Management of Complicated Urinary Tract Infection in Older Patients
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Yoshikawa, Thomas T. MD*; Nicolle, Lindsay E. MD†; Norman, Dean C. MD‡

From the *Charles R. Drew University of Medicine and Science and King-Drew Medical Center, Los Angeles, California; the† University of Manitoba, Winnipeg, Canada; and‡ West Los Angeles Veterans Affairs Medical Center and the University of California, Los Angeles, California.

Address correspondence to Thomas T. Yoshikawa, MD, Department of Internal Medicine (MP-11), King-Drew Medical Center, 12021 S. Wilmington Ave., Los Angeles, California 90059.

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Abstract

Urinary tract infection (UTI) in older persons is a common medical problem that is seen in both the ambulatory and institutional settings. It affects older women and men with a gender prevalence ratio of 2:1, respectively. UTI in older persons can be a complex problem in terms of the approach to diagnosis, treatment, and prevention. In this report, the discussion will begin with the unique aspects of UTI in older persons, particularly as they relate to UTI in the younger, general population. The remaining discussion will then focus on three complicated clinical circumstances and conditions of UTI in the geriatric population: non-catheter recurrent UTI, asymptomatic bacteriuria, and catheter-related bacteriuria and UTI.

UNIQUE ASPECTS OF URINARY TRACT INFECTIONS IN OLDER PEOPLE

Epidemiology

In the general population, urinary tract infection (UTI) is primarily an infection of sexually active women, with women outnumbering men with UTI by a ratio of 30:1.1 With increasing age, the prevalence of UTI increases in both women and men, and the two women to men ratio becomes 2:1.1

UTI or bacteriuria is the most frequently found of all bacterial infections in the older population. Bacteriuria is defined here as the presence of at least 100,000 colony-forming units of a uropathogen per milliliter urine without regards to clinical symptoms. Virtually all bacteriuria in older persons elicits a host inflammatory response and is thus considered to be UTI. Colonization of urinary tract in aged persons has very little clinical relevance (see section "Asymptomatic Bacteriuria"). Asymptomatic bacteriuria is a UTI without clinical symptoms. Complicated UTI refers to infection that fails to resolve completely or recurs after standard chemotherapy (i.e., chronic bacteriuria, recurrent UTI, or catheter-related bacteriuria), regardless of cause, is associated with bacteremia or sepsis, or presents atypically (e.g., asymptomatic bacteriuria) or has an atypical clinical course.

Community studies consistently report an increasing prevalence of asymptomatic bacteriuria with age; 5 to 10% of women older than age 60 are bacteriuric. This prevalence increases to as much as 20 to 30% in women aged 80 years and older.1-7 For men, the prevalence of asymptomatic bacteriuria in the community is generally reported to be from 5 to 10% for those more than 70 years old 1,5,7-9(Table 1).

Table 1. Prevalence of Asymptomatic Bacteriuria in an Older Population Without Long-Term Indwelling Catheters

Institutionalized populations have a remarkable prevalence of bacteriuria. In several reports from different developing countries, 17 to 55% of women and 15 to 31% of men are bacteriuric (Table 1). Among the most highly functionally disabled persons, the prevalence of bacteriuria exceeds 50% for both women and men.

Diagnostic Considerations

The majority of younger adults with UTI experience uncomplicated disease. Approximately 80 to 85% of those UTI cases (generally women) will be caused by Escherichia coli. In such younger female patients (but not men), obtaining a culture of the urine before initiating therapy may not be necessary provided a diagnostic urinalysis (bacteria and leukocytes) is identified. Moreover, adults in the general population who acquire bacteriuria usually complain of genitourinary symptoms, which include frequency, dysuria, and urgency (dysuric syndrome), abdominal or flank pain, nausea, or fever or chills. In men, there may be obstructive complaints, i.e., hesitancy, poor stream, and dribbling.

In contrast to younger persons with UTI, older persons with urinary infections are more likely to experience uropathogens other than E. coli, i.e., other enterobacteriaceae, enterococci, and staphylococci. The severity of functional disability, nature of underlying illness, presence of anatomical and physiologic abnormalities of the genitourinary tract, and use of indwelling bladder catheter will determine the type(s) of organisms and chronicity of bacteriuria. The diversity of potential uropathogens mandates that urine cultures be obtained in all older persons with suspected UTI.

