

SPECIAL SECTION: AGING AND INFECTION

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Urinary Tract Infection in Long-Term-Care Facility Residents

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Urinary tract infection is the most frequent bacterial infection in residents of long-term-care facilities. Most infections are asymptomatic, with a remarkable prevalence of asymptomatic bacteriuria of 15%–50% among all residents. The major reasons for this high prevalence are chronic comorbid illnesses with neurogenic bladder and interventions to manage incontinence. Prospective, randomized, comparative trials of therapy and no therapy for asymptomatic bacteriuria among nursing home residents have repeatedly documented that antimicrobial treatment had no benefits. However, there is substantial diagnostic uncertainty in determining whether an individual with a positive urine culture has symptomatic or asymptomatic infection when there is clinical deterioration and there are no localized findings. In the noncatheterized resident, urinary infection is an infrequent source of fever but may not be definitively excluded. The use of antimicrobials for treatment of urinary infection is part of the larger concern about appropriate antimicrobial use in long-term-care facilities and the impacts of the selective pressure of antimicrobials on colonization and infection with resistant organisms.

Urinary tract infection is the most common infection in residents of long-term-care facilities [1]. Although most infections are asymptomatic, episodes of symptomatic infection do contribute to morbidity in this population. The term “colonization” is used by some individuals when discussing asymptomatic bacteriuria in this population. However, asymptomatic bacteriuria is virtually always associated with a host response and is, therefore, infection rather than colonization. In this article, the terms “asymptomatic bacteriuria” and “asymptomatic urinary infection” are used interchangeably. Aspects of urinary tract infection related to chronic urinary catheters differ from non-catheter bacteriuria and will not be discussed further in this paper. This discussion is restricted to issues relevant to urinary infection in residents without long-term indwelling catheters, unless otherwise noted.

Occurrence

Asymptomatic infection. The frequency of asymptomatic urinary infection, or asymptomatic bacteriuria, among residents of long-term-care facilities is remarkable [2]. Repeated

prevalence surveys in different facilities and countries consistently report that 15%–30% [2] of men and 25%–50% of women have positive urine cultures. The incidence of new episodes of asymptomatic bacteriuria is 45 cases per 100 patient-years for men, and 10% of previously nonbacteriuric men are reported to acquire bacteriuria every 3 months. Among previously bacteriuric women, the incidence of acquisition of either symptomatic or asymptomatic new infections is 0.87–1.67 cases per patient-year. Bacteriuric residents may become nonbacteriuric, often secondary to antimicrobial therapy for urinary or other infections, leading to a continuing “turnover” of bacteriuria. For instance, the rate of conversion from a negative to positive urine culture was 8% among women in 1 facility at 6 months, while the rate of conversion from a positive to negative urine culture was 31% [3].

The principle factors responsible for this high frequency of bacteriuria are chronic comorbid conditions, some of which may have caused the patients to be institutionalized. Residents with asymptomatic bacteriuria are more functionally impaired, with decreased cognitive function and incontinence of bladder and bowel, than residents without asymptomatic bacteriuria. Chronic degenerative neurological diseases, such as Alzheimer’s disease and Parkinson’s disease, and cerebrovascular accidents are associated with a neurogenic bladder. These conditions cause impaired bladder emptying and ureteric reflux, which contribute to the high frequency of bacteriuria. Interventions to manage incontinence may also promote infection. External condom drainage, which is used by incontinent men, doubles the frequency of bacteriuria, and the new onset of asympto-

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matic bacteriuria may occur with initiation of condom drainage [2]. Aging-associated physiological changes such as prostatic hypertrophy in men and estrogen deficiency in women may also contribute to asymptomatic bacteriuria; however, their relative importance is not well defined, and they may have greater impact in ambulatory rather than institutionalized populations.

