Chapter 113: Catheter-associated Urinary Tract Infections in the ICU

CATHETER-ASSOCIATED URINARY TRACT INFECTIONS IN THE ICU: IMPLICATIONS FOR CLINICAL PRACTICE

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OBJECTIVE

Intensive care units (ICUs) represent a meeting point between the most seriously ill patients receiving aggressive therapy and the most resistant pathogens that are selected by the use of broad-spectrum antimicrobial therapy. Most patients who are hospitalized in ICUs receive an indwelling urinary catheter to monitor urine output. Urinary tract infection (UTI) remains a leading cause of nosocomial infections with significant morbidity, mortality, and, hence, additional hospital costs (1). Although UTI represents 10% to 40% of nosocomial infections (1,2), its prevalence in patients admitted to the ICU is approximately 20% (3). In a large European survey, UTI was the third most common cause of nosocomial infections in the ICU (3). Another study suggests that the incidence of urosepsis, defined as an inflammation of the upper urinary tract that causes sepsis, occurs in approximately 20% of patients who are hospitalized in ICUs (4). The aim of this chapter is to focus on the prevention and management of UTI in patients hospitalized in the ICU.

DEFINITIONS

The Centers for Disease Control and Prevention (CDC) definitions of symptomatic UTIs and asymptomatic UTIs are collected in Tables 113.1, 113.2, and 113.3 (5). In the ICU, UTI is the consequence of placement of an indwelling catheter. This results in the concept of catheter-associated UTI, the definition of which is restricted to the presence of bacteria in the bladder of a patient with an indwelling catheter. Bacteriuria is defined as the detection of greater than or equal to 10^5 micro-organisms/mL of urine with no more than two species of organisms (5). It is of interest to note that, contrary to non-ICU-acquired urinary tract infections, this definition does not take into account the clinical symptoms.

PATHOPHYSIOLOGY

With the exception of the distal urethra, the urinary tract is normally sterile. Resistance to UTI is influenced by exposure to uropathogenic bacteria, age, hormonal status, and urine flow...
TABLE 113.1
DEFINITIONS FOR SYMPTOMATIC URINARY TRACT INFECTIONS

| CRITERION 1 | Patient has at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness and patient has a positive urine culture with ≥10^5 micro-organisms/mL of urine with no more than two species of micro-organisms. |
| CRITERION 2 | Patient has at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness and at least one of the following: (a) positive dipstick for leukocyte esterase and/or nitrate; (b) pyuria (urine specimen with 10 white blood cells/μL or ≥3 WBC/high-power field of unspun urine); (c) organisms seen on Gram stain of unspun urine; (d) at least two urine cultures with repeated isolation of the same uropathogen (Gram-negative bacteria or Staphylococcus saprophyticus) with ≥10^5 colonies/mL in nonvoided specimens; (e) ≤10^2 colonies/mL of a single uropathogen (Gram-negative bacteria or S. saprophyticus) in a patient being treated with an effective antimicrobial agent for a urinary tract infection; (f) physician diagnosis of a urinary tract infection; or (g) physician institutes appropriate therapy for a urinary tract infection. |
| CRITERION 3 | Patient ≤1 year of age with at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, dysuria, lethargy, or vomiting and positive urine culture with ≥10^5 micro-organisms/mL of urine with no more than two species of micro-organisms. |
| CRITERION 4 | Patient ≤1 year of age with at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, dysuria, lethargy, or vomiting and (a) positive dipstick for leukocyte esterase and/or nitrate; (b) pyuria (urine specimen with 10 WBC/μL or ≥3 WBC/high-power field of unspun urine); (c) organisms seen on Gram stain of unspun urine; (d) at least two urine cultures with repeated isolation of the same uropathogen (Gram-negative bacteria or S. saprophyticus) with ≥10^5 colonies/mL in nonvoided specimens; (e) ≤10^2 colonies/mL of a single uropathogen (Gram-negative bacteria or S. saprophyticus) in a patient being treated with an effective antimicrobial agent for a urinary tract infection; (f) physician diagnosis of a urinary tract infection; or (g) physician institutes appropriate therapy for a urinary tract infection. |


(6). Insertion of a catheter allows organisms to gain access to the bladder. The catheter induces an inflammation of the urethra, allowing bacteria to ascend into the bladder in the space between the urethral mucosa and the catheter. Catheter-associated UTI usually follows the formation of biofilm, which consists of adherent micro-organisms, their extracellular products, and host components deposited on both the internal and external catheter surfaces. The biofilm protects the organisms from both antimicrobials and the host immune response (7). The ascending route of infection is predominant in women, owing to their short urethra and contamination with anal flora. An internal route of contamination (i.e., through the lumen of the catheter) is less frequent and related to reflux of pathogens from the drainage system into the bladder. This contamination occurs when the drainage system fails to close or contamination of urine in the collection bag.

