UTI

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KUMS
DEFINITIONS:

• **UTI** is an inflammatory response of the urothelium to bacterial invasion that is usually associated with bacteriuria and pyuria.

• Bacteria may be in the urothelium in the absence of bacteriuria.

• Alternatively, bacteriuria may represent bacterial contamination of an abacteriuric specimen during collection.
• **Pyuria, the presence of white blood cells (WBCs) in the urine**

• indicator of infection and/or an inflammatory response of the urothelium to the bacterium, stones, or other indwelling foreign body.

• Bacteriuria without pyuria is generally indicative of **bacterial colonization** without infection of the urinary tract.

• Pyuria without bacteriuria warrants evaluation for **tuberculosis, stones, or cancer**.
• INCIDENCE AND EPIDEMIOLOGY:

• UTIs are considered to be the most common bacterial infection.

• They account for 1.2% of all office visits by women and 0.6% of all office visits by men.

• The overall prevalence of bacteriuria in women has been estimated at 3.5%, with prevalence generally increasing with age in a linear trend.
• Nearly 30% of women will have had a symptomatic UTI requiring antimicrobial therapy by age 24, and almost half of all women will experience a UTI during their lifetime.

• The prevalence of bacteriuria in young women is 30 times more than in men.

• However, with increasing age, the ratio of women to men with bacteriuria progressively decreases. At least 20% of women and 10% of men older than 65 years have bacteriuria.
• The incidence of bacteriuria also increases with institutionalization or hospitalization and concurrent disease.

• Catheter-associated UTIs (CAUTIs) are the most common nosocomial infection.

• The incidence of UTIs is also increased:
  - pregnancy
  - spinal cord injuries
  - diabetes
  - multiple sclerosis
  - (HIV) and (AIDS).
Prevalence of bacteriuria in females

Onset of sexual intercourse

Prevalence probably declines at puberty and teenage years before sexual activity
• no association between recurrent infections and renal scarring, hypertension, or progressive renal azotemia has been established unless comorbidities are present

• In pregnant women, the prevalence and rate of recurrent infection are the same, but their bacteriuria progresses to acute clinical pyelonephritis more frequently than in nonpregnant women
• **PATHOGENESIS:**

• **Routes of Infection:**
  - **Ascending Route**
    - soilage of the perineum with feces
    - spermicidal agents
    - intermittent or indwelling catheters.
    - VUR
    - edema associated with cystitis
    - Gram-negative bacteria and their endotoxins, as well as pregnancy and ureteral obstruction, have a significant antiperistaltic effect.
  - **Hematogenous Route** *Staphylococcus aureus bacteremia originating from oral sites or with Candida fungemia*
  - **Lymphatic Route** severe bowel infection or retroperitoneal abscesses
• **Urinary Pathogens**

  • *E. coli* is by far the most common cause of UTIs, accounting for 85% of community-acquired and 50% of hospital-acquired infections.

  • Other gram-negative *Enterobacteriaceae*, including *Proteus* and *Klebsiella*, and gram-positive *E. faecalis* and *Staphylococcus saprophyticus* are responsible for the remainder of most community-acquired infections.

  • Nosocomial infections are caused by *E. coli*, *Klebsiella*, *Enterobacter*, *Citrobacter*, *Serratia*, *Pseudomonas aeruginosa*, *Providencia*, *E. faecalis*, and *S. epidermidis*.
• Less common organisms such as *Gardnerella vaginalis*, *Mycoplasma species*, and *Ureaplasma urealyticum* may infect patients with intermittent or indwelling catheters.

• *S. saprophyticus* is now recognized as causing approximately 10% of symptomatic lower UTIs in young, sexually active females.

• *Anaerobes* organisms must be suspected when a patient with bladder irritative symptoms has cocci or gram-negative rods seen on microscopic examination of the centrifuged urine (catheterized, suprapubic aspirated, or voided midstream urine) and routine quantitative aerobic cultures fail to grow organisms.
• Anaerobic organisms are frequently found in **suppurative infections** of the genitourinary tract. **cystitis emphysematosa**- scrotal, prostatic, and perinephric abscesses

• **Bacteroides species**, including **B. fragilis**, **Fusobacterium species**, anaerobic cocci, and **Clostridium perfringens**
UTI

Bacterial Virulence Factors
- Pili

Epithelial Cell Receptivity
- Vaginal Cells
- Bladder Cells

Natural Defenses of the Urinary Tract
- Normal flora of the vaginal introitus, the periurethral area, and the urethra
- Urine
- Immune Response
Alterations in Host Defense Mechanisms

- Vesicoureteral Reflux
  - Renal Papillary Necrosis
- Obstruction
- Underlying Disease
  - Diabetes Mellitus
  - Human Immunodeficiency Virus
- Pregnancy
- Spinal Cord Injury with High-Pressure Bladders
### BOX 12-6  Risk Factors for Urinary Tract Infections