Therapeutic Approach

Currently, young adult women with uncomplicated lower UTI are generally treated with 3 days of antimicrobial therapy. Adult men with cystitis require 7 to 10 days of therapy. In both women and men with uncomplicated pyelonephritis, 14 days of antimicrobial agents are recommended.

However, abbreviated courses (less than 7 days) of treatment for UTI are not recommended for older patients because of the relatively high rates of failure and relapse. Most older women with uncomplicated lower tract UTI should be treated with antibiotics for 10 days; older men are generally treated for 14 days. Upper tract UTI (e.g., presence of urosepsis, flank tenderness, fever over 101°F) in both men and women requires 14 days of therapy.

NON-CATHETER-RECURRENT URINARY TRACT INFECTIONS
Recurrent UTI

In the absence of an indwelling bladder catheter, recurrent UTI is defined here as three or more episodes of symptomatic bacteriuria within 1 year.22 (Other investigators define recurrence as two or more UTIs in 1 year.23) Recurrent UTI is classified as either relapse or reinfection.

Relapse UTI

Relapse UTI is the condition in which infected urine is rendered temporarily or partially "sterile" by therapy, but bacteriuria with the uneradicated pathogen recurs, generally within 2 weeks after completion of antibiotics.24,25 Table 2 summarizes the predisposing risk factors or underlying conditions for both relapse and reinfection UTIs.17,22

<table>
<thead>
<tr>
<th>Relapse UTI</th>
<th>Risk Factors or Underlying Conditions Associated with Recurrent UTI</th>
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<tbody>
<tr>
<td>Genitourinary (GU) anatomic abnormalities (e.g., vesicoureteral reflux)</td>
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<tr>
<td>GU calculi</td>
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<td>Pyelonephritis</td>
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<td>Renal abscesses</td>
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<tr>
<td>Perinephric abscesses</td>
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<td>Urinary diversion procedures (e.g., fistula bladder)</td>
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<td>Chronic bacterial prostatitis</td>
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<tr>
<td>Reinfection UTI</td>
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<tr>
<td>Sexual intercourse</td>
<td></td>
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<tr>
<td>Incomplete bladder emptying</td>
<td></td>
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<tr>
<td>Lack of good personal hygiene</td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
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</tr>
</tbody>
</table>

Depending on the overall management goals for each patient, select older (or any age) patients with relapse UTI require a full genitourinary evaluation.17 This evaluation should include determination of renal function, quantitation of postvoid residual bladder urine volume, and investigation of the upper urinary tract architecture (ultrasonography; computed tomography in select cases). Urologic consultation should be sought if there are obstructive uropathy, calculi, abscesses, or genitourinary anatomical abnormalities.

In older men, chronic bacterial prostatitis (CBP) may be a cause of relapse UTI. The method of diagnosis of CBP is not precise and is dependent on a combination of culture results from segmented urine specimens and prostatic secretions. The technique of urine collection and the significance of the results are shown in Table 3.26 The diagnosis of CBP is suggested when the bacterial colony counts from the urethra/prostate urine (UPU) specimen or expressed prostatic secretion (EPS) are at least tenfold greater than counts from the urethral urine (UU) sample. Prostatic secretions should also be examined by wet mount or Gram stain to confirm presence of inflammation, i.e., presence of neutrophils. The bladder urine (BU) specimen must be sterile for proper interpretation of culture results. If bladder bacteriuria is suspected, urine should be sterilized with nitrofurantoin for 2 or 3 days; this antibiotic does not penetrate the prostatic tissue.

| Table 3. Diagnosis of Chronic Bacterial Prostatitis (CBP) by Segmented Urine Cultures |

Therapy of relapse UTI depends on the underlying cause(s) and correction or alleviation of this (these) problem(s). For CBP, treatment with long-term (at least 4 weeks) oral antimicrobial agents such as a quinolone, carbenicillin, or trimethoprim-sulfamethoxazole is recommended.27-29

Reinfection UTI

Reinfection UTI is the occurrence of a new UTI following successful eradication of a previous infection. Generally, reinfection UTI occurs 4 weeks or more after the previous infection has been cured; the reinfesting organism is frequently a different pathogen from earlier infections, although they can be the same.