TABLE 113.2
DEFINITIONS FOR ASYMPTOMATIC URINARY TRACT INFECTIONS

| CRITERION 1 | Patient has had an indwelling urinary catheter within 7 d before the culture and patient has a positive urine culture with ≥10^5 micro-organisms/mL of urine with no more than two species of micro-organisms and patient has no fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness. |
| CRITERION 2 | Patient has not had an indwelling urinary catheter within 7 d before the first positive culture and patient has had at least two positive urine cultures with ≥10^5 micro-organisms/mL with repeated isolation of the same micro-organism and no more than two species of micro-organisms and patient has no fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness. |

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TABLE 113.3

OTHER URINARY TRACT INFECTIONS

One of the following criteria:

| CRITERION 1 | Patient has organisms isolated from culture of fluid (other than urine) or tissue from affected site. |
| CRITERION 2 | Patient has an abscess or other evidence of infection seen on direct examination, during surgical operation, or during a histopathologic examination. |
| CRITERION 3 | Patient has at least two of the following signs or symptoms with no other recognized cause: fever (>38°C), localized pain, or tenderness at the involved site and at least one of the following: (a) purulent drainage from affected site; (b) organisms cultured from blood that are compatible with suspected site of infection; (c) radiographic evidence of infection (e.g., abnormal ultrasound, computed tomography [CT] scan, magnetic resonance imaging [MRI], or radiolabel scan); (d) physician diagnosis of infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space; or (e) physician institutes appropriate therapy for an infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space. |
| CRITERION 4 | Patient ≥3 year of age with at least one of the following signs or symptoms with no other recognized cause: fever (>38°C), hypothermia (<37°C), apnea, bradycardia, dysuria, lethargy, or vomiting and at least one of the following: (a) purulent drainage from affected site; (b) organisms cultured from blood that are compatible with suspected site of infection; (c) radiographic evidence of infection (e.g., abnormal ultrasound, CT scan, MRI, or radiolabel scan); (d) physician diagnosis of infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space; or (e) physician institutes appropriate therapy for an infection of the kidney, ureter, bladder, urethra, or tissues surrounding the retroperitoneal or perinephric space. |


MICROBIOLOGY

The isolated pathogens in ICU patients with bacteriuria are essentially relatively few: Escherichia coli, Pseudomonas aeruginosa, and Enterococcus species (Table 113.4) (8–10). Polymicrobial infections represent a relatively small percentage—5% to 12% (8,9)—of total infections. In a large report investigating nosocomial infections in ICU patients, Gram-negative bacteria caused 71% of UTIs, with stability over a 17-year period of surveillance (10). Resistance to antimicrobials increased during this period, with rates of resistance to third-generation cephalosporins up to 20% for E. coli (10,11). Although its role is demonstrated in a urologic ward, cross-transmission probably plays a much greater role than suggested up to the present (12).

RISK FACTORS

As stated, in ICU patients, UTIs are associated with the presence of indwelling catheters. The first step of prevention is to highlight the risk factors of catheter-associated UTI in this specific population. In a study assessing risk factors for bacteriuria in 553 patients with a urinary catheter for more than 48 hours and hospitalized in an ICU (8), female sex, length of ICU stay, prior use of antibiotics, severity score on admission, and duration of catheterization were independently associated with an increased risk of catheter-associated bacteriuria; these results mirrored those from a previous clinical study (13). Such results emphasize that reducing the duration of catheterization appears to be the most important clinical step that can be identified for prevention. One notable study showed that in 21% of 202 patients, the initial indication for the placement of a urinary catheter was unjustified. In a medical intensive care unit, excessive duration of urinary catheter use for monitoring urine output resulted in 64% of the total of unjustified patient-days (14).

IMPACT OF URINARY TRACT INFECTIONS IN THE INTENSIVE CARE UNIT

Although adverse consequences of asymptomatic UTIs have been described during pregnancy or in nursing home patients (15), the real impact of ICU-acquired UTIs on outcome remains unclear. In a general hospital population, Platt et al. showed that nosocomial UTIs were associated with significant attributable mortality (16). The picture is probably different in a specific ICU population. Indeed, even after controlling for many risk factors, UTIs have a higher incidence in ICUs as compared to other wards (17), although the urinary tract is the source of sepsis in only 10% to 14% of the cases, which is far less than the lung (Table 113.5) (18,19). Development of ICU-acquired UTIs is associated with both an increase in the length of ICU stay and the crude rate of mortality (8,9). However, adequately powered studies demonstrate that UTIs are not dependent factors for mortality (9,17). Urosepsis is defined as an inflammation of the upper urinary tract that causes seeding of the blood with bacteria, resulting in local and distant destruction of tissue. A retrospective study evaluated 126 trauma patients with a urinary catheter for...
TABLE 113.4
PERCENTAGE OF PATHOGENS ASSOCIATED WITH NOSOCOMIAL URINARY TRACT INFECTIONS

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Percentage of isolates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Leone et al.(^{a})</td>
</tr>
<tr>
<td></td>
<td>(n = 53)</td>
</tr>
<tr>
<td>Gram negative</td>
<td></td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>39</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>22</td>
</tr>
<tr>
<td>Enterobacter species</td>
<td>15</td>
</tr>
<tr>
<td>Acinetobacter species</td>
<td>11</td>
</tr>
<tr>
<td>Proteus species</td>
<td>11</td>
</tr>
<tr>
<td>Klebsiella species</td>
<td>11</td>
</tr>
<tr>
<td>Citrobacter species</td>
<td>2</td>
</tr>
<tr>
<td>Gram positive</td>
<td></td>
</tr>
<tr>
<td>Enterococcius species</td>
<td>4</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2</td>
</tr>
<tr>
<td>Coagulase-negative Staphylococcus</td>
<td>2</td>
</tr>
<tr>
<td>Yeast</td>
<td></td>
</tr>
<tr>
<td>Candida albicans</td>
<td>2</td>
</tr>
<tr>
<td>Candida non-albicans</td>
<td>8</td>
</tr>
</tbody>
</table>


Finally, UTIs can incur significant additional cost. An episode of symptomatic nosocomial UTI in a hospitalized patient is expected to result in an average of $676 in additional cost (22). Interestingly, however, a Turkish study calculated the daily antibiotic costs per infected ICU patient. Among the sites of nosocomial infections, urinary tract infections had the lowest daily antibiotic cost per infected patient ($32) (23).

