Urinary Tract Infection

Philippine Clinical Practice Guidelines 2015 Update

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Urinary tract infections (UTI) are among the leading indications for seeking healthcare and using antimicrobials in the community and hospital settings. The current guidelines further update the recommendations following an extensive review of more recent literature. The outputs are consensus recommendations of a panel of clinicians from different societies (PSMID, POGS, PSN, PAFP, PUA).

The focus of this 2015 update will be on Asymptomatic bacteriuria, Recurrent UTI, and Complicated UTI.

Asymptomatic bacteriuria

Asymptomatic bacteriuria in adults

- Defined as bacterial counts **more than or equal to 100,000 cfu/mL**
  - Asymptomatic women: 2 consecutive voided urine specimens with isolation of the same bacterial strain
  - Men: single, clean-catch voided urine specimen with one bacterial species isolated
  - Both men and women: single catheterized urine specimen with one bacterial species isolated

- All diagnosis should be based on results of urine culture specimens that are collected **aseptically** and with **no contamination.**

Who should be screened and treated?

- Patients who will undergo genitourinary manipulation and instrumentation
- All pregnant women

*choice of antibiotic depends on culture results

** 7-day regimen is recommended

Table 2. Antibiotics that can be used for ASB in pregnancy

Antibiotics	Recommended dose and duration	FDA Risk Category
Cephalexin	500 mg BID for 7 days	B
Cefuroxime axetil	500 mg BID for 7 days	B
Fosfomycin trometamol	3 g single dose	B
Amoxicillin-clavulanate	625mg BID for 7 days	B
Nitrofurantoin* macrocrystal	100 mg QID for 7 days; 100 mg BID for 7 days for monohydrate macrocrystal formulation (not available locally)	B
Trimethoprim-sulfamethoxazole	160/800 mg BID for 7 days	C (avoid in 1st and 3rd trimester)

Who should NOT be screened and treated?

- All healthy adults
- Patients with diabetes mellitus
- Elderly patients
- Patients with indwelling catheters
- Solid organ transplant patients
- PLHIV
- Spinal cord injury patients
- Patients with urologic abnormalities

PEARLS!!!

Pyuria with ASB is not an indication for antimicrobial treatment among patients whom screening and treatment is not recommended

Optimal screening test for ASB

- **Urine culture** is the gold standard for diagnosing ASB
- In the absence of facilities with urine culture:
  - Significant pyuria (>10 wbc/hpf)*
  - Positive gram stain on unspun urine (>2 microorganisms/oif)*
- If **(-) pyuria** and **(-) organisms** → no need for urine CS

*in two consecutive midstream urine samples

Recurrent Urinary Tract Infection

Recurrent UTI in women

- Acute uncomplicated cystitis in a healthy non-pregnant woman with no known urinary tract abnormalities as documented by urine culture
  - 3 or more episodes in a 12-month period
  - 2 or more episodes in a 6-month period

- May either be a **relapse** or a **reinfection**

Relapse VS **Reinfection**	
Initial organism persists within the urinary tract and re-emerges despite adequate treatment occurring 1-2 weeks after stopping treatment	Infection is caused by a different bacterial isolate, OR by the previously isolated bacteria after a negative culture or an adequate period (>= 2 weeks) between infections

Who should be screened?

- Recommended for patients in the following situations:
  - No response to appropriate antimicrobial therapy or rapid relapse after such therapy
  - Gross hematuria during a UTI episode OR persistent microscopic hematuria
  - Obstructive symptoms
  - Clinical impression of persistent infection
  - Infection with urea-splitting bacteria (Proteus, Morganella, Providencia)
  - History of pyelonephritis
  - History of or symptoms suggestive of urolithiasis
  - History of childhood UTI
  - Elevated serum creatinine
- Patients with the factors stated above **MAY BENEFIT** from further diagnostic evaluation

Diagnostic work-ups

- All women with Recurrent UTI should undergo a complete history and PE first to evaluate urogenital anatomy and estrogenization of vaginal tissues and to detect prolapse.

