

# Health Care–Associated Urinary Tract Infections: Prevention and Management

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## ABSTRACT

**Objective:** To review management issues regarding health care–associated urinary tract infections (UTIs) commonly encountered by practicing clinicians.

**Methods:** Review of the literature.

**Results:** Because urinary catheter (UC) placement plays a major role in the development of catheter-associated UTIs (CA-UTI), clinicians should be aware of the appropriate and inappropriate uses of UCs and their association with CA-UTI development. Removal of a UC when no longer necessary is key to preventing CA-UTI. Treatment of asymptomatic bacteriuria is generally not indicated. Percutaneous nephrostomy and ureteral stenting need close monitoring, and early removal should be performed if infection is suspected. Candiduria rarely leads to symptoms unless it is related to an ascending process. Proper urine collection is crucial in determining whether contamination, colonization, or infection is present. Fluconazole is recommended in most cases of *Candida* UTI, while intravenous amphotericin B is recommended for fluconazole-resistant *Candida* species.

**Conclusion:** Continued use of evidence-based strategies for preventing and managing health care–associated UTI should lead to further improvements in patient outcomes and overall decreased rates of infection.

**Keywords:** bacteriuria; catheter-associated UTI; catheterization; percutaneous nephrostomy; candiduria.

Health care–associated urinary tract infections (UTIs) are estimated to be the most common adverse infectious event in U.S. hospitals, occurring in 1 of 10 admitted patients.<sup>1–3</sup> Approximately 32% of all health care–associated infections are UTIs.<sup>1</sup> Furthermore, urinary catheters (UCs) are associated with 8% to 21% of health care–associated infections that occur in the intensive care unit.<sup>4</sup> The most important predisposing factor for nosocomial UTI is urinary catheterization.<sup>5</sup> Genitourinary

manipulation and/or implementation also play a major role in the development of nosocomial UTIs.

In 2008, the U.S. Centers for Medicare & Medicaid Services instituted a new policy that reduced reimbursement rates for hospitalizations linked to health care–associated infections.<sup>6</sup> Indwelling UCs are among the most overused health care devices in the hospital setting. They are placed in an estimated 15% to 25% of all hospitalized patients,<sup>7,8</sup> and are often inserted in the emergency department (ED) without a physician order or appropriate indication.<sup>9</sup> Intermittent straight catheterization, male or female condom catheterization, and/or placement of an indwelling UC are the most common causes of catheter-associated asymptomatic bacteriuria (CA-ASB) and catheter-associated UTIs (CA-UTI).<sup>5</sup> Prevention and management of CA-ASB and CA-UTI can be challenging and require an evidence-based approach. Furthermore, guidelines for the management of UTIs in the setting of active percutaneous nephrostomy (PCN) drainage and/or ureteral stenting are not established.<sup>5</sup> This may leave clinicians with little mainstream data to aid in management decisions.

In 2009 the Centers for Disease Control and Prevention provided a guideline for the appropriate and inappropriate use of indwelling UCs to help promote their proper use.<sup>10</sup> In the time since the guideline's initiatives were instituted around the United States, published data have shown some improvement in the use of UCs,<sup>11,12</sup> but other recent reports indicate that rates of UC use have remained unchanged.<sup>13</sup> This review discusses management issues regarding health care–associated UTIs that are commonly encountered by practicing clinicians, with a focus on current guidelines and evidence.

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## Catheter-Associated UTI

CA-UTI is defined as the presence of signs or symptoms of UTI with no other explainable infectious source along with  $\geq 1000$  colony-forming units (cfu) of  $\geq 1$  bacterial species per milliliter in a urine specimen from a catheter that has been changed within 48 hours of collection of the urine specimen.<sup>5</sup> Signs and symptoms of CA-UTI include, but are not limited to: new-onset or worsening fever, chills, altered sensorium from baseline, lethargy, malaise, flank pain, pelvic pain, costovertebral angle tenderness, and acute hematuria.<sup>5</sup> New-onset “foul-smelling” (odorous) urine and “cloudy” urine are neither sensitive nor specific when assessing for CA-UTI, and do not have significant clinical relevance when found alone.<sup>14,15</sup> Patients who have removed or exchanged the UC during this event and then experience dysuria, increased frequency, urgency, or suprapubic pain are likely having symptoms of CA-UTI.<sup>5</sup>

### **What is the recommended method for collecting urine samples when CA-UTI is suspected?**

In a patient with an indwelling catheter that has been in place for more than 2 weeks at the onset of a suspected CA-UTI, the catheter should be replaced (if still indicated) or removed to accelerate resolution of symptoms and to reduce the risk of subsequent catheter-associated bacteriuria and CA-UTI. The urine culture should be acquired from the freshly placed UC.<sup>5</sup>