TABLE 113.5
RATES OF SEPSIS ACCORDING TO EACH SITE

<table>
<thead>
<tr>
<th>Sites</th>
<th>Percentages of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vincent et al.(^{a})</td>
</tr>
<tr>
<td></td>
<td>(n = 1,177)</td>
</tr>
<tr>
<td>Lung</td>
<td>68%</td>
</tr>
<tr>
<td>Abdomen</td>
<td>22%</td>
</tr>
<tr>
<td>Blood</td>
<td>20%</td>
</tr>
<tr>
<td>Urine</td>
<td>14%</td>
</tr>
</tbody>
</table>


Urosepsis should be suspected any time a patient has a febrile episode. Because of the prevalence of bacteriuria in patients with urinary catheters, some have advocated daily monitoring of urine in catheterized patients. Routine daily bacteriologic monitoring of the urine from all catheterized patients is not an effective way to decrease the incidence of symptomatic, catheter-associated UTI, and is not recommended (24).

Three clinical trials have assessed the effectiveness of urinary dipsticks (leukocyte esterase and nitrite) for screening patients instead of quantitative urine culture in the ICU (Table 113.6) (25–27). Leukocyte esterase activity is an indicator of pyuria, and urinary nitrite production is an indicator of bacteriuria. In the medical ICU, it has been demonstrated that the urinary dipstick strategy is a rapid and cost-effective test with which to screen asymptomatic catheterized patients. This effectiveness is observed only for a positive quantitative urine culture level of 10⁵ micro-organisms/mL. The urinary dipstick
strategy decreases the cost of diagnosis of nosocomial infection and the daily workload in the microbiology laboratory (25). One limitation of this study is that the incidence of asymptomatic bacteriuria was 31%, as compared with 6% to 9% in other studies (8,9).

In a prior study, analysis of 102 urine samples determined a positive predictive value of 81%. Those authors did not recommend the use of urinary dipsticks (27). Our best sense of these data is that the use of dipsticks—instead of quantitative urine culture—cannot be recommended for symptomatic UTIs in ICU patients. The Infectious Disease Society of America (IDSA) guidelines recommend that asymptomatic bacteriuria or funguria not be screened in patients with an indwelling urethral catheter (28). Hence, in symptomatic patients, quantitative urine culture with Gram stain examination is recommended to obtain rapid identification of the pathogen.

### PREVENTION

The best prevention of ICU-acquired UTIs is to simply reduce the use of indwelling urethral catheters. In a medical ICU, an independent observer determined that 64% of the total unjustified patient-days with urethral catheter resulted from its prolonged use for monitoring urine output (14). Hence, each member of the critical care medicine team should attempt to reduce the length of urethral catheterization and, whenever possible, this evaluation should occur during daily rounds. Other measures, described below, can be useful only in units with a restrictive policy of catheterization (Table 113.7).

#### Urinary Drainage System

In order to prevent infection, the maintenance of a closed sterile drainage system is recommended as the most successful method (29). A closed drainage system was described for the first time in 1928 (30), and its benefit has been subsequently re-enforced (16). A subgroup analysis of a randomized study, in which analyzyed patients did not receive antibiotic treatment, showed a reduction in mortality in the group using the closed system (16). Historically, “open systems” were large, uncapped glass bottles. The drainage catheters were inserted into the glass bottles,

### TABLE 113.6

<table>
<thead>
<tr>
<th>Tissot et al.</th>
<th>Mimoz et al.</th>
<th>Legras et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence (%)</td>
<td>31</td>
<td>38</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>87</td>
<td>84</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>61</td>
<td>41</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>31</td>
<td>46</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>96</td>
<td>81</td>
</tr>
</tbody>
</table>


### TABLE 113.7

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Method (number of patients)</td>
<td>Prospective Not randomized (311)</td>
<td>Prospective Randomized (224)</td>
<td>Prospective Randomized Multicenter (199)</td>
</tr>
<tr>
<td>Rate of bacteriuria (%)</td>
<td>8</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Study group</td>
<td>Two-chamber simple closed drainage system</td>
<td>Two-chamber simple closed drainage system</td>
<td>Catheter coated with hydrogel and silver salts</td>
</tr>
<tr>
<td>Control group</td>
<td>Complex closed system</td>
<td>Complex closed system</td>
<td>Standard catheter</td>
</tr>
<tr>
<td>Conclusion</td>
<td>No difference</td>
<td>No difference</td>
<td>No difference</td>
</tr>
</tbody>
</table>

often below the level of urine. Urine was stagnant, and bacteriuria could easily grow and ascend through the drainage catheter. The introduction of closed drainage systems was a major improvement, and their use has greatly reduced the rate of bacteriuria. However, in the modern era, several studies have failed to confirm the benefit of complex closed systems compared with simple devices (31–33).