Symptomatic infection. Prospective studies of infections in residents of long-term-care facilities report an incidence of symptomatic urinary infection that varies from 0.1 to 2.4 cases per 1000 resident-days [1]. The wide variation reflects differences in patient populations among institutions and variability in surveillance definitions. These studies also included residents with long-term indwelling catheters. Prospective studies of urinary infection in noncatheterized subjects with restrictive definitions for symptomatic infection report an incidence of 0.11 episode per year for men and 0.33–0.46 episode per year for women [1, 4]. In another study [5], the incidence of more severe morbidity, manifested as febrile urinary infection, was 0.49–1.04 cases per 10,000 resident-days.

Diagnosis

Microbiological diagnosis. The microbiological diagnosis of urinary infection requires that a specimen be collected appropriately, in a manner to limit contamination, and that it be delivered promptly to the laboratory. A clean catch urine specimen can usually be obtained from men and is reliable. Where a clean catch specimen cannot be obtained, collection from a freshly applied condom catheter may be used, with a quantitative count of $\geq 10^5$ cfu/mL diagnostic of bacteriuria [2]. For women, a clean catch specimen is more difficult to obtain, and bacterial contamination is problematic in women unable to cooperate with specimen collection. If a urine specimen for culture is essential for clinical management, in-and-out catheterization is the preferred method for collection. The use of bedpans or pedibags for collection of urine specimens from women is associated with substantial contamination and cannot currently be recommended.

The diagnostic criterion for asymptomatic bacteriuria is a quantitative count $\geq 10^5$ cfu/mL in 2 consecutive urine specimens. From 10% to 25% of men or women have infection with >1 organism; therefore, isolation of >1 organism in appropriate quantitative counts should not be dismissed as contamination [1]. For symptomatic urinary infection, $\geq 10^5$ cfu/mL is the diagnostic standard. Although lower quantitative counts of bacteria occur in some clinical presentations, alternate criteria for quantitative urine culture have not been validated for this population, and no definitive recommendations for lower quantitative counts can be made.

Enterobacteriaceae are the most common infecting organisms [1]. *Escherichia coli* infection is most common among women, and *E. coli* infection and *Proteus mirabilis* infection occur with equal frequency among men. However, a greater variety of

organisms is isolated from residents in long-term care facilities than from the community population. Other organisms frequently isolated include *Providencia stuartii*, *Pseudomonas aeruginosa*, *Citrobacter* species, *Klebsiella* species, *Enterobacter* species, and gram-positive organisms such as *Enterococcus*, group B *Streptococcus*, and coagulase-negative staphylococci. Bacteria that infect residents of long-term care facilities tend to have greater antimicrobial resistance, because repeated courses of antimicrobial therapy select for such organisms, and because infection is acquired in the institutional setting.

Clinical diagnosis. Symptomatic infection may present with the classic clinical genitourinary symptoms characteristic of younger populations. These are lower tract irritative symptoms, which for bladder infection include new onset or increased frequency of incontinence and for acute pyelonephritis include fever with costovertebral angle pain or tenderness. The diagnosis of symptomatic urinary infection, however, is often problematic [6]. Acute symptoms may be difficult to recognize because of impaired communication with patients who are deaf or because of dysarthria, dementia, or chronic symptoms associated with comorbid illnesses. Many patients have incontinence that is associated with neurogenic bladder or prostatic hypertrophy. Chronic genitourinary symptoms are frequent in this population but have not been shown to occur with greater frequency among patients with bacteriuria. Thus, chronic symptoms are not due to urinary infection, although many residents with chronic genitourinary symptoms have positive urine cultures [2, 7].

Although the febrile response is blunted in the elderly population, most serious urinary infections will still be associated with fever [5]. In some younger populations, the association of fever and a positive urine culture may be sufficient for a diagnosis of urinary infection; this is not the case for residents of nursing homes. Given the high prevalence of bacteriuria, a positive urine culture is not diagnostic for symptomatic urinary infection in a febrile patient, although a negative urine culture will exclude the diagnosis. In a prospective study of fever in bacteriuric subjects without localized findings were due to urinary infection. The positive predictive value of a positive urine culture for residents with fever and no localized genitourinary symptoms was only 12%. Thus, for the febrile patient with no symptoms referable to the genitourinary tract and a positive urine culture, the diagnosis of urinary infection is unlikely and often cannot be made definitively. Where acute symptoms referable to the urinary tract were present, 43% of patients with episodes of fever had an antibody response consistent with infection, and the positive predictive value of a positive urine culture was 19%.

