

Urinary Tract Infection (Adult)

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1. Introduction

Urinary tract infections (UTIs) are one of the most common conditions encountered by the medical profession. UTI is defined by **symptoms** localized to the urinary tract combined with objective evidence of **inflammation** (pyuria) from urinalysis and urine culture with an identified urinary pathogen. It is important to distinguish the term "cystitis" from UTI. "Cystitis" implies inflammation but does not necessarily mean infectious etiology. Patients presenting to the urologist for UTIs usually have either recurrent or difficult treat infections. These infections may lead to frustration from consultants and patients due to the trial and error of antibiotic therapy, recurrent painful symptoms, spread of infection, and side effects of therapy. **The urologist's role is to manage the complex UTI (see definition Table 1) and infectious complications and to find and treat the underlying etiology so as to prevent or reduce further episodes.** In an era of increasing antibiotic resistance, UTIs have become more complex to manage, making it prudent to frequently engage infectious disease specialists. Herein, we will examine the various common patient-specific scenarios important to urologists (**Figure 1**). Basic definitions are listed in **Table 1**. One of the **most important goals in treating UTIs for the urologist is to identify patients at risk for recurrent infection or complications and mitigate the risks where possible. This will be detailed below and the remedies vary based on the patient population and risk factors.** One of the first tasks is to determine if the current infection represents a complicated UTI or an uncomplicated UTI, which impacts choice and duration of antibiotic treatment (see **Table 1**).

Table 1. Basic Definitions

Bacteriuria	Bacteria in the urine sample
Asymptomatic Bacteriuria (ASB)	Presence of bacteria in the urine that causes no illness or symptoms
Pyuria	White blood cells in the urine sample
Sterile Pyuria	Urinalysis with white blood cells present with negative urine culture indicates the presence of inflammation that can arise from atypical bacteria (chlamydia, mycoplasma, ureaplasma), stones, tuberculosis or other organisms which are not able to grow aerobically in a urine culture ¹
Acute bacterial cystitis	A culture-proven infection of the urinary tract with a bacterial pathogen associated with acute-onset symptoms such as dysuria in conjunction with variable degrees of increased urinary urgency and frequency, hematuria, and new or worsening incontinence
Uncomplicated UTI	An infection of the urinary tract in a healthy patient with an anatomically and functionally normal urinary tract and no known factors that would make them susceptible to develop a UTI
Complicated UTI	An infection in a patient in which one or more complicating factors may put them at higher risk for development of a UTI and potentially decrease efficacy of therapy Such factors include the following <ul style="list-style-type: none">• Male gender• Anatomic or functional abnormality of the urinary tract (e.g, stone disease, diverticulum, neurogenic bladder)• Immunocompromised host• Multi-drug resistant bacteria
Recurrent UTI (rUTI)	Two separate culture-prove episodes of acute bacterial cystitis and associated symptoms within six months or three episodes within one year
Cystitis	Clinical syndrome of inflammation or infection of the urinary bladder
Pyelonephritis	Inflammation or infection of the kidneys that tends to arise from an ascending genitourinary tract infection
Isolated UTI	First documented UTI either in their lifetime or after a prolonged period of time without having a UTI
Persistent UTI	Persistent infection despite antibiotic therapy

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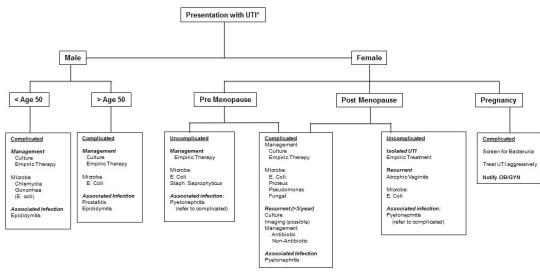


Figure 1: Presentation with UTI

2. Epidemiology

Greater than 50% of all women and 12% of all men will experience a UTI in their lifetime.² UTIs accounted for 10.5 million office visits and 2-3 million emergency department visits in the United States in 2007.³ UTIs also have considerable medical costs, with estimates of over \$2.6 billion dollars annually, and can substantially impact an individual's productivity and quality of life.⁴ UTIs are usually present as cystitis or inflammation of the bladder but can potentially spread to other organs such as the kidney, commonly in women, and epididymitis or orchitis in men.² Due to increasing rates of bacterial resistance, the usual antibiotic therapies are becoming less efficacious and more patients are presenting with "recurrent" UTIs.⁵ **Table 2** describes the top 8 bacteria that cause UTIs.⁶

Table 2. Top 8 Bacterial Causes of Urinary Tract Infections

Uropathogenic <i>Escherichia coli</i>	<i>Staphylococcus saprophyticus</i>	Klebsiella species
Enterococcus species	Group B Streptococcus	<i>Proteus mirabilis</i>
<i>Pseudomonas aeruginosa</i>	<i>Staphylococcus aureus</i>	
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3. Risk Factors

Risk factors for UTI have generally been categorized into three groups: **genetic, biologic, and behavioral**.

Certain medical conditions such as **diabetes, obesity, sickle cell trait or neurologic disorders also confer an increased risk, as do anatomic congenital abnormalities, urologic stones, and any condition requiring repeated or indwelling catheterization or instrumentation**. These risks can be categorized into genetic, biologic, or behavioral factors and all should be explored during the evaluation process.^{7,8}

For pre-menopausal women, additional risk factors include sexual activity, spermicide or diaphragm use, first UTI at a young age, maternal history of a UTI, personal history of UTI and increasing parity.

For post menopausal women, additional risk factors include sexual activity, personal history of UTI, and incontinence.⁹ Urinary tract infections in this population are a symptom genitourinary syndrome of menopause, which results from the effect of estrogen deficiency in the female genitourinary tract.¹⁰

For men, additional risk factors include benign prostatic hyperplasia, incomplete bladder emptying and incontinence.¹¹

4. Patient Evaluation

UTIs are diagnosed with the combination of symptoms and a positive urinalysis (UA) or urine culture. The urine dipstick can yield immediate results as it is done in-office as a point of care test, making it one of the most popular methods of diagnosis. Although the negative predictive value of UA is very high, UA lacks specificity and many have recommended that positive results should be confirmed!¹² This varies based on the population tested and clinical setting. **Microscopic exam**, either in-office or in-lab may provide more reliable results, and a urine culture is considered the most specific diagnostic modality. **Figures 2-16** is a detailed atlas of some important findings on microscopic urine exam. For a detailed discussion on in-office urinalysis please refer to Simerville "Urinalysis: A Comprehensive Review".²



Figure 2: uric acid crystals. Courtesy of Indiana Pathology Images (www.ipimages.com)

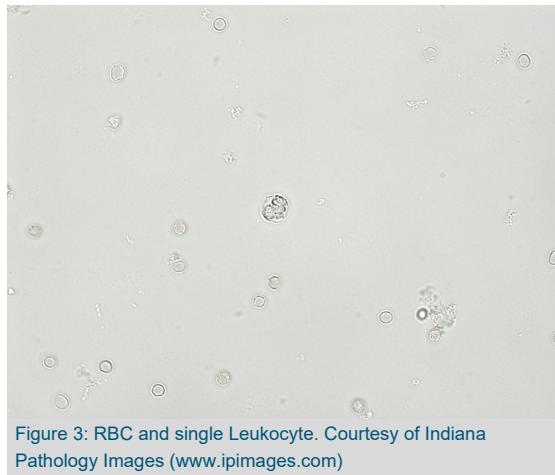
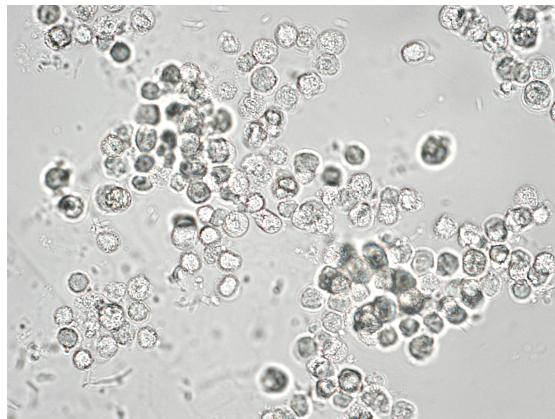


Figure 3: RBC and single Leukocyte. Courtesy of Indiana Pathology Images (www.ipimages.com)



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Figure 4: Multiple WBCs. Courtesy of Indiana Pathology Images (www.ipimages.com)



Figure 5: Transitional epithelial cells. Courtesy of Indiana Pathology Images (www.ipimages.com)

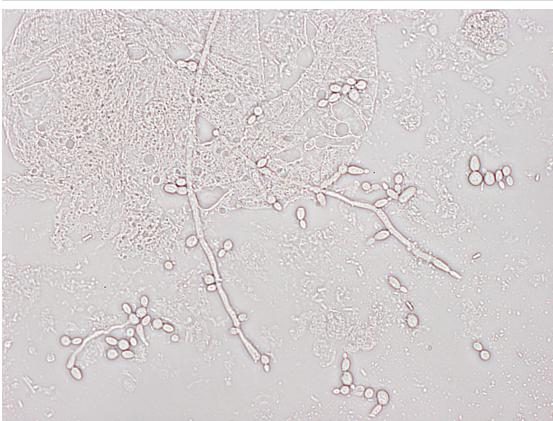


Figure 6: Yeast (budding and pseudohyphae), bacteria, amorphous crystals. Courtesy of Indiana Pathology Images (www.ipimages.com)



Figure 7: Struvite/triple phosphate crystals, bacteria. Courtesy of Indiana Pathology Images (www.ipimages.com)

