

# Urinary Tract Infection and Asymptomatic Bacteriuria in Older Adults



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## KEYWORDS

• Older adults • Urinary tract infection • Asymptomatic bacteriuria

## KEY POINTS

- Differentiating urinary tract infection (UTI) from asymptomatic bacteriuria (ASB) helps health care providers avoid harming older adults with inappropriate antibiotic therapy.
- Testing for UTI should be ordered only when suggestive clinical symptoms are present because laboratory tests alone cannot differentiate ASB from infection.
- The role of testing for UTI is primarily to exclude the diagnosis. With rare exceptions, treatment of UTI should not be given when a patient has a negative urinalysis or urine culture.
- In a clinically stable older adult without genitourinary tract symptoms, active monitoring and oral hydration may obviate antibiotic use.

## INTRODUCTION

Urinary tract infections (UTIs) are responsible for an estimated 7 million office visits, 1 million emergency room visits, and 100,000 hospitalizations each year, accounting for some 25% of all infections in geriatric patients.<sup>1</sup> Health care providers often confuse asymptomatic bacteriuria (ASB), defined as bacteria in the urine without any symptoms, with UTI, and unnecessary antibiotic treatment of ASB in older adults is common.<sup>2</sup> In the United States, the prevalence of antimicrobial resistance in urinary organisms in the

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community is increasing, including in older adults.<sup>3–5</sup> In nursing home settings, colonization with multidrug-resistant organisms (MDROs) is high, and these organisms spread to other settings along with the colonized patients.<sup>6</sup> Multidrug-resistant bacteria implicated in UTIs include extended-spectrum beta-lactamase (ESBL)–producing organisms, carbapenem-resistant *Enterobacteriaceae*, and now colistin-resistant gram-negative bacilli.<sup>7–9</sup> At the same time, the severe and sometimes life-threatening adverse events associated with commonly prescribed antibiotics increasingly recognize.<sup>10</sup> These trends highlight the need for a renewed emphasis on antimicrobial stewardship in the treatment of UTIs, which includes increased recognition of ASB.

Confusion about several key issues complicates the approach to the spectrum of syndromes included in the broad category of UTI. Particularly among older adults, these issues include:

- Poorly defined clinical criteria to diagnose UTIs
- Reliance on laboratory criteria rather than clinical symptoms to define infection
- Limited guidance regarding the use and interpretation of diagnostic tests
- Challenges for selecting empiric antimicrobial therapy
- Difficulty distinguishing ASB from UTI, particularly in older adults with dementia
- Increased risk of adverse events and drug interactions related to antibiotic use.

This article summarizes the epidemiology, microbiology, and pathogenesis of UTI in older adults; provides clinically applicable definitions; discusses the approach to diagnostic testing for UTIs in this population; and offers guidance regarding optimal treatment of UTIs in elderly patients when treatment is indicated. UTI in the older adult is framed as a diagnosis of exclusion throughout. Much of inappropriate antibiotic prescribing for UTIs comes from diagnoses based on nonspecific findings, such as leukocytosis, weakness, and malaise.<sup>11</sup> Given that the risk of harm in delaying UTI treatment in clinically stable patients is low,<sup>12</sup> in general, the risk-benefit balance favors a cautious approach to diagnosing and prescribing antibiotics for UTIs in the absence of localizing signs and symptoms.

## EPIDEMIOLOGY, MICROBIOLOGY, AND PATHOGENESIS OF URINARY TRACT INFECTIONS

### *Epidemiology*

Among patients older than 65 years, UTIs cause 15.5% of hospitalizations and 6.2% of deaths attributable to an infectious disease.<sup>13</sup> UTIs are the most common type of infection among institutionalized adults and make up more than one-third of all infections in this population.<sup>14,15</sup> Estimates suggest the overall incidence of UTIs in elderly men and women is in the range of 1 infection per 14 to 20 person-years (0.05–0.07 infections per person-year).<sup>16,17</sup> These estimates, however, are based on administrative data that are limited by variations in what the practitioners considered to be a UTI.