**REDUCED URINE FLOW**
- Outflow obstruction, prostatic hyperplasia, prostatic carcinoma, urethral stricture, foreign body (calculus)
- Neurogenic bladder
- Inadequate fluid intake (dehydration)

**PROMOTE COLONIZATION**
- Sexual activity—increased inoculation
- Spermicide—increased binding
- Estrogen depletion—increased binding
- Antimicrobial agents—decreased indigenous flora

**FACILITATE ASCENT**
- Catheterization
- Urinary incontinence
- Fecal incontinence
- Residual urine with ischemia of bladder wall
• **Urine Collection:**

-Voided urine:

- The **first 10 mL of urine (representative of the urethra)** and a **midstream specimen (representative of the bladder)** should be obtained.

- **Prostatic fluid** is obtained by performing digital prostatic massage and collecting the expressed prostatic fluid on a glass slide. In addition, **collection of**

- the **first 10 mL of voided urine** after massage will reflect the prostatic fluid added to the urethral specimen.

-Catheterized Specimens

- Catheterization of a male patient for urine culture is not indicated unless the patient cannot urinate.

- In women the voided specimen is contaminated if it shows evidence of vaginal epithelial cells and lactobacilli on urinalysis, and a midcatheterized specimen should be collected.
• Catheterization and collection of a midcathterized specimen is more accurate than a voided specimen, but carries a risk of iatrogenic infection.
• Although a single dose of an oral antimicrobial agent such as trimethoprim-sulfamethoxazole (TMP-SMX) may be effective for prophylaxis because antimicrobial usage encourages development of bacterial resistance, prophylaxis should be limited to high-risk patients.
- Suprapubic Aspiration
• Suprapubic aspiration is highly accurate, but because it carries some morbidity there is limited clinical usefulness except for a patient who cannot urinate on command, such as patients with spinal cord injuries.
• It is highly useful in newborns and in patients with paraplegia
• Urinalysis

• Microscopic bacteriuria is found in more than 90% of infections with counts of 10^5 colony forming units (cfu) per milliliter of urine or greater and is a highly specific finding.

• However, bacteria are usually not detectable microscopically with lower colony count infections (10^2 to 10^4/mL) → a negative urinalysis for bacteria never excludes the presence of bacteria in numbers of 30,000/mL and less.
• The second error of urinalysis (i.e., a false-positive result) is the reverse of the first error: bacteria are seen in the microscopic sediment, but the urine culture shows no growth. The voided urine from a female patient can contain many thousands of lactobacilli and corynebacteria.

• The validation of the midstream urine specimen can be questioned if numerous squamous epithelial cells (indicative of preputial, vaginal, or urethral contaminants) are present.
• The presence of bacteriuria has a sensitivity for UTI of 40% to 70%, and a specificity of 85% to 95%, depending on the number of bacteria observed

• More than 2 WBCs per HPF in a centrifuged specimen or 10 WBCs/mm3 of urine correlates well with the presence of bacteriuria and is rarely seen in nonbacteriuric patients
• In clinical studies, determination of pyuria in voided urine specimens has a reported sensitivity of 80% to 95% and a specificity of 50% to 76% for UTI.

• The absence of pyuria should cause the diagnosis of UTI to be questioned until urine culture data are available.
• tuberculosis is the well-recognized example of abacterial pyuria, staghorn calculi and stones of smaller size can produce intense pyuria with clumps of WBCs in the absence of UTI.

• Almost any injury to the urinary tract, from chlamydial urethritis to glomerulonephritis and interstitial cystitis, can elicit large numbers of fresh polymorphonuclear leukocytes (glitter cells).
• Microscopic hematuria is found in 40% to 60% of cases of cystitis and is uncommon in other dysuric syndromes.

• Rapid Screen Methods.
  - nitrite in urine
  - leukocyte esterase activity

Although false-positive results are relatively uncommon, the borderline sensitivity of these tests, especially among patients with less characteristic symptoms of UTIs, does not allow these inexpensive tests to replace careful microscopic urinalysis in symptomatic patients. Their main role is in screening asymptomatic patients.
Urine Culture

• 20% to 40% of women with symptomatic UTIs present with bacteria counts of 10^2 to 10^4 cfu/mL of urine probably because of the slow doubling time of bacteria in urine (every 30 to 45 minutes) combined with frequent bladder emptying (every 15 to 30 minutes) from irritation.

