Uncomplicated and Complicated UTIs: A Review of Management

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Muskoka Algonquin Healthcare

Disclosures

No disclosures to declare.

Learning Objectives

1. List the difference between complicated and uncomplicated UTIs.

2. Describe the presentation and management in special/at-risk populations – (old, pregnant, immunocompromised and patients with indwelling catheters).

3. Describe antibiotic stewardship principles – empiric therapy vs. tailored treatment; resistance patterns.

Case 1

Clinical vignette

- 62-year-old postmenopausal woman presented with 6-month history of recurrent simple cystitis (4 episodes), each resolving temporarily with antibiotics.

Vitals

- T: 36.8
- BP: 128/76
- PR: 76 BPM
- SpO_2: 98% on RA

Urinalysis

- WBCs: 5-10/hpf
- Nitrites: Neg
- Leukocyte esterase: +++

Bloods

- WBC: 6.5 x 10^9/L
- Hb: 132 g/L
- Platelets: 240 x 10^9/L
- Creatinine: 72 umol/L
- BUN: 5.8 mmol/L
- HbA1c: 5.5%

Case 2

Clinical vignette

- 99-year-old-female presented to the ED with lower abdominal and left flank pain on a known background of stage IV CKD with in-situ indwelling urinary catheter.

Vitals

- T: 37.8
- BP: 127/58
- PR: 75 BPM
- SpO_2: 95% on RA

Urinalysis

- Leukocytes 3-5
- Trace blood
- Negative nitrites

Bloods

- WBC: 16.6
- Neutrophil count: 13.8
- Hb: 88
- BUN: 32.3
- Creatinine 529
- Na: 138
- K: 2.2
- Cl: 112

Plan/Management:

1. Started on Macrobid
2. Urine & BC done
3. Called nephrology:

- Hold Lasix
- IV fluids
- K replacement

Case 3

Clinical vignette

- 95-year-old-male was admitted to the ED with decreased appetite, SOB, and vomiting 3 days ago. His retirement home notably had a respiratory and gastroenteritis outbreak at the time of admission. This is on a known past medical background of end-stage CHF, CAD, A fib, CKD, HTN, DM, mild-moderate dementia, and BPH with indwelling catheter.

Current Medications

- Ramipril
- Spironolactone
- Lasix
- Apixaban
- Jardiance
- Levothyroxine
- Fluoxetine
- Pantoprazole
- KCl

O/E:

- No distress
- Vitals stable
- Chest – diffuse bilateral mild wheezing & fine crepitations
- No evidence of fluid overload

Investigations

- Urine: Blood +++; nitrites +++; leukocytes +++
- WBC: 14.7
- Creatinine: 130 (up from baseline 130-140)
- CXR: multifocal pneumonia

Plan:

1. Azithromycin + ceftriaxone
2. IV fluids

Case 3 Con’t:

Day 3:

- Urine cultures grow S. aureus (MRSA); no vancomycin resistant enterococcus isolated

Plan:

Septra (1 tablet BID) was added to the existing regimen while awaiting culture sensitivity results

Case 4

Clinical vignette

- 45-year-old male presented with 3-month history of recurrent dysuria, urinary frequency, and incomplete bladder emptying. He was treated twice for presumed UTI with 7-day course of Abx, with only partial relief. Symptoms recurred soon after treatment. Post-treatment urine cultures show E. coli growth.

Vitals
- T: 37.1
- BP: 124/78
- PR: 80 BPM
- SpO_2: 99% on RA

Bloods
- WBC: 7.8 x 10^9/L
- Hb: 140 g/L
- Platelets: 260 x 10^9/L
- Creatinine: 85 umol/L
- BUN: 5.5 mmol/L
- CRP: 12 mg/L

Urinalysis
- WBCs > 10
- Nitrites: +++
- Leukocyte esterase: +++
- Urine cultures: E. coli > 10^5 CFU/mL, sensitive to ciprofloxacin

UTI: Definition, Epidemiology and Clinical Relevance

Definition:

Urinary tract infections are broadly divided into:

- **Simple cystitis** – infection confined to the bladder
- **Complicated UTI** – infection of the urinary tract that extends beyond the bladder to the kidneys (pyelonephritis) or systemically

Epidemiology

- UTIs occur >4x more frequently in F vs. M
- Globally, ~405,000,000 cases, ~235,000 deaths (2.4x mortality from 1990-2019), and ~520,000 DALYs were estimated in 2019