### **When should a patient be empirically treated?**

A patient presenting with evidence of sepsis should be empirically treated with antimicrobials. Empiric coverage should be based on risk factors for multidrug-resistant organisms and data pertaining to local antimicrobial resistance patterns. A urine specimen for urinalysis and possible culture should be sent prior to administering empiric antibiotics (if possible) in a symptomatic patient.<sup>5</sup>

### **What bacteria are commonly associated with CA-UTI?**

The bacteria most commonly associated with CA-UTI are found in or around the gastrointestinal and genitourinary tracts and also are part of the normal skin flora. The introduction and/or facilitated ascension of these microorganisms is believed to occur during UC inser-

tion.<sup>16,17</sup> Two-thirds of all isolated uropathogens in those with indwelling UCs are extraluminally acquired (via ascension along the catheter-urethral mucosa interface), and one-third are believed to be intraluminally acquired.<sup>18</sup>

The most commonly isolated bacteria in CA-UTI are Enterobacteriaceae, which include *Escherichia coli* (most common), *Klebsiella* species (*K. oxytoca*, *K. pneumoniae*), *Serratia* species (*S. marcescens*), *Citrobacter* species (*C. koseri*), *Enterobacter* species (*E. cloacae*), and *Proteus* species; non-Enterobacteriaceae such as *Pseudomonas* species; and gram-positive cocci, which include coagulase-negative staphylococci (*S. saprophyticus*), *Staphylococcus aureus*, group B streptococci, and *Enterococcus* species (*E. faecalis*, *E. faecium*).<sup>19-21</sup> Coagulase-negative staphylococci and *Enterococcus* species can lead to CA-UTI but are usually avirulent and more commonly isolated from asymptomatic individuals.<sup>19</sup> Also, coagulase-negative staphylococci such as *S. epidermidis* and *S. lugdunensis* are usually the manifestation of contamination during the collection process and their presence should prompt a repeat sample collection under sterile techniques. Monomicrobial infection is usually seen in those with short-term catheter use and CA-UTI. In contrast, polymicrobial infection is more common in those with long-term indwelling UCs and CA-UTI.<sup>19</sup> *Providencia stuartii*, *Proteus mirabilis*, *S. aureus*, and *Morganella morganii* have all been associated with CA-UTI in those with long-term indwelling UCs.

Growth of *S. aureus* in the urine should prompt further investigation with blood cultures to explore the possibility of hematogenous dissemination to the urinary tract. Organisms leading to bacteremia due to CA-UTI are most commonly gram-negative bacilli (*E. coli*, *Klebsiella* species, *Pseudomonas aeruginosa*) and *E. faecalis*.<sup>21</sup>

### **What is the difference between CA-ASB and CA-UTI?**

CA-ASB is defined as the presence of  $\geq 1$  bacteria species growing on urine culture at  $\geq 100,000$  cfu/mL in a patient with a history of urinary catheterization and/or indwelling UC who lacks signs or symptoms of UTI. In a man with a condom catheter, CA-ASB is defined using the same criteria, but the urine sample is collected after a fresh condom catheter is applied.<sup>5</sup> The difference between CA-ASB and CA-UTI is simply the presence or absence of signs and symptoms related to UTI. Currently, there is no standard definition for significant bacte-

riuria in a catheterized patient.<sup>5</sup> Pyuria found on urinalysis is indicative of genitourinary inflammation and can be present in both CA-ASB and CA-UTI. The absence, presence, and/or degree of pyuria in catheterized patients does not accurately differentiate between CA-ASB and CA-UTI.<sup>5,22,23</sup> On the other hand, the absence of pyuria in a symptomatic catheterized patient suggests an etiology other than CA-UTI.<sup>5</sup>

### ***How can CA-UTI be prevented in patients with a short-term indwelling urinary catheter?***

If a short-term UC is essential, the most important approach to preventing CA-UTI is limiting the duration of time it will be used. Strategies such as computer-based order entry and care maps with automated discontinuation of UCs have been shown to decrease catheter usage.<sup>19</sup> Using closed-systems for UC collection with ports in the distal catheter for needle aspiration of urine has also been shown to decrease the incidence of CA-UTI.<sup>5</sup> Securing the UC to avoid urethral trauma, aseptic techniques for insertion and repositioning, and placement of the tubing and collection bag below the level of the bladder to prevent reflux will likely also prevent CA-UTI, but these strategies have not been evaluated thoroughly.<sup>19</sup>