• Thus, in dysuric patients, an appropriate threshold value for defining significant bacteriuria is 10^2 cfu/mL of a known pathogen
• The second limitation of the 105 cutoff in midstream voided culture is overdiagnosis in:
  - women
  - uncircumcised men without careful preparation.
Localization

- Fever and Flank Pain
- Ureteral Catheterization (Stamey)
- Tissue and Stone Cultures → research
- Prostate and Urethral Localization Studies
IMAGING TECHNIQUES

- Imaging studies are not required in most cases of UTI because clinical and laboratory findings alone are sufficient for correct diagnosis and adequate management of most patients.

Indication:
- most men
- compromised host
- febrile infection
- signs or symptoms of urinary tract obstruction
- failure to respond to appropriate therapy
- a pattern of recurrent infections suggesting bacterial persistence within the urinary tract
- acute clinical pyelonephritis persist after 5 to 6 days of appropriate antimicrobial therapy
BOX 12-3 Indications for Radiologic Investigation in Acute Clinical Pyelonephritis

Potential ureteral obstruction (e.g., caused by stone, ureteral stricture, tumor)
History of calculi, especially infection (struvite) stones
Potential papillary necrosis (e.g., patients with sickle cell anemia, severe diabetes mellitus, analgesic abuse)
History of genitourinary surgery that predisposes to obstruction, such as ureteral reimplantation or ureteral diversion
Poor response to appropriate antimicrobial agents after 5 to 6 days of treatment
Diabetes mellitus
Polycystic kidneys in patients in dialysis or with severe renal insufficiency
Neuropathic bladder
Unusual infecting organisms, such as tuberculosis, fungus, or urea-splitting organisms (e.g., Proteus)
Ultrasonography

• important renal imaging technique because it is noninvasive, easy to perform, and rapid and offers no radiation or contrast agent risk to the patient.
• It is particularly useful in identifying calculi and hydronephrosis, pyonephrosis, and perirenal abscesses
• It is useful for diagnosing postvoid residual urine.
• A disadvantage is that the study is dependent on the interpretative and performance skills of the examiner.
• Furthermore, the study may be technically poor in patients who are obese or who have dressings, drainage tubes, or open wounds overlying the area of interest.
Computed Tomography and Magnetic Resonance Imaging

• best anatomic detail
• They are more sensitive than excretory urography or ultrasonography in the diagnosis of acute focal bacterial nephritis, renal and perirenal abscesses, and radiolucent calculi. When used to localize renal and perirenal abscesses,
• CT improves the approach to surgical drainage and permits percutaneous approaches.
• MRI has not superseded CT in the evaluation of renal inflammation, but it has provided some advantages in delineating extrarenal extension of inflammation.
Voiding Cystourethrogram

- The voiding cystourethrogram is an important examination in assessing vesicoureteral reflux.
- It may be used to evaluate patients with neuropathic bladders.
- The rare female patient who has a urethral diverticulum causing her persistent infections.
• **Radionuclide Studies**

• Hippuran I-131 and technetium-99m (99mTc) glucoheptonate scans are used to detect focal parenchymal damage, renal function impairment, and decreased renal perfusion in acute renal infections.

• Although gallium-67 scanning has been reported to be useful in the diagnosis of pyelonephritis and renal abscess, it is uncommonly required and may be positive in noninfectious entities.

• Indium-111–labeled WBC studies have limited efficacy in establishing the presence of an inflammatory focus, particularly when the patient’s clinical presentation does not suggest an infectious process.
Classification:

- Asymptomatic bacteriuria - screening bacteriuria
- Cystitis: Uncomplicated - complicated
- Acute pyelonephritis: Uncomplicated - complicated
- Chronic pyelonephritis
- Unresolved UTIs
- Recurrent UTIs
• **A first or isolated infection** is one that occurs in an individual who has never had a UTI or has one remote infection from a previous UTI.

• **An unresolved infection** is one that has not responded to antimicrobial therapy and is documented to be the same organism with a similar resistance profile.

• **A recurrent infection** is one that occurs after documented, successful resolution of an antecedent infection. Consider these two different types of recurrent infection:

  1. **Reinfection** describes a new event associated with reintroduction of bacteria into the urinary tract from outside.

  2. **Bacterial persistence** refers to a recurrent UTI caused by the same bacteria reemerging from a focus within the urinary tract, such as an infectious stone or the prostate. **Relapse** is frequently used interchangeably.
• **Domiciliary or outpatient UTIs** occur in patients who are not hospitalized or institutionalized at the time they become infected. The infections are generally caused by common bowel bacteria (e.g., Enterobacteriaceae or *Enterococcus faecalis*) which are susceptible to most antimicrobial agents.

• **Nosocomial or health care–associated UTIs** occur in patients who are hospitalized or institutionalized, and these are typically caused by *Pseudomonas* and other more antimicrobial-resistant strains.
• **Uncomplicated describes an infection in a healthy patient with** a structurally and functionally normal urinary tract.

• The majority of these patients are women with isolated or recurrent bacterial cystitis or acute pyelonephritis, and the infecting pathogens are usually susceptible to and eradicated by a short course of inexpensive oral antimicrobial therapy.

