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URINARY TRACT INFECTIONS (JACK D. SOBEL, SECTION EDITOR)

Update in Adult Urinary Tract Infection

Lindsay E. Nicolle

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Abstract Urinary tract infection remains a common problem for many populations. Recent studies have expanded our understanding of the host innate immune response and its role in the familial association observed for recurrent uncomplicated urinary tract infection in healthy women. Therapeutic management for uncomplicated infection has been compromised by increasing antimicrobial resistance, particularly global dissemination of the CTXM-15 extended spectrum β-lactamase (ESBL) producing *Escherichia coli* ST-131 strain. Prevention strategies exploring non-antimicrobial approaches continue to show limited promise, and approaches to limit empiric antimicrobials are now being explored. For complicated urinary tract infection, increasing antimicrobial resistance limits therapeutic options for many patients. In addition to ESBL producing *E. coli*, NDM-1 *E. coli* and *Klebsiella pneumoniae* and other resistant Gram negatives, such as Acinetobacter species, are being isolated more frequently. There has been renewed interest in catheter-acquired urinary tract infection, the most common health–care associated infection, with several recent evidence-based guidelines for infection prevention available. However, technologic progress in development of adherence-resistant catheter materials remains disappointing.

Keywords Urinary tract infection · Uncomplicated · Complicated · Antimicrobial resistance · Antimicrobial therapy · Pyelonephritis · Catheter-acquired

L. E. Nicolle (✉)
Department of Internal Medicine and Medical Microbiology,
University of Manitoba, Health Sciences Centre,
Room GG443–820 Sherbrook Street,
Winnipeg, MB R3A 1R9, Canada
e-mail: lnicolle@hsc.mb.ca

Introduction

Urinary tract infection is the most common bacterial illness occurring in adults. The clinical presentation varies from asymptomatic bacteriuria or trivial voiding irritation to life-threatening septic shock. Acute uncomplicated urinary infection (acute cystitis) occurs in healthy women, while complicated urinary infection occurs in men or women with underlying functional or structural genitourinary abnormalities. Asymptomatic bacteriuria is common in all populations who experience symptomatic urinary infection, but is of clinical significance only for pregnant women or individuals who undergo invasive genitourinary procedures while bacteriuric. Prostatitis, a presentation of urinary infection in men, will not be discussed here.

Acute Uncomplicated Urinary Infection

Pathogenesis: Host Factors

From 2% to 5% of healthy women experience recurrent acute uncomplicated urinary tract infection at some time during their lifetime. Risk factors for recurrent infection are both genetic and behavioral. The important behavioral determinants promoting infection in premenopausal women are sexual intercourse and spermicide use for birth control. The strong familial association observed in women with recurrent infection supports a genetic propensity and was documented again by Scholes et al. [1•] in a cohort of 1261 women aged 18 to 49 years enrolled in a northwestern United States health plan. For 71% of 431 women with recurrent cystitis, 75% of 400 with pyelonephritis, and 42% of 430 controls, one or more first degree female relatives were reported to have a history of urinary tract infection.

The odds ratios for recurrent infection with one first degree female relative affected were 3.1 (95% confidence intervals [CI] 2.1, 4.7) and 3.3 (CI: 2.2, 5.0) for cystitis and pyelonephritis, respectively, and for two first degree relatives, 5.0 (CI: 3.1, 8.1) and 5.5 (CI: 3.4, 9.0).

Women who are nonsecretors of the blood group substances have an increased frequency of recurrent infection, an association strongest for post-menopausal women, where the major behavioral risk factors have little impact. Other than this association, the genetic determinants of familial susceptibility are not well characterized. Recently, polymorphisms affecting components of the innate immune response have been explored. Toll-like receptors (TLR) on uroepithelial cells, principally TLR-1 and TLR-4, are activated by bacteria in the urine, either directly by lipopolysaccharide or following bacterial adherence. This stimulates local urinary production of chemokines such as CXCL8, leading to migration of neutrophils and other responder inflammatory cells into the urinary tract [2•]. The intensity of this response is one determinant of whether infection is asymptomatic or symptomatic [3•].

