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#### **TERMINOLOGY**

The term *cystitis* has been used to describe the syndrome involving dysuria, frequency, urgency, and occasionally suprapubic tenderness.

However, these symptoms may be related to lower tract inflammation without bacterial infection and can be caused by urethritis (e.g., gonorrhea, chlamydial urethritis). Furthermore, the presence of symptoms of lower tract infection without upper tract symptoms by no means excludes upper tract infection, which may also be present.

- Acute pyelonephritis describes the clinical syndrome characterized by flank pain, tenderness, or both, and fever, often associated with dysuria, urgency, and frequency. However, these symptoms can occur in the absence of infection (e.g., in renal infarction or renal calculus).
- *Uncomplicated* UTI refers to infection in a structurally and neurologically normal urinary tract.

- The generally accepted definition of complicated UTI includes:
  - infection in the presence of factors that predispose to persistent or relapsing infection, such as foreign bodies (e.g., calculi, indwelling catheters or other drainage devices);
  - obstruction;
  - immunosuppression;
  - renal failure;
  - renal transplantation; and
  - urinary retention from neurologic disease.
  - In addition, infection in men, pregnant women, children, and patients who are hospitalized or in health care—associated settings may be considered complicated.

• In the patient with complicated infection, infecting microorganisms are more

likely to be resistant to antimicrobial agents.

- Recurrences of UTI may be relapses or reinfections.
- Relapse of bacteriuria refers to a recurrence of bacteriuria with the same infecting microorganism that was present before therapy was started. This is caused by the persistence of the organism in the urinary tract.
- Reinfection is a recurrence of bacteriuria with a microorganism different from the original infecting bacterium. It is a new infection. Reinfection may occur with the same microorganism, which may have persisted in the vagina or feces. This can be mistaken for a relapse.

- The term **urosepsis** has been commonly used to describe the sepsis syndrome caused by UTI.

  Although used in the literature, this term should not be used in clinical documentation because it is not considered synonymous with sepsis for the purposes of coding. Utilizing the term *sepsis* and indicating the specific clinical syndrome to which the sepsis is secondary (e.g., pyelonephritis or acute prostatitis) is a better way to refer to sepsis secondary to infection in the urinary tract.
- Increasingly the term *febrile urinary tract infection* is utilized; these infections can occur with or without concomitant sepsis.



## SEPSIS STEPS

#### **SIRS**

T: >100.4 F

< 96.8 F

RR: >20

HR: >90

WBC: >12,000

<4,000

>10% bands

PCO2 < 32 mmHg

#### SEPSIS

2 SIRS

+

Confirmed
or suspected
infection

#### SEVERE SEPSIS

Sepsis +

Signs of End Organ Damage

Hypotension (SBP <90)

Lactate >4 mmol

## SEPTIC SHOCK

Severe Sepsis with persistent:

Signs of End Organ Damage

Hypotension (SBP <90)

Lactate >4 mmol

Slides Courtesy of Curtis Merritt, D.O.

- Escherichia coli is the most frequent infecting organism in initial infections.
- In recurrent UTIs, especially with complicated UTI (e.g., obstructive uropathy, congenital anomalies, neurogenic bladder, fistulous communication involving the urinary tract), the relative frequency of infection caused by bacteria such as Proteus, Pseudomonas, Klebsiella, and Enterobacter spp., by antibiotic-resistant E. coli, and by enterococci and staphylococci increases greatly. In the presence of complicated UTI, it is not uncommon to isolate multiple organisms from the urine.

• UTIs are much more common in women than in men. Premenopausal women are at especially high risk for acute cystitis. The strongest risk factors in premenopausal women include sexual intercourse, use of spermicides, and history of previous UTI, as well as diabetes. In this population, risk factors suggesting a genetic component are a history of maternal UTI and age of first UTI.

• At least 10% of men and 20% of women older than 65 years have asymptomatic bacteriuria. In contrast to young adults, in whom bacteriuria is 30 times more frequent in women than in men, in those older than 65 years the ratio alters dramatically, with a progressive decrease in the female-to-male ratio.

- . Possible reasons for the high frequency of asymptomatic bacteriuria in older patients include:
  - obstructive uropathy from the prostate (with resultant instrumentation)
  - loss of the bactericidal activity of prostatic secretions in men,
  - poor emptying of the bladder because of prolapse in women,
  - soiling of the perineum from fecal incontinence in demented women,
  - and neuromuscular diseases and increased instrumentation and bladder catheter usage in both genders.

