Urinary Tract Infection at the Age Extremes: Pediatrics and Geriatrics

Linda M. Dairiki Shortliffe, MD, Jack D. McCue, MD, FACP, AGSF

Urinary tract infections (UTIs) are common and generally benign conditions among healthy, sexually active young women without long-term medical sequelae. In contrast, UTIs are more complicated among those individuals at either end of the age spectrum: infants/young children and geriatrics. UTI in children younger than 2 years has been associated with significant morbidity and long-term medical consequences, necessitating an extensive and somewhat invasive imaging evaluation to identify possible underlying functional or anatomic abnormalities. Pediatric UTI should be considered complicated until proved otherwise, and treatment should reflect the severity of signs and symptoms. Management in the acutely ill child frequently involves parenteral broad-spectrum antimicrobial agents, and less ill children can be treated with trimethoprim-sulfamethoxazole (TMP-SMX), β-lactams, and cephalosporins.

UTI among older patients (>65 years) may be complicated by comorbidities, the baseline presence of asymptomatic bacteriuria, and benign urinary symptoms that can complicate diagnosis. The etiology of UTI encompasses a broader spectrum of infecting organisms than is seen among younger patients and includes more gram-positive organisms. Symptomatic UTI is generally more difficult to treat than among younger populations. Management should be conservative, of longer treatment durations, and cover a broad spectrum of possible uropathogens. Oral or parenteral treatment with a fluoroquinolone for 7 days is the preferred empiric approach. TMP-SMX can also be considered a first-line agent in women only, but only if the pathogen is known to be TMP-SMX sensitive. *Am J Med.* 2002;113(1A):55S–66S.

From the Department of Urology, Stanford University School of Medicine, Stanford, California, and the Department of Medicine, University of California, San Francisco, San Francisco, California, USA.

Requests for reprints should be addressed to Linda M. Dairiki Shortliffe, MD, Department of Urology, Stanford University School of Medicine, MC:5118, 300 Pasteur Drive, Room S287, Stanford, California 94305-5118.

Urinary tract infections (UTIs) are common and generally benign conditions among healthy, sexually active young women without long-term medical sequelae. In contrast, UTIs are more complicated among those at either end of the age spectrum: infants/young children and geriatrics. UTI in children younger than 2 years has been associated with significant morbidity and long-term medical consequences. In addition to appropriate antibacterial management, pediatric UTI necessitates an in-depth diagnostic process to identify possible underlying functional or anatomic abnormalities. Similarly, UTI among older patients (>65 years) may be complicated by comorbidities as well as the baseline presence of asymptomatic bacteriuria and benign urinary symptoms that can complicate diagnosis. In addition, great diversity in geriatric health and living arrangements, ranging from independent community dwelling to institutionalized or long-term care (LTC) settings, affects the etiology, diagnosis, and management of UTI within geriatric populations. In summary, the diagnosis and management of UTI among very young or very old persons represent a challenge to the practicing clinician.

PEDIATRIC PATIENTS

There are important differences in the clinical course, medical sequelae, and diagnostic and management approaches of UTIs between infants and pediatric patients and adults. Unlike the generally benign nature of UTI among young women, UTI in pediatric populations is associated with significantly greater morbidity and long-term consequences, such as impaired renal function, hypertension, end-stage renal disease, and complications of pregnancy as an adult. In children with risk factors, recurrent UTI (RUTI) may increase the progression of UTI to pyelonephritis and subsequent risk of renal scarring. Genitourinary abnormalities must be considered subsequent to a diagnosis of pediatric UTI, and accurate and early diagnosis and management of UTI can provide patients with an improved long-term prognosis.

Epidemiology, Pathogenesis, and Etiology

The difficulties inherent in determining the incidence and prevalence of UTI among adults impede the determination of the true incidence of UTI among pediatric populations. Nevertheless, UTI is believed to be one of the most common bacterial infections seen by clinicians who treat pediatric patients. It has been estimated that approximately 3% of prepubertal girls and 1% of prepuber-

tal boys are diagnosed with UTIs.[1] Recent estimates suggest up to 8% of prepubertal girls are affected by UTI.[2] It may be that UTI that occurs during the first 8 to 12 weeks of life more likely results from hematogenous seeding associated with bacteremia, whereas UTIs occurring after the third or later months of life reflect an ascending seeding after bacterial entrance through the urethra, the pathogenesis routinely associated with older children and adults. Similar to the predominance of Enterobacteriaceae infections in adults, Enterobacteriaceae are the most common pathogens isolated from uncomplicated pediatric UTI.

There are multiple risk factors for UTI in pediatric patients, including age, sex, periurethral or colonization factors, native immunity, genitourinary abnormalities, and genetic and iatrogenic factors[3,4] (**Table 1**). UTI is more prevalent among boys than girls younger than 1 year. However, at all other ages, even among the very elderly, UTI is far more prevalent among females than males.[1] Approximately 2.7% of boys experience UTI during the first year of life, which decreases to 0.03% to 1.2% during the school years. In contrast, the rate of UTI increases from 0.7 during the first 12 months to 1% to 3% during school years in girls.[1] However, there appears to be a slight decrease in UTI among girls 11 to 15 years of age, after which the rate increases again throughout the mid-20s.[5] Breastfeeding may confer some protection against pediatric UTI.[6]

Epidemiologic data demonstrate lower rates of UTI among circumcised male infants.[7,8] The periurethral bacterial flora of uncircumcised male infants (younger than 6 months) contain a greater quantity of both *Escherichia coli* and gram-negative uropathogens (*Klebsiella* and *Enterobacter* spp., *Proteus mirabilis*, and *Pseudomonas aeruginosa*) compared with circumcised boys through 12 months of age ($P < 0.003$).[7] Evidence suggests that this significantly greater bacterial colonization of the preputial skin in uncircumcised infants before age 6 months decreases over time and is uncommon after 5 years of age. As a result, uncircumcised boys have an overall 12-fold increased risk of urinary infection during their first 6 months compared with circumcised boys,[9] in addition to a significantly higher probability of hospital admission for UTI (7.02 of 1,000) as compared with circumcised boys (1.88 of 1,000; $P < 0.0001$).[10] These data suggest that cirumcision may confer some protection against UTI in male infants by decreasing periurethral bacterial colonization, but this appears to be lost after infancy. A case-control study of 144 boys under 5 years of age also demonstrated the protective effect of circumcision: among boys with microbiologically proven symptomatic UTI, 1.4% were circumcised versus 6.3% who were uncircumcised ($P = 0.02$).[8]

