Philippine Practice Guidelines Group in Infectious Diseases-Task Force on Urinary Tract Infections

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Algorithm on Evaluating a Woman with Symptoms of Acute Urinary Tract Infection

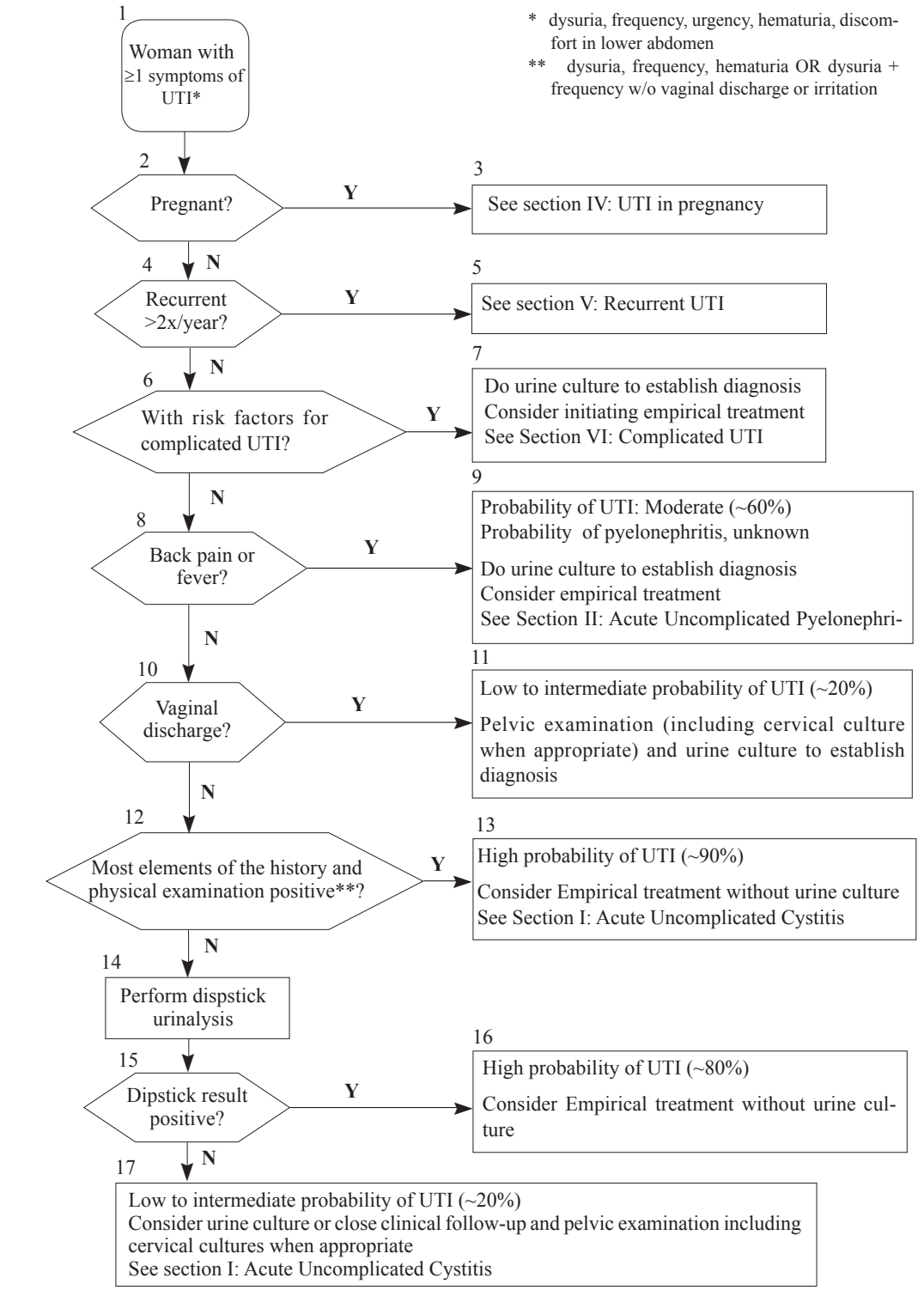
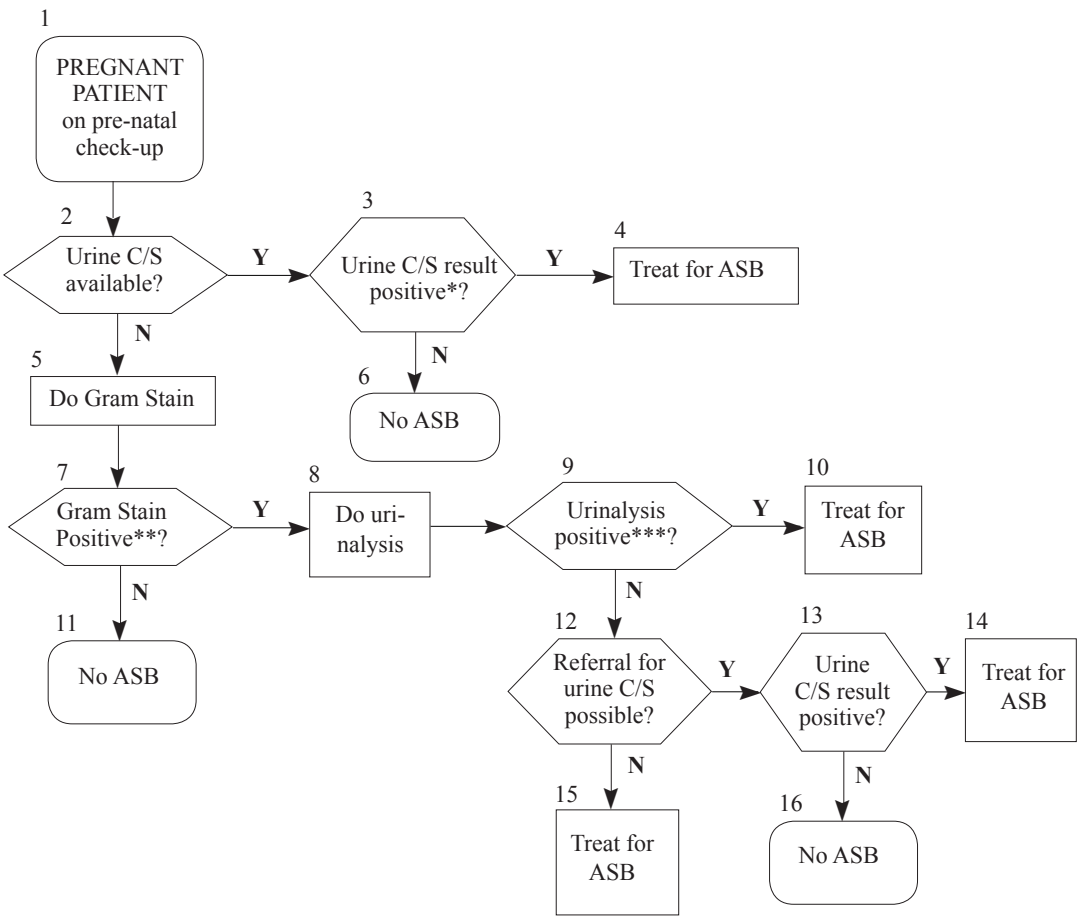