Lundstedt et al. [4] reported a familial association of pyelonephritis, but not cystitis, in girls and women with polymorphisms having significantly lower expression of CXCR1, an IL8 receptor. A comprehensive study of nine TLR-1, TLR-2, TLR-4, and TLR-5 pathway genes in subjects enrolled in the family history study [1•] reported TLR4_ A896G was associated with a lower risk of recurrent acute cystitis and TLR5 _ C1174T with an increased risk of recurrent cystitis, while TLR1 _ G1805T was protective against pyelonephritis [5••]. The same investigators reported TLR2 _ G2258A was associated with asymptomatic bacteriuria and CXCR 1 _ G827C with increased urine CXCL8 levels in subjects with asymptomatic bacteriuria [2•]. These studies are, however, compromised by multiple comparisons, and the associations were only modestly significant, with wide confidence intervals. Thus, the observations are not definitive, but do suggest polymorphisms affecting the innate immune response may explain some part of the genetic propensity observed in women with acute uncomplicated urinary infection.

Small molecular weight antimicrobial peptides are also effectors of the innate immune response. These molecules, expressed by neutrophils and epithelial cells, inhibit a range of microorganisms, although the mechanisms of action are not fully understood. Several have been identified in the urinary tract [6•]. An α defensin, HD5, is expressed in the vaginal epithelium, kidneys and upper ureters. In contrast, the β defensin HBD1 is expressed constitutively by epithelial cells of the loop of Hente, distal tubule, and collecting duct, although the urine levels are insufficient to lyse bacteria. Another β-defensin, HBD2, is induced by chronic renal infection, and increased bacteriuria has been reported in a knockout mouse model. Cathelicidin is expressed on all epithelial surfaces and induced following detection of microorganisms in the urinary tract, reaching high urine levels which peak within 5 min. Hepcidin serves a dual function as an iron regulatory protein and antimicrobial peptide, and is excreted in the urine as a 25 amino acid peptide. It has activity against Gram-positive and Gram-negative bacteria and yeast. Thus, an array of these molecules are present and variably expressed within the uninfected and infected urinary tract. The specific roles in prevention or response to infection require further characterization.

Voiding abnormalities attributed to pelvic floor dysfunction have been proposed to be an important clinical variable contributing to recurrent infection in women. A questionnaire survey of 1961 non-pregnant women in the 2005–2006 National Health and Nutrition Examination Survey (NHANES) reported 23.7% of women over 20 years had at least one pelvic floor disorder such as urinary incontinence, fecal incontinence, or symptomatic pelvic organ prolapse [7]. Minardi et al. [8•] undertook an open, randomized study enrolling women with a 3 year history of recurrent urinary infection into one of three interventions for treatment of dysfunctional voiding: uroflowmetry biofeedback, biofeedback training of the pelvic floor muscles, or the two combined. Outcomes evaluated were changes in symptoms, urodynamic measurements, and frequency of urinary infection. All three interventions showed significant improvement for all outcomes followed for 12 months, and there were no differences among the three approaches. However, at 24 months outcomes including urinary infection had returned to baseline for over one-half of study subjects. Thus, the impact of pelvic floor dysfunction and effectiveness of interventions to improve function in the management of recurrent urinary tract infection in women remain uncertain.

Pathogenesis: Organism Virulence

E. coli virulence is a determinant of clinical presentation for women with a genetic predisposition to urinary infection [3, 9]. Uropathogenic *E. coli* promote a more intense inflammatory response through greater activation of the innate immune system, resulting in symptomatic infection. Less virulent strains have more limited activation of the inflammatory cascade and may establish asymptomatic bacteriuria.

