# Microscopy, culture, and sensitive management of uncomplicated urinary tract infections in adults in the primary care setting

*Niroshan Sivathasan,* MBBS, MRCS (Eng), *Krzysztof R. Rakowski,* Medical Student.

## ABSTRACT

يشكل انتشار التهابات المسالك البولية عبئاً كبيراً يقع على عاتق الأنظمة الصحية، حيث يقوم الأطباء بالمبالغة في علاج المرض، كما أن هناك تباين في ممارساتهم الطبية، أضف إلى ذلك تأثير العوامل الاقتصادية والموردية على هذه المشكلة. تزيد نسبة المرضى الذين يُشتبه إصابتهم بالمرض ولكنهم غير مصابين بالالتهاب فعلاً عن 40%. لقد قمنا في هذا المقال بالاستعانة بالمكتبة الوطنية الأمريكية الطبية ( Pubmed ) وذلك من أجل تلخيص المقالات التي تطرقت لهذه المشكلة خلال الثلاثين سنة الماضية، كما أننا قمنا بإضافة بعض المقالات الفرعية التي غطت الحالات المصابة بالتهاب المسالك البولية الغير معقد لدى البالغين في عيادات الرعاية الصحية. وبهذه الطريقة تمت مراجعة الأدب الطبي الذي سلط الضوء على المشكلة وكيفية علاجها بفعالية. لقد اتضح من بحثنا هذا أنه ليس هناك فائدة من الفحص المجهري الروتيني أو زراعة العينات البولية عند وجود التاريخ المرضي واختبار تحليل البول باستخدام شريط حامض الفيريك، وإذا تعين صرف المضادات الحيوية فإن أخذها لمدة 3 أيام يعد كافياً. نحن بحاجة إلى المزيد من الدراسات الموسعة الخاصة بالأوبئة والتي تركز على الفئات المعرضة للمرض أكثر من غيرها، وقد تساعد مثل هذه الدراسات في الكشف عن الخصائص المميزة للمرض حتى يتم التوصل إلى العلاج المناسب.

The high prevalence of urinary tract infections (UTIs) places a significant burden on healthcare systems. Clinicians may over-manage the issue, and there is great variability in practice, with economic- and resource-implications. Up to 40% of patients with a suspected UTI do not have an infection. Using PubMed (Medline) to shortlist relevant papers in English from the last 30 years, and further sub-selection to include only uncomplicated UTIs in adults in primary care, we reviewed the literature pertaining to uncomplicated UTIs, and how it should be managed efficiently in the primary care setting. In general practice, there is no advantage to routinely request microscopy and culture of urine samples in the presence of an appropriate history and urinalysis reagent-strip testing. If antibiotics are required, then a 3-day course shall suffice. Larger epidemiological studies focusing on more susceptible sub-populations may provide better guidance for discriminatory factors to produce an algorithm for treatment.

Every single clinician is, almost certainly, involved in the management of a urinary tract infection (UTI) at some point. While most UTIs do not cause severe complications, the high prevalence of UTIs places a significant burden on the healthcare systems, particularly primary care, where most patients are managed.[1] Clinicians arguably tend to over-manage UTIs with great variability in practice, and consequently impact on finances and other resources, and this has been corroborated in the literature.[2] For example, most women in primary care are prescribed antibiotics,[3] despite evidence indicating that many women with bacteriological UTI recover without antibiotics.[4] The best sequence of management can be provided by understanding the pathology and course of such infections, especially for more junior clinicians who may find themselves under increasing pressure by patients to provide treatment due to unpleasant symptoms.[5] It has been shown that when a doctor is not that familiar with a patient presenting with lower urinary tract symptoms, the doctor will be 4.5 times more likely to assume a clinically significant infection.[6] Yet, 40% of patients with a suspected UTI do not have an infection.[3]

Symptoms and clinical signs associated with micturition and the genitourinary tract, together with the presence of bacteriuria indicate a UTI. Urine culture is the gold standard in the diagnosis of UTI, but there is limited concordance between the classical definition

of bacteriuria (>100,000 colony forming unit (cfu)/ml of a single type of organism), and clinical signs and symptoms.[7]

This is a brief evidence-based review of current literature that could help primary care physicians in managing UTIs in adults. Literature was gathered utilizing PubMed to shortlist articles on 'uncomplicated', 'adult', 'UTI' or 'urinary tract infection,' and 'primary care' in English. The 50 most generic papers were then sub-selected from the 100 that was shortlisted, on the basis of clinical- and functional- applicability, and relevance. Children with UTIs require a different management algorithm, and such is not considered in this article.