Figure 1

Algorithm on Alternative Diagnostic Evaluation for ASB in Pregnancy in Settings Where Urine Culture is Not Available



* Positive urine C/S: ≥100,000 cfu/mL of a uropathogen

** Positive Gram stain: >6 of 12 hpf with bacteria of same morphology in centrifuged urine

*** Positive urinalysis: ≥5 wbc/hpf of centrifuged urine

Figure 2

Algorithm for the Treatment of Acute Uncomplicated Cystitis in Non-Pregnant women

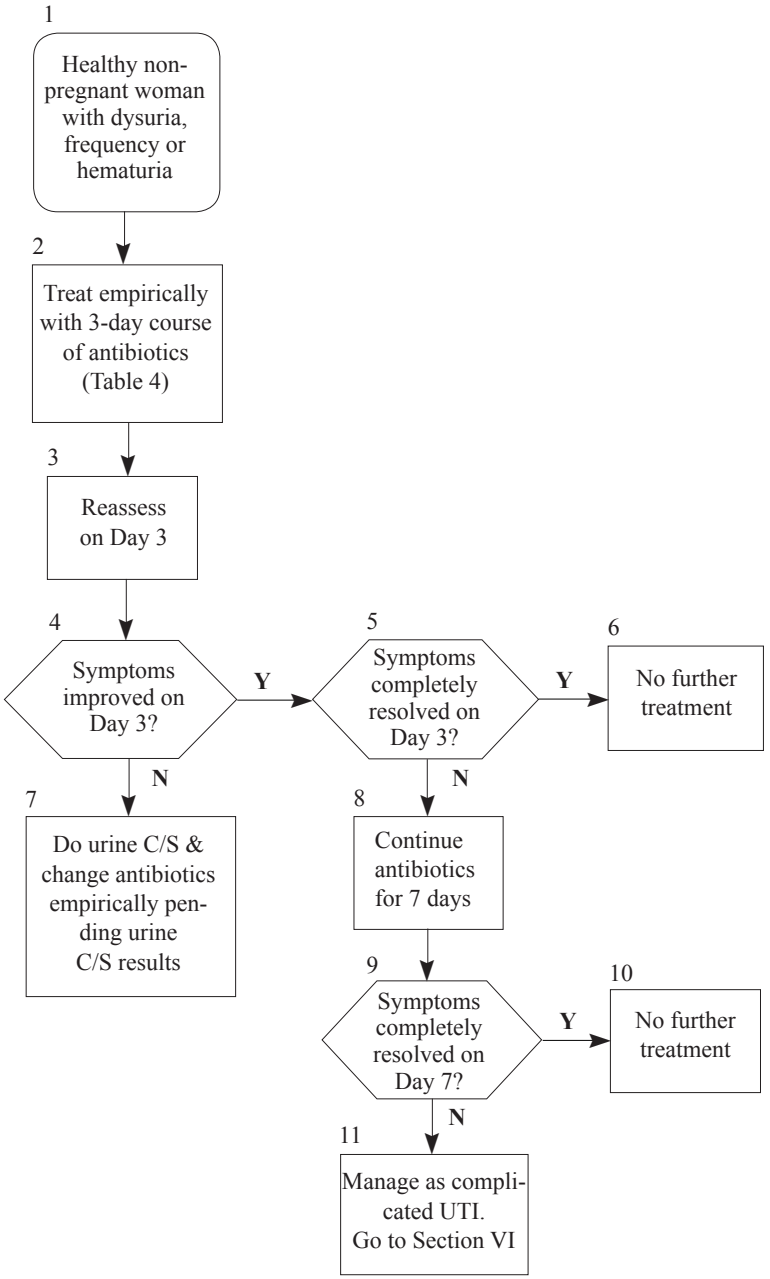


Figure 3

Algorithm for the Treatment of Acute Uncomplicated Pyelonephritis in Non-Pregnant Women