Gross hematuria in nursing home residents is more frequent in men than in women and is rarely directly due to infection (i.e., hemorrhagic cystitis) [8]. Thus, alternate causes for gross hematuria should always be sought. Most residents with

Table 1. Summary of prospective, randomized trials compared antibiotic therapy and no therapy for asymptomatic bacteriuria among residents of long-term-care facilities.

Reference	Population characteristics (mean age, y)	Outcome(s)
[12]	Men, veterans (82)	After 2 y, no difference in incidence of symptomatic urinary infection, no difference in prevalence of infection, and no difference in mortality rate
[13]	Women, nursing home residents (83.4)	After 1 y, monthly prevalence of urinary infection down 31% among women treated with antibiotics; incidence of symptomatic infection and mortality rate similar among treated and among untreated women; and among treated women, more adverse drug effects and reinfection with resistant bacteria
[11]	Women, geriatric apartment residents (81.1)	After 8 y, mortality similar in treated or untreated residents
[7]	Male and female nursing home residents with incontinence (85)	No decrease in frequency or volume of incontinence among women treated with antibiotics

hematuria have underlying abnormalities of the genitourinary tract, and a high proportion, 75% in one study [8], have positive urine cultures. The presence of gross hematuria usually indicates ulceration or trauma to the genitourinary mucosa, and secondary fever or bacteremia may occur in a bacteriuric subject; one report found that 30% of episodes were associated with fever [8]. Therefore, although hematuria per se is not caused by infection, individuals with gross hematuria frequently have secondary fever due to invasive infection in a traumatized genitourinary tract.

Pyuria. Over 90% of men or women with asymptomatic bacteriuria have associated pyuria [2]. Thus, the presence of pyuria does not differentiate asymptomatic from symptomatic infection. In residents with persistent asymptomatic bacteriuria, a high degree of pyuria may persist for many years [9]. Approximately 30% of elderly nursing home residents without bacteriuria have pyuria [2]. The reasons for this pyuria are not known, but associated genitourinary diseases such as interstitial nephritis, vaginal inflammation, or prostatitis may contribute to its occurrence. Thus, pyuria by itself is insufficient for a diagnosis of urinary infection. The absence of pyuria, however, has a high negative predictive value (80%–90%) for the absence of bacteriuria. Thus, the absence of pyuria is useful to exclude urinary infection; however, the presence of pyuria is not a valid diagnostic criterion for infection, nor does it differentiate symptomatic from asymptomatic infection.

Impact

Host response. A demonstrable host response is usually present with asymptomatic bacteriuria [2]. Therefore, this is infection rather than colonization. In addition to pyuria, 50% of subjects have elevated titers of urine or serum antibody to surface antigens of the infecting uropathogen, and antibody levels return to normal if bacteriuria is eradicated. Urine levels of cytokines such as IL-6, IL-8, and TNF- α are higher in elderly nursing home residents with asymptomatic bacteriuria than in residents without bacteriuria.

The response to symptomatic infection is similar to that ob-

served in younger populations. There are increases in the antibody level to the infecting organism in both the urine and serum [5], and increases in other measures of inflammation, such as urinary cytokine levels. In more severe clinical manifestations, the C-reactive protein level is elevated.

Morbidity and mortality. The presence of asymptomatic bacteriuria has not been shown to be associated with adverse outcomes in long-term-care facility residents [2]. There is no evidence for accelerated functional decline with asymptomatic bacteriuria or development or progression of renal failure. Symptomatic infection in subjects with asymptomatic bacteriuria occurs infrequently in the absence of genitourinary trauma or another abnormality of the genitourinary tract. Although urease-producing organisms such as *P. mirabilis* and *Providencia* species are frequently isolated and often cause persistent infection, urolithiasis has not been identified as a significant problem in these populations.

