Philippine Practice Guidelines Group in Infectious Diseases - An Initiative of the Philippine Society for Microbiology and Infectious Diseases

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Urinary Tract Infection: Clinical Practice Guideline.
PPGG-ID Philippine Society for Microbiology and Infectious Diseases.
Volume 1 No. 1 Quezon City, Philippines.
Algorithm for Urinary Tract Infection

1. Patients with symptoms of upper or lower UTI

2. Male?
   - Y: Go to Section VII: UTI in Males
   - N: Proceed to next step

3. Pregnant?
   - Y: Go to Section IV: UTI in Pregnancy
   - N: Proceed to next step

4. Any Risk Factor (Listed in Table 1)?
   - Y: Go to Section VI: Complicated UTI
   - N: Proceed to next step

5. Symptoms of Upper UTI?
   - Y: Go to Section II &/or Fig. C: Acute Uncomplicated Pyelonephritis
   - N: Proceed to next step

6. Recurrent (>2x/year)?
   - Y: Go to Section V: Recurrent UTI
   - N: Go to Section 1 &/or Fig. B: Acute Uncomplicated Cystitis

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1 Symptoms of lower UTI include any of the following: dysuria, frequency, urgency, gross hematuria or hypogastric pains.
The syndrome of upper UTI includes fever, chills, flank pain, costovertebral angle tenderness, nausea and vomiting, with or without lower UTI.
Algorithm for Acute Uncomplicated Cystitis

1. Acute Uncomplicated Cystitis
2. Treat Empirically with 3-Day Course of Antibiotics (Listed in Table 2)
3. Reassess on Day 3
4. Symptoms improved on Day 3?
5. Symptoms completely resolved on Day 3?
6. No further treatment
7. Do urine CS & change antibiotics empirically pending CS results
8. Continue antibiotics to Day 7
9. Symptoms completely resolved on Day 7?
10. Treat as Complicated UTI Go to Section VI

FIGURE B
Algorithm for Acute Uncomplicated Pyelonephritis

1. Acute Uncomplicated Pyelonephritis

2. Assess severity of illness and compliance

3. Too ill, septic or likely to be non-compliant?

4. - Hospitalize
   - Do urine GS, CS
   - Do blood CS 2x
   - Start IV antibiotics (Listed in Table 3)
   - Revise when CS results become available

5. - Treat as outpatient
   - Do urine GS, CS
   - Start oral antibiotics (Listed in Table 3)
   - Revise when CS results become available

6. Reassess within 72 hours

7. Symptoms improved on Day 3?

8. - Shift antibiotic to oral when patient afebrile for >24 hours
   - Continue antibiotics to Day 14
   (See Section II.3.4)

9. - Consider urologic evaluation
   - Refer to a specialist as necessary

FIGURE C
INTRODUCTION

Urinary tract infections (UTIs) are among the most common infections encountered by physicians. In out-patient clinics of tertiary centers in Manila, Cavite and Davao, they account for 5 to 17% of consultations. The Philippine Renal Disease Registry of the Philippine Society of Nephrology reports chronic pyelonephritis as the cause of end stage renal disease in 11% of patients undergoing maintenance dialysis and 8% of kidney transplant patients from six centers. UTIs also constitute over 40% of hospital-acquired infections.

The clinical practice guidelines (CPGs) on UTIs are formulated to assist practitioners in the diagnosis, treatment and prevention of UTI in adults. The targeted users are general practitioners, family physicians and specialists.

To cover the various important issues on UTI management, recommendations are provided for each of the following eight clinical syndrome, which differ from one another in terms of clinical presentation, epidemiologic setting and requirements for antimicrobial therapy: acute uncomplicated cystitis, acute uncomplicated pyelonephritis, asymptomatic bacteriuria, UTI in pregnancy, recurrent UTI, complicated UTI, UTI in men and catheter-associated UTI.

The standards are not intended to supplant good clinical judgment. This caveat applies to all recommendations, particularly those for which there is inadequate evidence for or against their use (Grade C). Despite lack of quality evidence, some recommendations which are based on clinical experience, descriptive studies and/or consensus reports of expert committees have been provided to specifically address common problems which confront health care providers and their patients.

I. ACUTE UNCOMPLICATED CYSTITIS IN WOMEN

1. Definition

1.1. Acute uncomplicated cystitis in women is defined as growth of >100 colony-forming units (cfu)/mL of midstream urine (msu) in non-pregnant women (18 to 50 years old), presenting with: (a) any of the following symptoms: dysuria, frequency, urgency, gross hematuria, or hypogastric pains; and (b) without symptoms of vaginitis, pyelonephritis, and risks factors for subacute pyelonephritis or complicated UTI (Table 1) (Grade A). For inclusion of patients in clinical trials, a diagnostic criterion of ≥1,000 cfu/mL is recommended (Grade C).

Note: A table summarizing laboratory criteria for significant bacteriuria and pyuria for various UTI syndromes is found in Appendix 2. Laboratory criteria are based on the requisite that urine specimens are properly collected and handled (see Appendix 4).

<table>
<thead>
<tr>
<th>Table 1. Risk factors for subacute pyelonephritis or complicated UTI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital acquired infection</td>
</tr>
<tr>
<td>Indwelling urinary catheter</td>
</tr>
<tr>
<td>Recent urinary tract infection</td>
</tr>
<tr>
<td>Recent urinary tract instrumentation (in the past 2 weeks)</td>
</tr>
<tr>
<td>Functional or anatomic abnormality of the urinary tract</td>
</tr>
<tr>
<td>Recent antimicrobial use (in the past 2 weeks)</td>
</tr>
<tr>
<td>Symptoms for &gt;7 days at presentation</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Immunosuppression</td>
</tr>
</tbody>
</table>

1.2. In the absence of a urine culture, the laboratory diagnosis of acute cystitis can be determined by the presence of significant pyuria defined as: (a) 8 or more pus cells/mm³ of uncentrifuged urine; or (b) 5 or more pus cells/hpf of centrifuged urine; or (c) positive leukocyte esterase test and nitrite test (Grade C).