After an initial UTI, many children may have a recurrence, and most recurrences occur 3 to 6 months after the initial episode. The likelihood of recurrence appears to relate to age at initial infection. For instance, the rate of RUTI within the next few months in children who get an initial UTI before age 1 year is 18% for boys and 26% for girls, but recurrence more than a year afterward is rare in either group.[1] In contrast, if the initial infection occurred in a boy older than 1 year, 32% become reinfected. For girls, the risk of RUTI within the year after the last UTI is proportional to the number of previous infections; that is, the risk of getting a RUTI within 1 year is >25% with 1 previous UTI and >75% after 3 previous childhood UTIs.[1] There is some evidence that the organisms associated with these RUTI are dependent on previous antibiotic exposure and may differ somewhat from those causing the initial UTI, with *Klebsiella* spp., *Proteus* spp., and *Enterobacter* spp. more prevalent in pediatric RUTI or among children who receive antibiotic prophylaxis.[11]

Girls with RUTI who have such risk factors as vesicoureteral reflux (VUR) are at increased risk of pyelonephritis infections and subsequent risk of renal scarring[5] with progressive renal disease in adulthood[12] (**Table 2**). Long-term studies indicate generally that an initial childhood UTI does not increase the risk of hypertension for up to 2 decades,[13] nor does it impact renal function, despite unilateral renal scarring.[14] However, long-term follow-up of children with renal scarring subsequent to pyelonephritis suggests that even unilateral scarring can increase the risk of serious long-term complications, including a smaller renal mass, lower glomerular filtration rate, and possibly higher diastolic blood pressure.[15]

The rate of reflux among children diagnosed with bacteriuria varies from 20% to almost 60%.[16–19] There is a genetic component involved in VUR, such that 8% to

Table 1. Urinary Tract Infection in Pediatric Patients

- One of the most common infections
  - —3% prepubertal girls
  - —1% prepubertal boys
- Etiology: Enterobacteriaceae spp.
- Multiple risk factors
  - —Age, sex
    - Girls > boys
    - Risk decreases with age in boys, increases in girls
  - —Periurethral/colonization factors
  - —Native immunity
  - —Genitourinary abnormalities
  - —Genetic/iatrogenic factors

Table 2. Recurrent Urinary Tract Infection (RUTI) in Pediatric Girls

↑↑Risk renal scarring
↑↑Risk pyelonephritis
↑↑Risk progressive renal disease in adulthood
Risk of renal scarring: 60% with ≥5 RUTI

Table 3. American Academy of Pediatrics Urinary Tract Infections (UTI) Treatment Guidelines: Recommendations

1. A UTI should be suspected with unexplained fever among children aged 2 months to 2 years.
2. There is a need to assess the degree of toxicity, dehydration, and the ability to retain oral intake.
3. If the child is ill enough to warrant immediate presumptive antibiotic usage, a urine specimen should be obtained by suprapubic aspiration or catheterization—not a "bagged" specimen.
4. When the child is not judged ill enough for immediate presumptive antibacterial therapy for UTI, a urine specimen can be obtained by SPA or catheterization, or by the most convenient means for urinalysis.
5. Diagnosis of UTI requires urine culture.
6. If the child is "toxic," dehydrated, or unable to retain fluids, initial antibacterial therapy should be given parenterally and hospitalization should be considered.
7. If the child is not judged ill enough to need immediate presumptive antibacterial therapy and has a urinalysis suggesting or culture confirming UTI, antibiotic therapy should be started (parenteral or oral).
8. If there is no clinical response within 2 days of antibiotic therapy, another urine specimen should be cultured.
9. Children whose treatment was initially given parenterally should complete 7 to 14 days of treatment (oral + parenteral).
10. Children should receive antibiotics in therapeutic or prophylactic dosage until imaging studies are complete.
11. Children who do not have the expected clinical response within 2 days should have prompt RBUS and VCUG. Children who have the expected clinical response should have RBUS and VCUG (RNC) at the earliest convenient time. Boys must have a standard fluoroscopic VCUG.

RBUS = renal and bladder ultrasound; RNC = radionuclide cystography; SPA = suprapubic aspiration; VCUG = voiding cystourethrogram.

Adapted from *Pediatrics.*[26]

45% of children born to parents with VUR, and 32% to 35% of children who have a sibling diagnosed with VUR, will also have VUR.[20] The rate of VUR among children younger than 18 months with a familial history of VUR is as high as 50%. There appears to be a direct relation between the severity of reflux and the incidence of renal scarring.[21,22]

Symptoms of voiding dysfunction, specifically nocturnal and diurnal enuresis, are common in children with RUTI, even when the enuretic episodes are as infrequent as once a week.[23] For this reason, urine culture is important for the evaluation of these patients. Moreover, this study revealed that 7-year-old girls who had their initial UTI when they were 3 years or older were more likely to have associated voiding dysfunction than those who had their initial UTI before that age. Furthermore, almost 20% of children who had RUTI developed new diurnal enuresis that could last as long as 1 year even though the UTI was treated and the urine reverted to normal.

RUTI also appears to be associated with bowel dysfunction and constipation.[24,25] When children with incontinence and RUTI are examined, many have signs and symptoms of constipation even though they may deny such on questioning.

American Academy of Pediatrics Guidelines

A multidisciplinary Committee on Quality Improvement of the American Academy of Pediatrics developed an evidence-based, consensus-based practice parameter for the diagnosis, treatment, and evaluation of initial UTI in febrile infants and young children 2 months through 2 years of age. The 11 recommendations of the practice parameter cover 4 areas of concern for current practitioners and future research endeavors: identifying children at risk, diagnosing UTI, treating acute UTI, and evaluating children for possible urinary tract abnormalities[26] (**Table 3**). In this practice parameter all children aged 2 months to 2 years who present with unexplained fever were identified as the subpopulation of pediatric patients at greater risk for renal damage from UTI than older children, and it was therefore recommended that these children be targeted for UTI evaluation. Approximately 5% of infants develop UTI, and they frequently present with few localizing symptoms.

The diagnostic recommendations address the need to culture appropriately collected urine specimens. Urinalysis alone is not sufficient for a diagnosis of UTI in this age group; similarly, culture of specimens from urine-collection bags is not recommended. It is recommended

that a specimen should be obtained by either suprapubic aspiration or catheterization in all infants requiring immediate presumptive antibiotics. Suprapubic aspiration or catheterization is also the preferred means for specimen collection among children not requiring immediate treatment. Although a negative urinalysis does not rule out UTI, a normal urinalysis in circumcised boys reduces the likelihood of UTI to only 0.1%.[26]

Recommendations on UTI management focus on treatment that reflects the severity of signs and symptoms. Pediatric UTI should be considered complicated until proved otherwise. Infants with severe UTI who are "toxic," dehydrated, and unable to retain fluids require initial parenteral antibiotic therapy, frequently on an inpatient basis. Outpatient antibiotic parenteral or oral therapy is initiated among children who are not ill enough to necessitate hospitalization but who have a urinalysis suggesting, or a culture confirming, UTI. The total duration of antibiotic treatment (oral plus parenteral) is 7 to 14 days. Therapeutic or prophylactic doses of antibiotics should be continued until imaging studies have been completed. This minimizes the risk of reinfection and possible renal damage should the child be found to have risk factors.