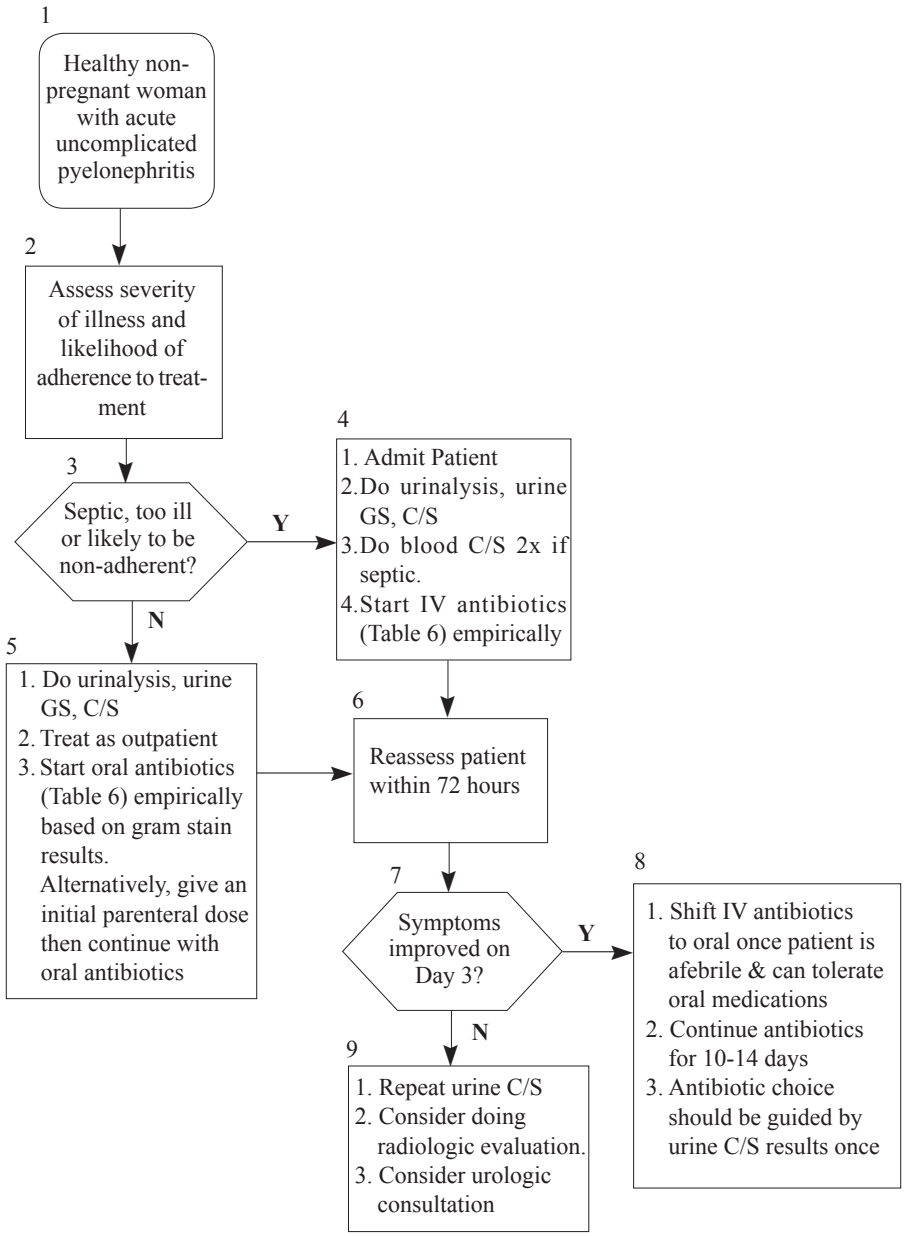


Figure 4

The Philippine Clinical Practice Guidelines on the Diagnosis and Management of Urinary Tract Infections in Adults

Update 2004 Quick Reference Guide

Background

Urinary Tract Infection (UTI) continues to be among the top five reasons for consultations in health facilities nationwide. With the progressive development of new diagnostic and treatment modalities, patients are exposed to wide variations in clinical care and to potentially irrational and expensive health care practices. The use of clinical practice guidelines (CPGs) can potentially minimize practice variations and irrational management decisions by providing systematically formulated management recommendations derived from a critical review of existing literature.

The Philippine Society for Microbiology and Infectious Disease (PSMID) has been active in CPG development for a number of years. Through the initiative of the PSMID, a consortium of collaborators was organized as the Philippine Practice Guidelines Group in Infectious Diseases (PPGG-ID) in 1997. The PPGG-ID was composed of 16 professional societies and its initial project was the development of evidence-based clinical practice guidelines on common infections in the Philippines.

