

Genitourinary System Module

Pharmacology

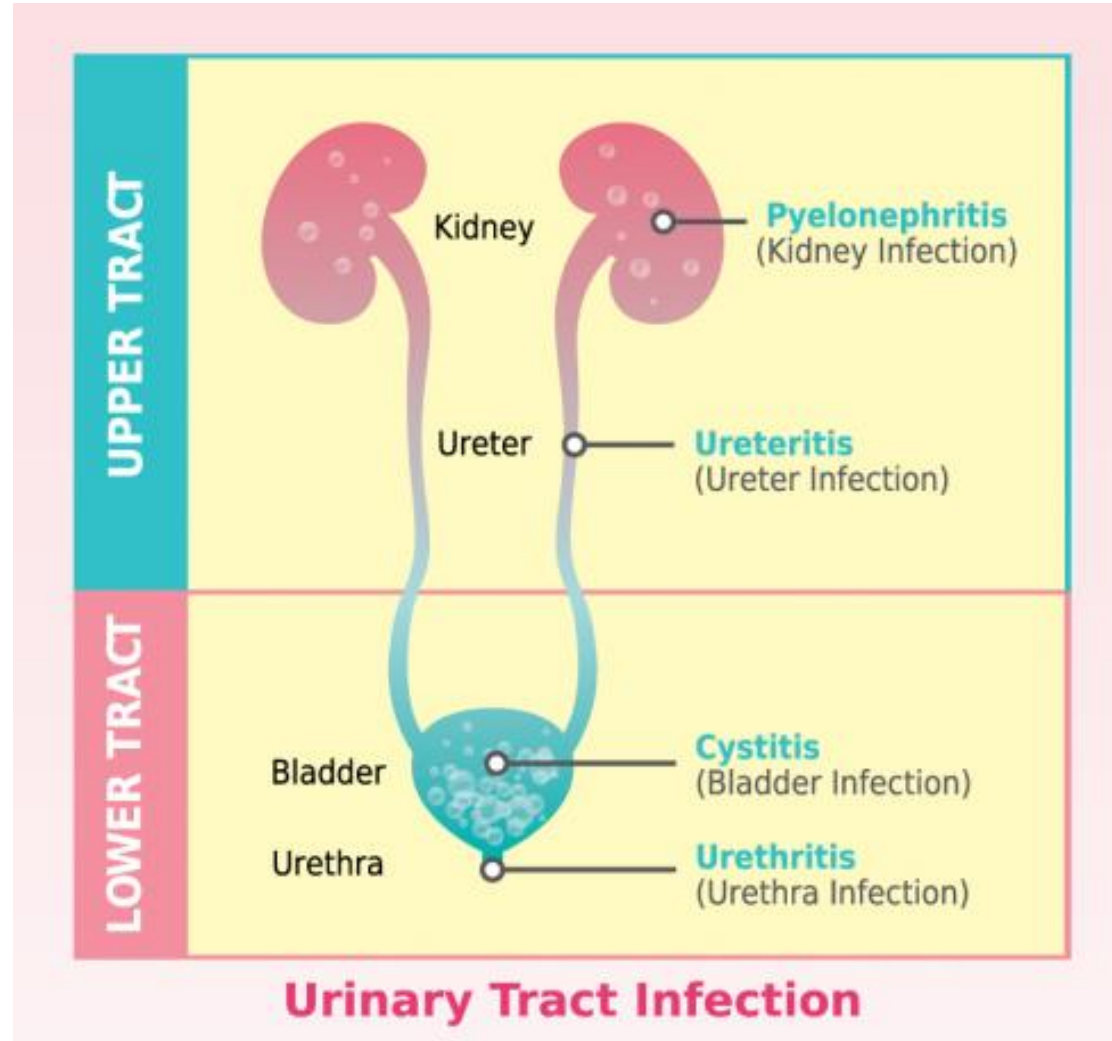
Treatment of UTI

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Upper and lower urinary tract infection



Urinary tract infection

- Among the most common bacterial infections encountered in clinical practice.
- UTI is much more common in female than male:
Female urethra is shorter, reducing the distance for bacterial ingress. Opens into the vulvar vestibule, i.e. a structure that is prone to infections and in close proximity of the rectum.
- 50 to 70% of women will have a UTI sometime during their lifetime, and 20 to 30% of women who have a UTI will have a recurrent UTI.
- Most UTIs are due to the colonization of the urogenital tract with rectal and perineal flora.
- *Escherichia coli* is the most common etiologic agent in uncomplicated UTIs in women, followed by *Klebsiella*.