A proposed virulence factor for *E. coli* which might promote recurrent urinary infection is uroepithelial cell entry and intracellular persistence. Hultgren and colleagues previously reported, in a mouse model, that uropathogenic *E. coli* persist in bladder uroepithelial cells despite antimicrobial treatment, and re-emerge to initiate recurrent infection [10]. Whether this phenomenon contributes to

recurrent infection in adult women, in whom 30% of early (< one month) recurrent cystitis is with the previously isolated *E. coli* strain, has been controversial. Rosen et al. [11] found that 41% of 80 premenopausal women with acute cystitis had filamentous bacterial forms in voided urine specimens and 18% had intracellular bacterial colonies observed. These features are similar to those described in the mouse model, and were not identified in any urine specimens from 20 asymptomatic women with a history of urinary tract infection. The authors suggest these findings support intracellular bacterial persistence as a mechanism of recurrent infection in healthy adult women. However, the same group subsequently enrolled 104 young women following an episode of acute cystitis and obtained daily urine and periurethral cultures until the next symptomatic recurrence [12•]. For 38 recurrent *E. coli* infections, the strain isolated from urine on the day of symptom onset had been isolated from periurethral swabs 24 h or more prior to symptom onset for over 90% of episodes. This supports reinfection from an external reservoir such as the gut or vaginal flora, rather than intracellular persistence within uroepithelial cells.

Diagnosis

The utility of serum markers of systemic infection in the management of acute pyelonephritis in women has been explored in several studies. Classens et al. [13•] enrolled 699 patients who presented to emergency departments in France with presumed acute pyelonephritis into a multicenter, prospective, observational study; 93% were women and the mean age was 30 years. Baseline C-reactive protein, procalcitonin or proatrial naturetic peptide levels did not discriminate between patients who required hospitalization or those treated successfully as outpatients. Previous studies have also concluded that neither serum procalictonin [14] nor serum C reactive protein levels [15•] predict the likelihood of adverse outcomes for patients hospitalized with pyelonephritis.

Treatment

The increasing prevalence of resistance to TMP/SMX and fluoroquinolones in community-acquired *E. coli*, including extended spectrum β-lactamase (ESBL) producing *E. coli* strains, has compromised empiric antimicrobial management of acute uncomplicated urinary infection. This increased resistance is largely attributable to the worldwide expansion of a restricted number of uropathogenic clones that have acquired resistance—025:H4-ST 131, 015:K52:H1, and A [16, 17]. Prior antimicrobial therapy is a risk factor for acquisition of infection with these strains [18, 19]. The impact of even limited antimicrobial exposure on normal gut flora is described comprehensively in a study using pyrosequencing methods to generate large numbers of 16S rDNA sequence tags [20]. Following 5 days of ciprofloxacin, the abundance of one third of the 3300–5700 bacterial taxa in the gut were altered, although the magnitude of the effect varied among individuals. While recovery of gut flora was usually apparent by 4 weeks, several taxa failed to achieve pre-antibiotic levels, even by 6 months. Thus, even limited antimicrobial courses, such as those recommended for acute cystitis, have extensive and prolonged effects on the gut bacterial community.

International guidelines for treatment of acute uncomplicated urinary infection have updated the Infectious Diseases Society of America (IDSA) treatment guideline of 1999 [21••]. The updated guidelines consider empiric antimicrobial therapy for acute cystitis in the context of the increasing global resistance observed in *E. coli* [22]. The term "collateral damage" is used to describe the propensity of an antimicrobial to induce resistance in gut flora which may then compromise infection management beyond cystitis. For empiric treatment of acute uncomplicated cystitis recommended first line agents are TMP/SMX or TMP by itself for 3 days if the local prevalence of resistance is less than 20%, nitrofurantoin for 5 days, pivmecillinam for 3–7 days, or fosfomycin as a single dose. Three of these agents—nitrofurantoin, pivmecillinam, and fosfomycin—currently have indications only for acute cystitis, and are unique classes of antimicrobials without cross-resistance with other agents. Fluoroquinolones given for three days may be 5% to 10% more effective in clinical trials than some of the recommended first line regimens, but are discouraged for use as first line therapy because of the propensity for "collateral damage."