### ***When should you screen for and treat CA-ASB?***

The 2009 Infectious Diseases Society of America (IDSA) guidelines recommend that the only patients who should be screened and treated for CA-ASB are pregnant women and those who will undergo a potentially traumatic urologic procedure for which mucosal breaching may occur, causing bleeding. Routinely screening or treating patients for CA-ASB is not recommended in any other group of patients and will lead to unnecessary antibiotic use and antibiotic resistance.<sup>5</sup>

### **UTI Associated with Percutaneous Nephrostomy and Ureteral Stenting**

Similar systemic symptoms of infection (fever, rigors, malaise, shock) are present in patients with and without percutaneous nephrostomy (PCN) and/or ureteral stent placement. Dysuria is not commonly present in those with PCN. The first signs of CA-UTI may be decreased urine output and pericatheter leakage due to an obstructive process resulting from the encrustation.<sup>24-27</sup> The most

common complaint among patients with either acute or chronic ureteral stenting is discomfort, which has been described as “urinary symptoms” and “body pain.”<sup>28</sup> This discomfort can be related to ureteral hyperperistalsis after placement of the stent and is usually self-limiting. Ureteral stent migration, usually at the distal end, can also lead to discomfort, but is easily rectified with cystoscopy.<sup>25</sup> Body pain and/or urinary symptoms in the setting of ureteral stenting are not indicative of infection alone.

### ***What is urinary catheter and/or ureteral stent encrustation?***

Encrustation is the formation of a conditioning film that develops on the surface of the UC or ureteral stent. The exact mechanism is not well understood, but it is believed to involve electrostatic interactions of urinary proteins that stimulate binding onto the stent or UC surface.<sup>25</sup> Encrustation increases exponentially with the dwell time. Among patients with ureteral stents placed due to urolithiasis, encrustation occurred in 9.2% of stents removed prior to 6 weeks, 47.5% of stents removed at 6 weeks, and 76.3% of stents removed at 12 weeks.<sup>26</sup> Encrustation is most common at the proximal and distal ends (pigtailed) of the ureteral stent and usually spares or presents last within the lumen.<sup>29</sup> Attempts have been made to prevent ureteral stent encrustation through the development of biodegradable, drug-eluting, and tissue-engineered substrates. These developments are promising, but currently there is limited observational data from large randomized trials to suggest that these new modalities decrease rates of encrustation.<sup>25</sup> Encrustation is highly associated with certain microorganisms, especially those that create biofilms.<sup>30</sup> Urease-producing bacteria, most commonly *P. mirabilis*, play a role in encrustation formation.<sup>31</sup> Bacteria most commonly associated with encrustation include *Proteus* species (*P. mirabilis* is most common), *P. aeruginosa*, *K. pneumoniae*, *Providencia* species (*P. stuartii* is most common), and *M. morganii*.

### ***Does ureteral stent bacterial colonization correlate with UTI?***

Ureteral stent colonization with bacteria increases with dwell time and is found in 40% to 98.5% of stents placed.<sup>32-35</sup> If UTI is suspected in a patient with an active indwelling ure-

teral stent, a sample of urine should be cultured while the stent is in place.<sup>25</sup> Typically, genitourinary and normal skin flora pathogens are found when the ureteral stent is cultured. The top 3 organisms cultured from ureteral stents are *S. aureus*, *P. aeruginosa*, and *E. faecalis*.<sup>34</sup> Urine culture usually does not correlate with stent culture results, which has brought up the debate of how bacterial colonization occurs. It has been postulated that colonization is actually a manifestation of contamination during the insertion procedure, but this has yet to be validated.<sup>25</sup> In patients with symptoms of UTI in the setting of an indwelling ureteral stent, a positive culture has low sensitivity, with estimates between 21% and 40%.<sup>35</sup> Therefore, a negative urine culture does not rule out UTI alone in a symptomatic patient. Multiple studies have suggested that colonization of the ureteral stent does not correlate strongly with developing a UTI.<sup>25,32-34</sup>