Note: Pyuria per se is not automatically equated with UTI. Other important causes are listed in Appendix 5.

2. Pre-treatment diagnostic tests
Pre-treatment urine culture and sensitivity is not recommended (Grade E). Standard urine microscopy, urine microscopy using a hemocytometer and dipstick leukocyte esterase test and nitrite tests are not pre-requisites for treatment (Grade D).

3. Duration of treatment
A 3-day course of antimicrobial therapy is effective. However, patients should be advised to come back if symptoms persist or recur (Grade C).

4. Choice of antibiotics
Any of the antimicrobials listed in Table 2 can be used (Grade A). Ampicillin and amoxicillin should not be used (Grade E). In areas where trimethoprim/sulfamethoxazole (TMP/SMX) resistance is not a problem, the first line drug is still TMP/SMX. The recommended antimicrobials may change depending on the local patterns of susceptibility. Cost and side effects are additional factors to be considered in the choice (Grade C). (See Appendix 6 for costs of antimicrobial regimens)
URINARY TRACT INFECTIONS

**Table 3. 3-day regimen for uncomplicated acute cystitis**

<table>
<thead>
<tr>
<th>Duration</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 days</td>
<td>TMP/SMX 160/800 mg BID, Nitrofurantoin 100 mg QID, Norfloxacin 200 mg BID, Ciprofloxacin 250 mg BID, Pefloxacin 400 mg BID, Ofloxacin 200 mg BID, Co-amoxyclav 375 mg TID</td>
</tr>
</tbody>
</table>

5. Post-treatment follow-up
5.1. Routine post-treatment urine culture and urinalysis in asymptomatic patients are not recommended (Grade C).
5.2. Patients whose symptoms worsen or do not improve after 3 days should have a urine culture and the antimicrobial should be empirically changed, pending result of sensitivity testing (Grade C).
5.3. Patients whose symptoms improve but do not completely resolve after 3 days should complete a 7-day course of the same antimicrobial. Patients whose symptoms fail to resolve after the 7-day treatment should be managed like a complicated urinary tract infection (see Section VI) (Grade C).

II. ACUTE UNCOMPPLICATED PYELONEPHRITIS

1. Definition
The classic syndrome of acute uncomplicated pyelonephritis (AUPN) is characterized by fever (>38°C), chills, flank pain, costovertebral angle tenderness, nausea and vomiting, with or without signs and symptoms of lower urinary tract infection (dysuria, frequency, urgency and hematuria) in an otherwise healthy female with no clinical or historical evidence of structural or functional urologic abnormalities (Rubin 1992).

Laboratory findings include pyuria (>5 wbc/hpf of centrifuged urine) and bacteriuria with counts of >10,000 cfu of a uropathogen/mL in culture of voided urine (Rubin 1992, Roberts 1986).

2. Etiologic Diagnosis
2.1. Gram stain of uncentrifuged urine is recommended to differentiate gram-positive from gram-negative bacteria, the result of which can guide choice of empiric therapy (Grade C). Quantitative urine culture and sensitivity test should also be performed routinely to allow for more precise and cost-effective use of antimicrobial agents and because of the potential for serious sequelae if an inappropriate antimicrobial regimen is used (Grade C).
2.2. Blood cultures (done twice) are recommended for those who are ill enough to require hospitalization, particularly those with suspected sepsis (Grade C).
3. Treatment

Premise: The main therapeutic objectives are to eradicate organisms invading the renal parenchyma and to anticipate the need to treat bacteremia and prevent metastatic infection. Choice of antimicrobial regimen depends on the locally prevailing sensitivity patterns of common uropathogens, ease of administration and relative costs.

3.1. Outpatient vs. inpatient therapy. Non-pregnant patients with no signs and symptoms of sepsis, who are compliant and are likely to return for follow-up if symptoms do not resolve, may be treated as outpatients (Grade C). The following are indications for admission: inability to maintain oral hydration or take medications; concern about compliance; uncertainty about the diagnosis; severe illness with high fever, severe pain, marked debility and signs of sepsis (Grade C).

3.2. Selection of antimicrobial therapy. Several regimens which have been found to be effective are recommended (see Table 3) (Grades A-B). The aminopenicillins (ampicillin or amoxicillin) and first-generation cephalosporins are not recommended (Grade E). If there is increasing resistance to TMP/SMX in the area, this drug is also not recommended (Grade E). Combining ampicillin with an aminoglycoside offers no added benefit, except when enterococcal infection is suspected (Grade C). The choice of continued antibiotic therapy should be guided by the urine culture and sensitivity result once available (Grade C).

**Table 3. Treatment regimens for uncomplicated acute pyelonephritis**

<table>
<thead>
<tr>
<th>Characteristic Pathogens</th>
<th>Clinical Situation</th>
<th>Empiric Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli, P. mirabilis, K. pneumoniae, S. saprophyticus</td>
<td>Moderate- to-severe illness</td>
<td>Oral* fluoroquinolone, TMP/SMX or co-amoxiclav for 14 days</td>
</tr>
<tr>
<td>Severe illness or possible urosepsis — hospitalization required</td>
<td>Parenteral** aminglycoside, fluoroquinolone or third generation cephalosporin until fever is gone (usually after 24-48 hrs), then oral fluoroquinolone or TMP/SMX to complete 14 days.</td>
<td></td>
</tr>
</tbody>
</table>

* Oral regimens: ciprofloxacin 500 mg every 12 hours; ofloxacin 200 mg every 12 hours; norfloxacin 400 mg every 12 hours; lomefloxacin 400 mg once a day; TMP/SMX 160-
** Parenteral regimens: ceftriaxone 1-2 g once a day; ciprofloxacin 200-400 mg every 12 hours; ofloxacin 200-400 mg every 12 hours; gentamicin 3-5 mg/kg once a day or 1 mg/kg every 8 hours.