There are only two studies in the literature specifically focused on ICU patients (34,35) and comparing a two-chamber, open drainage system with a complex closed drainage system. Both of them, which were performed by the same team of investigators, found similar results, although one of these studies was not randomized (34). In the randomized and prospective trial, 311 patients requiring an indwelling urinary catheter for longer than 48 hours were assigned to the two-chamber drainage system group or to the complex closed drainage system group to compare the rates of bacteriuria. The rates of UTIs were 12.1 and 12.8 episodes per 1,000 days of catheterization, respectively (35). The data extracted from the recent literature do not support the use of complex closed drainage systems in ICU patients in view of the increased cost.

Owing to the lack of specific ICU studies, the guidelines for the management of drainage systems should be viewed as recommendations at best.

The following are reasonable suggestions:

1. Only people who know the proper technique of aseptic insertion and maintenance of the catheter should handle catheters.
2. Hospital personnel should be given periodic in-service training stressing the proper techniques and potential complications of urinary catheterization.
3. Hand washing should be performed immediately before and after any manipulation of the catheter site or apparatus.
4. If small volumes of fresh urine are needed for examination, the distal end of the catheter, or preferably the sampling port of present, should be cleaned with a disinfectant, and urine then aspirated with a sterile needle and syringe.
5. Larger volumes of urine for special analyses should be obtained aseptically from the drainage bag.
6. Unobstructed flow should be maintained.
7. In order to achieve free flow of urine, (a) the catheter and collection tube should be kept from kinking; (b) the collection bag should be emptied regularly using a separate collecting container for each patient (the draining spigot and nonsterile collection container should never come into contact); (c) poorly functioning or obstructed catheters should be irrigated or, if necessary, replaced; (d) collection bags should always be kept below the level of the bladder; and (e) indwelling catheters should not be changed at arbitrary fixed intervals (36).

### Types of Urethral Catheters

There are a large number of articles in the literature that stress the efficacy of antiseptic-impregnated catheters, including silver oxide or silver alloy, and antibiotic-impregnated catheters in hospitalized patients (37–39). The results of two meta-analyses clarify some points (38,39) related to these devices.

Silver oxide catheters are not associated with a reduction in bacteriuria in short-term catheterized adults, whereas silver alloy catheters reduce the incidence of asymptomatic bacteriuria and the risk of symptomatic UTI in catheterized adults. Further, economic evaluation is required to confirm that the reduction of infection compensates for their increased cost. Catheters coated with a combination of minocycline and rifampin or nitrofurazone may also be beneficial in reducing bacteriuria in hospitalized men catheterized less than 1 week, but this requires further testing (38,39). No trials directly compare nitrofurazone-coated and silver alloy-coated catheters.

In a specific ICU patient population, a randomized, prospective, double-blind multicenter trial compared catheters coated with hydrogel and silver salt with classic urinary tract catheters in 199 patients requiring urethral catheterization for more than 3 days (40). The cumulative incidence of UTIs associated with catheterization was 11.1% overall, 11.9% for the control group, and 10% for the coated catheter group. The odds ratio was 0.82 (95% confidence interval [CI] 0.3–2.2). The differences between the two groups were not significant, although the power of the study was more than 90% (40). A prior trial, which included five hospitals selected to participate in a blinded prospective study, exchanged the standard latex Foley catheter for a hydrogel-latex Foley catheter with a monolayer of silver metal applied to the inner and outer surfaces of the device. The adjusted catheter-associated infection rate during the baseline and intervention periods was 8.1 and 4.9 infections per 1,000 catheter-days (p = 0.13), respectively (41).

### Meatal Care

Twice-daily cleansing of the urethral meatus with povidone-iodine solution and daily cleansing with soap and water have failed to reduce catheter-associated UTIs. Thus, at this time, daily meatal care with either of these two regimens cannot be endorsed.

A randomized, controlled, prospective clinical trial involving 696 patients hospitalized in medical and surgical units was undertaken to determine the effectiveness of 1% silver sulfadiazine cream applied twice daily to the urethral meatus in preventing transurethral catheter-associated bacteriuria. The overall incidence of bacteriuria was approximately 13% in both groups (p = 0.56) (42). The absence of data from an ICU-specific patient population, the current guidelines should be followed.

There are no data available on the level of sterility required to insert a urinary catheter. Experts recommend that catheters should be inserted using an aseptic technique and sterile equipment, including gloves, drapes, and sponges. However, in a prospective study conducted in the operating room, 156 patients underwent preoperative urethral catheterization, randomly allocated to “sterile” or “clean/sterile” technique groups. There was no statistical difference between the two groups with respect to the incidence of UTI, but the cost differed considerably between the two groups (43).

### Vesical Irrigation and Antiseptic in the Drainage System

The objective of antibiotic irrigation is to clear bacteria from the urinary tract. A randomized study compared 89 patients receiving a neomycin-polymyxin irrigation administered through
a closed urinary catheter to 98 patients not so irrigated. Al-
though the number of ICU patients was not specified in this
case study, 19 of the 98 (18.5%) patients not irrigated became
infected as compared with 14 out of the 89 (16%) of those who
were irrigated; the organisms from the irrigated patients were
more resistant (44). Another study also investigated in 264 uro-
ology patients, evaluating the effect of povidone-iodine bladder
irrigation prior to catheter removal on subsequent bacteriuria.
Of 264 patients, 138 received irrigation and 126 were controls.
Urines were positive in 22% in the control group and 18% in the study group (45). Thus, irrigation methods failed to
demonstrate efficacy in surgical patients, and its use is not
recommended in ICU patients.