*Etiology demographics.* The most common associated uropathogens include *Escherichia coli (E. coli)*, accounting for up to 90% especially in women, *Staphylococcus saprophyticus*, *Klebsiella spp.*, and *Proteus mirabilis*.[8] Uncomplicated UTIs (uUTIs) are common, and account for up to 3% of consultations in general/family practice.[6] A UTI may involve the kidney (pyelonephritis), bladder ((cystitis), or prostate (prostatitis). The prevalence of UTIs varies with age. They are up to 50 times more common in women than men, and up to 50% of women experience UTI, at least once in their lives.[9-11] There is a mean annual incidence of approximately 15% in women aged 15-39, and 10% in women aged 40-79.[12] Urinary tract infections are an increasingly prevalent problem for women, and the difference in age-range prevalence is thought to be due to greater sexual activity in younger women.[13,14] In women, the risk of acute cystitis significantly increases in the first 48 hours after sexual intercourse. In contrast, UTIs are very rare in young men with a rate of just 8 infections per 10,000 men from 21-50 of age.[15] In elderly men who are debilitated and living in nursing homes, the prevalence can be up to 50%.[15]

*Symptoms.* Common symptoms are dysuria, frequency (considering that the average person micturates 6 times per day), lower abdominal discomfort, offensive-smelling urine, and hematuria. One must not forget that these symptoms have numerous other causes. Dysuria, for example, can be caused by trauma, neoplasia, calculi, hypoestrogenism, psychogenic disorders, vaginitis, or chlamydia.[14,16] Back pain, costovertebral tenderness, and systemic symptoms should alert the clinician to the possibility of pyelonephritis and systemic involvement. A clinician must consider the possibility of autoimmune conditions, uroliths, and neoplasia, if hematuria is a symptom. The latter is of notable concern in older adults due to the increased risk of cancers of the bladder and prostate.

*Risk factors.* Most acute lower UTIs are uncomplicated and the management of these is
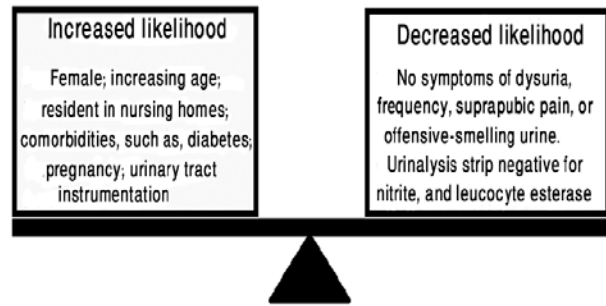


**Figure 1** - Factors that clinicians must consider when considering the likelihood of an uncomplicated urinary tract infection and the need to treat it.

simple, whereas complicated, systemic, or recurrent infections necessitate specialized input.[17] Acquired risk factors for UTIs include: urinary tract interventions, be it instrumentation, or an in-dwelling catheter; immunosuppression; diabetes mellitus; and pregnancy. These also increase the risk of complications.[12] In women, the main risk factors for acute UTIs are previous episodes, and recent, or frequent sexual activity.[18] Recurrent UTIs occur in up to one-third of women.[12] Studies suggest that post-coital voiding may not necessarily prevent cystitis.[18] **Figure 1** summarizes the factors that should be considered when assessing the likelihood of an uUTI.

*Diagnosis.* Despite the risk of contamination (approximately a 30% likelihood)[19] and impracticality, culture of fresh, mid-stream specimen of urine is the most accurate modality for diagnosing UTI, and it is the most common request for processing carried out in microbiology laboratories.[20] The use of urinalysis reagent strips (also known as dipsticks, dipstix, dipstrips) is cheap, simple, yields immediate results, and requires no expertise. Using a urinalysis strip, one can check for the presence of nitrites (not nitrates), blood, leucocyte esterase (not leucocytes), glucose, protein, and other substances such as acids, ketones, bilirubin, and urobilinogen. Various studies have evaluated the accuracy of this convenient test in detecting UTIs, and in the absence of upper UTI symptoms, a meta-analysis has demonstrated that if the result for both nitrites and leucocyte esterase is negative, then UTI can be excluded with a negative predictive value of 92%.[21-23] Conversely, in the presence of symptoms and positive nitrite and leucocyte esterase testing, the likelihood of a UTI is high.[24] The lack of genital discharge and irritation increases the likelihood of a UTI to well over 90%.[12,25] Laboratory testing is not necessary in this circumstance, and treatment can, in the absence of an upper tract or complicated infection be satisfactorily commenced,[16,17] due to the low possibility of increased

morbidity.[26] It has been suggested that a negative result on a urinalysis strip cannot reliably exclude an infection if the pre-test likelihood is high, and in such cases, it is advisable to obtain culture results.[17] This could partly be due to the presence of non-nitrate-reducing bacteria, such as *Staphylococci* and *Enterococci*.