The majority of older men with UTI have underlying urologic abnormalities. Urinary incontinence also contributes to UTI in postmenopausal women. There is a high rate of spontaneous cure and reinfection with asymptomatic bacteriuria in women and men. The spectrum of microorganisms is unaltered in the older adult population. Symptomatic infection uncommonly follows asymptomatic bacteriuria, and asymptomatic bacteriuria is much more frequent than symptomatic UTI in this age group.

 Asymptomatic bacteriuria in older persons does not seem to have any deleterious effects. Furthermore, there is no evidence to suggest that treatment of asymptomatic bacteriuria in older patients has any beneficial effects, including decreasing urinary incontinence. Therefore routine treatment of asymptomatic bacteriuria in older patients is not indicated. Effective management of symptomatic episodes in older males requires determining whether the site of infection is the kidney, bladder, or prostate.

## TABLE 72.3 Risk Factors for Urinary Tract Infection (UTI)

Age	Female	Male
All ages	Previous UTI  Urologic instrumentation or surgery Urethral catheterization Urinary tract obstruction, including calculi Neurogenic bladder Renal transplantation	Lack of circumcision (children and young adults) Urologic instrumentation or surgery Urethral catheterization Urinary tract obstruction, including calculi Neurogenic bladder Renal transplantation
Adults	UTIs in female relatives Sexual intercourse  New sex partner Lack of urination after intercourse Spermicidal contraceptive jellies Diaphragm use Pregnancy Lower socioeconomic group Diabetes Possibly sickle cell trait in pregnancy	Insertive rectal intercourse Vaginal <i>Escherichia coli</i> colonization in partner
Older age	Functional or mental impairment Estrogen deficiency (loss of vaginal lactobacilli) Bladder prolapse	Prostatic enlargement ndows  Condom catheter drainage

