DIAGNOSIS AND MANAGEMENT OF

Urinary Tract Infection in Adults

This CPM was created by the Antimicrobial Stewardship and Infectious Diseases services at Intermountain Healthcare. It guides treatment of adult patients with urinary tract infections (UTIs) presenting to the emergency department, urgent care, or primary care. These guidelines should not be used to treat patients with urinary tract devices (e.g., indwelling catheters, ureteral stents, or nephrostomy tubes), those undergoing urologic procedures, pregnant women, renal transplant recipients, or those with prostatitis.

Why Focus ON UTI?

- **UTIs are common.** In the US, there were approximately 2.7 million visits to the ED for UTIs in 2014.[RUI] In a random sample of 2000 adult women, > 10 % reported at least one presumed UTI in the previous 12 months.[FOX]
- **UTIs are overdiagnosed and over-treated.** Patients with positive urine cultures but lacking clinical signs and symptoms of UTI should not be prescribed antibiotics, yet up to half are treated unnecessarily with antibiotics.[FLO]
- **UTIs are costly.** The average cost of UTI hospitalizations nearly doubled between 2001 and 2011.[SIM]
- **Antimicrobial resistance complicates treatment**. With increasing rates of antimicrobial resistance to common first-line agents, prescribers face a challenge in treating UTIs.

Implementing best practices for UTI diagnosis and treatment will improve patient outcomes and cure rates by ensuring appropriate antibiotic therapy and reducing serious adverse events from unnecessary and inappropriate antibiotic use.

KEY POINTS

The focal points discussed in this CPM include:

- **Treating asymptomatic bacteriuria with antibiotics offers no benefit and may cause harm,** such as increased symptomatic recurrences, antimicrobial resistance, and *Clostridioides difficile* infection.
- **Ciprofloxacin and levofloxacin are no longer first-choice agents for cystitis**. The FDA released a warning against fluoroquinolone use for uncomplicated cystitis in 2016. Avoid when other options are available.
- **Nitrofurantoin is the preferred agent for cystitis** due to its efficacy, minimal resistance, and low propensity for collateral damage.

WHAT'S INSIDE?

MEASUREMENT & GOALS

Intermountain seeks to increase the number of UTI's that are correctly diagnosed and properly treated with the most effective course of antibiotics in order to improve patient outcomes and decrease the rates of antibiotic resistance. The following are key aims in this process:

- Reduce urine testing for patients without symptoms of UTI.
- Reduce the treatment of asymptomatic bacteriuria with any antibiotic.
- Improve appropriate empiric antibiotic choices and treatment durations for cystitis and pyelonephritis.
- Reduce the use of fluoroquinolones for uncomplicated cystitis.

Indicates an Intermountain measure

Intermountain® Healthcare

UTI SIGNS & SYMPTOMS

UTI symptoms are a prerequisite for urine testing and antibiotic treatment.

Specific (localized) signs/symptoms:

- Dysuria
- Urgency
- Frequency
- Suprapubic pain or pressure
- Flank pain

Nonspecific signs/symptoms:

CAUTION: Often associated with non-UTI etiologies

- Fever
- Leukocytosis
- Abdominal pain
- Altered mental status
- Nausea
- Vomiting

NOT UTI signs/symptoms:

Testing and treatment not recommended in the absence of other symptoms:

- Cloudy, foul-smelling, or dark urine
- Increased urine sediment

Clinically stable, asymptomatic patients with pyuria should not be treated with antibiotics. [NIC]

Treatment of asymptomatic bacteriuria may result in harm and offers no clinical benefit. [CAI1, CAI2, DIN]

UTI DIAGNOSIS

Neither urine testing nor antimicrobial treatment are appropriate in the absence of UTI symptoms. Interpret nonspecific signs and symptoms such as fever, rigors, nausea, vomiting, and delirium with caution since they are often present with other infectious and non-infectious etiologies. UTI diagnosis should be based on the presence of localized symptoms when possible (see sidebar at left).

Types of Urinary Tract Infections

Cystitis. Cystitis is an infection isolated to the bladder. Symptoms of cystitis are dysuria, urinary frequency, urgency, and suprapubic pain.

Pyelonephritis. Pyelonephritis is a severe UTI involving the kidneys, commonly referred to as an **upper urinary tract infection.** It typically presents with fever, chills, flank pain, nausea, and vomiting in addition to dysuria, frequency, urgency and suprapubic pain (although not all patients have bladder symptoms). Presentation with systemic symptoms suggests tissue inflammation of the urinary tract and may represent pyelonephritis, prostatitis, or urosepsis.

Uncomplicated v. Complicated UTI's

Uncomplicated infection: A UTI (cystitis or pyelonephritis) occurring in nonpregnant, premenopausal women with no known comorbidities or urologic abnormalities. Women with well-controlled diabetes mellitus (DM) or postmenopausal women without urologic abnormalities may also be classified as having an uncomplicated UTI. [GUP]

Complicated infection: A UTI (cystitis or pyelonephritis) that presents in patients meeting any of the following conditions: male, pregnant, poorly controlled diabetes mellitus (DM), urinary tract obstruction, acute/chronic kidney injury, immunosuppressed, abnormality of the urinary tract, presence of an external catheter or hospital-acquired infection. Some of these patient populations are outside the scope of this CPM.

Asymptomatic bacteriuria. Asymptomatic bacteriuria is defined as the presence of ≥ 100,000 cfu/ml in 1 (men) or 2 (women) consecutive, voided urine specimens in the absence of urinary symptoms. [NIC] Asymptomatic patients with bacteria in their urine (even with pyruria) should **not** receive antimicrobial treatment as doing so can increase the risk of future bladder infections with more antibiotic-resistant strains and potentially increase the risk of *C. difficile* infection. [CAI1, CAI2, DIN] **Neither pyuria nor cloudy or foul-smelling urine warrants testing or treatment in the absence of UTI symptoms.** Reducing the treatment of asymptomatic bacteriuria with antibiotics will decrease adverse drug events, mitigate the development of resistance, and lower *C. difficile* infection rates and prescription costs.

EXCEPTION: According to the guidelines published by the Infectious Disease Society of America (IDSA), pregnant women and patients undergoing transurethral resection of the prostate or other urologic procedures where mucosal bleeding is anticipated **should** be treated for asymptomatic bacteriuria. [NIC]

Types of urine testing

Urinalysis macroscopic (UMAC): This urine dipstick assay tests for specific gravity and pH, as well as leukocyte esterase, nitrite, hemoglobin, protein, ketone, and urobilinogen levels.

Urinalysis macroscopic with reflex to microscopic exam (UA): A urinalysis macroscopic evaluation is performed. If urine has abnormal appearance or is positive for protein, hemoglobin, nitrites, or leukocyte esterase, a microscopic examination will automatically be executed. The microscopic exam evaluates for white blood cells, red blood cells, epithelial cells and bacteria.

UA with reflex criteria to culture (CRITER): UA is performed and if abnormal, based on criteria set by provider, a urine culture will automatically result. The recommended reflex criteria is ≥ 5 WBC / hpf.