When parenteral treatment is needed, antimicrobial selection should cover a broad spectrum of organisms. Most often this includes combinations of an aminoglycoside and amoxicillin or similarly based drug, or a third-generation cephalosporin with or without an aminoglycoside. For initial oral treatment, any number of antimicrobial agents that reach systemic levels may be selected until organism sensitivities are available and allow selection of the least expensive drug with the narrowest spectrum. Once initial treatment is complete, the child should be maintained on a prophylactic agent such as trimethoprim-sulfamethoxazole (TMP-SMX), nitrofurantoin, or sulfisoxazole at a once-daily low dose.

This parameter emphasizes the importance of imaging evaluation in children who have documented evidence of UTI. Infants who do not respond clinically to antibiotic therapy within the first 2 days require another urine specimen for culturing to rule out resistance, as well as immediate renal and bladder ultrasound and voiding cystourethrogram to investigate potential anatomic abnormalities. Infants who do respond to antibiotic therapy should have renal and bladder ultrasound and voiding cystourethrogram as soon as the urine is sterile and bladder irritability has disappeared.

Diagnosis. Accurate and prompt diagnosis of UTI among neonates, infants, and children is of the utmost importance. When combined with appropriate and prompt antibiotic treatment and close medical follow-up, early diagnosis can minimize the long-term sequelae otherwise associated with pediatric UTI. Because UTIs may be considered a marker for genitourinary abnormalities in children, imaging studies are indicated after an initial febrile pediatric UTI.

Diagnosis of UTI in pediatric patients requires a culture. However, results from a urinalysis that support a presumptive diagnosis of UTI can be the basis for the initiation of empiric therapy (**Table 4**). Urine cultures with multiple organisms or with colony counts $<$50,000 to 100,000 colony-forming units/mL are suspect and may require additional confirmation. Catheter specimens are significantly less likely to be associated with contaminated culture results (9.1%) than "clean voided" bag specimens (62.8%; $P < 0.001$).[27] Because some have reported that nearly 2% of "bagged" urine specimens result in such adverse clinical outcomes as delayed diagnosis and treatment, unnecessary treatment or radiologic investigation, and unnecessary hospital admissions, the benefits of using the more invasive catheter specimen far exceed collecting a "noninvasive bagged" specimen.

VUR encompasses a variety of underlying conditions that together represent the most common abnormality observed in infants and young children.[28] VUR may be nonobstructive with no other urinary tract abnormality, or it may present with bladder outlet obstruction, hydronephrosis, and intrauterine renal damage. VUR can also be associated with voiding dysfunction and frequent UTIs. Children with intrauterine renal damage are at greatest risk of developing hypertension and for progression to end-stage renal disease.[28] Congenital genitourinary abnormalities, as well as abnormalities that impair bladder emptying, including neurogenic bladder, dysfunctional voiding problems,VUR, and partial obstruction and hydronephrosis, all increase the potential consequences of UTI among children. Of those children with documented UTI, 5% to 10% of boys and 1% to 2% of girls through age 16 years may have obstructive lesions. Finally, although the role of renal cortical scintigraphy with ^{99m}Tc–dimercaptosuccinic acid scan for the management of acute UTI is controversial, it is the standard imaging study to detect renal scarring and acute pyelonephritis in children.

Management. There are numerous options for the empiric management of UTI among pediatric patients. Selection of the initial agent should be based on the clinical status of the patient and need for parenteral versus oral therapy, knowledge of the predominant pathogens for the patient's age group, antibacterial sensitivity patterns in the patient's community, and the opportunity for close follow-up (**Table 5**).

Management of UTI in the acutely ill child frequently involves parenteral broad-spectrum antimicrobial treatment, such as ampicillin, plus an aminoglycoside or a third-generation cephalosporin. Less ill children who can tolerate oral antibiotics are frequently treated with TMP-

SMX, the β-lactams (penicillins and cephalosporins), and nalidixic acid. Antibiotic treatment durations are generally 3 to 5 days for children with acute uncomplicated UTI and 10 to 14 days for the management of acute pyelonephritis. Clinical and basic studies have shown that larger cortical renal defects correlate with longer delay of treatment[29–32] and longer length and severity of infection.[33]

Currently, in the United States, the quinolones other than nalidixic acid are not approved for use in persons younger than 18 years of age even though these agents are important and commonly used in the treatment of adults with complicated UTI. Early studies suggested quinolone-induced cartilage toxicity in experimental juvenile animals, and this has limited the use of the fluoroquinolones in children to compassionate-use situations in which the benefits outweigh the risks. In reports from these limited trials, however, the fluoroquinolones were well tolerated and adverse events minimal.[34–36] Studies examining the safety and indications for the fluoroquinolones in children are under way.

Antimicrobial prophylaxis should be considered in young children with a documented UTI until full imaging evaluation can be obtained to exclude anatomic abnormalities in which RUTI might pose further risk to the kidney. For this reason, prophylaxis might be prudent in children with a history of documented UTI who are younger than 3 to 6 months with VUR, with partial obstruction, or on immunosuppressive therapy. Furthermore, it might be considered in children with frequent recurrent symptomatic UTI (≥2 in a 6-month period) without underlying anatomic abnormalities.[37,38]

Summary. The potential for long-term medical sequelae as a result of pediatric versus adult UTI necessitates a more extensive diagnostic imaging regimen with more extended clinical follow-up when risk factors are detected. Diagnosis of pediatric UTI requires a reliable urine culture (often by suprapubic aspiration or urethral catheterization), and evaluation requires imaging studies to identify potential anatomic or functional abnormalities. Prompt diagnosis and management can minimize long-term sequelae. As such, it is recommended that all children aged 2 months to 2 years with unexplained fever be managed with high suspicion for UTI. Those in whom UTI is diagnosed and other children with documented UTI should undergo imaging evaluation. Neonates and infants with UTI are at increased risk for development of pyelonephritis with subsequent complications of renal scarring, RUTI, and progression of renal injury when they have underlying anatomic or functional abnormalities, and they therefore deserve special attention. Treatment depends on the severity of the illness, with parenteral antimicrobial drugs often needed for severe infections and appropriate oral medications used for those children who can tolerate it. Minimizing host susceptibility factors when possible may be beneficial. Improvement of voiding problems and constipation may be helpful in some children. It should be remembered, however, that first UTIs diagnosed in young children should be considered complicated until proved otherwise.

