



Brigham and Women's Hospital
Founding Member, Mass General Brigham

Urinary Tract Infections for Internal Medicine

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Conflicts

None (commercial)

Editorial:

IDSA UTI guidelines expert panel
UTI topic editor for DynaMed



Simple Cystitis: Principals in diagnosis and management

- UTI syndromic definitions
- When to test and what tests to order
- Selecting empiric and definitive therapy

OBJECTIVES

Challenges in UTI management

- Treating multi-drug-resistant organisms (MDRO)
- Treating cystitis and prostatitis in men
- Managing complicated and bacteremic UTI syndromes
- Approach to asymptomatic bacteriuria and catheter-associated UTI
- Evidence-based strategies in management of recurrent UTI



Case one – outpatient case

47-year-old woman, BMI 34.2, prediabetes (A1C 5.9), not pregnant, no other significant medical history, on no medications, calls to report a 3-day history of dysuria and urinary urgency. Prior similar episodes ~once per year.

No fever, nausea, vomiting, flank pain

No recent hospitalization or antibiotics except malaria prophylaxis for a recent trip.

Simple cystitis
AKA uncomplicated UTI

Classic lower tract symptoms
(dysuria, urgency, frequency)

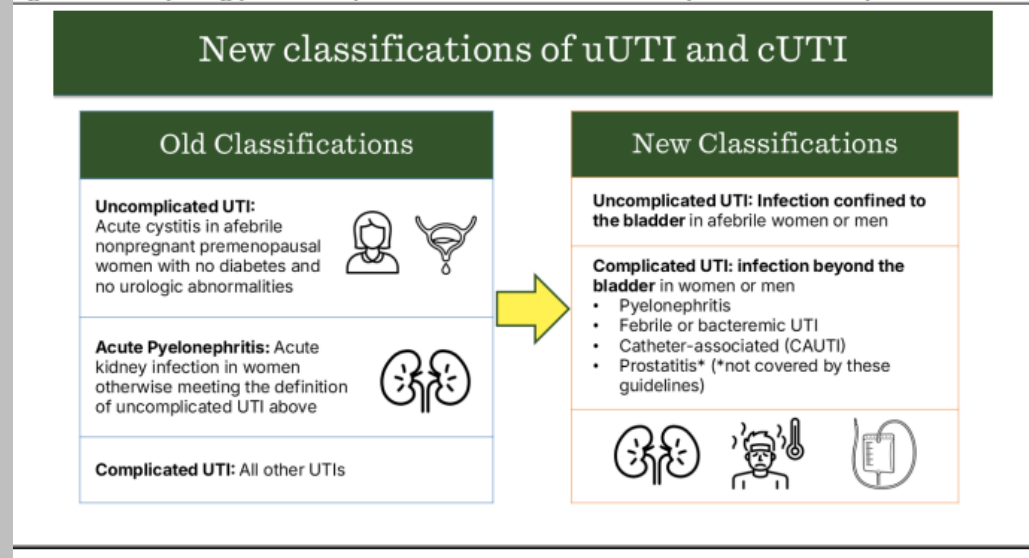
No upper tract symptoms or fever

Updated UTI Classification

Complicated UTI Guidelines

<https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/>

Figure 1.0 Comparing prior and updated classifications of uncomplicated and complicated UTI



IDSA PRACTICE GUIDELINES • CURRENT

Complicated Urinary Tract Infections (cUTI): Clinical Guidelines for Treatment and Management

 Published July 17, 2025

Evolving new Definitions of uUTI and cUTI

TRADITIONAL DEFINITION	EVOLVING DEFINITION
Uncomplicated UTI Acute cystitis in a healthy, non-pregnant young (premenopausal?) woman without diabetes or urologic abnormalities	Uncomplicated UTI Simple cystitis in men and women (assumes no fever on urinary instrumentation)
Acute Uncomplicated Pyelonephritis	Complicated UTI Everything else. <u>Examples:</u> - Pyelonephritis - Prostatitis - Fever or systemic toxicity - Bacteremia or sepsis - Obstruction
Complicated UTI Everything else (postmenopausal women, men, complicated UTI syndromes)	

Clinically stable, outpatient, premenopausal, with suspected symptomatic cystitis

Diagnostic and Management Decisions



**47F with simple
cystitis**

- Order tests or symptom-based empiric therapy?
- When obtaining tests:
 - What tests to order?
 - How to interpret results?
- When treating
 - Immediate versus delayed or deferred therapy?
 - Adequate empiric or culture based antibiotic choice and duration

Natural History of Untreated Simple Cystitis (young, normal GU tract)

- Episodes resolve at 2–4 weeks in ~40-50%
 - may account for some of response rate reported in antibiotic trials
- Majority (~70%) clear bacteriuria eventually (weeks to months)
- Progression to pyelonephritis or renal failure rare, if normal GU tract anatomy and function

Wigton, *et al.*, J Gen Int Med ,1999

Hooton, Infect Dis Clin North Am 2003, Hooton, CID, 2004, Christiaens, Br J Gen Pract. 2002, Falagas, J of Infection, 2009

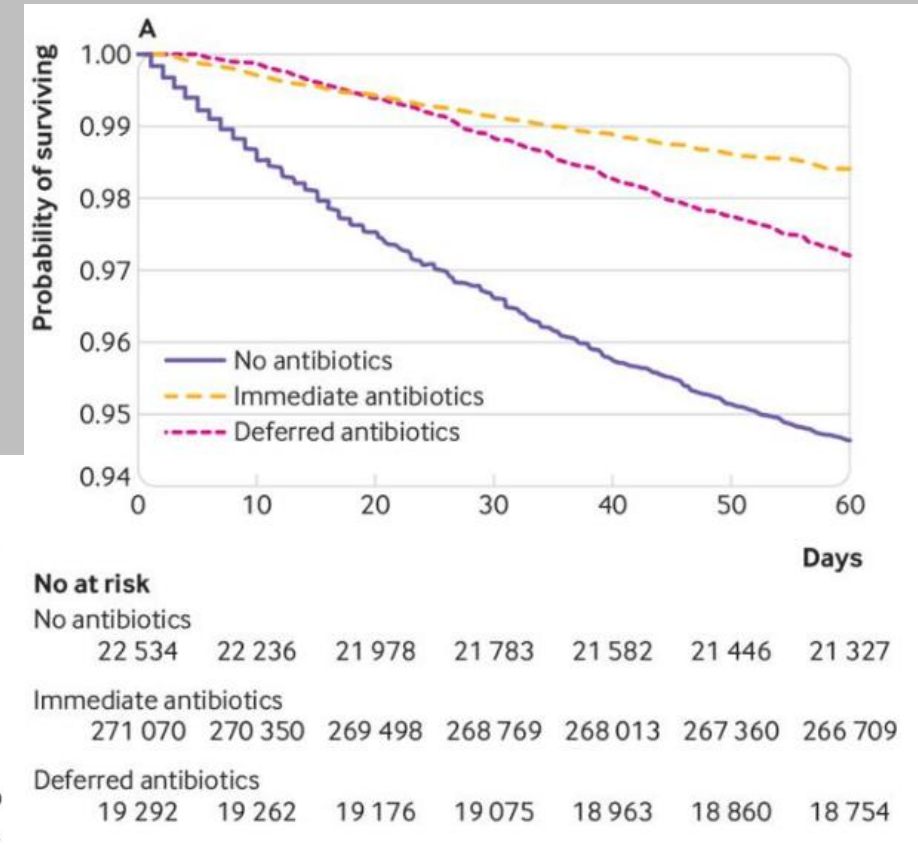
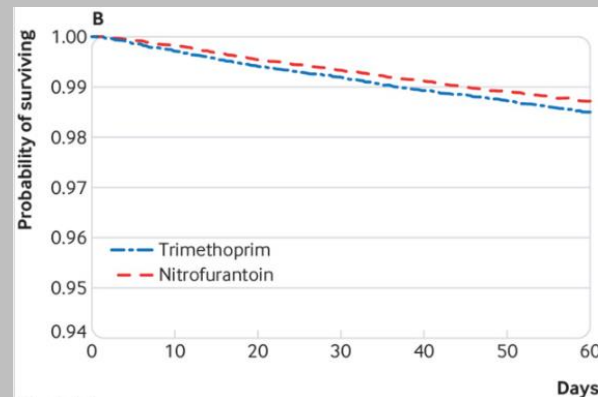
Table 3. Symptomatic and bacteriological effect of nitrofurantoin versus placebo
CFU/ml or more on inclusion, n = 56).