Urine culture: Organisms are isolated from urine sample, identified, and then screened for antimicrobial susceptibility.

Limits of urinalysis

Urinalysis is most **helpful for ruling out** a UTI, but is **not specific enough to rule in** a UTI on its own. Other signs and symptoms must be present. Reasons for this include:

- **Bacteria may colonize the bladder,** especially in elderly adults living in the community (10 – 20 %) or long-term care facilities (15 – 50 %), diabetic women (10 – 25 %), and patients with long-term catheter use (up to 100 %).[NIC]
- **Skin and vaginal flora can contaminate** the urine sample during collection.
- **Pyuria can have non-infectious causes** including dehydration, acute renal failure, recent urologic procedure, renal stone, or presence of a catheter.[WIS]

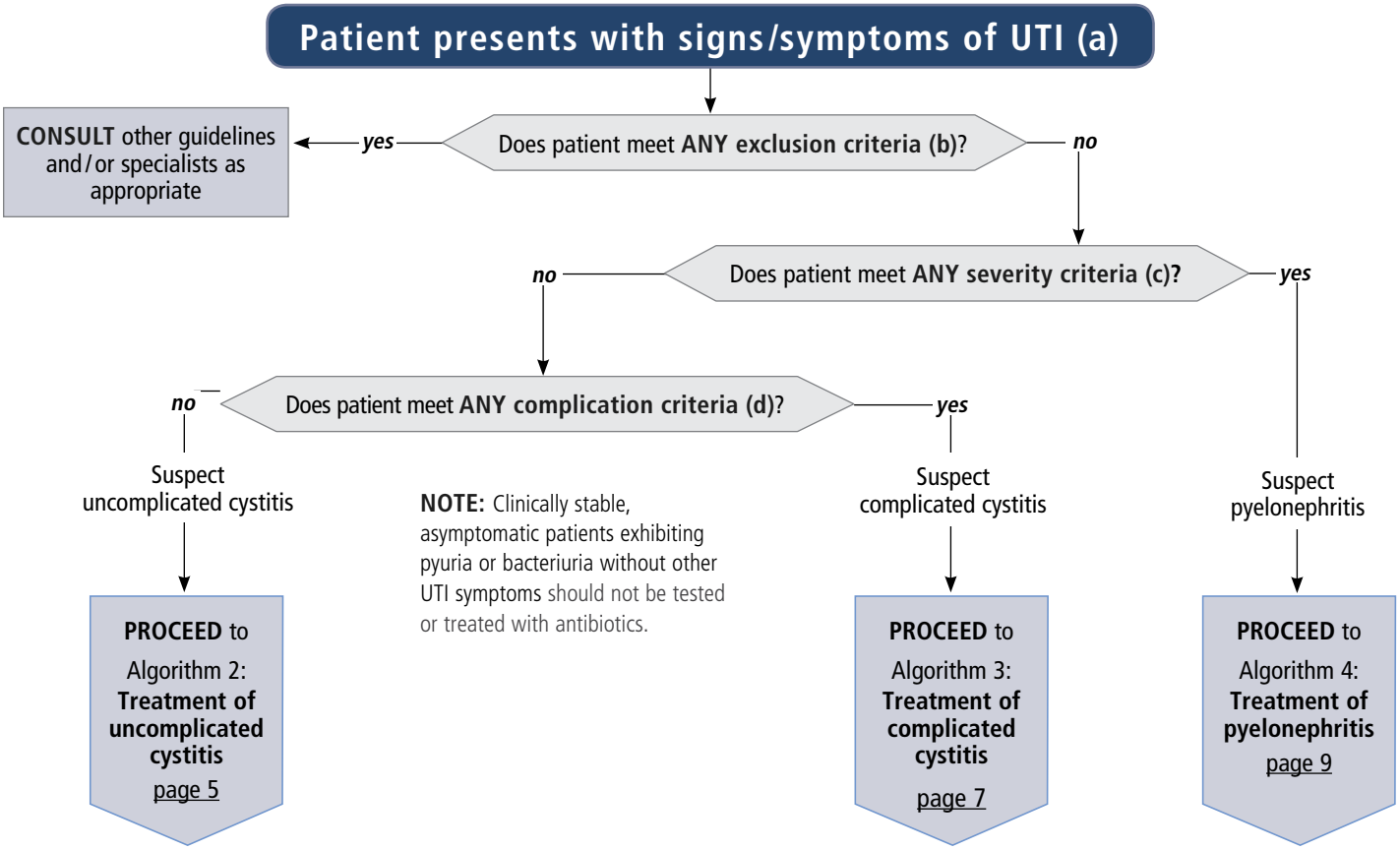
Use Table 1 below for guidelines on the appropriate use of urine testing.

TABLE 1. Appropriate use of urine testing

Indication for urine testing	UMAC	UA	UA with reflex to culture	Urine culture	No testing
Evaluation of noninfectious disease (e.g., kidney disease, nephrolithiasis, DM)		X			
Signs / symptoms of complicated UTI or recurrent uncomplicated UTI			X		
Signs / symptoms of uncomplicated UTI	X				
No signs / symptoms					X
Neutropenic and signs / symptoms of UTI				X	
Post UTI treatment (i.e. test of cure)					X
Unable to give a history and no clear source of infection			X		
Unable to give a history and clear non-urinary source of infection					X

Abbreviations: DM-Diabetes mellitus

ALGORITHM 1: PATIENT STRATIFICATION



ALGORITHM 1 NOTES

(a) Signs/Symptoms of UTI

Specific (localized)	**Nonspecific** (often associated with non-UTI etiologies)	
• Dysuria	• Fever	• Altered mental status
• Urgency	• Vomiting	• Abdominal pain
• Frequency	• Nausea	• Leukocytosis
• Suprapubic pain or pressure,		
• Flank pain		

(b) Exclusion criteria

Exclusion criteria include **ANY** of the following:

- Urinary tract devices (e.g., indwelling catheters, nephrostomy tubes)
- Undergoing a urologic procedure
- Pregnancy
- Recipient of renal transplant
- Prostatitis

(c) Severity criteria

Severity criteria include **ANY** of the following:

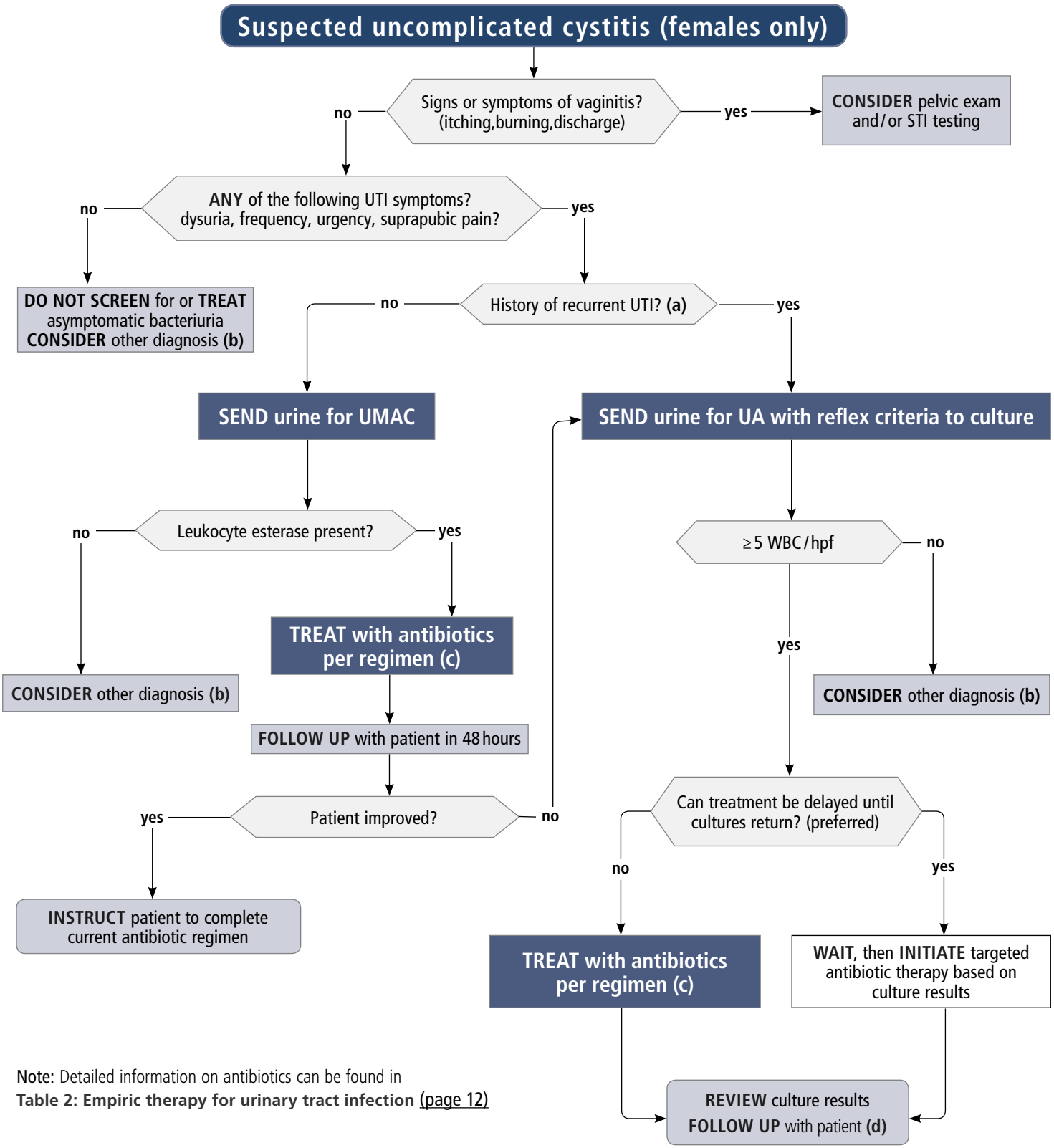
- Temperature > 38.3 °C (100.1° F) or < 36 °C (96.8° F)
- Heart rate > 90 beats per minute
- Respiratory rate > 20 breaths per minute
- Serum WBC > 12,000 / mm^3 or < 4,000 / mm^3
- Serum WBC > 10 % are immature (band) forms
- Chills
- Flank pain

(d) Complication criteria

Complication criteria include **ANY** of the following:

- Male
- Poorly controlled diabetes mellitus
- Immunosuppressed
- Hospital-acquired infection
- Obstruction of urinary tract
- Abnormality of urinary tract
- Acute or chronic kidney injury

ALGORITHM 2: TREATMENT OF UNCOMPLICATED CYSTITIS



Note: Detailed information on antibiotics can be found in **Table 2: Empiric therapy for urinary tract infection** (page 12)

Abbreviations: **UTI**-urinary tract infection; **WBC**-white blood cell; **hpf**-high powered field; **STI**-sexually transmitted infection; **UMAC**-urinalysis macroscopic; **UA**-urinalysis macroscopic with reflex to microscopic

ALGORITHM 2 NOTES

(a) Recurrent UTI criteria[DAS]

Consider recurrent UTI if **ANY** of the following:

- One UTI within the last 2 weeks
- Two UTIs within the last 6 months
- Three UTIs within the last 12 months

See page 13 for recurrent UTI prophylaxis recommendations. Carefully assess the risks and benefits prior to prescribing antimicrobial prophylaxis for women with recurrent UTI. Risk factors for recurrent UTI in premenopausal women include sexual intercourse, use of spermicides and diaphragms, prior UTI, and family history. Risk factors for recurrent UTI in postmenopausal women include cystocele, estrogen deficiency, urinary retention, urogenital surgery and prior UTI.[AYD]

(b) Other diagnoses (Cystitis mimics)

Vaginitis, atrophic vaginitis; STIs; malignancy; interstitial cystitis; overactive bladder; irritant contact dermatitis; urethral stricture; bladder diverticulum; prostatitis.