• **A complicated infection is associated with factors that increase** the chance of acquiring bacteria and decrease the efficacy of therapy.

• The urinary tract is structurally or functionally abnormal, the host is compromised, and/or the bacteria have increased virulence or antimicrobial resistance. The majority of these patients are men.
BOX 12-1  Factors That Suggest a Complicated Urinary Tract Infection

- Functional or anatomic abnormality of urinary tract
- Male gender
- Pregnancy
- Elderly patient
- Diabetes
- Immunosuppression
- Childhood urinary tract infection
- Recent antimicrobial agent use
- Indwelling urinary catheter
- Urinary tract instrumentation
- Hospital-acquired infection
- Symptoms for more than 7 days at presentation
Asymptomatic Bacteriuria
Asymptomatic bacteriuria is a microbiologic diagnosis based on the isolation of a specified quantitative count of bacteria in a properly collected specimen of urine from a patient who is without symptoms or signs referable to UTI.

<table>
<thead>
<tr>
<th>Category</th>
<th>Treatment Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal nonpregnant women</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Recommended</td>
</tr>
<tr>
<td>Diabetic women</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Older persons residing in the community</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Elderly institutionalized subjects</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Subjects with spinal cord injuries</td>
<td>Not recommended</td>
</tr>
<tr>
<td>Patients with indwelling urethral catheters</td>
<td>Not recommended</td>
</tr>
<tr>
<td><strong>Note:</strong> Antimicrobial treatment of asymptomatic women with catheter-associated bacteriuria that persists 48 hours after catheter removal may be considered.</td>
<td></td>
</tr>
<tr>
<td>Urologic interventions</td>
<td>Recommended</td>
</tr>
<tr>
<td>Immunocompromised patients and transplant patients</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>
BLADDER INFECTIONS
describes a clinical syndrome of dysuria, frequency, urgency, and occasionally suprapubic pain.
Clinical Presentation

- The presenting symptoms of cystitis are variable but usually include dysuria, frequency, and/or urgency.
- Suprapubic pain, hematuria, or foul-smelling urine may develop.
- Fever, chills, and other signs of dissemination are not present.
- Some patients may experience suprapubic tenderness, but most have no diagnostic physical findings.
- In women, physical examination should include the possibility of vaginitis, herpes, and urethral pathology, such as a diverticulum.
• *E. coli* is the causative organism in 75% to 90% of cases of acute cystitis in young women

• *S. saprophyticus*, a commensal organism of the skin, is the second most common cause of acute cystitis in young women, accounting for 10% to 20% of these infections

• Other organisms less commonly involved include *Klebsiella* and *Proteus* species and *Enterococcus*.

• In men, *E. coli* and other *Enterobacteriaceae* are the most commonly identified organisms.
Uncomplicated Cystitis
DEFINITION: single non recurrent Cystitis with duration < 7 days without:

- Functional/structural abnormalities of urinary tract
- Recent urinary tract instrumentation
- Recent antimicrobial agent use
- Diabetes mellitus
- Immunosuppression
- Pregnancy
- Hospital-acquired infection
• Most cases of uncomplicated cystitis occur in women.

• Although it is much less common, young men may also experience acute cystitis without underlying structural or functional abnormalities of the urinary tract.
Laboratory Diagnosis

• The presumptive laboratory diagnosis of acute cystitis is based on microscopic urinalysis, which indicates microscopic pyuria, bacteriuria, and occasionally hematuria.

• **Indirect dipstick tests for** bacteria (nitrite) or pyuria (leukocyte esterase) may also be informative and more convenient but are less sensitive than microscopic examination of the urine.

• Urine culture remains the definitive test; and in symptomatic patients, the presence of 10^2 cfu/mL or more of urine usually indicates infection.

• **However, routine urine cultures are often not necessary.**
Differential Diagnosis

• Vaginitis
• urethral infections caused by sexually transmitted pathogens
• miscellaneous noninflammatory causes of urethral discomfort
  • interstitial cystitis, bladder carcinoma, or calculi.
Vaginitis

- is characterized by irritative voiding associated with vaginal irritation and is subacute in onset.
- A history of vaginal discharge or odor and multiple or new sexual partners is common.
- Frequency, urgency, hematuria, and suprapubic pain are not present.
- Physical examination reveals a vaginal discharge
- examination of vaginal fluid demonstrates inflammatory cells.
- Differential diagnosis includes herpes simplex virus, gonorrhea, *Chlamydia, trichomoniasis, yeast, and bacterial vaginosis.*
Urethritis

