Complicated Urinary Tract Infections: A Practical Review of the 2025 IDSA Guidelines

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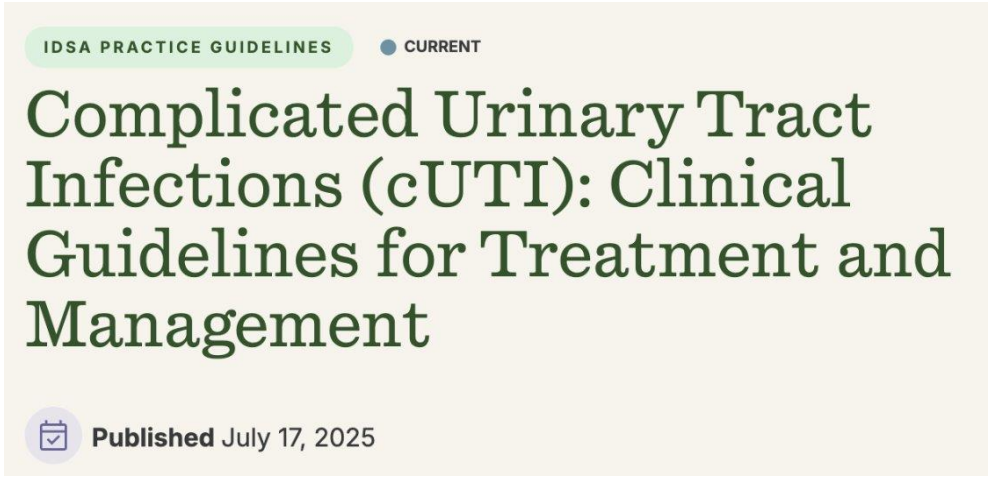
Why a New Guideline



- Prior IDSA guidance (2010)
  - Focused on acute uncomplicated cystitis & pyelonephritis in women
    - "diagnoses limited in these guidelines to premenopausal, non-pregnant women with no known urological abnormalities or co-morbidities"
- Updates guidance for
  - Definitions of uUTI and cUTI
  - Oral step-down therapy
  - Shorter duration of therapy (5-7 days most cUTI)
  - Men & catheters

New classifications of uUTI and cUTI

Old Classifications

Uncomplicated UTI: Acute cystitis in afebrile nonpregnant premenopausal women with no diabetes and no urologic abnormalities

Acute Pyelonephritis: Acute kidney infection in women otherwise meeting the definition of uncomplicated UTI above

Complicated UTI: All other UTIs

New Classifications

Uncomplicated UTI: Infection confined to the bladder in afebrile women or men

Complicated UTI: infection beyond the bladder in women or men

- Pyelonephritis
- Febrile or bacteremic UTI
- Catheter-associated (CAUTI)
- Prostatitis* (*not covered by these guidelines)

Complicated UTI: infection beyond the bladder

- Pyelonephritis
- Febrile OR bacteremic UTI
- Catheter associated UTI
  - "Patients with systemic symtpoms associated with trans-uretheral, supra pubic, or intermittent cath is encompassed in cUTI"
- Prostatitis (not covered by these guidelines)

Box 1: Complicated UTI classifications for guidelines purposes (intended to guide treatment not diagnosis)

- Clinical presentation:
  - Complicated UTI is accompanied by symptoms which suggest an infection extending beyond the bladder, including:
    - Fever
    - Other signs or symptoms of systemic illness (including chills, rigors, or hemodynamic instability)
    - Flank pain
    - Costovertebral angle tenderness
  - Pyelonephritis is encompassed in complicated UTI.
  - UTI with systemic symptoms associated with transurethral, suprapubic, or intermittent catheterization is encompassed in complicated UTI.
- Populations:
  - Patients with complicated UTIs may have an indwelling urinary catheter, neurogenic bladder, urinary obstruction, or urinary retention as an underlying condition.
  - These guidelines are not intended to apply to bacterial prostatitis, epididymitis, or orchitis.

