



Debates in infection prevention

The Diagnosis and Management of UTI in >65s: To Dipstick or Not? The Argument Against Dipsticks

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Background

In 2018 Public Health England (PHE) published guidelines on the diagnosis of urinary tract infections (UTI) in primary care. For the first time they recommended against the use of urine dipsticks in frail older patients, an approach already well-established in Scotland and a number of other countries. [1,2] As part of the Commissioning Quality and Innovation scheme (CQUIN) 2019/20 for acute hospitals NHS improvement used these guidelines to incentivise a 'no dipstick' approach when diagnosing UTIs in older adults. [3] This has been controversial, due to the widespread and embedded use of urine dipsticks as accepted medical practice across primary and secondary care.

Urine is not sterile

Contrary to classical medical doctrine, urine is not sterile. Changes to the urinary microbiome are increasingly reported in a variety of conditions such as preterm labour, interstitial cystitis and overactive bladder. [4,5] Heavy and persistent colonisation with one predominant organism in the absence of localising urinary symptoms has been termed 'asymptomatic

bacteriuria' (bacteriuria $>10^5$ colony forming units per millilitre [cfu/mL] of the same organism on two separate urine specimens) [6]; a clinical entity more common in certain patient groups. The prevalence of asymptomatic bacteriuria rises from 5% of premenopausal women, to 80% of frail older women. [6,7] In the absence of acute urinary symptoms, this colonisation state has a benign natural history and may even be protective against symptomatic UTI. [8] Treatment of asymptomatic bacteriuria in older people confers no benefit and may cause harm. [9] Distinguishing this heavy colonisation from acute infection can be a significant challenge in older patients and the current available diagnostic tests, including urine dipsticks, do not help clinicians or patients.

Flaws in the test

"Diagnostic or therapeutic decisions should not be based on the basis of a single result." [10] This statement is from the packaging insert of a widely-used brand of dipsticks. Yet this warning is ignored on a daily basis throughout healthcare settings and across patient groups. Are urine dipsticks really good enough to be basing diagnostic and therapeutic decisions upon?

Urine dipsticks were already ubiquitous in clinical practice when standards regarding the introduction and implementation of point-of-care diagnostics were introduced by regulatory bodies. [11] The requirements to perform regular quality controls, follow a standard operating procedure and keep comprehensive records are seldom met. [11] If the requirement for prior 'consideration of available evidence on the test' were reviewed in this present era of diagnostic and antimicrobial stewardship, the risks of inappropriate antibiotic use and misdiagnosis due to over-reliance upon and misinterpretation of dipstick results would be clear. [12,13].

The sensitivity and specificity of leucocyte esterase and nitrite positivity have been mainly studied in children and premenopausal women, in whom asymptomatic bacteriuria is uncommon. The gold-standard comparison commonly used to derive test performance is quantitative urine culture, usually to the standard of $>10^5$ cfu/mL. However, this 'gold-standard'

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has not been revised since it was first defined in the 1960s by Kass and colleagues. Studies have since shown that as little as 10^2 cfu/mL can be relevant in strongly symptomatic patients and that infections of a recurrent, chronic or interstitial nature are frequently missed by both urinalysis and standard quantitative culture techniques. [14,15] Fastidious, intra-cellular or antibiotic-inhibited bacteria are commonly missed by standard laboratory methods. [15].

Nitrites are only produced by the common Gram-negative uropathogens when there is sufficient dietary nitrate present in urine and sufficient bladder dwell time for metabolism to occur. Gram-positive uropathogens such as *Enterococcus sp.*, *Staphylococcus saprophyticus*, *Actinotignum schaalii* and *Aerococcus sp.* (particularly relevant in older patients) will result in a negative nitrite result and this may lead to erroneous exclusion of UTI. Pyuria, causing positive leucocyte esterase, can be present due to asymptomatic bacteriuria, non-urinary infections (e.g. intra-abdominal infection, pneumonia), renal pathologies, inflammatory conditions, malignancies and common drugs (e.g. proton pump inhibitors). [16,17] Whilst the negative predictive value of a negative leucocyte esterase result (and to some extent nitrite) may possibly be used to support an alternative diagnosis to UTI, this requires reliable user understanding of performance characteristics of the test; understanding that is currently not widespread. In older people, urine dipsticks are both too insensitive and too non-specific to be used in clinical decision-making regarding diagnosis and management of possible infection.

The power of the positive result

Older frail patients presenting to hospital without specific or localising symptoms frequently undergo urine dipstick and culture, tests that are designed to detect heavy growth of urinary bacteria – bacteria that, for the majority of older patients, are harmless bystanders to the clinical presentation. Many hospitals have a 'routine' dipstick in admissions protocols regardless of the reason for admission. Patients with conditions such as acute or chronic kidney disease and diabetes undergo regular dipsticking for protein, blood, glucose or ketones. Due to the multiplex nature of commonly available brands, more indicators than are required by the user are produced simultaneously. This includes leucocyte esterase and nitrites, the indicators interpreted (often incorrectly) as diagnostic of UTI.

The belief that a positive urine dipstick supports the diagnosis of UTI is common in nurses and to some extent doctors. [18] In our institution baseline knowledge of staff prior to implementation of an education programme was low, with staff frequently confident that a positive dipstick confirmed a UTI even in the absence of symptoms. The Bayesian reasoning approach to diagnosis (with understanding of pre-test probabilities, sensitivity and specificity of tests and how these vary with changing prevalence of the condition) is rarely taught or applied; thus a 'positive' result is frequently perceived to be diagnostic. [19] Even if it is not initially misinterpreted, once a 'positive' result has been documented, its effects on decision-making can be long-lasting. Bias is introduced to the diagnostic thought process and clinicians may fall foul of the unconscious impact of such results, sometimes even when there is knowledge and understanding about asymptomatic bacteriuria. [19] Confirmation bias may occur when the urine culture result then

'confirms' a UTI in an older frail person (when there is a high likelihood of colonisation) thus 'justifying' the antibiotics that were started. [19] A urine dipstick can convert the diagnostic challenge of a complex frail older patient presenting non-specifically unwell, to a straightforward case requiring a short-course of antibiotics. It is therefore not surprising that dipsticks are so popular, but taking cognitive shortcuts does not lead to patients being appropriately investigated and managed; more likely, missed diagnoses and over-use of antibiotics. The potential harm from inappropriate antibiotics is significant with older people at higher risk of these adverse effects. [20] A study in nursing home residents found that the combination of dysuria, change in character of urine and altered mental status were most predictive of bacteriuria plus pyuria, and in the absence of these clinical features, 25% patients had bacteriuria plus pyuria. [21] One approach may be to reserve immediate antibiotics for patients with clinical signs of sepsis, whilst for non-specifically unwell older frail patients completing a thorough clinical assessment, microbiological culture of possible infection sites (including urine) and regular review for evolving evidence of infection may be a reasonable alternative to upfront prescribing.

Ditch the dipstick for diagnosing UTI in older people

Diagnostic stewardship is equally as important as antimicrobial stewardship if we are to tackle rising microbial resistance. The correct implementation of diagnostics has the potential to impact hugely on the safe and judicious use of antimicrobials. New diagnostic tests are desperately needed for urinary tract infections across different patient groups, especially in older patients where distinguishing asymptomatic bacteriuria from acute infection could greatly improve patient management and reduce unnecessary antibiotic use.

Conflict of Interest

I have no conflicts of interest with this publication and there has been no funding relevant to the publication of this manuscript.

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