- causes dysuria that is usually subacute in onset and is associated with a history of discharge and new or multiple sexual partners.
- Frequency and urgency of urination may be present but are less pronounced than in patients with cystitis, and fever and chills are absent.
- Urethral discharge with inflammatory cells or initial pyuria in the male is characteristic.
- The common causes of urethritis include Neisseria gonorrhoeae, Chlamydia, herpes simplex virus, and trichomoniasis.
- Appropriate cultures and immunologic tests are indicated.
<table>
<thead>
<tr>
<th>CIRCUMSTANCES</th>
<th>ROUTE</th>
<th>DRUG</th>
<th>DOSAGE (mg)</th>
<th>FREQUENCY PER DOSE</th>
<th>DURATION (DAYS)</th>
<th>COST PER DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WOMEN</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy</td>
<td>Oral</td>
<td>Nitrofurantoin macrocrystals</td>
<td>100 mg</td>
<td>bid</td>
<td>5</td>
<td>$3.24</td>
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<td></td>
<td></td>
<td>TMP-SMX</td>
<td>1 double-strength tablet (160-800 mg)</td>
<td>bid</td>
<td>3</td>
<td>$0.26</td>
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<td></td>
<td></td>
<td>Trimethoprim</td>
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<td>bid</td>
<td>3</td>
<td>$1.32</td>
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<td></td>
<td></td>
<td>Fosfomycin trometamol</td>
<td>3 g</td>
<td>Single dose</td>
<td>—</td>
<td>$47.99</td>
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<td>Pivmecillinam</td>
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<td>bid</td>
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<td>Not available in the U.S.</td>
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<td></td>
<td></td>
<td>Ciprofloxacin</td>
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<td>3</td>
<td>$0.50</td>
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<tr>
<td></td>
<td></td>
<td>Levofloxacin</td>
<td>250 mg†</td>
<td>qd</td>
<td>3</td>
<td>$5.07</td>
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<tr>
<td>Symptoms for &gt;7 days, recent urinary tract infection, age &gt;65 yr, diabetes, diaphragm use</td>
<td></td>
<td>TMP-SMX or fluoroquinolone</td>
<td>As above</td>
<td>As above</td>
<td>7</td>
<td>As above</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Oral</td>
<td>Amoxicillin</td>
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<td>Cephalexin</td>
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<tr>
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<tr>
<td></td>
<td></td>
<td>TMP-SMX*</td>
<td>As above</td>
<td>As above</td>
<td></td>
<td>As above</td>
</tr>
<tr>
<td><strong>MEN</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Healthy and age &lt;50 yr</td>
<td>Oral</td>
<td>TMP-SMX</td>
<td>As above</td>
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<td>7</td>
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<tr>
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<td>Levofloxacin</td>
<td>500 mg</td>
<td>qd</td>
<td>7</td>
<td>As above</td>
</tr>
</tbody>
</table>
• Three-day therapy is the preferred regimen for uncomplicated cystitis in women.
• Seven-day therapy is the preferred regimen in uncomplicated cystitis in men.
• A follow-up visit or culture is not required in young women who are asymptomatic after therapy.

• A follow-up visit, urinalysis, and urine culture are recommended in older women or those with potential risk factors and in men.

• Urologic evaluation is unnecessary in women and is usually unnecessary in young men who respond to therapy

• However, UTIs in most men should be considered complicated until proven otherwise.
Complicated Cystitis
These infections can be caused by a broad range of bacteria with resistance to multiple antimicrobial agents. Therefore urine cultures are mandatory to identify the bacteria and its antimicrobial susceptibility.

- guidelines for empirical therapy are limited

- For patients with mild to moderate illness who can be treated as an outpatient with oral therapy, the fluoroquinolones provide a broad spectrum of activity with excellent urine and tissue levels and safety.

- If the susceptibility pattern of the pathogen is known, TMP-SMX may be effective.
• 7-14 day
• Because therapy will be compromised without addressing complicating factors, every effort should be made to correct any underlying urinary tract abnormalities and treat host factors that exacerbate the infection.
• Repeat urine cultures should be performed if the patient fails to respond to therapy.
Unresolved UTIs
Clinical Presentation:

- Unresolved infection indicates that initial therapy has been inadequate in eliminating symptoms and/or bacterial growth in the urinary tract.
- If the symptoms of UTI do not resolve by the end of treatment or if symptoms recur shortly after therapy, urinalysis and urine culture with susceptibility testing should be obtained.
- If the patient’s symptoms are significant, empirical therapy with a fluoroquinolone is appropriate, pending results of the culture and susceptibility testing.
Rapid reinfection that mimics unresolved bacteriuria should alert the clinician to the possibility of an enterovesical fistula.