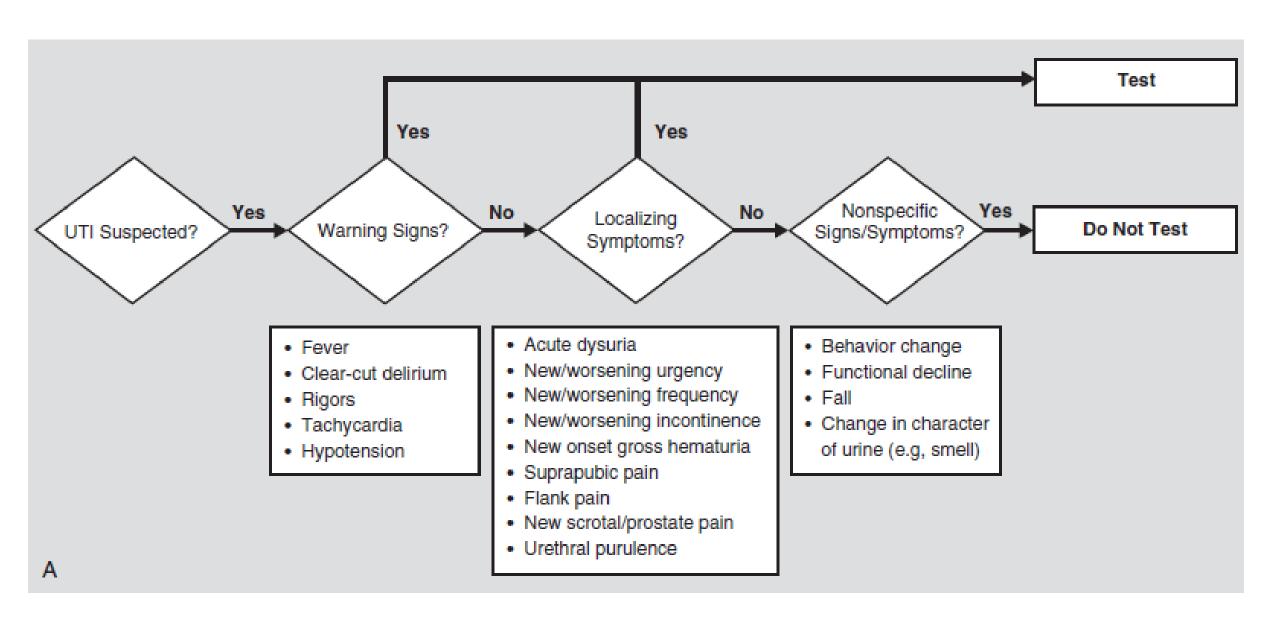
#### DIAGNOSIS

- Presumptive Diagnosis of Urinary Tract Infection
- Using the preferred definition of pyuria, which is at least 10 leukocytes/ mm3 of midstream urine by counting chamber, the vast majority of patients with symptomatic or asymptomatic bacteriuria have pyuria. In fact, with symptomatic infection, most have hundreds of leukocytes per cubic millimeter. A less reliable method uses a urine specimen that is centrifuged for 5 minutes at 2000 rpm and then the sediment is examined under high power. With this method, 5 to 10 leukocytes/high-power field in the sediment is the upper limit of normal. It should be emphasized that the finding of pyuria is nonspecific, and patients with pyuria may or may not have infection. The absence of pyuria should strongly call into question a diagnosis of UTI.

 The dipstick leukocyte esterase test is a rapid screening test for detecting pyuria and has largely replaced microscopic methods. Although the sensitivity and specificity are high for detecting more than 10 white blood cells/mm<sub>3</sub> of urine (75%–96% and 94%–98%, respectively), a positive test by no means indicates UTI; in patients with a negative leukocyte esterase test and UTI symptoms, a urine microscopic examination for pyuria or a urine culture should be considered.

- Microscopic or sometimes gross hematuria is occasionally seen in patients with UTI (i.e., hemorrhagic cystitis). However, red blood cells may be indicative of other disorders, such as calculi, tumor, vasculitis, glomerulonephritis, and renal tuberculosis.
- White cell casts in the presence of an acute infectious process are strong evidence for pyelonephritis, but the absence of white cell casts does not rule out upper tract infection. White cell casts can also be seen in renal disease in the absence of infection.
- Proteinuria is a common although not universal finding in UTI. Most patients with UTI excrete less than 2 g of protein/24 h; excretion of 3 g/24 h or more suggests glomerular disease.

• The ability to identify bacteria in the urine depends on whether the specimen has been centrifuged and on whether it has been stained with Gram or methylene blue stain. Smaller numbers of bacteria can be detected microscopically in a stained than in an unstained specimen, and smaller numbers can be detected in centrifuged than in uncentrifuged urine. The presence of at least one bacterium per oil immersion field in a midstream clean-catch, Gram-stained, uncentrifuged urine specimen correlates with 10 bacteria/mL of urine or more.



#### **Acute Uncomplicated Cystitis**

• Case 1: A 27-year-old woman calls her physician's office reporting 3 days of a burning sensation during urination with urinary frequency and discomfort in her lower abdomen. She recalls having the same symptoms a year ago, which was the only other time she was treated for a UTI. She is otherwise healthy and takes no medications. Her last menstrual period was 2 weeks ago.

Question 1: What is the best next step in the management of this patient?

- (a) Ask her to submit a urine sample for urinalysis and urine culture and recommend antibiotics pending culture results.
- (b) Prescribe ciprofloxacin 500 mg twice daily for 7 days.
- (c) Prescribe nitrofurantoin 100 mg twice daily for 5 days.
- (d) Prescribe amoxicillin 875 mg twice daily for 5 days.
- (e) Prescribe cefpodoxime 100 mg twice daily for 5 days.

#### **Diagnosis and Testing**

- Acute uncomplicated cystitis (also known as "simple cystitis") is a type of UTI, specifically an infection of the bladder in an otherwise immunocompetent host with normal urinary tract anatomy.
- The classic symptoms are dysuria, urinary frequency, urinary urgency, or suprapubic pain in the absence of systemic illness (eg, fever, rigors, or vomiting) or upper urinary tract involvement (eg, flank pain or costovertebral angle tenderness).

 Testing with urinalysis or urine culture up front is not indicated in most cases of uncomplicated cystitis. Having classic symptoms of acute uncomplicated cystitis, as in case 1, can be sufficient to make a clinical diagnosis.

