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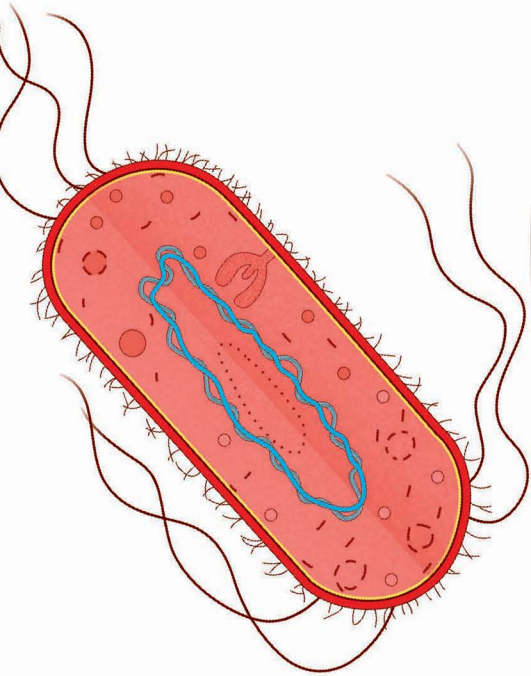

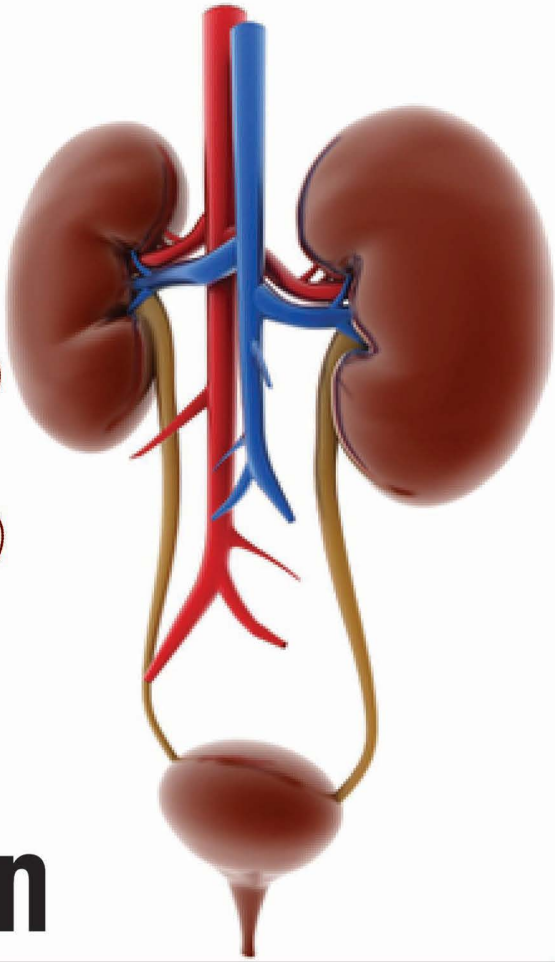

Update on Urinary Tract Infections

Rakesh Khera

Foreword
Naresh Trehan

JAYPEE

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CHAPTER

4 Urinary Tract Infection in Intensive Care Unit

Chitra Mehta

INTRODUCTION

Urinary tract infection (UTI) has been found to account for 25% of all cases of sepsis. It may be either community or hospital acquired. In intensive care unit (ICU), one may encounter both severe community acquired and/or a hospital acquired UTI. In a study in US, UTI accounted for 40% of patients presenting with septic shock to the emergency department (ED). It was found to be responsible for 25% of septic shocks due to hospital-acquired infections. Similarly, an Australian study found UTI to account for 30.2% of patients with septic shock being admitted in the ED.

Urinary tract infection forms about 20–50% of all intensive care acquired infections. This is related to rampant use of indwelling catheters in these settings. Presence of indwelling catheter increases the risk of acquiring bacteriuria by 3–10% every day. Out of these about 10–25% patients develop UTI. The incidence of catheter-associated UTI (CAUTI) ranges from 2% to 6% in the first 10 days of catheterization. It is nearly 100% at 30 days of catheterization. Incidence of UTI in ICU has been observed to be approximately 7%.