Uncomplicated UTI

- Cystitis: dysuria, urgency/frequency, and suprapubic pain
  - No fevers
  - No other signs of systemic illness (no chills, rigors, "unstable vital signs")
  - No flank pain or CVA tenderness
- Populations:
  - Can occur in females or males
  - Underlying urologic abnormalities
    - Except catheters
  - Immunocompromised
  - T2DM

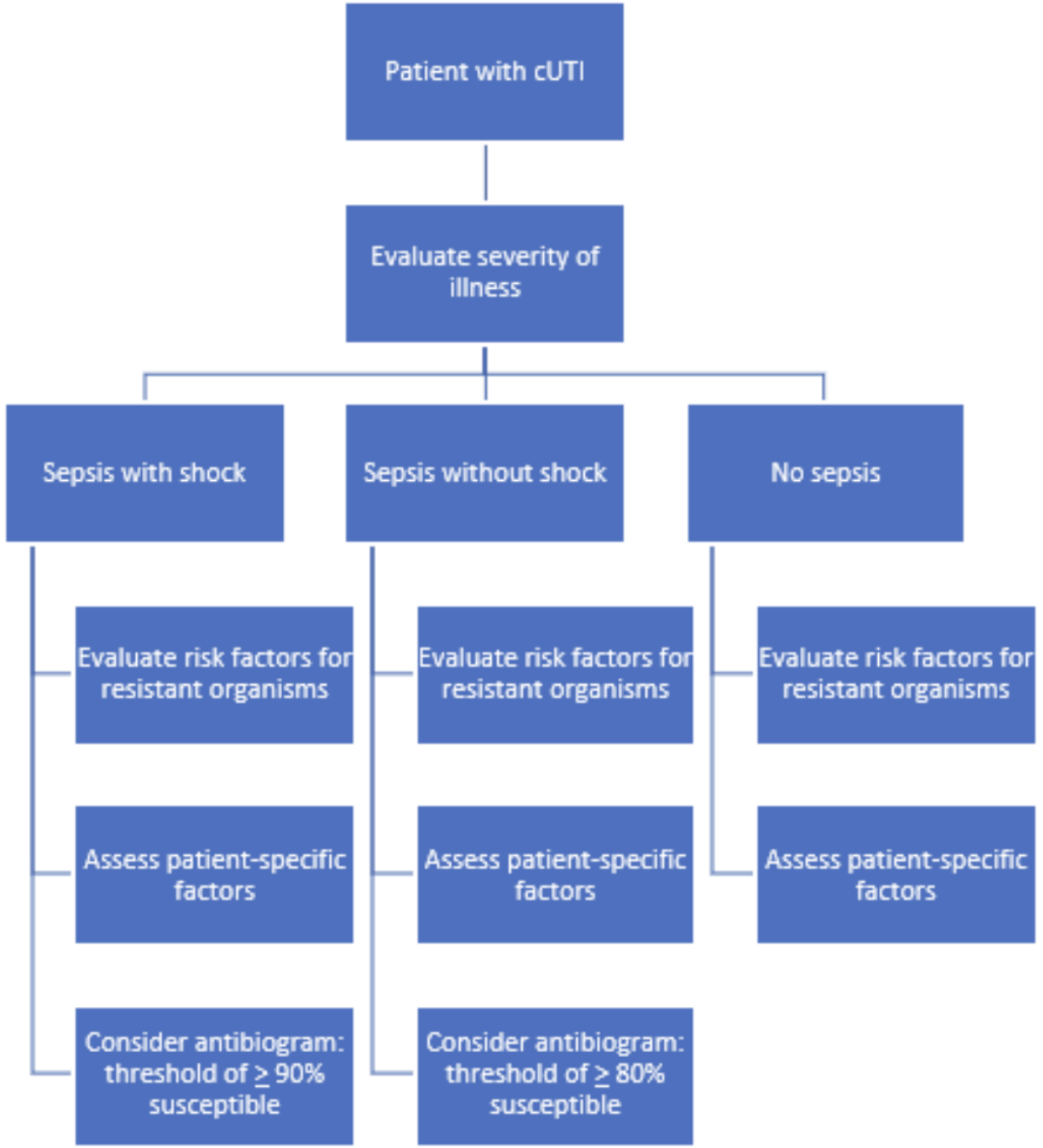
Box 2: Uncomplicated UTI classifications for guidelines purposes (intended to guide treatment, not diagnosis)

- Clinical presentation:
  - A clinical syndrome characterized by local bladder signs and symptoms such as dysuria, urgency, frequency, and suprapubic pain.
  - Uncomplicated UTI is presumed to be confined to the bladder and is defined by absence of signs or symptoms which suggest an infection extending beyond the bladder:
    - No fever, unless explained by a non-UTI cause
    - No other signs or symptoms of systemic illness (including chills, rigors, or unstable vital signs), unless explained by a non-UTI cause
    - No flank pain
    - No costovertebral angle tenderness
- Populations:
  - Uncomplicated UTI can occur in females or males, patients with underlying urologic abnormalities, patients with immunocompromise, and persons with diabetes. Recurrent UTI can be uncomplicated.
  - Patients with urinary catheters (including transurethral, suprapubic, and intermittent catheterization), stents, and percutaneous nephrostomy tubes generally do not have uncomplicated UTI.
  - These guidelines are not intended to apply to bacterial prostatitis, epididymitis, or orchitis.