Increasing age is itself a risk factor for UTIs. This risk is likely multifactorial, with increasing rates of urinary incontinence and urinary retention, hospitalizations and accompanying urinary catheterizations, long-term medical institutionalization, and immune senescence all contributing. Potentially modifiable factors contributing to UTIs include anatomic abnormalities of the urinary tract, particularly those that produce incontinence or urinary retention (eg, prostatic hyperplasia), uncontrolled diabetes mellitus, treatment with the sodium-glucose cotransporter 2 inhibitors (eg, canagliflozin and dapagliflozin), vaginal atrophy in postmenopausal women, sexual intercourse, which is a risk factor for both men and women, and, most critically in the elderly population, urinary catheterization.<sup>18–24</sup>

### Microbiology

Epidemiologic surveillance of outpatient urine cultures offers important insights into the changing prevalence and antibiotic susceptibilities of specific uropathogens. Among patients older than 65 years with uncomplicated cystitis, *Escherichia coli* remains the predominant pathogen, causing nearly two-thirds of cases, followed by *Klebsiella oxytoca* (~15% of cases), and *Proteus mirabilis* (~7% of cases). Taken together, gram-negative bacteria are present in more than 90% of cases of cystitis in older adults.<sup>4</sup> The microbiology of catheter-associated UTI (CAUTI) is more much diverse. In a review of multicenter data on CAUTIs reported to the National Healthcare Safety Network between 2011 and 2014, *E coli* was still the most common pathogen but made up only 23.9% of cases, whereas rates of *Candida* spp (17.8%), *Enterococcus* spp (13.8%), and *Pseudomonas aeruginosa* (10.3%) were significantly higher than those reported in uncatheterized patients.<sup>25</sup>

Colonization and infection with antibiotic-resistant bacteria increases with age, though the degree to which resistance increases varies by antibiotic class, likely reflecting variation in rates of antibiotic prescribing. For example, among female outpatients in 2012, susceptibility to ceftriaxone among urinary isolates was similar between girls aged 0 to 17 and women older than 65 years (83.4% and 84.3%), whereas for ciprofloxacin the rates of susceptibility dropped from 95.4% to 75% between those groups.<sup>4,26</sup> A limitation to these surveillance data is that, in the outpatient setting, a significant proportion of women may receive treatment of cystitis without a urine culture. Consequently, antimicrobial resistance patterns in the community may differ somewhat from the results based on surveillance data.<sup>27</sup> In the case of older adults with UTI, particular attention should be paid to any history of colonization or infection (including infections other than UTIs) with MDROs, as well the patient's history of antibiotic exposure (ie, which antibiotics the patient received in the past several months). Both prior carriage of MDROs and prior receipt of antimicrobials, the latter producing selective pressure for MDROs, are risk factors for infections with resistant bacteria. Special attention should also be paid to the local susceptibilities of *E coli*, which is responsible for most infections in uncatheterized patients. The resistance profile of *E coli* in the community, which providers may assess using their local antibiogram, will help inform the selection of antibiotics likely to be effective when empiric treatment of UTIs is necessary.

### Pathogenesis

Several recent genomic sequencing-based studies of human urine demonstrate that the urinary tract is not sterile even when urine cultures are negative; instead, the healthy urinary tract is host to a unique community of bacteria and viruses.<sup>28–30</sup> Notably, the bladder microbiome of patients with ASB is ecologically distinct from that of healthy patients with negative cultures.<sup>31</sup> Disruption of the urinary microbiota correlates with several genitourinary diseases, including urinary urgency and incontinence, chronic prostatitis, and symptom flares in chronic pelvic pain.<sup>32–34</sup>

The urinary microbiota may also mediate susceptibility to UTIs.<sup>35,36</sup> In theory, constituents of the healthy urinary microbiome may play a role in preventing UTIs by occupying attachment sites at the genitourinary epithelium, competing for limited nutrients, and limiting the proliferation of uropathogens via bacteriophage infection. Persistent urinary dysbiosis may compromise host defenses and lead to recurrent UTIs much in the same way that persistent disruption of intestinal microbiota predispose people to recurrence of *Clostridium difficile* infections. This model challenges the assumption that ASB is necessarily a prelude to symptomatic UTI and further suggests a role for

nonantibiotic approaches to managing recurrent UTI. So far, probiotic supplementation has not shown consistent benefit in preventing UTIs, though the quantity and quality of evidence is limited.<sup>37</sup>