The addition of antimicrobial agents to the drainage device
has not been studied in the ICU. The largest reported clinical
trial evaluating the effect of H2O2 insertion into the drainage
device of 353 patients, and comparing this to 315 control pa-
tients, failed to show a benefit in the treatment group. It is
of interest to note that 68% of these patients required an in-
dwelling catheter for hemodynamic monitoring, with anti-
microbial therapy prescribed in 75% of the patients, suggesting
that these results may apply to ICU patients (46). Expert opin-
ion recommends that we not use irrigation unless obstruction
is anticipated, as might occur with bleeding after prostatic or
bladder surgery.

Alternatives to a Urinary Catheter

For selected patients, other methods of urinary drainage, such
as condom catheterization, suprapubic catheterization, and intermit-
tent urethral catheterization, should be considered as alterna-
tives to indwelling urethral catheterization. There are limited
ICU data available to assess these alternative devices. There is
evidence, however, that suprapubic catheterization is advan-
tageous, as compared to indwelling catheters, with respect to
bacteriuria, recatheterization, and discomfort (47,48). The use
of a condom connected to a collection bag has been evalu-
at ed in a study comparing 167 patients over two periods of
6 months. The occurrence of bacteriuria was significantly de-
creased for the period using the condom catheters (26.7 vs.
2.4%) (49). However, this issue merits further study to deter-
mine whether or not this alternative method may actually re-
duce bacteriuria rates. The use of intermittent catheterization is
also associated with a lower risk of bacteriuria than indwelling
urethral catheter, although such a procedure has never been
investigated in ICU patients (48,50,51).

Miscellaneous Measures

While there is a low risk of bacteremia during urinary catheter-
ization (52), the administration of antimicrobial therapy at the
time the device is placed leads to a reduction in bacteriuria
(53–55). The efficacy of antibiotic treatment has been assessed
as optimal for catheterization lasting less than 14 days (54).
However, the prophylactic use of antibiotic in the ICU can
be detrimental to the bacterial ecology by increasing the pres-
sure for antimicrobial resistance among bacteria. The practice
of administration of prophylactic antimicrobials in this man-
ner must be discouraged in our ICUs. It should be noted that
in most ICU studies, 75% of the patients with an indwelling
catheter require antibiotics for reasons unrelated to the urinary
catheter (8). Further, all measures aimed at reducing the burden
of nosocomial infections can reduce the rate of UTIs (56–58).

TREATMENT AND MANAGEMENT

The management of catheter-associated UTI has not been eval-
uated in ICU patients. Several nonspecific measures, including
hydration, have been advocated in the therapy of UTI. Ade-
quate hydration would appear to be important, although there
is no evidence that it improves the effectiveness of an appro-
priate antimicrobial therapy (59). The management of compli-
cated UTIs in the ICU may include mechanical intervention.
Consequently, appropriate diagnostic tests and urologic con-
sultation should be included in the algorithm of the manage-
ment of these patients (Fig. 113.1).

Management of Asymptomatic Bacteriuria

According to leaders in our field, asymptomatic catheter-
associated UTI does not require treatment (28). However, an-
timicrobial treatment may be considered for asymptomatic
women with a catheter-acquired UTI that persists 48 hours
after catheter removal (60). In a specific ICU patient popula-
tion, 60 patients with an indwelling urethral catheter for longer
than 48 hours who developed an asymptomatic positive urine
culture were randomized to receive either a 3-day course of
antibiotics associated with the replacement of the indwelling
urethral catheter 4 hours after the first antibiotic administra-
tion or no antibiotics and no catheter replacement. Six patients
equally distributed in the two groups developed urosepsis. The
profile of bacterial resistance was similar in the two groups.
Hence, treating a positive urine culture in an asymptomatic
patient with an indwelling urethral catheter does not reduce the
occurrence of urosepsis (20).

Management of Symptomatic Urinary Tract Infections

Choice of Antimicrobial Agents

The optimal characteristics of agents to treat urinary tract in-
fec tion must include activity against the major pathogens in-
volved in these infections, good tissue penetration, and minimal
side effects. High urinary levels should be present for an ade-
quate period to eliminate the organisms, since disappearance
of bacteriuria correlates with the sensitivity of the pathogen
to the concentration of the antimicrobial agent achieved in the
urine (61). Inhibitory urinary concentrations are achieved af-
ter administration of essentially all commonly used antibiotics.
However, an antibiotic that achieves active concentrations in
the renal tissue is required for infection of the renal tissue. The
antibiotic concentration in the serum or plasma can be used as
surrogate markers for the antibiotic concentrations in the renal
tissue (62). For drugs with concentration-dependent time-kill
activity such as the aminoglycosides or the fluoroquinolones,
the peak antibiotic concentration is the most important pa-
rameter for the in vivo effect. Experimentally, gentamicin and
fluoroquinolone treatment are both more effective than the β-lactam antibiotics in rapid bacterial killing (62).

Most clinical studies have shown that the renal concentrations of the cephalosporins remained higher than the minimal inhibitory concentration for the most common bacteria during the time interval between the administration of two doses (63–65). By contrast, β-lactam antibiotics, which have a low pKa and poor lipid solubility, penetrate poorly into the prostate, except for some cephalosporins. Good to excellent penetration into the prostatic tissue has been demonstrated with many antimicrobial agents, such as aminoglycosides, fluoroquinolones, sulfonamides, and nitrofurantoin (66).

