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CONTENTS

An alternative approach to the diagnosis of

UTI IN ADULTS

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An alternative approach to the diagnosis of **UTI IN ADULTS**

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Introduction

Whether they are aware of it or not, in most situations clinicians use mental processes akin to Bayesian probabilities when arriving at a diagnosis. As each possible diagnosis emerges in the clinician's mind, it is ranked against the other diagnoses most recently considered. Questions are asked, signs are sought and investigations requested in such a way that the most probable and most serious diagnoses become more or less likely. Each finding is weighted according to past experience and evidence from the literature. Eventually, one or more diagnoses are considered likely enough that treatment for that condition is commenced, or else a treatable condition is excluded for the time being.

In contrast, the traditional approach to the diagnosis of UTI is categorical, requiring clinical features in combination with urine microscopy, culture and susceptibility testing. Over three million of these tests are claimed through Medicare each year, the vast majority requested for adult women seen in general practice. In this article, we challenge the notion that urine microscopy, culture and susceptibility testing is always necessary for the diagnosis and management of UTI.

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Urinary tract infections

The spectrum of UTIs in an otherwise normal urinary tract includes urethritis or cystitis with typical symptoms but without significant bacteriuria, classic uncomplicated UTI and pyelonephritis. Further permutations arise when pregnancy, an immune deficiency, a foreign body or an abnormality of the urinary tract are present. Asymptomatic bacteriuria is a closely related condition that, by definition, is not a UTI but a form of colonisation of the urinary tract (see Table 1). This spectrum of normal health and disease makes clinical context essential for the interpretation of laboratory findings of urine (see Table 2).

The diagnosis of UTI can be improved by a return to the same Bayesian approach used in other clinical situations, and this article describes the quantitative details of the application of Bayesian probability to the diagnosis of UTI. It is suggested that clinicians use this information as a background to developing the same diagnostic strategy used for other disease processes.

The Bayesian approach

In a strictly Bayesian approach, the initial, or pre-test, probability of the presence of a particular disease ($P_{pre\text{-}test}$) is modified by the application of diagnostic findings in the form of likelihood ratios. These likelihood ratios are properties of all diagnostic 'tests'. These 'tests' include any finding present in a different frequency in those with the disease compared with those without the disease, including features of the patient's history and physical examination. One result of such a test will increase the probability of the disease being present by a certain amount, while the other result will decrease the probability of that disease by a certain amount.

Test results can be accumulated until a satisfactory estimate of the probability of the presence of the disease is made ($P_{post\text{-}test}$). Once the odds of a diagnosis are high enough that the benefits of treatment outweigh the risks, treatment can be commenced. Alternatively, once the odds of a diagnosis are low enough that the risks and costs arising from further investigation outweigh the benefit, investigation can be stopped.

Table 1: Asymptomatic bacteriuria[1]

Bacteria are often present in significant numbers in the urine in the absence of any symptoms of UTI. Rates of asymptomatic bacteriuria can be as high as 100% in the setting of a long-term indwelling catheter, 25-50% in female nursing home residents and 1-5% in healthy, premenopausal women.

There is evidence from the following settings that treatment of asymptomatic bacteriuria provides no benefit, and may be harmful: non-pregnant premenopausal women; diabetic women; elderly patients living in the community; elderly patients living in a nursing home or similar institution; patients with spinal cord injury; and patients who have an indwelling catheter.

However, in the following circumstances there is some evidence of benefit with treatment of asymptomatic bacteriuria: pregnancy; and immediately before transurethral resection of the prostate.

The evidence for treatment of asymptomatic bacteriuria before transurethral resection of the prostate can probably be extrapolated to other procedures involving breaches of mucosal barriers in the urinary tract.

The mere presence of numbers of bacteria above a certain limit in a urine specimen does not by itself indicate UTI. Nor does the combination of leucocytes and bacteria guarantee UTI. Particularly in settings where the prevalence of asymptomatic bacteriuria is high, the use of urine microscopy and culture to determine the presence of UTI can be misleading, unless there is a strong suspicion on clinical grounds.

1. *Clinical Infectious Diseases* 2005; 40:643–54.

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Table 2: The objectives of laboratory testing of urine for UTI

From the perspective of primary care, urine microscopy, culture and antibiotic susceptibility testing can help resolve three questions.

1. Does this patient have a UTI?
The diagnosis of UTI requires a constellation of symptoms and signs. The results of urine microscopy, culture and antibiotic susceptibility can support those findings, but in isolation, cannot make a diagnosis of UTI, because of the existence of asymptomatic bacteriuria (see Table 1). This is a distinct entity that in many cases does not require treatment.