	Nitrofurantoin (Day 1, n = 29)	Placebo (Day 1, n = 27)
Day 3 — bacteriology: (nitrofurantoin n = 26, placebo n = 25; symptoms: nitrofurantoin n = 25, placebo n = 25 ^c		
Bacteriological cure	21 (81)	5 (20)
Symptomatic cure or improvement	20 (80)	11 (44)
Day 7 — bacteriology: (nitrofurantoin n = 23, placebo n = 22; symptoms: nitrofurantoin n = 24, placebo n = 24		
Bacteriological cure	17 (74)	9 (41)
Symptomatic cure or improvement	21 (88)	13 (54)

Impact of immediate versus Deferred antibiotics may be age Dependent

No antibiotics vs deferred or immediate ABX for symptomatic UTI in the elderly

- UK NHS observational study
- Primary care and adults >65y
- no or deferred versus immediate antibiotics for symptomatic UTI:
 - increased risk of bloodstream infection
 - Increase all-cause mortality



Testing for Simple Cystitis in Women with simple (outpatient) cystitis

PROS

Diagnostic accuracy: sensitivity if only 1 symptom ~50% (dysuria a bit higher)

A negative urinalysis can exclude a UTI

Resistance on the rise – tailor antibiotic to organism

Societal / environmental and personal costs of antibiotic overuse

Testing for Simple Cystitis in Women with simple (outpatient) cystitis

CONS

Sensitivity of symptom-triad for cystitis (healthy non-pregnant cis-woman) ~96%

Causative organisms predictable

Most respond clinically to a standard empiric antibiotic course

Cost of visit and tests

- Several phone triage studies show it's a cost-effective approach ¹⁻²

PROS

Diagnostic accuracy: sensitivity if only 1 symptom ~50% (dysuria a bit higher)

A negative urinalysis can exclude a UTI

Resistance in the community on the rise – tailor antibiotic to organism

Societal / environmental and personal costs of antibiotic overuse

Non-culture Diagnostic Options Looking for evidence of inflammation Pyuria or Leukocyte Esterase



≥ 10 WBC/mL in midstream urine (≥ 5 in a sediment of spun urine)



Pyuria present in nearly all cystitis . Pyuria absent: UTI unlikely (unless neutropenic or obstructed)

Sensitivity high: > 90%



Pyuria without acute cystitis is common

Specificity low: ~70%



Dipstick leukocyte esterase – rapid screening test for pyuria

Sensitivity (for detecting >10WBC/mL): 75-96%

Specificity for pyuria 94-98%

Non-Culture Diagnostic Options

Looking for evidence of Bacteriuria (symptomatic and asymptomatic)

Nitrite (positive helpful, negative doesn't rule out)

- Sensitivity poor: ~20-50%
 - Colony counts (<100,000)
 - Organism dependent: non-producers of nitrite: *Enterococci*, *S. saprophyticus*, *Acinetobacter*
 - Bladder dwell time (high frequency = less time to produce nitrate) dilute urine
- Specificity for bacteriuria high: ~95% (GOOD)
 - Strong rule in for presence of nitrite producing bacteria

Kuijper, *et al.* Eur. J. Clin. Micro Infect Dis 22; 228 (2003)

Urinalysis, Positive and Negative Predictive Values for positive culture (by age group)

Table 1

Diagnostic performance of test strips and sediment microscopy in all subjects and different age groups.

Test	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
<i>LE</i>				
All	71.0 (67.6–74.2)	83.6 (83.2–84.2)	9.2 (8.5–10.0)	99.3 (99.1–99.4)
0–1	63.7 (53.6–73.0)	68.8 (67.5–70.0)	4.0 (3.1–5.0)	98.9 (98.5–99.3)
2–17	65.7 (58.7–72.2)	88.6 (88.1–89.0)	5.3 (4.4–6.3)	99.6 (99.5–99.7)
18–69	77.0 (71.3–82.0)	80.8 (79.8–81.8)	14.6 (12.8–16.6)	98.8 (98.5–99.1)
≥ 70	72.4 (65.6–78.5)	66.0 (62.0–69.8)	42.1 (36.8–47.5)	87.5 (84.0–90.4)
<i>Nitrite</i>				
All	17.7 (15.0–20.6)	90.1 (89.7–90.4)	4.0 (3.4–4.7)	97.9 (97.7–98.2)
0–1	6.9 (2.8–13.6)	90.1 (89.2–90.9)	1.4 (0.6–2.8)	93.0 (97.5–98.3)
2–17	21.9 (16.4–28.3)	97.3 (97.1–97.5)	7.4 (5.4–9.8)	99.2 (99.1–99.3)
18–69	19.9 (15.2–25.4)	68.1 (66.9–69.2)	2.6 (1.9–3.4)	95.2 (94.5–95.8)
≥ 70	16.1 (11.3–21.9)	60.1 (56.0–64.1)	12.1 (8.4–16.7)	67.7 (63.5–71.7)
<i>Bacteriuria</i>				
All	78.8 (75.7–81.6)	97.8 (97.6–97.9)	45.4 (42.7–48.1)	99.5 (99.4–99.6)
0–1	43.1 (33.4–53.3)	98.0 (97.5–98.3)	30.1 (22.8–38.3)	93.8 (98.5–99.1)
2–17	72.6 (65.9–78.7)	98.3 (98.2–98.5)	29.8 (25.8–34.1)	99.7 (99.6–99.8)
18–69	91.8 (87.7–94.9)	97.0 (96.5–97.4)	56.4 (51.4–61.2)	99.6 (99.4–99.8)
≥ 70	86.4 (80.9–90.9)	84.4 (81.2–87.2)	65.4 (59.3–71.1)	94.8 (92.5–96.5)
<i>WBC</i>				
All	68.2 (64.8–71.5)	87.8 (87.5–88.2)	11.7 (10.7–12.6)	99.2 (99.0–99.3)
0–1	49.0 (39.0–59.1)	81.9 (80.9–83.0)	5.2 (3.9–6.8)	98.8 (98.4–99.1)
2–17	41.8 (34.9–48.9)	90.3 (89.8–90.7)	4.0 (3.2–4.9)	99.4 (99.3–99.5)
18–69	84.0 (78.9–88.3)	85.6 (84.7–86.5)	20.0 (17.6–22.5)	99.2 (98.9–99.4)
≥ 70	84.4 (78.6–89.2)	76.0 (72.3–79.4)	54.6 (48.8–60.2)	93.5 (90.1–95.5)

Urinalysis, Positive and Negative Predictive Values for positive culture (by age group)

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≥ 70	84.4 (78.6–89.2)	76.0 (72.3–79.4)	54.6 (48.8–60.2)	93.5 (90.1–95.5)