For oral treatment of acute nonobstructive pyelonephritis, ciprofloxacin, ofloxacin or levofloxacin are recommended [21••]. TMP/SMX or TMP are effective alternate oral agents if the infecting organism is known to be susceptible. When TMP/SMX is used empirically, an initial parenteral dose of an aminoglycoside or ceftriaxone is suggested for coverage of potential TMP/SMX resistant organisms pending culture results. Empiric parenteral therapy for pyelonephritis is little changed from the 1999 guidelines. Suggested regimens include an aminoglycoside with or without ampicillin, a third generation cephalosporin, or a fluoroquinolone.

Antimicrobial stewardship considerations for the treatment of community acquired infections have prompted an exploration of treatment strategies for acute cystitis which may limit antimicrobial exposure. A randomized, controlled trial in Britain evaluated five management approaches in 309 non-pregnant women aged 18 to 70 years [23••]. The different strategies were immediate antibiotics at presentation, antibiotics delayed until symptom reassessment at 48 h, antibiotics prescribed based on a symptom score (two or more of urine cloudy, offensive smell, moderately severe

dysuria, or nocturia), antibiotics prescribed based on a dipstick algorithm (antibiotics if nitrites or leukocytes and trace blood detected), or consistent collection of midstream urine with only symptomatic treatment given until microbiology results were available to direct antimicrobial choice. Clinicians recommended the initial antibiotic management for patients based on the randomization, but immediate empiric antibiotics or dipstick or midstream urine testing could be initiated for any subject, depending on patient expectations or clinical assessment. There were no significant differences in duration or severity of symptoms among the five groups (P=0.177), but antibiotic use was 97% for immediate empiric therapy, 77% for therapy delayed 48 h, 90% for the symptom score, 80% using a dipstick algorithm, and 81% when antibiotics were withheld pending urine culture results (P=0.011). Total antibiotic use was significantly less for each of the four approaches other than immediate empiric antibiotics. Patients who waited 48 h before starting antibiotics had on average a 37% longer duration of symptoms than those taking immediate antibiotics. The authors concluded that all management approaches achieved similar symptom control, and there were no advantages with routine midstream urine collection for every patient.

A cost effectiveness analysis derived from this same study concluded that the strategy of antibiotics prescribed based on dipstick testing was cost effective if the value of saving a day of moderately bad symptoms was 10 pounds or more [24]. However, there was considerable uncertainty surrounding the cost estimates. A third publication described a qualitative interview study of women's views of the different management approaches and causes of urinary tract infection [25]. In general, women preferred not to take antibiotics and were open to alternative management approaches, including antibiotic delay. However, with antibiotic delay, some women felt a lack of validation or respect from the general practitioner. The authors concluded that if the clinician wished to delay therapy, careful explanation of the rationale for not prescribing immediate antibiotics was necessary.

A pilot study enrolling patients from 29 German general practices describes a blinded, randomized trial of 80 women presenting with symptoms consistent with acute cystitis who were treated with either 3 days ibuprofen or 3 days ciprofloxacin [26••]. Symptom resolution was similar at day 4 for both arms—58.3% of ibuprofen subjects and 51.5% ciprofloxacin, and at day 7, 75% and 61%, respectively. While 33% of the ibuprofen subjects required subsequent antimicrobial therapy because of persistent or recurrent symptoms, 18.2% of the ciprofloxacin subjects also required a second antimicrobial. Further clinical trials of the effectiveness and acceptability of symptomatic treatment rather than immediate empiric antimicrobial therapy will be necessary to understand when this approach is appropriate.

