

INFECTION

The shortcomings of standard tests and treatments for UTI

Standard tests for the detection of urinary tract infection (UTI) have serious flaws that compromise patient care. A UK-based research team has concluded that dipstick testing and microscopy “should no longer be recommended for screening” of patients with lower urinary tract symptoms (LUTS) in the absence of acute frequency and dysuria.

Guidelines currently advocate use of dipsticks for UTI screening. The easy-to-use strips indirectly indicate the presence of pyuria by detecting leukocyte esterase and bacterially produced nitrite. The reliability of these diagnostic aids has been questioned for many years, but their use remains ubiquitous.

On-the-spot dipstick testing of a midstream urine sample is usually followed by culture in media specific for *Enterobacter* species, the pathogens most likely to cause ‘typical’ UTI accompanied by acute frequency and dysuria. In the absence of these symptoms, how likely are these standard tests to detect clinically important infection?

Not likely enough, according to the results of a new study performed by Rajvinder Khasriya and colleagues at the Whittington Hospital in London. Patients referred to the hospital’s incontinence clinic for first assessment of LUTS were recruited. Only those without acute frequency and dysuria were enrolled.

Midstream samples from more than 500 predominantly female participants were processed. The sensitivities of leukocyte esterase and nitrite, relative to the current gold standard of culture that grows at least 10^5 colony-forming units (cfu) per ml, were 56% and 10%, respectively. The sensitivity of microscopic detection of white blood cells in fresh aliquots of urine—a third, but less-frequently employed, standard screening test for UTI—was also 56%. Specificities were

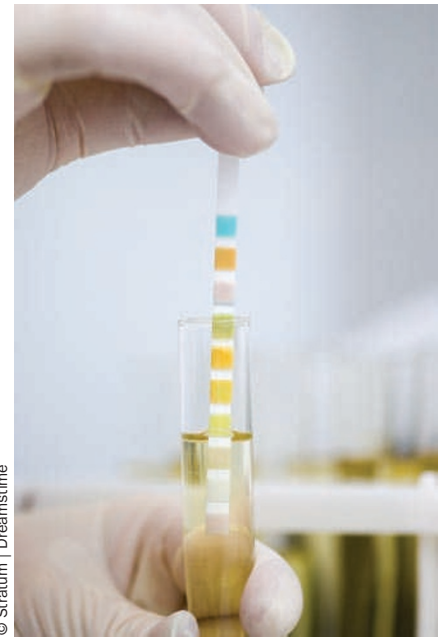
66%, 99% and 72% for leukocyte esterase, nitrite and microscopy, respectively.

On the basis of these poor results, the authors propose that dipsticks and microscopy be abandoned as standard tests for UTI among patients with LUTS. They are investigating alternative bedside methods in an effort to develop a test that combines the convenience of dipsticks with superior diagnostic capacity. Detection of bacterial ATP activity is the focus of their ongoing research in this area.

Khasriya *et al.* are also scrutinizing the performance of the gold-standard culture method. The widely-accepted threshold for positivity is 10^5 cfu/ml after incubation in *Enterobacter*-specific medium. The authors’ recent study included an experiment in which urine collected via catheter from 470 women with LUTS was submitted for culture. Relative to the 10^5 cfu/ml cutoff, twice as many cultures were positive when a benchmark of 10^2 cfu/ml was applied after growth in nonspecific medium. These findings indicate that current best practice is failing to detect infection in a significant proportion of patients with painless LUTS.

In the absence of reliable diagnostic tools, what should clinicians do? Khasriya stresses the importance of “listening to the patient’s symptoms and individualizing treatment, rather than relying on test results”. The team is working on a urine sediment test that captures adherent bacteria, which might cause the type of painless UTI harbored by a subgroup of LUTS sufferers.

Symptoms of overactive bladder (OAB) were reported by three-quarters of the LUTS patients from whom Khasriya *et al.* collected midstream urine samples. The fact that almost half of the study participants with OAB had abnormal urine test results raises intriguing questions as to the etiology of this



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condition. Could infection be a causative factor in a subset of OAB cases?

Regardless of detection method and species of causative agent, antibiotics remain the mainstay of UTI management. A paper published recently in the *Archives of Internal Medicine* highlights the potentially serious consequences of prescribing certain anti-infective agents to elderly patients taking warfarin.

Hadas Fischer and co-workers used information from Canadian health-care databases to show that co-administration of warfarin and cotrimoxazole—commonly prescribed for UTI—increases the odds of hospitalization for an upper gastrointestinal tract bleed fourfold. The risk rose twofold when ciprofloxacin and warfarin were administered concomitantly. One-tenth of those hospitalized died.

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Original articles Khasriya, R. *et al.* The inadequacy of urinary dipstick and microscopy as surrogate markers of urinary tract infection in urological outpatients with lower urinary tract symptoms without acute frequency and dysuria. *J. Urol.* **183**, 1843–1847 (2010) | Fischer, H. D. *et al.* Hemorrhage during warfarin therapy associated with cotrimoxazole and other urinary tract anti-infective agents. *Arch. Intern. Med.* **170**, 617–621 (2010)