Key Statistics

- Most common in F aged 16 – 35
- ~40% of F in the USA will develop a UTI during their lifetime
- ~10% of F experience a UTI annually
- Recurrence is common; ~50% experiencing a second infection within a year
- ~9.4% of hospitalized patients are diagnosed with healthcare-associated UTIs annually
- In hospitalized patients, UTIs attribute to 2.3% of mortality and cost ~340 to 450 USD to treat in the USA alone

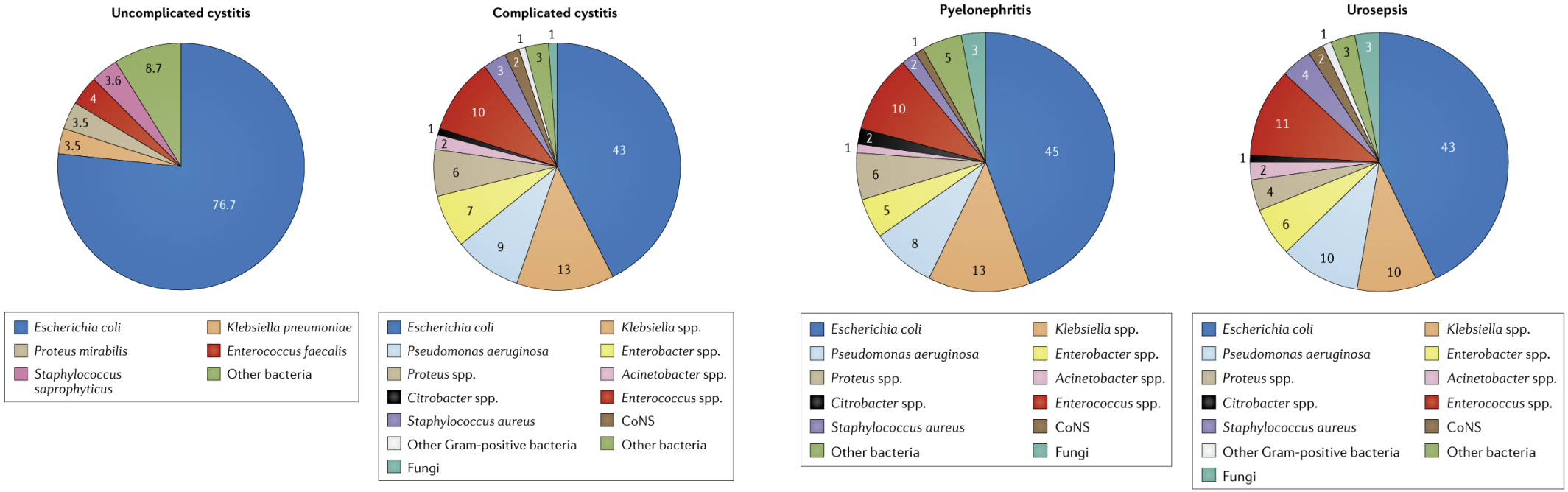
Clinical Presentations

Clinical Features of Simple Cystitis

- Dysuria
- Frequency
- Urgency
- Suprapubic pain
- WBCs (but not WBC casts) in urine