3.3. Route of administration. Patients with mild to moderate symptoms can be treated with oral antimicrobials for the total duration of treatment (Grade B). Parenteral therapy is recommended for initial management of patients who may have severe infection (presence of chills, fever, vomiting with or without shock) and for patients with nausea, vomiting or ileus (Grade C). Switching to an oral regimen is appropriate once the patient is afebrile for at least 24 hours and is able to take the drug orally (Grade C).

3.4. Duration of Therapy. The recommended duration of therapy for AUPN is 14 days for most antimicrobials, except for ciprofloxacin for which 7 days is sufficient (Grade A). Treatment for longer than 14 days has no additional benefit and is not recommended (Grade E).

4. Work-up for urologic abnormalities
Routine urologic evaluation and routine use of imaging procedures are not recommended (Grade D). Radiologic evaluation should be considered if the patient remains febrile within 72 hours of treatment to rule out the presence of nephrolithiasis, renal or perirenal abscesses, or other complications of pyelonephritis, or if there is recurrence of symptoms (Grade C). Urologic consultation should be obtained if deemed appropriate (Grade C).

5. Follow-up cultures during and post-therapy
In patients who are clinically responding to therapy (usually apparent in <72 hours after initiation of treatment), there is no need for a follow-up urine culture (Grade C). Routine post-treatment cultures in asymptomatic patients are also not indicated except in patients who initially present with sepsis (Grade C). In women whose symptoms do not improve during therapy and in those whose symptoms recur after treatment, a repeat urine culture and sensitivity test should be performed (Grade C).

6. Re-treatment
Recurrence of symptoms requires antibiotic treatment based on results of urine culture and sensitivity test, in addition to assessment for underlying genitourologic abnormality (Grade C). The duration of retreatment in the absence of a urologic abnormality is 2 weeks (Grade C). For those patients who relapse with the same strain as the initially infecting strain, a 4-6 week regimen is recommended (Grade C).

III. ASYMPTOMATIC BACTERIURI

1. Definition
Asymptomatic bacteriuria (ASB) is defined clinically by: (a) the presence of ≥100,000 cfu/mL of one or more uropathogens on two consecutive midstream urine specimens or on one catheterized urine specimen; and (b) the absence of symptoms attributable to urinary tract infection.

The risk groups most likely to have asymptomatic bacteriuria are: (1) the elderly population, especially women; (2) women with diabetes mellitus; (3) individuals with long-term indwelling catheters; (4) patients with genitourinary abnormalities; and (5) renal transplant recipients (Grade B). The risk of asymptomatic bacteriuria among pregnant women is discussed in Section IV. Infections in renal transplant recipients are discussed in Section VI.

2. Screening for bacteriuria
Periodic testing for asymptomatic bacteriuria and treatment with antimicrobials is not recommended in the elderly (Grade D), in individuals with indwelling catheters (Grade E), immunocompromised patients (Grade C) and in patients with urological abnormalities (Grade C).

Screening by urine culture is recommended in the following: patients with diabetes mellitus, patients who will undergo genitourinary manipulation or instrumentation, and after catheter removal (Grade C). The frequency of screening is left to the discretion of the clinician (Grade C).

In the absence of urine culture facilities, significant pyuria (>10 wbc/hpf) or a positive gram stain of unspun urine (2 microorganisms/oif) in 2 consecutive midstream urine samples can be used to screen for asymptomatic bacteriuria (Grade C). Urine culture and sensitivity testing are not necessary when urinalysis or gram stain of urine is normal (Grade C).

It should be noted that pyuria is not an accurate screening test for bacteriuria in patients with poor inflammatory response, e.g., immunosuppressed renal transplant recipients, or patients with diabetic nephropathy and azotemia.

3. Treatment of asymptomatic bacteriuria
Treatment of asymptomatic bacteriuria may be considered in the following patients: (a) persistent bacteriuria after catheter removal (Grade B); (b) patients who will undergo genitourinary manipulation or instrumentation; (c) diabetic patients; and (d) patients with abnormal genitourinary tract (Grade C). (See Section VI for treatment regimens).

For asymptomatic funguria, removal of predisposing factors, such as urinary catheters or prolonged antibiotic use, will generally result in spontaneous resolution (Grade C).

Treatment is not recommended in the following groups: (a) patients with long-term indwelling catheters (Grade E); (b) ambulatory elderly men and women (Grade D); and (c) patients with short-term indwelling catheters (Grade C).
IV. URINARY TRACT INFECTION IN PREGNANCY

A. Asymptomatic Bacteriuria (ASB) in Pregnancy

1. Definition
Asymptomatic bacteriuria in pregnancy is defined clinically by: (a) >100,000 cfu/mL with one or more organisms in two consecutive midstream urine specimens or one catheterized urine specimen, and (b) the absence of symptoms attributable to urinary infection.

2. Screening for asymptomatic bacteriuria in pregnancy

2.1. All pregnant women, particularly those at high risk of developing acute cystitis and acute pyelonephritis, e.g. diabetics and those with a previous history of UTI, must be screened for asymptomatic bacteriuria on their first prenatal visit (Grade A).

2.2. A standard urine culture using a clean catch midstream urine is the test of choice in screening for asymptomatic bacteriuria (Grade A). In areas where urine culture facilities are not available, a urine gram stain is an acceptable substitute (Grade C).

Leukocyte esterase and nitrite tests are not recommended for screening for ASB (Grade E). Urinalysis alone is not recommended for screening (Grade C).

3. Treatment of asymptomatic bacteriuria in pregnancy

3.1. Antibiotic treatment for asymptomatic bacteriuria is indicated to reduce the risk of acute cystitis and pyelonephritis in pregnancy as well as reduce the risk of LBW neonates and preterm infants (Grade A).

It is recommended that antibiotic treatment be initiated upon diagnosis of ASB in pregnancy (Grade A). Among the drugs which can be used are nitrofurantoin, amoxicillin, cephalexin, co-amoxiclav and TMP/SMX (not in 3rd trimester) (Grade C). A 7-day course is recommended (Grade C). A follow-up culture should be done one week after completing the course of therapy (Grade C).