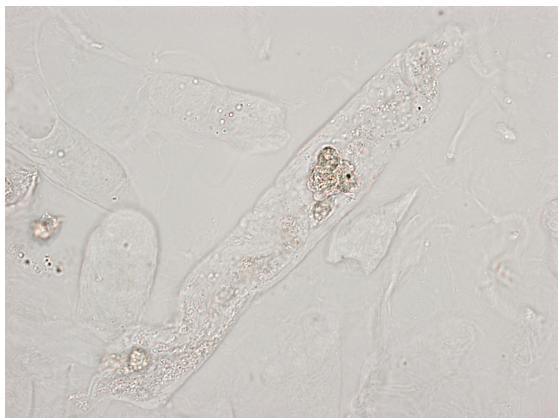


Figure 8: Hyaline casts, WBC cast. Courtesy of Indiana Pathology Images (www.ipimages.com)

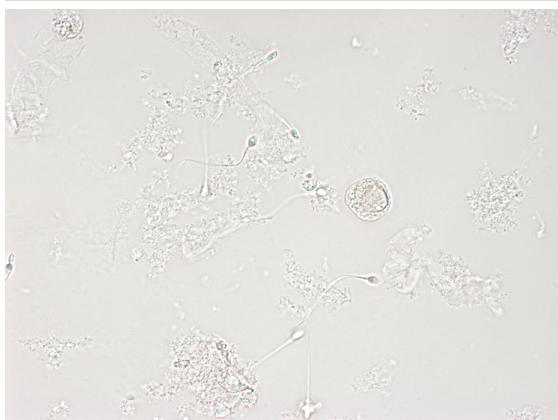


Figure 9: Sperm with renal tubular epithelial cell. Courtesy of Indiana Pathology Images (www.ipimages.com)



Figure 10: WBCs, bacteria. Courtesy of Indiana Pathology Images (www.ipimages.com)



Figure 11: Squamous epithelial cells, WBCs, bacteria. Courtesy



Figure 12: Renal tubular epithelial cells, WBCs. Courtesy of Indiana Pathology Images (www.ipimages.com)



Figure 13: Waxy cast. Courtesy of Indiana Pathology Images (www.ipimages.com)



Figure 14: WBC cast, mucous strands. Courtesy of Indiana Pathology Images (www.ipimages.com)

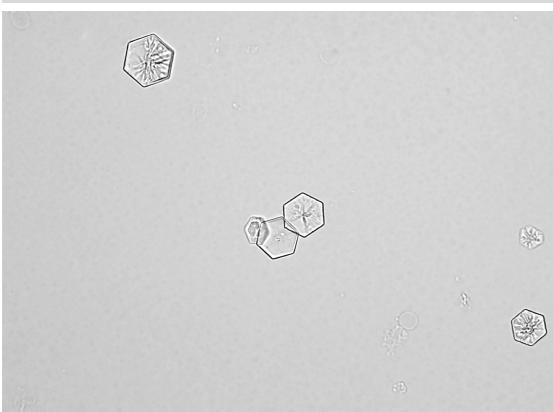


Figure 15: Cysteine crystals. Courtesy of Indiana Pathology Images (www.ipimages.com)

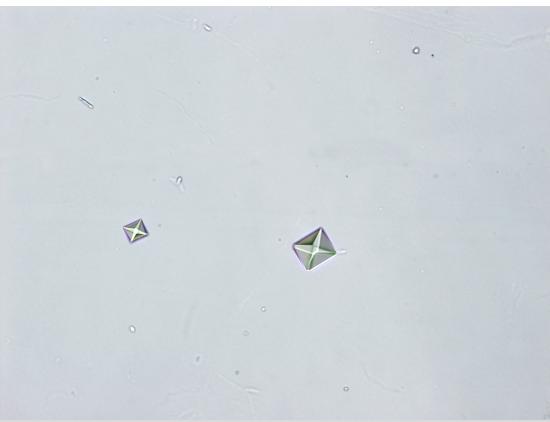


Figure 16: Calcium oxalate dihydrate crystals. Courtesy of Indiana Pathology Images (www.ipimages.com)

4.1 Asymptomatic Bacteriuria

Asymptomatic bacteriuria (ASB) defined as bacteria on urine culture, irrespective of the presence of pyuria, in the absence of signs or symptoms attributable to UTI.

The prevalence of ASB varies from 1-6% in premenopausal women, 2-10% in pregnancy, where it can lead to low birthweight and premature delivery, and can be as high as 2% in non-institutionalized elderly women. Outside of pregnancy, ASB carries so little risk that screening for asymptomatic bacteriuria has been given a grade D recommendation by the United States Task Force on Preventative Services (USPSTF), treatment is unnecessary and contributes to antibiotic resistance.³ The Infectious Diseases Society of America has published recommendations against treating asymptomatic bacteriuria with the exception of two scenarios: **pregnant women or patients undergoing genitourinary instrumentation**.¹²⁻¹³

- a. **Pregnant women:** During pregnancy, the gravid uterus imposes a temporary anatomic defect in the lower urinary tract and pregnancy is also a state of immunosuppression. The reason to treat ASB in pregnant women is to prevent bacteraemia and potential fetal infection.
 - Current recommendations are to collect a urine culture at one of the initial prenatal visits. There is insufficient evidence to inform a recommendation for or against repeat screening during pregnancy for a woman with an initial negative screening culture or following treatment of an initial episode of ASB
 - Optimal duration of the therapy depends on the antimicrobial given but the shortest effective course should be used. It is important to be cognizant of what antibiotic are teratogenic.
- b. **Persons scheduled for GU instrumentation:** In patients who will undergo endoscopic urologic procedures associated with mucosal trauma it is recommended to screen and treat for ASB prior to surgery
 - Recommendation for pre procedure urine culture so that targeted antimicrobial therapy can be prescribed
 - Consider a shorter course of antimicrobial therapy
 - See AUA White Paper: **Urologic Surgery Antimicrobial Prophylaxis** and AUA Updates 2019 Volume 38 Lesson 17: **What's New in Antimicrobial Prophylaxis I Urological Surgery**.

4.2 Patient History and Physical Examination

Typical symptoms of UTI include dysuria, urinary frequency, or urgency. Factors worth noting on history include: number of UTIs, history of urinary tract abnormalities, prior urologic surgeries, neurogenic bladder (spinal cord injuries, spine surgery, diabetes), immunologic status (diabetes, HIV/AIDS, immunosuppression), and recent antibiotic exposure. It is also important to query for the chance of pregnancy in this population as there are certain antibiotics to avoid in a pregnant patient.

Relevant Factors In Patient History

1. **Differential Diagnosis**
 - a. Patient Specific Factors (See [Figure 1](#))
 - b. The differential based on the chief complaint should guide targeted questioning to direct exam and diagnostic testing.
2. **Focused History**
 - a. Chief Complaint
 - i. Urethritis (constant vs. dysuria)
 - ii. Cystitis (Hematuria, Pneumaturia, Fecaluria)
 - iii. Flank Pain
 - b. Complaint History (OPQRST)
 - i. Onset
 - ii. Palliative factors/pain
 - iii. Quality of pain
 - iv. Region of body
 - v. Severity of pain (Visual Analog Scale 1-10)
 - vi. Timing
 - c. Infection History
 - i. Number of past UTI, culture results and treatments
 - ii. Anatomic abnormalities (horseshoe kidney, hydronephrosis, UPJ)
 - iii. Any other associated infections
 - d. Voiding History
 - i. Frequency of voiding
 - ii. Difficulty with voiding
 - iii. Incontinence

- iv. Use of medications for bladder
- e. Bowel History
 - i. Frequency of bowel movements
 - ii. Consistency of bowel movements
 - iii. Use of medications for bowels
- f. Social History
 - i. Occupation (r/o CIS/bladder cancer)
 - ii. IV Drug use
 - iii. Hygiene
- g. Sexual History
 - i. Previous STI's
 - ii. New sexual partners
 - iii. Sexual practices
 - iv. Lubricants and protection
 - v. Chance of pregnancy
- h. Family History
 - i. UTI in families
 - ii. History of urinary calculi
- i. Pediatric History
 - i. Pediatric urinary surgeries
 - ii. Pediatric UTI
 - iii. Dysfunctional voiding
- j. Medical History
 - i. Recent hospitalization
 - ii. Diabetes
 - iii. Spinal Cord Injury
 - iv. HIV/AIDS
- k. Surgical History
 - i. Spine Surgery
 - ii. Urinary Calculi
 - iii. Bladder/prostate/renal/ureteral surgery
 - iv. Prior vaginal mesh
- l. Medication History
 - i. Recent antibiotic exposure
 - ii. Recent anesthesia
 - iii. Pain medications
 - iv. Steroids or Immune compromising agents

• Physical Exam

- 3. Physical examination should focus on temperature, abdominal exam assessing for pain, back exam assessing for costovertebral tenderness, pelvic examination including wet prep, herpes PCR, and chlamydia testing if urethritis or vaginitis is suspected. Bladder and urethral palpation and inspection during the pelvic exam should be conducted to assess tenderness or for evidence of diverticulum or other masses. Laboratory testing to be conducted are listed in the section titled:

Laboratory Testing in Cystitis Evaluation. Other more invasive testing is generally not needed unless the UTI is a complicated UTI (see below).

• Other

- 3. Patient website

<https://www.urologyhealth.org/healthy-living/urologyhealth-extra/magazine-archives/summer-2014/urinary-tract-infections-learn-how-to-spot-and-treat-th>

4.3 Laboratory Testing in Cystitis Evaluation

1. Urine Dip Stick

- a. Positive:
 - i. Leukocyte Esterase – indicated presence of 5-15 WBC/HPF
 - ii. Nitrite – bacteria convert nitrates to nitrites
 - iii. Blood – hematuria, hemoglobinuria or myoglobinuria.
 - iv. Glucose – may indicate diabetes

b. Limitations: Improved performance using dip stick as a “rule out” UTI rather than diagnosis of UTI. Each test within the dip stick has false positives and negatives that should be understood as limitations of the test.

