



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

Urinary Tract Infections for Internal Medicine

Sigal Yawetz, MD

Division of Infections Diseases
Department of Medicine
Brigham and Womens' Hospital
Harvard Medical School



Sigal Yawetz, MD



Harvard Medical School

Medicine Residency @ WLVAMC, UCLA Medical School

Infectious Diseases and HIV fellowships @ BWH/MGH combined program, Harvard Medical School

Assistant Professor of Medicine @ HMS

Director, BWH Program for HIV in Women and Youth

Co-Chair, DEI Committee, BWH Division of Infectious Diseases

Conflicts

None (commercial)

Editorial:

IDSA UTI guidelines expert panel
UTI topic editor for DynaMed



Principals in diagnosis and management of simple urinary tract infections

- When to test, what tests to use, when to treat empirically
- Empiric therapy versus test-guided treatment choices

Challenges in diagnosis and management of urinary tract infections

- Multi-drug resistance organisms (MDRO)
- Antibiotic allergies in the way
- cUTI - antibiotic choice and duration in inpatient to outpatient transition
- Catheter associated Urinary tract infections
- Asymptomatic bacteriuria and funguria – when to test/treat?
- Prevention of recurrent UTI

Role of imaging and referrals in UTI management

OBJECTIVES

UTI for Internal Medicine

Case one

39F, A1C 6.1, BMI 32, no other significant PMH, no medications, comes once per year for routine physicals and labs.

Calls for a 3-day history of dysuria and urinary urgency

No fever, nausea, vomiting, flank pain.

Has had occasional cystitis ~once per year.

No recent hospitalization or antibiotics

Simple Cystitis
AKA Uncomplicated UTI

Classic Lower Tract symptoms
(dysuria, urgency, frequency)

No upper Tract symptoms or fever

Evolving new Definition of uUTI and cUTI

Credit: Barbara Trautner, IDWeek 2023, Sneak Preview to the IDSA UTI GL Update on cUTI

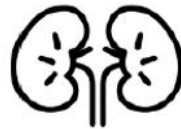
OLD DEFINITION

Uncomplicated UTI:

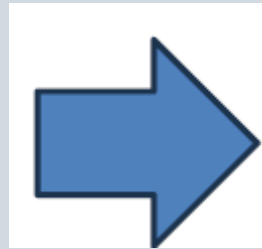
Acute cystitis in a healthy nonpregnant afebrile women with no diabetes and no urologic abnormalities



Acute Pyelonephritis:



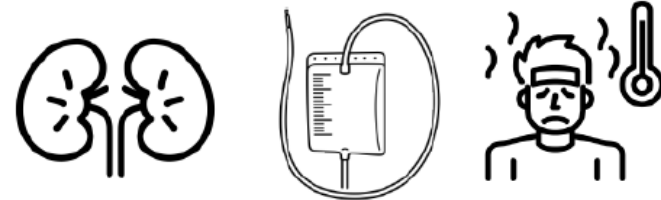
Complicated UTI: Everything else



NEW DEFINITION

Complicated UTI: infection beyond the bladder

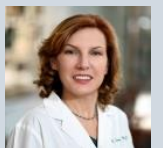
- Pyelonephritis
- CAUTI
- Febrile or bacteremic UTI



Uncomplicated UTI: Everything else (in women or men)

Images from *Noun Project*; see slide comments for attributions

IDSA
Infectious Diseases Society of America



Case one

39F, A1C 6.1, BMI 32, no other significant PMH, no medications, comes once per year for routine physicals and labs.

Calls for a 3-day history of dysuria and urinary urgency

No fever, nausea, vomiting, flank pain.

Has had occasional cystitis ~once per year.

No recent hospitalization or antibiotics

- A. Wait and see
- B. In-person urgent care visit
- C. Ask to come in for dipstick before antibiotics
- D. Order outpatient UA and culture before antibiotics
- E. Empiric antibiotics to a local pharmacy

Simple (afebrile or uncomplicated) Cystitis - what if wait and see?

Natural History of Untreated Simple Cystitis in Young cis-Women with a Normal Urinary Tract

- Episode resolution after 2–4 weeks ~ 50%
 - may account for some of response rate reported in antibiotic trials
- Majority (~70%) premenopausal w/ simple cystitis clear bacteriuria eventually (weeks to months)
- Progression to pyelonephritis & renal failure rare (if normal GU tract anatomy and function)

Wigton, *et al.*, J Gen Int Med 14:491 (1999)

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)

Hooton, Infect Dis Clin North Am 2003

Christiaens, Br J Gen Pract. 2002

Hooton, CID, 2004

Falagas, J of Infection, 2009



Testing for Simple Cystitis in Women

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



Testing for Simple Cystitis in Women

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

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Societal / environmental and personal costs of antibiotic overuse



