

## Recurrent Urinary Tract Infections in Adult Women

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**Urinary tract infections (UTIs)** disproportionately affect adult women. Postmenopausal women are especially vulnerable to recurrent UTI, commonly defined as culture-proven UTIs that have occurred at least twice within 6 months or 3 times within 12 months. Current prevalence estimates are lacking, despite the significant negative effect of recurrent UTI on quality of life and health care costs.<sup>1</sup> There is significant variation in patient care related to inconsistent recommendations from key professional societies due to lack of high-quality evidence supporting clinical guidelines.<sup>2-5</sup>

Most women with recurrent UTI initially present to their primary care clinician for management of symptomatic UTI. Although many adult women recall occasional, infrequent UTIs, most patients with recurrent UTI report a discrete change in the frequency of UTIs. The initial evaluation and treatment plan can be informed by reports of common life events associated with an increase in UTI frequency, including sexual debut, new sexual partner, new form of contraception, urinary catheter use, pelvic surgery, menopausal estrogen loss, fecal incontinence or diarrhea, or onset of a significant health condition (eg, immunosuppression, diabetes, neurological disease that affects bladder emptying) or associated treatment.

In addition to a focused history and physical examination, the initial evaluation of adult women with recurrent UTI should clarify the onset of frequent UTI; details of UTI events, including UTI testing results when available; prior treatment; antibiotic allergies; prevention and treatment preferences (antibiotic and antibiotic alternatives); and current prevention practices, such as postcoital voiding and drinking larger amounts of water (2-3 L/d). The symptoms that the patient attributes to the UTI should be documented, including duration and response to therapy, because these may vary between patients. Symptoms are typically acute in onset and include dysuria, urinary frequency and urgency, suprapubic or flank pain, hematuria, and/or documented fever. Patients often attribute foul-smelling or cloudy urine to UTI; however, testing for UTI should be based on clinician judgment because these symptoms are not pathognomic for UTI, especially in the absence of traditional UTI symptoms. Older patients, especially frail older women, with urine cultures positive for uropathogenic bacteria may present with acute onset of general fatigue and/or confusion; however, treatment in this instance is not recommended in the absence of additional symptoms or findings suggestive of UTI.<sup>3</sup> Physical examination should include abdominal and focused neurologic examinations as well as pelvic examination to detect manageable conditions, including genitourinary atrophy in postmenopausal women, urethral diverticulum, evidence of fecal soiling, and vaginal prolapse beyond the hymen. An assessment of bladder emptying should be considered by urethral catheterization or bladder scan (ultrasonography), especially in patients with neurologic disease or diabetes.

In the setting of recurrent UTIs, the patient and clinicians should develop a personalized plan that incorporates patient preference for empirical antibiotics, urine cultures, appropriate hormone use, or natural remedies for prevention, and treatment of subsequent UTI. It is important that clinicians understand that recurrent UTI is rarely a personal

hygiene issue and the patient is not to blame. A subgroup of patients with recurrent UTI have conditions that warrant accelerated evaluation and consideration of specialist referral, including patients with a pelvic mass, vaginal prolapse beyond the hymen, rectal prolapse, kidney stones, chronic catheterization, immunosuppression, atypical symptoms (eg, gross hematuria, pneumaturia following pelvic procedure), rapid progression to sepsis, presence of multidrug resistant pathogens, or a history of complicated UTIs. The Table details different patient characteristics and recurrent UTI management strategies.

Most patients with uncomplicated recurrent UTI are prescribed 3 to 5 days of an appropriate antibiotic for each cystitis episode. Clinicians should offer hydration and urinary analgesics for patient comfort while awaiting urine culture results. Patients who prefer prompt antibiotic therapy can provide urine samples for testing and initiate empirical therapy based on microbial history, allergy profile, and medical status (eg, kidney function). Treatment refinements can follow final urine culture results. Management of symptomatic UTIs should be informed by microbial identification and susceptibility, as well as the local antibiogram, which provides clinicians microbial resistance patterns in the local community. Oral antibiotic therapy is generally preferred, although specialists may recommend intravenous therapies in select patients. Intravesical therapy is infrequently used, but may be an alternative when it is important to avoid systemic therapy (ie, in women with a history of serious *Clostridioides* [formerly *Clostridium*] *difficile* infection).

Current guidelines recommend against the routine use of post-treatment testing, often referred to as *test of cure*, to verify bacteriologic resolution, although there are no rigorous studies to support this recommendation in women with recurrent UTI. However, in select patients with persistent symptoms, a test of cure can help determine the efficacy of prescribed therapy and further define the relationship between symptoms and bacteriuria. In patients with persistent symptoms despite bacteriuria resolution, alternative etiologies for the symptoms should be considered, including painful bladder syndrome, overactive bladder, carcinoma in situ, vulvar and vaginal infections, and, rarely, genitourinary tuberculosis. In patients with persistent symptoms and persistent bacteriuria despite appropriate antibiotic therapy, other diagnoses should be considered, including poor bladder emptying, presence of a foreign body, enterovesical fistula, urethral diverticulum, urinary stones, or anatomic abnormalities of the urinary tract.