Bacterial adhesion to the uroepithelium is a critical step in the pathogenesis of UTIs and thus a potential drug target. Cranberry proanthocyanidins inhibit adherence of *E coli* P-fimbria to uroepithelial cells and have provoked a longstanding interest in the use of various cranberry products for the prevention of UTI. However, multiple investigations on this topic have failed to show a consistent and clinically relevant benefit of cranberries in UTI prevention, and a recent randomized controlled trial showed no benefit of cranberry supplementation in preventing pyuria plus bacteriuria among older women in a nursing home setting.<sup>38,39</sup>

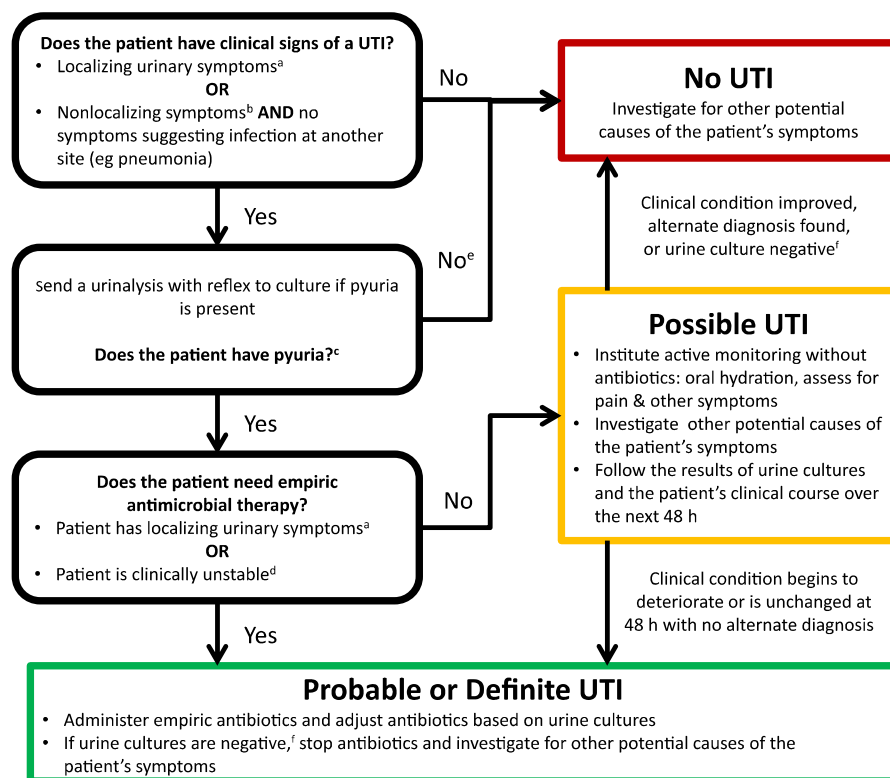
Urinary catheters, the most important risk factor for UTIs, function as portals for bacteria that are not part of the healthy urinary microbiome to enter the urinary tract. The catheter serves as a pathway for bacterial immigration into the ecological niche of the bladder such that bacterial colonization is ubiquitous in catheterized individuals. Although antibiotics can render the urine temporarily sterile, colonization invariably recurs days after antibiotic cessation. Because a persistently sterile urine culture is not a realistic goal for the patient with an indwelling urinary catheter, attempting to eliminate bacteriuria in such a patient with repeated antibiotic prescription merely selects for antibiotic-resistant organisms that may cause the patient future harm.<sup>40</sup>

#### DEFINING CLINICAL AND LABORATORY CRITERIA FOR URINARY TRACT INFECTION

As a clinical descriptor, UTI encompasses several clinical syndromes, including cystitis, pyelonephritis, and renal or perinephric abscess. Any of these conditions may be accompanied by systemic illness, including bacteremia and sepsis, and any of them can occur in the context of urinary catheterization, referred to as CAUTI. Providers' diagnostic uncertainty in differentiating UTI from ASB contributes to antibiotic overprescribing, and bacteriuria is a risk factor for both receipt of antibiotics for UTI and isolation of multidrug-resistant gram-negative rods in the urine of nursing home residents.<sup>41,42</sup> The authors propose definitions for ASB, which is generally not a clinical condition that merits treatment in older adults, and for the spectrum of conditions that comprise UTI. These definitions are used to differentiate older adults who are likely to benefit from receiving antibiotics from those who are not (Fig. 1). Note that this figure is intended to be used in clinical diagnosis and management of UTI. This criteria for UTI differs from the revised McGeer criteria, which are intended for surveillance for UTI in long-term care.<sup>43</sup>