**BOX 12-8 Causes of Unresolved Bacteriuria, in Descending Order of Importance**

- Bacterial resistance to the drug selected for treatment
- Development of resistance from initially susceptible bacteria
- Bacteriuria caused by two different bacterial species with mutually exclusive susceptibilities
- Rapid reinfection with a new, resistant species during initial therapy for the original susceptible organism
- Azotemia
- Papillary necrosis from analgesic abuse
- Giant staghorn calculi in which the “critical mass” of susceptible bacteria is too great for antimicrobial inhibition
- Self-inflicted infections or deception in taking antimicrobial drugs (a variant of Munchausen syndrome)
Management:

- Initial empirical antimicrobial selection should be based on the assumption that the bacteria are resistant. Therefore an antimicrobial agent different from the original agent should be selected.
- Fluoroquinolones offer excellent coverage in most cases and should be given for 7 days.
- When the bacterial susceptibilities are available, adjustments can be made if necessary.
- Urine cultures should be performed during and 7 days after therapy to ensure microbiologic efficacy.
Recurrent UTIs
• Recurrent UTIs are caused by either reemergence of bacteria from a site within the urinary tract (bacterial persistence) or new infections from bacteria outside the urinary tract (reinfection).

• Reinfections in men are uncommon and may be associated with an underlying abnormality, such as urethral stricture; therefore, at a minimum, endoscopic evaluation is indicated.
bacterial persistence
**BOX 12-4** Correctable Urologic Abnormalities That Cause Bacterial Persistence

- Infection stones
- Chronic bacterial prostatitis
- Unilateral infected atrophic kidneys
- Ureteral duplication and ectopic ureters
- Foreign bodies
- Urethral diverticula and infected periurethral glands
- Unilateral medullary sponge kidneys
- Nonrefluxing, normal-appearing, infected ureteral stumps after nephrectomy
- Infected urachal cysts
- Infected communicating cysts of the renal calyces
- Papillary necrosis
- Perivesical abscess with fistula to bladder
DX:

• A systematic radiologic and endoscopic evaluation of the urinary tract is mandatory.
• CT and cystoscopy provide the initia screening.
• Retrograde urography may be required in selected patients to delineate abnormalities, such as diverticulum or nonrefluxing ureteral stump.
Treatment:

=surgery

• In patients in whom the focus of infection cannot be eradicated, long-term, low-dose antimicrobial suppression is necessary to prevent symptoms of infection.

• The antimicrobial drugs used for These include nitrofurantoin, TMP-SMX, cephalexin, and the fluoroquinolones.
Reinfections
These reinfections most often occur in women and girls and are associated with ascending colonization from the bowel flora.

Reinfections in men are often associated with a urinary tract abnormality.

The possibility of a vesicoenteric or vesicovaginal fistula should be considered when the patient has any history of pneumaturia, fecaluria, diverticulitis, obstipation, previous pelvic surgery, or radiation therapy.
• Probability of recurrent UTIs increases with the number of previous infections and decreases in inverse proportion to the elapsed time between the first and the second infections.

• Most reinfections occurred after 2 weeks and within 5 months.

• Patients with frequent UTI who take prophylactic antimicrobial agents for extended periods (≥6 months) reduces morbidity and may decrease their infections during the time of prophylaxis, but the rate of infection returns to the pretreatment rate after prophylaxis is stopped.
• Evaluation of the patient with presumed reinfections must be individualized.

• Abnormalities should be corrected and urinary tract function restored by medical, pharmacologic, or surgical management.

• A thorough urologic evaluation is essential in all men and in women with evidence of upper tract infections (fevers, chills, flank pain, hemorrhagic cystitis, or other risk factors, such as history of unexplained hematuria, obstructive symptoms, neurogenic bladder dysfunction, renal calculi, fistula, analgesic abuse, or severe disease such as diabetes mellitus
• In women, diaphragm-spermicide use has been associated with an increased risk of UTI and vaginal colonization with *E. coli*

• Postmenopausal women have frequent reinfections. These infections are sometimes attributable to residual urine after voiding, which is often associated with bladder or uterine prolapse.

• In addition, the lack of estrogen causes marked changes in the vaginal microflora, including a loss of lactobacilli and increased colonization by *E. coli*
Urinary tract imaging will demonstrate the anatomy of the urinary tract and provide reasonable assessment of its functional status.

In healthy women, upper tract abnormalities associated with reinfections are very rare; therefore routine urologic imaging is not indicated.

Cystoscopy should be performed in men or women who have frequent reinfections and symptoms suggestive of obstruction, bladder dysfunction, and fistula.