Poor

Excellent

urinalysis with reflex to culture (UARC) algorithm

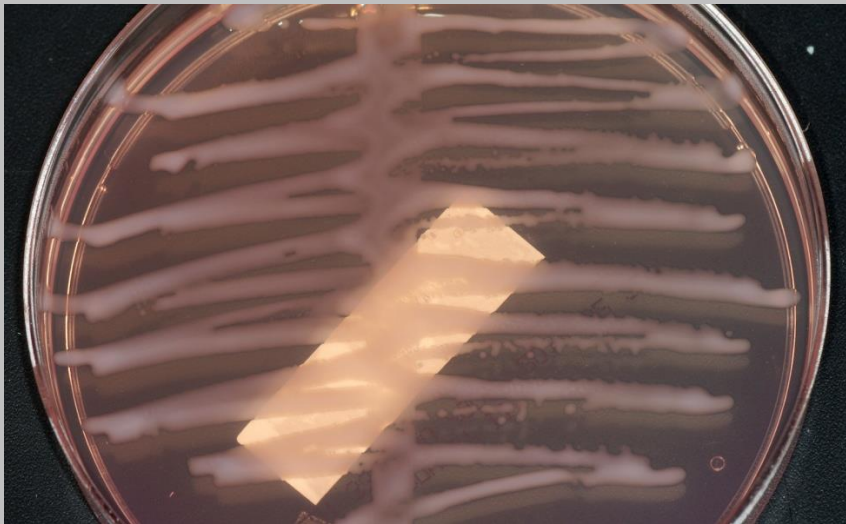
The Infectious Diseases Society of America (IDSA) and American Society for Microbiology (ASM) 2024 guide to utilization of Microbiology lab, 2024 <https://doi.org/10.1093/cid/ciae104>

Endorsed the concept of urinalysis with reflex to culture (UARC) in most adult patient populations

Exceptions: those with indication to treat asymptomatic Bacteriuria, neutropenia, obstructions, other clinician based decision

Urine Culture for Diagnostics

- Confirms the presence of significant bacteriuria
 - typically, a single uropathogen at diagnostic CFU/mL threshold
- Identifies organism
- Provides susceptibility testing to guide adequate therapy



Should $> 100,000$ (10^5) CFU/ mL be the threshold to diagnosed cystitis?

- Midstream and catheter urine compared in 18–49-year-old women with cystitis symptoms (Hooton et al. NEJM 2013)
- 70% had bacteriuria on catheterized samples
- For *E coli* 30–50% of those with catheterized bacteremia had colony counts of 10^2 to 10^4 CFU/mL on voided midstream urine — below the traditional $\geq 10^5$ CFU/mL threshold
- Enterococci and group B streptococci in midstream urine were not predictive of bladder infection at any colony count
- Reasons for “symptomatic abacteriuria”: urethritis (GC/ chlamdia /mycoplasma / trichomonas / other), genital herpes vaginitis, non-infectious process

Multiplex PCR in UTI Diagnosis

- Amplifies pathogen DNA + genotypic antibiotic resistance genes (ARGs) directly from urine:
 - results in < 24 h vs. 48–72 h for culture
- 15–30+ organisms including fastidious organisms
- Available only as laboratory-developed tests (LDTs) (no FDA approved panels)
- Many Limitations
 - Semi-quantitative
 - Oversensitive (normal flora, nonviable organisms)
 - Uropathogen versus normal flora, polymicrobial more likely
 - Concordance with phenotypic susceptibility limited (~ 60%)
- ASM/IDSA GL recommend against routine use (no regulatory oversight, risk of overtreatment, need more evidence)
- Interpretation with caution especially in critically ill in need of broad therapy

IDSA / International Guidelines (2010)

Treatment of Acute Uncomplicated Cystitis

Recommended

- Nitrofurantoin macrocrystals 100mg twice daily x 5 days
- TMP/SMX DS twice daily x 3 days
 - if *E. coli*'s resistance rates <20%
- Empiric Fosfomycin 3 gm x1
 - Best for *E coli* or *E fecalis*
- (Pivmecillinam 400 mg twice daily x 5 days)

Not recommended (2nd line)

- Fluoroquinolones x 3 days
- β -lactams x 5-7d
 - Cephalexin, amox (clav if needed), cefpodoxime)

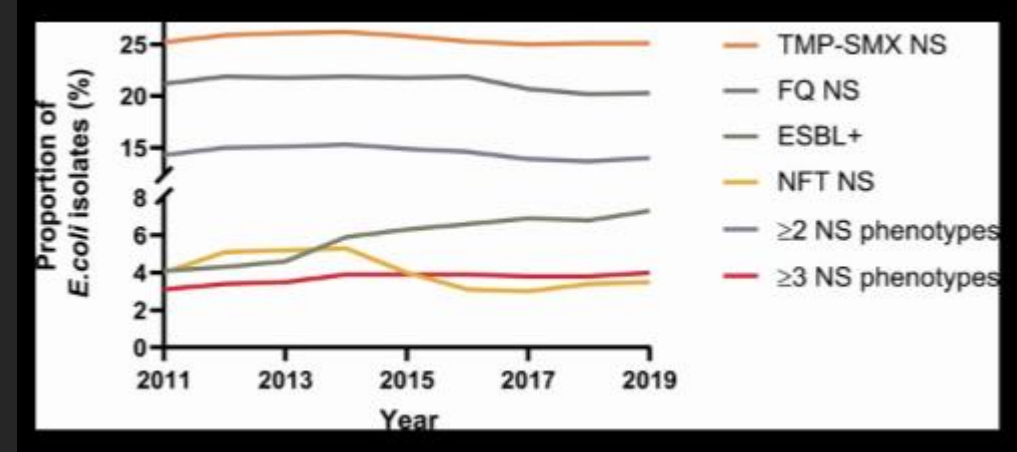
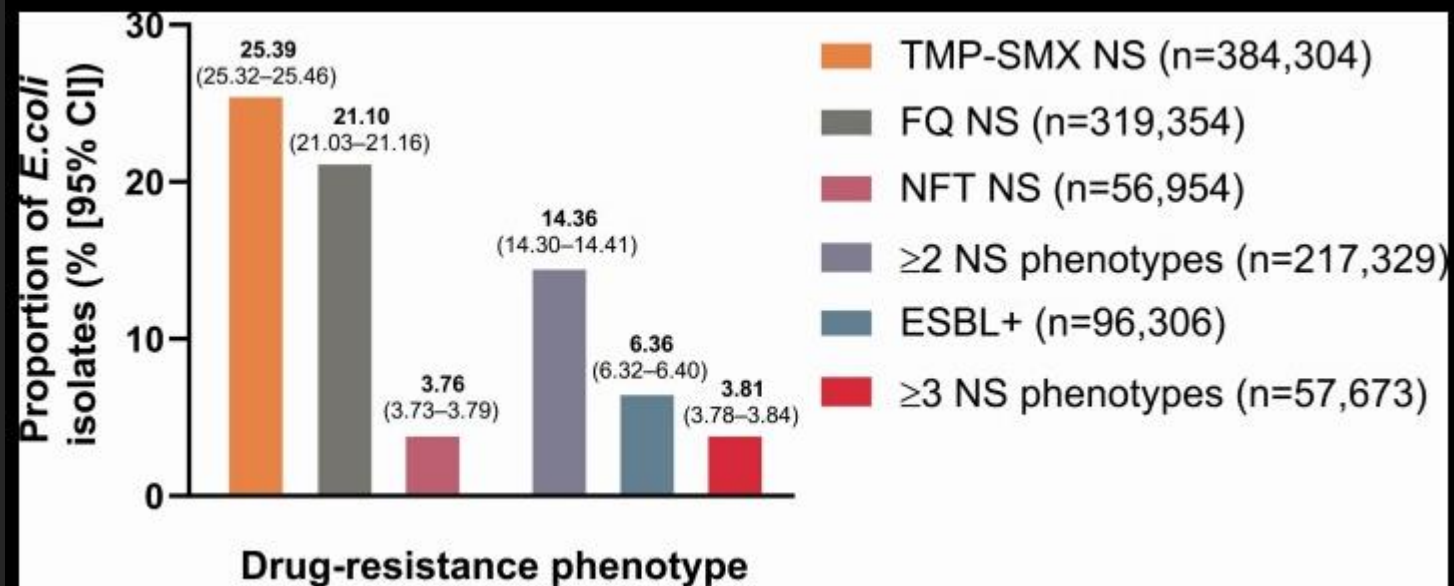
Resistance higher (not just to TMP/SXT)

Efficacy in some recent studies lower

Nitrofurantoin and fosfomycin NOT RECOMMENDED if early pyelonephritis suspected

- When diagnosis in question – urinalysis with reflex culture
- When resistance a concern – culture (may start empiric antibiotic while waiting)

1,513,882 *E. coli* isolates, from US female outpatients, 2011-19



48F, MS, takes ocrelizumab (B cell depleting agent), neurogenic bladder, CIC. Has h/o recurrent UTI. Childhood allergy to amoxicillin (rash). Admitted for meropenem therapy for MDR *E coli* cystitis

SX: malaise, dysuria, “bladder spasms”, leg spasms, low back discomfort, no flank pain, no nausea or systemic toxicity.