The Task Force on UTI was the first to publish evidence-based recommendation on the diagnosis and management of UTI in 1998. The Philippine Clinical Practice Guidelines on the Diagnosis and Management of Urinary Tract Infection has been widely used and disseminated among health care providers, educators and administrators. The Philippine Health Insurance Corporation has also adopted the guideline in implementing reimbursement schemes. Furthermore, specific strategies for dissemination, particularly interactive case-oriented sessions with audit and feedback discussions, were demonstrated to be effective in disseminating guidelines with improved adherence as the outcome measure in a quasi-experimental study conducted among private practitioners in four institutions in the country (Saniel 2004).

Since the publication of the 1998 Clinical Practice Guidelines on the Diagnosis and Management of Urinary Tract Infections, new developments in the field of urinary tract infections have occurred in the last 5 years providing us with current evidence in the diagnosis, treatment and prevention of urinary tract infections in adults. In recognition of these new developments, the UTI Task Force was reconvened in December 2002 to update the 1998 recommendations. Members consisted of infectious disease specialists, nephrologists, urologists, obstetrician-gynecologists, clinical epidemiologists and general practitioners.

In updating the guideline, the model of Shekelle [2001] was followed wherein new evidence was assessed not only in terms of validity but also in the context of patient values, available health resources and improvements in current performance.

Dissemination and implementation of the updated guidelines is equally important. Thus, the Task Force will also develop educational materials to facilitate dissemination, implementation and evaluation of this updated CPG. We are confident that this project, being the first CPG to be updated in the country, can serve as a model for updating and implementing other clinical guidelines.

Lastly, this update aims to provide health care providers with updated evidence-based recommendations on the rational diagnosis and management of UTI in adults. These guidelines however cannot encompass all scenarios and under no circumstances should it replace sound clinical judgment of the physician.

Saniel MC, Acuin CS, Arciaga RS et al. Improving private practitioners' adherence to clinical practice guidelines: a quasi-experimental study in the Philippines. 2004; for publication

Shekelle P, Eccles MP, Grimshaw JM, Woolf SH. When should guidelines be updated? BMJ 2001; 323:155-7

Methods

Phase I: Preparing the Evidence-Based Draft (EBD)

The UTI Task Force (TF) decided to update all the existing syndromes in the 1998 CPG and added 2 items- Section XII on non-pharmacologic interventions and urinary candidiasis in Section IV on complicated UTI. Designated TF members formulated the clinical questions for each of the syndromes. The Task Force discussed and approved the questions in a consensus meeting. The Technical Working Group (TWG) then searched the MEDLINE database up to March 2004 and the Cochrane Library up to Issue 2 2004. The HERDIN database was searched and experts in the field were

contacted for published and unpublished local literature. The assigned TF and TWG member reviewed the search yield and relevant literature was retrieved, including literature that was missed in the 1998 CPG. Reference lists of retrieved articles were also reviewed. New evidences were appraised for validity and applicability. Existing recommendations were modified and new recommendations formulated accordingly based on critical review of new data. The evidence was summarized to include updates on prevalence, accuracy of diagnostic tests, benefits, harms and cost-effectiveness of interventions. The EBD was circulated to all TF members who discussed and reviewed the updated recommendations using an iterative process. The Task Force and TWG graded the recommendations using the scale modified from the Infectious Diseases Society of America *(See Appendix 1)*.

Phase II: Preparing the Intermediate Draft

The EBD was circulated to all panelists for review two weeks before the en banc meeting that was held on April 23, 2004. The panelists consisted of experts in the field of family medicine, internal medicine, nephrology, urology, obstetrics and infectious diseases designated as representatives of their respective societies. Using the nominal group technique, each panelist commented on the recommendations during the en banc meeting. The panelists considered not only the quality and comprehensiveness of the evidence but values placed on the evidence, applicability and availability of health resources and experts' opinion. A consensus was reached when ≥75% of the panelists agreed on a recommendation through independent and secret balloting. All issues modifying the recommendations e.g. availability of resources were added in the respective sections to come up with an intermediate draft.

Phase III: Preparing the Penultimate Draft

Recommendations not resolved by consensus were circulated to the panelists by fax or e-mail using the modified Delphi Technique. The recommendations were again discussed and voted upon. Unresolved recommendations reached consensus after the first round and were incorporated in the penultimate draft.

Phase IV: Preparing the Final Report

The penultimate draft was circulated to non-panelists stakeholders that included representatives from various hospitals and universities, professional societies, pharmaceutical companies, health maintenance organizations, educational influentials, policy makers and administrators one week before the scheduled public forum. The stakeholders gave their oral or written comments and feedback during the public forum held on July 1, 2004. These comments were considered in preparing the final draft of the guidelines for publication.

Phase V: Preparing for Dissemination and Implementation

The Task Force will develop educational and training materials tailored for specific target groups (e.g. specialists, general practitioners, paramedical personnel, and patients). Other expected outputs are implementation checklist and performance indicators for monitoring and evaluation (e.g. change in prescribing habits and utilization of cost- effective interventions).