ASB is defined as the presence of bacteria in the urine, with or without pyuria, in the absence of clinical symptoms indicating a UTI. ASB is common in older adults; in 1 study of nursing home residents, 25% to 50% of subjects had bacteriuria at any given time.<sup>44</sup> After adjusting for other comorbidities, older adults with ASB do not experience increases in mortality.<sup>2,45</sup> Antibiotics administered for ASB do not reduce the rates of subsequent complication and perversely, may increase the risk for a subsequent symptomatic UTI.<sup>46</sup> Furthermore, unnecessary antibiotic treatment is associated with acquisition of drug-resistant pathogens, *C difficile* infection, and other drug-related adverse events.<sup>46–48</sup> Guidelines from the Infectious Diseases Society of America recommend treating ASB only in pregnant women or immediately before a urologic procedure likely to involve mucosal injury.<sup>2</sup>

UTIs are defined by 3 components. First, the patient should have clinical symptoms suggesting infection of the urinary tract. In older adults, accepted clinical



**Fig. 1.** Algorithmic approach to diagnosing ASB and possible, probable, or definite UTI.

<sup>a</sup> Dysuria, frequency, suprapubic pain, gross hematuria, costovertebral angle tenderness, or new or worsening urgency or urinary incontinence. <sup>b</sup> Fever, rigors, or clear-cut delirium.

<sup>c</sup> Greater than 10 white blood cells per high-powered field on microscopy or positive leukocyte esterase. <sup>d</sup> Fever, sepsis or acute illness requiring care within an intensive care unit. <sup>e</sup> UTI can still be considered in patients with neutropenia or other conditions that might cause the absence of pyuria. <sup>f</sup> Urine cultures may be negative if obtained after the patient has received antibiotics; in such cases, stop antibiotics given specifically for UTI if the patient's clinical condition is not improving.

criteria include dysuria alone or fever accompanied by frequency, suprapubic pain, gross hematuria, costovertebral angle tenderness, or new or worsening urgency or urinary incontinence.<sup>49</sup> For those with an indwelling urinary catheter or who had 1 removed in the previous 48 hours, fever, rigors, or delirium alone (all of which are nonspecific); or new costovertebral tenderness, may herald a CAUTI.<sup>49</sup> Note that the revised McGeer criteria for UTI, which were developed for epidemiologic surveillance of UTI, differ slightly in their definitions for UTI and CAUTI (eg, leukocytosis and acute functional decline with no alternate diagnosis in the criteria for CAUTI) than the criteria we propose, which are intended to guide antibiotic prescribing in clinical practice.

Determining whether a change in behavior or mental status is present can be particularly challenging, as evinced by documentation of interobserver variability among nursing home staff for these criteria in 5 nursing homes.<sup>50</sup> Fortunately, dysuria was identified reliably. The presence of dysuria appears to be among strongest predictors

of bacteriuria plus pyuria in nursing home residents, and new dysuria is the most helpful clinical finding in identifying UTI in older adults.<sup>51,52</sup>

Other signs and symptoms can be misleading and are often misinterpreted as an indication for urinary testing. Falls are often considered a reason to test a nursing home resident for UTI, but the association of falls and UTI is controversial. A prospective study in these same 5 nursing homes included 397 suspected episodes of UTI and did not find an association between falls and the presence of bacteriuria plus pyuria.<sup>53</sup> Urine turbidity, sediment color, and odor do not reliably correlate with the presence of infection and are not in themselves symptoms of UTI; they are, however, associated with antibiotic overprescribing.<sup>54–56</sup> Such changes in urine may suggest a need for increased oral hydration, reflecting a decreased thirst response in older adults, or may be due to their medications (eg, multivitamins) or diet (eg, asparagus).