The following are examples of situations where a urinalysis and urine culture should be sent when evaluating a patient for a UTI:

- Signs or symptoms of upper tract disease or systemic illness.
- Atypical symptoms, such as a patient who has dysuria and vaginal symptoms that are also suggestive of vaginitis.
- Patients at high risk of developing complications, such as those who are immunocompromised or have urological abnormalities.
- Patients at risk of infection with multidrug-resistant organisms (MDRO), such as those with a history of infections with MDROs or who have had recent courses of antibiotics or a recent hospitalization.
- Lack of improvement or progression of symptoms

Table 2. Oral Antibiotics for the Management of Cystitis and Pyelonephritis

Antibiotic	Acute Uncomplicated Cystitis	Pyelonephritis
Nitrofurantoin	<ul> <li>First-line agent</li> <li>100 mg twice daily for 5 days<sup>a</sup></li> </ul>	<ul> <li>Avoid due to suboptimal concentrations in renal parenchyma</li> </ul>
Trimethoprim- sulfamethoxazole	<ul> <li>First-line agent</li> <li>1 DS tablet twice daily for 3 days<sup>a</sup></li> <li>Avoid if used in the past 3 months or if prevalence of local resistance is known to exceed 20%. (Rates of TMP-SMX resistance in <i>E coli</i> isolates in most of the United States exceed 20%.)</li> </ul>	<ul> <li>Can be used if bacteria are identified to be susceptible.</li> <li>1 DS tablet twice daily</li> <li>Note: The Infectious Diseases Society of America (IDSA) recommends 14 days, but more recent data indicate that 7 days would be adequate provided the patient is improving clinically.</li> </ul>
Fosfomycin	<ul><li>First-line agent.</li><li>3 g as 1 dose</li></ul>	<ul> <li>Avoid due to suboptimal concentrations in renal parenchyma</li> </ul>
Oral β-lactams (eg, amoxicillin-clavulanic acid or cefpodoxime)	<ul> <li>Use only if the above first-line agents cannot be used</li> <li>Example (not comprehensive list):</li> <li>Amoxicillin, clavulanic acid 500/125 mg twice daily for 5-7 days<sup>a</sup></li> <li>Cefpodoxime, 100 mg twice daily for 5-7 days<sup>a</sup></li> </ul>	<ul> <li>Not recommended as an initial agent.</li> <li>Can consider using oral β-lactam agent if pathogen known to be susceptible and after the patient receives an initial intravenous dose of a long-acting parenteral antimicrobial, such as 1 g of ceftriaxone.</li> </ul>
Fluoroquinolones (eg, ciprofloxacin)	Effective but use only if alternative oral antimicrobials for acute cystitis are not available or possible     Example: Ciprofloxacin 250 mg twice daily	Ciprofloxacin 500 mg twice daily for 7 days  Activate Windows
	for 3 days	Go to Settings to activate

Doses listed in this table are for creatinine clearance > 60. Abbreviations: DS, double strength; TMP-SMX, trimethoprim-sulfamethoxazole.

<sup>&</sup>lt;sup>a</sup>Duration of therapy for cystitis are based on guideline recommendations for women. For uncomplicated cystitis in men, consider duration of ∼7 days provided there is no

#### **Review of Question 1**

• This patient had symptoms that would be classic for simple cystitis (burning, frequency, suprapubic pain), so she can be started on treatment without confirmatory laboratory testing. Of the treatment options listed, nitrofurantoin is the only first-line agent. Ciprofloxacin should be reserved for pyelonephritis or more complicated infections, and β-lactams such as amoxicillin are second-line agents. Thus, the answer is (c), prescribe nitrofurantoin 100 mg twice daily for 5 days.

#### **Pyelonephritis**

 Case 1, continued: The patient then developed subjective fevers and right lower back pain despite having taken the nitrofurantoin prescribed empirically by urgent care for 3 days. The diagnosis is pyelonephritis, and the urine cultures grew > 100,000 CFU/mL E coli which was resistant to nitrofurantoin and trimethoprimsulfamethoxazole but susceptible to ciprofloxacin. She was switched to ciprofloxacin 500 mg twice a day. She showed improvement in her symptoms by day 2 of treatment and resolution of all symptoms by day 3.

#### Question 2:

How many total days of ciprofloxacin would be recommended for this patient?

- (a) Treat for a total 3 days
- (b) Treat for a total 7 days
- (c) Treat for a total 14 days
- (d) Treat for a total 21 days
- (e) Determine treatment based on repeat urine culture results at day 7

- Pyelonephritis is a UTI that extends to the kidneys. The typical symptoms include flank pain, fevers, rigors, nausea, or vomiting. In contrast to cystitis, obtaining urinalysis and urine cultures is recommended for all cases of suspected pyelonephritis. The diagnosis of pyelonephritis should be made by clinical assessment and laboratory testing (urinalysis and urine culture).
- Imaging is not required for all comers and can be reserved for cases where the patient is critically ill, not improving on initial therapy, or suspected to have an obstruction or a complication.

