The New England Journal of Medicine

Most women have had at least one symptomatic urinary tract infection, and many have had multiple recurrences. In the United States, billions of dollars are spent annually and tens of millions of courses of antimicrobial therapy are prescribed for urinary tract infections. The majority of these infections are caused by bacteria that colonize and induce inflammation in the bladder. Although complications are rare, acute cystitis can be extremely uncomfortable and result in lost productivity.

The voided midstream urine culture represents a convenient, noninvasively obtained specimen that can aid in the diagnosis of urinary tract infection. However, such cultures do not perfectly reflect the microbiology of the bladder. For more than 50 years, quantitative criteria have been used to differentiate samples indicative of bladder infection from those that more likely represent contamination. Thirty years ago, a seminal study involving young women with acute symptoms of urinary tract infection lowered the threshold for interpretation of such cultures to 100 colony-forming units (CFU) of Escherichia coli and other gram-negative uropathogens per milliliter of urine from an earlier threshold of 100,000 CFU per milliliter; the earlier threshold was established on the basis of samples obtained from a broader spectrum of patients. However, clinical microbiology laboratories, which may not be equipped to enumerate bacteria in low concentrations, often use a threshold of more than 1000 or 10,000 pathogens per milliliter to indicate positivity. Furthermore, criteria for the diagnosis of urinary tract infection caused by gram-positive bacteria remain unclear.

In this issue of the Journal, Hooton et al. report the results of studies designed to examine in more detail the correlation between the results of voided midstream urine cultures and bladder colonization. In almost all the 202 episodes of possible urinary tract infection that they evaluated, patients had two or more symptoms that are classically associated with acute cystitis, and none had features of upper urinary tract disease or other complicating factors. The simple study design called for obtaining quantitative cultures of matched specimens of midstream urine and bladder urine, the latter obtained through a urethral catheter. Bacteria were identified even from mixed cultures and at concentrations as low as 10 CFU per milliliter.

The results of this study extend our understanding of the value of midstream urine cultures, especially regarding the role of gram-positive bacteria. Bacteria were grown from about three quarters of bladder specimens, and 95% of these bacteria were common uropathogens, usually in pure culture. In contrast, bacteria were present in almost all midstream urine samples, and 86% yielded more than one species. As had been found earlier, there was an excellent correlation between the concentration of either E. coli or Klebsiella pneumoniae in the midstream urine culture and the presence of the same bacterium in the bladder. Although Staphylococcus saprophyticus was detected in only six episodes of infection, the concentration of these bacteria in the midstream urine culture also closely matched that in the bladder. Of note, E. coli in a midstream urine culture, even when it was detected at a concentration of only 10 CFU per milliliter or with one or more other species, strongly predicted the presence of E. coli in the bladder.

More than one quarter of bladder specimens were sterile, but bacteria that are often considered to cause urinary tract infection grew from...
The value of a midstream urine culture in the treatment of patients with symptoms of acute uncomplicated lower urinary tract infection has been questioned, since outcomes in such patients do not appear to be improved by the information obtained by this test. Despite declining reliance on midstream urine cultures, millions are still performed annually. Several aspects of the current study in the context of clinical practice may further erode the potential utility of the midstream urine culture. In most clinical laboratories, midstream urine specimens that have a low concentration of E. coli or E. coli in conjunction with other bacteria are reported as negative or contaminated, yet they may represent false negative tests. Conversely, midstream urine cultures from which moderate or high concentrations of enterococci or group B streptococci are isolated probably represent false positive tests for cystitis. If the midstream urine culture is to remain useful for the diagnosis of uncomplicated cystitis, it may need to be refined.

The cause of the symptoms associated with urinary tract infection in patients in whom no bladder bacteria were detected remains obscure. In the past, Chlamydia trachomatis was found in many of these patients, but Hooton et al. did not make similar observations. It has been suggested that bacteria recovered from specimens of midstream urine but not catheter urine might cause symptomatic urethritis in some patients. If so, do such patients benefit from antimicrobial therapy? If not, it seems that a vast number of patients are currently receiving unnecessary treatment, causing avoidable adverse effects and contributing to the loss of efficacy of the remaining antimicrobial agents in our dwindling arsenal. Future studies should be designed to address this question. The answer could lead to renewed interest in a beleaguered test.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

From the Division of Infectious Diseases, University of Maryland School of Medicine, Baltimore.


The New England Journal of Medicine
Downloaded from nejm.org by BRADFORD KNEY on December 25, 2013. For personal use only. No other uses without permission.
Copyright © 2013 Massachusetts Medical Society. All rights reserved.