Second, laboratory evidence should demonstrate both pyuria and bacteriuria. Pyuria, which indicates an inflammatory reaction in the urinary tract, is generally defined as a positive leukocyte esterase on urine dipstick or greater than or equal to 10 white blood cells per high-powered field (WBCs/HPF), a threshold selected based on offering a negative predictive value for urine culture positivity and clinical UTI.<sup>57</sup> The accepted criteria for bacteriuria is at least 105 colony-forming units (CFUs) per 1 mL of a single organism in the urine of an uncatheterized patient or 103 CFU/mL greater than or equal to 1 bacterial species in the urine of a catheterized patient.<sup>2,24</sup>

Laboratory testing is primarily useful for excluding UTIs. Pyuria is sensitive but not specific for UTI, particularly among catheterized patients in whom its presence is ubiquitous. Reliance on pyuria alone for the diagnosis of UTI would lead to widespread antibiotic overtreatment, particularly because pyuria accompanies ASB.<sup>2,58</sup> Indeed, CAUTI is overdiagnosed, with retrospective studies showing that only 30% to 50% patients given the clinical diagnosis of CAUTI meet standardized criteria for CAUTI treatment.<sup>59</sup> Studies of the diagnostic value of the urinalysis for UTI have shown that it is an effective rule-out test but that poor specificity limits its value in ruling in UTI.<sup>60,61</sup> In this regard, the clinical utility of the urinalysis for diagnosing UTI is akin to that of the D-dimer for the diagnosis of a pulmonary embolism; a negative result is of great value for patients with all but the highest pretest probabilities of disease, whereas a positive result is necessary but not sufficient to establish the diagnosis.

Finally, the authors define UTI as a diagnosis that can only be made after a thorough search for other causes to explain the patient's symptoms and laboratory findings. This third criterion intends to avoid delays in appropriate therapy due to premature diagnosis of UTI and diagnostic closure. This is particularly relevant for older adults, in whom symptoms attributed to UTI are often not specific to the urinary tract (eg, fever, lethargy and confusion) and may belie infection at another site (eg, pneumonia), systemic infection (eg, influenza), or another cause entirely (eg, heart failure exacerbation).

The clinical presentation of UTI in older adults varies. In a multicenter evaluation of clinical features of UTI in nursing home patients, dysuria and change in mentation were 2 of the most frequently identified characteristics, with the important limitation that in this study UTI was defined by bacteriuria and pyuria alone, without consideration of clinical symptoms.<sup>51</sup> Factors that may complicate the diagnostic impression include urinary catheterization (which can obscure symptoms such as urinary frequency, urgency, or dysuria), baseline urologic comorbidities producing chronic urinary urgency or frequency, and a higher incidence of baseline cognitive impairments (ie, dementia) that can prevent the patient from effectively conveying their symptoms to the provider. In such cases, a careful history from caregivers, thorough physical examination of



the patient, and prudent laboratory testing may help differentiate UTI from other conditions.

For older adults especially, specific and clear criteria to diagnose UTIs are critical. First, recognition of ASB reduces unnecessary antibiotic exposure in a population rendered vulnerable to adverse drug events by comorbid conditions and polypharmacy.<sup>62</sup> Second, attributing clinical changes to a UTI without consideration of alternative diagnoses risks patient harm by delaying recognition and response to other medical problems. For example, a nursing home resident with a chronic indwelling urinary catheter who develops an acute change in mental status may be diagnosed with a UTI based on a urine dipstick showing pyuria. Providers may reflexively prescribe antibiotics, without considering other reasons for a clinical change, such as an acute cardiac event or ischemic stroke. This may delay appropriate interventions and lead to patient harm. Recognizing the high prevalence of ASB and the potential for misdiagnosis of UTIs based on laboratory findings, both The Society for Post-Acute Care and Long-Term Care Medicine and the American Geriatrics Society caution against ordering urine cultures in patients without urinary symptoms.<sup>63,64</sup>

#### QUALITY AND INTERPRETATION OF URINE SPECIMEN COLLECTION

Obtaining an adequate quality urine sample is frequently the first major barrier to appropriately diagnosing UTI in older adults. Guidelines specific to long-term care residents recommend collecting a midstream clean-catch urine specimen for urine studies.<sup>65</sup> In reality, such a collection is an often laborious process requiring the patient to possess not only urinary continence but a degree of cognition, coordination, and mobility that many older adults, particularly those who are institutionalized, may lack. For patients who cannot provide such a specimen, recommendations are to place an external condom catheter in men or perform in-out urinary catheterization in women, which can cause significant discomfort. Staff collecting urine specimens may use approaches that are not recommended by guidelines, such as obtaining the urine from a chronic urinary catheter or urine collection bag, both of which become contaminated with bacteria within hours of urinary catheter placement.<sup>24</sup> Finally, the person who interprets the results of urine studies may or may not be the same person who ordered the tests and is most certainly not the person who collected the sample.

