The Diagnosis of UTI: Liquid Gold and the Problem of Gold Standards

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Why is urine yellow? Because it is liquid gold! Pediatric nephrologist William Primack*

For >50 years, the gold standard for the diagnosis of urinary tract infections (UTIs) has been a positive culture result without regard for urinalysis findings. Both the definition of “positive” and the role of urinalysis stem from a publication in 1956. Edward Kass applied quantitative culture methods to urine specimens obtained from adults by catheterization to determine a dividing line between contamination and infection. The urine of most, but not all, patients with symptoms of acute pyelonephritis (chills, fever, flank pain, and dysuria) contained $10^5$ CFU/mL. Urine specimens from some asymptomatic women also had such high colony counts but most were much lower. Kass concluded: “For survey purposes, a count of $10^5$ bacteria or more per mL of urine has been designated arbitrarily as the dividing line between true bacilluria and contamination.” He acknowledged that for “individual clinical purposes,” lower colony counts needed to be considered and noted that pyuria did not reliably accompany bacteriuria in the asymptomatic women. During the subsequent decade, screening programs were widely conducted, applying $10^5$ CFU/mL as the diagnostic criterion without regard for the presence or absence of pyuria. The distinction between “survey” (screening) and “individual clinical purposes” became obscured; the threshold of $10^5$ became established in the minds of clinicians as absolute; and the significance of pyuria was overlooked.

By the end of the 1970s, asymptomatic bacteriuria (AB) was acknowledged to be a distinct entity involving colonization rather than infection, causing no morbidity except during pregnancy. Antimicrobial treatment was shown to be potentially harmful; bacterial replacement occurred with strains that increased the risk of symptomatic infection. Screening for AB was subsequently actively discouraged.

The question, however, is how to distinguish true UTI in an infant during a febrile illness from AB with the fever coming from a source other than the urinary tract, a situation akin to the dilemma with strep carriers who develop fever and have a throat culture performed. The distinction is that subjects with true UTI should have evidence of inflammation in their urine, whereas those with AB do not. By definition, therefore, the sensitivity of pyuria in a true UTI should be 100%. (The word “pyuria” is used here to indicate the presence of white blood cells and/or leukocyte esterase in the urine.) The finding of pyuria is particularly significant, because although bacteria are responsible for the infection, it is the host inflammatory response that damages the kidney. Other components of the urinalysis, such as nitrite and microscopically visible bacteria, indicate bacteriuria, but pyuria has a unique position of central importance regarding both the diagnosis of true infection and the risk of scarring. For
this reason, the American Academy of Pediatrics 2011 UTI guideline requires the presence of pyuria as well as a positive culture result for the diagnosis of UTI. 

Despite the importance of pyuria as noted here, its usefulness in the diagnosis of UTI was disregarded because of its apparent low sensitivity in various studies in adults, children, and young infants compared with culture as the gold standard. In this issue of Pediatrics, Schroeder et al raise the question of faulty gold standards, proposing that the observed sensitivity of pyuria compared with culture is reduced because, although some of the subjects studied had a true UTI, others likely had AB, and some may have had contaminated specimens. The authors compared the reported rate of AB in infants with the rate of bacteriuria in febrile infants and calculated that AB could account for the apparent low sensitivity of pyuria versus culture. They tested the validity of this proposition by studying a group of young infants with true UTI, as determined by the presence of the same organism in urine and blood. In these infants, the sensitivity of pyuria ranged from 96% to 99.5% (depending on the quantitative definition of pyuria), thus confirming its usefulness for diagnosis. Because pyuria can be detected at point of care, there is also great practical value to pyuria as a diagnostic criterion. By itself, pyuria is nonspecific and requires the addition of bacteriuria to establish the diagnosis of UTI, but the absence of pyuria should create great doubt about the presence of a UTI.

Schroeder et al also remind us that colony counts <100 000 CFU/mL may represent true UTIs, echoing the observation noted by Kass. Twenty years ago, Hoberman et al proposed 50 000 CFU/mL as a more appropriate threshold in children, adopted in the 2011 American Academy of Pediatrics guideline. Colony counts between 10 000 and 50 000 may also represent true UTIs, however, as recognized previously and now demonstrated by Schroeder et al when pyuria is associated with the same uropathogenic organism in urine and blood.

The article by Schroeder et al clarifies that, for "individual clinical purposes," establishing an accurate diagnosis of infection in specimens of "liquid gold" mandates a thoughtful reconsideration of what have traditionally been considered gold standards regarding pyuria and colony counts.

REFERENCES
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