(c) Recommended antibiotic regimen for uncomplicated cystitis

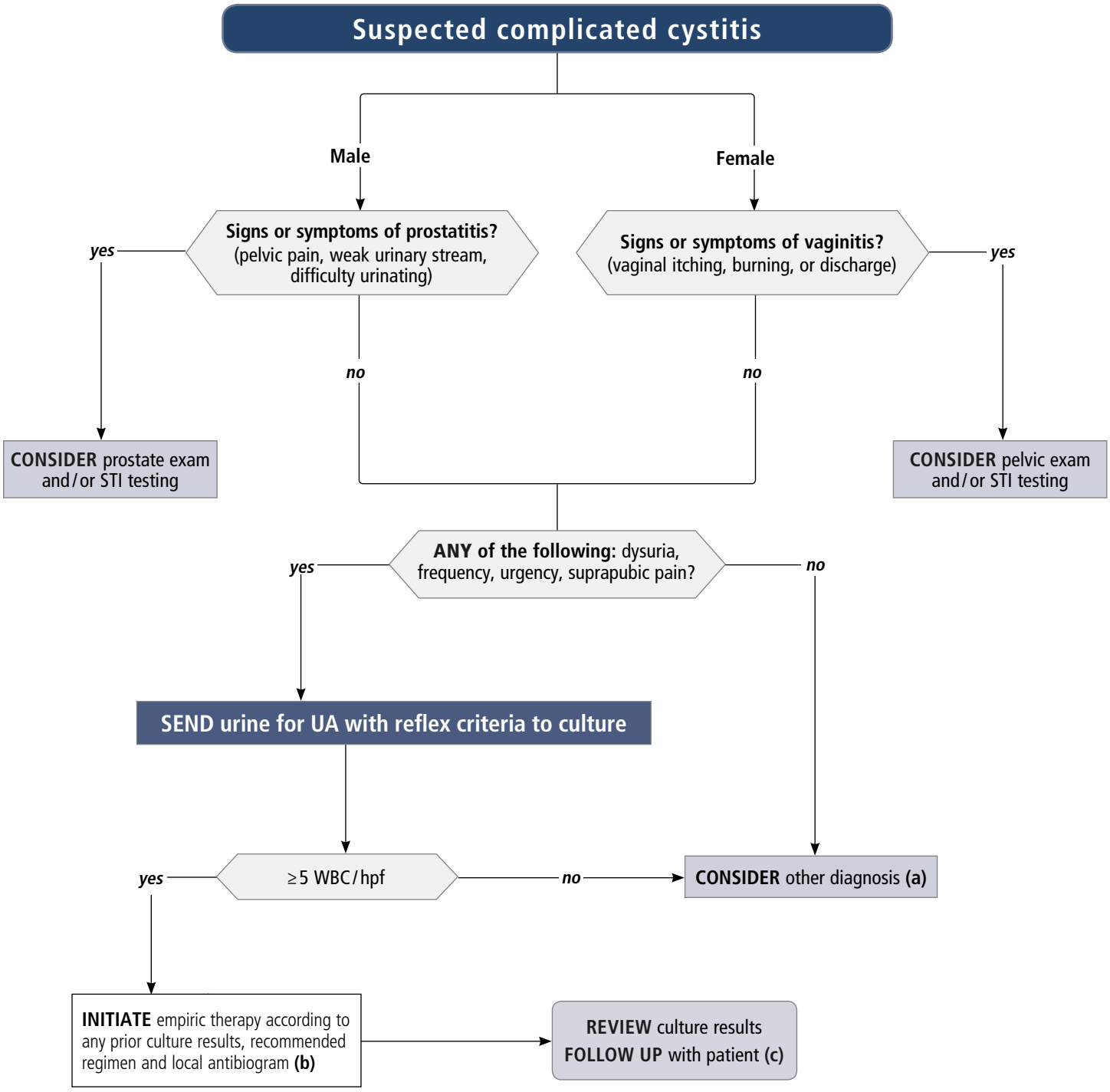
Antibiotic	Dosage and frequency	Notes
First Line Agent		
nitrofurantoin monohydrate (Macrobid)	100 mg orally two times per day for 5 days	If CrCl is 30–60 ml/min, consider use. Avoid use if CrCl < 30 ml/min; see page 12 for renal impairment information. Nitrofurantoin is **not** recommended for prostatitis.
nitrofurantoin macrocrystals (Macrodantin)	50–100 mg orally four times per day for 5 days	(see above)
Alternatives		
cephalexin	500 mg orally four times per day for 7 days (not recommended as first-line treatment for prostatitis)	
trimethoprim (TMP) /sulfamethoxazole (SMX) (double strength)	160 mg TMP/800 mg SMX orally two times per day for 3 days	
fosfomycin	3 g orally once	

(d) REVIEW culture results and FOLLOW UP with patient (24–48 hours)

Patient is improving	Patient is not improving	
	Results indicate that organism is susceptible to current antibiotic.	Results indicate that organism is resistant to current antibiotic
COMPLETE current antibiotic regimen regardless of reported antibiotic susceptibility	• **CONSIDER** cystitis mimics **(b)** • **REPEAT** urine culture • In the interim, **IF** cystitis mimics are ruled out: **INITIATE** change in antibiotic therapy; **TARGET** organism according to culture results.	**INITIATE** change in antibiotic therapy; **TARGET** organism according to culture results.

Abbreviations: **UTI**-urinary tract infection;**CrCl**-creatinine clearance; **STI**- sexually transmitted infection;

ALGORITHM 3: TREATMENT OF COMPLICATED CYSTITIS



Note: Detailed information on antibiotics can be found in
Table 2: **Empiric therapy for urinary tract infection** (page 12)

Abbrev: STI-sexually transmitted infection; UA-urinalysis macroscopic with reflex to microscopic; CrCl-creatinine clearance;

ALGORITHM 3 NOTES

(a) Other diagnoses (Cystitis mimics)

Vaginitis, atrophic vaginitis; STIs; malignancy; interstitial cystitis; overactive bladder; irritant contact dermatitis; urethral stricture; bladder diverticulum; prostatitis.

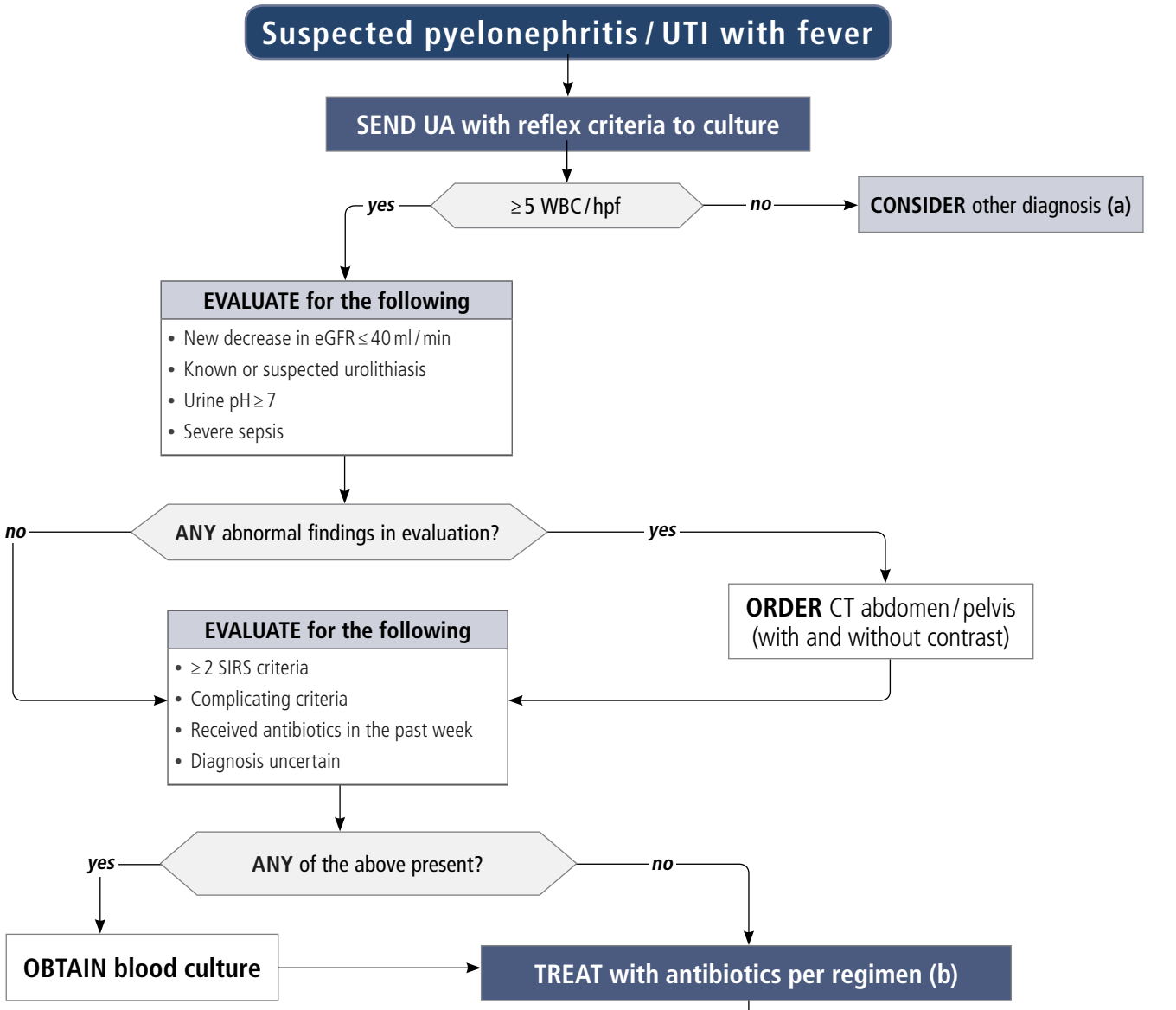
(b) Recommended antibiotic regimen for complicated cystitis