1. Fenwick. Brit J Gen Practice, 50: 635 (2000)

2. Saint, *et al.*, Am J Med, 106: 636 (1999)

Non-culture Diagnostic Options

Looking for Pyuria



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



Pyuria is present in almost all women with acute cystitis

Sensitivity high: ~90%



Pyuria without acute cystitis is common

Specificity lower: ~70%



Dipstick leukocyte esterase – rapid screening test for pyuria

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

Specificity for pyuria 94-98%

Non-Culture Diagnostic Options

Looking for Bacteriuria

Nitrite (positive helpful, negative not)

- Sensitivity poor: ~20%.
 - False negative: low (10^2 - 10^5 /mL) colony counts
 - non nitrite producer: *Enterococci*, *S. saprophyticus*, *Acinetobacter*, dilute urine
- Specificity for bacteriuria high: ~95% (GOOD)
 - false positives are rare

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)	98.0 (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)	98.8 (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)

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Poor

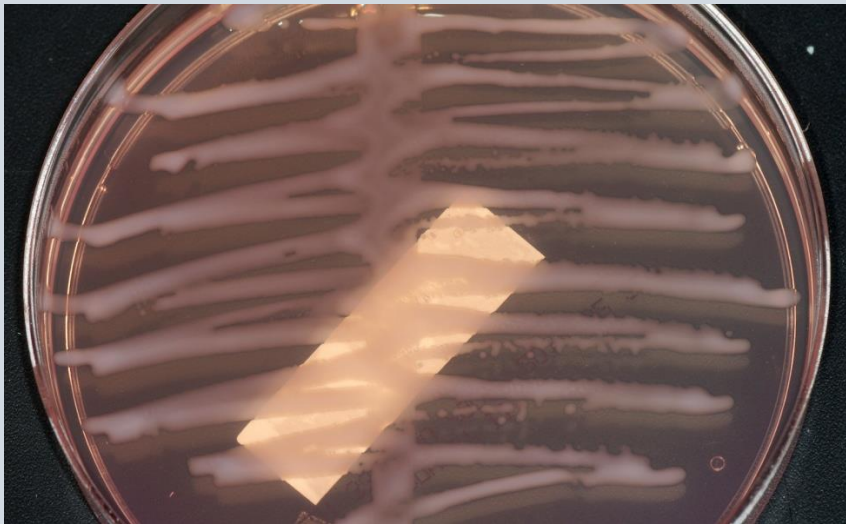
Excellent

Diagnostic Options - Culture

Why Culture?

- Confirms diagnosis (significant bacteriuria, >100,000 CFU/mL*?)
- Identifies causative organism
- Provides susceptibility testing to tailor therapy accordingly
 - Helps find narrowest agent
 - Assures no resistance

*CFU=colony forming units



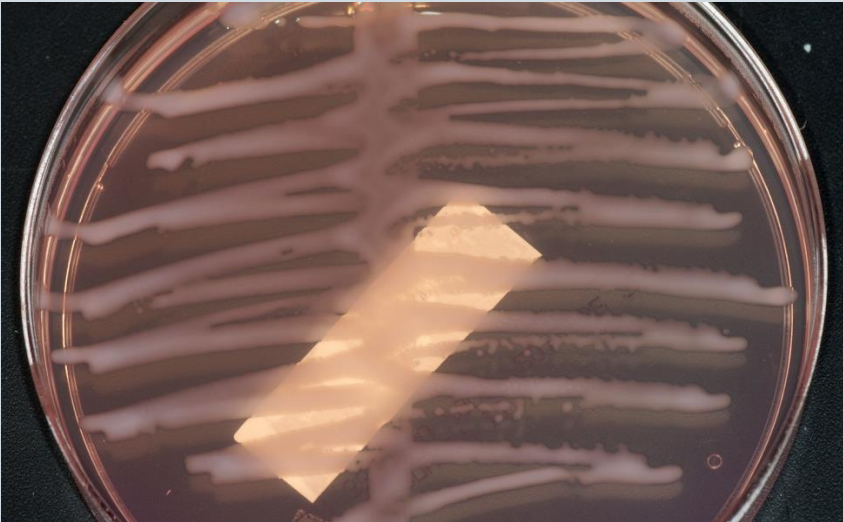
What percent of young women with simple cystitis (frequency, urgency, or dysuria) have $>10^5$ CFU/ mL of a single uropathogen in the urine?

- A. 85%
- B. 65%
- C. 50%
- D. 33%
- E. 25%



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- C. 50%
- D. 33%
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What about the other 50%?

Most have “acute urethral syndrome”

If therapy delayed 2d – 48% will have $>10^5$ (early presenters)

10^2 - 10^5 CFU 95% sensitive & 85% specific for UTI

Studies in young women: 10^2 cfu of GNR (e.g. *E. coli*) predictive of UTI (compared to catheterized urine)

Some have “symptomatic abacteriuria” e.g. urethritis (GC/chlamdia /mycoplasma / trichomonas / other), genital herpes vaginitis, non-infectious process



Simple cystitis in postmenopausal women

Is it truly [much more] complicated?