- **Renal ultrasound** or **CT scan/stonogram** may be done to screen for urologic abnormalities
  - If with anatomical abnormalities ⟶ refer to specialist (nephrologist or urologist) for further evaluation

Prophylaxis for Recurrent UTI

- Recommended in women whose frequency of recurrence is not acceptable to the patient in levels of discomfort OR in interference of daily activities

- Factors in determining a patient's risk-benefit profile for prophylactic strategies:
  - Frequency and pattern of recurrences
  - Patient's lifestyle, compliance and willingness to commit to a specific regimen
  - Plans for pregnancy
  - Antimicrobial resistance and susceptibility pattern of the organism causing the UTI
  - Risk of adverse events and drug allergies

- Only initiated after counseling and behaviour modification have been attempted

Non-antimicrobial strategies

- Behavioural changes
  - Post-defecation and anal cleansing antero-posteriorly always in women to avoid contaminating the periurethral area with fecal fora
  - Post-coital douche or post-coital urination
  - Liberal fluid intake especially after intercourse
  - Avoidance of tight fitting underwear
  - Use of alternative form of contraception for women using spermicide-containing contraceptives

- Biologic mediators
  - Cranberry products

Non-antimicrobial strategies

- Hormonal treatments in post-menopausal women
  - Application of intravaginal estriol cream once each night for 2 weeks
  - Use of estradiol releasing silicone vaginal ring for 3 months
  - However, there is no insufficient data to recommend vaginal estrogen over antibiotics for the prevention of recurrent UTI

- Immunoprophylaxis
  - Immunoprophylaxis using immune-active E. coli fractions
    - Once daily per orem for 3 months

Antimicrobial strategies

- Antibiotic prophylaxis
  - Continuous prophylaxis: daily intake of a low-dose of antibiotic for 6-12 months
  - Post-coital prophylaxis: intake of a single dose of antibiotic immediately after sexual intercourse
  - Intermittent prophylaxis: self-treatment with a single antibiotic dose based on patient's perceived need.

Table 4. Antibiotics proven effective in reducing the number of recurrences of UTI[3,8,10,26,28,29,31,32,70,71]

Antibiotics	Recommended doses		
	Continuous prophylaxis	Post-coital prophylaxis	Intermittent prophylaxis
Nitrofurantoin	50-100 mg at bedtime	50-100 mg	50 mg
Trimethoprim	100 mg at bedtime	100 mg	
Cotrimoxazole	40 mg/200 mg at bedtime	40 mg/200 mg	40 mg/200 mg
CotrimoxazolE	40 mg/200 mg 3x/week	80 mg/400 mg	
Ciprofloxacin	125 mg at bedtime	125 mg	125 mg
Norfloxacin	200 mg at bedtime	200 mg	200 mg
Ofloxacin		100 mg	
Pefloxacin	400 mg weekly		
Cefalexin	125-250 mg at bedtime	125-250 mg	
Cefaclor	250 mg at bedtime		250 mg
Fosfomycin	3 g every 10 days		
Amoxicillin			500 mg
Cefuroxime			250 mg

Antimicrobial strategies

- For individual episodes of UTI in women with recurrent UTI:
  - Any of the antibiotics for acute uncomplicated cystitis may be used
  - Consider intermittent self-administered therapy in highly educated, well-informed, motivated patients

Table 5. Antibiotics for acute uncomplicated cystitis

Antibiotics		*Recommended dose and duration*
Primary	Nitrofurantoin monohydrate macrocrystals (not sold locally)	100 mg BID for 5 days PO
	Nitrofurantoin macrocrystals	100 mg QID for 5 days PO
	Fosfomycin trometamol	3 g single dose PO
Alternative	Pivmecillinam (not sold locally)	400 mg BID for 3–7 days PO
	Ofloxacin	200 mg BID for 3 days PO
	Ciprofloxacin	250 mg BID for 3 days PO
	Ciprofloxacin extended release	500 mg OD for 3 days PO
	Levofloxacin	250 mg OD for 3 days PO
	Norfloxacin	400 mg BID for 3 days PO
	Amoxicillin-clavulanate	625 mg BID for 7 days PO
	Cefuroxime axetil	250 mg BID for 7 days PO
	Cefaclor	500 mg TID for 7 days PO
	Cefixime	200 mg BID for 7 days PO
	Cefpodoxime proxetil	100 mg BID for 7 days PO
	Ceftibuten	200 mg BID for 7 days PO
ONLY if with proven susceptibility	Trimethoprim-sulfamethoxazole (TMP-SMX)	160/800 mg BID for 3 days PO

MYTH BUSTERS!!