UA: >182W, nitrites.

Cx: “ESBL” producing *E. coli*.

Susceptible: amox/clav, pip/tazo, meropenem, imipenem.

Resistant: trimethoprim/sulfa, FQ, aminoglycosides.

48F, MS, takes ocrelizumab (B cell depleting agent), neurogenic bladder. Has h/o recurrent UTI. Childhood allergy to amoxicillin (rash). Admitted for meropenem therapy for MDR *E. coli* afebrile cystitis.

SX: malaise, dysuria, “bladder spasms”, leg spasms, low back discomfort, no flank pain, no nausea or systemic toxicity.

UA: >182W, nitrites.

Cx: “ESBL” producing *E. coli*.

Susceptible: amox/clav, pip/tazo, meropenem, imipenem.

Resistant: trimethoprim/sulfa, FQ, gentamicin.

Definition: afebrile, cystitis with MDR organism in a patient with abnormal bladder function

48F, MS, takes ocrelizumab (B cell depleting agent), neurogenic bladder, CIC. Has h/o recurrent UTI. Childhood allergy to amoxicillin (rash). Admitted for meropenem therapy for MDR *E. coli* cystitis

SX: malaise, dysuria, “bladder spasms”, leg spasms, low back discomfort, no flank pain, no nausea or systemic toxicity.

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Susceptible: amox/clav, pip/tazo, meropenem, imipenem

Resistant: trimethoprim/sulfa, FQ, gentamicin

Which of the following are adequate?

- A. Oral fosfomycin is adequate if susceptible (yes, cystitis)
- B. Oral nitrofurantoin adequate if susceptible (yes, cystitis)
- C. Amox/clav adequate after test dose or skin test (yes)
- D. Once daily IV ertapenem
- E. All of the above

UTI with Multidrug Resistant Organisms (MDRO)

- MDRO: resistance to at least 1 antibiotic in or ≥ 3 classes
 - Standard international definition: at least one antibiotic in 3 or more antibiotic classes; also used for NHSN (National Healthsafety Net)
 - CDC definition (≥ 1 class) often used for infection control hospital context (e.g. for MRSA/VRE) and correct answer on HealthStream at MGB
- Risk factors for MDRO
 - Urinary MDRO in the past
 - Recent stay at healthcare facility (hospital, LTAC)
 - Travel to areas with high rate of resistance
- Rates of both healthcare and community associated MDRO UTI on the rise:
 - Since early 2000's steady increase in community MDRO, especially ESBL-producing GNR in UTI
 - Many retain susceptibility to fosfomycin and nitrofurantoin

MDRO UTI

When can
oral agents
be used?

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Nitrofurantoin rapid

- Sole indication: simple cystitis
- IDSA guidelines dose 100 mg macrocrystals PO BID
- Broad and resistance rates remain low (1-3% *E.coli*, not for *Pseudomonas*)
- Low *C. diff* risk
- Barriers/limitations to use:
 - Tissue concentrations low: not for systemic/deep tissue infection (blood stream, kidney, prostate)
 - GFR: PDR: do not use at CrCl <60 ml/min (insufficient renal excretion, toxicity) BUT:
 - Short courses likely safe and effective in the elderly and with lower GFR (<30mL/Mim rather than <60 mL/min)
 - Side Effects
 - More common in elderly and with renal impairment
 - common: nausea (8%) & headache (6%)
 - less common but more serious: hepatitis, neuropathy
 - Rare, idiosyncratic, but serious: interstitial lung disease / pulmonary fibrosis

Fosfomycin rapid

Inhibits bacterial cell wall synthesis

- FDA approval and lab testing: *E. coli* and *E. faecalis* uncomplicated cystitis

Susceptibility in urinary isolates (overestimated?):

- ~90.6% of *Enterococci*, 90-94% of *Enterobacteriaceae*
- Resistance higher in experienced patients
- Usefull mostly for *E coli* and *E fecalis*

Response rates 3g single dose: 78%-83% (58% in a recent study)

Complicated cystitis: may repeat dose every 24-72 hours x 2-4 doses (or more)

Barriers/limitations to use:

- Susceptibility not routinely tested for
- Testing guidelines/approval in USA limited to *E coli* and *Enterococcus*
- \$\$\$, prior auth



Fosfomycin Key Pathogen Susceptibility Rates

studies published after 2020

Organism	Susceptibility to Oral Fosfomycin (%)	Notes (ESBL, MDR, etc.)	References
E. coli (all)	95–99	High activity, including ESBL	[1-5]
E. coli (ESBL+)	90–96	Slightly lower than non-ESBL	[1, 3-4, 6]
K. pneumoniae (all)	36–39	Low activity, not recommended	[4-5, 7]
Enterococcus faecalis	88–98	High activity	[1, 4-5, 8]
S. aureus	98	High activity	[1, 4, 8]
Proteus mirabilis	83	Moderate activity	[5]
Other Enterobacterales	<50	Variable, generally low	[1, 4, 7]

1. Karlowsky, J Antimicrob Chem 2022;77(11):3035 2. Tutone, Int J Antimicrob Agents 2022;59(5) 1065 3. Cai, Int Antimicrob Agents. 2023;62(5) 1069 4. Dombach JL, Microb Spec. 2025;13(3) 5. Massip C, J Antimicrob Chemo. 2024;79(10):2645 6. Goer A, J Clin Microb. 2022;60(7) 7 _Lima RC, European J of Ob, GYN, Repro Biol 2021;262:184 8. Ríos E, Med Micro & Immunol 2022;211(5-6):269

Fluoroquinolones in UTI rapid

Historically *E coli* resistance <10%, recently ~ 17% in community, 40% in some countries

For most GNR in UTI: cipro preferred (Few exceptions)

- Approved for UTI: ciprofloxacin and levofloxacin
- Moxifloxacin has poor PsA coverage

Notable advantages:

- Bioavailable, tissue penetration (prostate, abscesses, kidney), tolerability, bactericidal, inexpensive, broad
- Short oral courses studied