In ICU patients, the side effects of treatment should be minimized at both the individual and the community level. Many patients develop renal failure, associated with the inability to concentrate antimicrobial agents in the urine. Additionally, administration of drugs with potential renal toxicity may worsen renal insufficiency. This may be an important limiting factor for using aminoglycosides in patients with renal failure. Otherwise, antimicrobial treatment must produce a minimal effect on the bacterial flora of the community (67). From this standpoint, there is significant literature demonstrating that the use of fluoroquinolone is associated with the emergence of resistant pathogens (68–70). This implies that an indication for antibacterial therapy should be weighed thoroughly and fluoroquinolones should be used in accordance with sensitivity testing (70). Hence, it is of importance to stress that UTI should not be treated before the results of sensitivity testing, except in patients with pyelonephritis and those with severe sepsis or septic shock who require empirical antimicrobial therapy.

### Cystitis

As acute uncomplicated cystitis is infrequent in ICU patients, most recommendations focus on the treatment of nonhospitalized women, which makes their relevance in ICU patients questionable; _E. coli_ is the evident target pathogen. The 1999 IDSA guidelines recommend treatment with trimethoprim-sulfamethoxazole for 3 days as standard therapy for acute uncomplicated cystitis. Single-dose therapy is less effective in eradicating initial bacteriuria than longer durations of treatment with trimethoprim-sulfamethoxazole, trimethoprim, norfloxacin, ciprofloxacin, fleroxacin, and, as a group, β-lactam antibiotics (71). In contrast, a meta-analysis determined that 3 days of antibiotic therapy is similar to 5 to 10 days in achieving symptomatic cure during uncomplicated UTI treatment, while the longer treatment is more effective in obtaining bacteriologic cure. Consequently, such durations should be considered for treatment of women in whom eradication is critical (72). Quinolones are recommended for acute cystitis in regions where the level of resistance to trimethoprim-sulfamethoxazole is high. There were no significant differences in clinical or microbiologic efficacy between quinolones. The rate of adverse events causing antimicrobial withdrawal tends to be lower with norfloxacin and ciprofloxacin than with other quinolones (73).

Antibiotic treatment of UTI depends on the ability of the antibiotic to inhibit the growth or kill the bacteria present in the urinary tract. This is related to the concentration of antibiotics at the site of infection. Very high concentrations of antibiotics with renal clearance are obtained in urine. Consequently, even in the presence of pathogens exhibiting _in vitro_ resistance, the high concentrations of antibiotics in urine inhibit the growth of pathogens, rendering them effective to treat a UTI.

### Prostatitis

For outpatients, bacterial prostatitis is a common diagnosis and a frequent indication for antibiotics. Although urethral instrumentation and prostatic surgery are known causes of prostatitis, the incidence of prostatitis among ICU patients has never

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**FIGURE 113.1.** Suggested algorithm for the management of urinary tract infections related to an indwelling catheter in the intensive care unit. CT, computed tomography. *Discuss the need for antipseudomonal coverage according to the duration of hospitalization, prior medical history, and local ecology. Discuss renal failure.

**TABLE 113.1.** Duration of treatment for uncomplicated urinary tract infections (UTIs) in inpatient and outpatient settings.

<table>
<thead>
<tr>
<th>Inpatient Setting</th>
<th>Outpatient Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptomatic Cystitis</strong></td>
<td><strong>Acute Cystitis</strong></td>
</tr>
<tr>
<td>Single-dose therapy</td>
<td>Single-dose therapy</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Acute Pyelonephritis</strong></td>
<td><strong>Acute Pyelonephritis</strong></td>
</tr>
<tr>
<td>Parenteral therapy</td>
<td>Parenteral therapy</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe Pyelonephritis</strong></td>
<td><strong>Severe Pyelonephritis</strong></td>
</tr>
<tr>
<td>Parenteral therapy</td>
<td>Parenteral therapy</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urinary Tract Infection</strong></td>
<td><strong>Urinary Tract Infection</strong></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bacteriuria in patient with an indwelling urethral catheter</strong></td>
<td><strong>Bacteriuria in patient with an indwelling urethral catheter</strong></td>
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<tr>
<td></td>
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</tr>
</tbody>
</table>
been assessed, and there is only a weak relation between acute and chronic prostatitis.

Acute prostatitis is an acute infection producing local heat, tenderness, and fever, with the presence of IgA and IgG bacteria-specific immunoglobulins in the prostatic secretions. Few symptoms, usually perineal discomfort, are exhibited with prostatitis. Most patients with chronic prostatitis have no history of positive urine or urethral cultures (74).

In ICU patients, acute bacterial prostatitis is probably a common infection. The patient presents septic, but without an evident source of infection. There may be a history of urine retention due to bladder outlet obstruction. Rectal examination, a crucial step in the diagnosis, reveals a warm, swollen, and tender prostate. The prostatic fluid contains leukocytes and the pathogen responsible for the infection. However, massage of the prostate is proscribed to avoid bacteremia. Fluoroquinolones are the drugs of choice to treat acute prostatitis because of their excellent penetration in the tissue and excretions (75,76). The targeted pathogens are E. coli, Proteus sp., Klebsiella sp., Enterococcus sp., Staphylococcus aureus, Neisseria gonorrhoeae, and Chlamydia trachomatis. For acute prostatitis occurring without bacteremia, antimicrobial treatment consists of oral ofloxacin 200 mg twice per day for 28 days; ceftriaxone 2 g/day has good prostatic tissue penetration and represents an alternative to ofloxacin (77). Gentamicin 3 mg/kg/day is added in the presence of positive blood cultures (Table 113.8). Of importance, urethral instrumentation should be discouraged, and if acute retention occurs, suprapubic drainage of urine is required. Treatment of chronic prostatitis is based on the oral administration of ofloxacin 200 mg twice per day, or trimethoprim 160 mg–sulfamethoxazole 800 mg twice per day for at least 28 days. The indications for this treatment should be discussed with specialists.