Table 4. Diagnosis of Pediatric Urinary Tract Infection (UTI)

- Diagnosis requires culture
- Presumptive diagnosis with urinalysis to initiate empiric therapy
- Cultures with multiple organisms or <50,000–100,000 CFU/mL
  - —Considered suspect
  - —Require additional confirmation
- Specimen collected via suprapubic aspiration or catheterization
- Normal urinalysis in uncircumcised boys: rules out UTI
- Need for imaging studies

CFU = colony-forming unit.

Table 5. Therapeutic Management of Pediatric Urinary Tract Infection (UTI)

- Acutely ill
  - —Parenteral, broad-spectrum antimicrobial
    - Ampicillin + aminoglycoside
    - Third-generation cephalosporin
- Moderately ill
  - —Oral therapy
    - TMP-SMX
    - β-lactams
    - Nalidixic acid
- Duration of treatment
  - —Acute, uncomplicated UTI: 3–5 days
  - —Acute pyelonephritis: 10–14 days

TMP-SMX = trimethoprim-sulfamethoxazole.

GERIATRIC PATIENTS

The diagnosis and management of UTI among elderly persons can be particularly challenging to the clinician because of substantial differences between geriatric and otherwise healthy younger adults (**Table 6**). Geriatric patients with UTI frequently have an atypical clinical presentation, a higher prevalence of comorbidities, and an increased risk of drug–drug and disease–disease interactions. As such, the majority of presumably "uncomplicated" UTIs among the elderly would be characterized as "complicated" UTI in all other age groups.

In comparison to the relative homogeneity of UTI in pediatric populations or healthy adult populations, there is significant demographic and clinical diversity among the geriatric population with UTI. There is a wide range of living arrangements for the elderly: healthier patients

Table 6. Urinary Tract Infection (UTI) Bacteriuria in Younger Versus Older Patients

	Healthy Adults	Adults in Long-Term Care Facilities
Sex (Women:Men)	25:1	2–3:1
Etiology	Predominantly *Escherichia coli*	Wide variety gram-negative bacilli and enterococci
Clinical presentation	Lower UTI symptoms	Nonspecific symptoms Decline in function
Diagnostic approach	Leukocyte esterase sufficient; culture not necessary	Leukocyte esterase less reliable Urine culture necessary
Treatment	Short-course fluoroquinolone or TMP-SMX	Fluoroquinolone × 10 days for women 14–28 days for men
Outcome	Cure >90%–95%	Recurrences/failures common

TMP-SMX = trimethoprim-sulfamethoxazole.
Adapted from *Geriatrics.*[44]

generally reside independently in the community, debilitated patients often either live in a nursing home or require some type of permanent institutionalization.[39] Most of the research on UTI among the elderly has focused on the 5% of elderly patients who are institutionalized, overlooking the 95% of the elderly population (<65 years) who live independently in the community.[40]

Because of the prevalence of asymptomatic bacteriuria (ASB) among the elderly, diagnosis may be difficult. Unlike other age groups, a positive culture result does not confirm a diagnosis of UTI among elderly patients. A positive culture, with or without pyuria, may be ASB, a condition similar to colonization that does not ordinarily warrant or benefit from treatment. The diagnosis of UTI, rather than ASB, depends on the judgment of the clinician that signs or symptoms of infection are present. The benefit of treatment for ASB among the elderly is highly doubtful.

The etiology of UTI among geriatric patients differs from that of younger adults. It includes a broad range of gram-negative and gram-positive organisms. In addition, elderly patients may have polymicrobial infections, often necessitating broad-spectrum antibiotic agents for longer treatment durations for optimal treatment. Comorbidities common to the elderly, such as neurologic, hepatic, and cardiac conditions, can complicate and confuse the diagnosis and treatment of UTI. Finally, UTI among geriatric patients is more likely to cause infectious complications, such as bacteremia, and noninfectious complications, such as stroke or dehydration.

Epidemiology

Epidemiologic data regarding UTI among the elderly have focused predominantly on institutionalized patients rather than noninstitutionalized community-dwelling persons.[40] Early studies had small sample sizes and did not clearly define the demographics or disease states of the sample. In addition, the definition of "elderly" has aged with the aging of the US population and improvements in the general health of older US citizens.

Recent studies have nevertheless begun to address the epidemiology of UTI among the noninstitutionalized elderly. Genitourinary tract infections are the second most common form of infection, following respiratory tract infections, among otherwise healthy noninstitutionalized elderly persons[40–43] (**Table 7**).

A 24-month prospective study of 417 elderly (>65 years) noninstitutionalized persons found genitourinary infections accounted for 24% of all identified infections.[40] UTI or ASB was more common among people aged 65 to 74 years than among those >74 years. The risk of infection was independently associated with difficulty controlling urination and, curiously, a history of lung problems.

The high frequency of UTI is related, in part, to the increasing prevalence of incontinence among older women (33% to 50%).[41] Incontinence was the only independent predictor for infection among persons with multiple infections in 1 study.[40] Similarly, a longitudinal cohort study of elderly women in Sweden found that 61% of the random sample of 6,000 women had reported treatment for at least 1 UTI between 1986 and 1995; many women had received treatment for numerous UTIs.[41] A history of UTI significantly increased the risk of subsequent UTI ($P < 0.001$) and was also associated with an elevated risk of mortality versus age-matched controls ($P < 0.001$).

The majority of institutionalized geriatric patients are women, who are at greater risk of UTI (**Table 8**). The institutionalized elderly are more likely to have indwelling catheters, urologic anatomic or functional abnormalities, or other comorbidities that impact on UTI than their independent counterparts. They are also at greater risk for infection with nosocomial pathogens. Persons residing in LTC settings are most likely to have noncatheter

Table 7. Geriatric Urinary Tract Infection (UTI)

- Second most common infection (after RTI) (25% infections)
- Atypical presentations
- ↑↑Prevalence incontinence in older women
- ↑↑Rate comorbidities
- ↑↑Risk drug-drug interactions
- ↑↑Mortality with history of UTI
- "Uncomplicated" infections more likely to be "complicated"

RTI = respiratory tract infection.

Table 8. Institutionalized Elderly and Urinary Tract Infection

- Greater prevalence of women
- Greater prevalence of
  - —Indwelling catheters
  - —Urologic anatomic/functional abnormalities
  - —Comorbidities
- ↑↑Risk nosocomial infections
- ↑↑Risk catheter-associated UTI
- ↑↑Risk noncatheterized ASB

ASB = asymptomatic bacteriuria.

RUTIs, catheter-associated infections, or non–catheter-related asymptomatic bacteriuria.[44] In addition, LTC patients are at elevated risk for bacteremia and other septic complications associated with UTI.