I. ACUTE UNCOMPLICATED CYSTITIS IN WOMEN

1. When is acute uncomplicated cystitis suspected in women?

Clinically, acute uncomplicated cystitis (AUC) is diagnosed in non-pregnant women, presenting with dysuria, frequency, or gross hematuria, with or without back pain (Grade B). Risk factors for complicated urinary tract infection must be absent. (See Table 1.)
Women who present with the previously-mentioned symptoms plus vaginal irritation or vaginal discharge must undergo further diagnostic tests to confirm the presence of acute uncomplicated cystitis or other concomitant conditions (Grade B).
See Table 2.

2. In women suspected of having uncomplicated cystitis, what is the clinical utility of diagnostic tests performed before treatment?

Pre-treatment urine culture and sensitivity is not recommended (Grade E).

Standard urine microscopy and dipstick leukocyte esterase (LE) and nitrite tests are not prerequisites for treatment (Grade D).

Table 1. Risk factors for Complicated UTI

Hospital acquired infection
Indwelling urinary catheter
Recent urinary tract infection
Recent urinary tract instrumentation (in the past 2 weeks)
Functional or anatomic abnormality of the urinary tract
Recent antimicrobial use (in the past 2 weeks)
Symptoms for >7 days at presentation
Diabetes mellitus
Immunosuppression

Table 2. Accuracy of clinical signs and symptoms in the prediction of urinary tract infections*

Signs/Symptoms	Summary Positive Likelihood Ratios (95% Cl)	Summary Negative Like lihood Ratios (95% Cl)
Dysuria	1.5 (1.2-2.0)	0.5 (0.3-0.7)
Frequency	**1.8 (1.1-3.0)**	0.6 (0.4-1.0)
Hematuria	**2.0 (1.3-2.9)**	0.9 (0.9-1.0)
Fever	1.6 (1.0-2.6)	0.9 (0.9-1.0)
Flank pain	1.1 (0.9-1.4)	0.9 (0.8-1.1)
Lower abdominal pain	1.1 (0.9-1.4)	0.9 (0.8-1.1)
Absent vaginal discharge	3.1 (1.0-9.3)	**0.3 (0.1-0.9)**
Absent vaginal irritation	2.7 (0.9-8.5)	**0.2 (0.1-0.9)**
Back pain	1.6 (1.2-2.1)	0.8 (0.7-0.9)
Vaginal discharge on physical examination	1.1 (1.0-1.2)	**0.7 (0.5-0.9)**
Combination of symptoms		
1. dysuria & frequency present, vaginal discharge & irritation absent	22.6	
2. dysuria absent, vaginal discharge or irritation present	0.1-0.2	
3. dysuria or frequency present, vaginal discharge or irritation present	0.3-0.5	

"Adapted from Bent 2002. See Glossary for definition of likelihood ratios.

Table 3. Summary of performance characteristics of urinalysis and dipstick for LE/nitrites

Author (year)	Tests	Sensitivity (95% Cl)	Specificity (95% Cl)	Positive LR (95% Cl)	Negative LR (95% Cl)
Hurlbut (1991)	dipstick for LE/ nitrites			4.2	0.3
Sultana (2001)	dipstick for LE/ nitrites	82% (72 - 89)	84% (80 to 88)	1.27 (1.17-1.38)	0.22 (0.09-0.53)
Leman (2002)	urinalysis for pyuria	95.8% (84 - 99)	50% (32-72)	2.02 (1.24-3.20)	0.093 (0.02-0.38)
	dipstick for LE/ nitrites	87.5% (75- 95)	41.6% (20-61)	1.44 (0.98-2.12)	0.3 (0.11-0.84)
ACP PIER (2003)	urinalysis for pyuria	91%	50%		
	dipstick for LE/ nitrites	88-92%	66-67%		

Table 4. Antibiotics that can be used for acute uncomplicated cystitis

Antibiotics		Dose and Frequency	Duration	Unit Cost (PhP)	Total Cost (PhP)
TMP-SMX	(Grade A)	800/160 mg BID	3 days	27.50	165.00
Ciprofloxacin	(Grade A)	250 mg BID	3 days	56.00	336.00
Ofloxacin	(Grade A)	200 mg BID	3 days	50.00	300.00
Norfloxacin	(Grade A)	400 mg BID	3 days	27.75	166.50
Levofloxacin	(Grade A)	250 mg OD	3 days	112.50	337.50
Gatifloxacin	(Grade A)	400 mg	Single dose	199.75	199.75
Nitrofurantoin	(Grade A)	100 mg QID	7 days	22.25	623.00
Cefixime	(Grade B)	400 mg OD	3 days	116.75	700.50
Cefuroxime	(Grade B)	125-250 mg BID	3-7 days	80.50	483.00
Co-amoxiclav	(Grade B)	625 mg BID	7 days	89.25	1,249.50

NOTE: Cost is based on Mercury drug prices as of 2004.When multiple brands are available, the cost of the most frequently used brand was obtained.