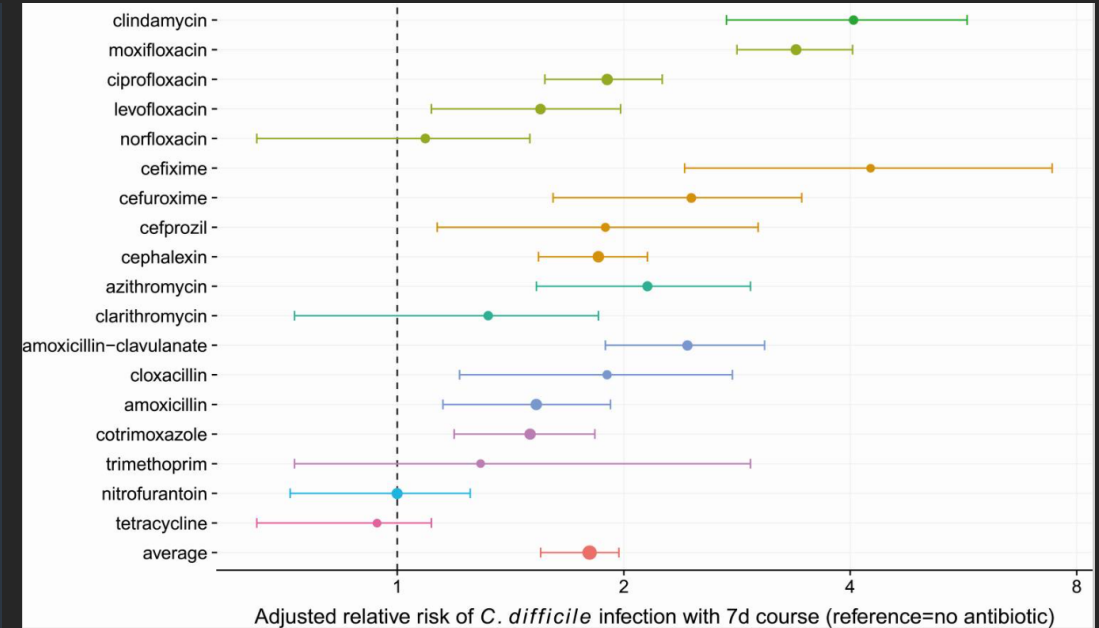
Barriers/limitations to use:

- Connective tissue damage: tendinopathy /tendon rupture/ aneurysms/retinal detachment (age>60 Aj RR 3), QT prolongation/arrhythmia, neuropsychiatric side effects/neuropathy, emerging resistance, hypoglycemia, teratogenic
- Stewardship: *C. difficile*, MRSA selection, selection for resistance, reserve for PsA
- Drug interactions (Mg, Fe, Ca, Al decrease absorption)

Oral Beta lactams for cystitis

(compared to TMP/S, NTF, FQ)

- ❖ Duration typically longer (5-7 days) for similar efficacy
- ❖ Higher return visit rates in recent machine learning study (Jones. *JAMA Net Open* 2025)
- ❖ Lower clearance rates of uropathogens from vagina
- ❖ High risk of C diff (Brown, CID, 2021)
- ❖ Amox first line *for Enterococcus* and effective against *Aerococcus*
- ❖ Cephalexin adequate for cystitis if organism is susceptible (urinary excreted and good bioavailability)





New / novel oral ABX for uUTI – 2025

Pivmecillinam

Not new (used since 1970s) 🧔

Aminopenicillin prodrug (resistant to hydrolysis by many ESBL)

FDA approved April/24

185 mg (1T) TID x(3)5-7d

Limited Gram+ and no PsA activity

Adult females

Gepotiacin

Non-FQ topoisomerase inhibitor (no cross-resistance)

1500 mg (2T) q12h x5d

May prolong QT

FDA approved March/25

QT prolongation, CYP 3A4 interactions, not for CrCl<30/HD

Females >12y/40kg



Sulopenem etzadroxil-probenecid

Oral carbapenem (~ertapenem in spectrum)

500/50 mg (1T) BID x5d

FDA approved Oct/24

Adult females with no other options

Avoid in gout; caution w/ NSAID, MTX, salicylate, CrCl<15

Anticipated and feared by ID



Simple cystitis in men

Treatment duration - 7 Versus 14 days?

- Afebrile cystitis (VA study): 272 men (69Y median age) give cipro or TMP/SXT for 7d or. Symptom resolution not significantly different ($\approx 92\%$). 28d recurrence of sx similar ($\approx 12\%$). No patients progressed to febrile or upper UTI
- Men with febrile UTI (French trial): 282 men, FQ use. Treatment success higher in 14-day group compared to 7-day group (sicker patients)
- For simple afebrile cystitis, without fever or evidence of prostatitis, 7 days likely adequate

Are antimicrobials penetrating prostate preferred for simple cystitis?

- Not addressed in above trials

Bacterial Prostatitis - General principals

Acute prostatitis

- Acute onset, typically febrile, lower tract urinary symptoms and pelvic or rectal pain/tenderness

Chronic prostatitis

- Indolent
- Typical presentation: short interval relapses of cystitis episodes, after adequate therapy, with same isolate
- Treatment duration: 6-12 weeks

Antibiotics for prostatitis:

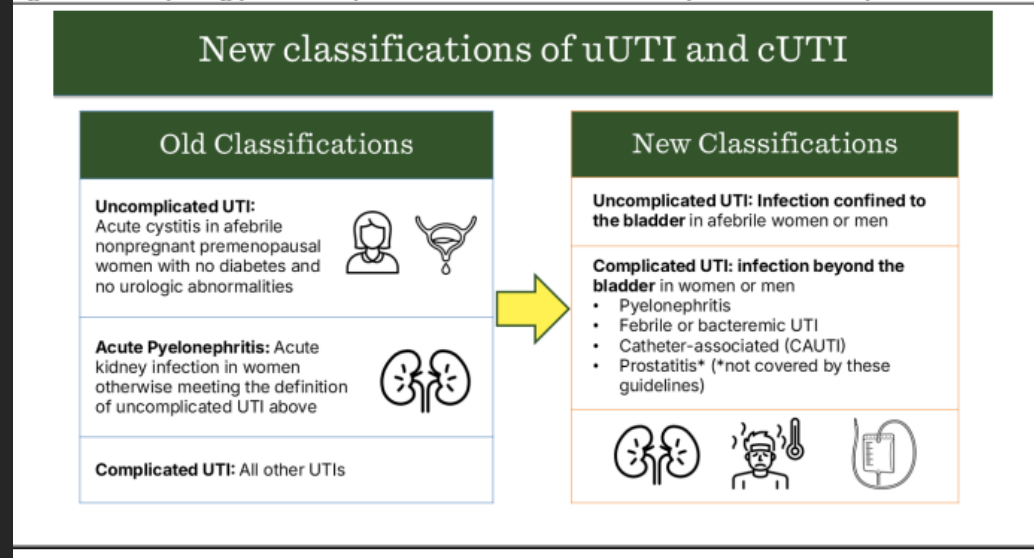
- Small, non-protein-bound, lipid-soluble, non-ionized, alkaline, penetrate prostate well
- Standard: TMP/SXT or FQ such as Cipro – good penetration.
- Doxycycline or azithromycin penetrate well
- Beta lactams penetrate less well (challenge in some gram-positive infections)
- In a study of chronic prostatitis used fosfomycin every 1-2 days for 6-12 days with good success (Karaiskos. *J Antimicrob Chemother* 2019; 74(5):1430-1437)

Updated UTI Classification

Complicated UTI Guidelines

<https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/>

Figure 1.0 Comparing prior and updated classifications of uncomplicated and complicated UTI



IDSA PRACTICE GUIDELINES • CURRENT

Complicated Urinary Tract Infections (cUTI): Clinical Guidelines for Treatment and Management

 Published July 17, 2025

IDSA 2025 Guidelines on complicated UTI

FOUR-STEP APPROACH TO EMPIRIC ANTIBIOTIC SELECTION

- Assess severity of illness (yes/no sepsis / SOFA ≥ 2)
- Consider resistance factors for MDR (previous urine culture, FQ exposure in 12m)
- Evaluate patient specific considerations (risk of tendinopathy, QT, etc)
- For sepsis: consult local antibiogram

EMPIRIC ANTIBIOTIC CHOICE BY SEVERITY

- cUTI with sepsis:
 - 3rd or 4th generation cephalosporins, carbapenems, piperacillin/tazobactam, Fluoroquinolone
 - ESBL/AMP-C considerations
- cUTI without sepsis:
 - Third- or fourth-generation cephalosporins, piperacillin-tazobactam, or fluoroquinolones
- Nitrofurantoin and fosfomycin should be generally avoided
- Newer agents and aminoglycosides for MDR, no other options



Complicated UTI Guidelines

<https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/>

Complicated UTI

Febrile UTI and Acute Pyelonephritis: ABX choice and duration – what about 5 days?