Table 1. Distribution of uropathogens that cause urinary tract infections in women.

Uropathogen	Frequency among women, by age group, % ^a	
	15–50 years of age	>50 years of age
<i>Escherichia coli</i>	72	53
<i>Klebsiella</i> species	6	12
<i>Proteus</i> species	4	6
<i>Enterobacter</i> species	2	2
<i>Pseudomonas aeruginosa</i>	1	4
Other gram-negative rod	2	4
<i>Enterococcus</i> species	5	12
<i>Staphylococcus aureus</i>	2	2
<i>Staphylococcus saprophyticus</i>	2	0.2
Coagulase-negative staphylococci	3	2
Other	1	3

**What changes after
menopause?**

Diversity of organism

Gupta *CID* 2001(33): 89

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
- Pivmecillinam 400 mg twice daily x 5 days*

Not recommended

- Fluoroquinolones 3 days
- β -lactams

- 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)

Fosfomycin (3-g x1) or Nitrofurantoin (100 mg thrice daily x 5 days) for UTI

93% completed trial, 73% + baseline CX

Resistance to both agents low for *E. coli*.

Klebsiella and *Proteus* resistance rates higher

Clinical Resolution 28d ($P < .004$, $.001$ for *E. coli*)

- Nitrofurantoin 70% (*E. coli* 78%)
- Fosfomycin 58% (*E. coli* 50%)

Micro Resolution 28d

- Nitrofurantoin 74% (*E. coli* 84%)
- Fosfomycin 63 % (*E. coli* 59%)

- Methodologic problems: open label, lots of LTF, positive cultures at baseline not required (27% did not have)
- Response rates lower than other studies for both arms
- Nitrofurantoin dose 100 mg TID (in US 100 mg BID)



Review question 1:

48F, MS previously on ocrelizumab (B cell depleting agent), neurogenic bladder. Has h/o recurrent UTI. Childhood allergy to amoxicillin (rash).

SX: dysuria, “bladder spasms”, 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.

What antibiotic options may be adequate?

Which of the following is correct
(may chose more than one correct
answer)

- A. Oral fosfomycin may be active if susceptible
- B. Oral nitrofurantoin may be active if susceptible
- C. Amox/clav may be given after a test dose or skin test
- D. Once daily ertapenem is likely adequate

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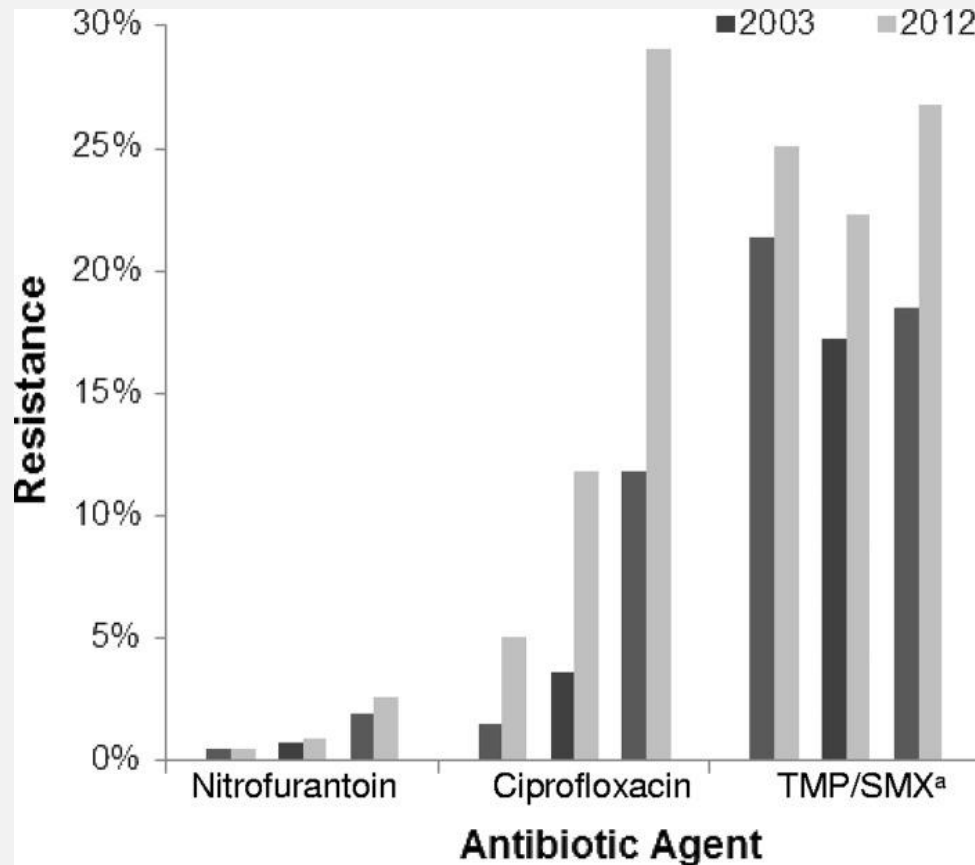
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Antibiotic Resistance among Urinary Isolates from Female Outpatients in the United States in 2003 and 2012