Catheter-associated UTI has been found to result in increased mortality, length of stay and healthcare costs. CAUTI prevention is an important patient safety goal, and is of vivid interest among ICU community. It is estimated that about 65–70% of CAUTIs are preventable.

Indwelling catheter is considered as short-term if it remains in situ for less than 30 days. If the catheter indwelling time is more than 30 days, it is considered as long-term. In ICU, the catheter use is generally short-term.[1-4]

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DEFINITIONS

Urinary tract infection is regarded as an inflammatory response to bacterial or fungal colonization of the urinary tract. Urinary tract infections can exhibit clinically in the form of uncomplicated urinary infection, complicated urinary infections, bacterial prostatitis and asymptomatic bacteriuria (ASB). The severity of infection depends upon the host response.

Asymptomatic bacteriuria is said to be present if a specific amount of bacteria is isolated from an adequately collected urine sample in an asymptomatic patient. The prevalence of ASB has been found to range from 1% to 100% in general population. Data regarding prevalence of ASB in hospitalized patients is somehow lacking.

Catheter-associated UTI needs to be defined with caution. It is difficult to differentiate between contamination, colonization, and true infection. More so in critically sick patients who are usually sedated, delirious or are unable to communicate. They may also not show typical signs and symptoms of UTI.

Catheter-associated bacteriuria is defined as presence of significant bacteriuria (defined as bacterial counts of more than or equal to 10^5 CFU/mL in urine specimen obtained from catheter) irrespective of symptoms. CAUTI has been defined by presence of significant bacteriuria from urine of a catheterized patient with signs and symptoms indicative of urinary infection. An ICU acquired UTI is defined by the presence of a positive urine culture on or later than Day 3 of ICU admission. Patients who develop positive urine culture within 48 hours of ICU discharge should also be considered as having ICU acquired UTI.

Catheter-associated UTI has been defined by Infectious Diseases Society of America (IDSA) as the presence of symptoms and signs of urinary infection with no other attributable source, plus more than or equal to 10^3 CFU/mL of one or more bacterial species in a single catheter urine specimen. It is also said to be present if similar counts are obtained in midstream urine specimen of a patient who has got his catheter removed in previous 48 hours. Catheter-associated ASB (CA-ASB) is said to be present if more than or

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equal to 10^5 CFU/mL of one or more bacterial species is grown in a single catheter urine specimen in an asymptomatic patient. Catheter-associated funguria is defined by presence of fungus in a catheterized or recently catheterized patient. Fungal colony counts have not been found to have meaningful interpretation.[5-7] However, some consider more than or equal to 10^4 CFU/mL an appropriate quantitative count for candiduria.

So far it has been difficult to accurately establish relationship between CA-ASB and CAUTI. Majority of patients with CA-ASB do not develop CAUTI, and factors influencing this progression have not been identified. Investigators have been targeting CA-ASB prevention in the hope of bringing down the incidence of CAUTI.

RISK FACTORS

Several factors have been found to be associated with bacteriuria. Many of them are important for critically sick patients especially CAUTI. Factors associated with risk of developing severe UTI have also been identified. These are enlisted in Table 1 and Box 1.[4,8]

Table 1: Risk factors for urinary tract infection.

Modifiable	*Nonmodifiable*
Prolonged catheterization	Diabetes mellitus
Antibiotics before or upon admission	Elevated creatinine
Other active sites of infection	Female gender
Nonadherence to aseptic catheter care	Rapidly fatal underlying illness
Catheterization outside operation room	Old age
Nonadherence to closed drainage system	Prolonged estrogen deficiency
Instrumentation of urinary tract	Hemodialysis
Ureteric stents	Admission due to acute disorder
Rigorous monitoring of urine output	Immune alterations
Urology services	
Urinary retention	
Prolonged intensive care unit stay	

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Box 1: Risk factors for severe urinary tract infection.

- Healthcare associated infection
- Female gender
- Infection with multidrug-resistant organisms
- Urinary obstruction
- Prolonged urologic surgery
- Mucosal trauma during catheterization
- Cirrhosis
- Prolonged intensive care unit length of stay
- Immunosuppression
- Structural urologic abnormalities
- Old age

Intensive care unit acquired CAUTI has not been found to impact mortality, but is associated with significant morbidity. Risk factors for developing bacteremia secondary to UTI in ICU have been found to be renal disease, male sex and neutropenia. Suprapubic catheterization has similar rates of UTI when compared to urethral catheterization. Intermittent catheterization reduces the risk but does not eliminate it.