Prevention

Prophylactic antimicrobial therapy given as a long term low dose or post intercourse regimen is the standard approach for prevention of frequent recurrent acute uncomplicated urinary infection. There is continuing interest, however, in identifying non-antimicrobial approaches for infection prevention. The effectiveness of cranberry juice to prevent recurrent acute cystitis is re-evaluated in a double-blind, randomized, placebo controlled trial of 319 college women treated with cranberry juice or placebo juice [27•]. By 6 months, 20% of cranberry juice subjects and 14% of placebo subjects experienced a recurrence. The presence of urinary symptoms at 3 days, 1–2 weeks, and beyond 1 month were also similar. The mean recurrence rate for all subjects in this study was 16.9% by 6 months which, as the authors note, is below the expected recurrence of 30% by 6 months. Increased daily fluid intake for both study arms or an antibacterial effect of ascorbic acid in the placebo juice are suggested as possible explanations for the unexpectedly low frequency of recurrence. The study also required a positive urine culture rather than symptoms alone for diagnosis of infection, and this could have contributed to the lower recurrence rate observed.

Development of a vaccine to prevent recurrent urinary infection by inducing local and systemic antibodies against uropathogenic *E. coli* remains a goal [28•]. However, no proposed vaccine candidates have yet been shown to be effective in human studies. A meta-analysis of immunoactive prophylaxis using bacterial lysates of *E. coli* or combinations of *E. coli* and other uropathogens as immune stimulants reported that two products—one oral and one intravaginal—had about 20% efficacy in clinical trials to decrease recurrent infection when given as a prime plus booster regimen [29•]. The limited characterization and standardization of specific antigens and other components in these bacterial extracts, however, limits widespread use.

Complicated Urinary Tract Infection

Febrile Urinary Tract Infection

van Nieuwkoop and colleagues [30•] in the Netherlands undertook a large, prospective, observational study of patients presenting to 35 primary health care centers or eight emergency departments with febrile pyelonephritis, and described a series of observations from this cohort. The subjects enrolled had a median age of 63 years and 58% had comorbidities, including 50% identified as complicated

urinary infection; 34% were male. The reliability of national guidelines which recommended referral to hospital only for management of pregnant women, failure of oral antibiotic treatment, or suspected deterioration to severe sepsis were evaluated in 395 patients [30•]. Outcomes were similar for patients treated as outpatients at primary care centers compared with patients managed at the emergency departments, with clinical failure at 30 days for 9% and 10%, respectively, and mortality rates 1% and 5%. A complicated outcome was observed in 6% of subjects managed in primary care and 10% of the emergency department group. Bacteremia was identified in 10% of patients in the primary healthcare group and 27% of patients referred to the emergency department. The authors concluded that, in a well organized primary health care system with appropriate national guidelines, management of adults with fever and acute pyelonephritis with home oral antibiotic therapy was safe and effective.

In a case control study, patients most likely to benefit from radiologic imaging were identified [31]. The derivation cohort included 346 patients, 71% of whom had radiologic imaging. A history of urolithiasis, urine pH ≥ 7.0, and renal insufficiency (estimated GFR ≤40 mL/min.), alone or in combination, predicted radiologic abnormalities requiring urgent intervention. The prediction rule developed from this derivation cohort was applied to a validation cohort of 131 individuals. The negative predictive value for clinically relevant radiologic findings was 89%, and positive predictive value 20%. For urgent urologic disorders the negative predictive value was 100% and positive predictive value 11%. The authors estimated that radiologic imaging for patients presenting with febrile pyelonephritis could be reduced by 40% if this prediction rule was applied uniformly.