Clinical symptoms that localize to the genitourinary tract should prompt testing urine for possible infection (see Fig. 1). In such patients, the diagnostic test of choice is a urinalysis with reflex to urine culture for specimens with pyuria ( $\geq 10$  WBCs/HPF or positive leukocyte esterase). The urinalysis has a negative predictive value for growth of bacteria in urine culture approaching 100%.<sup>66</sup> In patients who lack pyuria, attention should be turned away from UTI and toward other diagnostic considerations, except in rare cases in which neutropenia or other conditions may prevent pyuria. This algorithmic approach combining the urinalysis and urine culture offers both excellent sensitivity and specificity for UTI, with the reflex criteria averting inappropriate urine culture orders, a primary driver of unnecessary antibiotic prescription in patients with ASB.<sup>56,57</sup>

Because of older patients' higher burden of comorbidity and consequent risk of adverse events due to antibiotic therapy, we recommend active monitoring without antibiotics for older adults with possible UTI symptoms who are clinically stable (ie, no evidence of sepsis) until the results of the urinalysis and reflex culture are available. Active monitoring includes frequent assessment of vital signs for early detection of sepsis, parameters for hydration, and criteria for notifying the physician or other

provider if the patient's condition worsens.<sup>67</sup> If a patient spontaneously improves while waiting for the results of urine tests, a positive urine culture likely reflects ASB and the provider should consider other reasons for the patient's symptoms. If the patient deteriorates during a period of active monitoring, then providers should consider empiric antibiotic therapy until culture results become available or, depending on the clinical symptoms, consider other diagnoses. Order sets that support monitoring off antibiotics can help standardize active monitoring interventions.<sup>67</sup> When it is necessary to start antibiotics before culture results are known, facility antibiograms should inform selection of empiric treatment, if available.

Urine cultures should not be obtained in older adults unless clinical symptoms suggest a UTI and the accompanying urinalysis demonstrates pyuria (or the patient is neutropenic). Inappropriate ordering of urine cultures is harmful because, just as with a urinalysis, a urine culture does not distinguish between UTI and ASB. Detection of bacteriuria may lead to inappropriate antibiotic therapy, particularly when the patient has a peripheral leukocytosis or when the urine is colonized by a typical or multidrug-resistant uropathogen.<sup>11</sup> In older adults with both pyuria and clinical symptoms consistent with a UTI, obtaining a urine culture permits selecting antibiotics informed by microbiological results. Especially for older adults, we recommend against prescribing antibiotics for UTIs without first obtaining urine cultures to guide the choice of agent because the presence of antibiotic-resistant bacteria increases with age.<sup>4</sup>

#### TREATMENT OF URINARY TRACT INFECTIONS

For patients with a UTI, antibiotics provide symptomatic relief and may help prevent complications such as pyelonephritis, perinephric abscess, and bacteremia. The 2010 Infectious Diseases Society of America guidelines recommend 4 agents for the treatment of uncomplicated cystitis in women: nitrofurantoin; fosfomycin; pivmecillinam; and, where resistance rates are less than 20%, trimethoprim-sulfamethoxazole.<sup>68</sup> No recommendations have been made for UTI in men or empiric treatment of complicated UTI. However, when choosing empiric treatment in these settings, the provider should refer to the results of prior urine cultures. A study done in predominantly older men with UTI caused by MDROs found that prior urine culture results, even those collected as long ago as 2 years from the index case, were useful at predicting the causative pathogen and its susceptibilities.<sup>69</sup>

Currently, pivmecillinam is not available in the United States. Resistance to trimethoprim-sulfamethoxazole now exceeds 20% nationally among common uropathogens in older adults, emphasizing the importance of local antibiogram data in determining whether this agent remains an appropriate empiric agent in a provider's region of practice.<sup>4</sup> Nitrofurantoin is well-tolerated, and susceptibility of uropathogens to this agent remains high in older adults. However, nitrofurantoin achieves poor levels in tissue and serum and thus is only appropriate in patients who have cystitis without suspicion for upper tract disease. A retrospective study of male veterans with UTI treated with nitrofurantoin showed a clinical cure rate of 77% rate, which is comparable to other agents.<sup>70</sup> Decreased creatinine clearance predicted clinical failure in this study; however, 2 additional studies in older adults, 1 limited to women, refuted the concern that nitrofurantoin is less effective in treating UTI in patients with reduced creatinine clearance.<sup>71,72</sup> Particularly in older adults, for whom adverse event profile and collateral damage to the microbiome are important considerations, nitrofurantoin is a good choice for uncomplicated UTIs, including in men with preserved renal function.