Sanchez et al Antimicrob Agents Chemother. 2016 May; 60(5): 2680–2683



Surveillance Network USA

Urinary isolates from female outpatients
2012 ($n = 305,749$) *E. coli* in 64.9%

E. coli resistance to nitrofurantoin low (<3%)
across all age groups.

E. coli resistance to ciprofloxacin was high
among adults (11.8%) and elderly
outpatients (29.1%).

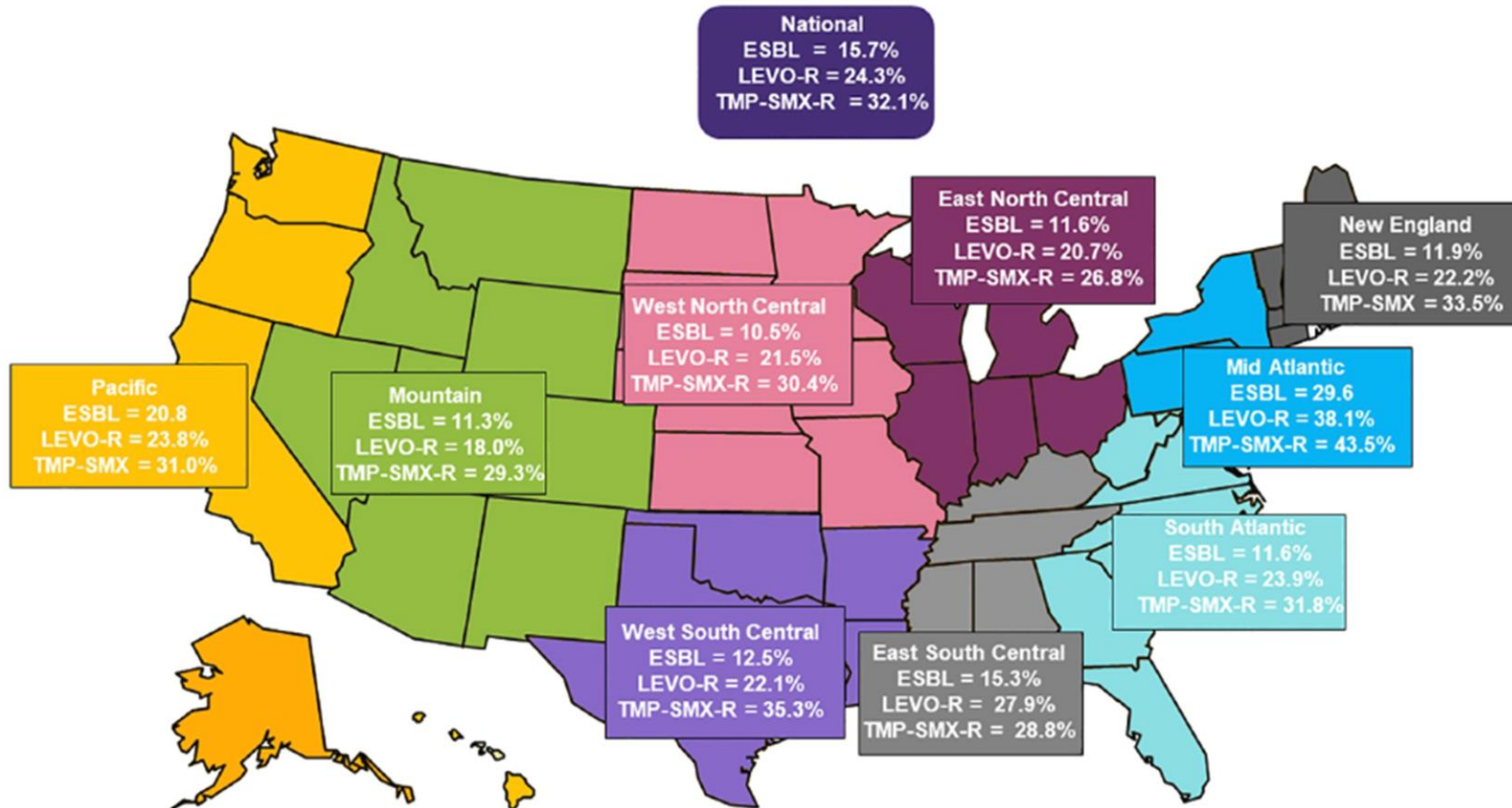


Fig 1. National and regional prevalence of ESBL phenotypes, levofloxacin- and trimethoprim-sulfamethoxazole-resistant phenotypes among 1831 isolates of *E. coli* from UTIs in the USA in 2017. ESBL = extended spectrum β -lactamase, LEVO-R = levofloxacin-resistant, TMP-SMX-R = trimethoprim-sulfamethoxazole-resistant.