The procalcitonin level was measured at presentation for 581 patients. A level >0.25 ug/L predicted bacteremia, and for bacteremic subjects procalcitonin level correlated with bacterial load measured as time to positive culture [32]. Of 136 bacteremic patients, 29 (21%) had urine cultures which were negative, contaminated, or grew an organism different from that isolated from the blood [33]. Antimicrobial pretreatment, an indwelling urinary catheter, and presence of malignancy were independently associated with bacteremic pyelonephritis without isolation of the organism from the urine. While antimicrobial pretreatment or presence of a catheter seem straightforward explanations, the reported association with malignancy is less obvious. The validity of the diagnosis of urinary infection for these patients could be questioned. Fluoroquinolone resistance was present in 12% of subjects with community onset *E. coli* febrile urinary tract infection. Independent risk factors for fluoroquinolone resistance were an indwelling urinary catheter (OR 3.1; 95% CI 0.9–11.6), requirement for hospitalization (OR 2.0; 95% CI 1.0–4.3), and fluoroquinolone use in the past 6 months (OR 17.5; 95% CI 6.0–50.7) [34]. The 30 and 90 day mortality rates were higher for individuals with fluoroquinolone resistant isolates (3.9% vs 1.9% and 5.9% vs 2.8%, respectively). Another subset of 153 cases, 40% of whom were male, completed a pelvic floor dysfunction questionnaire and responses were compared with those of controls who consulted the primary health care physician for causes other than fever or urinary infection [35]. Pelvic floor dysfunction measured by the questionnaire was similar for patients with febrile urinary tract infection and the control patients, and was not an independent risk factor for febrile pyelonephritis.

Overall, the observations and extensive analyses reported from this large cohort provide limited new or unexpected observations addressing febrile pyelonephritis. However, the size and comprehensiveness of the studies provides a useful contribution toward understanding some clinical aspects of this common problem.

Treatment of Resistant Organisms

Increasing antimicrobial resistance compromises the management of many patients with recurrent urinary tract infection. While ESBL producing *E. coli* are now frequently isolated from community onset acute uncomplicated urinary infection, studies exploring risk factors associated with urinary isolation of these organisms consistently identify complicated urinary tract infection as a major risk factor. In the Calgary Health Region, 28% of ESBL *E. coli* infections were healthcare acquired; for patients with community acquired infection, advancing age and co-morbidities were also significant associations [19]. Rodriguez-Bano et al. [18] in Spain reported that independent predictors of ESBL *E. coli* in community acquired infections, 93% of which were urinary infections, were age >60 years, female sex, diabetes mellitus, recurrent urinary tract infection, health care associated infection, and previous antimicrobial use. In an analysis of types of health care contact, only invasive urinary procedures remained a risk for acquisition [18]. More highly resistant organisms such as Acinetobacter species and New Delhi metalloprotease (NDM-1) producing *E. coli* and *K. pneumoniae* are now of increasing concern, and infections with these strains will further restrict therapeutic options.

Fosfomycin remains effective for most ESBL and NDM-1 producing *E. coli* strains [36•]. An in vitro study by Awer et al. [37•] reported over 95% of outpatient ESBL *E. coli* were susceptible to fosfomycin. Falagas [38••] summarized 17 in vitro studies and reported 96.8% of ESBL *E. coli* and 81.3% of ESBL *K. pneumoniae* were susceptible. In three clinical studies, fosfomycin was effective treatment for 93% to 94% of ESBL *E. coli* urinary infections [38]. However, this antimicrobial is not currently licensed for treatment of

complicated urinary infection, and the optimal dose and duration of therapy for this indication have not been evaluated in clinical trials. In addition, widespread fosfomycin use for treatment during a clonal outbreak of ESBL producing *E. coli* in one area of Madrid was followed by fosfomycin resistance in the outbreak strain, and the prevalence of resistance correlated with the intensity of fosfomycin use [39•].