Antibiotic	Dosage and Frequency	Notes
First Line Agent		
nitrofurantoin monohydrate (Macrobid)	100 mg orally twice per day for 7 days	If CrCl is 30–60 ml/min, consider use. Avoid use if CrCl < 30 ml/min; see page 12 for renal impairment information. Nitrofurantoin is **not** recommended for prostatitis.
nitrofurantoin macrocrystals (Macrodantin)	50–100 mg orally four times per day for 7 days	(see above)
Alternatives		
cephalexin	500 mg orally four times per day for 7 days (not recommended as first-line treatment for prostatitis)	
trimethoprim (TMP) / sulfamethoxazole (SMX) (double strength)	160 mg TMP/800 mg SMX orally two times per day for 7 days	
ciprofloxacin	500 mg orally two times per day for 7 days	**Use only in the absence of alternative options**

(c) REVIEW culture results and FOLLOW UP with patient (24–48 hours)

Patient is improving	Patient is not improving	
	Results indicate that organism is susceptible to current antibiotic.	Results indicate that organism is resistant to current antibiotic
COMPLETE current antibiotic regimen regardless of reported antibiotic susceptibility.	• **CONSIDER** cystitis mimics **(b)** • **REPEAT** urine culture • In the interim, **IF** cystitis mimics are ruled out: **INITIATE** change in antibiotic therapy; **TARGET** organism according to culture results	**INITIATE** change in antibiotic therapy; **TARGET** organism according to culture results.

ALGORITHM 4: TREATMENT OF PYELONEPHRITIS / UTI WITH FEVER



Note: Detailed information on antibiotics can be found in **Table 2: Empiric therapy for urinary tract infection** (page 12)

Treatment and Follow-up		
INPATIENT	**UNCERTAIN ADMISSION**	**OUTPATIENT**
• **CONTINUE** intravenous antibiotic treatment with ceftriaxone or ertapenem 1 g daily (if normal kidney function) • **REVIEW** culture results • **FOLLOW UP** with patient **(d)**	• **GIVE** supportive care (fluids, antiemetics) • **RESOLVE** admission criteria • **ADMIT** if unresolved	• **GIVE** oral antibiotics per regimen **(b)** • **REVIEW** culture results • **FOLLOW UP** with patient **(d)**

Abbreviations: **UTI**- Urinary Tract Infection; **WBC**-White Blood Cell; **hpf**-high powered field; **CT**- Computerized Tomography; **SIRS**- Systemic Inflammatory Response System; **UA**- urinalysis; **eGFR**-estimated glomerular filtration rate

ALGORITHM 4 NOTES

(a) Other diagnoses (pyelonephritis mimics)

Cholecystitis; appendicitis; urolithiasis; renal vein thrombosis; paraspinous muscle disorder; pelvic inflammatory disease (PID); lower lobe pneumonia; pancreatitis

(b) Recommended antibiotic regimen for pyelonephritis

Antibiotic	Dosage and Frequency
Use ceftriaxone PLUS one other oral antibiotic	
ceftriaxone (single dose)*	1 g intravenous or intramuscular one time
Oral antibiotics for use with ceftriaxone	
cephalexin**	500 mg orally four times per day for 10 days (uncomplicated) , 14 days (complicated)
trimethoprim (TMP)/sulfamethoxazole (SMX) (double strength)	160 mg TMP / 800 mg SMX orally two times per day for 10 days (uncomplicated) , 14 days (complicated)
ciprofloxacin	500 mg orally two times per day for 7 days (uncomplicated); 10 days (complicated)

*Use ertapenem instead of ceftriaxone (1 g intravenous or intramuscular one time) if patient has a severe cephalosporin allergy (ceftriaxone is safe for most PCN allergies) or if patient has a history of an extended-spectrum, beta-lactamase-producing organism (ESBL).

**ASSESS risk and benefit. Risk of lower efficacy beta-lactam agents (e.g. cephalexin) must be balanced with higher rates of resistance to trimethoprim / sulfamethoxazole and ciprofloxacin in common UTI pathogens.

(c) Absolute admission criteria	Relative admission criteria
ADMIT to hospital if patient has **ANY**:	**CONSIDER** hospital admission if patient has **ANY**:
• Hemodynamic instability (hypotension) • Abscess upon imaging • Obstructive uropathy • Unstable comorbidities and ≥ 2 SIRS criteria met: – Temperature > 38. 3 °C (100.1° F) or < 36 °C (96.8° F) – Heart rate > 90 beats per minute – Respiratory rate > 20 breaths per minute or $PaCO_2$ < 32 mm Hg – White blood cell (WBC) count > 12,000 / mm ^{3}, < 4,000 / mm ^{3}, or > 10 % are immature (band) forms	• Failed outpatient therapy • Inability to take oral medication • Neutropenia or severe immunosuppression with mild infection • Significant dehydration • Social / personal factors interfering with outpatient care • Mild-to-moderate immunosuppression with ≥ 2 SIRS criteria met • ≥ 2 SIRS criteria unresolved in the emergency department

(d) REVIEW culture results and FOLLOW UP with patient (24 – 48 hours)

Patient is improving	Patient is not improving	
	Results indicate that organism is susceptible to current antibiotic.	Results indicate that organism is resistant to current antibiotic
COMPLETE current antibiotic regimen regardless of reported antibiotic susceptibility. **Exception**: If patient has concomitant bacteremia adjust antibiotic based on lab results.	• **CONSIDER** pyelonephritis mimics **(a)** • **CONSIDER** CT of pelvis / abdomen if not performed previously • **REPEAT** urine culture • In the interim, **IF** cystitis mimics are ruled out: **INITIATE** change in antibiotic therapy; **TARGET** organism according to culture results	**INITIATE** change in antibiotic therapy; **TARGET** organism according to culture results

Abbreviations: **SIRS**- systemic inflammatory response System; **PCN**-Penicillin; **$PaCO_2$**-partial pressure of carbon dioxide

COMMON CULTURE CONTAMINANTS

When the following organisms appear in urine culture, they typically represent contamination from the normal flora of the skin, genitals, and rectal area:

- *Candida spp.*
- *Lactobacillus spp.*
- Diphtheroids (except *Corynebacterium urealyticum*)
- *Streptococcus viridans*
- *Micrococcus spp.*
- *Bacillus spp.*
- *Staphylococcus spp.* (except *Staphylococcus aureus* and *Staphylococcus saprophyticus*)

REFERRAL CRITERIA

Indications for a referral to urology include:

- Males <50
- Recurrent complicated UTI
- Nephrolithiasis
- Urinary retention
- Hydronephrosis
- Non-responsive to appropriate treatment
- Recurrent pyelonephritis
- Persistent hematuria following resolution of infection

UTI TREATMENT

Urine culture interpretation

Contamination

It is important to consider that contamination of the urine sample may have occurred when there are:

- Low bacterial colony counts (< 100,000 cfu/ml for clean catch, or < 100 cfu/ml for catheterized sample)
- Mixed organisms
- Common contaminant organisms (see sidebar at left)

If the patient presents with signs and symptoms of UTI and contamination is suspected, consider submitting a new urine sample.