In younger adults, reinfection, which is found primarily in women, occurs most often as a bladder infection, and is usually related to sexual intercourse. In older persons, reinfection also is primarily a lower tract disease, but the pathogenesis is unclear. Poor or incomplete bladder emptying, lack of good personal hygiene, and perhaps age-related diseases such as diabetes mellitus may be risk or contributing factors.2,3

Management of reinfection includes assessment of bladder anatomy and function, i.e., postvoid residual volume and voiding cystogram or cystoscopy (voiding cystogram for patients suspected of anatomical abnormalities; cystoscopy is reserved for possible bladder tumors or masses). Patients without heart failure or renal dysfunction should be encouraged to have good hydration; all patients should practice regular and complete emptying of the bladder and careful personal hygiene.22 The clinical can prescribe vitamin C and drinking of citrus fruit juice to acidify the urine (which inhibits bacterial growth), or perhaps cranberry juice (which limits microbial adherence to bladder epithelium).20 Alternatively, low-dose antibiotics, e.g., trimethoprim, 50-100 mg, or trimethoprim-sulfamethoxazole 40/200 mg, at bedtime should be recommended for 3 to 6 months in patients with reinfection without obstruction, stones, or neurogenic bladder.

ASYMPTOMATIC BACTERIURIA IN NON-CATHETERIZED PATIENTS

Occurrence

Prevalence and incidence of asymptomatic bacteriuria in older people are high. In an older ambulatory American population living in a geriatric home, Boscia et al. reported that 18% of women and 6% of men had asymptomatic bacteriuria at initial screening.1 The cumulative prevalence after 18 months, with screening every 6 months, was 10% for men and 30% for women. Mims et al.2 reported development of asymptomatic bacteriuria in only three (3.4%) of 87 initially nonbacteriuric older ambulant men followed less than 1 year and 17 (14%) of 122 followed for 1 to 4.5 years. In a group of highly functionally impaired older institutionalized men, new (asymptomatic) infections were identified at a rate of 45/100 patient years, including
10% of previously nonbacteriuric subjects who become bacteriuric in any 3-month period. However, a highly impaired bacteriuric population of institutionalized older women, an incidence of new (asymptomatic) infection of 1.2/resident year was observed.

Microbiology

E. coli is generally the organism isolated most frequently from noninstitutionalized older men and women with asymptomatic bacteriuria. However, Gram-positive cocci have been isolated in ambulatory older men with asymptomatic bacteriuria. The frequency of Gram-positive organisms such as coagulase-negative staphylococci, Enterococcus faecalis, and group B streptococci is increased relative to the distribution of organisms isolated from symptomatic infection in younger populations. Proteus mirabilis and Klebsiella pneumoniae are the Gram-negative organisms isolated with greatest frequency after E. coli. In institutionalized women, E. coli remains the organism isolated most frequently. For men, however, P. mirabilis is identified as frequently or more frequently than E. coli. Gram-negative organisms of increased antimicrobial resistance are isolated more frequently in the institutionalized population. These include Citrobacter freundii, Enterobacter cloacae, Pseudomonas aeruginosa, and Providencia stuartii. Infection with more than one organism is identified in 10 to 25% of institutionalized bacteriuric subjects.

Host Response

More than 90% of all older subjects with asymptomatic urinary infection have evidence of a local host response as measured by pyuria. However, as many as 30% of non-bacteriuric older institutionalized subjects also have pyuria. The use of pyuria to differentiate "colonization" from infection has not been shown to have clinical relevance.

Older subjects with asymptomatic bacteriuria demonstrate a spectrum of local urinary immune and inflammatory parameters in addition to pyuria. From one-quarter to one-half of subjects have an elevated urine antibody to the infecting uropathogen when compared with nonbacteriuric subjects; a similar proportion have measurable urinary interleukin (IL)6, IL1a,37 or IL8 (unpublished observations). Some older subjects with asymptomatic bacteriuria also have evidence for a systemic response as measured by persistently elevated serum antibody to potential uropathogens. The factors that influence frequency and extent of systemic host response are not yet described.

Morbidity

The associations of asymptomatic bacteriuria and symptomatic UTI in ambulant, noninstitutionalized older persons have not been well studied. Boscia et al. reported that, in 6 months of observations, 7.9 to 16% of women with asymptomatic bacteriuria developed symptomatic infection; it was not determined whether symptomatic infection was attributable to the organism isolated when the subject was asymptomatic or to reinfection with a different uropathogen.