#### ***How can UTI be prevented in those receiving PCN or ureteral stent placement?***

Antibiotic prophylaxis has been recommended to prevent UTI in patients who will undergo PCN or ureteral stent placement. The American Urological Association recommends empiric treatment even in the absence of signs and symptoms of UTI,<sup>36</sup> but substantial evidence is lacking that this approach prevents infection.<sup>37</sup> Ciprofloxacin or trimethoprim/sulfamethoxazole has been recommended by some for empiric coverage for enteric gram-negative bacilli and enterococcus in those undergoing genitourinary manipulation or instrumentation.<sup>32,38</sup> Most patients who develop CA-UTI and pyelonephritis do so within the first 2 to 6 weeks after placement.<sup>37,39</sup> Bacteriuria, candiduria, and/or pyuria are present in all patients approximately within 9 weeks even when sterile urine is confirmed prior to PCN placement.<sup>39</sup> Data on the effectiveness of antibiotic prophylaxis to prevent CA-UTI in those with PCN or ureteral stenting is limited. Currently, there are no recommendations from the IDSA on how to prevent infection in these situations.<sup>5</sup> Early or frequent stent removal or exchanges has been proven to reduce UTI in those with ureteral stenting.<sup>33</sup> Patients with diabetes mellitus and chronic renal failure are at high-risk for UTI when ureteral stents are in place. This population should undergo close monitoring for UTI development and may warrant more frequent stent exchanges.<sup>27,40</sup>

#### ***What is the treatment of CA-UTI associated with PCN and/or ureteral stenting?***

The IDSA guidelines do not apply to patients with PCN and/or ureteral stenting.<sup>5</sup> There is no treatment protocol for UTI related to these processes. Generally speaking, they are considered “complicated UTI” by most experts. Broad-spectrum, empiric antibiotic administration along with prompt removal of the PCN and/or ureteral stent is the gold standard of therapy.<sup>27</sup> The recommended duration of targeted antibiotic therapy is generally between 5 and 14 days.<sup>19</sup> Most clinicians will treat this complicated UTI for at least 10 to 14 days. Antibiotic administration should be continued even after removal of the catheter and/or stent to complete the full course. Repeat urinalysis and culture is not indicated at the end of therapy if the patient is clinically improving or has remission of symptoms.

#### ***What is the exchange rate for those who require chronic PCN and/or ureteral stent use?***

On average a PCN or ureteral stent should be exchanged every 2 to 3 months in patients who require chronic usage.<sup>24,27</sup> Some patients with persistent complications may require more frequent exchanges (< 10 weeks).<sup>27</sup> Encrustation and bacterial colonization become more prevalent the longer the devices are in place. This process is estimated to begin within the first 2 weeks after placement.<sup>27,33,34</sup> A “forgotten stent” is one that has been left in place after the patient is lost to follow-up. This unfortunate event can lead to massive encrustation, UTI, stent fracturing, and complete ureteral obstruction.<sup>24</sup> As noted, patients with diabetes mellitus, chronic renal failure, and frequent UTI may warrant more frequent exchanges, but this should be determined on a case-by-case basis.

#### ***Catheter-Associated UTI in Patients with Spinal Cord Injury***

Spinal cord injury (SCI) at any level can cause neurogenic bladder. This process ultimately leads to urinary stasis and colonization of the bladder with bacteria. According to the IDSA, the acceptable indications for UC insertion are: clinically significant urinary retention (if medical therapy is not effective), urinary incontinence, accurate urine output monitoring required, and patient is unable and/or unwilling to collect urine (**Table 1**).<sup>5</sup> Recently, further guidelines were

Table 1. IDSA 2009 Criteria for Acceptable Indications for Indwelling Urinary Catheter Insertion

Indications	Comments
Clinically significant urinary retention	If medical therapy is not effective and/or if surgical therapy is not indicated
Urinary incontinence	Comfort measures for a terminally ill patient Less invasive therapies fail (pharmacologic, behavioral, incontinence pads) External collection devices or effective alternatives are not available
Accurate urinary output monitoring	Conditions requiring strict input/output measuring
Patient is unwilling or unable to collect adequate urine sample	Surgical procedures requiring general or spinal anesthesia Urologic and gynecologic perioperative urine collection

Adapted from Hooton TM, Bradley SF, Cardenas DD, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50:625-663.  
IDSA, Infectious Diseases Society of America.

published regarding appropriate and inappropriate indwelling UC placement in hospitalized medical patients (**Table 2** and **Table 3**), expanding upon the earlier acceptable criteria provided by the IDSA.<sup>41</sup> According to the IDSA and Ann Arbor Criteria for Appropriate Urinary Catheter Use, patients with SCI and subsequent neurogenic bladder without obstruction where intermittent bladder straight catheterization for the drainage of urine is not feasible will likely need an indwelling UC.<sup>41</sup> SCI patients often experience decubitus ulcers, and an indwelling UC can be used if needed to help with wound healing if other urinary management alternatives have been attempted. Other such situations in which an indwelling UC can be used before attempting alternative approaches would be in a patient who is actively dying and is pursuing comfort care and/or hospice.<sup>41</sup>