B. Acute Cystitis in Pregnancy

1. Definition
Acute cystitis is characterized by urinary frequency and urgency, dysuria and bacteriuria but not by fever and costovertebral angle tenderness. Gross hematuria may also be present (Harris 1984).

In the absence of a urine culture, the laboratory diagnosis of acute cystitis can be determined by the presence of significant pyuria defined as (a) 8 or more pus cells/mm³ of uncentrifuged urine OR (b) 5 or more pus cells/hpf or centrifuged urine, and (c) positive leukocyte esterase and nitrate test (Grade C).

2. Treatment
Treatment of acute cystitis in pregnancy should be initiated immediately to prevent the spread of the infection to the kidney (Grade A). Since E. coli remains to be the most common organism isolated, drugs to which this organism is most sensitive and which are safe to give during pregnancy should be used (Grade A). A 7-day course is recommended (Grade C).

C. Acute Pyelonephritis in Pregnancy

1. Definition
Acute pyelonephritis, an inflammation of the renal parenchyma, is characterized by shaking chills, fever, flank pain, nausea and vomiting, with or without signs and symptoms of lower urinary tract infection (frequency, urgency, dysuria and hematuria) and physical findings of costovertebral angle tenderness. Urinalysis shows pyuria of ≥5 wbc/hpf of centrifuged urine and bacteriuria of >10,000 cfu of a uropathogen/mL of urine (Rubin 1992, Robert 1986, Harris 1984).

2. Etiologic diagnosis

2.1. Gram stain of uncentrifuged urine is recommended to differentiate gram positive from gram negative bacteriuria, the result of which can guide choice of empiric therapy (Grade C). Quantitative urine culture and sensitivity test should also be performed routinely to allow for more precise and cost-effective use of antimicrobial agents and because of the potential for serious sequelae if an inappropriate antimicrobial regimen is used (Grade C).

2.2. Blood cultures (done twice) are recommended for all pregnant patients with acute pyelonephritis (Grade C).

3. Treatment

3.1. All pregnant patients with acute pyelonephritis should be hospitalized and immediate antimicrobial therapy instituted (Grade A). Treatment duration is 14 days (Grade C). Choice of antibiotics is as for acute uncomplicated pyelonephritis except for drugs contraindicated in pregnancy (see Table 4) (Grade C).

Table 4. Antibiotic use in pregnancy.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Safe</th>
<th>Contra-indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalosporins</td>
<td>Amino-</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>glycoside</td>
<td>Fluoroquinolone</td>
</tr>
<tr>
<td>Ampicillin-</td>
<td>TMP/SMX</td>
<td>(1st &amp; 2nd trimester)</td>
</tr>
<tr>
<td>sulbactam</td>
<td>(3rd trimester)</td>
<td></td>
</tr>
<tr>
<td>Aztreonam</td>
<td></td>
<td>(probably)</td>
</tr>
<tr>
<td>(probably)</td>
<td></td>
<td>(Reese &amp; Betts 1996)</td>
</tr>
</tbody>
</table>

3.2. For pregnant patients with no signs and symptoms of sepsis and are able to take medications by mouth, oral antibiotics may be given as first line drugs (Grade A). Empiric choice should be based on local susceptibility patterns of uropathogens (Grade C).

V. RECURRENT URINARY TRACT INFECTION

1. Definition
Recurrent UTI is defined as episodes of acute
uncomplicated UTI documented by urine culture occurring more than twice a year in a non-pregnant woman with no known urinary tract abnormalities (Kraft 1977, Stamm 1980).

2. Treatment of individual episodes
Seven-day treatment with amoxicillin-clavulanate, cephradine, ciprofloxacin and lomefloxacin is effective (Grade A). Three-day treatment with any of the antibiotics for simple uncomplicated cystitis (see Section I) may be an acceptable alternative (Grade C). Intermittent self-administered therapy, wherein the patients are apprised of the common signs and symptoms of UTI and instructed to take four tablets of TMP/SMX (40 mg/200 mg) single dose as soon as symptoms first appear, may be recommended in well-instructed and highly educated patients (Grade A).

3. Prophylaxis
3.1 Indication for prophylaxis. Prophylaxis is recommended in women whose frequency of recurrence is not acceptable to the patient in terms of level of discomfort or interference with her normal activities. Prophylaxis may be withheld according to patient preference if the frequency of recurrence is tolerable to the patient (Grade C recommendation).

3.2. Prophylactic strategy. If prophylaxis is to be given, either of the following regimens is recommended: (1) continuous prophylaxis, defined as the daily intake of a low dose of antibiotic, or (2) post-coital prophylaxis, defined as the intake of a single dose of antibiotic immediately after sexual intercourse (Grade A).

3.3. Choice and dose of antibiotic. A number of antibiotics given continuously for 6 months have been proven to effectively reduce the number of episodes of UTI (See Table 5) (Grade A). Post-coital prophylaxis with a number of antibiotics has also been proven to be effective (see Table 5) (Grade A).

Table 5. Antibiotics which have been proven to be effective in reducing the number of recurrences of UTI and their recommended doses and regimens.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Recommended dose for continuous prophylaxis</th>
<th>Recommended dose for post-coital prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin</td>
<td>100 mg at bedtime</td>
<td>—</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>200 mg at bedtime</td>
<td>200 mg</td>
</tr>
<tr>
<td>TMP-SMX</td>
<td>40 mg/200 mg at bedtime</td>
<td>40 mg/200 mg</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>125 mg at bedtime</td>
<td>125 mg</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>—</td>
<td>100 mg</td>
</tr>
</tbody>
</table>


3.4. Duration of prophylaxis. Six-month continuous or post-coital prophylaxis effectively reduces the number of UTI episodes (Grade A).