ASB is a common and generally benign condition in this population, affecting up to 50% of women[42,45] and 30% of men, and increases in frequency with age and debility. Comorbid conditions that cause neurogenic bladder and incontinence increase the frequency of ASB.[46] It may be difficult for the clinician to distinguish ASB accurately from symptomatic infection.[45] Because most studies of ASB in LTC settings have documented a prevalence of up to 50% positive urine cultures, the chance that a febrile patient will have a positive urine culture is 1:2 to 1:3, regardless of the actual etiology of fever.

Hence, at least 33% to 50% of elderly patients with pneumonia will also have a positive urine culture that is unrelated to the cause of their fever. Indeed, a careful prospective study of nursing home patients with fever concluded that in only 10% of patients could the fever be attributed to UTI.[45] A majority of these patients had a positive urine culture because of underlying ASB. If the clinical assessment had stopped with a urinalysis and culture, serious causes of fever, such as pneumonia or abdominal sepsis, would have been missed.

Diagnosis and Clinical Course

The diagnosis of UTI among the elderly is often a diagnosis of exclusion. Older patients frequently present with atypical nonurinary symptoms, and many common urinary symptoms, such as frequent urination and incontinence, are already present in the older patient (**Table 9**). Nonurinary symptoms, including delirium, are most likely to be seen among patients with other medical problems (dehydration or multiple chronic diseases). As a result, clinicians must first often rule out other serious illnesses, such as pneumonia, acute myocardial infarction, and dehydration, before they can confidently diagnose UTI.

Table 9. Diagnosis of Urinary Tract Infection (UTI) in the Elderly

- Atypical presentations (including delirium)
- Pyuria not accurate predictor of bacteriuria
- Absence of pyuria: not a very good predictor of absence of bacteriuria
- Dipstick testing
  - —More useful in ruling out UTI than predicting UTI
  - —1 in 3 specimens from elderly "contaminated"

Table 10. Etiology and Pathogenesis of Urinary Tract Infection in the Elderly

- Broader spectrum uropathogens
  - —↑↑Gram-positive organisms
  - —*Escherichia coli* <50% isolates
- 1 in 3 infections: polymicrobial
- Antibiotic-selective pressure and high rates of resistance

In comparison to younger adult patients, pyuria is not an accurate predictor of bacteriuria among the elderly.[47–49] The absence of pyuria, moreover, is not a very good predictor for the absence of bacteriuria. In a study of chronically incontinent nursing home residents, 45% of patients had pyuria, and 43% had (presumably) asymptomatic bacteriuria; 34% of the residents had pyuria without bacteriuria.[48] An earlier study of elderly ambulatory women found pyuria without bacteriuria present in 52% of subjects.[47] High-titer bacteriuria, however, was almost always (94%) associated with pyuria.

There are differences in the sensitivity and specificity of leukocyte esterase tests among nursing home residents and office patients. In both cases, dipstick testing is far more useful in ruling out than in predicting UTI.[39] As is seen with pediatric patients, obtaining a proper midstream or clean-catch urine specimen can be difficult, particularly among the infirm elderly. In fact, almost 1 in 3 specimens taken from the elderly are "contaminated."[39] Suprapubic aspiration or in/out catheterization is usually indicated for a definitive evaluation.

Etiology and Pathogenesis

The etiology of UTI or ASB among geriatric patients encompasses a broader spectrum of infecting organisms than is seen among younger patients[39] and includes more gram-positive organisms (**Table 10**). Whereas *E coli* is the predominant pathogen isolated from among younger

sexually active women with acute cystitis, *E coli* accounts for <50% of isolates in the elderly. *Staphylococcus aureus* may be seen in older men, but *Staphylococcus saprophyticus* UTI in the elderly is rare. Enterococci are uncommon uropathogens in the elderly but usually represent colonization that resolves without treatment. Polymicrobial infections are also relatively common, affecting up to 1 in 3 geriatric patients with UTI. A recent microbiologic survey of LTC facilities found high rates of antibiotic resistance.[50] *E coli* organisms isolated in the elderly are more likely to be resistant to such traditional therapies as TMP-SMX because of both intrinsic resistance of the infecting species and selection of more resistant strains by frequent use of antibiotics in this population.

The pathogenesis of UTI in the elderly also varies according to living arrangements. Elderly patients residing independently in the community tend to have a pathogenesis similar to that of their younger cohorts. However, "meaningful contact," including touching or contact that facilitates communication of antibiotic resistant pathogens, between residents in LTC facilities is common (30% of patients each day) and has a significant impact on the pathogenesis of UTI in LTC settings.

Functional and anatomic predispositions associated with UTI are commonly observed in elderly patients (**Table 11**). Changes in prostatic function in men, as well as an increased risk of obstructive uropathy in both men and women, may increase susceptibility to UTI. Anatomic changes related to childbearing and/or reproductive surgery, as well as mucosal and smooth muscle changes related to postmenopausal estrogen deficiency with resultant changes in the vaginal flora, can predispose the postmenopausal woman to UTI.[51] Similarly, postmenopausal women with urinary incontinence, cystocele, postvoiding residual urine, or a history of premenopausal UTI are at increased risk of RUTI.[52]

Neurologic and other chronic diseases that cause incontinence and debility increase the risk of UTI. For example, Alzheimer disease is associated with incontinence, often a form of neurologic dysmotility syndrome, that can predispose to UTI and AB. Similarly, such drugs as antibiotics, anticholinergics, and psychotropics may have a negative effect on bladder function. Complications from UTI are more likely among the elderly, ranging from bacteremia and abscess to such noninfectious effects as dehydration, stroke, or functional losses.

Table 11. Functional and Anatomic Predispositions to Urinary Tract Infection (UTI) in the Elderly

- Men
  - —Changes in prostatic function
  - —Increased risk of obstructive uropathy
- Women
  - —Childbearing and reproductive surgeries
  - —Mucosal/smooth muscle changes from menopause
  - —Changes in vaginal flora
  - —Urinary incontinence
  - —Cystocele
  - —Postvoiding residual urine
  - —History of premenopausal UTI
- Both: Alzheimer disease and other neurologic disorders

Table 12. Management of Urinary Tract Infection (UTI) in the Elderly

- General approach
  - —Conservative
  - —Longer treatment durations
    - 10 days in women
    - 14–28 days in men
  - —Cover broad spectrum of uropathogens
- Antibiotic choice
  - —Fluoroquinolones
  - —TMP-SMX in women only (if sensitive)

TMP-SMX = trimethoprim-sulfamethoxazole.