Negative culture (no growth)

If culture is negative, consider an alternative diagnosis. If antecedent antibiotics are suspected as the cause, treat empirically if there is not a plausible alternative explanation for the symptoms. See page 3 for guidelines on the appropriate use of urine testing.

Drug-resistant organisms

Some organisms are resistant to common empiric antibiotic therapy, including *Enterococcus faecalis, E. faecium*, gram negative bacteria that produce extended-spectrum beta-lactamase (ESBL), and others. See Table 3 Resistant Pathogens: targeted antibiotic treatment (page 13) for further guidance regarding antibiotic treatment.

Staphylococcus aureus

Staphylococcus aureus is not a common cause of uncomplicated UTI. However, urinary catheterization or recent instrumentation are risk factors for the development of *S. aureus* bacteriuria. While a positive urine culture for *S. aureus* may represent a primary UTI, it is important to recognize that it could also indicate staphylococcal bacteremia with hematogenous seeding of the kidney. For this reason, ALL patients who grow *S. aureus* from urine culture should be evaluated for *S. aureus* bacteremia, (two sets of blood cultures and symptom-targeted imaging), and then assessed for endovascular infection if indicated. Consult with an infectious disease specialist.

Non-antimicrobial treatment

In a recent study, prescribing diclofenac alone for uncomplicated cystitis resulted in a delayed treatment response and increased the risk of progression to pyelonephritis compared to oral norfloxacin.[KRO] Therefore, any symptomatic management, such as ibuprofen, should be given together with antimicrobial therapy.

Note: Phenazopyridine is an option for the symptomatic management of UTI, but may or may not help relieve the patient's urinary symptoms.[ZEL] There is a risk of rare but serious adverse effects such as hemolytic anemia and renal failure.

FDA warning on fluoroquinolones for uncomplicated cystitis

According to a 2016 review by the FDA, **the risks of fluoroquinolones outweigh the benefits in treatment of uncomplicated cystitis.**[FDA] While the actual incidence of adverse reactions appears to be low, those that do occur can be disabling and potentially irreversible. Fluoroquinolone usage also carries a high risk of subsequent *C. difficile* infection. Use only for patients without alternative treatment options.

TABLE 2. Empiric therapy for urinary tract infection

Drug (normal renal function)	Dose and frequency	*E. coli* susceptibility [1]	Notes
Cystitis (first line)			
nitrofurantoin monohydrate (Macrobid)	100 mg orally two times per day for 5 days (uncomplicated); 7 days (complicated)	98 %	Recommended first-line treatment due to high efficacy and low resistance. Contraindicated for patients with CrCl < 30 ml / min. Ineffective for pyelonephritis or prostatitis.
nitrofurantoin macrocrystals (Macrodantin)	50 – 100 mg orally four times per day for 5 days (uncomplicated); 7 days (complicated)	98 %	(See above)
Cystitis (alternatives, in order of preference)			
cephalexin	500 mg orally four times per day for 7 days	89 %	Less resistance but higher relapse rate compared to other oral agents. (Not recommended as first-line treatment for prostatitis)
trimethoprim / sulfamethoxazole (double strength)	160 mg TMP / 800 mg SMX orally two times per day for 3 days (uncomplicated); 7 days (complicated)	78 %	Efficacious but high resistance rate.
ciprofloxacin	500 mg orally two times per day for 3 days (uncomplicated)*; 7 days (complicated)	87 %	Efficacious with lower resistance rate compared to other oral agents, but high risk of adverse effects. *FDA warning against use in uncomplicated cystitis (see page 11).
fosfomycin [2]	3 g orally once (uncomplicated); 3 g orally once ever 48 hours for a total of 3 doses (complicated)	Unknown	Lower cure rates compared to nitrofurantoin; [HUT] recommended for patients with history of ESBL or VRE organisms or significant allergies. [2] Ineffective orally for pyelonephritis.
Pyelonephritis (Use ceftriaxone PLUS one oral antibiotic)		Use patient's previous cultures to determine most appropriate oral therapy.	
ceftriaxone (single dose)	1 g intravenously or intramuscularly one time	95 %	If patient has a severe cephalosporin allergy (ceftriaxone is safe for most PCN allergies) or if patient has a history of an extended-spectrum, beta-lactamase-producing organism (ESBL) use ertapenem.
ertapenem	1 g intravenously or intramuscularly one time		Use only if ceftriaxone is not recommended. (See above)
Oral antibiotics for use with ceftriaxone			
cephalexin	500 mg orally four times per day for 10 days (uncomplicated) ; 14 days (complicated)	89 %	Less resistance but higher relapse rate compared to other oral agents.
trimethoprim (TMP) / sulfamethoxazole (SMX) (double strength)	160 mg TMP / 800 mg SMX orally two times per day for 10 days (uncomplicated) ; 14 days (complicated)	78 %	Efficacious but high resistance rate.
ciprofloxacin	500 mg orally two times per day for 7 days (uncomplicated); 10 days (complicated)	87 %	Efficacious with lower resistance rate compared to other oral agents, but high risk of adverse effects

1. Salt Lake Valley outpatient 2017 antibiogram (all sites). Link to: https://m.intermountain.net/Pharmacy/AntimicrobialStewardship/Pages/Tracking-and-Reporting.aspx for current antibiogram (Intermountain employee resource only)
2. Fosfomycin is a branded product and some insurance providers do not cover it. Pharmacies may have to order. For detailed information on the drug see Table 3 / note 3 (page 13).

Nitrofurantoin and renal impairment

Creatinine clearance (CrCl) less than 60 ml / min is listed in the package insert as a contraindication for nitrofurantoin due to increased risk of toxicity from impaired excretion although serious side effects are rare with a 5- to 7-day course as recommended for cystitis. [FEL, HOL, OPL] Retrospective studies suggest that cure rates for cystitis range from 70 – 79 % in patients with CrCl less than 60 ml / min. [BAI, GEE, ING] Current data support the following recommended practices:

- All patients receiving nitrofurantoin (regardless of renal function) should be advised to monitor for adverse effects, such as pulmonary, hepatic, or neuropathic symptoms.
- Nitrofurantoin is first-line for cystitis in patients with CrCl > 60 ml / min.
- Consider use if CrCl 30 – 60 ml / min.
- Avoid use if CrCl < 30 ml / min.