3.5. Treatment of breakthrough infections during prophylaxis. Breakthrough infections during prophylaxis should be initially treated with any of the antibiotics recommended for uncomplicated cystitis other than the antibiotic being given for prophylaxis (Grade B). A urine culture should be requested and the treatment modified accordingly.

4. Diagnostic work-up for urologic abnormalities.
4.1. Indication for screening. Screening is not recommended for all patients (Grade E). Certain risk factors associated with a higher incidence of urologic abnormalities have been identified. Screening is recommended for patients with (1) gross hematuria during a UTI episode; (2) obstructive symptoms; (3) clinical impression of persistent infection; (4) infection with urea-splitting bacteria; (5) history of pyelonephritis; (6) history of or symptoms suggestive of urolithiasis; (7) history of childhood UTI; and (8) elevated serum creatinine (Grade C).

4.2. Choice of screening procedure. A combination of a renal ultrasound and a plain abdominal radiograph is recommended (Grade B). Patients with anatomical abnormalities should be referred to a specialist (nephrologist or urologist) for further evaluation (Grade C).

5. Prophylaxis in post-menopausal women
Use of estriol. In post-menopausal women, application of intravaginal estriol cream applied once each night for two weeks followed by twice-weekly applications for 8 months is recommended (Grade A).

VI. COMPLICATED URINARY TRACT INFECTION

1. Definition
Complicated UTI is significant bacteriuria which occurs in the setting of functional or anatomic abnormalities of the urinary tract or kidneys. The conditions that define complicated UTI include the following (Rubin 1992): (a) the presence of an indwelling urinary catheter or use of intermittent catheterization; (b) incomplete emptying of the bladder with more than 100 mL of urine retained postvoiding; (c) obstructive uropathy due to obstruction of the bladder outlet, a calculus or other causes; (d) vesicoureteral reflux or other forms of urologic abnormalities including surgically created abnormalities; (e) azotemia due to intrinsic renal disease; and (f) renal transplantation.

Other authors (Ronald & Harding 1997, Williams 1996, Stamm & Hooton 1993, Nickel 1990) have broadened the definition to include UTI in patients with metabolic, hormonal or immunologic abnormalities, such as diabetes, impaired host responses and UTI caused by pathogens which are either unusual or resistant to antibiotics.
In addition, UTI in males is generally considered complicated except in young males presenting exclusively with symptomatic lower UTI (see Section VII.1.1).

The cut-off for significant bacteriuria in complicated UTI has been set at 100,000 cfu/mL (Rubin 1992). However in certain clinical situations, low-level bacteriuria or counts <100,000 cfu/mL may be significant as in catheterized patients (Stark and Maki 1984).

2. General recommendations for the management of complicated UTI

2.1. Etiologic diagnosis. A urine sample for gram stain, culture and sensitivity testing must always be obtained prior to the initiation of any therapy (Grade C).

2.2. Treatment. Patients with complicated UTI who are unable to maintain oral hydration or take oral medications, with concern about compliance, uncertainty in diagnosis, severe illness with high fever, severe pain, marked debility and signs of sepsis require hospitalization (Grade C). Patients who do not fall under the above categories may be treated on an outpatient basis (Grade C).

2.3. For mild to moderate illness, oral fluoroquinolones are recommended. For more severe illness, parenteral antibiotics with adequately broad coverage should be used, choice of which should depend on the expected pathogens, results of the urine gram stain and current surveillance data of microorganisms in the area (Grade C). (Refer to Table 7 for regimens).

<table>
<thead>
<tr>
<th>Antibiotic Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Regimen:</strong></td>
</tr>
<tr>
<td>Ciprofloxacin 250 mg po q 12 hrs x 14 days</td>
</tr>
<tr>
<td>Norfloxacin 400 mg BID po x 14 days</td>
</tr>
<tr>
<td>Ofloxacin 200 mg q 12 hrs x 14 days</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole 160/800 q 12 hrs po x 10 days</td>
</tr>
<tr>
<td><strong>Parenteral Regimen:</strong></td>
</tr>
<tr>
<td>Amoxicillin 1 gm q 6hrs IV + gentamicin 3 mg/kg/day OD IV</td>
</tr>
<tr>
<td>Ceftazidime 1-2 gm q 8 hrs IV</td>
</tr>
<tr>
<td>Ceftriaxone 1-2 gm OD IV</td>
</tr>
<tr>
<td>Ciprofloxacin 200-400 mg q 12 hrs IV</td>
</tr>
<tr>
<td>Imipenem-cilastatin 250-500 mg q 6-8 hrs IV</td>
</tr>
<tr>
<td>Ofloxacin 200-400 mg q 12 hrs IV</td>
</tr>
</tbody>
</table>

2.4. Antibiotics are modified according to the results of the urine culture and sensitivity test. Patients started with parenteral regimen may eventually be switched to oral therapy after clinical improvement has been noted. The optimal duration of treatment is not completely established. At least 14 days of therapy is recommended (Grade C).