PATHOGENESIS

In noncatheterized patients UTI occurs due to contamination with own fecal microflora. The flora colonizes the periurethral region and ascends up the urinary system. On the other hand, urinary catheterization is the most important predisposing factor for nosocomial UTI. It bypasses the host defense mechanisms and provides rapid access of organisms to the bladder. CAUTI may also result due to contamination from the hands of attending personnel during catheterization, or due to poor handling of the collection system. Extraluminally, microorganisms invade the bladder by moving upward in the mucus film coating the external surface of catheter. The biofilm formation, comprising of Tamm-Horsfall protein,

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organic molecules and electrolytes, protects uropathogens from antibiotics, urine flow and host defenses. Biofilm formation starts right after the catheter insertion, involving both interior and exterior surfaces. Biofilm formation has not been observed with synthetic materials. Intraluminal infection occurs secondary to contamination of the collecting bag, or failure to maintain closed drainage system. Both extraluminal and intraluminal routes of infection are important.[9,10]

MICROBIOLOGY

Nosocomial UTIs have a wide range of infecting organisms, commonly antibiotic resistant when compared to community acquired uncomplicated UTI. Most of the catheter related infections are monobacterial (commonly, gram-negative bacilli, and enterococci). *Escherichia coli* is the most common organism especially in community acquired UTI. Coagulase-negative *Staphylococcus*, enterococci, *Candida* species and non-fermenters like pseudomonas are frequently encountered in patients with indwelling catheter. Although multidrug-resistant organisms are more common in nosocomial UTI, extended spectrum B lactamases (ESBL) *Enterobacteriaceae*, and carbapenemases producing *E. coli* have been isolated in community acquired UTI as well. A study from Taiwan reported an incidence of 72% of ESBL producing *E. coli* and *Klebsiella pneumoniae* bacteremia due to urinary infection in patients admitted to ED. In ICU about 5–12% are polymicrobial UTIs. This usually occurs in presence of prolonged catheterization, neoplasm, stone, or in presence of fistula between vagina or bowel and the urinary tract. Incidence of gram-positive infections in ICU acquired UTI has been found to be 27.1%. There has been a recent increase in fungal UTIs with candiduria accounting for about one-third of ICU acquired UTI.

Proteus mirabilis, *Morganella morganii* and Providentia species are common organisms in patients with chronic indwelling catheters.

Isolation of *Staphylococcus aureus* in urine usually indicates a disseminated infection.[11-13]

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CLINICAL PRESENTATION

Urinary tract infections have wide range of presentations starting from bacteriuria with minimal symptoms to florid sepsis and septic shock. A typical UTI presents with high-grade fever, suprapubic pain, renal angle tenderness and burning micturition. These symptoms are lacking in majority of patients with CAUTI. It becomes even more difficult in ICU due to ongoing concurrent antibiotics, sedatives, analgesics, and mechanical ventilation. Patients with CAUTI may present with new onset fever, altered mentation, pelvic discomfort, urinary incontinence, cloudy urine, and flank pain. Patients with spinal cord injury, in addition to these symptoms, may have autonomic dysreflexia and increased spasticity.

In ICU, even in presence of indwelling catheter, fever, leukocytosis, it is difficult to make a diagnosis of CAUTI. It is basically a diagnosis of exclusion. Nevertheless, if a catheterized patient has signs and symptoms of UTI not explainable by another condition warrants treatment. And when the same organism is isolated simultaneously in urine and blood cultures, CAUTI should be thought responsible for bacteremia.[14,15]

DIAGNOSIS

As discussed earlier, IDSA has defined ASB and CAUTI based on the colony counts. In catheterized patients, pyuria is generally not indicative of CA-bacteriuria or CAUTI. In a large study the specificity of pyuria for CA-bacteriuria in catheterized patients was 90% but sensitivity was just 47%. So just on the basis of pyuria it is difficult to differentiate between CA-bacteriuria and CAUTI. Absence of pyuria in a symptomatic patient, however, usually points toward an alternative diagnosis.