Several recently introduced antimicrobials contribute little to the treatment of resistant organisms isolated from complicated urinary infection. In a prospective, randomized trial, doripenem 500 mg q8h and a low dose of levofloxacin 250 mg once daily had similar outcomes for complicated urinary infection and pyelonephritis [40•]. Doripenem, like ertapenem, has little activity against *Pseudomonas aeruginosa*. For the relatively few ESBL or other fluoroquinolone resistant Enterobacteriaceae isolates in this study, only 60% were microbiologically cured with doripenem and 20% with levofloxacin [41•]. Tigecycline has little renal excretion and is not indicated for treatment of urinary tract infection. Case reports describe success using this agent for ESBL *E. coli* infection of a renal cyst and prostatitis, both infections where tissue rather than urine levels would be important [42•]. The optimal therapy for treatment of candida urinary tract infection is addressed in the updated IDSA guidelines for management of candidiasis [43•]. Fluconazole, which is excreted renally, is the preferred therapy for both cystitis and pyelonephritis, with amphotericin B and flucytosine as alternatives. Echinocandins and azoles other than fluconazole are not excreted into the urine and are not recommended.

Catheter–Associated Urinary Tract Infection

Catheter–acquired urinary tract infection is the most common device associated health-care acquired infection. New paradigms for infection prevention and control which promote zero tolerance for device associated infections, together with funding changes in some American programs so health care acquired urinary infections are no longer reimbursed, have contributed to renewed interest in this problem. Three evidence-based guidelines addressing prevention of catheter-acquired urinary tract infection have recently been published [44, 45••, 46••]. These are the SHEA/IDSA Compendium to Prevent Health Care Associated Infections in Acute Care Hospitals [44], IDSA guidelines for the management of catheter-acquired urinary tract infection [45••], and a revision of the Healthcare Infection Control Practices Advisory Committee (HICPAC) guidelines initially published in 1983 [46••]. The guideline recommendations are generally consistent, but targeted to somewhat different audiences, including health care administration, patient safety practitioners, infection control, and practicing physicians. An important change is the revised National Healthcare Safety Network (NHSN) definition for surveillance in which asymptomatic bacteriuria has been removed, so only episodes of symptomatic infection are identified for surveillance of healthcare-acquired urinary infection [46••].

One inappropriate practice contributing to catheter-acquired urinary infection is failure of healthcare personnel to remove the catheter once it is no longer indicated for patient care. Meddings et al. [47•] reviewed evidence for the use of reminder systems to alert health care staff to reassess catheter indications and remove the catheter promptly when no longer indicated. In a systematic meta-analysis, use of reminders reduced catheter-acquired bacteriuria by 52% and the mean duration of catheterization by 37%. However, the impact of these interventions for preventing symptomatic urinary infection was not addressed.

The efficacy of antimicrobial coated catheters for prevention of catheter-acquired urinary tract infection remains controversial. While initial studies reported that silver alloy coated catheters decreased the short-term acquisition of bacteriuria, more recent reviews and clinical trials report no difference between silver alloy coated catheters compared with a similar catheter without the antimicrobial coating [44, 45••, 46••]. In vitro studies also report no differences in bacterial adherence between silver alloy silicone coated catheters and silicone catheters alone [48, 49]. A nitrofurazone coated catheter was effective in delaying onset of bacteriuria in clinical trials, but the impact on symptomatic infection has not been described. In vitro studies report that the nitrofurazone catheter may inhibit adherence of *E. coli* up to 5 days and *E. faecalis* for 1 day compared with a non-antimicrobial coated catheter [48, 49]. Thus, antimicrobial coated catheters appear to have limited, if any, impact on bacteriuria, and no benefit has been shown for preventing symptomatic infection. The guidelines consistently recommend against routine use of these devices.

Conclusions

Urinary tract infection remains a common and important clinical problem. Some new information further characterizes the complex interactions of organism virulence, host genetic susceptibility, and immune response, and may provide insights into why such a high proportion of healthy women experience recurrent urinary tract infection. For complicated urinary tract infection, there has been little progress made in management approaches. The increasing prevalence of resistant Gram-negative organisms will further compromise treatment of both complicated and uncomplicated urinary tract infections.

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- • Of importance
- •• Of major importance

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