 Complications of pyelonephritis include but are not limited to sepsis, acute renal failure, renal or perinephric abscess, kidney stones (eg, staghorn calculi), and emphysematous pyelonephritis (a serious necrotizing infection). Computed tomography (CT) scan of the abdomen with intravenous (IV) contrast is typically the primary mode of imaging in the majority of these cases. Renal ultrasound is less sensitive than a CT scan but is a reasonable alternative for patients where exposure to radiation or contrast is of concern.

#### **Review of Question 2**

• The patient's fever and flank pain indicated that she had progressed to pyelonephritis. The recommended duration for treatment of pyelonephritis with ciprofloxacin is 7 days, provided the patient is clinically improving as in this case. Tests of the cure with repeat urine cultures is not recommended. Thus, the answer is (b), 7 days.

 Case 2: A 53-year-old man with diabetes mellitus, incomplete bladder emptying, and a deceased donor renal transplant 2 years ago who is taking mycophenolate mofetil and tacrolimus presents to the emergency department (ED) with 5 days of dysuria, urinary frequency, and fatigue. On the fifth day, he developed fever with rigors, so he presented to the ED. In the ED he is hemodynamically stable with WBC of 15,000 with urinalysis showing >182 WBC, 2 red blood cells (RBC), + leukocyte esterase, and 4+ bacteria. Within 24 hours, his urine and a single blood culture bottle grow E coli that is multidrug resistant. His renal transplant ultrasound is normal. The patient has an estimated glomerular filtration rate (eGFR) of 48 and normal electrolytes; he clinically responds within 24 hours of appropriate antibiotic therapy.

#### Question 3:

- With which antibiotic and for what duration would you treat this patient?
- (a) 3 days of ertapenem
- (b) 7 days of nitrofurantoin
- (c) 9 days of trimethoprim-sulfamethoxazole after 5 days of ertapenem
- (d) 21 days of trimethoprim-sulfamethoxazole
- (e) 14 days of ciprofloxacin

 this is a case of pyelonephritis but in a renal transplant recipient and has an associated bloodstream infection. In this case, imaging of the genitourinary tract is performed to exclude an abscess or other transplant complication because these will likely impact management if found. The choice and duration of antibiotic in this case involves consideration of the host, the pathogen's susceptibility profile, and the associated bloodstream infection. The Infectious Disease (ID) Committee of Practice for the American Society of Transplantation recommends 14 days of treatment for complicated UTI/pyelonephritis.

#### **Review of Question 3**

• In general, 14 days of treatment is favored. Further, when acceptably bioavailable oral options exist, the total duration of treatment does not need to be parenteral. For that reason, answer (a) is incorrect; 3 days of ertapenem only is an insufficient course for pyelonephritis in general. Answer (b) is incorrect as well; nitrofurantoin should only be used for cystitis and never for upper tract disease or bacteremia. Although treatment with trimethoprim-sulfamethoxazole alone is reasonable, a 21day course is excessive without abscess and raises the risk of complications, thus making answer (d) incorrect. Answer (e) is also incorrect. Thus, in this case with the caveats as described, the best answer listed to this question is (c).

### **Asymptomatic Bacteriuria**

• Case 3: A 33-year-old woman with diabetes mellitus presents to her primary care doctor's office for a routine followup visit. She feels well and has no acute complaints. The urine sample she submitted for annual screening for albuminuria was also sent for urine microscopy and urine culture due to a processing error. The urine microscopy was notable for 5-10 WBC/high-power field (HPF), and the urine cultures grew more than 105 CFU/mL of pan-susceptible Klebsiella oxytoca.

#### Question 4:

In which of the following scenarios would antibiotic treatment targeted at urine culture results be indicated for this patient?

- (a) Pregnancy
- (b) Elective hernia repair scheduled in the next 48 hours
- (c) Elective cystoscopy in the next 48 hours
- (d) Placement of a Foley catheter
- (e) Liver transplant in the past year

 Asymptomatic bacteriuria (ASB) is defined as ≥105 CFU/mL in a voided urine specimen without signs or symptoms attributable to UTI. This is regardless of whether pyuria is present. ASB is a common benign finding in many populations including healthy women, residents in long-term care facilities, and patients with urinary tract abnormalities. Studies have shown that antimicrobial treatment for the majority of patient populations with ASB does not confer significant benefit but can increase the risk of antimicrobial resistance or Clostridioides difficile infection.