Empiric Therapy

4-Step Approach

1. Severity of illness
   - No sepsis
   - Sepsis w/o shock
   - Sepsis w/ shock
2. Risk factors for resistance
3. Patient specific factors
   - Risk of allergic reaction, contra-indications, DDI
4. Local antibiogram
   - Shock = empiric agent >90% susceptible
   - Sepsis >80% susceptible



Condition of the patient	Patient risk factors	Preferred	Alternative
Sepsis with or without shock	Risk of resistance Allergy Contraindications Drug-Drug interactions Antibiogram thresholds (>90% susceptible if shock, >80% if sepsis)	3rd or 4th gen cephalosporins, carbapenems, piperacillin-tazobactam, fluoroquinolones	Novel beta lactam-beta lactamase inhibitors (ceftolozane-tazo, ceftaz-avi, meropenem-vabor), cefiderocol, plazomicin, or older aminoglycosides
Without Sepsis, IV route of therapy	Risk of resistance Allergy Contraindications Drug-Drug interactions	3rd or 4th gen cephalosporins, piperacillin-tazobactam, fluoroquinolones	Carbapenems, newer agents (novel beta lactams-beta lactamase inhibitors, cefiderocol, plazomicin), or older aminoglycosides
Without sepsis, oral route of therapy	Risk of resistance Allergy Contraindications Drug-Drug interactions	Fluoroquinolones or trimethoprim-sulfamethoxazole	Amoxicillin-clavulanate or oral cephalosporins

Empiric antibiotics: Pearls

Resistant Uropathogen(s)

- Avoid antibiotic if prior resistance shown in urine
  - More recent urine cultures (6-12 months) may be better guide than distant cultures
- Avoid fluoroquinolones empiric if patient exposure within 12 months (suggestion)

Tailoring cUTI Empiric Therapy w/ Antibiogram

- Sepsis: suggest using antibiogram to further tailor empiric therapy choice
  - Use agent with >90% local susceptibility if septic shock, >80% if sepsis w/o shock
- Without sepsis: no specific recommendations about using antibiogram
  - Pts w/o sepsis have lower risk of mortality from cUTI (</= 5%)
  - Routine use of broader-spectrum agents in cUTI w/o sepsis may drive resistance w/o pt benefit

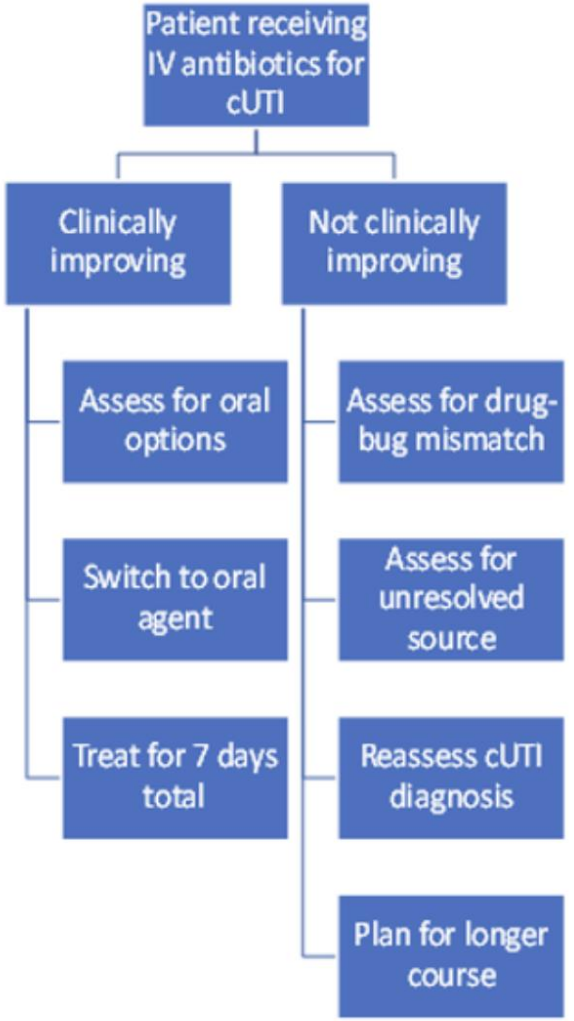
Oral Step-Down: Earlier Than You Think

Switch to Orals When:

1. Afebrile, improving, w/ source control
2. Reliable GI absorption
3. Susceptible organism

Usually 48-72 hours

Pts w/ or without bacteremia



Oral Step-Down Regimens

1st line agents: achieve therapeutic levels in urine and relevant tissue

- Fluoroquinolones (levofloxacin, moxifloxacin, ciprofloxacin)
- Trimethoprim-sulfamethoxazole

Alternatives:

- Oral beta-lactams
  - Studies comparing oral beta-lactams vs oral FQ/TMP-SMX have found lower clinical and microbiologic cure.
  - Concern standard dosing may not achieve adequate levels in urine/tissue

Beta-Lactam Caveats

Beta Lactams Considered to be bioavailable (optimized dosing):

- Amoxicillin 1000 mg Q8H (amoxicillin 80% oral absorb, 50-70 urinary excretion)
- Amoxicillin-clav 875-1000 mg Q8H (amoxicillin 80% oral absorb, 50-70 urine excretion)
- Cephalexin 500-1000 mg orally Q6H (90% oral absorb, ~90% urinary excretion)

Non-highly bioavailable, with supporting observational data

- Cefpodoxime 400 mg Q12H (50% oral absorb, 80% urinary excretion)
- Cefuroxime 500 mg Q12H (52% oral absorb, 90% urinary excretion)

Low bioavailability/tissue penetrations/limited-no use for cUTI:

- Cefdinir, cefadroxil, cefaclor, ampicillin
- Nitrofurantoin, fosfomycim not recommended (fosfomycin may be option for prostatitis)

Duration of Therapy

- 5-7 days: most cUTI who are improving clinically on effective therapy
  - 5-7 days of a fluoroquinolone
  - 7 days of a non-fluoroquinolone antibiotic
  - 7 days if bacteremic cUTI
- No default 10-14 days
- Caveats:
  - Men with febrile UTI in whom acute bacterial prostatitis is suspected may benefit from a longer treatment duration
  - Most studies supporting shorter duration excluded indwelling catheteers, immunocompromising conditions, CKD, complete urinary obstruction, or undergoing urologic surgical procedures

Supplemental Data for Oral Switch

- Inclusion:
  - RCTs including adults w/ cUTI w/ or w/o bacteremia
  - Intervention group switched to after single dose IV/IM orals when clinically stable
  - Control group continued parenteral therapy
- Excluded:
  - Children, renal transplant, neutropenia, pregnancies
- Studies:
  - Included 4 studies for review

Supplemental Data:

- 4 studies (Italy, Thailand x3)
- IV therapy x 3 days
  - Switch oral FQ 3/4 studies
  - Switch oral 3rd gen beta lactam in ¼
  - Duration total 10-14 days