2. Urine Microscopy (see Figures 2-16, also [AUA Update Series 2019 Volume 38 Lesson 30 Interpretation of Urinalysis](#))

- a. Laboratory or in Office

- i. Urine is centrifuged (1500-4000 RPM x 3-5 min)
 - 1. Decant supernatant, suspend pellet, drop on slide, add slide cover
 - 2. Examine at low power, high power, and phase contrast.
- ii. Squamous Cells – Indicator of quality. More “squams” = poor collection i.e. not midstream or presence of skin contamination.
- iii. White Blood Cells: Number of WBC's may assist in identification of true infection Pyuria ($10+$ WBC/HPF)
- iv. Red Blood Cells: More pertinent when deciding whether or not a microscopic hematuria work up (≥ 3 RBC/HPF) is needed if infection is not identified. A dipstick result is not sufficient.
- v. Bacteria – $5/\text{HPF} = 100,000 \text{ CFU/mL} = \text{UTI}$
- vi. Urine Crystals – indicates risk of urinary calculi
- vii. Urine Casts – may indicate medical renal disease

b. Limitations – In unilateral ureteral obstruction and infection the UA may be negative as the infected urine may not pass the obstruction to the bladder.

3. Gram Stain

- a. Differentiate gram positive and gram negative bacteruria
- b. The gram stain may alter empiric antibiotic choices

4. Urine Culture

- a. 10^3 colony forming units (CFU) is deemed to be a UTI by definition
- b. May take up to 3 or 4 days to receive the result with corresponding sensitivity profiles

5. Blood Culture

- a. Usually not indicated in outpatient cystitis presentation
 - b. If patient has rigors, abnormal vitals (fever, tachycardia, hypotension), or a suspecting associated infections (pyelonephritis) blood culture would be indicated.
6. Urine pregnancy test if applicable (qualitative HCG)

The clinician should be aware of many new and emerging technologies to address some weaknesses in traditional UA and urine culture. These include polymerase chain reaction (PCR), expanded quantitative urine culture (EQUC), and next generation sequencing (NGS).⁵ See section 5.1 Urinary Microbiome. For more information the reader is referred to [AUA University Podcast](#) on this topic.

4.4 Evaluation of Recurrent UTI

Recurrent UTI (rUTI) is defined as 3 UTIs within 12 months, or 2 within 6 months. (see [AUAUniversity Podcast: Second Opinion Cases Ask the Guidelines Recurrent UTI](#) and [AUA Guideline: Recurrent UTI](#)).

The initial evaluation starts similar to the evaluation of UTI. The goal of the evaluation of rUTI is to prevent further UTIs. Patients should be asked about inciting factors, such as the relationship of UTI with the time of coitus. For peri- and postmenopausal women presenting with rUTI the evaluation should also include evaluation of genitourinary syndrome of menopause.⁶

In addition to obtaining a complete patient history and performing a pelvic examination in women presenting with rUTIs, clinicians should:

- a. Clinicians must document positive cultures associated with the prior symptomatic episodes for the diagnosis of rUTI
- b. If there is question of contamination of prior cultures one should repeat and even consider obtaining a catheterized specimen
- c. If patient has comorbidities which may place them at risk for complicated UTI consider imaging of the urinary tract. If kidney stone is not suspected one may begin with renal/bladder ultrasound but may need to consider exams such as KUB, CT or VCUG.
- d. Pregnancy test should be performed in any woman prior to ordering any radiologic exams that may include radiation
- e. Cystoscopy should be considered if there are any comorbidities or risk factors for foreign body or malignancy

4.5 Complicated UTI

Risk factors for a complicated UTI include diabetes, immunosuppression, pyelonephritis, resistant organisms, urinary tract abnormalities, previous urologic surgery, a history of urologic stones, spinal cord injury or an indwelling catheter.⁷ **Table 3** details these. UTI in pregnancy is also, by definition, complicated. Many of these patients will initially present to the urologist for consultation.

Table 3. Complicated Urinary Tract Infections

Failure to respond to appropriate antimicrobial therapy

Fever ($>38^{\circ}\text{C}$)

Gross hematuria

Diabetes

Renal failure

Obstruction (upper or lower urinary tract)

History of calculi

Neuropathic bladder

Recent genitourinary surgery

Recent catheterization

Unusual organisms

Tuberculosis

Fungus

Urea-splitting organisms (Proteus, Staphylococcus, Klebsiella, Pseudomonas, Mycoplasma etc.)

Immune system compromise (Transplantation, HIV, Immunosuppressive medications, steroids)

Pregnancy

Male Gender

[View Image](#)

4.5.1 Evaluation of Complicated UTI

Evaluation is similar to a primary UTI. Urine culture is **required**. **Imaging** can be very helpful to narrow the differential of surgically correctable UTI etiologies. Typically, a KUB and ultrasound are sufficient for women of childbearing age.¹⁴ If a renal stone or obstruction is suspected, a CT scan without contrast may be useful. A CT scan with contrast may be useful in select patients where there is question of anatomic abnormality or concern for malignancy. **Cystoscopy** may be indicated for women with a suspected fistula, those who have undergone pelvic surgery, especially anti-incontinence surgery, those with a history of nephrolithiasis, persistent microhematuria, or gross hematuria. Cystoscopy allows for further examination of the urethra to investigate for diverticula, polyps, or other sources for recurrent infection. Elevated post-void residual using an in office automated ultrasound device with or without uroflowmetry may provide justification for cystoscopy or urodynamic study to rule out urethral stricture, urethral obstruction, or bladder contractility/neurogenic issues.

5. Microbiology

5.1 Urinary Microbiome

In the past decade there have been significant advances in the study of the urinary microbiome which have lead to the understanding that the healthy urinary tract contains fastidious microorganisms not previously detected by traditional culture techniques. Some of these can be detected by **expanded quantitative urine culture (EQUC)**.¹³ Polymerase chain reaction (PCR) and next generation sequencing techniques are more sensitive methods to detect these microorganisms. However, the clinical implications of more sensitive assays for microbial detection remain unclear and refinement and research are necessary to help guide clinical practice. (See **2019 AUA Panel Discussion on New Technologies for Diagnosing UTIs**). Future applications of this technology are likely to change to conversation from "infection" to "dysbiosis" and may lead to important insights to the etiology of idiopathic bladder conditions such as interstitial cystitis/painful bladder syndrome and overactive bladder.

5.2 Typical Uropathogens:

In men, culture studies of UTI *Escherichia coli*, *Enterococcus faecalis*, and *Staphylococcus* are some of the most common bacteria isolated in hospitalized men.¹⁵ Foley catheters were protective in men but not women (OR 0.71).¹⁶

In women, pathogens in the distal urethra are usually made up of vaginal and enteric flora. The vagina is colonized with *Lactobacillus*, which protects against uropathogens by altering the pH of the vagina. Bacteria from the gastrointestinal tract are the most common organisms causing UTIs in women. They ascend from the vaginal introitus through the urethra to the bladder. **For pre-menopausal women, 80-85% of UTIs are caused by *Escherichia coli*.**¹⁷ Other pathogens include *Staphylococcus saprophyticus* (10-15%), *Klebsiella pneumoniae* and *Proteus mirabilis*, each accounting for approximately 4% of UTIs in pre-menopausal women.¹⁸

5.3 Atypical Uropathogens

5.3.1 Candida UTI

Most fungal UTI are secondary to *Candida* species. *Candida* may represent vaginal contamination or actual infection. This requires repeat urine culture via midstream clean catch or repeat urethral catheterization. Most patients tend to be asymptomatic (no fever or leukocytosis) and thus do not warrant treatment. When associated with a catheter, it tends to be colonization, particularly when found in hospitalized patients already on broad-spectrum antibiotics.¹⁹ **However, one must be mindful of candiduria in more susceptible patients such as immunosuppressed, diabetic, ICU patients, and neutropenic patients. In these cases, candiduria may point to invasive candidiasis. In more susceptible patients, renal ultrasound may be helpful.**

5.3.2 Mycoplasma/Ureaplasma

Certain fastidious organisms are known to exist in the lower urinary tract and do not grow in typical laboratory settings.⁵ Four organisms (*m. genitalium*, *m. hominis*, *m. pneumoniae*, and *ureaplasma urealyticum*) are now thought to be responsible for some symptomatic infections as well as non-gonococcal urethritis.²⁰⁻²² The prevalence of *ureaplasma* varies but ranges from 27% to 52% in symptomatic women, and is less prevalent in men.^{17,20,23} It is more prevalent in women with multiple sexual partners.²⁴ In asymptomatic screened men and women, the prevalence of *ureaplasma urealyticum* is 8.2 and 8.9% respectively, much less than that of symptomatic individuals.²⁵ *Mycoplasma hominis* in women has been noted to be 7.1%.^{20,23} Studies describing the prevalence of *mycoplasma hominis* in asymptomatic men outside of Sexually Transmitted Infection clinics are rare, it has been noted to range from 0% to 3.6%. The presence of *mycoplasma hominis* and *ureaplasma urealyticum* has been correlated with LUTS in small studies^{22,23,25} but large scale, well powered trials are lacking. *M. hominis* and *U. urealyticum* can be treated with tetracycline where available, doxycycline, and azithromycin.