TABLE 3. Resistant Pathogens: Targeted antibiotic treatment.[1]

Urine culture result	First-line treatment, if susceptible	Second-line treatment, for resistant pathogens, if susceptible	Third-line treatment, if susceptible [2]
Yeast	fluconazole 200 mg orally daily for 7–14 days	N/A – limited options are available; for resistant species, contact an infectious disease specialist. Consider evaluation for fungal ball in persistently symptomatic patients.	
Enterococcus faecalis and *E faecium*	amoxicillin 500–1,000 mg orally three times per day for 7–14 days	nitrofurantoin 100 mg orally two times per day for 7 days (cystitis only) fosfomycin[3] 3 g orally once (cystitis only)	linezolid 600 mg orally two times per day for 7–14 days
Gram negative, extended spectrum beta-lactamase (ESBL)	nitrofurantoin 100 mg orally twice per day for 7 days (cystitis only) OR trimethoprim/sulfamethoxazole DS (160 mg TMP/800 mg SMX) orally two times per day for 7–14 days OR ciprofloxacin 500 mg orally two times per day for 3–10 days	fosfomycin[3] 3 g orally once (cystitis only)	ertapenem 1 g intravenously daily for 7–14 days

1. Check patient allergies and relevant contraindications prior to prescribing. Move to the next-line treatment option if the first- or second-line options are not appropriate.
2. If the organism is not susceptible to any of the listed agents, contact your antimicrobial stewardship pharmacist for guidance.
3. **For complicated cystitis:** If renal function > 50 ml/min, give 3 g every 48 hours for 6 days (3 total doses). If renal function is 10–50 ml/min, give 3 g every 72 hours for 9 days (a total of 3 doses). **Spectrum of activity of fosfomycin:** Fosfomycin is an antibiotic with a unique mechanism of action blocking cell wall synthesis via enolpyruvate transferase (MurA) inhibition. It is indicated only for uncomplicated cystitis, but has been used off-label for complicated cystitis. It is not effective against pyelonephritis. Susceptibility to fosfomycin is not routinely performed and must be requested from the lab. Its activity against *Escherichia coli, Proteus mirabilis,* and *Citrobacter spp.* is high enough that empiric therapy without known susceptibilities is appropriate for uncomplicated cystitis, given the long turnaround time for susceptibilities. Request susceptibilities if treating complicated or recurrent cystitis. Fosfomycin has limited-to-no activity against *Morganella morganii, Pseudomonas aeruginosa* and *Acinetobacter baumannii.* [FRI]

TABLE 4. Recommended prophylaxis for women with recurrent UTI[DAS] (see algorithm 2 note (a) on page 6)

Prophylactic agent	Recommended dose	Comments
nitrofurantoin	100 mg orally daily or once within 2 hours of coitus	Base antibiotic choice on: • Antimicrobial susceptibilitiers on previous urine cultures • Local antibiogram (Intermountain antibiograms) • Allergy history **Risks of prolonged antibiotic therapy include** *C. difficile* infection, antimicrobial resistance, and adverse drug events. Nitrofurantoin may be associated with higher rates of adverse effects. [PRI] If sexual intercourse is the precipitating factor, postcoital prophylaxis is likely to be beneficial.
trimethoprim	100 mg orally daily or once within 2 hours of coitus	
trimethoprim (TMP)/sulfamethoxazole (SMX) (single strength)	80 mg TMP/400 mg SMX orally three times weekly or once within 2 hours of coitus	
ciprofloxacin	125 mg orally daily or once within 2 hours of coitus	
fosfomycin	3 g orally once every 10 days	
cephalexin	250 mg orally once per day or once within 2 hours of coitus	
topical estrogen	Various products available; see product information for dosing	Reduced symptomatic UTI episodes in a small trial; however, 28 % of patients discontinued treatment due to localized vaginal irritation. [RAZ]
estradiol vaginal ring (Estring)	Insert for 12 weeks, 3 times (total of 36 weeks)	Reduced the 36-week incidence of symptomatic UTI from 80 % to 51 %; however, some experienced discomfort and withdrew from the study. [ERI] May be expensive.
methenamine hippurate	1000 mg orally twice per day	Efficacy demonstrated in women undergoing urologic surgeries treated for ≤ 7 days. Not effective in those with neuropathic bladder. [LEE] Note: If choosing mandelate, prescribe 1000 mg PO four times per day.

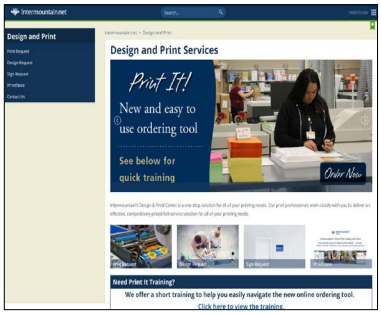
NOTE: **Prescribe antimicrobial UTI prophylaxis for women with recurrent UTI only after carefully assessing the risks and benefits. For sexually active women, limiting spermicide use, postcoital voiding, and cranberry products may offer some benefit, but data supporting clinical efficacy are limited.**

LOCATING PATIENT EDUCATION MATERIALS

Intermountain education materials are designed to support your efforts to educate and engage patients and families. They complement and reinforce interventions by providing a means for patients to reflect and learn in another mode and at their own pace. To access these materials:

- **In iCentra,** search for Intermountain items in the patient education module.
- **Log in to** Intermountainphysician.org**,** and search for the patient education library under A–Z. Then, search item number and title in the appropriate area.

- **Use** Print It! at Intermountain's Design and Print Center for one-stop access and ordering for Intermountain-approved education, such as fact sheets, booklets, and trackers.



CPM DEVELOPMENT TEAM

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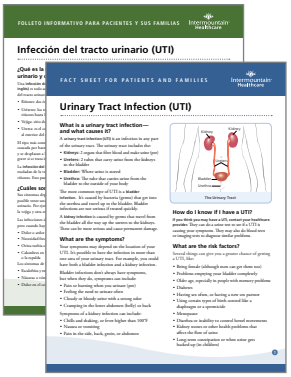
RESOURCES

Patient resources

Intermountain clinicians and the Patient and the Provider Publications team have developed patient education materials to directly support treatment recommendations in this care process model. Education for patients and families increases patient compliance with a treatment plan.