If the patient has residual urine that is judged to be significant (e.g., 100 mL) and due to a narrowing of the urethra, a single dilation of the urethra to improve bladder emptying
• Antimicrobial management in women who have had two or more symptomatic UTIs over a 6-month period or three or more episodes within a 12-month period involves one of three regimens:

1-low-dose continuous prophylaxis
2-self-start intermittent therapy
3-postintercourse prophylaxis.
The oral antimicrobial agents with minimal adverse effects on the bowel and vaginal flora are:

- TMP-SMX or TMP alone
- nitrofurantoin
- cephalexin (in minimal dosage)
- fluoroquinolones
Because the fluoroquinolones are expensive and can be used only in nonpregnant women, we favor their use only when antimicrobial resistance or patient intolerance to TMP-SMX, TMP, nitrofurantoin, or cephalexin occurs.
-When breakthrough infections occur, they are not necessarily accompanied by symptoms; therefore we advocate monitoring for infections every 1 to 3 months, even in asymptomatic patients.

-Breakthrough infections usually respond to full-dose therapy with the drug used for prophylaxis. However, cultures and susceptibility tests may indicate that another drug is indicated.

- Low-dose prophylaxis is usually discontinued after about 6 months, and the patient is monitored for reinfection.
self-start intermittent therapy:

- the patient is given a dip slide device to culture the urine and is instructed to perform a urine culture when symptoms of UTI occur.
- The patient is also provided a 3-day course of empirical, full-dose antimicrobial therapy to be started immediately after performing the culture.
- It is important that the antimicrobial agent selected for self-start therapy have a broad spectrum of activity and achieve high urinary levels to minimize development of resistant mutants.
- In addition, there should be minimal or no side effects on the bowelflora.
- Fluoroquinolones are ideal for self-start therapy because they have a spectrum of activity broader than any of the other oral agents and are superior to many parenteral antimicrobials, including aminoglycosides.

- Nitrofurantoin and TMP-SMX are acceptable alternatives, although they are somewhat less effective.

- Antimicrobial agents such as tetracycline, ampicillin, SMX, and cephalexin in full doses should be avoided because they can give rise to resistant bacteria
• The culture is brought to the office as soon as possible.

• If the culture is positive and the patient is asymptomatic, a culture is performed 7 to 10 days after therapy to determine efficacy.

• If the patient has symptoms that do not respond to initial antimicrobial therapy, a repeat culture and susceptibility testing of the initial culture specimen are performed and therapy adjusted accordingly.

• If symptoms of infection are not associated with positive cultures, urologic evaluation should be performed to rule out other causes of irritative bladder symptoms, including carcinoma in situ, interstitial cystitis, and neurogenic bladder dysfunction.
Postintercourse therapy with antimicrobial agents, such as nitrofurantoin, cephalexin, TMP-SMX, or a fluoroquinolone taken as a single dose, will effectively reduce the incidence of reinfection.
Symptoms and Signs of Recurrent Urinary Tract Infection (No Fever or Flank Pain)

1. History
2. Urinalysis
3. Culture
   - Positive
     - Antimicrobial therapy
     - Repeated infections: same species at short intervals
       - Yes: Bacterial persistence
         - Urologic evaluation
           - Yes: Removal of infectious focus
           - No
             - No: Related to coitus
               - Yes: Postcoital prophylaxis
               - No: Low-dose prophylaxis
             - Yes: Self-start therapy
     - No
       - Reinfection
         - Risk factors
           - Yes
             - Related to coitus
               - Yes: Postcoital prophylaxis
               - No: Low-dose prophylaxis
           - No
             - Appropriate therapy

Figure 12-14. Management of recurrent urinary tract infection.
Acute Pyelonephritis
Acute pyelonephritis:

- clinical syndrome of chills, fever, and flank pain that is accompanied by bacteriuria and pyuria,

- a combination that is reasonably specific for an acute bacterial infection of the kidney.

- The term should not be used if flank pain is absent.

- There may be serious difficulties in diagnosing spinal cord–injured and elderly patients who may be unable to localize the site of their discomfort.
• less prevalent than bladder infection
• significant renal infection may be associated with an insidious onset of nonspecific local or systemic symptoms, or it may be entirely asymptomatic.
• Therefore a high clinical index of suspicion and appropriate radiologic and laboratory studies are required to establish the diagnosis of renal infection.
• Unfortunately, the relationship between laboratory findings and the presence of renal infection often is poor. Bacteriuria and pyuria, the hallmarks of UTI, are not predictive of renal infection.

• Conversely, patients with significant renal infection may have sterile urine if the ureter draining the kidney is obstructed or the infection is outside of the collecting system.
On physical examination, there often is tenderness to deep palpation in the costovertebral angle. Variations of this clinical presentation have been recognized.

Acute pyelonephritis may also simulate gastrointestinal tract abnormalities with abdominal pain, nausea, vomiting, and diarrhea.