Urine culture is considered the gold standard for diagnosing UTI. It can be quantified based on colony counts in patients with or without indwelling catheter (quantitative urine culture). It is imperative to collect urine sample with due precautions to make the accurate diagnosis. Ideally the urine specimen should be obtained from a freshly placed catheter, or from a voided midstream specimen in noncatheterized patients or in whom the catheter has been

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discontinued. Urine specimen should be collected directly from the catheter collection port or through needle puncture of tubing in order to maintain a closed drainage system. In a US based study the sensitivity of urine testing in combination with urine culture was detected to be 100% with a specificity of 24.1% in diagnosing CAUTI.

BLOOD CULTURES

A positive blood culture along with a positive urine culture is highly suggestive of urosepsis. But it is found to be positive in only 18% of total patients. It is essential that similar organisms are grown in both urine and blood cultures. In presence of multiple organisms on urine culture, positive blood culture may help in identifying clinically most important organism leading to optimization of antimicrobial therapy.[16,17]

Polymerase chain reaction is increasingly being utilized for early diagnosis of UTI. However, it is not readily available, is costly and may not be able to differentiate between ASB and UTI.

INFLAMMATORY MARKERS

Elevated procalcitonin is predictive of bacteremia in patients with symptomatic urinary infection. It needs to be evaluated further for its utility in predicting the outcomes in UTI. Its role also needs to be better defined in the management of life-threatening urinary infection.

DIAGNOSTIC IMAGING

In patients presenting with severe sepsis to ICU and suspected to have urinary cause should undergo early imaging. Imaging helps in identification of abnormalities requiring source control. It may also establish a unilateral or bilateral pathology, pyelonephritis, renal abscess, emphysematous pyelonephritis and any obstruction in the urinary tract. A contrast enhanced computed tomographic examination is considered appropriate. Magnetic resonance imaging is

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not sensitive for identifying stones or gas in tissues and thus not recommended. Renal and pelvic ultrasounds are also less sensitive, though these can be performed easily bedside.[7,18-20]

COMPLICATIONS

Urinary tract infections account for 15% of nosocomial bacteremias. About one-fourth patients with CA-ASB develop CAUTI. Four percent patients with CA-bacteriuria develop bacteremia. CA-bacteriuria has been found to be the most common source of gram-negative bacteremia in hospitalized population. CA-bacteriuria is felt to contribute significantly to problem of antibiotic resistance in healthcare facilities. Firstly, it comprises of a large pool of antibiotic resistant organisms that can easily be transmitted to other patients who have invasive devices. Secondly, CA-bacteriuria is frequently treated inappropriately resulting in emergence of multidrug-resistant organisms. Inappropriate antimicrobial therapy also contributes toward appearance of nosocomial clostridium difficile colitis.[21,22]

Patients with prolonged ICU stay with extended indwelling catheter time are at an increased risk of developing polymicrobial bacteriuria, catheter obstruction, bacteremia, incontinence, fistula formation and local genitourinary infections. *Proteus* mirabilis is most commonly isolated organism during prolonged catheterization. It hydrolyses urea to ammonia resulting in formation of apatite and struvite crystals within the catheter lumen resulting in obstruction.

MANAGEMENT

Antimicrobial therapy should be initiated as early as possible in a patient presenting with suspected urinary source of sepsis or septic shock, community or hospital acquired. In critically sick patients it may be worthwhile ensuring antimicrobial coverage for UTI, even when another potential source has been identified. It must be kept in mind that antibiotics alone may not be sufficient. It should be accompanied with source control (when indicated), correction of anatomical or functional defects and discontinuation of catheter at earliest feasible.

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URINE CULTURE AND CATHETER REPLACEMENT BEFORE TREATMENT

Urine specimen for culture should be collected before the initiation of antibiotic therapy, especially if the patient is catheterized. If however the indwelling catheter duration is more than 2 weeks, and if there is a continuous need for catheterization, then the catheter should be replaced. In this situation, the urine specimen for culture should be obtained from a freshly placed catheter. And if catheter can be discontinued, voided midstream urine specimen should be sent for culture after its removal.