2.5. Further work-up to identify and correct the anatomical, functional or metabolic abnormality is

### Table 6. Pathogens identified in complicated UTI:

<table>
<thead>
<tr>
<th>Type of Complicated UTI</th>
<th>Pathogens</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter-associated UTI</td>
<td>E. coli, Pseudomonas aeruginosa</td>
<td>Warren 1997</td>
</tr>
<tr>
<td>Short-term (&lt;1 week)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Long-term (&gt;1 week)</td>
<td>Proteus mirabilis, Enterobacter Usually polymicrobial E. coli, P. aeruginosa P. mirabilis, Providencia stuartii, Morganella morgagnii, Citrobacter, Enterococcus, Candida sp.</td>
<td>Ouslander 1987</td>
</tr>
<tr>
<td>Anatomic abnormalities</td>
<td>E. coli, Klebsiella pneumoniae (37%), P. aeruginosa, Proteus mirabilis</td>
<td>Childs 1993</td>
</tr>
<tr>
<td>UTI in Diabetics</td>
<td>E. coli, Klebsiella pneumoniae, Proteus mirabilis, Enterobacter, Enterococcus, P. aeruginosa, Candida</td>
<td>Patterson and Andriele 1997</td>
</tr>
<tr>
<td>Renal Transplant Recipients</td>
<td>E. coli (29-61%), Proteus mirabilis &amp; Klebsiella pneumoniae (30%), Gram positive cocci (20%), Enterobacter, Enterococci, Serratia, Acinetobacter, Citrobacter, Pseudomonas aeruginosa</td>
<td>Schmaldienst and Horl 1997</td>
</tr>
<tr>
<td>Neutropenic Patients</td>
<td>Gram negative bacilli spec. Pseudomonas aeruginosa, Staphylococcus aureus, Candida</td>
<td>Korzeniowski 1991</td>
</tr>
<tr>
<td>UTI in AIDS</td>
<td>E. coli, Enterobacter, Klebsiella pneumoniae, Pseudomonas, enterococci, Staphylococcus aureus, Cytomegalovirus, Adenovirus, Toxoplasma, Pneumocystis carinii, Blastomyces dermatidis, Mycobacterium tuberculosis</td>
<td>Sharifi and Lee 1997</td>
</tr>
</tbody>
</table>
indicated. Referral to the appropriate specialists, such as infectious diseases, nephrology or urology should be made as necessary (Grade C).

2.6. Urine culture should be repeated one to two weeks after completion of medications (Grade C). Significant bacteriuria post-treatment needs appropriate referral (Grade C).

3. Special issues

3.1. Catheter-associated UTI. Catheterized patients with significant bacteriuria of $10^3$ cfu/mL of urine, who develop fever or other signs of bacteremia should be treated as complicated UTI (Grade B). Catheterized patients with no risk factors who are otherwise asymptomatic need not be treated with antibiotics (Grade E). Whenever possible, the indwelling catheter should be removed to help eradicate the bacteriuria (Grade A).

3.2. Patients with diabetes. Acute uncomplicated cystitis in diabetic patients require pre-treatment urine gram stain and culture and a post-treatment urine culture. At least 7-14 days of oral antibiotics is recommended (Grade C).

Diabetic patients who present with UTI and signs of sepsis should be hospitalized. Failure to respond to appropriate therapy within 48 to 72 hours warrants a plain abdominal radiograph and a renal ultrasound (Grade C).

3.3. Renal transplant patients. UTI which develop in the first three months post-operatively, as well as other UTIs which develop later with signs of pyelonephritis or sepsis, be treated with parenteral broad-spectrum antibiotics until the urine cultures become negative. Therapy can be switched to oral agents according to the culture and sensitivity results and continued to complete 4-6 weeks (Grade C).

For renal transplant patients who develop UTI within the first three months post-transplant with no evidence of sepsis may be treated as outpatients with oral antibiotics for more than 14 days (Grade C).

For renal transplant patients, TMP/SMX (160/800 mg) twice daily during the hospitalization period immediately post-surgery, then once daily upon discharge is recommended (Grade A). The actual dose of TMP/SMX should be adjusted to the renal function. Duration of prophylaxis should be given for 3 months (Grade C).

3.4. Patients with acquired immunodeficiency syndrome. In addition to the general management of complicated UTI, patients with AIDS and UTI should be evaluated to include other non-bacterial pathogens if clinically suspected and should be referred to an appropriate specialist (Grade C).

VII. URINARY TRACT INFECTION IN MALES

A. Uncomplicated UTI in Young Males

1. Definition

Urinary tract infection in males is generally considered complicated. However, the first episode of symptomatic lower urinary tract infection occurring in a young (15-40 yrs. old) otherwise healthy sexually active male with no clinical or historical evidence of a structural or functional urologic abnormality is considered as uncomplicated UTI.

2. Diagnosis

Significant pyuria in men is defined as $\geq 10$ wbc/mm$^3$ or $5$ wbc/hpf in a clean catch midstream urine specimen. This shows good correlation with bladder bacteriuria and the growth of $\geq 1000$ colonies of one predominant species/mL of urine and best differentiates sterile from infected bladder urine (Grade C).

3. Recommended diagnostic work-up

The recommended diagnostic work-up includes a urinalysis and urine culture (Grade C). Routine urologic evaluation and use of imaging procedures are not recommended (Grade C).

4. Treatment

TMP/SMX or a fluoroquinolone given for seven days is recommended (Grade C). Ampicillin, sulfonamides, tetracyclines and cephalothin are not recommended because of increasing resistance (Grade C). Choice of antibiotics should be guided by the prevailing resistance and sensitivity patterns in the community (Grade C).

B. Prostatitis

(Note: Current clinical practice guidelines include only acute and chronic bacterial prostatitis and not non-bacterial prostatitis and prostatodynia syndromes)

1. Definition

1.1. Acute bacterial prostatitis. Acute prostatitis is defined as a febrile illness with abrupt onset marked by chills, low back and perineal pain, generalized malaise and prostration. Irritative voiding symptoms including dysuria, urgency frequency and nocturia are characteristic. Rectal examination reveals a markedly tender prostate that is swoolen, firm and warm.

1.2. Chronic bacterial prostatitis. Chronic bacterial prostatitis is a more subtle illness than acute prostatitis typified by relapsing recurrent UTI caused by persistence of the pathogen in the prostate despite courses of antibacterial therapy. Symptoms consist of varying degrees of irritative voiding and pain perceived in various sites - suprapubic, perineal, low back, scrotal, penile or even the inner thighs. Rectal examination discloses no specific nor characteristic finding.

1.3. Diagnosis. In chronic bacterial prostatitis, direct microscopic examination of the expressed prostatic secretions (EPS) identifies significant prostatic inflammation at $>10$ wbc/hpf. The presence of lipid-laden macrophages is more prostate specific and strengthens the diagnosis.

Diagnosis can be further confirmed by doing the triple
voided urine test. In this examination, prostatitis can only be diagnosed if the VBI specimen is free of WBC. The diagnosis of prostatic infection is confirmed when the quantitative bacterial colony counts of EPS and the next 5 to 10 mL (VB3) of urine significantly exceed those of the urethral (VB1) and bladder (VB2) specimens. The colony count of the EPS and VB3 should exceed the VB1 by at least 1 logarithm (Grade C).

