Nosocomial urinary tract infection is a major cause of morbidity in hospitalized patients in general, and in postoperative surgical patients in particular. The major predisposing factor to the development of a urinary tract infection is the presence of a urinary catheter. The risk of infection increases with the duration of catheterization. It has been estimated that the risk of urinary tract infection increases by 5% to 10% per catheter day after the second day of catheterization.1,2

RISK FACTORS

A recent analysis of data from the National Surgical Infection Prevention Project revealed that 86% of patients undergoing major operations had indwelling urinary catheters in the perioperative period, with half of the patients remaining catheterized for more than 2 days. As expected, catheterization for more than 2 days was a significant risk factor for urinary tract infection (9.4% versus 4.5%; P = .004). Prolonged catheterization was also associated with a decreased likelihood for discharge to home, and with increased 30-day mortality.3 Previously, duration of catheterization had not been linked to mortality.4 The National Health Safety Network, a project of the Centers for Disease Control and Prevention, also investigated catheter use and catheter-related urinary tract infection as part of its surveillance activities. In 2006, it reported a catheter use index in surgically oriented intensive care units (ICUs). This index, a ratio of urinary catheter days to patient days, ranged from 0.69 to 0.91. In these same ICUs, there were 4.0 to 7.5 catheter-associated urinary tract infections per 1000 urinary catheter days.5 Thus, perioperative catheterization is near ubiquitous, is a major risk factor for nosocomial urinary tract infection, and is linked to, if not directly causative of, a decreased likelihood of discharge to home and an increased 30-day mortality.

MICROBIOLOGY AND DIAGNOSIS

The most common causative agents of catheter-related urinary tract infection are the patients’ own colonic flora. Additional organisms are usually not found until duration of
catheterization exceeds 30 days. The most common organisms causing these infections with short-term catheterizations are *Escherichia coli*, enterococci, *Pseudomonas*, *Klebsiella*, *Enterobacter*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Serratia*. Exogenous sources can also lead to catheter-related urinary tract infection, commonly with staphylococci, *Serratia marcescens*, *Burkholderia cepacia*, and *Stenotrophomonas maltophilia*.

Wagenlehner and colleagues recently analyzed their 12-year experience with urinary tract infections in hospitalized urology patients in one German hospital. *E coli* initially accounted for approximately one third of the urinary tract infections. This increased over the 12 years to approximately 40%, primarily displacing infections due to *Pseudomonas aeruginosa*. Other gram negatives accounted for another one third of the infections, and gram positives caused the remaining one third. Increasing resistance of *E coli* to the commonly used trimethoprim/sulfamethoxazole was noted, highlighting the importance of culture and sensitivity data not only in treating the individual patient, but also for planning effective empiric treatment strategies. The investigators did not include fungal urinary tract infections as part of their study.

Urinary cultures have been the standard means for diagnosing urinary tract infections. The standard cutoff has been the growth of $10^5$ or more organisms per milliliter of urine. This number was originally based on studies of symptomatic patients with cystitis, and not hospitalized patients with infections related to indwelling urinary catheter. Nonetheless, this remains the number used to diagnose the presence of urinary tract infection in surgical patients, and in reporting the incidence of such infections to regulatory agencies.

In more critically ill surgical patients, candiduria remains a vexing clinical problem. It typically occurs in patients who have a multitude of reasons to manifest sepsis. Sobel and Lundstrom reviewed the development of candiduria in 2001 and pointed out that 10% to 15% of nosocomial urinary tract infections are now caused by *Candida* sp, with the highest prevalence being in patients housed in ICUs, and those with leukemia or who had undergone bone marrow transplant. Diabetes predisposes to the development of candiduria in multiple ways. In women, diabetes promotes colonization of the vulvovestibular area with *Candida*. Glycosuria, if present, enhances urinary fungal growth. Diabetes also impairs host defenses, particularly phagocytosis. Finally, the development of a neurogenic bladder allows for urinary stasis and increases the likelihood that the urinary tract will be instrumented. Fungal urinary tract infections are also promoted in diabetics and nondiabetics alike by antibiotic therapy, which leads to fungal overgrowth in the colon and perineal area due to suppression of normal bacterial flora; the fungal organisms can then ascend the Foley catheter into the urinary system. Bukhary in 2008 also identified similar risk factors in a review of 37 years of English-language literature on the topic of candiduria. This review indicated that the risk factors for candiduria were indwelling urinary catheters, use of antibiotics, advanced age, underlying anatomic urologic abnormality, previous surgery, and the presence of diabetes.