ANTIMICROBIAL THERAPY

Once the microbiological sampling of urine and blood are done, antibiotics should be administered within the first hour, especially in septic patients. Antibiotics that have renal excretion achieve high drug levels in kidneys and urine, and therefore are considered appropriate. Antibiotics not excreted through the renal route may be able to treat bacteriuria effectively but fail to eradicate organisms from the urinary tract. There is also a possibility of relapse upon discontinuation of these antibiotics. High levels of antibiotics in urinary system may also not be achieved in presence of renal failure, urinary obstruction and unilateral nonfunctioning kidney. This may warrant a prolonged antimicrobial therapy.

Appropriate empirical antibiotic therapy in right dosages is of utmost importance. Inappropriate therapy has been associated with high mortality. Decision of empirical antibiotics should be based upon the urine gram stain results, expected bacterial spectrum, institutional resistance profile, previous urine culture results, and individual patient's requirement. Different empirical treatment regimens are shown in Box 2.[23-25]

Antibiotics should be appropriately targeted once the culture results are available. The optimal duration of antimicrobial therapy in CAUTI is unknown. But latest IDSA guidelines recommended duration is mentioned in Box 2.[26-28]

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Box 2: Empirical antimicrobial choices for catheter-associated urinary tract infection (CAUTI).

- Mild-to-moderate infection ± fever
  - Urinary fluoroquinolones: Levofloxacin and ciprofloxacin (PO)
- Severe infection ± fever
  - Ceftriaxone, cefepime, and ceftazidime
  - Piperacillin-tazobactam combination
  - Carbapenems: Meropenem, Imipenem-cilastatin, ertapenem, and doripenem
  - Aztreonam
  - Gentamicin ± ampicillin, tobramycin ± ampicillin, and amikacin ± ampicillin
  - IV levofloxacin
  - Fosfomycin
- Pyelonephritis/urosepsis
  - Piperacillin-tazobactam or carbapenems
- Gram-positive cocci on Gram stain
  - + vancomycin
- Extended spectrum B lactamases (ESBL) strain suspected
  - Carbapenems
- Vancomycin-resistant enterococci (VRE)
  - Linezolid
- Carbapenemase-producing organisms
  - Colistimethate
- Previous exposure to antibiotics within 3–6 months
  - Alternative class to be chosen
- Duration of treatment
  - 5 days if not severely ill
  - 7 days if there is resolution of symptoms in sick patients
  - 10–14 days if there is a delayed response
  - 3 days in women more than 65 years, having no urinary symptoms, and catheter already removed

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ASYMPTOMATIC BACTERIURIA

In a febrile ICU patient it is very common to overdiagnose and overtreat patients with ASB. Treatment of ASB is generally not indicated except in high-risk individuals like patients undergoing genitourinary surgery, and pregnant women. These patients are at high-risk of developing pyelonephritis or bloodstream infections. ASB persisting beyond 48 hours of removal of catheter should also be treated, as there is an increased risk of developing symptomatic UTI. Nonpregnant women, elderly patients living in community, catheterized patients, diabetics and persons with spinal cord injury should not receive treatment for ASB. In ICU, ASB has been found to be associated with increased hospital stay. There is limited data whether ASB in patients undergoing major surgical procedures should be treated or not.[29,30]

FUNGAL URINARY TRACT INFECTION

Fungal infection, mainly *Candida* species, account for about 10–15% of nosocomial UTI. Their incidence in burns ICU is the highest, about three times of that observed in medical/surgical ICUs. There has been a recent emergence of *Candida glabrata* as the dominant yeast in urinary tract. This is secondary to rampant use of fluconazole. Nosocomial funguria is most common in presence of diabetes, previous antibiotic exposure, concomitant nonfungal infection, urinary tract abnormalities and underlying malignancy. Candiduria may either represent contamination of voided urine, colonized stents or catheters, bladder infection or true renal infection with candidemia. Asymptomatic nosocomial candiduria does not require treatment. However, possibility of disseminated candidiasis should be kept in mind in all hospitalized patients with candiduria, especially if candiduria is common in that particular facility. Candiduria warrants treatment in a symptomatic patient, and blood cultures and appropriate imaging to detect disseminated infection should accompany it. Fluconazole and amphotericin B deoxycholate are antifungals of choice. These drugs have a good renal excretion and thus appropriate drug levels are achieved locally. Echinocandins,