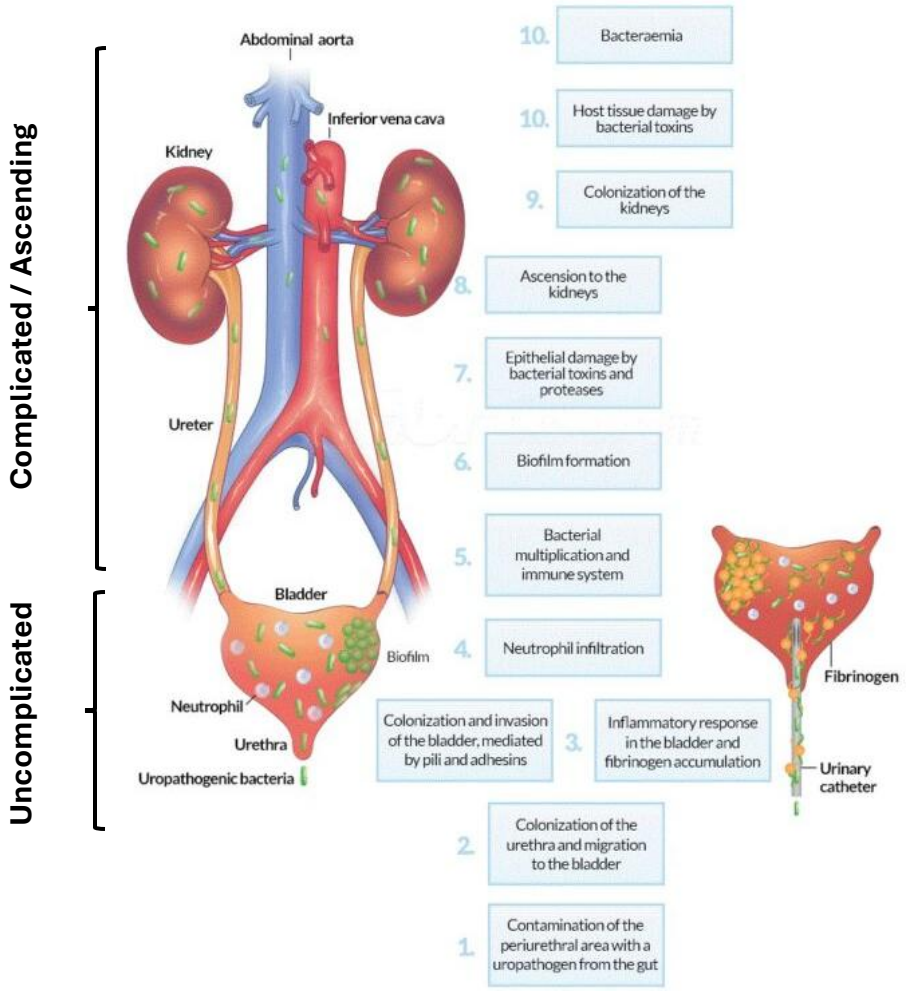
Risk Factors

- Obstruction (ex. kidney stone, BPH)
- Kidney surgery (transplant)
- Catheterization
- Congenital GU malformation (ex. vesicoureteral reflux)
- Diabetes, pregnancy, immune suppression



Wagenlehner et al. Nature Reviews Urology. 2020.

UTI Pathogenesis



Physical defense against UTI (urothelial cells)

- Produce IL-1, IL-6, and IL-18
- Encapsulate bacteria in fusiform vesicles, and if heavily infected, shed superficial layer to reduce bacterial load
- Local lactobacilli in premenopausal women occupy space to physically prevent colonization by uropathogens

Urine antimicrobial properties

- pH < 5
- High urea levels
- Hyperosmolality
- Organic acids, proteins (Tamm-Horsfall glycoprotein), and nitrites serve as bacterial growth inhibitors

Effect of SGLT2i on UTI?

UTI Classifications, Severity and Features

Review > Nat Rev Urol. 2020 Oct;17(10):586-600. doi: 10.1038/s41585-020-0362-4.
Epub 2020 Aug 25.

Epidemiology, definition and treatment of complicated urinary tract infections

Florian M E Wagenlehner [1], Truls E Bjerklund Johansen [2 3], Tommaso Cai [4], Bela Koves [5], Jennifer Kranz [6 7], Adrian Pilatz [8], Zafer Tandogdu [2 3 9]