Fosfomycin is administered as a single-dose oral packet (sachet) that is mixed with water then consumed. Fosfomycin is effective in the treatment of UTI, but its use is limited by availability, cost, and lack of standardized susceptibility testing. Furthermore, similar to nitrofurantoin, fosfomycin has poor tissue penetration, precluding its use in patients known or suspected to have upper urinary tract disease. In addition, this agent is among few remaining oral agents with reliable activity against ESBL-producing uropathogens, suggesting that its use might be justifiably reserved for people known to have these organisms.

Considered a second-line therapy, tetracycline antibiotics achieve therapeutic levels in urine, are well-tolerated, and may have an emerging role as an oral option for UTIs caused by ESBL-producing and carbapenem-resistant organisms. Most laboratories, however, do not routinely test urinary isolates for susceptibility to tetracyclines. Furthermore, uropathogens that are MDROs may also be resistant to tetracyclines, and only limited clinical data support using tetracyclines to treat UTIs.<sup>73,74</sup>

Other second-line therapies for uncomplicated UTIs include fluoroquinolones, aminoglycosides,  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations, and extended-spectrum cephalosporins. Although narrow-spectrum  $\beta$ -lactams and first-generation cephalosporins have historically played a minor role in the treatment of uncomplicated UTI due to concerns about inferior efficacy versus other agents, they are effective in treating urinary isolates known to be susceptible.<sup>68</sup> Using fluoroquinolones to treat UTIs has become commonplace, in part due to their high oral bioavailability and broad spectrum. In May 2016, however, the US Food and Drug Administration (FDA) advised that the risks of these medications generally outweigh their benefits for uncomplicated cystitis when other treatment options are available.<sup>10</sup> Beyond the prevalence of resistant organisms, fluoroquinolones increase the risk of several adverse events to which older adults are particularly vulnerable: QT prolongation, tendonitis and tendon rupture, seizures, delirium, and *C difficile* colitis.<sup>48,75–78</sup> Susceptibility to aminoglycosides remains high among most uropathogens. However, the lack of oral formulations of these drugs, the need to monitor serum drug levels, and the risk of major adverse events, including nephrotoxicity, vestibular toxicity, and ototoxicity, limit the role of this class in treating UTIs outside of the inpatient setting.  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations and extended-spectrum cephalosporins are broad-spectrum agents, which may lead to increased collateral damage to the patient's microbiome and selection of ESBL-producing organisms.

For patients with severe or systemic infections arising from the urinary tract, including pyelonephritis or bacteremia, empiric therapy with broad-spectrum agents is appropriate.<sup>68</sup> In these cases, fluoroquinolones,  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations, such as piperacillin-tazobactam, and extended-spectrum cephalosporins represent reasonable choices until culture results permit identification of an appropriate narrow-spectrum agent.

The duration of treatment of acute nonsevere UTI is best established in women, for whom the recommended duration of therapy varies by drug from 1 to 5 days.<sup>68</sup> Fosfomycin is given in a single dose, trimethoprim-sulfamethoxazole is given over 3 days, and nitrofurantoin requires a 5-day course of therapy. No clinical trial has demonstrated the superiority of extended (7–14 day) courses of therapy in male UTI or CAUTI versus shorter courses, whereas the harms of unnecessary antibiotic therapy are clear. In older adults, who are particularly susceptible to antibiotic-related adverse events, the risk-benefit calculus of antibiotic treatment favors shorter lengths of therapy. Mounting evidence demonstrates that clinical cure can be effectively achieved for CAUTI using a short course of antibiotics ( $\leq 7$  days) when the catheter is removed if the

patient is responding rapidly to initial therapy.<sup>79–81</sup> Similarly, longer lengths of therapy (>7 days) do not prevent recurrent UTIs and instead are associated with increased *C difficile* infection.<sup>18</sup>

Until more data are available, longer duration antibiotic therapy (ie, 10–14 days) remains reasonable for patients with severe urinary tract disease, including pyelonephritis and perinephric abscess, bacteremia, or need for hospitalization due to unstable clinical condition. However, we have intentionally chosen to avoid the labels uncomplicated UTI and complicated UTI in this discussion. We find the latter term problematic because it encompasses a heterogeneous group of conditions, some of which lack strong data supporting the need for extended courses of therapy (eg, UTI in men and diabetic women) and others for which extended antibiotic therapy alone may be inadequate (eg, UTI in the setting of urinary obstruction requiring mechanical intervention). Instead, we advocate that UTIs be classified by the extent of urinary tract and systemic involvement, and that potentially complicating factors, such as diabetes and urinary obstruction, be identified and addressed separately, tailoring the antibiotic duration to the complication and the patient's response to therapy.