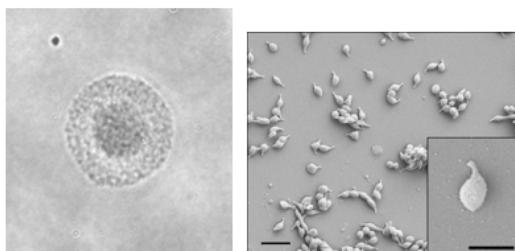


Figure 17: Micrograph of Mycoplasma colony (left, 100x) and *Mycoplasma genitalium* (right, SEM). Courtesy Ryan Relich, PhD, IU School of Medicine

5.3.3 Genitourinary Tuberculosis (Consult Infectious Disease)

Genitourinary tuberculosis is the 3rd most common presentation of extrapulmonary tuberculosis acquired through hematogenous spread of pulmonary tuberculosis. This usually occurs with HIV disease or other forms of immunosuppression, but can occur in healthy individuals where TB is endemic. Granulomas form in the renal cortex. This can present as sterile pyuria, proteinuria, or hematuria. Upon reactivation the disease progresses to the medulla causing papillary necrosis or progression down the ureters, bladder, and testes. Genitourinary tuberculosis can cause glomerulonephritis and chronic kidney disease. Patients being considered for renal transplant with a history of a positive PPD or Quantiferon should be evaluated by an infectious disease consultant. The Quantiferon test is a peripheral blood test which evaluates for a memory CD4T cell response against tuberculosis antigens.²⁶ A positive Quantiferon Gold, unlike a positive Tuberculin skin test (PPD), reflects active tuberculosis infection (and to a lesser degree latent TB infection) and will not be positive for individuals with prior BCG immunization. These patients usually require at least the initiation of isoniazid prophylaxis (+ pyridoxin prior to transplantation). Symptoms of post-transplant tuberculosis include reactivation of pulmonary tuberculosis with weight loss, fever, and night sweats, but can also present disseminated tuberculosis with hypercalcemia without renal injury. Diagnostic tests include acid-fast bacilli smears of the urine with mycobacterial culture +/- PCR when sterile pyuria is noted, chest X-ray, and imaging of the GU system to look for calcifications and other structural defects. **Suspicion for genitourinary TB warrants an infectious disease consult and Department of Public Health notification. Treatment entails two months of a four-drug regimen followed by seven months of isoniazid plus a**

rifampin regimen (If a patient is HIV positive, rifampin may be changed to rifabutin depending on antiretroviral therapy). **Prior to initiation of ethambutol, patients need a baseline ophthalmology exam, as ethambutol can cause optic neuritis.** If there is renal impairment, caution must be taken when using ethambutol or aminoglycosides.

5.3.4 Parasites of the genitourinary Tract (Consult Infectious Disease)

It is very important to obtain a travel history from patients before considering parasites in the differential diagnosis. Important helminthic parasites of the genitourinary tract include ***schistosomiasis*, *echinococcus*, and *filaria***. Genitourinary schistosomiasis is caused by *Schistosoma haemotobium*, which is endemic to Africa and the Middle East. The intermediary host is the snail, which releases the organism into fresh water. **The organism penetrates human skin and travels through the venous/lymphatic system to settle in the pelvic veins eventually causing symptoms of hematuria about 10-12 weeks after infection.** Chronic disease manifests as granulomas within the bladder, calcifications in the prostate and seminal vesicles, painful micturition due to bladder outlet obstruction and bladder cancer. Diagnosis is based on ELISA to demonstrate prior exposure. One can also filter urine for ova for identification. **Praziquantel is the treatment of choice;** it causes muscular contractions and detachment from the vein, killing the adult worm.

Hydatid cysts are secondary to *Echinococcus* species. The source of infection is usually accidental ingestion of ova from the feces of the primary host, e.g. dogs. The larvae penetrate the intestinal wall and enter the portal system to eventually settle in the liver. The organism can settle in the kidneys and encyst there, though this occurs rarely. A patient may present with flank pain from pressure. On ultrasound there are hypoechoic septated lesions within the GU system. **Medical treatment entails prolonged albendazole**, which may shrink the cyst. Any attempt at a cure requires surgical removal with care not to spill the contents of the cyst. **Do not attempt to percutaneously drain hydatid cysts** due to the severe reaction that may ensue. This may require partial nephrectomy.

Filariasis can present as chyluria with the patient reporting intermittent milky urine. The organism invades the lymphatic system and can obstruct the lymphatics when it dies causing elephantiasis. The infection is contracted in the subtropics and tropics. **Treatment for mild disease is albendazole.** For severe chyluria, retrograde injection of sclerosing agent may lead to palliation. For severe scrotal elephantiasis, reconstructive surgery is necessary.

Important non-helminthic parasites include *Trichomonas vaginalis*, *Plasmodium falciparum*, and *Entamoeba histolytica*. *Trichomonas vaginalis* can cause inflammation around the urethra and vagina. Diagnosis is through identification of a motile organism on wet mount. **Treatment consists of metronidazole for 7 days.** *Plasmodium falciparum*, the most common of the 4 plasmodium species responsible for malaria, presents as cyclical fevers and if left untreated can progress to hemolysis and renal damage, with free hemoglobin passing through the kidneys into the urine, termed "blackwater fever" secondary to severe hemolysis. Making this diagnosis, again, requires a detailed travel history and malaria smear.

6. Management

6.1 Acute UTI

6.1.1 Symptom Control

Acute onset dysuria is a central symptom of UTI and can cause significant discomfort to patients. Offering patients methods to manage symptoms in addition to antibiotic therapy can help relieve discomfort. Strategies that can decrease bladder symptoms of UTI include increase in fluids, use of acetaminophen or non-steroidal anti-inflammatory medications, and phenazopyridine. This is especially critical in patients who are awaiting culture results prior to treatment.

In uncomplicated patients with acute cystitis, the risk of progression to complicated UTI or soft tissue infection (pyelonephritis) is minimal. The natural history of uncomplicated acute cystitis is typically self limited and rarely progresses.¹³ Randomized trials of placebo, analgesics and hydration versus antibiotic evidence showed that antibiotic treatment offers only a mild improvement in symptoms compared to placebo.²⁷⁻²⁸ Given this data the AUA guidelines on recurrent UTI suggests that "supportive care can be reasonably attempted with antibiotic treatment reserved for those patients in whom it would be anticipated to impact prognosis."¹³

6.1.2 Antibiotic Treatment

Empiric vs. culture directed treatment

Empiric antibiotic treatment, before culture results return, may be acceptable based on symptoms alone in certain situations, but AUA guidelines recommend that if possible one should obtain a urine culture in all patients presenting with symptoms.¹³⁻¹⁷⁻¹⁹ In patients with mild symptoms, culture directed treatment (awaiting urine culture and sensitivities and specificity before prescribing antibiotics) can decrease inappropriate use of antibiotics in context of negative culture or resistant cultures. Offering patients supportive care options and educating them on the low risk of progression in a shared decision making model can help decrease patient symptoms while culture is pending.¹³

Antibiotic Considerations

Fewer antibiotics are being developed and antibiotic stewardship is the responsibility of all clinicians. Despite this, it has been estimated that inappropriate use of antibiotics is as high as 68% in the US.²⁹ Understanding the most common bacteria to cause UTIs and choosing antibiotics wisely will likely improve outcomes, reduce resistance, and preserve antibiotics needed for special situations and populations.

See Management of Antimicrobial Resistance is discussed in the **AUA Update Volume 35, Lesson 22, 2016**, see also **World Health Organization policy guidance on integrated antimicrobial stewardship activities**.³⁰ For a comprehensive list of all antimicrobial agents in use and in development worldwide please refer to **2020 Antibacterial Agents In Clinical And Preclinical Development: An Overview And Analysis**.³¹

Table 4 represents a basic table for antibiotic review in order to quickly access a basic understanding of antibiotic class, mechanism of action, adverse effects, and specific spectrum of bacteria each antibiotic targets. Patient information on treatment of UTI can be found at <https://www.urologyhealth.org/educational-materials/urinary-tract-infection-treatment-and-antibiotic-tips>.

Table 4. Medication Treatment Table/Antibiotic Summary Table

Class	Examples	Mechanism of Action	Adverse Effect	Spectrum
Penicillin	<ul style="list-style-type: none">• Ampicillin• Amoxicillin	<ul style="list-style-type: none">• Disrupts cell wall	<ul style="list-style-type: none">• Diarrhea• Rash	<ul style="list-style-type: none">• Streptococcus• Enterococcus
Anti-Staphylococcal Penicillin	<ul style="list-style-type: none">• Nafcillin• Oxacillin• Dicloxacillin	<ul style="list-style-type: none">• Disrupts cell wall	<ul style="list-style-type: none">• Acute interstitial nephritis (AIN)	<ul style="list-style-type: none">• MSSA• Streptococcus
Extended Spectrum Penicillin	<ul style="list-style-type: none">• Piperacillin/Tazobactam	<ul style="list-style-type: none">• Cell wall inhibitor• Beta lactamase inhibitor	<ul style="list-style-type: none">• GI upset• Candidiasis• C. difficile	<ul style="list-style-type: none">• Streptococcus• Enterococcus• MSSA• GNRs• Anaerobes
Amoxicillin/Clavulanic Acid Ampicillin/Sulbactam	<ul style="list-style-type: none">• Augmentin• Unasyn	<ul style="list-style-type: none">• Cell wall inhibitor• Beta lactamase inhibitor	<ul style="list-style-type: none">• GI upset• Candidiasis• C. difficile	<ul style="list-style-type: none">• Streptococcus• Enterococcus• some GNRs• anaerobes
Cephalosporin 1 st Generation	<ul style="list-style-type: none">• Cefazolin• Cephalexin	<ul style="list-style-type: none">• Disrupts cell wall	<ul style="list-style-type: none">• Diarrhea• Rash• Elevated LFTs• Pruritus	<ul style="list-style-type: none">• Gram Positives• MSSA• Streptococcus• <i>E. coli</i>• <i>Klebsiella</i>• <i>Proteus mirabilis</i>
Cephalosporin 2 nd Generation	<ul style="list-style-type: none">• Cefuroxime• Cefoxitin	<ul style="list-style-type: none">• Disrupts cell wall	<ul style="list-style-type: none">• Diarrhea• Rash• Elevated LFTs• Pruritus	<ul style="list-style-type: none">• GP Coverage• Increased GNR coverage• Anaerobeso <i>Peptostreptococcus</i>o <i>Clostridium</i>
Cephalosporin 3 rd Generation	<ul style="list-style-type: none">• Ceftriaxone• Cefpodoxime• Ceftazidime (anti-pseudomonal)	<ul style="list-style-type: none">• Disrupts cell wall	<ul style="list-style-type: none">• Diarrhea• Rash• Elevated LFTs• Pruritus	<ul style="list-style-type: none">• Strep• GNR• Neisseria
Cephalosporin 4 th Generation	Cefepime	<ul style="list-style-type: none">• Disrupts cell wall	<ul style="list-style-type: none">• Diarrhea• Rash• Elevated LFTs• Pruritus	<ul style="list-style-type: none">• GNRs• <i>Pseudomonas aeruginosa</i>
Cephalosporin 5 th Generation	Ceftaroline	<ul style="list-style-type: none">• Disrupts cell wall	<ul style="list-style-type: none">• Diarrhea• Rash• Elevated LFTs• Pruritus	<ul style="list-style-type: none">• GNRs• MRSA