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lipid formulations of amphotericin B and other azoles (voriconazole, itraconazole, and posaconazole) are not excreted in urine, and therefore not recommended. There have been some case reports regarding effectiveness of caspofungin and micafungin in *C. glabrata* related UTI. Relapse rates remain high in candiduria despite apparently successful systemic or local antifungal therapy. 5-fluorocytosine may be used for some strains but requires close hematological monitoring. There is no consensus regarding the exact duration of treatment for candiduria.[31,32]

PREVENTION

Several guidelines are available for prevention of CAUTIs. Most important determinants are judicious catheterization and strict adherence to hand hygiene practices. Use of multidimensional infection control programs for prevention of CAUTI has shown impressive results. Preventive strategies have been summarized in Box 3.[33-35]

The single most important preventive factor is rationale use of indwelling catheters. Catheterization should be performed for following indications:

- Urinary incontinence in presence of open perineal or sacral wounds
- Acute anatomic or functional urinary obstruction or retention
- Perioperative use in selective surgical procedures
- Improving comfort for terminally sick or end of life care patients
- If accurate monitoring of urine output is required
- Pressure ulcer healing for incontinent patients
- Patient preference.

Recently various bundles of interventions have been proposed for prevention of healthcare associated infections. Many researchers have also exhibited their successful implementation and outcomes. This aspect seems to have a huge potential that needs to be explored.

SUMMARY

Urinary tract infections are one of the major cause of nosocomial infections in critical care units. CAUTI is costly, and associated

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Box 3: Preventive strategies for catheter-associated urinary tract infection (CAUTI).

- Preventive strategies that should be routine
  - Robust institutional infection control programs
  - Surveillance programs in high-risk groups or units
  - Rationale catheterization
  - Early removal of catheter
  - Aseptic technique during insertion of catheter
  - Intermittent or condom catheterization where appropriate
  - Use of closed drainage systems
  - Placement of collection system below the level of bladder at all times
  - Aseptic technique for cleaning the urethral meatus
  - Avoidance of disconnection of catheter and drainage tubes
  - Maintain unobstructed urine flow
  - Adherence to hand hygiene practices
  - Education of health care personnel about techniques of CAUTI prevention
- Preventive strategies with possible benefit
  - Use of antimicrobial coated catheters in patients requiring short-term catheterization
  - Suprapubic catheterization for short-term catheterization
  - Use of methenamine salts in patients requiring catheterization for more than 7 days after gynecologic surgery
- Preventive strategies not routinely recommended
  - Use of prophylactic antimicrobials
  - Use of complex closed drainage systems
  - Use of hydrophilic catheters
  - Use of cranberry products
  - Catheter irrigation with antimicrobials or normal saline
  - Routine addition of antimicrobials or antiseptics to the drainage bag
  - Screening for catheter-associated asymptomatic bacteriuria (CA-ASB)
  - Daily meatal cleaning with povidone-iodine solution, polyantibiotic ointment or cream, soap and water in catheterized patients
  - Routine catheter change
  - Prophylactic antibiotic therapy on catheter replacement or removal

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with significant patient morbidity. Wise use of catheterization has an immense capacity to reduce the incidence of CAUTI. Timely removal of catheter is another strategy to this effect. Diagnosing CAUTI in ICU is not straightforward. It is essential to differentiate between ASB and true infection. Appropriate antibiotics should be initiated at the earliest once there is a clinical suspicion. Antimicrobial resistance is increasingly becoming common in CAUTI. It is thus essential to keep local susceptibility patterns in mind while deciding the empirical regimen. Prevention of CAUTI is an important patient safety goal.

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Update on
Urinary Tract Infections

In today's era the unhealthy world of people is mesmerised by bigger names of diseases like HIV, cancers, organ failures and such tough ones. Actually people forgot that the basic diseases are much more common and still remain the same as before. These are urinary tract infections and respiratory infections. It is also the case with doctors who need to know more about these problems with time but tend to ignore it. This book helps attract the attention toward the present scenario in UTI in various fields. This starts right from microbiology to the ICU setting.



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ISBN 978-93-5270-172-8