<https://doi.org/10.1371/journal.pone.0200065.g001>

National trends
in urinary *E.*
coli
susceptibilities

UTI with Multidrug Resistant Organisms (MDRO)

- MDRO: resistance to ≥ 1 antibiotic classes (prior definition 3 or more classes)
- 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:
 - Before 2003 most ESBL producing Enterobacteriaceae were health-care associated *Klebsiella*
 - Since 2003 steady increase in highly resistant and ESBL- producing *E. coli* in community associated UTI
 - Many of those retain susceptibility to fosfomycin and nitrofurantoin

* ESBL: Extended spectrum beta lactamase producing *Enterobacteriaceae*

Nitrofurantoin

Only one indication: **afebrile (simple) cystitis**

IDSA guidelines dose 100 mg PO BID (some countries TID)

Broad, resistance rates remain **low** (1-3% MDR *E.coli*)

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)
 - 2015 Beers criteria revision: **more liberal CrCl threshold in elderly** (<30 rather than <60 mL/min) if short term (≤7 days)
- Side Effects
 - More common in elderly, 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

Phosphonic acid, 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* (~95% *E. coli*, 90-95% *Klebsiella*), 89.7% PsA
Interpretation of susceptibility varies

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:

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

Hirsch. *Int J Antimicrob Agents* 2015; 46 :642
Liu. *J Microbiol Immunol Infect* 2011; 44:364

Fluoroquinolones in UTI

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

For GNR in UTI: cipro preferred

- levofloxacin/moxifloxacin add atypical/respiratory coverage ,moxifloxacin loses PsA

Notable advantages:

- Bioavailability, tissue penetration (prostate, abscesses, kidney), tolerability, bactericidal, inexpensive, broad
- Shorter oral courses

Barriers/limitations to use:

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

MDRO – when to use oral options

Patient able to take oral medicine

An effective oral option for the syndrome is available

- nitrofurantoin (simple cystitis), TMP/SXT, amox/clav, cefpodoxime, FQ, fosfomycin

Also for de-escalation: cUTI or febrile UTI on parenteral therapy, showing clinical improvement, for whom source control has been achieved

- nitrofurantoin or fosfomycin may not be appropriate as step-down for pyelonephritis/bacteremia

Confirm allergies, consider [graded?] challenge or skin test based on history

When only tetracyclines are the oral option... 😞

- not stable in urine, hepatically cleared - if feasible chose alternatives
- typically, not in bacteremia
- when considered, tetracycline has higher urinary clearance, doxycycline used for prostatitis, urethritis

Duration of antibiotics for cUTI Short (7d) vs long (10-14d)

Acute febrile UTI/pyelonephritis: clinical response + source control?

Data support shorter (5-7d FQ, 7d other) vs longer courses (10-14 days)

- ❖ Most acute pyelonephritis studies looked at FQ
- ❖ Who may require longer? foreign body (catheters, stones), severe sepsis, immunosuppression, prostatitis (acute or chronic), CKD
- ❖ Most studies *E coli* dominant, excluded catheterized patients

Bacteremic UTI

- ❖ 7d may be adequate if source control achieved, response by d3-5, effective ABX (w/ blood/urine levels) available (Yahav. CID. 2019 69:1091 | von Dach JAMA. 2020; **323**: 2160 | Molina Clin Microbiol Infect. 2022; **28**: 550-557)

Recent febrile UTI study in men: 7d inferior to 14d (Lafaurie, CID, 2023)

What if 75M, with frequent relapses or *E. coli* UTI, whom you have just decided to treat for **chronic prostatitis**

UA: >182W, nitrites.

Cx: “ESBL” producing *E. coli*.

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

Not checked: Ertapenem

Resistant: trimethoprim/sulfa, FQ, aminoglycosides.

He’s directly admitted to medicine for IV meropenem and home hospital or VNA transfer

Which of the following is correct (may chose more than one correct answer)



- A. Oral fosfomycin is adequate if susceptible
- B. Oral nitrofurantoin is adequate if susceptible
- C. Amox/clav may be given after a test dose or skin test
- D. Once daily ertapenem is likely adequate

What if 75M, with frequent relapses or *E. coli* UTI, whom you have just decided to treat for **chronic prostatitis**

UA: >182W, nitrites.

Cx: "ESBL" producing *E. coli*.





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

Not checked: Ertapenem

Resistant: trimethoprim/sulfa, FQ, aminoglycosides.

He's directly admitted to medicine for IV meropenem and home hospital or VNA transfer

Which of the following is correct (may chose more than one correct answer)

- A. Oral fosfomycin is adequate if susceptible 
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Cystitis in Men Therapeutic Dilemmas

- Treatment duration: simple cystitis
 - 7 or 14 days? are antimicrobials penetrating prostate preferred for simple cystitis?
- 7 Versus 14 days?
 - Favors 7 days: VA study*, 272 AFEBRILE men (69Y median age) randomized within 7d of starting cipro or TMP/SXT to stop at 7d or continue for 14d. Symptom resolution not significantly different ($\approx 92\%$). 28d recurrence of sx similar ($\approx 12\%$). No patients progressed to febrile or upper UTI
 - Favored longer: French trial: 282 men with FEBRILE UTI, FQ use. Treatment success higher in 14-day group.