2. Was my choice of treatment for a presumed UTI appropriate?
There is a delay between the time of patient consultation with symptoms of a UTI and the time at which all the results of urine microscopy, culture and sensitivity are available. In most circumstances, it is not appropriate to wait for antimicrobial susceptibility results before prescribing therapy for a UTI. In the case of short-course treatment of uncomplicated UTI, the patient may have completed most of their course of antimicrobial therapy by the time antibiotic susceptibility data is available. If the pathogen that is isolated is not susceptible to the agent that was prescribed, then the patient's condition can be reviewed and if they remain symptomatic, an alternative agent can be prescribed.

3. What treatment should I use for recurrent or subsequent presumed UTI?
Antimicrobial susceptibility results accumulated over time show the typical susceptibility patterns and trends in antimicrobial resistance within the population. They can also be collected for a particular practice to provide local data or, in the simplest scenario, collected for a single patient with recurrent UTI. These types of data allow informed decisions about the prescription of antimicrobial agents.

Summary

Returning to the three questions:

1. Does this patient have a UTI?

This question is fundamental, but if there is already good evidence for UTI, then microscopy, culture and sensitivity will not be needed to help give an answer.

2. Was my choice of treatment for a presumed UTI appropriate?

This receives an answer too late for the vast majority of uncomplicated UTIs, but is necessary if the patient is at high risk of complications or treatment failure.

3. What treatment should I use for recurrent or subsequent presumed UTIs?

This question is in most instances epidemiological in nature, and is probably better answered by searching the literature or by consulting antibiotic guidelines than by maintaining and analysing a practice-specific database of susceptibility results.

In the application of Bayesian logic to the diagnosis of UTI, the probability of UTI can be quantified using readily available data, likelihood ratios found in the literature and the following formula:

$$P_{UTI} = P_{pre\text{-}test} \times likelihood\ ratio\ (LR)$$

Local data collected from a GP's own practice will provide the best estimate of the prevalence of UTI in various populations, but the Bettering the Evaluation and Care of Health study of general practice provides a good starting point[2]. UTI was a final diagnosis in 1.7% of all general practice encounters. Thus the odds of a diagnosis of UTI in an undifferentiated population attending a GP are about one in 60. These odds should be adjusted upwards or downwards for various risk groups. For example, the odds of UTI will be higher in women than in men.

Likelihood ratios found in the literature for features of the history and physical examination are displayed in Table 3. Table 4 shows likelihood ratios for laboratory findings.

Table 3: Likelihood ratios (LR) for significant growth of a uropathogen arising from features of the patient's history and physical examination

Symptom or sign		LR	95% CI	Reference
History of dysuria	Present	1.5	1.2 – 2.0	3
	Absent	0.5	0.3 – 0.7	3
History of urinary frequency	Present	1.8	1.1 – 3.0	3
	Absent	0.6	0.4 – 1.0	3
History of haematuria	Present	2.0	1.3 – 2.9	3
	Absent	0.9	0.9 – 1.0	3
History of vaginal discharge	Present	0.3	0.1 – 0.9	3
	Absent	3.1	1.0 – 9.3	3
Palpation of costovertebral angle	Tender	1.7	1.1 – 2.5	3
	Non-tender	0.9	0.8 – 1.0	3
Nitrites on urine dipstick	Present	5.3	3.2 – 8.8	4
	Absent	0.6	0.3 – 0.9	4
Leucocyte esterase on urine dipstick	Present	2.1	1.5 – 2.9	4
	Absent	0.5	0.4 – 0.8	4

Case study 1

A 24-year-old woman presents with two days of dysuria and urinary frequency. She has noticed no haematuria or vaginal discharge and has no costovertebral angle tenderness. Urinalysis reveals the presence of leucocyte esterase and nitrites. You estimate that one in 20 young women presenting to your practice have a UTI.

How should you proceed?

Using the likelihood ratios in Table 3,

$$P_{UTI} = 1{:}19 \times 1.5 \times 1.8 \times 0.9 \times 3.1 \times 0.9 \times 5.3 \times 2.1$$
$$\approx 4{:}1 \text{ or } 80\%$$

A $P_{post\text{-}test}$ of 80% warrants empirical treatment.

If there is a need to answer the questions "was my choice of treatment for a presumed UTI appropriate?" or "what treatment should I use for subsequent presumed UTIs?", sending a specimen for microscopy, culture and antibiotic susceptibility testing will be warranted. If, as in the above case, the patient's history and co-morbidities do not provide a reason for caution or curiosity, laboratory urine testing is unnecessary.