### **Which indwelling UCs should be used in patients with SCI?**

Efforts to reduce the likelihood of infection in patients with SCI have led to several advances in the design and manufacturing of UCs. UCs are made of either latex, plastic, silicone, or polytetrafluoroethylene (Teflon). None of these substrates is free of complications, but of them latex UCs have been studied the most in regards to their associated complications. Aside from being allergenic in nature, latex UCs have an increased propensity to allow bacteria to adhere to their surface due to microscopic planes of unevenness.<sup>42</sup> Silicone UCs are less frequently associated with infection but are more rigid, leading to increased discomfort.<sup>43,44</sup> Hydrophilic and silver-hydrogel coatings are innovative methods that have been

developed to increase comfort and reduce the likelihood of infection. Hydrophilic-coated UCs are associated with reduced microbial adherence, decreased encrustation, and better patient satisfaction.<sup>45,46</sup> In SCI patients, these UCs have demonstrated lower complication rates, including UTI; fewer episodes of post-, intra-, and inter-catheterization bleeding; and decreased rates of antibiotic-resistant bacteria.<sup>45,46</sup> Silver-hydrogel-coated UCs are less well studied but have also demonstrated reduced UTI rates in SCI patients; however, their efficacy over the long term has yet to be determined. Antibiotic-impregnated UCs are not currently recommended for either short- or long-term indwelling UC use.<sup>5</sup>

### **How can CA-UTI be prevented in a patient who will require a long-term indwelling catheter?**

At this time, the data is insufficient to make a recommendation on routine UC exchange (eg, every 2 to 4 weeks) in patients who require long-term indwelling urethral or suprapubic catheters in an attempt to reduce the risk of CA-ASB or CA-UTI. This is also true for those who experience even repeated early catheter blockage from encrustation.<sup>5</sup> Thus, the rate at which these exchanges occur can be controversial, but typically around every 4 weeks is a common approach. Some would argue that if the patient has repeated CA-UTI, an exchange rate of every 2 weeks might be needed, but data is currently lacking to support this practice.<sup>5</sup> If intermittent urinary catheterization is feasible, it should be done at least every 6 hours and before bedtime. In general, when the volume of urine in the bladder reaches approximately 400 mL, the patient should undergo bladder



Table 2. **Appropriate Indwelling Urinary Catheter Use in Hospitalized Medical Patients**

Indwelling Urinary Catheter Indications	Comments
Acute urinary retention without bladder outlet obstruction	Example: medication-induced urinary retention
Acute urinary retention with bladder obstruction secondary to noninfectious or nontraumatic etiology	Example: exacerbation of benign prostatic hyperplasia (urology consultation may be considered)
Chronic urinary retention with and without bladder outlet obstruction	Example: neurogenic bladder when ISC is not a feasible option or is contraindicated
Decubitus ulcer (stage III, IV, unstageable) or severe wounds that cannot be kept clear from urine despite adequate wound care or other urinary management strategies	Urinary management strategies: barrier creams, absorbent pads, prompted toileting, non-indwelling catheters
Urinary incontinence in patients who require skin care but circumstances restrict adequate urinary management strategies and resources are limited	Examples: turning leads to hemodynamic instability or respiratory distress; morbid obesity (weight >300 lb); unstable spine or pelvic fracture; strict immobility after surgical procedure
Hourly urine volume collection for treatment purposes	Examples: patients requiring drips (vasopressors, inotropes); life-supportive therapy in critically ill patients
Daily urine volume collection for treatment purposes	When daily weight measurement and physical exam findings are not sufficient for monitoring: acute renal and heart failure management and fluid overload states requiring intravenous diuretics
Single 24-hour urine collection for diagnostic testing when other urine collection modalities are not acceptable	These modalities include: urinal, bedside commode, bedpan, external catheter, ISC
Reducing acute pain that is severe with movement when other urinary management strategies are not efficacious	Example: pelvic or hip fracture that is unrepaired
Assisting comfort in an actively dying patient	Example: comfort care measures in a patient with severe urinary retention who is agitated with ISC
Gross hematuria in a patient with clots	Example: blood clots in urine that are obstructive
Clinical condition in which ISC and/or external urinary catheterization cannot be accomplished	Examples: experienced nurse or physician unable to place after attempting; bladder emptying was inadequate with ISC or external collection devices