Study *(Lead author, Year of publication, Name of trial, Countries)*	**Population** *(Type UTI, Year of enrollment, n randomised, F (%), Age in Intervention vs Comparator groups)*	**Study design** *(Non-inferiority margin if applicable, primary outcome with its timing)*	**Main uro-pathogens** *(% of resistance)*	**Timing of randomisation / Criteria for transition to PO**	**Intervention** *(IV and PO antibiotics, total duration)*	**Comparator** *(IV antibiotics, total duration)*
Concia 2006 Italy (multicentric)	cUTI or uUTI associated with confirmed/ suspected sepsis (not admitted to ICU) Year of enrollment: NR N= 47 F: NR Age (mean): 49.0 vs 59.0y	Descriptive trial CC 1 to 5 days after EOT	*E. coli* (87.5%) R: NR	Randomisation: at day 1 Criteria for transition to PO: after at least 3 days of IV if resolution of at least one of the clinical symptoms, afebrile on two consecutive measures, clinically stable with normal CNS and no GI disorders	IV levofloxacin with/without IV amikacin X 3-7 days followed by oral levofloxacin (switch occurred at a median of 5 days in 82.6% of this arm) Total duration: maximum of 14 days (median 11 days received)	IV piperacillin-tazobactam +/- IV amikacin X 3-7 days Total duration: maximum of 14 days (median of 17 days received)
Malaisri 2017 Thailand	Non-bacteremic presumptive AP caused by ESBL-*E. coli* 2012-2015 N= 36 F: 66.7% Age (median): 72.3 vs 65.0y	Descriptive trial CC at day EOT	*E. coli* (100%) R: ESBL-*E.coli* (100%), but 0% to ertapenem and 5.6% (2/36) to sitafloxacin	Randomisation: at day 3 Criteria for transition to PO: NR	IV carbapenems (meropenem, imipenem, doripenem or ertapenem) followed by oral sitafloxacin Total duration: 10 days	IV ertapenem Total duration: 10 days
Monmaturapoj 2012 Thailand	Presumptive AP 2010-2011 N= 82 F: 96.3% Age (mean): 41.7 vs 48.6y	Non-inferiority trial Margin 25% for CC at EOT	*E. coli* (83.5%) R: 31.6% to fluoroquinolones but 0% to studied drugs	Randomisation: at day 3 if criteria for transition to PO meet Criteria for transition to PO: (1) clinical improvement for at least 24 h from the initial presentation; (2) functioning GI tract; (3) afebrile; (4) trend towards normalized white blood cells and neutrophil count values	IV ceftriaxone x 3 days, followed by oral cefditoren pivoxil Total duration: 10 days	IV ceftriaxone Total duration: 10 days
So-Ngern 2023 Thailand (multicenter)	Non-bacteremic and bacteremic presumptive AP caused by ESBL producing organisms 2015-2020 N=21	Superiority trial CC at TOC	*E. coli* (85.7%) R: ESBL (100%), but no resistance to both studied drugs	Randomisation: at day 4 if criteria for transition to PO meet Criteria for transition to PO: (1) afebrile; (2) hemodynamically stable; (3) improvement in signs,	IV empiric antibiotics (most received a 3rd gen cephalosporin but 2 received ertapenem and 1 piperacillin-tazobactam),	IV empiric antibiotics (all received a 3rd gen cephalosporin), followed by IV ertapenem

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Transition IV to PO*	Completion with IV*	Relative (95% CI)	Absolute (95% CI)		
Clinical cure (at End Of Therapy (EOT) or Test-Of-Cure (TOC))												
4[1-4]	randomised trials	serious[a]	not serious	not serious[b]	serious[c,d]	none	85/94 (90.4%)	83/92 (90.2%)	**RR 1.02** (0.96 to 1.08)	**18 more per 1,000** (from 36 fewer to 72 more)	⊕⊕◯◯ Low	CRITICAL
Recurrence of UTI (at 4 to 6 weeks)												
3[1,2,4]	randomised trials	serious[a]	not serious	not serious[b]	serious[d,e]	none	0/70 (0.0%)	2/67 (3.0%)	**RR 0.33** (0.04 to 3.05)	**20 fewer per 1,000** (from 29 fewer to 61 more)	⊕⊕◯◯ Low	IMPORTANT
Length of hospital stay (days)												
1[3]	randomised trials	serious[f]	not serious	serious[g]	serious[c]	none	Median 10.9 days (n=23)	Median 17.2 days (n=24)	-	MD **6.3 days fewer** (11.78 fewer to 0.82 fewer)	⊕◯◯◯ Very low	IMPORTANT
Serious Antibiotic Adverse Events												
4[1-,4]	randomised trials	serious[f]	not serious	not serious[c]	serious[e]	none	1/94 (1.1%)	2/92 (2.2%)	**RR: 0.65** (0.11 to 3.88)	**8 fewer per 1,000** (from 19 fewer to 63 more)	⊕⊕◯◯ Low	IMPORTANT
IV Catheter Related Adverse Events												
1[1]	randomised trials	serious[a]	not serious	not serious[b]	very serious[e,h]	none	0/41 (0.0%)	2/41 (4.9%)	**RR 0.20** (0.01 to 4.04)	**49 fewer per 1,000** (from 115 fewer to 17 more)	⊕◯◯◯ Very low	IMPORTANT
Non-Serious Antibiotic Adverse Events												
3[1,2,4]	randomised trials	serious[a]	not serious	not serious[b]	very serious[e,h]	none	3/71 (4.2%)	2/68 (2.9%)	**RR 1.35** (0.27 to 6.67)	**10 more per 1,000** (from 21 fewer to 167 more)	⊕◯◯◯ Very low	IMPORTANT