Uncomplicated vs complicated UTI

- The definition can vary.
- The distinction between uncomplicated and complicated UTI is based on gender and/or presence of risk factors, and it is used to guide the choice and duration of antibiotic treatment.
- Uncomplicated UTI: Acute cystitis (lower tract infection)in immunocompetent, **premenopausal**, **non-pregnant** women without urinary tract abnormality, and no signs of systemic inflammation (e.g., fever, chills, and malaise).
- Complicated UTI: All others are considered complicated UTI.

Treatment of simple cystitis in women

- Infection of the bladder in non-febrile, immunocompetent, non-menopausal women.
- Symptoms includes:
 - pain on urination (dysuria), frequent urination (frequency), inability to start the urine stream (hesitancy), sudden onset of the need to urinate (urgency), suprapubic pain or discomfort, bladder spasms, and blood in the urine (hematuria).

Treatment of simple cystitis in women

- Antibiotic treatment has varied historically from 3 to 5 days or 5 to 7 days.
- *E. coli* resistance to common antimicrobials varies in different areas of the country. Another drug should be chosen if the resistance rate is >50% to any particular antibiotic.
- **Empiric antimicrobial selection** — The selection of an antimicrobial regimen for acute simple cystitis depends on the risk of infection with a multidrug-resistant (MDR) gram-negative organism, patient circumstances (allergy, tolerability, expected adherence), local community resistance prevalence, availability, cost. If the patient has taken one of the agents in the preceding three months, a different one should be selected.

First line agents

- **Nitrofurantoin:** bacteriostatic, used for 5 to 7 days. It has several mechanisms of action that affect bacteria, so resistance is relatively uncommon. It is only effective in the lower urinary tract due to poor tissue concentrations and cannot be used for presumed or possible pyelonephritis. It is the preferred drug for low-dose long-term prophylaxis in patients with recurrent UTIs.
- **Sulfamethoxazole/trimethoprim** for 3 days is good mini-dose therapy, but resistance rates are high. It should not be used in patients with a sulfa allergy. Sulfamethoxazole/trimethoprim is generally the alternate drug of choice for long-term prophylaxis in patients with recurrent UTIs.
- **Fosfomycin** : used when there is significant resistance to other antimicrobials. A single dose will provide therapeutic urinary concentrations for 2 to 4 days and is comparable to 7- to 10-day therapy with other agents. Can not be used in case of suspected pyelonephritis, because not achieve adequate renal tissue levels.
- **Pivmecillinam** It is not recommended in pyelonephritis or suspected systemic infections due to inadequate tissue penetration.

Because fosfomycin retains activity against many MDR isolates and overuse may result in increasing rates of resistance, we favor reserving it for suspected MDR infections or when other first-line agents cannot be used.

Second line agents

➤ **Oral beta-lactams** (other than [pivmecillinam](#)) are appropriate options, and if beta-lactams cannot be used, a **fluoroquinolone** is reasonable.

➤ Beta lactams:

[amoxicillin-clavulanate](#), [cefpodoxime](#), and [cefadroxil](#), each given for five to seven days

In general, beta-lactams are second-line agents because they are less effective and have more potential adverse effects than other UTI antimicrobials.

➤ Fluoroquinolones can be used if beta-lactams cannot be used (eg, because of severe allergy):

Including [ciprofloxacin](#) and [levofloxacin](#). Increasing rates of resistance mitigate the utility of the fluoroquinolone class. Furthermore, because of concerns about the adverse effects of fluoroquinolones, the risk-benefit balance for acute cystitis favors the use of fluoroquinolones only if other agents (including beta-lactams) cannot be used.

Treatment of recurrent UTI in women

- Defined as 2 or more acute UTIs within 6 months or 3 in a year
- Approximately 1 in 3 women suffer an uncomplicated urinary tract infection (UTI) before the age of 24
- Managing recurrent UTIs typically involves optimizing personal hygiene, using vitamin C as a urinary acidifier, taking extra precautions after sexual contact, and using prophylactic antibiotics.
- Anti-biotic prophylaxis: Post-coital prophylaxis, Long-term low-dose antibiotic prophylaxis (requires patient compliance, has a long duration of therapy (at least 6 months), and risks increasing antibiotic resistance. It should be used in the most intractable cases where more conservative measures have failed or cannot be effectively utilized.
- **Nitrofurantoin** low-dose long-term prophylaxis is the standard therapy for recurrent UTIs. It is well tolerated; treatment is limited to the urinary tract, which minimizes side effects, bacterial resistance is relatively low, and allergies or intolerance is rare. Sulfamethoxazole/trimethoprim or trimethoprim alone are alternative agents.
- **Estrogen vaginal cream** applied twice weekly can be helpful in postmenopausal women with atrophic vaginitis
- **Increased fluid intake is** helpful in women with low urinary volumes
- **Contraceptive modification:** changing to an alternate method of contraception that does not include a spermicide containing would be expected to reduce the risk of cystitis.
- **Hygiene** : wiping from front to back to avoid perineal contamination with fecal flora is routinely recommended as a prevention measure