Management

Cure of symptomatic UTI in the elderly is more difficult than among younger populations. As such, it is recommended that management should be conservative, of longer treatment durations (10 days in women and a minimum of 14 days in men),[53–55] and cover a broad spectrum of possible uropathogens (**Table 12**). Treatment with a fluoroquinolone (oral or initially parenteral) is the preferred empiric approach to UTI. TMP-SMX can also be considered a first-line agent in women only, but only if the pathogen is known to be TMP-SMX sensitive. Fluoroquinolones have superior penetration into the prostate gland, and therefore are always the preferred treatment for UTI in older men. Antimicrobial resistance rates are greater in the elderly than among younger cohorts, particularly among elderly patients residing in LTC facilities, as a result of antibiotic-selective pressure for resistance among patients frequently treated with antibiotics or exposed to individuals frequently treated with antibiotics.[50]

Fluoroquinolones are the first-line class of agent for the management of UTI in the elderly, and selection of the most appropriate fluoroquinolone is especially important for this population (**Table 13**). There are differences in the spectrum of antimicrobial coverage and side-effect profiles of the 7 fluoroquinolones that are indicated for the management of UTI.[56–62] Levofloxacin and gatifloxacin provide the broadest spectrum of activity, including gram-positive and gram-negative pathogens as well as numerous atypical pathogens. However, gatifloxacin has been associated with prolongation of the QTc interval and may therefore not be appropriate for elderly patients with cardiac comorbidities. In addition, recent post-marketing surveillance data on gatifloxacin

Table 13. Fluoroquinolone Selection in Geriatric Urinary Tract Infection (UTI)

	Broadest Coverage	Drug Interactions (theophylline, methylxanthines, cyclosporins)	Prolongs QTc Interval	Neurologic Effects	Phototoxic Effects
Ciprofloxacin		✓			
Enoxacin		✓		✓	
Gatifloxacin	✓		✓		
Levofloxacin	✓				
Lomefloxacin		✓		✓	✓
Norfloxacin		✓		✓	
Ofloxacin				✓	

have also reported serious disturbances of glucose homeostasis. These events were of particular concern for very elderly patients (>75 years of age). (Please see article by Dr. Schaeffer [page 49S] for revised gatifloxacin labeling information.) Four antibiotics, ciprofloxacin, enoxacin, lomefloxacin, and norfloxacin, can potentially interact with theophylline, methylxanthines, such as caffeine, and cyclosporine. There may be an increased risk of neurologic effects, including seizures, convulsions, and hallucinations, with use of ofloxacin, norfloxacin, enoxacin, and lomefloxacin. Lomefloxacin is also associated with an increased risk of phototoxicity. The decreased renal function associated with natural aging may result in slower drug elimination among elderly patients. Hence, elderly patients with renal impairment may require dosing adjustments.

Currently, levofloxacin and ciprofloxacin are among the most widely used and methodically studied fluoroquinolones, and each has demonstrated a consistently high safety profile covering more than a decade of use. The potential for drug interactions associated with ciprofloxacin, however, may limit its use among some elderly patients.

A recent study compared the efficacy of ciprofloxacin with TMP-SMX among elderly patients.[63] The activity of ciprofloxacin against uropathogens was much higher (96%) than that of TMP-SMX (87%). Furthermore, the increased rate of resistance had important clinical ramifications: the success rate with TMP-SMX was only 84%, with a 33% failure rate among patients receiving TMP-SMX with TMP-SMX–resistant organisms. In addition, TMP-SMX is associated with higher side-effect and discontinuation rates in the elderly than the fluoroquinolones (2% of patients receiving ciprofloxacin discontinued vs. 11% of patients receiving TMP-SMX) because of allergic reactions with TMP-SMX.

Short-course therapy should not be used in the elderly. Earlier research found that a 3-day course of oral antibiotics with cefadroxil, TMP-SMX, or norfloxacin cleared bacteriuria in 70% of patients at 1 week.[53] However, only 25% of the patients remained infection free at 6 months. Both TMP-SMX and norfloxacin were more effective than cefadroxil.

All oral β-lactams and nitrofurantoin are second-choice agents. Although nitrofurantoin is not approved by the US Food and Drug Administration for complicated UTI because of its high failure rate in acute infections, macrocrystalline nitrofurantoin 50 mg at bedtime may be a safe and effective option for the prophylaxis of RUTI among elderly women.[64] The use of topical estrogen therapy among postmenopausal women with RUTI has been shown to reduce the frequency of UTI by >50% and should always be tried.[51,65] The benefits of systemic estrogen therapy are, as yet, unclear but probably are less effective than topical estrogens.[66]

Finally, despite the high prevalence of asymptomatic bacteriuria among the elderly, it is not a condition requiring antibiotic therapy. Paradoxically, 33% of antibiotic prescriptions for elderly patients living in LTC settings for a urinary indication were for ASB.[67] Although treating ASB may prevent a few UTIs, unnecessary use of antibiotics increases the risk of resistant pathogens.[43] Cost–benefit analyses have consistently concluded that antibiotic treatment of ASB probably does more harm than good.

Summary

Despite a high prevalence of UTIs, and particularly asymptomatic bacteriuria, among elderly persons living independently in the community as well as in LTC settings, numerous questions remain regarding their diagnosis and management. Of particular importance is the lack of information regarding UTI in the independent elderly patient; a majority of the research on geriatric UTI has focused on the 5% of elderly persons residing in LTC settings and not the 95% of healthier older patients.

Among the confounding variables that affect the diagnosis and management of UTI among the elderly are comorbidities, risk of drug–drug interactions, and the frequent presence of non–disease-related urinary symptoms in this population.

Empiric management in the elderly should be a sys-

temic fluoroquinolone for 10 days for women and 14 to 28 days for men. Selection of the most appropriate fluoroquinolone must consider the spectrum of activity as well as side-effect profile. Underlying heart, liver, or renal dysfunction may limit the selection. In contrast to ciprofloxacin, levofloxacin has no drug interactions and can be used in patients with these comorbidities. An inexpensive alternative option for women is TMP-SMX, but only if susceptibility is known in advance.

The need for additional research on UTI among the elderly is imperative. There are currently very few studies determining the appropriate dosing and course duration for antimicrobial therapy. Little is known regarding any possible interaction between AB and symptomatic UTI or between the route of administration of estrogen and potential for UTI. Finally, additional research is needed to determine the meaning of asymptomatic pyuria among the elderly.