The high prevalence of both chronic genitourinary symptoms and bacteriuria in institutionalized older populations makes the assessment of potential morbidity from UTI problematic. However, it is clear that chronic genitourinary symptoms such as frequency, dysuria, urgency, and incontinence, as well as nonspecific general complaints without localizing genitourinary symptoms, may not be caused by UTI, although many of these individuals are bacteriuric. In addition, hemorrhagic cystitis manifesting as gross hematuria is not caused by asymptomatic bacteriuria in the institutionalized population.
The contribution of asymptomatic bacteriuria to symptomatic genitourinary morbidity in institutionalized older adults is small relative to the high prevalence and incidence of bacteriuria. Symptomatic infection, however, may occasionally be caused by an organism previously causing asymptomatic infection. This usually occurs following invasive genitourinary procedures or other trauma to the genitourinary mucosa but, rarely, may be caused by alteration in virulence expression by the infecting organism such as new pilus expression by E. coli. There is little evidence that asymptomatic bacteriuria by itself leads to potentially negative long-term outcomes such as renal failure or hypertension.

Initial reports from Greece and Finland suggested asymptomatic bacteriuria was associated with decreased survival in ambulatory older men and women. These studies, however, did not provide an explanation for this association. Subsequent community-based studies from Sweden and Finland have failed to confirm this association. In the Swedish study, other bacteriuria men did have a poorer survival record, but this association did not persist after correction for the presence of associated genitourinary malignancy. Prospective studies in institutionalized populations have consistently failed to identify a contribution of asymptomatic bacteriuria to mortality. Finally, UTI is virtually never identified as an immediate cause of death in autopsy series of nursing home residents. Thus, there is currently no evidence to support a causal relationship of asymptomatic bacteriuria and mortality in the older population.

Management of Asymptomatic Bacteriuria

Studies that report observations of the treatment of asymptomatic bacteriuria in older populations without indwelling catheters are summarized in Table 4. These studies consistently document no benefits from treatment of asymptomatic bacteriuria. In fact, with increased adverse events secondary to antimicrobials and potential facilitation of emergence of antimicrobial-resistant organisms, there are some negative outcomes following attempts at therapy.

![Table 4. Studies Reporting Treatment or Nontreatment of Asymptomatic Bacteriuria in Older People](http://gateway.ut.ovid.com/gw1/ovidweb.cgi?QS=SoKamkUxtxWX%2fgR%2fn0h1PXBZ... 8/12/2004)
asymptomatic bacteriuria in this population would require frequent screening for bacteriuria and repeated antimicrobial courses for a substantial proportion of institutionalized residents.

Remaining Questions

Although current evidence is compelling that antimicrobial treatment of asymptomatic bacteriuria is not indicated, urinary infection remains the most frequent reason for prescribing antibiotics in long-term care facilities. Much of this antimicrobial use is for symptomatic infection and reflects diagnostic uncertainty or use of coexisting pyuria as an indication for treatment. Thus, further exploration of this common problem is warranted. Specific issues include identification of subgroups within the bacteriuria older population at increased risk for adverse outcomes as well as efforts to measure the morbidity of asymptomatic infection or symptomatic episodes more precisely. In addition, a clearer measurement of the impact of antimicrobial therapy in promoting emergence of resistance within the infected urine is essential, given the current concerns with antimicrobial resistance emergence.

URINARY CATHETER INFECTIONS

Catheters are still used frequently in older patients and are often used inappropriately. Long-term catheterization results in bacteriuria, which may lead to symptomatic UTI and other complications.

Epidemiology

Urethral catheterization of the bladder causes bacteriuria to occur at the rate of 3 to 10% per day while the catheter is in place, and in older people, a single in-out catheterization may cause bacteriuria in as many as 20%. Because as many as 15 to 25% of acute care hospitalized adult patients undergo urinary catheterization, though usually for a short term, catheter-associated bacteriuria is the most common nosocomial infection. By 30 days, which is the conventional cutoff between short- and long-term catheterization, most patients are bacteriuria. It is estimated that at any given time, as many as 100,000 older nursing home patients have long-term indwelling urinary catheters.