Sobel and Lundstrom indicated that *Candida albicans* is the most common fungal species causing urinary fungal infections, with *Candida glabrata* being the second most common fungal pathogen. More than one candidal species are found simultaneously in 10% of cases. Bukhary cited multiple reviews of the epidemiology of candiduria, and confirmed that with only one exception the overwhelming majority of candiduria is due to *C albicans*. *C glabrata* accounts for 12% to 18% of cases, *Candida tropicalis* for 8% to 22%, and all remaining species for less than 5% in almost all studies. Urinary tract infections due to noncandidal fungal organisms are very uncommon in surgical patients, and are usually encountered as part of a disseminated mycotic disease in highly immunosuppressed patients.
The diagnosis of a urinary tract infection due to *Candida* is difficult because *Candida* in the urine can represent contamination, colonization of the drainage device, or a true infection. Small numbers of yeast from a colonized catheter, collection device, or the vulva may multiply rapidly in the collected urine, producing high colony counts that do not necessarily indicate infection. Further, although the presence of pyuria usually supports the diagnosis of infection, the mere presence of an indwelling catheter can lead to pyuria, as can a coexisting bacterial urinary tract infection. Thus, clinical judgment must be used in making the diagnosis, particularly in asymptomatic patients. Notably, asymptomatic candiduria rarely, if ever, leads to candidemia.9

**PREVENTION**

European and Asian guidelines have been developed based on a comprehensive review and meta-analysis of data on prevention and treatment of urinary catheter-associated infections. Not surprisingly, the principal findings are that minimization of duration of catheterization and maintenance of a closed system are the best means of avoiding infection.6

These 2008 European and Asian guidelines for the prevention of catheter-associated urinary tract infections are listed below. The letters in parentheses indicate the grade of the guideline recommendation. An “A” recommendation is based on clinical studies of good quality and consistency, including at least one randomized trial; a “B” recommendation is based on well-conducted clinical studies, but without randomized clinical trials; and a “C” recommendation is one developed by the expert panel in the absence of directly applicable clinical studies of good quality.

- The catheter system should remain closed (A).
- The duration of catheterization should be minimal (A).
- Topical antiseptics or antibiotics applied to the catheter, urethra, or meatus are not recommended (A).
- Benefits from prophylactic antibiotics and antiseptic substances have never been established; therefore, they are not recommended (A).
- Removal of the indwelling catheter after a nonurological operation before midnight may be beneficial (B).
- Long-term indwelling catheters should be changed in intervals adapted to the individual patient, but must be changed before blockage is likely to occur (B); however, there is no evidence for the exact intervals of changing catheters. Chronic antibiotic suppressive therapy is generally not recommended (A).

Adherence to these basic recommendations could significantly decrease the risk of catheter-associated urinary tract infections. In a 10-year study of infection control and surveillance practices emphasizing some of these principles, there was a decrease of 70% over time in the risk of urinary tract infections in an ICU population.11

Nonetheless, prolonged use of urinary catheters is necessary in certain surgical patients. In such cases, clinicians cannot use the best tool for preventing catheter-associated infections—early removal of the devices. Therefore, there has been interest in the use of catheters that might be less prone to allowing an infection. One key way in which catheters predispose to urinary tract infection is by serving as a site for bacterial pathogens to create a biofilm. The organisms associated with catheter-associated urinary tract infection grow in a glycocalyx, protected from the antibiotics concentrated in the urine. This biofilm gradually thickens and can encapsulate all surfaces of the catheter. Within this dense biofilm, the bacteria create their own microenvironment,
become metabolically inactive as compared with planktonic bacteria, and thereby become resistant to antibiotics because of the lack of metabolic activity. Attempts have been made to reduce catheter-associated urinary tract infection through use of advanced catheters designed to inhibit biofilm formation. The primary technology for this is the use of antibiotic- or antiseptic-coated catheters. There have been two systematic reviews of silver alloy and nitrofurazone-impregnated urinary catheters in recent years. The difficulty in evaluating the utility of these products is stressed in one of these reviews, which included trials that were deemed to be of variable levels of quality. The combined data available on all 13,319 participants suggested that antimicrobial urinary catheters prevented or delayed the onset of catheter-associated bacteriuria compared with control catheters. However, the magnitude of this effect varied, and was systematically overestimated in many studies because of dropouts and exclusions. The effects of these catheters on morbidity, including bloodstream infection, remained unknown.

Thus, although these devises seem promising, the analysis of the literature by Tenke and colleagues described in the European and Asian guidelines suggests that the role of these devices is limited at the present time, with the indications for their use remaining to be established. Recommendations and their level of evidence included:

Antibiotic-impregnated catheters may decrease the frequency of asymptomatic bacteriuria within 1 week. There is, however, no evidence they decrease symptomatic infection. Therefore, they cannot be recommended routinely (B).

Silver alloy catheters significantly reduce the incidence of asymptomatic bacteriuria, but only for less than 1 week. There was some evidence of reduced risk for symptomatic urinary tract infection. Therefore, such catheters may be useful in some settings (B).

Research into urinary catheter design continues because of the clear need to reduce the incidence of catheter-associated urinary tract infections. The newest technology involves use of protamine sulfate and chlorhexidine to prevent or delay biofilm formation. These catheters proved less likely to become colonized in vivo than silver-coated or uncoated catheters, but their clinical efficacy, as with the older types of impregnated catheters, has yet to be proven.