### Acute Pyelonephritis

There are no specific data available in the literature on the management of acute pyelonephritis in the ICU. The urine of all patients with suspicion of complicated pyelonephritis should be cultured and a Gram stain of the spun urine performed. Blood cultures, which are positive in 36% of women not admitted to the ICU, are also required (78). All patients with acute pyelonephritis should have an ultrasound examination or a renal computed tomography scan to evaluate for obstruction and stones.

For uncomplicated acute pyelonephritis, the IDSA, in 1999, derived two conclusions from the analysis of randomized clinical trials. The first is that trimethoprim-sulfamethoxazole is preferred over ampicillin. Indeed, there is a relatively high prevalence of organisms causing acute pyelonephritis that are resistant to ampicillin, and even for susceptible organisms, there is a significantly increased recurrence rate in patients given ampicillin compared with those given trimethoprim-sulfamethoxazole. The second conclusion is that 10 to 14 days of therapy appears to be adequate for the majority of women (71). There has been little additional information since the publication of these recommendations. However, 255 outpatients were randomized to oral ciprofloxacin, 500 mg twice per day for 7 days, followed by placebo for 7 days versus trimethoprim-sulfamethoxazole, 160/800 mg twice per day for 14 days. In this study, a 7-day ciprofloxacin regimen was associated with greater bacteriologic and clinical cure rates than a 14-day trimethoprim-sulfamethoxazole regimen (79).

### Table 113.8

<table>
<thead>
<tr>
<th>Source of infection</th>
<th>Pathogens</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute prostatitis (without bacteremia)</td>
<td>Escherichia coli, Proteus sp., Klebsiella sp., Enterococcus sp., Staphylococcus aureus, Neisseria gonorrhoeae, Chlamydia trachomatis</td>
<td>Ofloxacin 200 mg twice daily (oral)</td>
<td>28 d</td>
</tr>
<tr>
<td>Acute prostatitis (with bacteremia)</td>
<td>E. coli, Proteus sp., Klebsiella sp., Enterococcus sp., S. aureus, N. gonorrhoeae, C. trachomatis</td>
<td>Ofloxacin 200 mg twice daily (oral) or Ceftriaxone 2 g/d and gentamicin 3 mg/kg/d IV</td>
<td>28 d</td>
</tr>
<tr>
<td>Chronic bacterial prostatitis</td>
<td>E. coli, Proteus sp., Klebsiella sp., Enterococcus sp., S. aureus, N. gonorrhoeae, C. trachomatis</td>
<td>Ofloxacin 200 mg twice daily (oral) or Trimethoprim 160 mg–sulfamethoxazole 800 mg twice daily (oral)</td>
<td>28 d</td>
</tr>
<tr>
<td>Acute pyelonephritis (uncomplicated)</td>
<td>Enterobacteriaceae, E. coli, Proteus sp., Enterococcus sp.</td>
<td>Ciprofloxacin 500 mg twice daily (oral)</td>
<td>14 d</td>
</tr>
<tr>
<td>Acute pyelonephritis (complicated)</td>
<td>Enterobacteriaceae, E. coli, Proteus sp., Enterococcus sp.</td>
<td>Ciprofloxacin 500 mg twice daily (oral) or Ceftriaxone 2 g/d IV AND Gentamicin 3 mg/kg/d</td>
<td>14–21 d</td>
</tr>
</tbody>
</table>

Each empirical treatment must be adapted to the susceptibility testing results.
Patients with complicated acute pyelonephritis should be hospitalized and initial administration of broad-spectrum intravenous antibiotics begun. The targeted bacteria are *Enterobacter* sp., *E. coli*, *Proteus* sp., and *Enterococcus* sp. Ciprofloxacin, 500 mg twice daily, is administered orally for 14 to 21 days. Gentamicin, 3 mg/kg/day intravenously, is added during the first 3 days. Interestingly, oral ciprofloxacin is as effective as the intravenous regimen in the initial empirical management of complicated pyelonephritis (81), and ciprofloxacin is as effective as ciprofloxacin (80). If needed, ceftriaxone, 2 g/day intravenously, is an alternative choice to ciprofloxacin. Further, the success rates are similar in patients given ceftriaxone or erythromycin (82).

The drainage of urine must be urgently performed using bladder catheterization, percutaneous nephrostomy drainage, or definitive surgery. Antimicrobial treatment is administered after urine and blood specimen collection. The antibiotic selection is based on the result of the Gram stain of the urine and the knowledge of the local ecology. Antimicrobial treatment should be adapted to the susceptibility testing results as soon as possible, and de-escalation should be performed in favor of a narrow-spectrum antibiotic.