Monobactam	Aztreonam	<ul style="list-style-type: none"> • Disrupts cell wall by inhibiting division 	<ul style="list-style-type: none"> • GI upset • Candidiasis • <i>C. difficile</i> 	<ul style="list-style-type: none"> • GNRs • Pseudomonas Poor GP Coverage • Poor anaerobic coverage
Carbapenems	<ul style="list-style-type: none"> • Imipenem • Ertapenem • Meropenem • Doripenem 	<ul style="list-style-type: none"> • Disrupts cell wall 	<ul style="list-style-type: none"> • Diarrhea • Vomiting • Lowers seizure threshold 	<ul style="list-style-type: none"> • ESBL coverage: **Ertapenem • Does not Cover Enterococcus o Pseudomonas o RSA coverage
Aminoglycosides	<ul style="list-style-type: none"> • Gentamicin • Amikacin • Tobramycin 	<ul style="list-style-type: none"> • Inhibits bacterial protein synthesis 	<ul style="list-style-type: none"> • ATN • Ototoxicity • Peripheral neuropathy 	Aerobic GNRs
Trimethoprim Sulfamethoxazole	Bactrim	<ul style="list-style-type: none"> • Depletes folic acid. • Bacteria cannot synthesize nucleic acid and proteins 	<ul style="list-style-type: none"> • Rash • Stevens-Johnson syndrome (SJS) • Methemoglobinemia • Aseptic meningitis • AIN 	<ul style="list-style-type: none"> • MRSA • Streptococcus
Fluorquinolones [†]	<ul style="list-style-type: none"> • Ciprofloxacin • Moxifloxacin • Levofloxacin • Lomefloxacin 	<ul style="list-style-type: none"> • Inhibits DNA gyrase • Topoisomerase IV 	<ul style="list-style-type: none"> • QT prolongation* • Tendonitis/Achilles Rupture • Lowers seizure threshold • Retinal Detachment* • May enhance the effect of warfarin 	<ul style="list-style-type: none"> • GNRs (including Pseudomonas) • some GPC coverage
Tetracyclines (not usual 1 st line treatment for UTIs)	<ul style="list-style-type: none"> • Doxycycline • Tetracycline • Tigecycline (not good for UTIs) 	<ul style="list-style-type: none"> • Inhibits protein synthesis • (Bacteriostatic) 	<ul style="list-style-type: none"> • Photosensitivity • Diarrhea • Vaginal candidiasis 	<ul style="list-style-type: none"> • Chlamydia • Mycoplasma • Ureaplasma • MRSA
Glycopeptide/lipopeptide	Vancomycin	<ul style="list-style-type: none"> • Disrupts cell wall and RNA synthesis 	<ul style="list-style-type: none"> • Red Man Syndrome (just slow infusion down) • Nephrotoxicity • Ototoxicity 	GPCs including MRSA
Glycopeptide/lipopeptide	Daptomycin	<ul style="list-style-type: none"> • Depolarizes cell membrane • Inhibits protein, DNA, RNA synthesis 	<ul style="list-style-type: none"> • Myopathy/Rhabdomyolysis (ATN) • SJS • Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) 	GPC including MRSA and VRE
Oxazolidinone	Linezolid	<ul style="list-style-type: none"> • Inhibits protein synthesis 	<ul style="list-style-type: none"> • Myelosuppression with prolonged use • Serotonin syndrome in patients on SSRIs 	Aerobic GPC including MRSA and VRE
Nitrofurantoin	Macrobid	<ul style="list-style-type: none"> • Blocks bacterial carbohydrate metabolism (Bacteriostatic) 	<ul style="list-style-type: none"> • Neurotoxicity • Lupus-like symptoms • Pneumonitis (Baseline CXR and LFTs if used for long term bacterial suppression)** • Rash • hemolysis in G6PD patients 	<ul style="list-style-type: none"> • <i>E. coli</i> • <i>Staphylococcus saprophyticus</i> • <i>Enterococcus</i>

Macrolides	<ul style="list-style-type: none"> Erythromycin Azithromycin 	<ul style="list-style-type: none"> Inhibits protein synthesis 	<ul style="list-style-type: none"> QT prolongation GI side effects (diarrhea, etc) Rash 	<ul style="list-style-type: none"> Mycoplasma Chalmydia
Fosfomycin	Fosfomycin	<ul style="list-style-type: none"> Cell wall synthesis inhibitor 	<ul style="list-style-type: none"> Diarrhea Dizziness Vomiting Vaginitis 	<ul style="list-style-type: none"> GNRs ESBL organisms KPC organisms (Neuner 2012). Enterococcus

† Recent FDA Warning to not use as first line therapy for uncomplicated UTI. www.fda.gov/Drugs/DrugSafety/ucm500143.htm

6.1.3 Decision For Admission

If the patient has tachycardia, hypotension, high fever, and flank pain or appears toxic, admit the patient and obtain a CT scan. **A UTI in the context of obstructive uropathy stones is a urologic emergency.** Other significant factors regarding the decision for inpatient management include the **inability to tolerate oral hydration, significant complicating comorbidities, immunocompromised state, mental status changes, or an elderly/disabled patient not able to appropriately care for themselves.** The patient should undergo urine culture and subsequently receive IV antimicrobial therapy, keeping in mind the local antibiogram. Prompt infectious disease consultation is warranted in more complicated scenarios or with multi-drug resistant organisms. Consider broad spectrum antibiotics if the patient has been recently hospitalized, had recent surgery or instrumentation, or is immunocompromised. Surgical management may be necessary for patients with an associated abscess, emphysematous pyelonephritis or ureteral obstruction.

6.2 Management of recurrent UTI

In patients with rUTI (two separate culture-proven episodes of acute bacterial cystitis and associated symptoms within six months or three episodes within one year), clinicians should continue to obtain urinalysis and urine culture for each symptomatic acute cystitis episode prior to initiating antibiotic treatment. Offer supportive measures (hydration, analgesics) and expectant management while cultures are pending.¹³ Urine culture results typically take at least 48 hours, therefore in patients with severe symptoms or complicated UTI, first-line therapy (i.e., nitrofurantoin, TMP-SMX, fosfomycin) can be initiated prior to urine culture results based on past urine culture sensitivities and when no available, on the local antibiogram.

- a. Clinicians should treat rUTI patients experiencing acute cystitis episodes with as short a duration of antibiotics as reasonable, generally no longer than seven days.¹⁵⁻³²
- b. When urine culture reveals resistance to all available oral antibiotics, clinicians may treat with culture-directed parenteral antibiotics for as short a course as possible, generally no longer than seven days.¹⁵⁻³²
- c. There is no evidence that a longer duration of antibiotic use (10-14 days) is more effective than a 7 day course, and some evidence that a 3 day course leads to bacteria persistence at 4-10 weeks' follow up.³³⁻³⁴⁻³⁵ Clinicians may offer patient-initiated treatment (self start treatment) to select rUTI patients with acute episodes which awaiting urine cultures, but urine cultures should always be sent per the AUA recurrent UTI guidelines.³²

6.2.1 Prevention of rUTI

There are many myths surrounding rUTI and hygiene practices. The **AUA guidelines on recurrent UTI** note that "case-control studies clearly demonstrate that changes in hygiene practices (e.g., front to back wiping), pre- and post-coital voiding, avoidance of hot tubs, tampon use, and douching do not play a role in rUTI prevention."¹³⁻¹⁵

Many women develop UTIs after specific life changes. UTIs may occur when first becoming sexually active or with new sexual partners. It is important to evaluate sexual practices as this may reveal practices which increase the risk for a UTI. Peri and post menopausal women may develop recurrent UTI due to estrogen loss within the peri-urethral tissue; this can occur even among women who are on systemic estrogen replacement. Several reviews on recurrent UTI are available including **AUA Update Series 2019 Volume 3** **Lesson 6**, Smith et al Journal of Urology 2018 and Laan and Geerlings Lancet Infectious Disease 2019.³⁶⁻¹⁴

Patient materials on UTI prevention are at (<https://www.urologyhealth.org/educational-materials/urinary-tract-infection-prevention>)

6.2.2 Non-antibiotic therapy for prevention of UTI

See References 37,38.