TREATMENT

Treatment of nosocomial urinary tract infections needs to be considered separately for patients with asymptomatic bacteriuria and for those with symptomatic urinary tract infection. In general, asymptomatic bacteriuria in catheterized patients should not be treated. Removal of the catheter allows resolution of bacteriuria in one third to one half of cases. The European and Asian guidelines recommend treatment of asymptomatic bacteriuria in the following circumstances:

For patients undergoing urological surgery or implantation of prostheses (A)
When treatment may be part of a plan to control nosocomial infection due to a particularly virulent organism prevailing in a treatment unit (B)
For patients who have a high risk of serious infectious complications (eg, patients who are immunosuppressed) (C)
For infections caused by strains causing a high incidence of bacteremia (eg, S marcescens) (B)
Treatment of symptomatic urinary tract infection is usually more straightforward. Clinical symptoms and signs, such as frequency, dysuria, or suprapubic pain directly attributable to an infection, are an indication for treatment.

The most common symptom attributed to a urinary tract infection in hospitalized patients is usually fever. Bacteriuria may or may not be the source of a fever or another nonspecific indicator of infection, such as leukocytosis. It has been suggested that if the patient has a low-grade fever, is clinically stable, and has no other indication for antibiotics, observation, rather than immediate antimicrobial therapy, can be entertained. In these patients, it may also be useful to replace the catheter with a new one to eliminate the burden of the existing biofilm.7

If the patient is systemically ill, empiric antibiotics should be started, based on knowledge of the local bacterial ecology, and then tailored based on definitive culture and susceptibility results. There are no adequate clinical studies to guide the duration of therapy; clinical judgment and patient response should be used to determine the duration of the antibiotic course.7 The choice of antibiotic may be complicated by the development of resistant bacteria. In particular, there is greater resistance of E. coli, other Enterobacteriaceae, and P. aeruginosa in catheterized patients compared with noncatheterized patients.16 In the absence of an indwelling catheter, as with community-acquired urinary tract infections, resistance has not generally been an important issue because antibiotics typically used for community-acquired infections, such as amoxicillin, cephalaxin, trimethoprim/sulfamethoxazole, ciprofloxacin, and levofloxacin, are highly concentrated in the urine, from nearly 100 up to several hundred times.17 However, in patients with nosocomial urinary tract infections, who may have indwelling urinary catheters and highly resistant pathogens, the perception that bacterial susceptibilities are unimportant may not necessarily be accurate. Thus, clinical judgment and the patient’s response to therapy dictate the degree to which susceptibility data are used to direct treatment of symptomatic urinary tract infections in hospitalized patients.

Some of these same considerations apply to the dilemma as to whether or not to treat the patient with candiduria. In the past, when the only option for treatment was amphotericin B, patients were rarely treated. The development of fluconazole and other less toxic antifungal agents has greatly increased the likelihood that clinicians will treat patients with candiduria. As with other asymptomatic urinary tract infections, however, asymptomatic candiduria needs no pharmacologic therapy, and can usually be treated by removal of Foley catheters or replacement of the catheter to reduce the biofilm burden. Pharmacologic therapy with an antifungal agent should generally be limited to patients with symptomatic candiduria after confirmation of the infection from a second urine sample.18

Unfortunately, the critically ill patient is the one most likely to have candiduria, and the one least likely to be able to complain of symptoms. Furthermore, this is the patient most likely to suffer a poor outcome if a necessary treatment is withheld. Thus, it is somewhat difficult to define which of these patients should be treated. Suggested indications for the treatment of candiduria include low birth weight infants and patients who have undergone renal transplantation, have neutropenia, or who have a planned invasive urologic procedure. If asymptomatic candiduria progresses to symptomatic cystitis, it ought to be treated as well.9

Fluconazole is the antifungal agent most commonly given to eradicate candiduria. Oral fluconazole is both convenient and effective, and should be used if it is feasible to give the patient an oral or enteral agent. Because fluconazole concentrates in the urine to more than 100 μg/mL after a 400-mg dose, even C. glabrata, which is relatively resistant to fluconazole with a minimal inhibitory concentration of 8 to 16 μg/mL, can
be successfully treated with fluconazole. Candiduria frequently recurs 2 weeks after successful treatment with fluconazole if the underlying patient conditions conducive to the development of candiduria have not been eliminated. In the presence of renal failure, when a drug cannot be effectively delivered into the urinary tract, amphotericin B bladder irrigations can be used to treat a lower urinary tract infection due to *Candida*.

**SUMMARY**

Nosocomial urinary tract infections are a common complication in surgical patients. The use of urinary catheters is the major risk factor for the development of these infections. Discontinuation of catheterization within 2 days is key to avoiding nosocomial urinary tract infections. Patients with asymptomatic bacteriuria can generally be treated initially with catheter removal or catheter exchange, and do not necessarily need antimicrobial therapy. Symptomatic patients should receive antibiotic therapy. Resistance of urinary pathogens to common antibiotics is not usually an issue because of the concentration of most antibiotics in the urine. However, it is uncertain if different empiric antimicrobial regimens are needed when highly resistant bacteria are involved in nosocomial urinary tract infections. The treatment of patients with candiduria generally follows the same principles. Patients with asymptomatic candiduria usually can be treated with catheter removal or exchange, and do not need specific antifungal therapy. However, selected high-risk patients as well as those with symptomatic fungal urinary tract infections should receive antifungal therapy, generally using fluconazole.

**REFERENCES**