Mortality rates among elderly subjects with asymptomatic bacteriuria are similar to the rates among subjects without asymptomatic bacteriuria, despite the consistent observation that residents with asymptomatic bacteriuria have more impaired functional status [10, 11]. The mortality rate among elderly residents with asymptomatic bacteriuria and elevated titers of urine antibody is significantly greater than among those with normal titers of urine antibody [14]. There is no evidence, however, that this is causal, and the presence of urine antibody probably simply identifies elderly subjects with immune dysregulation who have a greater likelihood of death. This observation requires further investigation.

Management

Asymptomatic bacteriuria. Prospective, randomized, comparative trials of antimicrobial therapy or no therapy in which elderly male and female nursing home residents with asymptomatic bacteriuria were enrolled consistently document no benefits of antimicrobial therapy (table 1). Specifically, there is no decrease in the frequency of symptomatic episodes, and no improvement in survival [7, 11–13]. In fact, at 12 or 24 months,

there is a trend toward increased mortality with intense antimicrobial therapy for eradication of bacteriuria [11–13]. Subjects with asymptomatic bacteriuria and chronic incontinence who are treated with bacteriuria have no decrease in the frequency or volume of incontinence [7]. On the other hand, treatment with antimicrobial therapy increases the occurrence of adverse drug effects and reinfection with resistant organisms, and increases the cost of treatment. Therefore, asymptomatic bacteriuria in elderly residents of long-term-care facilities should not be treated with antibiotics. It follows that screening for asymptomatic bacteriuria is also not advised. Pyuria is not an indication for treatment of bacteriuria in the absence of clinical symptoms, and urinalysis screening of asymptomatic subjects for pyuria is also not indicated.

There has been substantial interest in the use of “natural substances” such as cranberry juice in the management of urinary infection in elderly patients. The theoretical underpinnings include the presence of hippuric acid, an antiseptic, in cranberry juice, and *in vitro* studies reporting interference with adherence of organisms to uroepithelial cells with cranberry juice. One randomized, placebo-controlled trial of cranberry use to treat urinary infection in elderly female nursing home residents reported that daily intake of cranberry juice decreased the prevalence of bacteriuria with pyuria [15]; however, it did not decrease the prevalence of bacteriuria overall, nor did it decrease the number of episodes of symptomatic infection. In addition, the randomized groups in this study were unbalanced, and the group randomized to nontreatment had had an increased occurrence of infection before treatment. Thus, there is currently no evidence that daily ingestion of cranberry juice improves clinical outcomes, and its impact on bacteriuria remains unresolved.

Despite consistent evidence that asymptomatic bacteriuria in nursing home residents should not be treated, urinary infection remains the most frequent reason for prescribing antimicrobials in nursing homes, and much of the prescriptions are for treatment of asymptomatic infection [16, 17]. Some of these prescriptions reflect the diagnostic uncertainty. However, some courses are also prescribed because of a perceived need to treat a positive urine culture, especially if there is pyuria. It remains a challenge to translate the substantial and consistent evidence that supports nontreatment of asymptomatic urinary infection in long-term-care facilities into practice. Specific problems contributing to this challenge include diagnostic uncertainty and the fact that physicians are not always available in long-term-care facilities, so that initial evaluation and subsequent monitoring of patients who are not treated are often managed by nonphysician staff [18]. Approaches to deal with this practice problem need to be identified and evaluated.