- i. **Increased water intake to greater than 1.5 Liters per day** - there is randomized trial evidence showing that premenopausal women who drank more than 1.5L of water per day for 12 months had less frequent UTI than women who drank less than 1.5L of water per day.³⁹⁻⁴⁰
- ii. **Cranberry** - controversial since a recent Cochrane review suggests it is no more effective than placebo⁴¹
- iii. **Urine acidification** - typically with vitamin C, can be accomplished with methenamine as well
- iv. **Methenamine salts** - Methenamine is converted to formaldehyde in acidic urine.⁴²⁻⁴³
- v. **Probiotics** - controversial as a recent Cochrane review suggests no benefit was demonstrated compared to placebo or no treatment⁴⁴
- vi. **D-mannose** - has been shown to be as effective as nitrofurantoin in one small RCT with fewer side effects, a large RCT is pending⁷
- vii. **Vaginal Estrogen** - A decrease in estrogen leads to an increase in vaginal pH which can alter the microbial flora, leading to bacterial colonization with different predilections to causing UTIs.⁴⁵ Per the **AUA Guidelines on Recurrent UTI** in women vaginal estrogen is appropriate for the prevention of rUTI in post menopausal women but systemic (oral) formulations have not been shown to reduce rUTI.¹³ It is important to note that vaginal estrogen products have black box warning for "endometrial cancer, cardiovascular disorders, breast cancer and probably dementia" this data is extrapolated from systemic hormone therapy and those side effects have not been noted in vaginal formulations.¹³⁻⁴⁶ **Table 5** details some common vaginal estrogen formulations.

Table 5 Commonly used vaginal estrogen therapy (from AUA Guidelines on Recurrent UTI)¹³

Formulation	Composition	Strength and Dosage
Vaginal tablet	Estradiol hemihydrate*	10 mcg per day for 2 weeks, then 10 mcg 2–3 times weekly
Vaginal ring	17 β -estradiol	2 mg ring released 7.5 mcg per day for 3 months (changed by patient or provider)
Vaginal cream	17 β -estradiol	2 g daily for 2 weeks, then 1 g 2-3 times per week
	Conjugate equine estrogen or phytoestrogen	0.5 g daily for 2 weeks, then 0.5 g twice weekly

*Estradiol hemihydrate comes in a 4 mcg tablet; however, this has not been studied for prevention of rUTI.

[View Image](#)

Other, less studied, strategies for rUTI prevention include:

- i. **Vaginal pH manipulation** – Trimo-San™ vaginal jelly (8-Hydroxyquinoline Sulfate) is commonly used to maintain healthy vaginal pH and odor control for pessary users, and has weak but anecdotal evidence for prevention of UTI
- ii. **Intravesical agents** – acetic acid 0.25% has been used for refractory cases of rUTI but also is commonly used for prevention of UTI in chronically catheterized patients, is Chlorpactin™ 0.05% (oxychloroserine) however no high quality RCT data exists to support the efficacy of either intravesical agent, although a single RCT with some methodological flaws supports use of acetic acid.⁴⁷ Despite lack of evidence these agents have become popular for prevention of catheter associated UTIs (CAUTIs).

6.2.3 Antibiotic Prophylaxis

Following discussion of the risks, benefits, and alternatives, clinicians may prescribe antibiotic prophylaxis to decrease the risk of future UTIs in women of all ages previously diagnosed with UTIs. There have been several reviews of the literature regarding both antibiotic and non antibiotic based prophylaxis⁸⁻⁴⁹

Management of rUTI relies on a combination of therapies. This requires a trusting patient-physician relationship. Much of the management is trial and error, as there is no one-size-fits-all strategy. Management can be divided into three groups: (1) suppressive therapy (2) self-start therapy (3) post-coital therapy.

Antibiotic suppressive therapy comprises three strategies.

- i. Daily antibiotic prophylaxis with **re-evaluation after 6-12 months** (nitrofurantoin, cephalaxin, trimethoprim, TMP-SMX). Nitrofurantoin is commonly used if long-term prophylaxis is anticipated. A baseline chest x-ray and liver function panel may help in future assessment of rare lung and liver complications from this therapy. In prescribing fluoroquinolones one must be aware of the multiple FDA warnings on adverse events to include aortic dissection, mental health side effects, tenditis and tendon rupture.⁵⁰
- ii. Full-dose antibiotic suppressive therapy (beware long-term side effects of antibiotics)
- iii. Intravesical antimicrobial therapy. Patients must be capable of clean intermittent catheterization and can use solutions of gentamicin, neomycin, neomycin/polymyxin, or colostin daily with less risk of systemic effects. There is still a risk of antibiotic resistance.⁸

Self-start antibiotic therapy: The patient is given a specimen cup, a standing laboratory order for urinalysis/urine culture and an antibiotic prescription. If the patient has urinary symptoms, she collects a mid-stream urinary specimen and then starts antibiotic therapy. The patient should notify the physician, as urine culture results may change the antibiotic treatment.

Post-coital prophylaxis: For women in whom recurrent UTIs are related to sexual intercourse, they take an antibiotic post-coitus.

6.3.3 Follow-up Evaluation

Clinicians should **not** perform a post-treatment test of cure urinalysis or urine culture in asymptomatic patients. Repeat urine cultures should only be done to guide management when UTI symptoms persist following antimicrobial therapy.

As mentioned above, any patient on antibiotic prophylaxis should have follow up to reassess the need for continued antibiotic prophylaxis.

6.4 Complications of Urinary Tract Infection

6.4.1. Pyelonephritis

Pyelonephritis arises from an ascending GU tract infection. For uncomplicated pyelonephritis, patients present with UTI symptoms plus flank pain.⁵¹ These patients need a urinalysis and culture. Treatment duration usually ranges from 7-14 days depending on the organism and whether there are any underlying structural abnormalities.⁵² Patients requiring hospitalization should receive appropriate IV antibiotics. This usually entails appropriate GNR coverage. **If the patient is septic, broad-spectrum antibiotics are appropriate.**⁵³ Always review prior microbial history to ensure adequate coverage for a potential multidrug resistant organism. **Septic patients should have imaging of the kidneys to ensure there is no stone, perinephric abscess, or structural abnormality (UPJ obstruction, staghorn calculus) that may predispose to pyelonephritis.** When the patient is ready for discharge, antibiotics can be narrowed to an oral regimen, depending on the bacterial sensitivities.

6.4.2 Emphysematous Cystitis & Pyelonephritis

Emphysematous cystitis is characterized by gas within the bladder wall or lumen (in absence of manipulation). Treatment includes broad spectrum antibiotics, decompression of the bladder and treatment of underlying conditions such as poorly controlled diabetes mellitus.⁵⁴ Surgical debridement is rarely needed and is reserved for those with necrotizing infections.

Emphysematous pyelonephritis is a urologic emergency characterized by necrotizing infection of the kidneys with the formation of gas visualized on CT. Common bacterial pathogens include *E. coli*, *K. pneumoniae*, and *Proteus mirabilis*, with diabetics comprising the majority of patients. Type I emphysematous pyelonephritis is described as dry and is best treated with nephrectomy while Type II emphysematous pyelonephritis is wet and can be treated with percutaneous drainage.⁵⁵⁻⁵⁶

7. Evaluation & Management in Specific Populations

7.1 UTIs in Women

UTIs are much more prevalent in women than men. **Up to 60% of adult women report having had a UTI at least once in their lifetime and 11% report having at least one per year.**²⁻¹⁷ Urine culture for females is typically obtained as a clean catch, midstream specimen, although catheterization can be used. With the clean catch method, the Cent for Disease Control defines a UTI as symptoms plus 10⁵ colony forming units (CFU)/mL. With a catheterized specimen, the concentration of the pathogen can be as low as 10³ CFU/mL to qualify as a UTI.

In general, first line therapy has been to treat empirically with trimethoprim-sulfamethoxazole (TMP-SMX) and await optional culture results. The Infectious Disease Society of America (IDSA) Guidelines (2010) recommend TMP-SMX (1 DS tablet BID x 3 days) or nitrofurantoin (100mg BID x 5 days, avoid if suspect pyelonephritis) or fosfomycin (3g single dose) as first line therapy.⁵⁷⁻⁵⁸⁻⁵⁹ Amoxicillin or ampicillin alone should not be used as first line therapy. If TMP-SMX resistance is greater than 20% and the clinician cannot use nitrofurantoin, use fluoroquinolones or a β lactam (not amoxicillin or ampicillin) as a second line agent.⁵⁷ (See **Table 6**)

Guidelines should not replace clinical judgment. Knowledge of the institutional antibiogram regarding drug resistant organisms, when available, can assist in clinical decision-making.²⁹ The general approach to evaluation and treatment depends upon the population to which the woman belongs: pre-menopausal, post-menopausal or pregnant.

Table 6: Infectious Disease Society of America Drugs Commonly Used for Outpatient Cystitis in Non Pregnant Women

First Line Therapy	Macrobid 100mg BID x 5 days Bactrim 1 DS tablet (160mg/800mg) BID x 3 days Fosfomycin trometamol 3 gm in a single dose
Second Line Therapy	Ciprofloxacin 250mg q12 hours x 3 days or 500mg qday x 3 days
Other Commonly Used Antibiotics for Inpatient Use	Ceftriaxone 1g q24 hours Zosyn 3.375g q6 hours or higher for Pseudomonas aeruginosa dosing Tobramycin 3mg/kg/day
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7.1.1 Premenopausal Women Presenting with Uncomplicated UTI

Symptoms of a UTI in a premenopausal woman include **dysuria, frequency and urgency**. These alone can predict a UTI with 90% probability in the absence of vaginal discharge.^{25-34,35} It is important to remember that this age group is at risk for sexually transmitted infections. Therefore, a history and physical exam should be targeted at eliminating STIs as a possible source for symptoms of cystitis/urethritis. Urethritis from sexually transmitted infections such as **chlamydia, gonorrhea, trichomoniasis or Herpes Simplex Virus (HSV) 1** should be considered when pyuria and dysuria are present in the setting of a negative culture. If vaginal discharge is present with symptoms of vulvar irritation, external dysuria, pruritus, dyspareunia and odor, vaginitis is high on the differential. Common etiologies of vaginitis include **yeast, trichomoniasis and bacterial vaginosis**. Another less common diagnosis is a urethral diverticulum. This can be diagnosed on physical exam and imaging with pelvic MRI.³² In the setting of a negative culture with recurrent symptoms of frequency, urgency and dysuria, patients should be evaluated for Painful Bladder Syndrome/Interstitial Cystitis (www.urologyhealth.org/educational-materials/interstitial-cystitis/bladder-pain-syndrome-patient-guide). The prevalence of interstitial cystitis has increased with greater awareness among clinicians and patients. A useful tool for following progress longitudinally are the IC/PBS specific symptom questionnaires but recent evidence demonstrates need to include both pain and urinary symptom indices.¹⁸ These include the pelvic pain and urgency/frequency (PUF) symptom scale questionnaire as well as O'Leary-Sant Symptom Index and the Genitourinary Pain Index (GUPI).^{19,47-48,49}

Other causes of cystitis include: **foreign body in the bladder, neoplasms, atypical infections such as fungal infections or tuberculosis, nephrolithiasis, pelvic inflammatory disease**.