Table 5. Antimicrobial resistance rates of *E. coli* outpatient urine isolates by disc diffusion*

Year	1999-2000**	2000	2001	2002	2003 (n=694)
Ampicillin	53% (Amoxicillin)	79%	79%	79%	80%
Co-amoxiclav	29%	27%	32%	25%	29%
Cefuroxime	2%	11%	12%	13%	18%
Cephalothin	18% (Cephalexin)	51%	--	52%	50%
Nitrofurantoin	0%	14%	12%	40%	26%
Ciprofloxacin	--	30%	--	45%	44%
Cotrimoxazole	31%	85%	65%	70%	70%

* *Source: Carlos C. The 2000 - 2003 DOH Antimicrobial Resistance Surveillance Data*
** *51 E coli isolates from outpatient pregnant women with asymptomatic bacteriuria [Sescon NI et al. PJMID 2003]*

In women who present with additional symptoms such as vaginal discharge or vaginal irritation, either a standard urine microscopy or dipstick for LE and nitrites must be done to confirm the diagnosis (Grade B).
See Table 3.

3. Which antibiotics are effective for acute uncomplicated cystitis?

Any of the antibiotics listed in Table 4 can be used for acute uncomplicated cystitis depending on local susceptibility patterns and host factors. The recommended antibiotics may change depending on the local patterns of susceptibility (see Table 5). Costs, pharmacologic properties and adverse effects are additional factors to consider in the choice of antibiotics.

Ampicillin and amoxicillin should not be used (GradeE).

4. What is the effective duration of treatment for acute uncomplicated cystitis?

Three-day therapy is the recommended duration (Grade A) except for nitrofurantoin, which must be given for 7 days (Grade A).

5. In elderly women (>65 years) with acute uncomplicated cystitis what is the effective duration of treatment?

In otherwise healthy elderly women presenting with signs and symptoms of acute cystitis, a three-day course of any of the antibiotics listed in Table 4 is also recommended (Grade A).

6. What should be done for women whose symptoms worsen, do not completely resolve or do not improve after completion of a 3-day therapy?

Patients whose symptoms worsen or do not improve after 3 days should have a urine culture and the antibiotic should be empirically changed, pending result of sensitivity testing (Grade C).

Patients whose symptoms fail to resolve after the 7-day treatment should be managed as a complicated urinary tract infection (Grade C). (See Section VI)

7. What is the clinical utility of a post-treatment urine culture?

Routine post-treatment urine culture and urinalysis in patients whose symptoms have completely resolved are not recommended (Grade D).

II. ACUTE UNCOMPLICATED PYELONEPHRITIS IN WOMEN

1. When is acute uncomplicated pyelonephritis suspected?

In otherwise healthy women with no clinical or historical evidence of structural or functional urologic abnormalities, the classic syndrome of acute uncomplicated pyelonephritis (AUPN) is characterized by fever (T ≥38°C), chills, flank pain, costovertebral angle tenderness, nausea and vomiting, with or without signs and symptoms of lower urinary tract infection.

Laboratory findings include pyuria (≥5 wbc/hpf of centrifuged urine) on urinalysis and bacteriuria with counts of ≥10,000 cfu of a uropathogen/mL on urine culture.

2. What are the recommended diagnostic tests for acute uncomplicated pyelonephritis?

Urinalysis and Gram stain are recommended (Grade B).

Urine culture and sensitivity test should also be performed routinely to facilitate cost-effective use of antimicrobial agents because of the potential for serious sequelae if an inappropriate antimicrobial regimen is used (Grade B).

Blood cultures are not routinely recommended (Grade D).

Blood cultures done twice are recommended for patients with signs of sepsis defined as presence of any 2 of the following: T >38°C or < 36°C, leukopenia (WBC < 4,000) or leukocytosis (WBC >12,000), tachycardia (HR >90 beats/min), tachypnea (RR >20/min or $PaCO_2$ <32mmHg), or hypotension (SBP <90mmHg or >40mmHg drop from baseline) (Grade C).

3. Treatment

3.1 Can patients with acute uncomplicated pyelonephritis be treated as outpatients?

Non-pregnant patients with no signs and symptoms of sepsis, who are adherent to treatment and are likely to return for follow-up, may be treated as outpatients (Grade B).

An initial parenteral dose of ceftriaxone may be given followed by oral antibiotics (Grade B). Other parenteral antibiotics with similar efficacy as ceftriaxone may also be considered (Grade C). See Table 6.

The following are considered indications for admission: Inability to maintain oral hydration or take medications; concern about adherence to treatment; presence of possible complicating conditions; severe illness with severe pain, marked debility and signs of sepsis (Grade B).

3.2 What drugs can be used for empiric treatment of acute uncomplicated pyelonephritis?

Several regimens that have been found to be effective are recommended (Grade A). See Table 6.

The aminopenicillins (ampicillin or amoxicillin) and first generation cephalosporins are not recommended because of the high prevalence of resistance and increased recurrence rates in patients given these β-lactams (Grade E).

Because of high resistance rates to TMP-SMX (See Table 5), this drug is not recommended for empiric treatment (Grade E) but can be used when the organism is susceptible on urine culture and sensitivity test.

Combining ampicillin with an aminoglycoside offers no added benefit, except when enterococcal infection is suspected (Grade C).

IV antibiotics can be shifted to any of the listed oral antibiotics (See Table 6) once the patient is afebrile and can tolerate oral drugs (Grade B). The choice of continued antibiotic therapy should be guided by the urine culture and sensitivity results once available (Grade B).

3.3 What is the effective duration of treatment for acute uncomplicated pyelonephritis?

The recommended duration of treatment is 14 days. Selected fluoroquinolones (see Table 6) can be given for 7-10 days (Grade A).