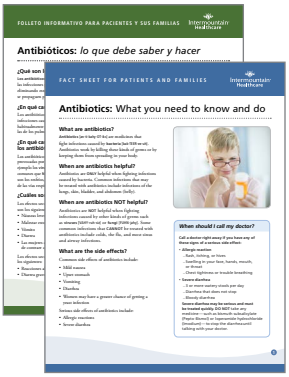
Intermountain-approved patient education materials

The following Intermountain-approved patient education resources can be accessed and ordered online at minimal cost. **See access and ordering information at left.**



Urinary Tract Infection

Available in English and Spanish

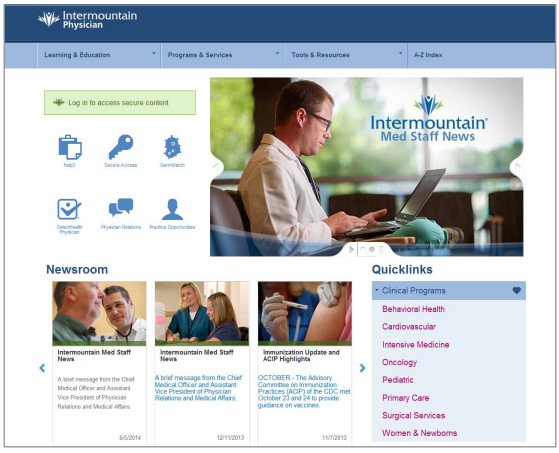


Antibiotics: What you need to know and do

Available in English and Spanish

Provider resources

To find all CPMs and Best Practice Flash Cards published by Intermountain, clinicians can go to intermountainphysician.org/tools and resources



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BAI Bains A, Buna D, Hoag NA. A retrospective review assessing the efficacy and safety of nitrofurantoin in renal impairment. *Can Pharm J.* 2009;142(5):248-252.

CAI1 Cai T, Mazzoli S, Mondaini N, et al. The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: To treat or not to treat? *Clin Infect Dis.* 2012 Sep;55(6):771-777.

CAI2 Cai T, Nesi G, Mazzoli S, et al. Asymptomatic bacteriuria treatment is associated with a higher prevalence of antibiotic resistant strains in women with urinary tract infections. *Clin Infect Dis.* 2015 Dec 1;61(11):1655-1661.

DAS Dason S, Dason JT, Kapoor A. Guidelines for the diagnosis and management of recurrent urinary tract infection in women. *Can Urol Assoc J* 2011;5(5):316-322.

DIN Dingle KE, Didelot X, Quan TP, et al. Effects of control interventions on *Clostridium difficile* in England: an observational study. *Lancet Infect Dis* 2017;17(4):411-421.

ERI Eriksen B. A randomized, open, parallel-group study on the preventive effect of an estradiol-releasing vaginal ring (Estring) on recurrent urinary tract infections in postmenopausal women. *Am J Obstet Gynecol.* 1999;180(5):1072-1079.

FDA Food and Drug Administration. FDA drug safety communication: FDA updates warnings for oral and injectable fluoroquinolone antibiotics due to disabling side effects. https://www.fda.gov/Drugs/DrugSafety/ucm511530.htm. Accessed March 5, 2019.

FEL Felts JH, Hayes DM, Gergen JA, Toole JF. Neural, hematologic and bacteriologic effects of nitrofurantoin in renal insufficiency. *Am J Med.* 1971;51(3):331-339.

FLO Flokas ME, Andreatos N, Alevizakos M, Kalbasi A, Onur P, Mylonakis E. Inappropriate management of asymptomatic patients with positive urine cultures: A systematic review and meta-analysis. *Open Forum Infect Dis.* 2017;4(4):ofx207.

FOX Foxman B, Barlow R, D'Arcy H, Gillespie B, Sobel JD. Urinary tract infection: Self-reported incidence and associated costs. *Ann Epidemiol.* 2000;10(8):509-515.

FRI Frimodt-Moller N. Fosfomycin. In: Grayson ML, ed. Kucers' *The Use of Antibiotics.* Roca Raton, FL: CRC Press; 2018. p. 1392-1406.

GEE Geerts AFJ, Eppenga WL, Heerdink R, et al. Ineffectiveness and adverse events of nitrofurantoin in women with urinary tract infection and renal impairment in primary care. *Eur J Clin Pharmacol.* 2013;69(9):1701-1707.

GUP Gupta K, Hooton TM, Naber KG, et al. 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. *Clin Infect Dis.* 2011;52(5):e103-20.

HOL Holmberg L, Boman G, Böttiger LE, et al. Adverse reactions to nitrofurantoin. Analysis of 921 reports. *Am J Med.* 1980;69(5): 733-738.

HUT Huttner A, Kowalczyk A, Turjeman A, et al. Effect of 5-day nitrofurantoin vs single-dose fosfomycin on clinical resolution of uncomplicated lower urinary tract infection in women. *JAMA.* 2018;319(17):1781.

ING Ingalsbe ML, Wojciechowski AL, Smith KA, Mergenhagen KA. Effectiveness and safety of nitrofurantoin in outpatient male veterans. *Ther Adv Urol.* 2015 Aug;7(4):186-193.

KRO Kronenberg A, Butikofer L, Odutayo A, et al. Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting: randomized, double-blind trial. *BMJ* 2017;359:j4784.

LEE Lee BSB, Bhuta T, Simpson JM, Craig JC. Methenamine hippurate for preventing urinary tract infections. *Cochrane Database Syst Rev.* 2012;10:CD003265.

NIC Nicolle LE, Bradley S, Colgan R, et al. Infectious Disease Society of America guidelines for the diagnosis and treatment of asymptomatic bacteriuria in adults. *Clin Infect Dis* 2005 40(5):643-654

NIC2 Nicolle LE. Consequences of asymptomatic bacteriuria in the elderly. *Int J Antimicrob Agents* 1994. June 4;4(2) 107-110.

OPL Oplinger M, Andrews CO. Nitrofurantoin contraindication in patients with a creatinine clearance below 60 mL/min: Looking for the evidence. *Ann Pharmacother.* 2013;47(1):106-111.

PRI Price JR, Guran LA, Gregory T, McDonagh MS. Nitrofurantoin vs other prophylactic agents in reducing recurrent urinary tract infections in adult women: a systematic review and meta-analysis. *Am J Obstet Gyn* 2016;548-560.

RAZ Raz R, Stamm WE. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. *N Engl J Med* 1993;329:753-756.

RUI Rui P, Kang K. National Hospital Ambulatory Medical Care Survey: 2014. Emergency Department Summary Tables. https://www.cdc.gov/nchs/data/nhamcs/web_tables/2014_ed_web_tables.pdf. Accessed March 5, 2019.

SIM Simmering JE, Tang F, Cavanaugh JE, Polgreen LA, Polgreen PM. The increase in hospitalizations for urinary tract infections and the associated costs in the United States, 1998-2011. *Open Forum Infect Dis.* 2017;4(1):ofw281.

WIS Wise GJ, Schlegel PN. Sterile pyuria. *N Engl J Med* 2015;372(11):1048-1054.

ZEL Zelenitsky SA, Zhanel GG. Phenazopyridine in urinary tract infections. *Ann Pharmacother.* 1996 Jul-Aug;30(7-8):866-868.

This CPM presents a model of best care based on the best available scientific evidence at the time of publication. It is not a prescription for every physician or every patient, nor does it replace clinical judgment. All statements, protocols, and recommendations herein are viewed as transitory and iterative. Although physicians are encouraged to follow the CPM to help focus on and measure quality, deviations are a means for discovering improvements in patient care and expanding the knowledge base. Send feedback to Stephanie Gelman, MD, Infectious Disease, Intermountain Healthcare (Stephanie.Gelman@imail.org).

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