Asymptomatic progression of acute pyelonephritis to chronic pyelonephritis, particularly in compromised hosts, may occur in the absence of overt symptoms.
• The effect of renal infection on renal function is varied
• nonobstructive pyelonephritis is no longer recognized as a major cause of renal failure
• Acute renal failure may be present in the rare case
Laboratory Diagnosis:

- leukocytosis with a predominance of neutrophils
- Urinalysis → WBCs, often in clumps, and bacterial rods or chains of cocci.
- The presence of large amounts of granular or leukocyte casts in the urinary sediment is suggestive of acute pyelonephritis.
specific type of urinary cast → bacteria in its matrix

- increased erythrocyte sedimentation rate
- elevated C-reactive protein levels
- elevated creatinine levels if renal failure is present
- creatinine clearance may be decreased.
- Blood cultures may be positive.
Bacteriology

- Urine cultures are positive
- but about 20% of patients have urine cultures with fewer than $10^5$ cfu/mL and therefore negative results on Gram staining of the urine
- *E. coli*, which constitutes a unique subgroup that possesses special virulence factors, accounts for 80% of cases.
If vesicoureteral reflux is absent, a patient bearing the P blood group phenotype may have special susceptibility to recurrent pyelonephritis caused by *E. coli* that have *P* pilis and bind to the P blood group antigen receptors.

Bacterial K antigens and endotoxins also may contribute to pathogenicity.
• Many cases of community-acquired pyelonephritis are caused by a limited number of multiantimicrobial-resistant clonal groups.

• More resistant species, such as *Proteus*, *Klebsiella*, *Pseudomonas*, *Serratia*, *Enterobacter*, or *Citrobacter*, should be suspected in patients who have recurrent UTIs, are hospitalized, or have indwelling catheters, as well as in those who required recent urinary tract instrumentation.

• Except for *E. faecalis*, *S. epidermidis*, and *S. aureus*, gram-positive bacteria rarely cause pyelonephritis.
• Blood cultures are positive in about 25% of cases of uncomplicated pyelonephritis in women, and the majority replicate the urine culture and do not influence decisions regarding therapy. Therefore blood cultures should not be routinely obtained for the evaluation of uncomplicated pyelonephritis in women.

• However, they should be performed in:
  - men and women with systemic toxicity
  - in those requiring hospitalization
  - risk factors such as pregnancy
Renal Ultrasonography and Computed Tomography:

- *These* studies are commonly used to evaluate patients initially for complicated UTIs or factors or to reevaluate patients who do not respond after 72 hours of therapy.

- Ultrasonography and CT show renal enlargement, hypoechoic or attenuated parenchyma, and a compressed collecting system. They also may delineate focal bacterial nephritis and obstruction.

- When parenchymal destruction becomes pronounced, a more disorganized parenchyma and abscess formation associated with complicated renal and perirenal infections may be identified.
Differential Diagnosis:

1- Acute appendicitis
2- Diverticulitis
3- Pancreatitis

Location of the pain often is different.

Results of the urine examination are usually normal.

4- Herpes zoster can cause superficial pain in the region of the kidney but is not associated with symptoms of UTI.
Management:

(1) uncomplicated infection that does not warrant hospitalization

(2) uncomplicated infection in patients with normal urinary tracts who are ill enough to warrant hospitalization. For parenteral therapy

(3) complicated infection associated with hospitalization, catheterization, urologic surgery, or urinary tract abnormalities
Figure 12-20. Management of acute pyelonephritis.
OUT PATIENT:

- Many physicians administer a single parenteral dose of an antimicrobial agent (ceftriaxone, gentamicin, or a fluoroquinolone) before initiating oral therapy.
- If a gram-positive organism is suspected, amoxicillin or amoxicillin/clavulanic acid is recommended.

IN PATIENT:

- Parenteral fluoroquinolone, an aminoglycoside with or without ampicillin, or an extended-spectrum cephalosporin with or without an aminoglycoside is recommended.
- If gram-positive cocci are causative, ampicillin/sulbactam with or without an aminoglycoside is recommended.
• complicated pyelonephritis and positive blood cultures should be treated with parenteral therapy until clinically stable.

• If blood cultures are negative, 2- to 3-day parenteral therapy is sufficient.

• Following parenteral therapy, an appropriate oral antimicrobial drug (fluoroquinolone, TMP, TMP-SMX, or amoxicillin or amoxicillin/clavulanic acid for gram-positive organisms) should be continued in full dosage for an additional 10 to 14 days. (B/C Positive $\rightarrow$ 14-21d)

• In patients with fever lasting longer than 72 hours, CT is most helpful for ruling out obstruction and identifying renal and perirenal infections.
Follow-Up:

- urine cultures → fifth to the seventh day of therapy and 10 to 14 days after discontinuing antimicrobial therapy

- Patients who relapse usually are cured by a second 14-day course of therapy, but occasionally a 6-week course is necessary
• **Chronic pyelonephritis**

• *describes a shrunken, scarred kidney, diagnosed by morphologic, radiologic, or functional evidence of renal disease that may be postinfectious but is frequently not associated with UTI.*
THANK YOU