4. Who will require work up for urologic abnormalities?

Routine urologic evaluation and routine imaging procedures are not recommended (Grade D).
Consider radiologic evaluation if the patient remains

Table 6. Empiric treatment regimens for uncomplicated acute pyelonephritis

Antibiotic and Dose	Frequency and Duration
ORAL	
Ofloxacin 400 mg	BID; 14 days
Ciprofloxacin 500 mg	BID; 7-10 days
Gatifloxacin 400 mg	OD; 7-10 days
Levofloxacin 250 mg	OD; 7-10 days
Cefixime 400 mg	OD; 14 days
Cefuroxime 500 mg	BID; 10-14 days
Amoxicillin-clavulanate 625 mg (when Gram stain shows Gram positive organisms)	TID; 14 days
PARENTERAL (given until patient is afebrile)	
Ceftriaxone 1-2 g	Q 24
Ciprofloxacin 200-400 mg	Q 12
Levofloxacin 250-500 mg	Q 24
Gatifloxacin 400 mg	Q 24
Gentamicin 3-5 mg/kg BW (± ampicillin)	Q 24
Ampi-sulbactam 1.5 g (when Gram stain shows Gram positive organisms)	Q 6
Piperacillin-tazobactam 2.25 - 4.5 g	Q 6-8

febrile within 72 hours of treatment or when there is recurrence of symptoms to rule out the presence of nephrolithiasis, urinary tract obstruction, renal or perirenal abscesses, or other complications of pyelonephritis (Grade C). Urologic consultation should be obtained if work up shows these abnormalities (Grade C).

5. Is a follow-up urine culture recommended?

In patients who are clinically responding to therapy (usually apparent in <72 hours after initiation of treatment), a follow-up urine culture is not necessary (Grade C).

Routine post-treatment cultures in patients who are clinically improved are also not recommended (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. What is the recommended management for patients whose symptoms recur?

Recurrence of symptoms requires a change in antibiotics 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 patients whose symptoms recur and whose culture shows the same organism as the initial infecting organism, a 4-6 week regimen is recommended (Grade C).

III. ASYMPTOMATIC BACTERIURIA IN ADULTS

1. When is asymptomatic bacteriuria diagnosed?

Asymptomatic bacteriuria (ASB) is defined as the presence of ≥100,000 cfu/mL of one or more uropathogens in two consecutive midstream urine specimens or in one catheterized urine specimen in the absence of symptoms attributable to a urinary tract infection.

2. Who are the patients that should be screened and treated for ASB?

Screening and treatment is recommended in the following: (1) patients who will undergo genitourinary manipulation or instrumentation (Grade B); (2) post-renal transplant patients up to the first 6 months (Grade B); (3) diabetes mellitus patients with poor glycemic control, autonomic neuropathy or azotemia (Grade C); and (4) all pregnant women (Grade A).

Any of the antibiotics for acute uncomplicated cystitis

listed in Table 4) can be used for treatment of ASB in the above group of patients (Grade C). A 7 to 14 day course is recommended (Grade C). For specific recommendations on pregnant women, please refer to Section IV.

3. Who should not be screened and treated for ASB?

Routine screening and treatment for asymptomatic bacteriuria is not recommended for healthy adults (Grade D). Likewise, periodic screening and treatment for asymptomatic bacteriuria is not recommended in the following: (1) diabetes mellitus patients with adequate glycemic control and no autonomic neuropathy or azotemia (Grade E); (2) elderly patients (Grade D); (3) patients with indwelling catheters (Grade E); (4) immunocompromised patients (Grade C); (5) other solid organ transplant patients (Grade C); (6) HIV patients (Grade C); (7) spinal cord injury patients (Grade D) and (8) patients with urological abnormalities (Grade C).

4. What is the optimal screening test for ASB?

Urine culture is the recommended screening test (Grade A).

In the absence of facilities for urine culture, 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 ASB (Grade C). Urine culture and sensitivity testing are not necessary when urinalysis is negative for pyuria or if Gram stain of urine is negative for organisms (Grade B).

IV. URINARY TRACT INFECTION IN PREGNANCY

A. Asymptomatic Bacteriuria in Pregnancy

1. When is asymptomatic bacteriuria in pregnancy diagnosed?

Asymptomatic bacteriuria in pregnancy is the presence of ≥100,000 cfu/mL of one or more uropathogens in two consecutive midstream urine specimens or one catheterized urine specimen, in the absence of symptoms attributable to a urinary tract infection.

In situations or settings where obtaining 2 consecutive urine cultures are not feasible or difficult, 1 urine culture is an acceptable alternative for the diagnosis of ASB in pregnancy (Grade C).

2. Do all pregnant women have to be screened for ASB?

A pregnant women must be screened for ASB on their first prenatal visit between the 9th to 17th weeks, preferably on the 16th week age of gestation (Grade A).

3. What is the optimal screening test for ASB in pregnancy?

A standard urine culture of clean-catch midstream urine is the test of choice in screening for asymptomatic bacteriuria (Grade A).