Complicated UTI

- UTI other than a simple UTI.
- tend to be caused by a much wider range of organisms which is significant because multidrug resistance is increasing, and therefore specific antibiotic regimens will vary.
- *Escherichia coli*, *Enterococcus*, *Klebsiella*, *Pseudomonas*, and other *Enterococcus* or *Staphylococcus* species.
- Antibiotic therapy in complicated UTIs is typically 10 to 14 days. Treatment response should be evident in 24 to 48 hours in most cases. A poor response may indicate an inappropriate antibiotic selection, polymicrobial infections, atypical infections, obstructing stone causing pyonephrosis, complications such as a perinephric abscess or emphysematous UTI, obstructive urinary tract lesions, urinary calculi.

Complicated UTI

- Examples of a complicated UTI include:
 - UTIs in males.
 - Infections occurring due to an immunocompromised state, for example, steroid use, postchemotherapy, diabetes, HIV, older individuals.
 - Infections occurring in pregnancy (including asymptomatic bacteriuria).
 - Infections occurring after instrumentation, such as placing Foley catheters.
 - Infections occurring due to anatomical abnormalities, for example, an obstruction, hydronephrosis, renal tract calculi, or colovesical fistula.

Treatment of Bacteriuria and pyelonephritis in Pregnancy

- Those who have bacteria in the urine but no symptoms should not generally be treated with antibiotics. Exception is in pregnancy or patients undergoing urologic procedures in which mucosal bleeding is expected.
- 2 - 7% of pregnant women will develop asymptomatic bacteriuria, usually early in their pregnancy
- Without treatment, up to 35% will progress to a symptomatic UTI and/or pyelonephritis during the pregnancy
- Most studies suggest untreated bacteriuria during pregnancy is associated with an increased risk of low birth weight babies, prematurity, preeclampsia, and perinatal mortality.
- Treatment of asymptomatic bacteriuria and cystitis generally includes 3 to 7 days of amoxicillin-clavulanate, cephalexin, cefpodoxime, or a single dose of fosfomycin. Nitrofurantoin and sulfamethoxazole/trimethoprim may also be used but not during the first trimester or close to term.
- Pyelonephritis has also been associated with poor pregnancy outcomes, particularly prematurity.
- Pyelonephritis during pregnancy can be challenging and generally requires hospitalization. Standard therapy would include ceftriaxone, cefepime. Aztreonam is suggested if there is a beta-lactam allergy. Treatment can be adjusted after culture reports are available. Aminoglycosides should be used cautiously due to potential fetal ototoxicity.

UTI in men

- While technically, any UTI in a male is considered a "complicated UTI," many experts will treat an unambiguous lower urinary tract infection in healthy man with no known bladder dysfunction, stones, or other high-risk factors the same as a simple UTI with first-line antibiotic agents such trimethoprim-sulfamethoxazole, or nitrofurantoin. The length of trx should be 7-10 days. In recurrent infections, prostatitis should be suspected and treated accordingly, especially if the same organism is encountered.
- Men presenting with recurrent UTIs or bacterial prostatitis may require 4 to 6 weeks or longer to eradicate their infecting bacteria completely. Men with benign prostatic hyperplasia (BPH) and recurrent or intractable UTIs should be considered for surgical therapy. Nitrofurantoin is not generally recommended if kidneys, testicles, or prostate are involved.

Catheter associated UTI

- A catheter-associated urinary tract infection (CAUTI) is a UTI in which the positive culture was taken when an indwelling urinary catheter had been in place for > 2 calendar days.
- Patients with indwelling bladder catheters are predisposed to bacteriuria and UTIs.
- Symptoms may be vague or may suggest sepsis.
- The most effective preventive measures are avoiding unnecessary catheterization and removing catheters as soon as possible.
- Antibiotic prophylaxis and antibiotic-coated catheters are no longer recommended for patients who require long-term indwelling catheters.
- Once culture and susceptibility results are available, the antimicrobial regimen should be tailored to the specific organism isolated.