UTI and Faulty Gold Standards

I read with interest the article by Shaikh et al[1] on the association between pyuria and uropathogen type in children being evaluated for urinary tract infection (UTI). Their conclusion differs from our related investigation[2] in *Pediatrics*, in which we concluded that the sensitivity of the urinalysis (UA) has been previously underestimated due to a faulty gold standard, namely, urine cultures that are falsely positive because of contamination and asymptomatic bacteruria (AB). In our sample of young infants with bacteremic UTI, a condition that cannot be explained by contamination or AB, 99.5% of subjects had a UA that was positive for either leukocyte esterase or pyuria (≥3 white blood cells per high-power field).[2] The accompanying commentary to our article concluded that "the absence of pyuria should create great doubt about the presence of a UTI."[3]

In this recent investigation, Shaikh et al[1] present data consistent with previous reports that pyuria on the UA is imperfectly sensitive, and provide new information suggesting that the sensitivity might differ by uropathogen. They report that the sensitivity of pyuria of only 90% cannot be explained by AB, because the prevalence of AB is "too low (<1%)." The actual prevalence of AB (detected via suprapubic aspirate) in the study by Wettergren et al,[4] which the authors cite in making this claim, is 1.4%: 0.9% in girls and 2.5% in boys. Nonetheless, even a prevalence of AB as low as 1% could have a substantial impact on the apparent sensitivity of the UA. In the Shaikh et al[1] study, for example, the estimated prevalence of UTI was ∼5% (1394/26 151). If the population prevalence of AB is 1% in children, then an estimated 1 of 5 positive cultures in their sample will be falsely positive (ie, a positive urine culture with a negative UA). Therefore, if this population were similar to the population of Wettergren et al,[4] the sensitivity of even a perfect screening test applied to this population would theoretically be ∼80%. As long as urine cultures alone are used as a gold standard to define UTI, we are unlikely to ever see UA sensitivities that approach 100%. The fact that sensitivities in this study appear to differ by pathogen also could be explained by the varying likelihoods of certain organisms to colonize the genitourinary tract and/or contaminate a urine sample.

Shaikh et al[1] also reiterate concerns that a delay in the diagnosis of UTI (as might occur if a physician is misled by a negative UA) may increase the risk of renal scarring. However, this concern is belied by data from their own meta-analysis demonstrating that fever >24 hours before diagnosis of UTI is not associated with renal scarring (odds ratio 1.11, 95% confidence interval 0.72–1.71).[5]

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POTENTIAL CONFLICT OF INTEREST: The author has indicated he has no potential conflicts of interest to disclose.

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doi:10.1542/peds.20163814A

Should We Believe the Urinalysis?

In the post–Haemophilus influenzae type b, postpneumococcal immunization era, urinary tract infections (UTIs) are the most common serious bacterial infection in infants and young children. The diagnosis of UTI is challenging in this population and has received much attention, including a 2011 American Academy of Pediatrics clinical practice guideline (CPG) on diagnosis and management of UTI in febrile infants and young children.[1] The recent article by Shaikh et al[2] in *Pediatrics* on the association between uropathogens and pyuria and the accompanying commentary by Aaron Friedman[3] support the importance of a urine culture even in the absence of a negative urinalysis (UA). On the other hand, Schroeder et al[4] find that in infants <3 months with a true UTI, UA sensitivity is higher than previously reported for UTI, suggesting that the UA is reliable even in young infants. What is a clinician to do?

As Dr Lewis First suggests in his commentary, let's look at the context.[5] The discrepancy regarding the utility of a UA as a screening test for UTI may be due to the different populations that these studies are addressing. Shaikh et al[2] evaluated children with "symptoms consistent with a diagnosis of a UTI" in whom it would make sense to have a high index of suspicion even with a negative UA and perhaps have a lower threshold for starting antibiotics pending urine culture results, which always should be obtained. Such an approach may be too conservative in a well-appearing (likely not bacteremic) patient with fever without localizing source with a low

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Pediatrics 2017;139;
DOI: 10.1542/peds.2016-3814A originally published online February 28, 2017;

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Pediatrics 2017;139;
DOI: 10.1542/peds.2016-3814A originally published online February 28, 2017;