2. Treatment
2.1. For acute prostatitis, empiric treatment with TMP/SMX (160/800 mg) or an oral fluoroquinolone may be started until culture and sensitivity results are known. The course of treatment should extend to at least 30 days to help prevent the development of chronic prostatitis (Grade C).

Seriously ill patients require hospitalization and parenteral antimicrobial therapy, such as an aminoglycoside-penicillin derivative combination or fluoroquinolones (Grade C). When complications of urinary retention or the development of a prostatic abscess occurs, referral to a urologist is strongly recommended (Grade C).

2.2. For chronic bacterial prostatitis, TMP/SMX or fluoroquinolones are indicated for two to three months (Grade C).

2.3. Men with recalcitrant chronic bacterial prostatitis can be treated with radical transurethral resection of the prostate. Symptomatic relief can be achieved with Sitz baths, anti-inflammatory agents and prostatic massage and other supportive measures (Grade C).

Long-term, low-dose suppressive therapy may be required for patients who do not respond to full dose treatment. TMP/SMX 80 mg/400 mg once daily is recommended (Grade C).

VIII. PREVENTION OF CATHETER-ASSOCIATED URINARY TRACT INFECTION

1. Personnel
1.1. Only persons trained in correct aseptic techniques of catheter insertion and care should handle urinary catheters (Grade B).

1.2. Handwashing should be done immediately before and after catheter insertion or care (Grade C).

2. The catheter
2.1. Avoid unnecessary catheter use (Grade C).

2.2. Limit catheter use to carefully selected patients (Grade C). Routine catheterization during labor or immediately post-partum for collection of urine sample is not recommended (Grade C).

2.3. Catheters should be inserted using aseptic technique and sterile equipment (Grade A).

2.4. Maintain a sterile, closed catheter system at all times. Open drainage is unacceptable (Grade D).

2.5. Urine specimens should be obtained aseptically without opening the catheter-collection junction (Grade B).

2.6. Maintain unobstructed and adequate urine flow at all times (Grade B).

2.7. Do not change catheters at arbitrary fixed intervals (Grade C).

2.8. Remove the urinary catheter as soon as possible (Grade A).

3. Methods to prevent endogenous infection
3.1. Daily meatal care is not recommended (Grade E).

4. Methods to prevent exogenous infection
4.1. Irrigation of the bladder with antimicrobial agents is not useful (Grade D).

4.2. Instillation of disinfectants into the bag and the use of antireflux valves and vents are not helpful (Grade D).

4.3. Segregate infected from uninfected catheterized patients (Grade C).

5. Bacteriologic monitoring and treatment of asymptomatic bacteriuria to prevent complications (Secondary prevention).

5.1. Regular bacteriologic monitoring of catheterized patients is not recommended (Grade D).

5.2. Use of systemic antibiotic prophylaxis in catheterized patients is discouraged (Grade C).

5.3. Patients at high-risk for complications of catheter-associated bacteriuria, such as renal transplant and granulocytopenic patients may benefit from antibiotic prophylaxis (Grade B).

References:


Appendix 1
Grading System for Recommendations

Categories reflecting the strength of recommendation

GRADE | DEFINITION
-------|--------------------------------------------------
A      | Good evidence to support a recommendation for use.
B      | Moderate evidence to support a recommendation for use.
C      | Poor evidence to support a recommendation for or against use.
D      | Moderate evidence to support a recommendation against use.
E      | Good evidence to support a recommendation against use.

Appendix 2
Quality Filters in assessing the evidence from the literature

1. Studies on effectiveness of treatment and accuracy of diagnostic tests

Level of quality of evidence

I. Evidence from at least one properly randomized controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies (preferably from more than one center), from multiple time-series studies, or from dramatic results in uncontrolled experiments.
III. Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees.

2. Studies on prognosis or causation

Criteria for assessing quality of evidence:

A. An inception cohort was chosen.
B. Reproducible inclusion and exclusion criteria were used.
C. Follow-up was complete for at least 80% of subjects.
D. Statistical adjustment was carried out for confounders or extraneous factors.
E. Reproducible descriptions of outcome measures were used.

Level of Quality of Evidence:

I. All of the criteria were satisfied.
II. An inception cohort was selected but only 3 of 4 remaining criteria were satisfied.
III. An inception cohort was selected but only 2 of 4 remaining criteria were satisfied.
IV. An inception cohort was selected but only 1 of 4 remaining criteria was satisfied.
V. An inception cohort was selected but only 1 of 4 remaining criteria was satisfied.
VI. None of the 5 criteria was met.

Appendix 4
Key points about urine collection:

1. Clean-voided urine is recommended for adult females.
2. No special preparation is needed to collect specimens from pre-pubertal females.
3. No special preparation is needed for males, but the foreskin should be retracted.
4. Urthral catheterization may be needed in adults who are suspected to have infection and cannot provide a clean-voided specimen. In such case, the laboratory should be informed that the specimen is catheterized urine.
5. First void morning specimens yield the highest bacterial counts. In practice, the best time to collect is when the patient is able to provide an adequate sample.
6. Urine specimens should be delivered to the laboratory without delay and should be cultured within one hour after voiding or be refrigerated.