Table 4: Likelihood ratios (LR) for significant growth of a uropathogen arising from microscopic examination

Feature		LR	95% CI	Reference
Number of leucocytes seen by urine microscopy	$\geq 100\times10^6$/L	9.6	6.1 – 15	5
	$\geq 10\times10^6$/L	5.8	4.2 – 8.0	5
	$<10\times10^6$/L	0.4	0.3 – 0.5	5
Bacteria in urine Gram stain	Present	13.7	4.2 – 44	6
	Absent	0.05	0.02 – 0.12	6

Values given for urine Gram stain are for UTI in children[6], but compatible results have been published for UTI in adults[7,8,9].

Case study 2

A 63-year-old man presents with four days of dysuria plus haematuria, but no urinary frequency. He complains of costovertebral angle tenderness. Urinalysis reveals the presence of leucocyte esterase but no nitrites. You estimate that 1 in 60 men in this age group presenting to you have a UTI.

How should you proceed?

$$P_{UTI} = 1{:}59 \times 1.5 \times 0.6 \times 2.0 \times 1.7 \times 0.6 \times 2.1$$
$$\approx 1{:}15 \text{ or } 6\%$$

In this scenario, the odds are against the final diagnosis of this presentation being UTI. Empirical therapy for UTI is not justified.

You remain concerned that this man has a potentially serious condition involving his genitourinary tract, and send a urine specimen to the laboratory for investigation of his haematuria. Using the laboratory's electronic result interface, you discover that there were 10-100×10^6 leucocytes per litre, more than 100×10^6 red blood cells per litre, and that no bacteria were seen on the urine Gram stain.

Using the most recent odds of UTI and the likelihood ratios given in Table 4,

$$P_{UTI} = 1{:}15 \times 5.8 \times 0.05$$
$$\approx 1{:}52 \text{ or } 2\%$$

The odds of UTI are now very low. Further investigation is required to determine the cause of this patient's haematuria.

Case study 3

A young woman presents with symptoms and physical findings that indicate a diagnosis of UTI. You treat her according to therapeutic guidelines with three days of trimethoprim.

She returns to see you one week later, saying her symptoms improved briefly, but have now recurred. She has dysuria and frequency. She does not have vaginal discharge or haematuria. Urinalysis is positive for leucocytes and nitrites.

How would you proceed?

UTI is highly likely by Bayesian probabilities, but diagnosis is no longer the most important issue. Treatment of her UTI has failed. There are many possible reasons, and urine microscopy, culture and antibiotic susceptibility testing is an important part of your approach to treatment in this woman.

You send a urine specimen to the microbiology laboratory and commence empirical therapy with a second-line agent. Later that day, you note that as expected on clinical grounds, microscopy reveals the presence of more than 100×10^{6} leucocytes per litre, and bacteria are seen on Gram stain. The organism is identified as *Klebsiella* species, and is reported to be resistant to trimethoprim and susceptible to your second-line agent. You continue treating the patient on the basis of the susceptibility data provided by the laboratory.

Conclusion

Case 1 is one of the most common presentations of UTI seen in general practice, and demonstrates that using a Bayesian approach, a confident diagnosis can be made without recourse to laboratory testing.

In case 2, the Bayesian approach enabled the exclusion of UTI as a cause of the patient's haematuria on the day of his initial presentation. If a hypothesis is disproved through a Bayesian approach, this allows the clinician to consider other explanations for the patient's presentation until the diagnosis of a treatable condition becomes unlikely.

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Case 3 shows the role of laboratory testing in the relatively uncommon situation of failed empirical treatment. In the absence of signs of severe illness, there are few consequences of delaying urine microscopy, culture and susceptibility testing until treatment failure becomes apparent.

When a categorical approach is used in the diagnosis of UTI, it may lead to unnecessary laboratory investigation. With a Bayesian approach, in many cases, the probability of UTI will be high enough at the initial consultation to start treatment without the need for laboratory testing.

Practice point

It is not proposed that clinicians consult tables of odds and employ a calculator when making a diagnosis of UTI. However, familiarity with the likelihood ratios provided in Tables 3 and 4 and a Bayesian approach to the evaluation of UTI will lead to rapid and accurate diagnosis. This approach is simple, and allows the integration of prevalence data and those clinical findings for which likelihood values are available in the literature. It also allows a more rational and effective use of the pathology laboratory.

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