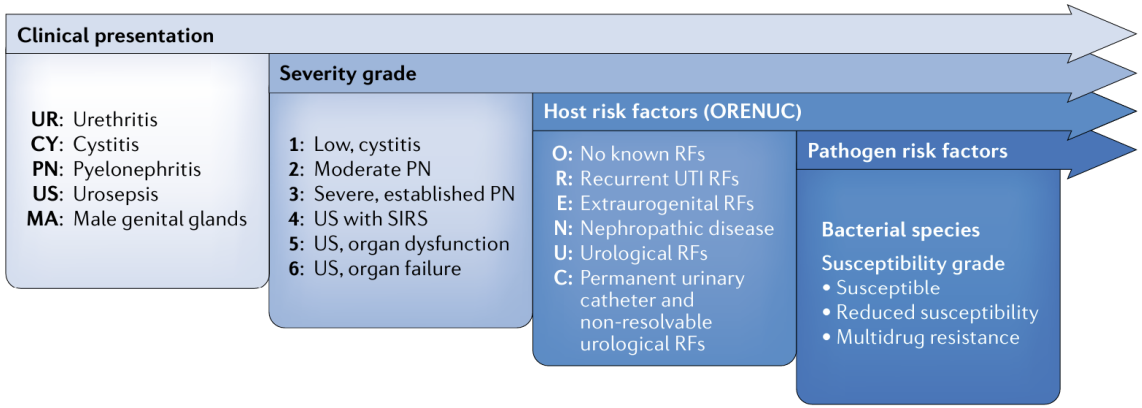


Table 1 | **Classical symptoms of different UTI entities**

Acronym	Clinical diagnosis	Clinical symptoms	Severity grade
CY-1	Cystitis	Dysuria, frequency, urgency, suprapubic pain; sometimes unspecific symptoms	1
PN-2	Mild to moderate pyelonephritis	Fever, flank pain[a], CVA tenderness[a]; sometimes unspecific symptoms with or without symptoms of cystitis	2
PN-3	Severe pyelonephritis	As for PN-2, but, in addition, nausea and vomiting with or without symptoms of cystitis	3
US-4[b]	SIRS	Temperature >38 °C or <36 °C, heart rate >90 beats/min, respiratory rate >20 breaths/min or $PaCO_2$ <32 mm Hg (<4.3 kPa), WBCs >12,000 cells/mm^3 or <4,000 cells/mm^3 or ≤10% immature (band) forms with or without symptoms of cystitis or pyelonephritis (>2 SIRS criteria must be met for US-4 diagnosis)	4
US-5[b]	Severe urosepsis	As for US-4, as well as organ dysfunction, hypoperfusion or hypotension; hypoperfusion and perfusion abnormalities may include but are not limited to lactic acidosis, oliguria or an acute change in mental status	5
US-6[b]	Uroseptic shock	As for US-4 or US-5, as well as hypotension despite adequate fluid resuscitation and the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria or an acute change in mental status; patients who are on inotropic or vasopressor agents may not be hypotensive when perfusion abnormalities are measured	6

Reinfection / Relapse

Relapse is defined as recurrence within 2 weeks of completion of treatment with the same uropathogen.

Reinfection is defined as infection that occurs 2 weeks after the treatment with complete resolution of the symptoms after the first episode even if it is the same organism.

Most recurrences of simple cystitis appear to be reinfections.

Most women with recurrent cystitis do not warrant imaging or urological evaluation. It is only reserved for women who have other features suggestive of structural or functional abnormalities.

Workup and Mx for Uncomplicated UTI

IDSA GUIDELINES

International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases

Kalpana Gupta,[1] Thomas M. Hooton,[2] Kurt G. Naber,[9] Björn Wullt,[10] Richard Colgan,[3] Loren G. Miller,[4] Gregory J. Moran,[5] Lindsay E. Nicolle,[8] Raul Raz,[11] Anthony J. Schaeffer,[6] and David E. Soper[7]