- [Mostly] 7 days courses
 - for acute pyelonephritis, febrile cystitis, quick to improve bacteremic UTI
- patients who are improving clinically on effective therapy
 - 5-7 days of a fluoroquinolone (conditional recommendation) or
 - 7 days of a non-fluoroquinolone antibiotic (*conditional recommendation*) rather than a longer course (10-14d)
 - Considerations for acute pyelonephritis:
 - Most studies *E coli* dominant
 - Most studies looked at FQ
 - Some patients require longer course: e.g. foreign body (catheters, stones), obstruction, severe sepsis at onset, immunosuppression, slow to respond, pregnant, abscess
- **Ultimately clinical response + source control guide decision on duration**



Complicated UTI Guidelines

<https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/>

Duration of Antibiotics for cUTI & sepsis of urinary source

Study (Year, Journal)	Population	Design	Intervention	Main Findings
Yahav, CID 2019	Hospital uncomplicated GNR bacteremia	RCT, noninferiority 411/604 urinary source	7 vs 14 d	7 noninferior to 14 composite outcome
McAteer, CID, 2023	Hospital cUTI & bacteremia,	Observational, propensity-weighted, n=1099	7 vs 10 vs 14 d	7d effective if highly bioavailable oral agents
Zahavi, Clin Microbiol Infect, 2025	cUTI or pyelonephritis (many w/ sepsis),	Systematic review/meta-analysis of RCTs, n=4643 (2274 w/ bacteremia)	5–7 vs 10–14 d	No significant difference in clinical, microbiological cure, relapse, mortality
Rudrabhatla PLOS one, 2018	Hospital pyelonephritis (excluding severe sepsis)	RCT n=54	7 vs 14 d (non-FQ)	7d noninferior to 14d in recurrence, adverse events
BALANCE 2025 NEJM and BMJopen	Hospital bacteremia (42% urinary source)	RCT, ~1516/3608 urinary source	7 vs 14 d	7d noninferior to 14d 90d mortality, urinary subgroup

Patients

- 3608 patients
- Median age, 70 years
- Male: 53%; Female: 47%



7-Day Group



N = 1814

14-Day Group

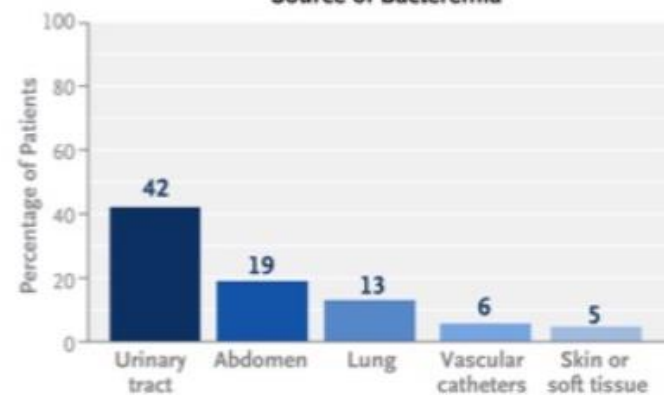


N = 1794

Death from Any Cause within 90 Days



Source of Bacteremia



BALANCE trial

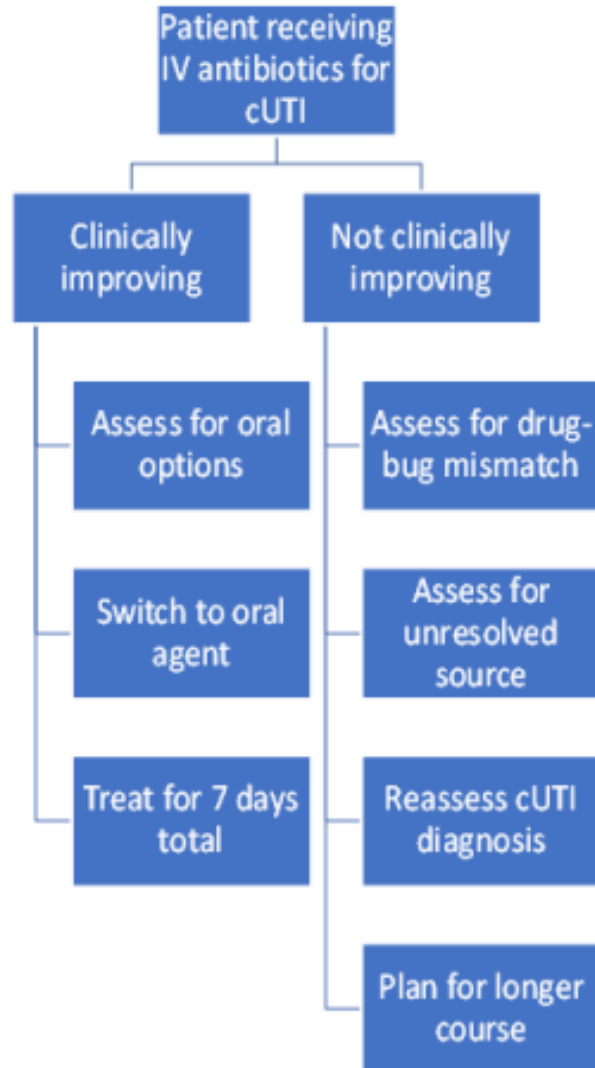
NEJM 2025;392:1065-1078 DOI: 10.1056/NEJMoa240499

UTI substudy: <https://bmjopen.bmj.com/content/10/5/e038300>



Bacteremic UTI

Transition to oral antibiotics



cUTI with gram-negative bacteremia on IV therapy: clinically improving (by 3-5d) + able to take oral med + effective oral option = source control achieved & no “complicating factors”

- Transition to oral antibiotics (rather than continued IV)
- Shorter (7d) rather than longer (14d) course

■ **Some indications for longer therapy:**

- obstruction (after relieved), abscess, slow response, incomplete source control (infected stone?), pregnancy (guidelines: 14d), prostatitis (14d), epididymitis, orchitis, ??other male with febrile UTI

Drugs	Oral absorption (%)	Urinary excretion (%)	Dose for patients with normal renal function
Amoxicillin-clavulanate	80 (amoxicillin) ⁴⁰ variable (clavulanate) ⁴¹	50-70 (amoxicillin) ⁴⁰ 25-40% (clavulanate) ⁴⁰	875mg-125mg every 8 to 12 hours ^{12,32-34,39,42-45} Other regimens may be more effective ^a
Cefixime	50 ⁴⁶	50 ⁴⁶	400mg once daily ⁷
Cefpodoxime	50 ⁴⁶	80 ⁴⁶	200mg to 400mg every 12 hours ^{29,34,47}
Ceftibuten	75-90 ⁴⁶	73 ⁴⁶	9mg/kg daily (children) 400mg daily or 200mg every 12 hours (adults) ^{48,49}
Cefuroxime	52 ^{46,50}	90 ^{46,50}	500mg every 12 hours ^{34,51}
Cephalexin	90 ⁴⁶	90 ⁴⁶	500mg to 1000mg every 6 hours ^{12,28,32,33,39,42-44,52} Other regimens may be more effective ^a
Ciprofloxacin	70 ⁵³	40-50 ⁵³	500mg to 750mg every 12 hours ^{20,28,34,39,54}
Levofloxacin	99 ⁵⁵	64-100 ⁵⁵	500mg to 750mg daily ^{28,47,54,56}
Other oral beta-lactams (e.g. amoxicillin, cefadroxil, cefaclor, cefdinir)	Comparative clinical outcomes data vs highly bioavailable oral alternatives are more limited and/or discouraging; consider use with infectious disease pharmacist consultation if alternatives are not available.		
Trimethoprim-sulfamethoxazole	70-90 ⁵⁷	84 (sulfamethoxazole), 66 (trimethoprim) ⁵⁷	800mg-160mg every 12 hours ^{20,34}

^aDespite routine use of optimized dosing, the majority of studies comparing switch to oral beta-lactams versus fluoroquinolones or trimethoprim-sulfamethoxazole for cUTI have found inferior outcomes with oral beta-lactams when amoxicillin-clavulanate or cephalexin

 **Complicated UTI Guidelines**
<https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/>

Oral antibiotic doses for cUTI may
higher than for simple cystitis

Table 2.1: Dosing of intravenous (IV) antibiotics for complicated UTI used in clinical studies presented in alphabetical order.