**Specificities of Complicated Urinary Tract Infections in the Intensive Care Unit**

Although there is little in the literature on the treatment of UTI in the ICU, one presumes the need for intravenous antibiotics for these patients because of the possibility of bacteremia or sepsis. The guidelines from the Surviving Sepsis Campaign state that (a) antibiotic therapy should be started within the first hour of recognition of severe sepsis, after appropriate cultures have been obtained; (b) initial empirical anti-infective therapy should include one or more drugs that have activity against the likely pathogens and that penetrate the presumed source of sepsis; and (c) monotherapy is as effective as combination therapy with a β-lactam and an aminoglycoside as empiric therapy of patients with severe sepsis or septic shock (83). Hence, empirical antimicrobial therapy should include drugs with good penetration in the urinary tract, and the choice is guided by the susceptibility patterns of micro-organisms in the hospital. For the septic shock patients whose presumed source is urine, we recommend, empirically, a combination of a β-lactam antibiotic with antipseudomonal activity and a fluoroquinolone. This broad-spectrum treatment is narrowed as soon as the results of the susceptibility testing are known. The durations of treatment should be tailored to the source of infection.

**Management of Candiduria**

Candiduria represents from 3% to 51% of catheter-associated UTI in the ICU (8,9,13). *Candida albicans* and *Candida glabrata* are found in 46% and 31% of cases, respectively (84). According to the International Conference for the Development of a Consensus on the Management and Prevention of Severe Candidal Infections, colonized patients without evidence of infection do not require treatment, but the contributing cause should be addressed, such as changing or removing the indwelling catheter and discontinuing inappropriate antibiotic therapy. Fluconazole may be the best option for treating a candiduria (85), but only if the species is *C. albicans*. Voriconazole may be more effective against non-*albicans* species.

Clinician reaction to isolating *Candida* organisms in urine was assessed in a retrospective review of 133 consecutive patients. The average patient age was 68.8 years old, most (78%) had an indwelling catheter, and many (35%) were in the ICU. In response to culture results, clinicians initiated antifungal therapy in 80% of patients. Treatment was often based on a single culture result without evidence of infection (66%) and in the absence of risk of invasive disease. Removal of the indwelling catheter was never attempted and antibiotics were rarely discontinued or modified (1.3%). Fluconazole was most frequently utilized (52%), followed by amphotericin B bladder irrigation (32%) and combined fluconazole/amphotericin B bladder irrigation (13%). Therapy was more frequently initiated in ICU cases (77 vs. 36%; p = 0.02) (86). These results show the poor adherence to guidelines.

A prospective, randomized trial compared fungal eradication rates among 316 hospitalized patients with candiduria treated with fluconazole (200 mg) or placebo daily for 14 days. Candiduria cleared by day 14 in 50% of the patients receiving fluconazole and 29% of those receiving placebo, with higher eradication rates among patients completing 14 days of therapy. Fluconazole initially produced high eradication rates, but cultures at 2 weeks revealed similar candiduria rates among treated and untreated patients. In 41% of the catheterized subjects, candiduria was resolved as the result of catheter removal only. The outcomes of patients were not provided in the results (87).

Bladder irrigation using amphotericin B has been proposed as an alternative technique to clear *Candida* from the urine. A comparative and randomized study of 109 elderly patients showed that funguria was eradicated in 96% of the patients treated with amphotericin B and 77% of those treated with fluconazole (p < 0.05). One month after study enrollment, the mortality rate associated with all causes was greater among patients who were treated with amphotericin B bladder irrigation than among those who received oral fluconazole therapy (41% vs. 22%, respectively; p < 0.05). This finding suggests that irrigation therapy could be associated with poorer survival (88).

There has only been one study performed in ICU patients developing candiduria, which reached the same conclusions; unfortunately, methodologic issues restrict the interest of this study. The authors retrospectively compared three means to manage candiduria in ICU patients: successful bladder irrigation with amphotericin B (10 of 27 patients), failure of bladder irrigation requiring the use of parenteral amphotericin B (17 of 27), and patients treated with parenteral fluconazole (n = 20). Severity score on admission day was significantly lower in the first group than in the two others. However, the mortality rate was 53% and 5% in patients experiencing a failure of bladder irrigation and in patients receiving fluconazole, respectively (89). These results must be considered with caution because of serious methodologic limitations. However, these data indicate that bladder irrigation of critically ill patients has a negative survival advantage.

**SUMMARY**

Bacteria in the bladder constitute a reservoir for the development of multiresistant bacterial strains, and the rate of bacteriuria may be used as a marker of the level of care in the...
ICU. Prevention of UTIs in the ICU is not improved by the use of expensive devices, but can reflect the level of general unit hygiene. While management of UTIs in the ICU is poorly described in the literature, it is reasonably clear that there is no need to treat asymptomatic bacteriuria. However, although infection, isolated episodes with a urinary source requires empirical broad-spectrum antimicrobial treatment based on the local bacteriologic ecology. Treatment is de-escalated after identification of the broad-pathogen and reporting of the susceptibility testing.

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CHAPTER 114  ■  FUNGAL AND VIRAL INFECTIONS

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FUNGAL INFECTIONS

Fungal Pathogens

Medically relevant fungi are classically considered as one of three types of organisms: yeasts, molds, or dimorphic agents.

The yeasts grow as smooth colonies on culture plates. Microscopically, they are oval or spherical, and they reproduce by budding. The two most common human yeast pathogens are Candida spp. and Cryptococcus spp., the molds appear as fuzzy colonies on agar plates. Microscopically, they have hyphae, which are tubular or filamentous morphologies that grow by branching and longitudinal extension. Hyphae can

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