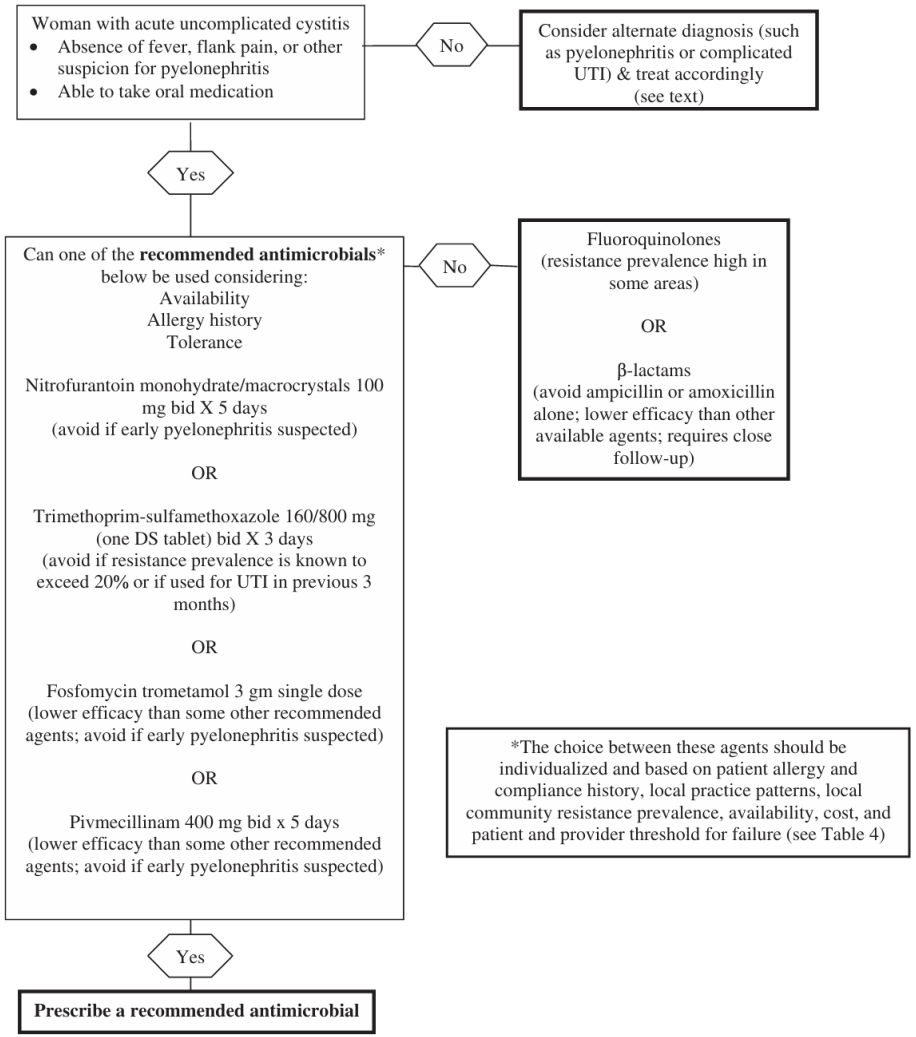


Figure 1. Approach to choosing an optimal antimicrobial agent for empirical treatment of acute uncomplicated cystitis. DS, double-strength; UTI, urinary tract infection.

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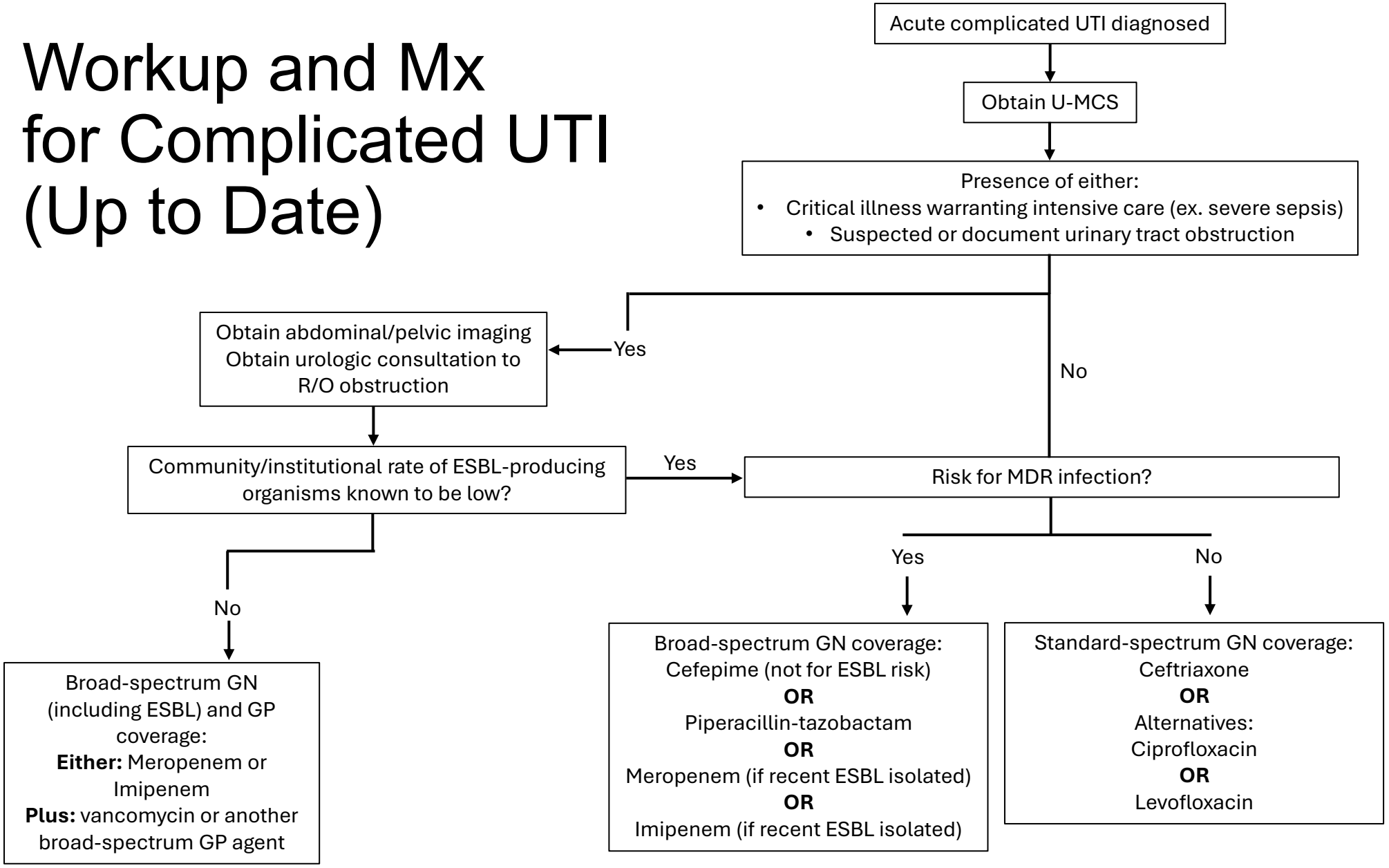
Workup and Mx for Complicated UTI (Up to Date)