7.1.2 Post-menopausal Women Presenting with UTI

Postmenopausal women can have similar symptoms to premenopausal women; however, **these women are more prone to atypical symptoms**. Elderly women may only present with altered mental status, however the causality of this association remains in question.⁵⁰⁻⁶⁰ A decrease in estrogen leads to an increase in vaginal pH which can alter microbial flora, leading to bacterial colonization with different predilections to causing UTIs.⁴⁵ Older women are more likely to have undergone other surgical procedures or have been recently hospitalized, both of which are important historical questions that may change management. Urethral diverticulum and potentially urethral cancer may be more common in elderly patients. Other causes of cystitis such as foreign body in the bladder, neoplasm, atypical infections such as fungal infections or tuberculosis, and nephrolithiasis should be investigated.

The risk factors are similar to premenopausal women. Decreased vaginal estrogen leads to reduced Lactobacillus colonization, vaginal alkalinization, and increased colonization with *Enterobacteriaceae* (e. *coli*, *p. mirabilis*, *k. pneumoniae*, *enterobacter species*, *serratia species*, and other gram-negative bacteria).⁶¹ Additional post-menopausal risk factors include incomplete bladder emptying, poor perineal hygiene, urinary and fecal incontinence, pelvic organ prolapse, lifetime history of UTI and diabetes.⁷

Empiric treatment is acceptable based on symptoms alone.¹⁷⁻¹⁹ UTI prevention focuses on increasing fluid intake to increase urination and reduce bacterial count and evaluating for vaginal atrophy.

7.1.3 Post-menopausal Women Presenting with Recurrent UTI

Evaluation and management of the post-menopausal woman presenting with rUTI or complicated UTI is similar to that for the pre-menopausal woman. Briefly, culture is mandatory and imaging with abdominal x-ray (kidneys, ureter and bladder) and ultrasound may be useful in identifying complicating factors. An in-office post-void residual (PVR) measurement may be helpful at guiding therapy. An exam should also be performed to assess for vaginal atrophy. Studies including a Cochrane review have shown that vaginal estrogen treatment has shown clinical benefit for prevention of UTIs in women with genitourinary syndrome of menopause and should be considered at the initial visit.⁶³ Based on this Cochrane review oral estrogens are not as effective as vaginal formulations in this population for the prevention of UTI.⁶² While vaginal estrogen products have black box warning, the data for these warnings is extrapolated from systemic hormone therapy and experts feel that vaginal estrogen does not portend these risks due to low systemic absorption, absence of randomized trial evidence or consistent observational evidence, and lack of evidence that small changes in blood hormone levels increase risk of these effects.⁴⁶ **Cystoscopy may be warranted in those patients with a clinical suspicion of obstruction, hematuria, malignancy, and complicated UTI.**

7.1.4 UTIs During Pregnancy

UTI in pregnancy is, by definition, complicated. There is an increased risk for pyelonephritis due to decreased ureteral peristalsis, obstruction of the ureters by the enlarged uterus, increased filtration leading to reduced antibiotic levels, and the immunocompromised state of pregnancy. **UTIs will affect 17-20% of pregnancies. Asymptomatic bacteriuria occurs in 2-10% of pregnancies with 2-4% of pregnant women developing pyelonephritis.** UTIs can be devastating in pregnancy resulting in **maternal septic shock, respiratory and renal insufficiency, fluid balance disorders and even death. Asymptomatic bacteriuria has also been associated with premature rupture of membranes, preterm labor, chorioamnionitis and postpartum fever.** (See [AUA Update Series 2019 Volume 38 Lesson 34 Urologic Complications Pregnancy-section on UTI](#))

Evaluation is similar to premenopausal women with a few very specific differences.

- a. Urine culture is mandatory.
- b. Aggressive management of the UTI is necessary.
- c. Attempts should be made to limit ionizing radiation due to fetal risk.
- d. **Screening with urine culture is recommended at one of the initial prenatal visits by the American College of Obstetricians and Gynecologists.** There is insufficient evidence to inform a recommendation for or against repeat screening during pregnancy for a woman with an initial negative screening culture or following treatment of an initial episode of ASB.

Nitrofurantoin is often used as **fluoroquinolones and TMP-SMX are both contraindicated in pregnancy**.⁶⁴⁻⁶⁵ If a pregnant woman has one episode of pyelonephritis, two episodes of a UTI or asymptomatic bacteriuria defined as 10^5 CFU, daily suppression with either nitrofurantoin or cephalexin should be considered for the remainder of the pregnancy. If nitrofurantoin is used, however, this is generally discontinued at 35 weeks of gestation due to an increased risk of hemolytic anemia in the neonate ([Table 7](#)).⁶⁶

If a pregnant woman develops pyelonephritis, she should be hospitalized and aggressively treated to avoid maternal and fetal morbidity. Antibiotic treatment should be tailored based on the sensitivities of urine culture. However, typically ceftriaxone 1g IV daily is used until clinical improvement, after which the patient may be transitioned to oral antibiotics. If improvement is not seen within 72 hours of antibiotics, a renal ultrasound should be performed to assess for stone, obstruction, urinary tract abnormality or abscess. If there is a strong suspicion of a urologic stone that cannot be seen with ultrasound, a plain radiograph of the abdomen or a low-dose spiral CT should be considered in urgent cases.

Table 7: Pregnancy Antibiotic Choices

Class	Pregnancy Class (FDA)
Penicillin (Amoxicillin)	B
Cephalosporin (Keflex)	B
Nitrofurantoin	B
Fosfomycin	B
View Image	

7.2 UTI in Men

UTIs in men are always considered complicated. Just as in women, bacteria and/or white blood cells (WBCs) in urine must be accompanied by symptoms. A urine culture is an important test. UTIs in men are much less common than in women, so a PVR is always appropriate as part of the workup in men presenting with UTI symptoms. Importantly one must exclude extension of infection into a secondary organ, complicating the treatment. **Common sites of extension include prostatitis, epididymitis, and pyelonephritis.** A thorough history and exam of these organs sites should be performed. For more details about prostatitis please see [AUA Core Curriculum Prostatitis](#).

7.2.1 Men Under Age 50 Years

Classically, men from their teenage years to age 50 are more likely to present with an sexually transmitted infection (STI). This needs to be excluded at the first visit. A history, physical exam, and urinalysis can help with the diagnosis. If an STI is suspected, laboratory examination using urethral swab or urine nucleic acid amplification testing (NAAT) gonorrhea and chlamydia must be performed. These patients require appropriate counseling including notification of sexual partners and treatment through the Department of Public Health. Additional etiologies include anatomic abnormalities causing urinary obstruction or stasis, as well as a urinary stone which can be a nidus for infection. As noted previously, PVR is recommended.

7.2.2 Men Over Age 50 Years

Men over the age of 50 years more commonly have an enlarged prostate causing bladder outlet obstruction. There are also multiple other issues with UTI in older men complicated by chronic prostatitis, asymptomatic bacteria, and urologic abnormalities.⁶⁷ These men can present with lower urinary tract symptoms which may be similar to symptoms of a UTI. On the other hand, **elderly men may present with atypical or absent symptoms of a UTI, only noting vague symptoms, failure to thrive, or sudden change in mental status.** Older men may have an STI or other associated infections making a careful history and examination necessary. **Special attention should be placed on history, focusing on recent urinary tract instrumentation, recent hospitalization, or recent treatment with broad-spectrum antibiotics, as these increase the risk of resistant organisms.** PVR is always recommended as part of the initial evaluation.

It may be useful for the patient to complete the AUA Symptom Score (see Relevant Factors In Patient History). Physical examination should focus on the prostate examination and postvoid residual where appropriate. Laboratory analyses include urinalysis, urine culture, and STI screening where appropriate.

7.3 UTI in patients with Neurogenic Lower Urinary Tract Dysfunction (NLUTD)

Patients with NLUTD can present with atypical symptoms. Some patients present with new or worsening leakage of urine, bladder spasms, worsened muscle spasms. **Cloudy malodorous urine can be due to hydration status and without other symptoms is not considered specific for UTI.** Patients with spinal cord injury at or above T6 may present with **autonomic dysreflexia (hypertension, bradycardia, flushing, diaphoresis).**

Patients with NLUTD are at higher risk for UTIs due to bladder dysfunction that can cause retention but because of instrumentation of the genitourinary tract with catheters which causes colonizations. These devices along with the bladder dysfunction and propensity for stone formation can complicate management, as these can result in resistant polymicrobial UTIs. There is a constant concern for skin breakdown, which may serve as a nidus for systemic infection. Antibiotic treatment of decubitus ulcers may result in multidrug resistant bacteria. In this patient population non-antibiotic bladder irrigation as mentioned previously is favored for prevention of recurrent UTIs.