 Therefore, screening or treatment for ASB should be avoided in most patients. The main exceptions to this are the following 2 populations. The first is pregnant women because treatment decreases the risk of pyelonephritis and negative fetal outcomes. The second population that may benefit from a course of antibiotics are patients who will undergo urologic procedures associated with significant mucosal bleeding and trauma (eg, transurethral surgery of the prostate or the bladder, or percutaneous stone surgery). Relatedly, most of the data available do not support treatment of ASB in renal transplant patients. This, however, continues to be studied; currently, because of the lack of data on the immediate transplant period (1-2 months after transplant), many centers will treat ASB if found coincidently during this time, but they do not routinely screen for such.

 Review of Question 4 Pregnancy is an indication for the treatment of ASB, so the answer is (a). Uncomplicated diagnostic cystoscopy or Foley catheter placement have a low risk of infection. Although urine culture results can help guide the standard 1-2 doses of perioperative prophylaxis for cystoscopy, a UTI treatment course with multiple days of antibiotics is considered unnecessary. Patients with solid organ transplants, other than early renal transplant, do not require treatment for ASB.

### **Catheter-associated Urinary Tract Infection**

Case 4: You are seeing a 64-year-old man with diabetes mellitus and heart failure with reduced ejection fraction who was admitted to the cardiac intensive care unit with acute decompensated heart failure. He did not have a fever or leukocytosis on presentation. An indwelling urinary catheter was placed on hospital day 1 to assist with intravenous diuresis. On hospital day 4, the patient was noted to have a fever to 38.5C. Blood cultures were drawn and are pending. The urinalysis revealed moderate leukocyte esterase and >182 WBC/HPF. The urine culture grew >100,000 CFU/mL of Klebsiella pneumoniae

Question 5: Which of the following is consistent with the Centers for Disease Control and Prevention (CDC) surveillance definition of a catheter-associated urinary tract infection (CAUTI)?

- (a) Indwelling catheter in place for at least 2 weeks
- (b) Urine culture with 1 organism with bacterium of >105 CFU/mL
- (c) Hemodynamic instability (ie, hypotension, tachycardia)
- (d) Presence of E coli or other Gram-negative rod isolated in urine culture
- (e) Admission to a hospital for less than 48 hours

- The CDC surveillance definition of a CAUTI necessitates that patients meet the following 3 criteria:
- 1. Indwelling catheter in place for more than 2 consecutive days in an inpatient location.
- 2. Urine culture with no more than 2 organisms present and 1 organism with bacterium of >105 CFU/mL.
- 3. Presence of at least 1 of the following: fever (38C), suprapubic tenderness, costovertebral angle pain or tenderness, urinary urgency, urinary frequency, or dysuria. The patient in case 4 above meets each of the 3 CAUTI criteria. CAUTI is the most frequent health care—related infection worldwide, and it has been associated with the development of bacteremia and increased mortality. The diagnosis of CAUTI can be difficult because pyuria is an expected finding in patients, and the symptoms are often nonspecific if the catheter is still present.

 The treatment for CAUTI includes first discontinuing the indwelling catheter or replacing the catheter (if still needed) if it has been in place for more than 2 weeks. Because urine cultures from long-term indwelling catheters may reflect the microbiology of the catheter's biofilm instead of the infection in the bladder, obtaining a urine culture from a newly placed catheter is recommended to guide antimicrobial therapy. Antimicrobial therapy should be initiated in patients with suspected CAUTI and tailored to the urine culture results. Common bacterial causes of CAUTI include E coli, Klebsiella spp, Pseudomonas aeruginosa, and Enterococcus spp. A duration of 7 days of antimicrobial therapy is likely sufficient, provided that the patient improves clinically after starting antimicrobials.

### **Review of Question 5**

• The CDC surveillance definition of CAUTI includes the 3 criteria detailed previously. Of the answer choices, only (b) is consistent with 1 of the criteria: urine culture with 1 organism with a bacterium of >105 CFU/mL. Note that indwelling catheters only need to be in place for 2 consecutive days in an inpatient location to meet the surveillance definition. Also, although CAUTI often are caused by Gram-negative organisms, Enterococcus spp, Staphylococcus spp, and Candida spp are also possible causative pathogens.

#### **Acute Bacterial Prostatitis**

 Case 4, continued: After CAUTI was diagnosed in the previous patient, he was started on intravenous ceftriaxone. However, he continued to have temperatures above 38.0C over the next 2 hospital days. A digital rectal examination revealed that the patient's prostate was tender and swollen. A CT scan of his abdomen and pelvis showed a heterogeneous-appearing prostate without abscesses or other intraabdominal pathology. The patient slowly begins to show clinical improvement, and you plan a treatment course for acute bacterial prostatitis (ABP).