For simple afebrile cystitis, without evidence of prostatitis, 7 days likely adequate

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)
- Recent 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)



Board review question 2 (x6)

Patients below is asymptomatic.

Urine sediment: 50 WBC Urine culture: >100,000 cfu of ciprofloxacin R E. coli. Whom will you given antibiotics for? What duration?

32, pregnant, first prenatal visit

48, new diagnosis of diabetes, A1C 14.2%, glucose 396, malodorous urine

36, quadriplegic man, chronic indwelling Foley, LTAC, cloudy urine, leg spasm

62, pre-op eval for a transurethral resection of prostate (TURP)

78 R THR 2016, L THR 2018, simple cystoscopy

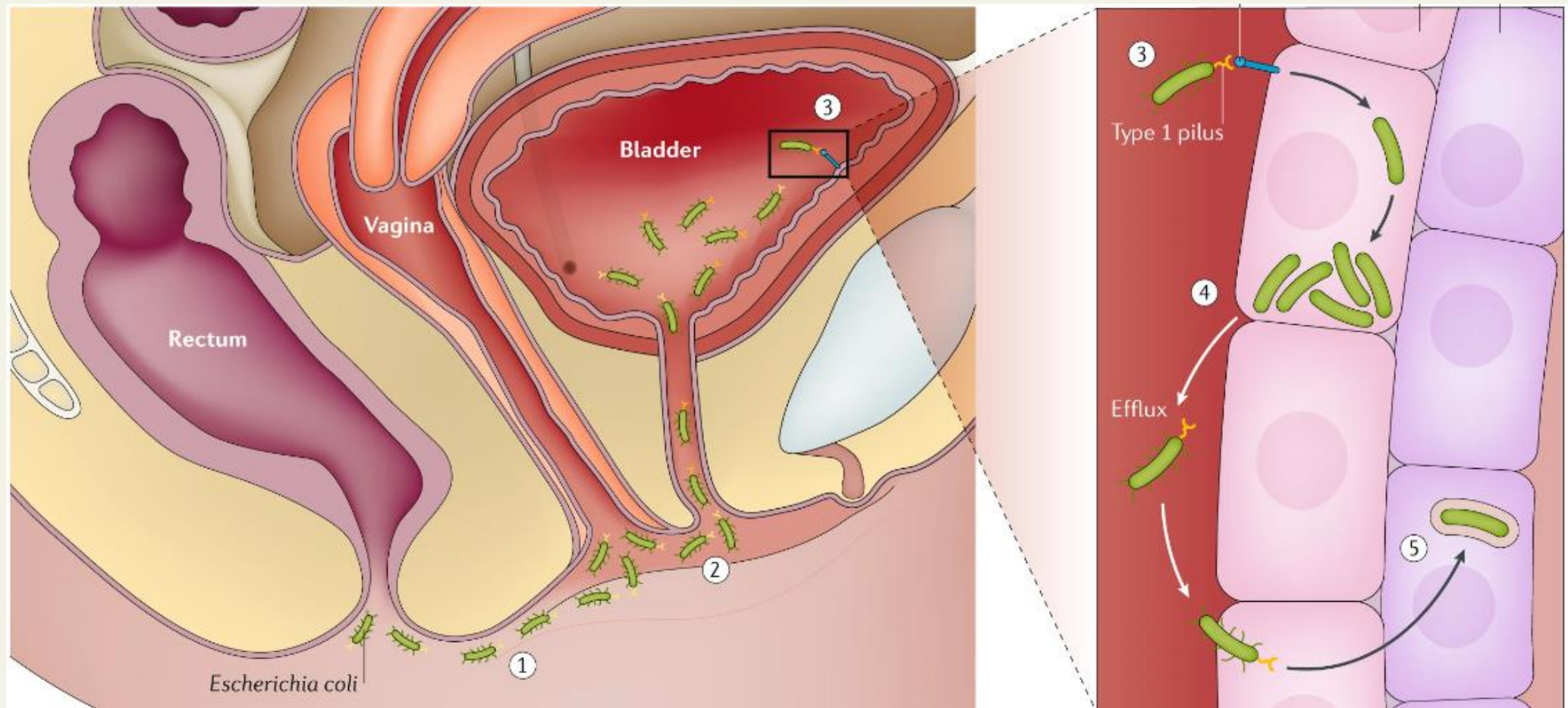
68F, stones, recurrent urosepsis, for stent exchange, nephrostomy exchange, possible lithotripsy, culture always positive