- Cranberry juice and cranberry products for the treatment of UTI → **NOT RECOMMENDED**
- Coconut juice in the prevention and treatment of UTI → **NO AVAILABLE EVIDENCE**
- Oral water rehydration (2-2.5 liters/day) in the prevention or treatment of UTI → **INSUFFICIENT EVIDENCE**
- Drinking more water and voiding before and after intercourse to prevent UTI → **INSUFFICIENT EVIDENCE**

Complicated Urinary Tract Infection

Complicated UTI

- Significant bacteriuria plus clinical symptoms, which occurs in the setting of:
  - Functional or anatomic abnormalities of the urinary tract or kidneys
  - The presence of an underlying disease that interferes with host defense mechanisms
  - Any condition that increases the risk of acquiring [persistent] infection and/or treatment failure

Table 6. Conditions that define complicated UTI

Presence of structural abnormalities causing urinary stasis and obstruction of the genitourinary tract Obstructive uropathy due to carcinoma, bladder outlet obstruction, calculus, or cystocoele Urethral or ureteric strictures, tumors, calculi and other urologic anatomic abnormalities Polycystic kidney disease
Functional abnormalities that affect normal urine outflow Incomplete emptying of the bladder with >100 ml retained urine post-voiding Vesico-ureteral reflux Neurogenic bladder, spina bifida, multiple sclerosis
Conditions that interfere with host defense mechanisms Azotemia due to intrinsic renal disease Renal transplantation Diabetes mellitus Immunosuppressive conditions – e.g. febrile neutropenia, myeloproliferative disorders, chemotherapy
Iatrogenic conditions Presence of an indwelling urinary catheter or intermittent catheterization, stents Peri- or post-operative UTI Surgically created abnormalities
Pathogen-related complicating factors UTI caused by unusual pathogens (M. tuberculosis, Candida spp.) UTI caused by antibiotic-resistant or multi-drug resistant organisms (MDROs)
Others UTI in males except in young males presenting exclusively with lower UTI symptoms Chemical or radiation injuries of the uroepithelium Urosepsis or severe pyelonephritis

Complicated UTI

- Patients with complicated UTI that need hospitalization:
  - Patients with marked debility and signs of sepsis
  - Patients in whom there is uncertainty in diagnosis
  - Patients in whom there is concern about adherence to treatment
  - Patients who are unable to maintain oral hydration or take oral medications

- Patients with mild to moderate illness (symptoms of fever and lower or upper UTI **WITHOUT** urosepsis, circulatory failure and/or organ dysfunction or failure), and those who do not fall under the above categories may be treated on an **OUTPATIENT** basis.

Diagnostic work-ups

- **Urine gram stain** and **culture and sensitivity** testing must be done before initiating any treatment

- Imaging of the urinary tract is warranted in the following cases:
  - Pyelonephritis that is not responding to usual treatment
  - Severe pyelonephritis in certain high-risk groups
  - Recurrent UTI in a man

- Imaging modality to be used may depend on local availability
  - **CT Scan** >> KUB ultrasound

Treatment

- For mild to moderate illness:
  - Oral fluoroquinolones OR Amoxicillin/Clavulanic acid (if there are no risk factors for infection with antibiotic resistant organisms)

- For severely-ill patients:
  - Broad-spectrum parenteral antibiotics which would depend on:
    - Expected pathogens
    - Result of urine gram stain
    - Current susceptibility patterns
    - Risk factors for the acquisition of drug-resistant organism
  - Fluoroquinolones are not recommended as empiric treatment