Personalized prevention strategies may include increased water intake (individualized volume based on a patient's specific circumstances), frequent voiding intervals (not holding urine too long), perineal hygiene, low-dose vaginal estrogen in the absence of contraindications, and various options for postcoital or chronic antibiotic suppression. Some women clearly attribute UTIs to sexual activity despite healthy sexual practices; this problem can be limited to activities with a specific sexual partner or occur with all or most sexual partners. Clinicians recognize the efficacy of a single dose of a low-dose, pericoital antibiotic as an effective prevention strategy. In postmenopausal women with recurrent UTI associated with genitourinary atrophy, 3 to 6 months of low-dose vaginal estrogen is often

**Table. Treatment and Consultation Recommendations for Women With Recurrent Urinary Tract Infections (UTIs)**

Patient Characteristic	Key Aspects of History and Physical Examination	Acute Treatment <sup>a</sup>	Prevention
Premenopausal	Related to sexual activity	Appropriate antibiotic	Modify sexual practices (eg, avoid anal intercourse); postcoital antibiotic
Postmenopausal	Genitourinary atrophy	Appropriate antibiotic	Vaginal estrogen
	Related to sexual activity	Appropriate antibiotic	Modify sexual practices (eg, avoid anal intercourse); postcoital antibiotics
	Atypical symptoms (eg, systemic symptoms with a change in baseline urinary status)	Appropriate antibiotic	Assess risk factors
Pyelonephritis	Fever and symptoms	Appropriate antibiotic	Assess risk factors
Intermittent or indwelling urinary catheter	Varying symptoms	Appropriate antibiotic only when symptomatic	Catheter care
Poor bladder emptying	Varying symptoms	Appropriate antibiotic	Refer to specialty care to facilitate better bladder emptying
Diabetes (typically with neuropathy)	Varying symptoms	Appropriate antibiotic	Manage glucosuria; assess bladder emptying
Advanced uterine prolapse	Varying symptoms	Appropriate antibiotic	Surgical correction; vaginal pessary
Enterovesical fistula	Pneumaturia typically associated with history of diverticulitis or abdominal surgery	Appropriate antibiotic for symptomatic UTIs only	Consider suppressive antibiotic until resolved
Nephrolithiasis	Recurrent UTI with the same organism, varying symptoms	Appropriate antibiotic	Consider stone removal
Urethral diverticulum	Varying symptoms, postvoid dribbling, dyspareunia, vaginal bulge	Antibiotic for symptomatic UTI only	Consider suppressive antibiotic until diverticulum managed (surgery)
Kidney transplant	Symptoms of pyelonephritis	Antibiotic twice per wk	Lower immunosuppression or suppressive antibiotic; assess for structural abnormalities
	Asymptomatic bacteriuria	Only treat within the first 3-12 mo	

<sup>a</sup> Appropriate antibiotic is based on clinical diagnosis, patient allergies, microbial sensitivities, and local antibiogram.

beneficial and, if helpful, it can be continued longer. Discussions of estrogen therapy should address the negligible levels of systemic absorption and appropriately address concerns about cancer risk. Antibiotic prophylaxis may be appropriate in a highly select group of patients who have frequent recurrences. Prophylactic antibiotics commonly used are nitrofurantoin (50-100 mg once daily), trimethoprim-sulfamethoxazole (0.5-1 single-strength tablet [40 mg/200 mg] once daily to 3 times weekly), and cephalexin (125 to 250 mg once daily). Once-weekly fosfomycin (3 gm) can be used in the case of drug-resistant infections as well. Duration of prophylactic UTI antibiotics is usually 3 to 6 months, which may be enough time to ascertain and manage underlying predisposing factors; monitoring for adverse events is important while receiving prophylactic UTI antibiotics, as is monitoring for development of drug resistance.

There is limited evidence supporting most nonantibiotic prevention strategies, including vitamin C, oral probiotics, vaginal lactobacillus capsules, garlic and cranberry extract, and L-arginine

and D-mannose supplements; most of these strategies are unregulated and lack high-quality evidence for efficacy.

The term *asymptomatic bacteriuria* is evolving following the recent discovery of a healthy urinary microbiome in the bladder. Currently, asymptomatic bacteriuria treatment is only indicated prior to invasive urological procedures and during pregnancy; asymptomatic bacteriuria treatment in nonpregnant adult women in clinical scenarios does not improve patient outcomes, including in older patients and patients with recurrent UTI.<sup>3</sup> Attempts to sterilize the urine in these patients with systemic antibiotics is generally not effective and can lead to development of resistant organisms, adverse events from antibiotics, and *C difficile* infection.

Primary care physicians play a key role in the workup and management of recurrent UTI in adult women. An individualized approach to further evaluation, prevention, and treatment can be informed by the likely etiology, the risk of serious underlying condition, the risk of pyelonephritis/sepsis, and patient preferences.

#### ARTICLE INFORMATION

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**Published Online:** January 29, 2020.  
doi:10.1001/jama.2019.21377

**Conflict of Interest Disclosures:** Dr Aslam reported receiving personal fees as a consultant from Merck. Dr Brubaker reported receiving grants from the National Institutes of Health and editorial stipends from Female Pelvic Medicine & Reconstructive Surgery and UpToDate. No other disclosures were reported.

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