*Treatment.* It has been shown in most women not treated with antibiotics that they get better on their own accord, although more slowly, and infrequently, experience complications.[27] Nonetheless, common empirical treatments include trimethoprim and cefaclor, and a 3-day course is considered to result in quicker eradication of bacteria from the urinary tract than a single-dose (94% versus 87%). Any other longer courses are neither more effective in eradicating the infection, nor in preventing recurrence, but are instead associated with significantly more adverse effects (30% versus 18% in a 3-day course and 11% in a single-dose).[17] In patients with recurrent UTIs, a common approach has been the use of low-dose once-daily antibiotics. Recently, there has been considerable interest into non-antimicrobial-based approaches, such as probiotics, intravaginal suppositories, vaccines, and interference with bacterial adherence, however, the results have not been conclusive. Cranberry products are generally considered to be useful in preventing UTIs, but not in treating them, and work by impairing the adhesion of fimbriated uropathogens, such as *E. coli*.[10] However, a valid comparison of the different cranberry products has not yet been carried out in part, due to lack of standardization of the active compounds, and the heterogeneity of the different studies.[10]

*General management.* Management of uUTIs can frequently be triaged to non-physician healthcare personnel without adverse clinical consequences, and it has been shown that a telephone-based algorithm can allow for successful and safe management for most women with symptoms of uUTIs.[12,28] This approach is unlikely to harm patients, but such automation would result in a significant percentage of the population receiving antibiotics, and this is likely to exacerbate resistance to antibiotics. As such, it is more important than before for doctors to adopt an evidence-based approach to managing uUTIs. Twenty percent of bacteria causing UTIs are resistant to trimethoprim and cephalosporins, and 50% to amoxicillin.[29] Other examples include nitrofurantoin and fluoroquinolones. A remarkable increase in antibiotic resistance has already been noted in uUTIs, and therefore, the choice of antibiotic when indicated must be governed by local patterns of microbial sensitivity, and the response to therapy determines further treatment and follow-up.[1,30]

One must not forget that the cost of diagnosing and managing any health condition extends beyond the health system. Absence from work and loss of productivity must be weighed-up in any consideration, and this also holds true for UTIs. One study suggested that symptoms were of shorter duration, and less severe when the doctor took a positive approach to diagnosis and prognosis, whereas, a more patient-centered approach made no appreciable difference.[4] Clinicians must also remember that on a background of severe baseline symptoms and a history of recurrence, the patient is likely to have severe symptoms for at least 3 days.[4] Indeed, in a population-based, cross-sectional study of 319 women, 85 years and older women with UTI had a significant impact on their morale, or subjective well-being ($p<0.001$).[31]

In conclusion, we believe there is no advantage to routinely request microscopy and culture of urine samples.[29] Therefore, we advise that on the basis of a suggestive history and symptoms, urine culture should be performed on the following: all patients with symptoms that suggest pyelonephritis; females with regular recurrence (for example, monthly); all pregnant women; all males with recurrence; if symptoms persist for over 3 days despite the use of antibiotics; and if either the nitrite or leucocyte esterase is negative. If the patient is nitrite positive and leucocyte esterase negative, then consider commencing antibiotics. If the leucocyte esterase is positive and nitrite is negative, then consider a deferred prescription pending the results of microscopy and culture, by which time symptoms may have also resolved.

The conflict between the judicious use of antibiotics, patients' expectations, and the resolution of symptoms is awkward. One must not forget that a doctor's input and influence can enhance a particular management strategy. Larger epidemiological studies focusing on more susceptible subpopulations may provide better guidance for discriminatory factors to produce an algorithm for treatment. A dramatic, clinically significant increase in the antimicrobial resistance of uropathogens over the past 5-10 years calls for new concepts in the treatment of UTIs.[32] In the mean time, it is more important than ever for general practitioners to be regularly updated by primary care trusts with regard to common etiological pathogens in their locality, along with suggested empirical antibiotics, which should be used on a 'rolling basis'. In addition, we must keep in mind that children should be managed differently, primarily with regard to careful investigation after a UTI.

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