CONCLUSION

UTIs are common across all ages and are consistently more prevalent among females than males across almost all generations. The greatest incidence of acute, community-acquired uncomplicated UTI is found among young sexually active women. Such infections are benign conditions with no long-term medical sequelae. In comparison, UTIs that occur in the very young patient can have significant and severe long-term ramifications, including renal scarring and end-stage renal disease. As such, the American Academy of Pediatrics recommends that UTI be suspected in any infant aged 2 months to 2 years presenting with unexplained fever and that comprehensive diagnostic testing, including culture and imaging studies, promptly be performed. Treatment of UTI and underlying physical or functional conditions can provide the infant with an enhanced prognosis. Antibiotic management is TMP-SMX in those geographic regions with known low resistance ($<$10% to 20%). Alternatives include the β-lactams and nalidixic acid.

The diagnosis of UTI among geriatric patients is more difficult than in younger persons, because many elderly patients have a greater prevalence of baseline urinary symptoms. The high prevalence of comorbidities, asymptomatic pyuria, and asymptomatic bacteriuria in this population reduces the efficacy of diagnostic testing and interpretations. Up to 50% of elderly patients have asymptomatic bacteriuria and would therefore not benefit from antimicrobial management. Symptomatic UTI among the elderly requires antibiotic treatment for at least 10 days for women and 14 to 28 days for men. Fluoroquinolones are the preferred agents. Selection of the most appropriate fluoroquinolone must consider comorbidities and concomitant drug use. Of the 7 agents with an indication for UTI, levofloxacin and gatifloxacin cover the broadest spectrum of uropathogens and have minimal drug–drug interactions. Gatifloxacin prolongs the QTc interval. Ciprofloxacin has a greater number of drug interactions than levofloxacin and must be administered twice daily.

Ultimately, UTI in the very young or very old patient can be particularly challenging to the practicing clinician. Accurate diagnosis, including appropriate imaging studies and identification of the causative pathogen, is often of the utmost importance. Treatment must integrate underlying host factors, local susceptibility trends, and potential for adverse effects and drug–drug interactions.

REFERENCES

1. Winberg J, Bergstron T, Jacobsson B. Morbidity, age and sex distribution, recurrences and renal scarring in symptomatic urinary tract infection in childhood. *Kidney Int Suppl*. 1975;4(suppl):S101–S106.
2. Stark H. Urinary tract infections in girls: the cost-effectiveness of currently recommended investigative routines. *Pediatr Nephrol*. 1997;11:174–177.
3. Shortliffe LD. Urinary tract infections in infants and children. In: Walsh P, Retik AB, Vaughn ED, Wein AJ. *Campbell's Urology*, vol. 2, 7th ed. Philadelphia: WB Saunders, 1997: 1681–1707.
4. Shortliffe LD. Urinary tract infections in infants and children. In: Walsh P, Retik A, Vaughan E, Wein A. *Campbell's Urology*, vol. 2. Philadelphia: WB Saunders, 2001. 7th ed.
5. Martinell J, Claesson I, Lidin-Janson G, Jodal U. Urinary infection, reflux and renal scarring in females continuously followed for 13–38 years. *Pediatr Nephrol*. 1995;9: 131–136.
6. Pisacane A, Graziano L, Mazzarella G, et al. Breast-feeding and urinary tract infection. *J Pediatr*. 1992;120:87–89.
7. Wiswell TE, Miller GM, Gelston HM Jr, et al. Effect of circumcision status on periurethral bacterial flora during the first year of life. *J Pediatr*. 1988;113:442–446.
8. Craig JC, Knight JF, Sureshkumar P, et al. Effect of circumcision on incidence of urinary tract infection in preschool boys. *J Pediatr*. 1996;128:23–27.
9. Wiswell TE, Hachey WE. Urinary tract infections and the uncircumcised state: an update. *Clin Pediatr (Phila)*. 1993; 32:130–134.
10. To T, Agha M, Dick PT, Feldman W. Cohort study on circumcision of newborn boys and subsequent risk of urinary-tract infection. *Lancet*. 1998;352:1813–1816.
11. Mangiarotti P, Pizzini C, Fanos V. Antibiotic prophylaxis in children with relapsing urinary tract infections: review. *J Chemother*. 2000;12:115–123.
12. Wennerstrom M, Hansson S, Jodal U, Stokland E. Primary and acquired renal scarring in boys and girls with urinary tract infection. *J Pediatr*. 2000;136:2–4.
13. Wennerstrom M, Hansson S, Hedner T, et al. Ambulatory blood pressure 16–26 years after the first urinary tract infection in childhood. *J Hypertens*. 2000;18:485–491.
14. Wennerstrom M, Hansson S, Jodal U, et al. Renal function 16 to 26 years after the first urinary tract infection in childhood. *Arch Pediatr Adolesc Med*. 2000;154:339–345.
15. Jacobson SH, Eklof O, Lins LE, et al. Long-term prognosis of post-infectious renal scarring in relation to radiological findings in childhood—a 27-year follow-up. *Pediatr Nephrol*. 1992;6:19–24.