The Infectious Diseases Society of America (IDSA) 2009 guidelines emphasize reduction of catheter use as effective and important measures to reduce UTIs in this specific population.⁶⁸ Patients with long-term catheters (>10 days) will invariably have asymptomatic bacteriuria. Anti-microbial treatment for asymptomatic bacteriuria in NLUTD patient is not recommended.^{69,70}

In the event of a febrile UTI with positive urine culture, or increased frequency of recurrent UTI, the patient must be fully evaluated with specifically fluoroscopic urodynamic (FUDS) testing once the infection has resolved. **FUDS may reveal high-pressure storage or voiding, vesicoureteral reflux, sphincteric urinary obstruction, diverticular disease, or other issues which may require surgical correction.** Additional imaging is recommended to rule out calculi, hydronephrosis from high bladder pressure or urinary obstruction. Cystoscopy may be necessary due to the elevated risk of bladder cancer in SCI patients.⁷¹

7.4 Catheter associated UTI

See AUAUniversity Podcast: [Infections in prostheses](#).

A catheter-associated UTI (CAUTI) is **defined as a UTI that occurs after a catheter has been left in place for 48 hours.**⁶⁸ Biofilms form on urinary catheters and can ascend into the bladder within 1-3 days after of urinary catheter placement. In most scenarios, this is catheter-associated asymptomatic bacteriuria (CA-ASB), which does not require treatment. However, **when associated with fever, costovertebral angle tenderness or suprapubic pain, a urine culture must be obtained and antibiotic treatment initiated.** Interestingly, bacteriuria is inevitable with urinary catheters, as is pyuria. When collecting a specimen for urinalysis and culture, **ensure that the specimen is collected from an upstream port and not from the collection bag.** It is best to collect urine from a freshly exchanged catheter. In general, asymptomatic otherwise healthy patients (no fever, no leukocytosis) do not require treatment. Prolonged antibiotic treatment of bacterial colonization will lead to the development of multi-drug resistant bacteria. CAUTI treatment requires removal and replacement of indwelling catheter, if in place for more than 2 weeks. Treatment duration for a CAUTI is 7 days, if prompt resolution of symptoms. The Infectious Diseases Society of America (IDSA) 2009 guidelines encourage strategies to reduce the use of catheterization, as it has been proven to reduce UTIs and bacteriuria.⁶⁸ Additionally, CAUTI prevention techniques have been supported by the Agency for Healthcare Research and quality who supported a CAUTI prevention program in non-intensive care units.⁷²

7.5 UTI in Immunocompromised populations

7.5.1 Patients with Kidney Transplants

Given the significant immunosuppressed state of a transplant recipient, particularly within the first few months of transplantation, recognition and treatment of UTI in this population is of utmost importance, and may be critical for the survival of the graft.⁷³ **These patients often have refluxing grafts to decrease anastomotic stenosis rates.** Risk factors for infection include cadaveric graft, diabetes, urinary retention, prolonged hemodialysis prior to transplantation, two episodes of asymptomatic bacteriuria, and female gender.⁷⁴ Patients may present with nonspecific symptoms that are not localized to the urinary tract. Part of the exam should assess for graft tenderness.⁷⁵

Treatment duration may depend upon time from transplant. Patients in the early post transplantation period (first 6 months) should be treated 7-10 days for simple cystitis, but may receive a short 5-7 day course beyond this 6 month period. For all renal transplant patients with pyelonephritis or sepsis it is recommended for a longer 14-21 day course. If the kidney donor has asymptomatic bacteriuria at the time of transplantation, the recipient should be treated. Recipients commonly receive TMP-SMX for *Pneumocystis carinii* prophylaxis which will also reduce UTIs but may also place the patient at increased risk of infection with organisms resistant to TMP-SMX.⁷⁶ Fungal infections should also be suspected early in the immunocompromised as well as the poorly controlled diabetic populations (**Table 8**) summarizes the common antifungals, it is important to note that significant interactions can occur between the antifungals and immunosuppressive agents.

Treatment of ASB is dependent on timing from transplant. Current recommendations are to do screening cultures the post-transplant period but to only treat if the bacteria is persistent. It is recommended to avoid routinely collecting urine cultures or treating bacteriuria in asymptomatic patients who are more than 2 months out from their transplant. It is also strongly recommended not to treat multi-drug resistant ASB⁷⁷

Table 8: Antifungals

Class	Examples	Mechanism of Action	Adverse Effect
Nystatin	Topical	Binds to ergosterol	Skin irritation
Amphotericin B	Ambisome	Binds to ergosterol forming pore	Nephrotoxicity, Elevated LFTs
Azoles	Fluconazole	Inhibits fungal sterol synthesis	Hepatotoxicity
Echinocandins	Micafungin	Inhibits 1,3-Beta glucan	Fever, Nausea, vomiting

[View Image](#)

7.5.2 Patients with HIV Disease

HIV is an independent risk factor for lower urinary tract symptoms and is associated with a higher rate of UTIs.⁷⁶⁷⁷ There is a broader differential when HIV progresses to AIDS (CD4 count <200 cells/mm³ or an AIDS defining illness).⁷⁷ The bacterial etiologies are broader with higher rates of *Acinetobacter* and *Salmonella* species in HIV positive patients compared to HIV negative patients. Patients with AIDS are at higher risk for atypical infections including fungal (*Candida* species, *Aspergillus* species, *Cryptococcus neoformans*) and other endemic fungi such as Histoplasma- **Table 8**, mycobacterial (tuberculosis and non-tuberculosis mycobacteria), and viral (CMV and adenoviruses).⁷⁶⁷⁸ Patients with a CD4 count <200 cells/mm³ are commonly given *Pneumocystis jirovecii* pneumonia prophylaxis, which tends to be TMP-SMX, unless the patient has a sulfa allergy or G6PD deficiency. TMP-SMX prophylaxis decreases the risk of UTI.⁷⁷

8. Abbreviations

UTI: Urinary Tract Infection
TMP-SMX: trimethoprim-sulfamethoxazole
IDSA: Infectious Diseases Society of America
HSV: Herpes Simplex Virus
PBS/IC: Painful Bladder Syndrome / Interstitial Cystitis
PUF: Pelvic pain and Urgency/Frequency symptom scale
HIV: Human Immunodeficiency Virus
AIDS: Acquired Immunodeficiency Syndrome
GU: Genitourinary
KUB: Kidney Ureter Bladder
VCUG: Voiding Cystourethrogram
CT Scan: Computed Tomography Scan
TB: Tuberculosis
PPD: Purified Protein Derivative
WBC: White Blood Cell
AUA : America Urologic Association
STI: Sexually Transmitted Infection
SCI: Spinal Cord Injury
CA-ASB: Catheter Associated Asymptomatic Bacteriuria
CAUTI: Catheter Associated Urinary Tract Infection
CD4: Cluster of Differentiation 4
G6PD: Glugose-6-phosphate-dehydrogenase
UPJ: Ureteropelvic Junction
ICU: Intensive Care Unit
ASB: Asymptomatic Bacteriuria
rUTI: Recurrent Urinary Tract Infection
AIN: Acute Interstitial Nephritis
SJS: Stevens Johnson Syndrome
DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms
FUDS: Fluoroscopic urodynamics

9. Additional References

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2. Naber, K. G., Cho Y-H, Matsumoto T, et al.: Immunoactive prophylaxis of recurrent urinary tract infections: a meta-analysis. *International Journal of Antimicrobial Agents* 33: 111, 2009.
3. Rourke E, Kraus SR, Liss, MA. Adult Urinary Tract Infections. AUA Update Lesson 37.

10. Top 5 Articles for Urinary Tract Infection

1. Gupta, K, Hooton, T M, Naber, K G, et al. (2011). International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clinical infectious diseases*, 52(5), e103-e120.

The IDSA has 3 categories regarding **FEMALE** GU tract infections: Asymptomatic Bacteria in Adults, Catheter-Associated Urinary Tract Infection, and Uncomplicated Cystitis and Pyelonephritis.
2. Gad MH, AbdelAziz HH. Catheter-Associated Urinary Tract Infections in the Adult Patient Group: A Qualitative Systematic Review on the Adopted Preventative and Interventional Protocols From the Literature. *Cureus.* 2021 Jul 9;13(7):e16284. doi: 10.7759/cureus.16284. PMID: 34422457; PMCID: PMC8366179.

Gad et. Al review 59 studies that meet inclusion criteria and provide conclusive evidence for measures that reduce CAUTIs, such as removing catheters at the earliest time, reducing the number of catheters inserted, decrease antibiotic administration unless clinically needed, raising more awareness and provide training of nursing personnel on the latest guidelines, and even benefit for antibiotic-impregnated catheters.
3. Naber, K. G., Cho Y-H, Matsumoto T, et al.: Immunoactive prophylaxis of recurrent urinary tract infections: a meta-analysis. *International Journal of Antimicrobial Agents* 33: 111, 2009.

Meta-analysis of non-antibiotic options for prevention of rUTI.

7. Rourke E, Kraus SR, Liss, MA. Adult Urinary Tract Infections. AUA Update Lesson 37.
Helpful review of adult UTI diagnosis and treatment.
5. Nickel, J C. (2005). Management of urinary tract infections: historical perspective and current strategies: Part 2--Modern management. *The Journal of urology*, 173(1), 27-32.
Reason: In a two part series, Dr. Nickel outlines the history of UTIs and antibiotic use and highlights many helpful references. These articles may change your own antibiotic practices.
Reason: Covers some key radiographic findings that should not be missed for complicated UTIs.

Videos

Urinary Tract Infection Presentation

Presentations

Urinary Tract Infection Presentation 1

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