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48, new diagnosis of diabetes, A1C 14.2%, glucose 396, malodorous urine	x
36, quadriplegic man, chronic indwelling Foley, LTAC, cloudy urine, leg spasm	x
62, pre-op eval for a transurethral resection of prostate (TURP)	+
78 R THR 2016, L THR 2018, simple cystoscopy	x
68F, stones, recurrent urosepsis, for stent exchange, nephrostomy exchange, possible lithotripsy, culture always positive	+



UTI pathogenesis

Understanding colonization and Clinical Infection

Asymptomatic Bacteriuria

- 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
 - For patients **before TURP & other urologic procedures** where mucosal injuries may occur

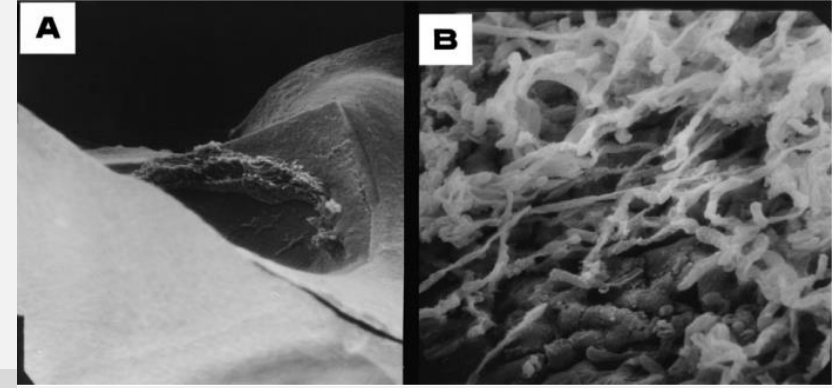
Screening and treatment for ASB before non-urologic surgery

- **Joint arthroplasty:** common procedure despite lack of prospective evidence (observational data suggest association between ASB and prosthetic joint infection[PJI])
- **Cardiac Surgery:** less available data, but no prospective data to support treating ASB for this indication

NOT INDICATED

Candida UTI

- Most commonly **catheter colonizer or vaginal contaminant**
- Adheres well to plastics, less well to bladder epithelium (promoted by *E. coli* and *Klebsiella*) – majority are hospitalized patients on antibiotics – not symptomatic - no treatment needed
 - **Possible Exclusions:**
 - retrograde upper tract infection, obstruction, fungal balls
 - Systemic infection suspected: think fungemia with seeding of urinary tract (get blood cultures)
 - Convincing urinary symptoms and no alternative explanation
- Fluconazole preferred but echinocandins and liposomal amphotericin work as well



Not all yeast is Candida; other fungal forms and molds should raise concern for disseminated infection



Catheter-associated UTI (CA-UTI) and Bacteriuria



- The presence, absence, or degree of **pyuria** should not be used to differentiate CA-ASB from CA-UTI – may be irritative
- Diagnosis should be made **clinically**
 - Fever, most common, but without localizing findings a challenge to interpret; attribute only when other causes excluded
- Consider prostatitis in symptomatic men with chronic catheters
- Focus on **prevention**
- Treatment of catheter associated UTI (not urinary sepsis):
 - 7 days for most (10-14 if delayed response)
 - 3 days may be considered in a young woman whose catheter was removed
 - Remove or replace catheters at the onset of therapy (especially if in place for >14 days)

Management of Recurrent Cystitis

Non-ABX Options

- Assess treatable causes
 - after menopause: emptying, cystocele, vaginal atrophy men: bladder outlet obstruction/BPH, aging: neurogenic bladder
- Inhibition of bacterial adherence:
 - cranberry products and D-mannose(2g daily max) – E. coli prevention
- Probiotics:
 - small RCTs of intravaginal lactobacillus results in high colonization and prevents UTI
- Liberal water intake
 - RCT: adding 1.5L daily reduced cystitis rate by 50% (JAMA IM 2018)
- Acidifying urine: (e.g. vitamin C 500 mg twice daily)
 - may work in some scenarios (small effect), beware of crystals/dehydration (minimal effect)
- Methenamine salts (methenamine mandelate)
 - Mandelate / Hippurate reduce urine pH (can add vitamin C) → methenamine hydrolyzed to ammonia & formaldehyde → bactericidal = antiseptic
- Topical estrogen products: shift vaginal pH and flora
 - Target population: postmenopausal
 - Two randomized studies demonstrated a relative risk of symptomatic UTI of 0.25 (95% CI 0.13–0.50) and 0.64 (95% CI 0.47–0.86)

Methenamine Hippurate not inferior to low dose antibiotic prophylaxis for treatment of recurrent UTIs in women

- *BMJ* 2022; 376 doi: <https://doi.org/10.1136/bmj-2021-0068229> (Published 09 March 2022)



Summary



Methenamine hippurate could be an appropriate non-antibiotic alternative to prophylactic antibiotics for women with recurrent UTIs, informed by patient preferences and antibiotic stewardship