Antimicrobial doses

Beta-lactam/beta-lactamase inhibitors:
- Piperacillin-tazobactam 3.375 g IV every 6 hours

Cephalosporins:
- Ceftriaxone 1 g IV once daily
- Cefepime 2 g IV every 12 hours

Fluoroquinolones:
- Ciprofloxacin 400 mg IV every 12 hours
- Ciprofloxacin 500 mg orally twice daily
- Ciprofloxacin extended-release 1000 mg orally once daily
- Levofloxacin 750 mg IV once daily
- Levofloxacin 750 mg orally once daily

Carbapenems:
- Meropenem 1 g IV every 8 hours, infused over 3 hours
- Imipenem 500 mg IV every 6 hours, infused over 3 hours

Broad-spectrum gram-positive agents:
- Vancomycin 15 mg/kg IV every 12 hours
- Daptomycin 6 to 8 mg/kg IV every 24 hours
- Linezolid 600 mg IV or PO every 12 hours

Screening & Tx Recommendations for At-Risk Populations

Patient Demographic	IDSA Screening & Up-To-Date Antibiotic Recommendations
Pediatric patients	Screening: Yes Antibiotic: Cephalosporin + RBUS if age <2 +/- voiding cystourethrogram
Asymptomatic Pregnant women	Screening: Yes Antibiotic: Beta-lactams and Fosfomycin; avoid Nitrofurantoin in first trimester
Older, community-dwelling residents who with functional impairment	No
Older residents in long-term care facilities	No
Diabetics	No
Renal transplant recipients	Yes; recommended for patients with renal transplant surgery >1 month prior Antibiotic prophylaxis recommendation: trimethoprim-sulfamethoxazole to prevent PCP Simple cystitis (choose one): ciprofloxacin, levofloxacin, cefpodoxime, Bactrim Complicated UTI: empiric Tx with piperacillin-tazobactam, meropenem, or combination with vancomycin + cefepime
Nonrenal transplant recipients	No
Neutropenic patients	No recommendation made
Indwelling urethral catheter	Short term IDC (<30 days) – No Long term IDC – Yes; Antibiotic – empiric tx followed by culture-driven Screening at time of IDC removal – not given

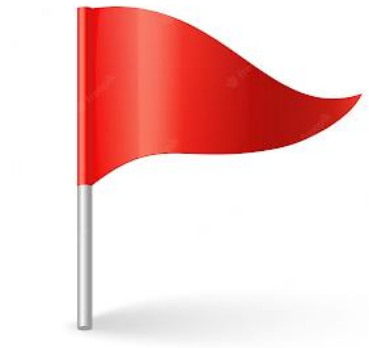
Infectious Disease Society of America. 2019. *Clinical Infectious Disease*

Prevention and Management of Recurrent UTI

Recurrent cystitis in women	
Definition	• ≥2 infections in 6 months • ≥3 infections in a year
Risk factors	• Sexually active • Postmenopausal • 1st UTI at age <15 • Spermicide use

Lifestyle Management	Non-Abx Treatment	Abx Prophylaxis
Avoiding certain activities: prolonged bicycling, motorcycling, and horseback riding	**Cranberry products** (controversial) – proanthocyanidins decrease bacterial urothelial adherence?	**First-line for recurrent UTI**: • Nitrofurantoin 50-100 mg • SMX-TMP 40/200 mg • Trimethoprim 100 mg (CI eGFR <15 mL/min)
Empty bladder and stay **hydrated** when physically active	**D-mannose** - conflicting evidence + expensive	**Second-line for recurrent UTI**: • Cephalexin 125/250 mg • Cefaclor 250 mg • Fosfomycin 3g every 10 d • Norfloxacin 400 mg • Pivmecillinam 185 mg (CI eGFR <10 mL/min)
Post-coital voiding and **hydration**	**Methenamine prophylaxis** – reduces urine pH <5.5	
Over-the-counter **washcloths**	**Estrogen vaginal cream**	
Avoid irritating foods like caffeine, alcohol, hot spices, chocolate, and soft drinks	**MV140 vaccine** – contains heat-inactivated E. coli, K. pneumoniae, E. faecalis, and P. vulgaris (not approved in Canada or USA)	