#### Question 6:

If ABP is diagnosed, as with the patient in case 4, how long should the patient receive antibiotics, assuming continued clinical improvement?

- (a) 3-5 days
- (b) 7 days
- (c) 7-14 days
- (d) 14-28 days
- (e) 42 days or longer

• ABP is typically characterized by the abrupt onset of voiding symptoms and is also often accompanied by systemic symptoms, though it can be difficult to diagnose because helpful diagnostics are limited. As in this case, an indwelling urinary catheter or urinary manipulation is a risk factor for development of ABP in men. On digital prostate palpation (which should be done gently to avoid risk of bacteremia), the prostate is often tender, swollen, and warm.

• . Prostatic abscess is a rare complication of ABP in general, but it may be more common in patients with ABP in the setting of recent urinary tract manipulation. Imaging to assess for prostatic abscess should be pursued if clinical improvement is not seen with antimicrobial therapy. Imaging modalities to diagnose prostatic abscess include prostate ultrasonography, CT, and magnetic resonance imaging.

### **Review of Question 6**

• Though there is a relative paucity of data regarding optimal treatment duration of ABP, most guidance recommends 2- 4 weeks of therapy. Therefore, the correct answer is (c), 14-28 days.

 The management of ABP typically requires 2-4 weeks of antimicrobial therapy, ideally tailored to the results of the urine culture if available. ABP is most commonly caused by E coli, P aeruginosa, Klebsiella spp, and Enterococcus spp; in sexually active men, Neisseria gonorrhoeae and Chlamydia trachomatis should also be evaluated with urine nucleic acid amplification testing. Though most antibiotics will penetrate acutely inflamed prostate tissue as these patients improve clinically, care should be taken to ensure antimicrobial agents are chosen that achieve adequate concentration in prostate tissue such as fluoroquinolones or trimethoprim-sulfamethoxazole.

#### **Recurrent UTI**

Case 7: A 78-year-old woman comes to see her primary care doctor after her third episode of cystitis in the last 9 months. She notes that each episode was heralded by urinary frequency, urgency, and dysuria. She has no known other medical conditions except for well-controlled hypertension on a single medication and osteoarthritis of her knees. Her pelvic examination does not reveal a prolapse but does show changes consistent with atrophic vaginitis. Her laboratory results reveal normal kidney function and no evidence of diabetes. Her urinalysis on evaluation when she is asymptomatic is normal, without any cells in sediment. She asks for something to prevent further infections.

Question 10: What advice would you give as an initial intervention to this patient?

- (a) Prescribe continuous antibiotic prophylaxis with ciprofloxacin
- (b) Start vaginal estrogen
- (c) Recommend cranberry juice supplementation
- (d) Initiate episodic antibiotic prophylaxis with intercourse
- (e) Explain to her that there are no evidence-based methods to reduce the frequency of UTIs in postmenopausal women

 Recurrent UTIs take many different forms. They can be precipitated by sexual intercourse most frequently in premenopausal women but also in postmenopausal women. Postmenopausal women are especially prone to recurrent UTIs due to the increased incidence of atrophic vaginitis and changes in the vaginal microbiome precipitated by lack of estrogenization of the tissues in the vaginal and lower urinary tracts. A detailed review of this pathophysiology is included in the recommended reading. In general, recurrent UTIs in men are often associated with underlying structural issues leading to urinary retention or the presence of an indwelling catheter.

• When undertaking the care of a patient with recurrent UTI, there is frequently no single intervention that "heals all." There are associations with recurrent UTIs related to sexual activity related to spermicidal contraceptives; if a woman is using this form of contraception, changing to a different agent may provide benefit. It is not clear that other behavior modifications such as early voiding after sexual intercourse or increased hydration to precipitate more frequent urination are effective in isolation, but certainly these are low-risk interventions that are easy to do.