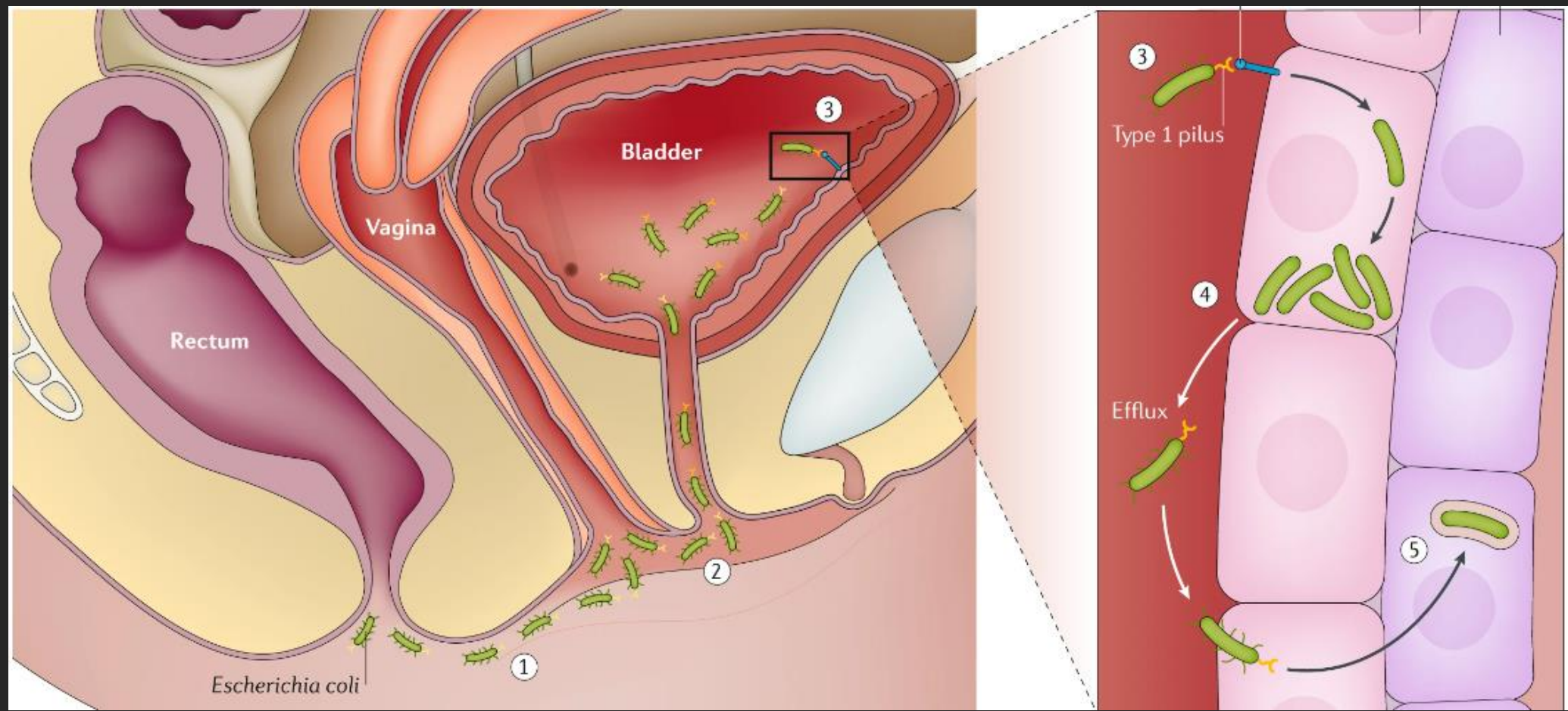
Drug	Dosing regimen used in clinical trials for patients with normal renal function
Cefepime	1-2g every 8 to 12 hours ^{7,8}
Cefepime-enmetazobactam	2g/0.5g (infused over 2 hours) every 8 hours ⁹
Cefiderocol	2g (infused over 3 hours) every 8 hours ^{10,11}
Cefotaxime	1-2g every 8 hours ¹²
Ceftazidime	1-2g every 8 hours ^{13,14}
Ceftazidime-avibactam	2.5g (infused over 2 hours) every 8 hours ¹⁵⁻¹⁷
Ceftolozane-tazobactam	1.5g every 8 hours ¹⁸
Ceftriaxone	1-2g daily ^{19,20}
Ertapenem	1g daily ²⁰
Fosfomycin	6g every 8 hours ²¹
Imipenem-cilastatin	500mg every 6 hours ^{17,22} 1g every 8 hours ¹¹
Imipenem-cilastatin-relebactam	500mg/125mg every 6 hours ²²
Meropenem	1g every 8 hours ^{19,23}
Meropenem-vaborbactam	2g/2g (infused over 3 hours) every 8 hours ²⁴
Piperacillin-tazobactam	4.5g every 8 hours ^{9,21,24}
Plazomicin	10-15mg/kg daily ^{23,25}

Table 2.1 includes IV dosing for cUTI based on review of randomized controlled trials among patients with complicated UTI.

Complicated UTI Guidelines

<https://www.idsociety.org/practice-guideline/complicated-urinary-tract-infections/>

IV antibiotic dosing
used in cUTI studies
(alphabetical order)



UTI pathogenesis

Understanding colonization and Clinical Infection

Asymptomatic Bacteriuria

Definition: significant bacteriuria in a person without symptoms of a urinary tract infection

Screening (and treatment) for asymptomatic bacteriuria is recommended for:

- **Pregnant** at least once, and if positive “periodically”
Many, but not all studies, link untreated bacteriuria to preterm birth, low birth weight, perinatal mortality and bacterial sepsis
- Patients undergoing **urologic procedures where mucosal injuries may occur** (e.g. TURP, cystoscopy with biopsy)

Screening and treatment for ASB before non-urologic surgery

Joint arthroplasty: common practice despite lack of prospective evidence (observational data suggest association between ASB and prosthetic joint infection[PJI])

NOT INDICATED

Cardiac Surgery: less available data, but no prospective data to support treating ASB for this indication

Clin Infect Dis (2017) 64 (6): 806, *Clin Infect Dis* 2014; 59 :41; *Clin Orthop Relat Res* 2013; 471:3822

Catheter Associated UTI, Rapid

- Pyuria/bacteriuria common – not diagnostic
 - Lower tract symptoms may be masked – early clinical diagnosis challenging
 - Most funguria = biofilm/colonization - hard to eradicate rarely requires therapy (⚠ do not miss fungemia, crypto)
- Replace in conjunction with UTI therapy?
- Considerations: duration & biofilm, culture accuracy, burden & risk from exchange
 - › Foley: some guidelines support exchange for clean culture; data on failure or mortality mixed
 - › Stent: no strong evidence for routine exchange; potential benefit if biofilm; remove if obstruction
 - › PCN: no strong evidence for routine exchange; exchange may increase risk of infection

Recurrent UTI Case

60-year-old woman with history of recurrent symptomatic afebrile cystitis. Frequency of infections increasing. She drinks a lot of water and has cranberries by the bushel. Anything else you would do?