UTI Mimics and Red Flags



Mimics

- Bladder or renal stones
- Sexually transmitted infection
- Medication adverse effects
- Overactive bladder
- PID
- Prostatitis
- Urethritis
- Vaginitis

Red Flags

- Fever > 38
- Chills or rigors
- Flank pain (suggests upper tract infection)
- N/V (especially if severe)
- Sepsis signs (hypotension, tachycardia, altered mental status)
- Persistent or worsening symptoms despites 48-72h of Abx treatment
- New confusion (especially in elderly)
- History of urinary tract abnormalities (ex. stones, strictures)
- Immunocompromised state
- Pregnancy

Genitourinary Syndrome of Menopause

Vaginal estrogen has effectively reduced the incidence of cystitis in a small trial of post menopausal females.

In a randomized trial of 93 post menopausal women history of recurrent cystitis, vaginal estrogen over an 8-month course reduced the incidence of cystitis compared to placebo (0.5 vs. 5.9 episodes per patient year: RR 0.25, 95% CL 0.13-0.50).

Nevertheless, vaginal estrogen does not seem to be as effective as Abx prophylaxis. In a randomized trial of 171 post menopausal women was higher with vaginal estrogen compared to daily Nitrofurantoin (2 vs. 0.8 episodes per pat year).

Chronic Bacterial Prostatitis

Pathogenesis is the same as an acute infection. Microorganisms enter into the prostatic ducts through the urethra/bladder with intraprostatic reflux of urine.

Chronic prostatitis may be a complication of acute prostatitis following inadequate and/or too short treatment.

It usually affects young and middle-age men. The presentation can be quite subtle. Classically, men present with symptoms of recurrent frequency, dysuria, urgency, perineal discomfort and perhaps low -rade fever. Most patients however have one or some of these features.

Some men can be asymptomatic and might have persistent, recurrent bacteriuria.

Other symptoms can include pain in the lower abdomen, testicles, penis, and with ejaculation and sometimes blood in the ejaculate.

On rectal exam, there may be prostatic hypertrophy, tenderness, edema, and nodularity. However, prostate exam is frequently normal.

Chronic Bacterial Prostatitis

Laboratory findings suggestive of infection or inflammation are usually absent. PSA might only be elevated in 25% patients.

The diagnostic standard is finding of high levels of bacteria in the prostatic fluid. However, maneuvers to express prostatic fluid are cumbersome and practically not possible.

Most of the times it is a clinical diagnosis, and patients respond to antibiotic therapy.

Prolonged antibiotic therapy (at least 6 weeks) with an agent that has good penetration into the prostatic tissue is generally necessary.

A fluoroquinolone is generally a drug of choice for both initial and recurrent episodes.

UTI in Catheterized Patients

Urinary tract infection associated with catheterization may be extraluminal/ intra-luminal.

Extra luminal is via entry of bacteria into the bladder along the biofilm that forms around the catheter.

Intraluminal infection occurs due to urinary stasis because of drainage failure or due to contamination of urinary bag.

The causative pathogens are the same as any complicated UTI.

Patients with catheter associated UTIs often present with the localizing symptoms like dysuria, urinary urgency, suprapubic discomfort, flank pain or costovertebral angle tenderness and systemic symptoms like fever.

Cloudy or foul smelling urine is not suggestive of a UTI in a patient with long standing indwelling catheter.

UTI in Catheterized Patients Cont'd

Patients with spinal cord injury may have especially atypical and non-specific symptoms including increased spasticity, malaise, lethargy and autoimmune dysreflexia.

Rarely purple discolouration of urine/ collecting bag and tubing (PUBS: purple urine bag syndrome) can occur due to metabolic by products of certain bacteria like Providencia spp, Klebsiella and Proteus. PUBS is benign and does not necessarily indicate presence of a UTI.

The diagnosis of catheter associated UTI is made by identifying bacteriuria plus pyuria in catheterized patients who have signs and symptoms that are consistent with UTI or systemic infection that is otherwise unexplained.

