It's time we recognised chronic urinary tract infection

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Many clinicians remain unfamiliar with the diagnosis of chronic urinary tract infection, leaving many women and girls to suffer without the right support.

Urinary tract infection (UTI) accounts for <u>a large workload in general practice</u> and as many as <u>one in eight preventable admissions to Australian hospitals</u>. So common and distressing is acute UTI that it has become <u>a political issue</u> with government-funded "prescribing trials" aimed towards women experiencing symptoms out of hours. The <u>popularity of such schemes with politicians</u> speaks to the distress that UTIs cause for so many people across the community.

Bacterial cystitis is common and <u>half of all women will develop a UTI during their lives</u>: unfortunately, <u>25% of adult women (and a high proportion of girls) who experience a first episode, will go on to experience recurrent infections</u>. Indeed, <u>studies suggest</u> that as many as one-third of patients treated according to current clinical guidelines, fail to respond to treatment.

As our understanding evolves, it is evident that some infections can be chronic or persistent: this is an important paradigm shift imparting practice and policy implications. Recent <u>media coverage</u> has drawn attention to chronic UTI (cUTI), and community-based advocacy groups, especially <u>Chronic UTI Australia</u>, have become a vital information repository and source of support for thousands of affected women.

Chronic UTI has caused unremitting suffering in many women and their physical pain has often been compounded by a lack of understanding of the condition. For example, Pippa, an <u>Adelaide mother</u>, who contracted a UTI aged 28 that did not resolve after an initial short course of antibiotics, experienced constant urinary urgency and disabling bladder pain that frequently left her housebound for the following decade. "I was told for years what I had was interstitial cystitis, that I was incurable," she says.

She was treated for cUTI with an extended course of full-dosage antibiotics and, now, has been symptom-free for over three years since finishing treatment. "I could have got 10 years of my life back if somebody just had the right knowledge," she says.



Adelaide based Pippa Anderson-Ward, 45, has suffered UTIs for over a decade. After receiving treatment in London (long term antibiotics) she has now been infection free for several years (Emma Brasier/TWAM).

If there is a clinical suspicion of cUTI, <u>confirmation of the diagnosis can present challenges</u>. Traditional dipstick testing of urine is of very limited value and the utility of standard urine microbiology has lagged compared to diagnostics in other areas. A substantial body of evidence now suggests that our diagnostic criteria <u>are neither sensitive nor specific enough to detect many cUTI</u>.

<u>In cUTI</u>, white cell thresholds may not exceed the accepted level of 10 cells used for acute bacterial cystitis. Similarly, a bacterial concentration of 10⁵ colony-forming units (CFUs) per mL — well below the threshold of 10⁶ used for acute infection — is typical. <u>The presence of mixed bacteria in a specimen</u> does not necessarily signify contamination as many cUTI are polymicrobial. Finally epithelial cells — traditionally thought to be evidence of "contamination" and believed to be evidence of a poorly obtained specimen — may represent infected bladder wall cells.

There is now <u>strong evidence</u> that bacteria, such as *Enterococcus faecalis* and other organisms, can overcome the bladder's innate defences and develop communities within the bladder epithelial cells: <u>the bladder wall itself becomes a reservoir for pathogens</u>. When this intracellular colonisation occurs, urine tests may show features of infection yet not meet traditional microbiological thresholds, leading to inappropriate reassurance and antibiotic avoidance.

Urothelial cells in the urine of patients with cUTI are commonly misinterpreted as vaginal squamous cells. Confocal microscopy has, however, demonstrated these are urothelial cells being sloughed by the bladder as a defence mechanism to eradicate cUTI. Some patients have chronic symptoms and others have bladder wall colonies remaining quiescent for prolonged periods yet causing recurrent symptomatic infection. Research to improve the understanding of, and therapies for, cUTI is occurring here in Australia and globally with an evidence base for this built using genomic techniques and expanded quantitative urine cultures. For the moment, cUTI is defined by a persistent fluctuating uncomfortable or painful urinary symptoms that respond to antibiotics, with associated white and epithelial cells present in the urine.

Recognition of persistent UTI in patients with congenital anomalies, kidney stones, bladder emptying disorders, neurogenic bladder, or cystocoele is not new. What is new is recognition that a normal urinary tract may develop cUTI. Methenamine, topical estradiol, urine vaccines such as Uromune and closely monitored chronic low-dose antibiotic protocols appear to <u>resolve a high proportion of cases</u> of cUTI and recurrent UTI.

Following an acute or recurrent episode of infection, it is crucial to ensure that patients make a full symptomatic recovery and urinary cells normalise. A <u>number of protocols involving the long term use of antibiotics have been studied</u> and found effective in specialised hands. The key to management of women with cUTI lies in making the diagnosis in the first place; being alert to the diagnosis, taking a thorough history, recognising the challenges in interpreting standard diagnostic tests, and looking at urinalysis results with fresh eyes. In refractory cases, effective management will likely require specialised management from a team that includes the patient's GP. Because of the false reassurance of many affected people, predominantly women, compassionate assessment and management protocols go beyond medications.

Many specialists — gynaecologists, urologists, infectious disease physicians, and GPs — remain unfamiliar with the diagnosis of cUTI and the failings inherent in our current interpretation of investigations. The time has come to recognise a condition that has been a source of misery for many

women and girls. Clinical awareness followed by treatment aimed at eliminating chronic bladder wall colonisation of pathogens may lead to complete recovery. Ultimately this will benefit antibiotic stewardship and reduce antibiotic resistance; lifting an enormous burden for thousands of women.

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