Instructions to the adult female to collect a clean-voided specimen:

1. Remove underpants completely so they will not get soiled.
2. Sit backwards on the toilet seat. Swing knee to the side as far as you can.
3. Spread your genitals with one hand, and continue to hold yourself spread while you clean and collect the specimen.
4. Before you collect urine, clean between the folds of your genitals around the area from which you pass urine with soaped wash cloth, rinse the wash cloth with tap water, dry yourself with clean cloth and void into a clean jar with
Conditions that may be associated with sterile pyuria

- Contamination during collection
- Vaginal secretions
- Foreskin secretions

Non-infectious causes of pyuria
- Vesicoureteral reflux
- Analgesic nephropathy
- Uric acid nephropathy
- Polycystic kidney
- Acute tubular necrosis
- Transplant rejection
- Allergic interstitial nephritis
- Sarcoioidosis
- Glomerulonephritis
- Hypercalcemic nephropathy
- Lithium toxicity
- Hyperoxalosis
- Heavy metal toxicity
- Carcinoma of bladder
- Renal calculi
- Sickle cell disease
- Idiopathic interstitial cystitis

Infectious diseases
- Tuberculosis
- Chlamydial and gonococcal urethritis

Leptospirosis
- Viral cystitis

Infections adjacent to the urinary tract
- Appendicitis
- Diverticulitis

Cost of Antimicrobial Prophylaxis Regimens for Recurrent UTI

<table>
<thead>
<tr>
<th>Daily Regimen</th>
<th>Cost (pesos)/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrofurantoin 50 mg</td>
<td>PhP 7.50</td>
</tr>
<tr>
<td>Co-trimoxazole 40/200 mg</td>
<td>6.40</td>
</tr>
<tr>
<td>(1/2 tab) (Generic)</td>
<td></td>
</tr>
<tr>
<td>Norfloxacin 200 mg</td>
<td>14.50</td>
</tr>
<tr>
<td>Cephalxin 250 mg</td>
<td>12.01</td>
</tr>
<tr>
<td>500 mg</td>
<td>21.88</td>
</tr>
</tbody>
</table>

Cost of Parenteral Regimens for UTI

<table>
<thead>
<tr>
<th>Drug/Regimen</th>
<th>Cost (pesos)/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin (Generic)</td>
<td>PhP 406.40</td>
</tr>
<tr>
<td>1 g q 6h</td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td></td>
</tr>
<tr>
<td>200 mg q 12h</td>
<td>1,638.00</td>
</tr>
<tr>
<td>400 mg q 12h</td>
<td>3,276.00</td>
</tr>
<tr>
<td>Ceftriaxone 2 g q 24h</td>
<td>1,910.00</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td></td>
</tr>
<tr>
<td>160/800 mg q 12h</td>
<td>555.00</td>
</tr>
<tr>
<td>Gentamicin 240 mg q 24h</td>
<td>252.42</td>
</tr>
<tr>
<td>Amikacin 1000 mg q 24h</td>
<td>1,580.00</td>
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</tbody>
</table>

Appendix 3

Laboratory criteria for significant pyuria and bacteriuria

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cut-off for pyuria</th>
<th>Strength of recommendation</th>
<th>Cut-off for bacteriuria</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acute uncomplicated cystitis</td>
<td>a. &gt;8 pus cells/mm³</td>
<td>C</td>
<td>&gt;100 cfu/mL</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>b. &gt;5 pus cells/hpf</td>
<td>C</td>
<td>&gt;1000 cfu/mL (clinical trials)</td>
<td>C</td>
</tr>
<tr>
<td>2. Acute uncomplicated pyelonephritis</td>
<td>&gt;5 pus cells/hpf</td>
<td>C</td>
<td>&gt;10,000 cfu/mL</td>
<td>B</td>
</tr>
<tr>
<td>3. Asymptomatic bacteriuria</td>
<td>&gt;10 pus cells/hpf</td>
<td>C</td>
<td>&gt;10,000 cfu/mL</td>
<td>A</td>
</tr>
<tr>
<td>4. Complicated UTI</td>
<td>—</td>
<td>—</td>
<td>≥100,000 cfu/mL (with exceptions)</td>
<td>C</td>
</tr>
<tr>
<td>5. UTI in males</td>
<td>a. ≥10 pus cells/mm³</td>
<td>C</td>
<td>≥1000 cfu/mL</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>b. ≥5 pus cells/hpf</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Pus cells per mm³ and per hpf refer to number found in uncentrifuged and centrifuged urine.
## Cost of Oral Drugs Commonly Used for UTI

<table>
<thead>
<tr>
<th>Drug/Regimen</th>
<th>3-day</th>
<th>7-day</th>
<th>14-day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-trimoxazole (Generic)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>160/800 mg q 12h</td>
<td>PhP 66.00</td>
<td>PhP 154.00</td>
<td>PhP 308.00</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>178.20</td>
<td>415.80</td>
<td>831.60</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanate</td>
<td>546.48</td>
<td>1,575.12</td>
<td>3,150.24</td>
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<tr>
<td>375 mg q 8h</td>
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<tr>
<td>Ciprofloxacin</td>
<td>180.00</td>
<td>420.00</td>
<td>840.00</td>
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<tr>
<td>250 mg q 12h</td>
<td>245.70</td>
<td>573.30</td>
<td>1,146.60</td>
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<tr>
<td>500 mg q 12h</td>
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<tr>
<td>Ofloxacin</td>
<td>204.78</td>
<td>477.82</td>
<td>955.64</td>
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<td>200 mg q 12h</td>
<td>256.02</td>
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</tr>
<tr>
<td>400 mg q 12h</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>120.00</td>
<td>280.00</td>
<td>560.00</td>
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<tr>
<td>400 mg q 12h</td>
<td>87.00</td>
<td>203.00</td>
<td>406.00</td>
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</table>
Drugs Mentioned in the Treatment Guideline

This index lists drugs/drug classifications mentioned in the treatment guideline. Prescribing Information of these drugs can be found in the Philippine Pharmaceutical Directory (PPD) 7th edition. Opposite the brand name is its page number in the PPD 7th edition.

<table>
<thead>
<tr>
<th>Aminoglycoside</th>
<th>Cefradine</th>
<th>Qinolon</th>
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<tbody>
<tr>
<td>Amikacin sulfate</td>
<td>Sedinef</td>
<td>Pefloxacin</td>
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<td>Velosef</td>
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<td>Nica</td>
<td>Ceftriazide</td>
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<td>Penicillins</td>
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<td>Amoxicillin</td>
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