Symptomatic infection. Antimicrobial selection for the treatment of symptomatic urinary infection in elderly nursing home residents does not differ from that for younger popu-

lations. There are limited comparative clinical trials to define optimal agents or regimens. Wherever possible, a urine culture should be performed, and the results should be available before initiating therapy. If empirical therapy must be given, preferred agents for oral therapy are trimethoprim-sulfamethoxazole and nitrofurantoin [18]. For subjects who are more ill, require parenteral therapy, and do not have renal impairment, an aminoglycoside (im or iv) is preferred. In this situation, the need for aminoglycoside therapy is reassessed following the results of urine culture, which is usually available within 3–4 days. Many other agents will certainly be effective, including extended-spectrum cephalosporins and the quinolones, but these agents should be reserved as therapy for individuals known to be infected with resistant organisms or who have intolerance to other antimicrobial agents, in order to limit the selective pressure of antimicrobials and, hopefully, the emergence of resistant organisms [18].

Where the clinical presentation is consistent with acute cystitis or acute pyelonephritis or bacteremia is present, the diagnosis may be straightforward. However, as previously noted, the diagnosis is often problematic, and although the probability is low, it cannot be dismissed in many cases [5]. In these situations, observation is preferred to empirical antimicrobial therapy if the patient is not significantly ill with high-grade fever, leukocytosis or left shift, or hemodynamic instability. Careful observation is warranted if empirical therapy is given to monitor the clinical course and reassess the possibility of alternate diagnoses.

The appropriate duration of therapy for bacteriuria in nursing home residents has not been well studied [19]. Short-course therapy is less effective in older women than in younger women. For patients presenting with lower tract symptoms, 7 days of therapy is recommended. For individuals presenting with fever or more severe systemic manifestations, 10–14 days of therapy is recommended. The only current indication for prophylactic antimicrobial therapy for this population is as periprocedure prophylaxis for bacteriuric subjects who are to undergo an invasive urologic procedure. The use of suppressive therapy should be limited to selected cases where symptomatic infection can be controlled only with ongoing antimicrobial therapy or where struvite stones are known to be present and prevention of stone enlargement is the therapeutic goal.

Early microbiological recurrence after therapy is the norm. Thus, by 4–6 weeks, 50%–70% of treated individuals will again have positive urine cultures [2]. The positive culture will often not be associated with recurrence of symptoms. If symptoms recur after treatment, repeated urine culture should be performed before treatment is given again. In the absence of symptoms, posttherapy urine cultures are not indicated. The goal in this population is to ameliorate symptoms, not to sterilize the urine.

Prevention

The major determinants of bacteriuria are not modifiable. Therefore, it is unlikely that the high prevalence of urinary infection in long-term-care facilities can be substantially decreased. The use of intravaginal estrogen in institutionalized women who had a high frequency of infection was reported to decrease the frequency of both symptomatic and asymptomatic infection [20]. However, in one group of elderly women, some of whom were institutionalized, the frequency of infection among those receiving low doses of estrogen as prophylaxis was similar to the frequency among those receiving placebo [21]. Therefore, the role of estrogen therapy in preventing urinary infection in this population requires further study.

The frequency of infection among men may be decreased by avoiding the use of condom catheters and, where they are used, ensuring unobstructed drainage of urine from the catheter to the drainage bag. It is not currently known whether different approaches to cleaning of leg bags will alter the frequency of urinary infection. For patients with voiding managed by intermittent catheterization, a clean technique is associated with a frequency of infection similar to that of a sterile technique and is less costly [22]. Avoidance of use of long-term indwelling catheters may decrease the overall prevalence, because persistent infection may occur following catheter removal. Invasive infection with bacteremia and sepsis may be minimized by early identification of retention and appropriate use of periprocedure antimicrobial prophylaxis for bacteriuric subjects who undergo invasive procedures with trauma to the genitourinary mucosa.

Summary

Urinary infection is an important clinical problem in long-term-care facility residents. Several aspects of management differ from those for other populations. Physicians who care for patients in this setting must understand the high frequency and appropriate management of asymptomatic bacteriuria, the diagnostic uncertainty in identifying symptomatic infection, and appropriate treatment of symptomatic infection. Many issues require further evaluation. One of the most important is to identify optimal approaches to antimicrobial therapy for individuals with suspected symptomatic urinary infection.

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