Pathogenesis and Duration of Bacteriuria

Bacteria most frequently gain access to the urinary tract first through periurethral colonization usually with the patient's own colonic flora. Subsequent migration of periurethral microorganisms between the catheter and the uroepithelium into the bladder and potentially the upper urinary tract may then occur. Less commonly, external introduction of pathogens during catheterization or from breakdowns in the closed collection system (e.g., opening catheter/collecting tube connection or draining the bag) occurs. Furthermore, bacteria are capable of colonizing the intraluminal surface of the catheter and bag and can migrate against the urinary flow into the lower urinary tract.

Microbiology

Short-term catheterization (STC)-associated bacteriuria usually involves a single pathogen, most frequently \textit{E. coli}. Bacteriuria associated with long-term catheterization (LTC) is dynamic and typically polymicrobial, with original pathogens persisting or being replaced or coexisting with newer pathogens. LTC-associated bacteriuria usually contains two to five isolates with \textit{E. coli}, \textit{P. mirabilis}, \textit{K. pneumoniae}, \textit{Enterococcus}, \textit{Providencia stuartii}, and \textit{Morganella morgani} the common isolates. Many other bacterial species and yeasts have also been isolated.
Yeasts are typically associated with antibiotic use. Urease-producing strains of bacteria such as *P. mirabilis* cause high urine pH, which may lead to stone formation and catheter obstruction.64

Urine cultures obtained from the catheter lumen may contain more species than are actually present in the bladder, and some experts advise removing the catheter and replacing it with a new catheter before obtaining urine cultures.63

**Complications and Treatment of Bacteriuria**

Complications of STC and LTC other than asymptomatic bacteriuria include symptomatic infection (fever, acute pyelonephritis, bacteremia, sepsis, and death). Long-term catheterization is also associated with urethritis, nephrolithiasis, cystolithiasis, epididymitis, vesicourethral reflux, and newly recognized chronic pyelonephritis and chronic tubulo-interstitial nephritis with deformed calyces and parenchymal scarring.65 The incidence of symptomatic UTI in STC is not well established, but it may be as high as 10 to 30%. LTC causes approximately one febrile episode per 100 days of catheterization.57,65-67

**Treatment**

Current data do not support treatment of asymptomatic bacteriuria for either STC or LTC.57,58,68 Antibiotics may delay onset of bacteriuria in STC but do not reduce complications and may select resistant pathogens. Persistent bacteriuria after removal of the catheter may require antibiotic treatment.69

Symptomatic UTI following STC or LTC is treated with as narrow-spectrum agent as possible, based on culture and sensitivity results. The optimal duration of therapy is not well established and depends on severity of infection; however, it usually ranges from 5 to 14 days or longer. Empiric therapy for LTC symptomatic UTI should cover for possible polymicrobial flora. For routine cases in which it is unlikely that multi-drug resistant pathogens are present and where the patient is not critically ill, parenteral or oral trimethoprim-sulfamethoxazole or second-generation cephalosporin will generally be effective. However, for seriously ill patients or those who are septic, a two-drug combination of ampicillin plus a third-generation cephalosporin, aztreonam, an aminoglycoside, or a quinolone is recommended. The removal and replacement of the catheter is recommended by some experts as part of the therapy of symptomatic catheter-associated UTI.63

**Prevention of Bacteriuria and its Complications**

Every effort should be made to minimize the duration of catheterization and avoid long-term catheterization. It is also important to maintain the integrity of the closed urinary collection system and avoid breakdowns in sterile technique. There is little evidence that bladder irrigation, the placement of antibacterials in urine collection bags, silver-coated catheters, and use of methenamine reduce the incidence of bacteriuria. Ultimately, other experimental measures such as intra-urethral devices for urinary obstruction may hold promise for reducing bacteriuria and symptomatic UTI.57,58,68

Because there are no effective methods to reduce the incidence of bacteriuria from LTC, the best strategy is to avoid their use unless absolutely necessary. Ouslander and Schnelle have published strict criteria for the use of long-term indwelling bladder catheters based on an extensive review of the literature.70 Briefly, these criteria include (1) urinary retention that cannot be managed surgically or medically and condom and intermittent catheterization, which have lower complication rates, are not practical; (2) where incontinence is exacerbating wounds;
(3) care of terminally ill or severely impaired individuals where frequent changing of clothes or linen would be very uncomfortable; and (4) preference of patient who has not responded to specific incontinence treatments.

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