

Should the Diagnosis of UTI in Young Febrile Infants Require a Positive Urinalysis?

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Reduction of antibiotic overuse is an important goal for improving the quality of care for children and is highlighted in many of the *Choosing Wisely*[®] recommendations across disciplines.¹⁻³ However, the evidence supporting these recommendations vary widely and many are derived from expert opinion and clinical practice guidelines rather than from original research studies.² In this issue of the *Journal of Hospital Medicine*, Schroeder and colleagues identify a potential area of antibiotic overuse among young febrile infants with possible urinary tract infection (UTI).⁴ A wide variation in antibiotic treatment rates (0%-35%) was observed across 124 hospitals in the United States for febrile infants 7-60 days of age with uropathogen detection by urine culture but a negative urinalysis (UA). Treated infants with a negative UA were more likely to be younger (7-30 days), have respiratory symptoms, and were less likely to have abnormal inflammatory markers than infants with a positive UA.

Clinicians faced with the decision of whether or not to treat a febrile infant with uropathogen detection in the setting of a negative UA must weigh the potential benefits and harms of antibiotic use in this population. Withholding antibiotics for a young infant with UTI may increase the risk of recurrent UTI and renal scarring,^{5,6} while antibiotic treatment in young infants can lead to the disruption of the gut microbiome, resulting in long-term consequences that are only beginning to be understood.⁷⁻¹⁰

The American Academy of Pediatrics (AAP) UTI practice parameter requires a positive UA to establish the diagnosis of UTI in children 2-24 months of age.¹¹ This recommendation is based primarily on studies demonstrating that uropathogen detection in the setting of a negative UA commonly represents asymptomatic bacteriuria or contamination rather than true infection.¹²⁻¹⁴ This is supported by research showing that the UA demonstrates near perfect (>99%) sensitivity for UTI in children with bacteremic UTI,^{12,15} and studies demonstrating lower rates of subsequent urinary infections and renal injury among infants with uropathogen detection and a negative UA compared with those with uropathogen detection and a positive UA.^{13,14,16}

An important question is whether febrile infants within the first two months of life with uropathogen detection should be treated with antimicrobials regardless of UA findings or specifically in the setting of a negative UA. The AAP practice guideline¹¹ deliberately omits these young infants, recognizing that evidence derived from studies of older infants and children may not be applicable to this young age group, as they may not mount as robust an inflammatory response and thus may not demonstrate pyuria in the setting of a bacterial urinary infection. Schroeder et al. demonstrate lower rates of abnormal inflammatory markers in UA negative compared with UA positive infants, a finding the authors argue supports the possibility of asymptomatic bacteriuria or contamination rather than true infection.⁴ The counterargument is that young infants may not mount a significant inflammatory response to true infections.

The authors appropriately highlight the paucity of literature to help differentiate true infection from asymptomatic bacteriuria or contamination in infants less than two months of age. As infants in this age group are usually treated with antibiotics for a positive urine culture regardless of UA result, robust data on short- and long-term outcomes of untreated infants are lacking. Much of the existing literature evaluates the test performance of the UA for UTI using the urine culture as the reference standard, which presents inherent limitations with incorporating the results of the UA into the definition of UTI using these data. Additionally, reported test performance of the UA for UTI varies by uropathogen type,¹⁷ fever duration,¹⁸ associated bacteremia,¹⁹ and urine concentration,²⁰ which are important considerations when applying a strict definition of UTI that includes the UA in this age group. Conversely, more recent studies have demonstrated improved sensitivity of the dipstick and microscopic UA for the detection of UTI.^{15,20,21} The improved test performance may not only enhance the use of the UA as a screen for UTI in this high-risk population but also allow its potential inclusion into the definition of UTI as the authors suggest, as previous false-negative UTIs would be less frequent with improved UA testing modalities.

Ultimately, what's missing from the equation is whether treatment of young febrile infants with uropathogen detection in the setting of a negative UA affects either short-term or long-term complications of UTI. Unfortunately, limited information exists to help inform the decision to initiate antibiotic treatment for these infants. Ideally, this question can only be answered by either an observational study evaluating outcomes of untreated infants or a randomized trial of antibiot-

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ics for infants less than two months of age with uropathogen detection in the setting of a negative UA. Until then, we may continue to observe a wide variation in antibiotic treatment rates for febrile young infants with uropathogen detection in the setting of a negative UA.

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