Study design



Randomised non-inferiority trial

Open label

Recruited women from eight centres across the UK

Population



240 adult women with recurrent UTIs requiring prophylactic treatment

Median average 6 UTIs in 12 months before trial entry in both groups
Peri-/post-menopausal: 59%
Average age: 50 years

Comparison

Experimental

Methenamine hippurate
Taken twice daily for 12 months

120

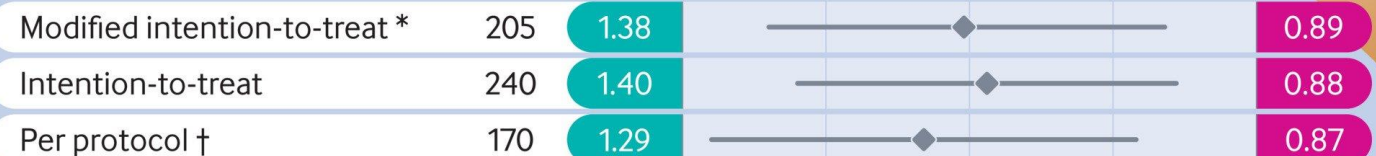
Control

Antibiotic prophylaxis
Nitrofurantoin, trimethoprim, or cefalexin taken daily for 12 months

120

Outcomes

Incidence of symptomatic, antibiotic treated UTIs over the 12 month treatment period



* All participants observed for \geq six months

† Participants who achieved \geq 90% adherence

‡ Methenamine hippurate minus antibiotic prophylaxis

Recurrent Cystitis

Antibiotic approach

- Preferred:
 - self diagnosis, self treatment (with or without standing UA/reflex culture order)
= pill in pocket
 - Postcoital PPX: single dose after intercourse, treatment dose x1
 - TMP-SMX SS
 - nitrofurantoin, 50–100 mg
 - cephalexin, 250 mg
- When all else fails, a period of continuous prophylaxis: daily (typically bedtime) dose (keep brief)
 - 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 10 days
 - Reassess need after a few months

- ≥ 66 Y years
- 4.7% prophylaxis 3.6% controls required ED visit or hospitalization for UTI, sepsis, or bloodstream infection
- More C diff with ABX
- Limitations: retrospective, populations may differ

Risks may outweigh benefits for urinary tract infection (UTI) prophylaxis in older adults



Antibiotic prophylaxis

was defined as at least 30 days of antibiotics after a positive urine culture for presumed prevention of UTI in adults over 66 years

1.7%

of patients received antibiotic prophylaxis

Antibiotic prophylaxis recipients experienced more harm

compared to patients without antibiotic prophylaxis



1.3x risk of hospital visit



1.6x risk of *C. difficile* diarrhea



1.3x risk of antibiotic resistance



1.6x risk of side effects

Langford BJ, Brown KA, Diong C, Marchand-Austin A, Adomako K, Saedi A, Schwartz KL, Johnstone J, MacFadden DR, Matukas LM, Patel SN, Garber G, Daneman N. The Benefits and Harms of Antibiotic Prophylaxis for Urinary Tract Infection in Older Adults. *Clinical Infectious Diseases*. 2021



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Imaging and Urologic Workup of Patients with UTI, rUTI

- Most outpatient uUTI or rUTI don't warrant imaging or urologic evaluation
 - Yield of evaluation low for recurrent cystitis, single simple pyelonephritis episode
 - Postvoid residual measurement / voiding assessment useful after menopause
- CT or renal ultrasound guided by clinical concern:
 - rUTI: relapse/suspicion for nidus or complications
 - ?nephrolithiasis (e.g. recurrent *Proteus*/urea splitters, persistent haematuria, pain)
 - Anatomic issues (e.g. prior surgery/adhesions)
 - non-response to adequate therapy
 - Remember: obstructed UTI = medical emergency = urgent imaging
- Urology or urogynaecology evaluation
 - Suspected neurogenic bladder or voiding issues (UDS), anatomic issues (stricture, diverticula)
 - Need for cystoscopy to assess bladder for alternative or reversible dx (e.g. interstitial cystitis, cystitis cystica, neoplasms)
 - Nephrolithiasis
- ID role
 - Education, prevention, stewardship, challenging cases

Takeaways/Summary (MOC points)

- Select patients with simple cystitis may be treated empirically, without laboratory studies (organisms and likelihood of resistance predictable)
- A negative urinalysis has excellent negative predictive value for a clinical significant urinary infection
- Community drug resistance is on the rise (know and assess risk factors)
- Some cUTI, including bacteremic, may be treated with a short (7d) course
 - must demonstrate clinical improvement + source control
- Indications to treat asymptomatic bacteriuria are narrow (preg, urologic procedures)
- For rUTI prevention prioritize stewardship - begin with non antibiotic approaches
- Imaging, urologic, and urogynecologic referrals should be guided by a clinical suspicion for a treatable finding



Additional Selected References (more in individual slides)

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