Adapted from Meddings J, Saint S, Fowler KE, et al. The Ann Arbor criteria for appropriate urinary catheter use in hospitalized medical patients: results obtained by using the RAND/UCLA appropriateness method. *Ann Intern Med.* 2015;162(9 Suppl):S1-34.  
ISC, intermittent self-catheterization.

catheterization to prevent stasis and infection.<sup>47</sup> A closed drainage system is recommended in all patients who require long-term indwelling UC use.<sup>48,49</sup> Placement of the collection bag above the catheter or above the level of the bladder and a breach in the closed drainage system have been shown to result in higher rates of catheter-associated bacteriuria.<sup>48,50</sup> Proper hand hygiene and sterile and/or clean techniques should be used when placing or exchanging a UC. However, in one study there was no difference in bacteremia or UTIs when using sterile versus clean techniques.<sup>51</sup>

Asymptomatic bacteriuria should not be treated in patients with long-term indwelling UCs, and prophylactic antibiotics have led to the emergence of resistance.<sup>52</sup> At this time it is not clear whether prophylactic weekly

oral cyclic antibiotic administration can effectively reduce the frequency of CA-UTI in patients with SCI and chronic indwelling UC use.

### ***What are the signs and symptoms of CA-UTI in a patient with SCI?***

Subjective and objective findings may be limited when a patient with SCI presents with CA-UTI. These patients often lack the usual symptoms of UTI (dysuria, suprapubic discomfort, urgency, increased frequency) and pyelonephritis (flank pain, costovertebral angle tenderness). Caregivers and health care providers should be aware that nonspecific symptoms such as foul-smelling urine, pyuria, increased residual volume of urine in the

Table 3. **Inappropriate Use of Indwelling Urinary Catheter in Hospitalized Medical Patients**

Inappropriate UC Uses	Comments
Urinary incontinence in the presence of skin abnormalities that is amenable to nursing care and/or other urinary management strategies	Resources available for proper skin care Intact skin, decubitus ulcer stage I and II Incontinence-associated dermatitis Closed deep-tissue injury
Indwelling catheter use in the ICU without an appropriate indication	Indwelling UC should be removed in critically ill patients when indications are no longer met (eg, resolution of acute renal failure)
Postvoid residual volume assessment	Bladder ultrasound in the best option to assess for urinary retention
Random or 24-hour urine collection when other urine collection modalities are acceptable	These modalities include urinal, bedside commode, bedpan, external catheter, ISC
Family or patient requesting UC placement in a non-dying patient without expected difficulties with urinary management	Risk of developing CA-UTI outweighs the benefit of temporary UC placement  Patients' request for a "break" from ISC should be weighed against risks and benefits of developing CA-UTI and the possibility of inability to continue ISC as an outpatient
UC placement to manage urinary incontinence or retention only for purposes of transportation	Risk of developing CA-UTI outweighs the benefit of temporary UC placement  Nursing staff should be sent with patient if needed
"Bed rest" order when strict immobility is not indicated	Patient should be properly assessed for strict bed rest orders and their indication
Management of frequent and painful UTI	Placement of UC in this situation will likely lead to colonization of UC with pathologic organism
Preventing UTI in a patient with fecal incontinence	No proven benefit in preventing UTI in this population

Adapted from Meddings J, Saint S, Fowler KE, et al. The Ann Arbor criteria for appropriate urinary catheter use in hospitalized medical patients: results obtained by using the RAND/UCLA appropriateness method. *Ann Intern Med.* 2015;162(9 Suppl):S1-34.

CA-HAUTI, catheter-associated urinary tract infection; ISC, intermittent self-catheterization; UC, urinary catheter; UTI, urinary tract infection.

bladder, change in voiding habits, worsening detrusor spasticity, and aggravation of autonomic dysreflexia can be the only initial presenting symptoms.<sup>53</sup>

## ***What is the duration of therapy for CA-UTI in SCI, and how can antibiotic stewardship principles be applied in this patient population?***

Antibiotic therapy is indicated for a duration of 7 days if there is prompt resolution of symptoms, or for a total of 10 to 14 days if the response is delayed, regardless of whether the patient remains with a UC.<sup>5</sup> Antibiotic stewardship is very important to reduce the risk for developing drug resistance in this high-risk population. Methods such as prescriber education practices, institution protocols, guideline implementation, auditing and feedback, restriction and reauthorization practices, computer-assisted programs, de-escalation or streamlining,

and antibiotic cycling or dosage optimization have all been shown to assist in antibiotic stewardship in UTIs.<sup>54</sup>