## PREVENTION OF URINARY TRACT INFECTION

### *Effective Approaches to Catheter-Associated Urinary Tract Infection Prevention in Long-Term Care*

Removing indwelling urinary catheters is key to managing CAUTI because this both prevents further bacterial influx into the urinary tract and eliminates the reservoir of bacteria in biofilms that adhere to the catheter. Practically speaking, CAUTI prevention hinges on routine reevaluation of catheterized patients to determine whether they continue to have an indication for an indwelling urinary catheter, as well as identifying and treating the underlying comorbidities necessitating the catheter, and replacing indwelling catheters with clean intermittent catheterization when appropriate.

Removing catheters that are no longer necessary is an example of a technical intervention, defined as providing professional development and training in urinary catheter utilization, care, and maintenance. More recently, CAUTI prevention efforts have also included a socioadaptive component, specifically encouraging improvements in attitudes and behavior concerning patient safety. Two large-scale studies of CAUTI prevention in acute care and long-term care suggest that interventions that combine both cultural change and technical training can be successful at decreasing CAUTI.<sup>82,83</sup>

### *Ineffective Approaches to Catheter-Associated Urinary Tract Infection Prevention*

Long-term indwelling urinary catheters need be exchanged only when clinically indicated (eg, obstructed catheter flow, leakage from around the catheter insertion site, physical defect in the catheter, or CAUTI) rather than routinely because there is inadequate evidence that the latter practice reduces rates of CAUTI.<sup>84</sup> Attempts to decrease rates of CAUTI and bacteriuria by coating catheters with antibiotics or antiseptic materials have been largely unsuccessful, with either no or limited reductions in clinical outcome at the expense of increased patient discomfort and higher costs.<sup>85</sup> Systemic antibiotic prophylaxis for patients with long-term urinary catheters does not reduce rates of bacteriuria, CAUTI, or death.<sup>84</sup>

## SUMMARY

UTIs cause significant morbidity and mortality among older adults. Unfortunately, inappropriate or unnecessary antibiotics prescribed to older adults to treat suspected

UTI based on nonspecific symptoms or positive urine studies also leads to adverse events. The authors favor an approach to diagnosing UTIs rooted in the recognition of clinical signs and symptoms localizing to the genitourinary tract. Furthermore, we emphasize the value of the urinalysis as an exclusionary rather a confirmatory tools for UTIs. For instances when long-term care residents exhibit nonspecific changes, active monitoring, including hydration, treating pain, and reviewing medications, offers the possibility of avoiding unnecessary antibiotics while assuring residents and their family members that the health care team is responding to their concerns. Posting criteria for ordering urine studies, reviewing methods to collect good-quality urine specimens, implementing active monitoring order sets, and offering clinical decision support all represent systems-based approaches that may help curb inappropriate orders for urine studies and for antibiotics.

Developing technologies, such as colonizing the bladder with nonpathogenic bacteria or using catheters impregnated with bacteriophage cocktails are intriguing; however, currently, the most important means to prevent UTIs is by identifying and addressing modifiable risk factors. When older adults develop UTIs, providers should give preference to narrow-spectrum agents and short courses of therapy in most cases, with empiric antibiotic selections informed by local antibiogram data. Treatment and overtreatment of UTIs represents a significant proportion of antibiotic prescribing for older adults, driving the proliferation of resistant organisms in the community. Also, because older adults are particularly susceptible to adverse events associated with antibiotic treatment, whereas the harms associated with delays in appropriate antimicrobial therapy for UTI are small for most clinically stable patients, providers should take an approach to the diagnosis and treatment of UTIs that balances the potential benefit for the individual patient with both the risk of harm to that individual and the provider's duty as an antibiotic steward to protect the health of the larger community.

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