Supplemental Data:

- 4 studies (Italy, Thailand x3)
- IV therapy x 3 days
  - Switch oral FQ 3/4 studies
  - Switch oral 3rd gen beta lactam in ¼
  - Duration total 10-14 days
- Low certainty of evidence, net balance of effects favors switch to oral

Study *(Lead author, Year of publication, Name of trial, Countries)*	**Population** *(Type UTI, Year of enrollment, n randomised, F (%), Age in Intervention vs Comparator groups)*	**Study design** *(Non-inferiority margin if applicable, primary outcome with its timing)*	**Main uro-pathogens** *(% of resistance)*	**Timing of randomisation / Criteria for transition to PO**	**Intervention** *(IV and PO antibiotics, total duration)*	**Comparator** *(IV antibiotics, total duration)*
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Cases

72-year-old man with T2DM, HTN, and BPH presents with fevers and flank pain. Blood and urine cultures grow E coli (Susceptible to FQ, TMP-SMX, and ceftriaxone). Exam remarkable for CVA TTP, the prostate is non-tender. After 48 hours of ceftriaxone, he is afebrile, HDS, and tolerating oral intake

Which is the best next step?

A. Continue IV ceftriaxone 7 days
B. Switch to oral ciprofloxacin to complete 7 days total
C. Switch to oral TMP-SMX to complete 10 days total
D. Continue IV ceftriaxone until blood cultures clear

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72-year-old man with T2DM, HTN, and BPH presents with fevers and flank pain. Blood and urine cultures grow E coli (Susceptible to FQ, TMP-SMX, and ceftriaxone). Exam remarkable for CVA TTP, the prostate is non-tender. After 48 hours of ceftriaxone, he is afebrile, HDS, and tolerating oral intake

Which is the best next step?

A. Continue IV ceftriaxone 7 days
B. Switch to oral ciprofloxacin to complete 7 days total (assuming no contra-indications)
C. Switch to oral TMP-SMX to complete 10 days total
D. Continue IV ceftriaxone until blood cultures clear

Cases

A.70-year-old woman with obstructive uropathy undergoes stent placement for infected hydronephrosis. She improves rapidly after drainage and antibiotics

What primarily determines antibiotic duration

A. Presence of prior obstruction
B. Need for urologic intervention
C. Clinical response after source control
D. Organism virulence

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C. Clinical response after source control (7 day duration)
D. Organism virulence

Cases

- 24-year-old women admitted with pyelonephritis remains febrile on day 3 of antibiotic therapy with ceftriaxone -> ciprofloxacin. Urine cultures show pan-sensitive E coli. CT A/P shows no obstruction, abscess or undrained source.

What is the best response

- Extend antibiotic duration
- Switch back to ceftriaxone
- Switch to ertapenem
- Continue current therapy without change

Cases

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What is the best response

- Extend antibiotic duration
- Switch back to ceftriaxone
- Switch to ertapenem
- **Continue current therapy without change**

Cases

49-year-old man with spinal cord injury requiring intermittent self-catheterization presents with suprapubic pain, dysuria, and fever. He is started on ceftriaxone, and after cultures/clinical improvement, switched to tmp-smx.

what is your total duration of therapy?

- 3 days
- 5 days
- 7 days
- 10 days

Cases

49-year-old man with spinal cord injury requiring intermittent self-catheterization presents with suprapubic pain, dysuria, and fever. He is started on ceftriaxone, and after cultures/clinical improvement, switched to tmp-smx.

what is your total duration of therapy?

- 3 days
- 5 days
- 7 days cUTI guidelines consider intermittent catheterization as CAUTI, and suggest 7 day course similar to other cUTI
- 10 days

Take Home Points

- Complicated UTI involves extension of infection beyond the bladder (fever, bacteremia, pyelonephritis) or indwelling catheter
- Choose empiric therapy based on illness severity, risk factors for MDR, DDI/CI, and local antibiogram
- Antibiogram adjustment may not be necessary in cUTI prior to final susceptibilities without sepsis or septic shock
- Oral step-down therapy is safe and effective after clinical improvement, with susceptible pathogen, and good tissue penetration agent
- 1st line oral agents for cUTI include FQ and TMP-SMX,
- Antibiotic duration 5-7 days is usually enough for cUTI

Questions/Comments?

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