## **Candida UTI**

### ***What is the initial evaluation for a patient with candiduria?***

The workup for candiduria hinges on determining whether the candiduria likely represents contamination, colonization, or infection; certain predisposing risk factors are associated with *Candida* UTI (**Table 4**).<sup>55-57</sup> The most important aspect to candiduria is the patient's clinical status and comorbid conditions.<sup>58</sup> Among funguria, *Candida* species are the most common and represent 95% of organisms isolated on urine cultures (**Table 5**).<sup>59</sup> Candiduria is usually present in those with significant comorbidities and rarely is associated with healthy individuals.<sup>59,60</sup> Candiduria is increasing in prevalence

Table 4. **Predisposing Risk Factors for Candiduria/Funguria**

Strong Risk Factor	Possible Risk Factor
Diabetes mellitus	Pregnancy
Recent antibiotic use	Malignancy
Genitourinary instrumentation	Recent surgery
Indwelling urinary catheter	Immunosuppression
Intermittent self-catheterization	Neutropenia
Urologic procedure	Steroid use
Urinary tract disease	Renal transplant
Neurogenic bladder	Bedridden status
Urolithiasis	
Bladder outlet obstruction	
Ureteropelvic junction obstruction	
Female gender	
Age > 60 years	

among hospitalized patients, representing 22% to 40% of all nosocomial UTIs.<sup>59,60</sup> Markers in the urine (leukocyte esterase, colony count of culture growth, presence or absence of *Candida* casts and pseudohyphae) cannot alone differentiate colonization from infection.<sup>55</sup> When candiduria is discovered in a patient with symptoms related to UTI in the setting of predisposing risk factors, it should be considered a real infection until proven otherwise.

In a situation where an asymptomatic patient without an indwelling UC has *Candida* species isolated from a urine culture, a repeat culture (clean-catch midstream sample) should be performed to assess for a likely contaminated collection.<sup>55</sup> If the patient has an indwelling UC then it should be exchanged and urine collected from the fresh catheter.<sup>61</sup> When candiduria is found in healthy asymptomatic adults, it is most commonly associated with poor collection techniques or postcollection contamination.<sup>59</sup> If candiduria persists in an asymptomatic patient, the patient should be assessed for predisposing factors. This includes checking hemoglobin A1C for developing diabetes and renal ultrasound looking for urolithiasis, renal abscess, hydronephrosis, and fungus ball. Postvoid residual urinary retention should also be ruled out with bladder ultrasound. Treatment of predisposing factors can lead to resolution of candiduria without antifungal treatment, and a urine culture should be repeated (1 to 2 weeks later).<sup>61</sup> Asymptomatic

Table 5. **Common *Candida* Species Responsible for Candiduria and Urinary Tract Infection**

#### ***Candida albicans***

Most common (50% to 75% of isolates)

Usually sensitive to fluconazole

#### ***Candida glabrata***

Increasing nosocomial infection and common in elderly

Known for resistance to fluconazole

Usually sensitive to echinocandins (echinocandins achieve low urinary concentration)

Highly resistant strains are emerging

#### ***Candida tropicalis***

Usually sensitive to fluconazole

Common cause of candiduria

#### ***Candida krusei***

Uncommon urinary pathogen

Innately resistant to fluconazole

Usually sensitive to echinocandins (echinocandins achieve low urinary concentration)

#### ***Candida parapsilosis***

Associated with central venous line-associated candidemia

Usually fluconazole sensitive

MIC to echinocandins higher than with other species (low urinary concentration)

patients lacking any predisposing factors can be observed with repeat urine cultures in 1 to 3 months.<sup>61</sup>

Candiduria may actually represent candidemia in those patients who have a predisposing risk factor for disseminated candidiasis. These risk factors include central venous catheters, administration of total parental nutrition, antibiotic use (especially broad spectrum), critical illness, recent surgical intervention (especially intra-abdominal), acute renal failure, nasogastric tube use, and active gastric acid suppression (ie, proton pump inhibitors).<sup>62,63</sup> The hematogenous spread of *Candida* can lead to the detection of candiduria in 46% to 80% of persons who are experiencing candidemia.<sup>59</sup> If the patient is at risk for candidemia, then blood fungal cultures should be drawn. It is not unreasonable to also order a serum-D-glucan assay if suspicions are high. A thorough skin assessment should be completed and ophthalmology consulted for a detailed eye exam in the event that the patient has candi-



demia. Candiduria is highly prevalent among those who are candidemic, but overall candidemia is encountered in less than 5% of patients in most intensive care units.<sup>59</sup> Thus, most patients with candiduria do not have disseminated candidiasis.