Treatment

- Antibiotic treatment should be at least taken for **7-14 days**
  - May be extended depending on clinical situation
- Antibiotics are **modified** according to results of the urine culture and sensitivity tests
- Outpatient Parenteral Antibiotic Therapy (OPAT)
  - When an oral regimen is not available
  - If continuation of an IV-administered antibiotic is necessary
  - Criteria:
    - Indication for parenteral antibiotic therapy in the absence of an oral or alternate route of delivery
    - No other clinical indication for hospitalization
    - Consent of the patient and/or caregiver to participate
    - Outpatient environment safe and adequate to support care

Table 10. Antibiotics that may be used as empiric therapy for complicated UTI

Oral Regimen • Ciprofloxacin 500 -750 mg BID or 1000 mg extended release tablet OD x 7-14d* • Norfloxacin 400 mg BID x 7-14d* • Ofloxacin 200 mg BID x 10-14d* • Levofloxacin 500-750 mg OD x 7-14d* • Amoxicillin/clavulanate 500 mg/125mg TID or 875 mg/125 mg BID x 7-14d
Parenteral Regimen • Amikacin 15mg/kg q24h+ • Doripenem 500 mg q8h • Ertapenem 1 gm. q24h • Gentamicin 3-5 mg/kg/day q24h+ • Imipenem-cilastin 250-500 mg q6-8h • Meropenem 1g q8h • Piperacillin-Tazobactam 2.25-4.5 gms q6-8h

**Determine if patient has risk factors for drug-resistance prior to use.*
+Monitor kidney function especially for patients with impaired renal function at baseline

Post-treatment

- After completion of antibiotics:
  - Urine culture should be **repeated** 1-2 weeks after completion
  - If significant bacteriuria persists → refer to specialists (IDS, Nephro, Uro, etc)

Specific Issues of Concern in Complicated UTI

UTI in Diabetic Patients

- Diabetic patients require **pre-treatment** urine GSCS and a **post-treatment** urine culture
  - Antibiotic therapy of at least 7-14 days (oral or parenteral)

- If with sepsis → **HOSPITALIZATION**
  - Before starting therapy, get blood culture + urine culture
  - Failure to respond to empiric therapy within 48-72 hours warrants the following:
    - Plain abdominal radiograph of the KUB
    - Renal ultrasound
    - CT-scan

- Screening and treatment for ASB in diabetic patients → **NOT RECOMMENDED**

Catheter-associated UTI

- Diagnosis of CA-UTI
  - Fever or other signs and symptoms of UTI with no other identifiable source
  - At least 10^3 CFU/mL of at least 1 bacterial species in a single catheter urine specimen or midstream voided urine specimen
  - In a patient with an indwelling, suprapubic or condom catheter or undergoing catheterization within the previous 48 hrs

- Screening and treatment for asymptomatic cases **not recommended**
  - Only for pregnant and will undergo urologic procedures
  - However data is insufficient for post-solid organ transplant and neutropenic patients

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- Pyuria alone or presence or absence of odor or cloudy urine alone are **not indications** for starting treatment

Management Catheter-associated UTI

Antibiotic	Recommended Dose and Duration
Amikacin *(First line)*	15 mg/kg q24h
Ertapenem	1g IV q24h[1]
Anti-Pseudomonal carbapenems	
Doripenem[2] Imipenem-cilastin[3] Meropenem[4]	500 mg q8h 500 mg q6h 1 g q8h
Vancomycin	1g IV q 12
Colistin (Colistimethate sodium)	
Colomycin[5]	31,250–62,500 IU/kg per day, divided in 2-4 equal doses (240-480 mg/kg/day)
Coly-Mycin	Double the dose of colomycin (400-800 mg/kg/day)

Tigecycline	100 mg IV loading dose then 50 mg IV q12
Ampicillin	1-2 g IV q6-8h
Cefepime	1-2 g IV q8-12h
Ceftazidime	1-2 g IV q8h+
Piperacillin-Tazobactam	4.5 g IV q24
Levofloxacin	750 mg q24h
Fluconazole	
Amphotericin B ± 5-flucytosine	