For patients with indwelling catheter, it is recommended that the catheter is changed and the first void from the new catheter is sent for urine culture.

If that cannot be done, catheter should at least be changed before the initiation of the antimicrobial treatment.

Case 1 Revisited

Clinical vignette

- 62-year-old postmenopausal woman presented with 6-month history of recurrent simple cystitis (4 episodes), each resolving temporarily with antibiotics. She also reported vaginal dryness and dyspareunia. Pelvic exam shows thin pale vaginal mucosa without discharge. Patient denied symptoms suggestive of functional or structural abnormality.

Vitals

- T: 36.8
- BP: 128/76
- PR: 76 BPM
- SpO_2: 98% on RA

Urinalysis

- WBCs: 5-10/hpf
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- HbA1c: 5.5%

Plan/Management:

1. Start vaginal estrogen cream (estradiol 0.5 g twice weekly)
2. Counsel on hydration and post-coital voiding
3. Follow-up in 8-12 weeks
4. Consider prophylactic Abx if UTIs persist despite estrogen
5. Reassure regarding minimal systemic absorption of topical estrogen

Case 2: Complicated UTU/ Pyelonephritis

Clinical vignette

- 99-year-old-female presented to the ED with lower abdominal and left flank pain on a known background of stage IV CKD with in-situ indwelling urinary catheter.

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Urinalysis

- Leukocytes 3-5
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- Neutrophil count: 13.8
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- Cl: 112

Plan/Management:

1. Started on Macrobid
2. Urine & BC done
3. Called nephrology:

- Hold Lasix
- IV fluids
- K replacement

Macrobid is not appropriate for complicated UTI and is also CI if eGFR<30

Case 3 Revisited

Clinical vignette

95-year-old-male was admitted to the ED with decreased appetite, SOB, and vomiting 3 days ago. His retirement home notably had a respiratory and gastroenteritis outbreak at the time of admission. This is on a known past medical background of end-stage CHF, CAD, A fib, CKD, HTN, DM, mild-moderate dementia, and BPH with indwelling catheter.

Current Medications

- Ramipril
- Spironolactone
- Lasix
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- Levothyroxine
- Fluoxetine
- Pantoprazole
- KCl

O/E:

- No distress
- Vitals stable
- Chest – diffuse bilateral mild wheezing & fine crepitations
- No evidence of fluid overload

Investigations

- Urine: negative after catheter change

Plan:

1. Azithromycin + ceftriaxone
2. IV fluids

No need to treat in absence of UTI symptoms

Septra increases risk for hyperkalemia in CKD patients/ nephrotoxic medications

Case 3 Revisited Con't:

Day 3:

- Urine cultures grow S. aureus (MRSA); no vancomycin resistant enterococcus isolated

Day 3 Investigations

- Creatinine: 116 – 132 - 168

Plan:

1. Hold Jardiance, Lasix, spironolactone, and ramipril
2. Cease Septra

Case 4: Chronic Bacterial Prostatitis

Clinical vignette

45-year-old male presented with 3-month history of recurrent dysuria, urinary frequency, perineal discomfort, and incomplete bladder emptying. He was treated twice for presumed UTI with 7-day course of Abx, with only partial relief. Symptoms recurred soon after treatment. Post-treatment urine cultures show E. coli growth. DRE revealed mildly tender, boggy prostate

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Urinalysis

- WBCs > 10
- Nitrites: +++
- Leukocyte esterase: +++
- Urine cultures: E. coli > 10^5 CFU/mL, sensitive to ciprofloxacin

Examination and Investigations:

1. DRE
2. PSA
3. USG KUB – negative

Plan/Management:

1. Start ciprofloxacin 500 mg PO BID for 4-6 weeks
2. Consider tamsulosin for voiding symptoms
3. Offer NSAIDs for pain if needed
4. Repeat urine culture 1-2 weeks post-treatment
5. Urology referral if persistent symptoms

Summary & Take Home Message

1. Differentiate simple from complicated UTI early to guide appropriate investigation and management – recognizing patient-specific risk factors is key.

2. Tailor antibiotic therapy carefully based on severity, patient population (ex. elderly, pregnant, immunocompromised, catheterized), and local resistance patterns to optimize outcomes and reduce harm.

3. Prioritize antimicrobial stewardship: always reassess the need for antibiotics, use the narrowest effective agent, and appropriately limit treatment duration to prevent resistance.

Thank You! ☺