “amalgamation effect,” (Simpson’s paradox) in which individual studies may trend in one direction but when combined show an opposite conclusion. This is often seen when studies of differing sizes are combined and when confounding effects are unaccounted: for example, bag specimens, circumcision status, drug compliance, or bladder and bowel dysfunction.

The relationship between renal damage and number of known febrile UTIs (see p. 605 of the Guidelines, Fig 4) is well established; the incidence of scarring roughly doubles after the second febrile UTI. The recommendation in the new Guidelines (to wait until there is a second febrile UTI) is making the assumption that reducing the number of initial VCUGs is worth the risk of increased renal scarring; this is a value judgment, not a scientific conclusion, and should be discussed and acknowledged as such.

The general conclusion that treatment of reflux offers no clinical benefit ignores the prior literature showing that antireflux surgery reduces recurrent febrile UTI among children with grade III and IV VUR. Thus, even if antibiotic prophylaxis is found to be less effective in some children, there are advantages to early detection and surgical therapy.

Action Statement 6, that a “VCUG should not be performed” with the first febrile UTI, will send the inappropriate and incorrect message to pediatricians and other primary care clinicians that this issue is a settled scientific fact. The real-world consequence is that it will imply that deferring the VCUG is now the standard of care and may cause many to infer wrongly that choosing to order an initial VCUG is substandard care. The impact may be felt particularly among those children who are most disadvantaged. Under the prior 1999 Guidelines, less than half of children diagnosed with a UTI aged <1 year received the recommended anatomic imaging. This was particularly true for those on Medicaid. This recommendation also ignores the fact that many children do not have consistent primary caregivers, and, therefore, a pediatrician might not even be aware that a first UTI has occurred. A heavy burden is placed on parents and guardians who are now responsible for identifying the next febrile episode as a UTI. Finally, it assumes that the first febrile infection diagnosed is truly the first febrile infection that has occurred.

The literature on the use of RBUS-centered clinical decision protocols on deciding which children should undergo VCUG testing is not encouraging. The 2007 UK National Institute for Health and Clinical Excellence (NICE) guidelines limited the use of VCUG only to those patients who had an abnormal RBUS. An analysis of the effect of applying these guidelines in infants with UTI aged <6 months (98 patients, 196 kidneys) found that 25 refluxing ureters and 22 scarred kidneys would have been missed.

The members of the Section on Urology are aware that the understanding of VUR, its evaluation, and treatment remains incomplete and that there is a need to better determine who needs to be evaluated and treated. There are many children in whom VUR is not a dangerous condition and in whom little, if any, therapy is necessary. However, it is equally clear that there are many children in whom VUR is a serious condition, and prompt early detection and therapy can prevent kidney infection, damage, and loss of function. Our membership has been and continues to be actively engaged in research that may permit a better differentiation of these patients. However, we do not believe that the current data support a paradigm shift in the decision to defer a VCUG in children aged 2 months to 2 years after a febrile UTI. We strongly believe that the VCUG should not be omitted but should remain an accepted option after a febrile UTI until there is more definitive evidence to conclude otherwise.

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REFERENCES


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