- Obtain a urine gram stain and culture **before** starting antibiotics
  - Urine should be obtained from the freshly placed catheter by aspirating from the catheter port or by puncturing the distal end of the catheter with a sterile needle
  - If the catheter has been removed, a mid-stream collection should be obtained
  - All urine should be processed as soon as possible or refrigerated and used within 24 hrs
- Antibiotics are institution specific and dependent on local susceptibility patterns
- Remove the indwelling catheter whenever possible or replace with new catheters before initiating therapy for UTI

Strategies for Reducing Risk

Strategy	Strength of Recommendation
Use indwelling catheters only when necessary	Strong
Use aseptic technique including appropriate hand hygiene and sterile gloves	Strong
Allow only trained health personnel to insert Foley catheters	Weak
Properly secure catheters after insertion to prevent movement and urethral traction	Weak
Maintain a closed sterile drainage system.	Strong
Maintain good hygiene at the catheter-urethral interface.	Strong
Maintain unobstructed urine flow	Strong
Remove catheters when no longer needed.	Strong
Do not change indwelling catheters or drainage bags at fixed intervals.	Weak

- Periodic assessment of compliances is recommended
- Alternatives to indwelling catheter:
  - Condom catheter provided post void urine is minimal and patient has no cognitive impairment
  - Intermittent catheterization but requires a trained healthcare staff and a cooperative patient
  - Suprapubic catheterization when there are excellent support mechanisms from the surgical and caregiver staff
- **AVOID**
  - Use of antibiotic coated catheters
  - Use of systemic prophylactic antibiotics
  - Catheter or irrigation with antimicrobial agents
  - Addition of antibiotics or antiseptics to drainage bags and valves
  - Daily meatal care
  - Arbitrarily changing catheters and bags

Renal abscess

- Strongly considered in :
  - diabetic patients presenting with **hypotension** and **renal impairment**
  - Patients suspected to have upper UTI who remain afebrile and hypotensive **72 hours after** initial IV antibiotic administration

- Diagnostics
  - CT scan >> ultrasound
  - Urine and blood cultures
  - Abscess aspirate culture (if possible)

Renal abscess

- Management
  - Empiric treatment
    - Should have activity against gram-negative organisms (Escherichia coli, Klebsiella sp., and Proteus mirabilis)
    - Guided by local antimicrobial susceptibility patterns
  - Surgical intervention
    - Lesions <5cm - not needed; antibiotics given alone for 4-10 weeks until abscess has regressed as evidenced by CT scan
    - Lesions >5cm - Percutaneous drainage considered; if unsuccessful, open drainage should be considered (antibiotics given for min 4 weeks)
  - Vancomycin
    - Given if there is another source of infection where *S. aureus* is suspected

UTI in Renal Transplant Patients

- Management
  - Initial: **empiric broad-spectrum antibiotics** → If with cultures, specific therapy initiated
  - Patients with early UTI OR UTI with s/sx of pyelonephritis or sepsis:
    - Admitted and started on IV antibiotics
    - If with cultures, IV antibiotics → oral
  - Late cystitis vs Late pyelonephritis
    - **Late cystitis**: treated for 7 days abx
    - **Late pyelonephritis:** treated for 14 days abx
  - Patients with recurrent or relapsing UTI:
    - Worked up for any functional or anatomic abnormalities

Table 17. Recommended empiric antibiotics for early post–kidney transplant UTI

Gram-Negative Organism	Gram-Positive Organism
meropenem	vancomycin
ertapenem	linezolid
imipenem	nitrofurantoin*
doripenem	tetracycline*
amikacin	
nitrofurantoin*	

* Reserved for asymptomatic bacteriuria or cystitis only

UTI in Renal Transplant Patients

- Prophylaxis
  - Oral Trimethoprim-sulfamethoxazole 160mg/800mg BID immediately post-transplant
    - OD as soon as catheter is removed or patient is discharged x 6 months

REFERENCES:

Philippine Clinical Practice Guidelines on the Diagnosis and Management of Urinary Tract Infections in Adults 2015 Update: Part 2 Asymptomatic Bacteriuria in Adults, Recurrent Urinary Tract Infection, and Complicated Urinary Tract Infection.

THANK YOU!