• For postmenopausal women, especially those in whom there may be associated incontinence, a pelvic examination to exclude pelvic floor dysfunction or prolapse is advised. If there is no correctable anatomic issue, then vaginal estrogens are a well-tolerated, low-risk intervention to undertake. Vaginal estrogens can be applied in many forms including vaginal rings, creams, and tablets. Utilization of supplements such as cranberry extracts and D-mannose have been tried, and some individuals may find benefit, but the data are mixed (as presented in a recent Cochrane review). Investigators are studying the use of vaginal probiotics, which may have efficacy in combination with estrogens

For those who are unable to derive benefit from these interventions, antibiotic prophylaxis is often tried. Postcoital antibiotics can be effective in decreasing the incidence of UTI and the most well-studied agent is trimethoprim/sulfamethoxazole. Continuous prophylaxis has been shown to be effective in clinical trials, but the efficacy is lost once prophylaxis is stopped. Further, prophylaxis is not usually 100% effective, so UTIs will likely be less frequent but still present, and when they occur, organisms present are likely to have antimicrobial resistance to the class of prophylactic drug.

### **Review of Question 10**

The patient described in case 7 does not appear to have an anatomic issue to which her recurrent UTIs can be ascribed. Further, she has changes on examination that are consistent with atrophic vaginitis. Based on the sentinel randomized controlled trial this patient will likely derive benefit from vaginal estrogens. This study not only demonstrated decreased antimicrobial use for UTI in the estrogen group over the follow-up period but also demonstrated other benefits such as decreased vaginal colonization with Enterobacterales with lower vaginal pH and recolonization with Lactobacillus spp (normal vaginal flora). Thus, the correct answer is (b), start vaginal estrogen as an initial intervention

### **Approaching Candiduria**

 Case 6: A 64-year-old man is admitted to the intensive care unit after a coronary artery bypass graft procedure. A Foley catheter was placed during the procedure. On postoperative day 3, the patient has a fever of 38.3C. Blood cultures are obtained and are pending. His urinalysis is notable for the presence of leukocyte esterase and >50 WBC/HPF. The urine culture ultimately grows >100,000 CFU/mL Candida albicans.

Question 9: What is the most appropriate next step in management?

- (a) Initiate antifungal treatment with fluconazole.
- (b) Replace the indwelling urinary catheter and repeat the urine culture.
- (c) Obtain a renal ultrasound.
- (d) Replace the indwelling urinary catheter and start treatment with fluconazole.
- (e) Initiate antifungal treatment with micafungin.

 The task of clinicians when approaching patients with candiduria is to determine whether the isolated Candida indicates contamination, colonization, or infection. For patients with indwelling catheters and Candida isolated from urine culture, the catheter should be discontinued (if possible) and a repeat urine culture obtained to investigate whether Candida is still present. If an indwelling catheter is still required, the catheter should be exchanged and a new culture obtained to again assess for persistence of candiduria. If Candida is again isolated, the clinician must then determine whether the patient has continued colonization versus cystitis or upper tract infection.

 Note that pyuria is an expected finding in patients who have indwelling catheters and is not helpful in delineating colonization versus infection. Treatment of Candida UTI is only indicated in cases of persistent candiduria in patients who have symptoms consistent with UTI without an alternative etiology (ie, concurrent bacteriuria). Imaging such as renal ultrasound or CT abdomen/pelvis should also be obtained in the setting of persistent candiduria to assess for obstruction and need for urology consultation. • For candiduria in patients without indwelling catheters, the management approach is similar. First, a repeat clean catch urine sample should be obtained (or a specimen from the catheter if clean catch is not feasible) to see if Candida is again isolated. If applicable, patients should also be assessed for the presence of concurrent vaginitis. For patients who reisolate Candida in urine, imaging is indicated to assess for obstruction; however, as with catheterized patients, treatment of candiduria is only indicated when patients have signs/symptoms consistent with UTI. Exceptions to this management approach include patients undergoing urologic procedures and neutropenic patients for which asymptomatic candiduria should be treated.

### **Review of Question 9**

• The patient in case 6 has evidence of a possible UTI with fever and a urine culture from an indwelling urinary catheter growing C. albicans. Though this could be consistent with fungal CAUTI causing fever, the isolation of C. albicans may also represent colonization of the catheter. Empiric treatment is not warranted at this stage. Replacement of the urinary catheter (if the catheter cannot be removed all together) followed by repeating the urine culture should be pursued. Unless Candida is reisolated or there is clinical evidence of an upper urinary tract obstruction, renal ultrasound is not necessary at this juncture. The answer is (b), replace the indwelling urinary catheter and repeat the urine culture.

- Treatment of symptomatic candiduria (dose and duration depending on severity and treatment response):
- Oral fluconazole 200 to 400 mg/d for 7 to 14 days or
- IV amphotericin B 0.5 to 0.7 mg/kg for 1 to 7 days (14 days for pyelonephritis).