Candiduria rarely leads to symptoms of UTI,<sup>58</sup> unless the pathogenesis is related to an ascending process.<sup>56</sup> Symptoms of *Candida* UTI are no different from those experienced from a bacterial etiology. Some patients may complain of pneumaturia and/or endorse seeing particulate matter in their urine.<sup>55</sup> Patients showing signs of sepsis (fever, chills, flank pain) should be investigated for possible *Candida* pyelonephritis in the setting of candiduria.<sup>64</sup>

### **When should asymptomatic candiduria be treated?**

In adult patients with asymptomatic candiduria, there are 2 situations in which antifungal therapy is recommended. A patient undergoing a traumatic urologic procedure would be treated to avoid the risk for candidemia caused by the procedure. Also, in neutropenic patients empiric antifungal therapy should be administered because there is a high likelihood that this candiduria may actually represent hematogenous spread from candidemia.<sup>61,65</sup>

### **What is the treatment for symptomatic *Candida* cystitis?**

Empiric treatment with oral fluconazole 200 to 400 mg daily for a total of 2 weeks is recommended in patients with persisting candiduria and symptoms of cystitis.<sup>65</sup> Identifying the species is a crucial step in the treatment of *Candida* UTI. Several species (*C. glabrata*, *C. krusei*) are known to be resistant to fluconazole. Species identification and antifungal sensitivities should be done and therapy directed after obtaining these results.<sup>55</sup>

### **What is the recommended treatment for *Candida* pyelonephritis?**

Treatment for pyelonephritis caused by fluconazole-susceptible *Candida* species is oral fluconazole 200 to 400 mg (3–6 mg/kg) for a total of 2 weeks.<sup>65</sup> A fluconazole-resistant organism should be suspected when a non-albicans *Candida* species is isolated, such as *C. krusei* or *C. glabrata*. In this circumstance, *in vitro*

antifungal susceptibility testing should be done. Echinocandins are not a good option in this situation because they do not reach adequate urine concentration and treatment failure is well documented.<sup>66–68</sup> Amphotericin B deoxycholate (AmB) 0.3 to 0.6 mg/kg daily for 1 to 7 days, with or without oral flucytosine (25 mg/kg) 4 times daily, is recommended by the IDSA for the treatment of fluconazole-resistant isolates of *C. glabrata* and *C. krusei*.<sup>65</sup> Further imaging with ultrasound, CT, or magnetic resonance should be done to rule out urinary tract obstruction and/or “fungus ball” formation. Emphysematous pyelonephritis and necrosis can occur and usually require nephrectomy. Perinephric abscess will need drainage, which can be accomplished through interventional radiological techniques.<sup>55</sup>

### **If a “fungus ball” is suspected in the kidney, how does the management change in a patient with *Candida* pyelonephritis?**

A fungus ball must be treated with both antifungals and surgical intervention. Antifungal therapy should be continued during the surgical removal process to avoid fungemia. Interventional radiology should be consulted and is usually the best option for removal. Fungus ball(s) can and often do cause urinary obstruction. Temporary nephrostomy tube placement may be warranted in these situations to relieve the obstruction.<sup>55,65</sup> AmB can be infused through the nephrostomy tube to increase local concentrations. This route of administration is not known to be nephrotoxic.<sup>55</sup> Fluconazole infusion through a nephrostomy tube has also been used in the successful treatment of a fungus ball.<sup>69</sup>

## **Summary**

Health care–associated UTIs are the most common nosocomial infection in the United States. UC placement and genitourinary manipulation or instrumentation play a major role in the development of CA-UTI. Clinicians should be aware of the appropriate and inappropriate use of UCs and their association with CA-UTI development. Removal of a UC when no longer necessary is key in prevention of CA-UTI. Treatment of asymptomatic bacteriuria is generally not indicated. A multidisciplinary approach is essential when managing chronic indwelling UCs in SCI. PCN and ureteral stenting need close monitoring, and early removal should

be performed if infection is suspected.

Candiduria is an emerging nosocomial source of UTI but rarely leads to symptoms unless related to an ascending process. Proper urine collection is crucial in determining whether you are dealing with contamination, colonization, or infection. If candiduria persists in an asymptomatic individual, then further investigations should be done in regards to possible predisposing risks factors. Fluconazole is recommended for treatment of most patients with *Candida* UTI, while intravenous AmB is the treatment of choice for fluconazole-resistant *Candida* species. As we continue to take an evidence-based approach to the prevention and management of health care-associated UTI, we will likely see continued improvement in patient outcomes and overall decreased rates of infection.

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Financial disclosures: None.

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