16. Abbott GD. Neonatal bacteriuria: a prospective study in 1460 infants. *BMJ*. 1972;1:267–269.
17. Kunin CM, Deutscher R, et al. Urinary tract infection in school children: an epidemiologic, clinical and laboratory study. *Medicine*. 1964;43:91–130.
18. Asscher AW, McLachlan MSF, Jones RV, et al. Screening for asymptomatic urinary-tract infection in schoolgirls. *Lancet*. 1973;2:1–4.
19. Newcastle Asymptomatic Bacteriuria Research Group. Asymptomatic bacteriuria in schoolchildren in Newcastle upon Tyne. *Arch Dis Child*. 1975;50:90–102.
20. Noe H. The long-term results of prospective sibling reflux screening. *J Urol*. 1992;148:1739–1742.
21. Govan DE. The current status of vesicoureteral reflux: a review. *Monogr Urol*. 1984;5:155–173.
22. Govan DE, Fair WR, Friedland GW, Filly RA. Management of children with urinary tract infections, the Stanford experience. *Urology*. 1975;6:273–286.
23. Hanson S. Urinary incontinence in children and associated problems. *Scand J Urol Nephrol*. 1992;141(suppl):47–55.
24. O'Regan SS, Yazbeck S, Schick E. Constipation, bladder instability, urinary tract infection syndrome. *Clin Nephrol*. 1985;23:152–154.
25. Loening-Baucke V. Urinary incontinence and urinary tract infection and their resolution with treatment of chronic constipation of childhood. *Pediatrics*. 1997;100: 228–232.
26. American Academy Pediatrics, Committee on Quality Improvement, et al. Practice parameter: the diagnosis, treatment, and evaluation of the initial urinary tract infection in febrile infants and young children. *Pediatrics*. 1999;103: 843–852.
27. Al-Orifi F, McGillivray D, Tange S, Kramer MS. Urine culture from bag specimens in young children: are the risks too high? *J Pediatr*. 2000;137:221–226.
28. Hellerstein S. The long-term consequences of urinary tract infections: a historic and contemporary perspective. *Pediatr Ann*. 1999;28:695–699.
29. Glauser MP, Lyons JM, Brauder AI. Prevention of chronic experimental pyelonephritis by suppression of acute suppuration. *J Clin Invest*. 1978;61:403–407.
30. Miller T, Phillips S. Pyelonephritis: the relationship between infection, renal scarring, and antimicrobial therapy. *Kidney Int*. 1981;19:654–662.
31. Shimamura T. Mechanisms of renal tissue destruction in an experimental acute pyelonephritis. *Exp Mol Pathol*. 1981; 34:34–42.
32. Slotki IN, Asscher AW. Prevention of scarring in experimental pyelonephritis in the rat by early antibiotic therapy. *Nephron*. 1982;30:262–268.
33. Jakobsson BL, Nolstedt L, Svensson L, et al. ^{99m}Technetium-dimercaptosuccinic acid scan in the diagnosis of acute pyelonephritis in children: relation to clinical and radiological findings. *Pediatr Nephrol*. 1992;6:328–334.
34. Freifeld A, Pizzo P. Use of fluoroquinolones for empirical management of febrile neutropenia in pediatric cancer patients. *Pediatr Infect Dis J*. 1997;16:140–145.
35. Hampel B, Hullmann R, Schmidl H, et al. Ciprofloxacin in pediatrics: worldwide clinical experience based on compassionate use—safety report [review]. *Pediatr Infect Dis J*. 1997;16:127–129.
36. Warren R. Rheumatologic aspects of pediatric cystic fibrosis patients treated with fluoroquinolones [review]. *Pediatr Infect Dis J*. 1997;16:118–122.
37. Lindert K, Shortliffe L. Evaluation and management of pediatric urinary tract infections. *Urol Clin North Am*. 1999;26: 719–728.
38. Shortliffe LD. The management of urinary tract infections in children without urinary tract abnormalities. *Urol Clin North Am*. 1995;22:67–74.
39. Hamilton-Miller JMT. Issues in urinary tract infections in the elderly. *World J Urol*. 1999;17:396–401.
40. Ruben FL, Dearwater ST, Norden CW. Clinical infections in the noninstitutionalized geriatric age group: methods utilized and incidence of infections. *Am J Epidemiol*. 1995; 141:145–157.
41. Molander U, Arvidsson L, Milsom I, Sandberg T. A longitudinal cohort study of elderly women with urinary tract infections. *Maturitas*. 2000;34:127–131.
42. Monane M, Gurwitz JH, Lipsitz LA, et al. Epidemiologic and diagnostic aspects of bacteriuria: a longitudinal study in older women. *J Am Geriatr Soc*. 1995;43:618–622.
43. Nicolle LE. Urinary tract infection in the elderly. *J Antimicrob Chemother*. 1994;33:99–109.
44. McCue JD. Complicated UTI. Effective treatment in the long-term care setting. *Geriatrics*. 2000;55:48–61.
45. Nicolle LE. Urinary infections in the elderly: symptomatic or asymptomatic? *Int J Antimicrob Agents*. 1999;11:265–268.
46. Nicolle LE. Urinary tract infection in long-term-care facility residents. *Clin Infect Dis*. 2000;31:757–761.
47. Boscia JA, Abrutyn E, Levison ME, Pitsakis PG, Kaye D. Pyuria and asymptomatic bacteriuria in elderly ambulatory women. *Ann Intern Med*. 1989;110:404–405.
48. Ouslander JG, Schapira M, Schnelle JF, Fingold S. Pyuria among chronically incontinent but otherwise asymptomatic nursing home residents. *J Am Geriatr Soc*. 1996;44:420–423.
49. Kunin CM. Urinary tract infections in females. *Clin Infect Dis*. 1994;18:1–12.
50. Smith PW, Seip CW, Schaefer SC, Bell-Dixon C. Microbiologic survey of long-term care facilities. *Am J Infect Control*. 2000;28:8–13.
51. Raz R, Stamm WE. A controlled trial of intravaginal estradiol in postmenopausal women with recurrent urinary tract infections. *N Engl J Med*. 1993;329:753–756.
52. Raz R, Gennesin Y, Wasser J, et al. Recurrent urinary tract infections in postmenopausal women. *Clin Infect Dis*. 2000; 30:152–156.
53. Tzias V, Dontas AS, Petrikkos G, et al. Three-day antibiotic therapy in bacteriuria of old age. *J Antimicrob Chemother*. 1990;26:705–711.
54. Norrby SR. Short-term treatment of uncomplicated lower urinary tract infections in women. *Rev Infect Dis*. 1990;12: 458–467.
55. Flanagan PG, Rooney PJ, Davies EA, Stout RW. A comparison of single-dose versus conventional dose antibiotic treatment of bacteriuria in elderly women. *Age Ageing*. 1991;20:206–211.
56. Ciprofloxacin package insert. West Haven, CT: Bayer Corporation, 2001.
57. Enoxacin package insert. Bridgewater, NJ: Aventis Pharmaceuticals, 2001.
58. Gatifloxacin package insert. Princeton, NJ: Bristol-Myers Squibb, 2001.
59. Levofloxacin package insert. Raritan, NJ: Ortho-McNeil Pharmaceutical Inc., 2001.
60. Lomefloxacin package insert. Deerfield, IL: Unimed Pharmaceuticals, 2001.
61. Norfloxacin package insert. West Point, PA: Merck & Company, 2001.

62. Ofloxacin package insert. Raritan, NJ: Ortho-McNeil Pharmaceutical Inc., 2001.
63. Gomolin IH, Siami PF, Reuning-Scherer J, Haverstock DC, Heyd A. Efficacy and safety of ciprofloxacin oral suspension versus trimethoprim-sulfamethoxazole oral suspension for treatment of older women with acute urinary tract infection. *J Am Geriatr Soc*. 2001;49:1606–1613.
64. Brumfitte W, Hamilton-Miller JM. Efficacy and safety profile of long-term nitrofurantoin in urinary infections: 18 years' experience. *J Antimicrob Chemother*. 1998;42:363–371.
65. Eriksen B. A randomized, open, parallel-group study on the preventive effect of an estradiol-releasing vaginal ring (Estring) on recurrent urinary tract infections in postmenopausal women. *Am J Obstet Gynecol*. 1999;180:1072–1079.
66. Cardozo L, Benness C, Abbott D. Low dose oestrogen prophylaxis for recurrent urinary tract infections in elderly women. *Br J Obstet Gynaecol*. 1998;105:403–407.
67. Loeb M, Simor AE, Landry L, et al. Antibiotic use in Ontario facilities that provide chronic care. *J Gen Intern Med*. 2001; 16:376–383.