- A. antibiotic prophylaxis
- B. vaginal estrogen
- C. add D-mannose

Recurrent Cystitis: Non-ABX options that work!



Liberal Water Drinking

- RCT showed that 1.5L daily reduced cystitis rate by 50% (JAMA IM 2018)



Topical estrogen products

- Increase healthy lactobacilli + reduce uropathogenic *E. coli*
- Target population: postmenopausal, no contraindication (?any)
- Two randomized studies showed a relative risk of symptomatic UTI of 0.25 (95% CI 0.13–0.50) and 0.64 (95% CI 0.47–0.86)

Recurrent Cystitis: Non-ABX options that sometimes work!



Methenamine salts

- Mandelate / Hippurate reduce urine pH (can add vitamin C) → methenamine hydrolyzed to ammonia & formaldehyde → bactericidal
- Used often if residual urine present (neurogenic bladder, spinal injury)
- Long-term efficacy not known; can't be used if CKD
- Not given with TMP/SMX



Probiotic Suppository

- small RCT of intravaginal lactobacillus showed effect

Recurrent Cystitis: Non-ABX options that may work for a subset of patients



Cranberry products

- Theoretical benefit – inhibits *E coli* from adhering to bladder epithelium (some negative studies)



D-Mannose

- May prevent *E coli* bacteria from binding to bladder epithelium
- Very limited data

<https://pubmed.ncbi.nlm.nih.gov/23633128/>
<https://pubmed.ncbi.nlm.nih.gov/8350884/>

■ Recurrent Simple Cystitis: If opting for Antibiotic approaches

Preferred:

- Self diagnosis, self treatment = pill in pocket (with or without standing UA/culture)
- Postcoital PPX: single dose after intercourse, treatment dose x1
 - TMP-SMX SS
 - Nitrofurantoin, 50–100 mg
 - Cephalexin, 250 mg

If opting for continuous antibiotics

- Define trial period, then pause (if feasible)
- Doses typically lower than treatment dose (confirm urine sterility at onset):
Nitrofurantoin, 50–100 mg, TMP-SMX SS QD or TIW, cephalexin, 125–250 mg,
Fosfomycin, 3-g sachet every 7-10 days

Takeaways / summary

- Negative urinalysis: excellent negative predictive value for a clinically significant urinary infection (few exclusions)
- Community and hospital drug resistance on the rise (know community data and assess individual history and risk factors)
 - For susceptible simple UTI nitrofurantoin (susceptibility remains high), TMP/S, fosfomicin, with second line beta lactams (including cephalexin, amoxicillin) and FQ
 - Exciting novel oral antibiotic options for MDR uUTI are here
- Most complicated and febrile UTI, including bacteremic, may be treated with short (7d) courses
 - If clinical improvement + source control / no complications
 - step down to adequate oral therapy okay
- Indications to treat asymptomatic bacteriuria are narrow (pregnancy, invasive urologic procedures)
- For rUTI prevention prioritizes stewardship - begin with non antibiotic approach (liberal water intake, vaginal estrogen, methenamine)

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- Trautner, B.W., 2021. Urinary tract infections as a continuum: implications for diagnostic and antibiotic stewardship. Clinical Infectious Diseases, 72(8), pp.1339-1341

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CAUTI

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ASB

- Nicolle LE, Gupta K, Bradley SF, et al. Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America. Clin Infect Dis 2019; 68:e83

Bacteremia, Antibiotic duration

- Turjeman, A., et al. ., 2023. Duration of antibiotic treatment for Gram-negative bacteremia—Systematic review and individual participant data (IPD) meta-analysis. EClinicalMedicine, 55.
- BALANCE Trial (Daneman et al., NEJM 2024) — Landmark RCT of 3,608 patients randomizing 7 vs. 14 days of antibiotics for bacteremia (42% urinary source); 7 days was non-inferior for 90-day mortality.

Recurrent UTI

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- Sihra, N., Goodman, A., Zakri, R., Sahai, A. and Malde, S., 2018. Nonantibiotic prevention and management of recurrent urinary tract infection. Nature Reviews Urology, 15(12), pp.750-776.

A 32-year-old non pregnant health woman has 3 days of dysuria, urinary frequency and urgency without vaginal discharge, fever, or flank pain. She has no known drug allergies, recent hospitalizations or recent antibiotic use. Which is the most appropriate empiric first line therapy?

- A. Ciprofloxacin 500 mg PO BID × 3 days
- B. Amoxicillin-clavulanate 875 mg PO BID × 7 days
- C. Cephalexin 500 mg PO QID × 7 days
- D. Nitrofurantoin monohydrate 100 mg PO BID × 5 days
- E. Obtain urine culture before starting antibiotics

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- D. Nitrofurantoin monohydrate 100 mg PO BID × 5 days

Nitrofurantoin, TMP-SMX (3 days), and fosfomycin (single dose) are **first-line agents** for simple cystitis per IDSA/ESCMID guidelines. Fluoroquinolones are reserved for more invasive or if there are no alternatives. resistant infections. β -lactams (amoxicillin-clavulanate, cephalexin) are second line therapy. For the most common organisms nitrofurantoin susceptibility remains high, and urine culture is not always required for a straightforward presentation simple cystitis in a young woman

A 60-year-old man is in the ICU for an upper gastrointestinal bleeding complicating warfarin therapy. The bleeding is controlled and the patient is hemodynamically stable. He has an indwelling urinary catheter. Owing to cloudy urine, a urine culture was sent and is growing $>100,000$ CFU/mL *Enterococcus faecalis*. Susceptibilities are pending. The patient has no fever, no flank tenderness, and upon questioning reports no dysuria.

What is the most appropriate next step?

- A. Start IV vancomycin while susceptibilities pending, then oral therapy
- B. Start oral levofloxacin
- C. Start oral amoxicillin
- D. Remove the catheter when feasible and repeat the culture at 48 hours
- E. Do not treat and reassess need for catheter

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- C. Start oral amoxicillin
- D. Remove the catheter when feasible and repeat the culture at 48 hours
- E. **Do not treat and reassess need for catheter**

This patient has catheter-associated asymptomatic bacteriuria. He has no signs or symptoms suggestive of infection or infection of urinary source. Pyuria, bacteriuria, malodor, and cloudy urine alone are not indications for treatment in a catheterized patient in the absence of clinical symptoms of or concern for infection. The most important intervention is to remove the catheter as soon as it's no longer indicated.

A 72-year-old woman presents with urinary urgency, frequency, mild confusion, tachycardia, and a temperature of (39°C). Urine culture grows >100,000 CFU/mL *E. coli* susceptible to ceftriaxone, co-trimoxazole and ciprofloxacin. 1 of 4 blood cultures bottles grow the same organism. She had prior Achilles tendinitis during ciprofloxacin therapy. GFR is 75 mL/min. WBC is 12,000. She is treated with IV ceftriaxone and improves clinically (back to baseline) on day 3. Repeat blood cultures are negative to-date. She's clinically ready for discharge home. A plan is made to complete the course of therapy with cotrimoxazole. What is the recommended total duration of antibiotic therapy?

- A. 3 days
- B. 5 days
- C. 7 days
- D. 10 days
- E. 14 days

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- A. 3 days
- B. 5 days
- C. 7 days
- D. 10 days
- E. 14 days

This patient has bacteremic cUTI. 7 (rather than 10-14) days of therapy are adequate for complicated UTI patients who are clinically improving, when an effective (adequate) oral agent is available and source control is achieved. This approach is supported by several trials and conditionally endorsed by the 2025 IDSA cUTI guidelines.