In areas where urine culture is not available, the following can be used for screening: An initial Gram stain of centrifuged urine (cut-off: same morphology of bacteria seen in >6 of 12 high power fields in centrifuged urine sample). If positive, this must be followed by a urinalysis to determine pyuria. A cut-off level of ≥5 wbc/hpf suggests ASB (Grade C). To minimize multiple visits to the laboratory and/or clinic, both tests can be requested simultaneously, but with the urinalysis being performed after a positive Gram stain result. (See Algorithm)

Urine dipsticks for leukocyte esterase and/or nitrite tests are not recommended for screening for ASB in pregnancy (Grade E).Urinalysis alone is not recommended for screening (Grade E). (See Tables 7, 8 and 9).

4. What is the effective treatment for ASB in pregnancy?

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

It is recommended that antibiotic treatment be initiated upon the diagnosis of ASB in pregnancy. Among the drugs that can be used are nitrofurantoin (not for those near-term), co-amoxiclav, cephalexin, and cotrimoxazole (not in the 1st and 3rd trimesters) depending on the sensitivity results of the urine isolate (Grade B). A 7-day course is recommended (Grade C).

Do follow-up cultures one week after completing the course of treatment (Grade C).

B. Acute Cystitis in Pregnancy

1. When do you suspect acute cystitis in pregnancy?

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.

Table 7. Performance characteristics of reagent strips

No	Study	Sensitivity	Specificity
1	Archbald 1984 (N=324)		
	Nitrites	37	100
	Microstix	33	98
2	Bachmann 1993 (N=1,047)		
	Leukocyte esterase (LE)	16.7	97.2
	Nitrites	45.8	99.7
	LE or Nitrites	50.0	96.9
	LE and Nitrites	12.5	100
3	McNeeley 1987 (N=694)		
	LE or Nitrites	69.6	83.4
4	Robertson 1986 (N=750)		
	LE 77.4	96.1	
	Nitrites	43.4	98.9
	LE or Nitrites	92.0	95.0
	LE and Nitrites	32.2	94.2
5	Tincello 1998 (N=893)		
	Nitrites	18.8	99.5
	Test combined	33.3	91.1
	Millar et al 2000 (N=383)	70	45
	Uriscreen	45	97
	Nitrites	69	69
	Leukocyte esterase (LE)	81	97
	Dipstick (LE+Nitrites)		
	Microscopic using hemocytometer chamber	67	80
	Pyuria (>5wbc/mL of centrifuged urine)	93	43
	Bacteria (≥1)	93	42
	Pyuria+Bacteriuria		
	McNair et al 2000 (N=528)	80.6	71.5
	Urinalysis	(63.4-91.2)	(67.3-75.4)
		47.2	80.3
	Reagent strips	(30.8-64.3)	(76.4-83.7)

1-5. From a *systematic review by Garingalao-Molina F. 2000*

Table 8. Performance characteristics of urine microscopy for pyuria

Study	Sensitivity (%)	Specificity (%)
Archbald 1984 (N=324)		
Pyuria:5 or more wbc/hpf	20	89
Bachmann 1993 (N=1,047)	25	99
Pyuria: >10 wbc/hpf	8.3	99.7
Adjusted cut-off: >50 wbc/hpf		

Table 9. Performance characteristics of urine Gram stain

Study	Sensitivity (95% CI)	Specificity (95% CI)
1. McNair 2000 (N=528)		
Gram stain of centrifuged urine (same morphology of bacteria seen in >6 of 12 hpfs)	100 (88-100)	7.7 (5.6-10.5)
2. Bachmann 1993 (N= 1,047)		
Gram Stain		
Definite positive: 2 or > organisms/OIF	83.3	94.9
Borderline (1 organism/OIF) or definite positive	91.7	89.2

2. Is a pretreatment diagnostic test required in acute cystitis in pregnancy?

In pregnant women suspected to have acute uncomplicated cystitis, obtain a urine culture and sensitivity test of a midstream clean-catch urine specimen (Grade C).

In the absence of a urine culture, the laboratory diagnosis of acute cystitis is determined by the presence of significant pyuria defined as (a) ≥8 pus cells/mm^3 of uncentrifuged urine; OR (b) ≥5 pus cells/hpf of centrifuged urine; and (c) a positive leukocyte esterase and nitrite test (Grade C).

3. What is the treatment for acute cystitis in pregnancy?

Treatment of acute cystitis in pregnancy should be instituted immediately to prevent the spread of the infection to the kidney (Grade A).

Since *E. coli* remains to be the most common organism isolated, antibiotics to which this organism is most sensitive and which are safe to give during pregnancy should be used (Grade A). TMP-SMX and fluoroquinolones are relatively contraindicated during pregnancy because of their potential teratogenicity and the third trimester risk of kernicterus with TMP-SMX. (See Table 10)

A 7- day course is recommended (Grade C).

In the absence of a urine culture and sensitivity test, empiric therapy should be based on local susceptibility patterns of uropathogens (Grade C).

4. In cases where the result of a urine culture shows an organism resistant to the empirically started antibiotic in a clinically improving patient, should the antibiotic be changed based on the susceptibility report?

Adjust antibiotic therapy based on urine culture results (Grade C).

Alternatively, repeat the urine culture. If sterile, continue with the same antibiotic. If bacteriuria persists, switch regimen based on culture result (Grade C).

5. What is the clinical utility of a post-treatment urine culture?

Post-treatment urine culture should be obtained to confirm eradication of bacteriuria and resolution of infection in pregnant women (Grade C).

Pregnant patients with pyelonephritis, recurrent UTIs, concurrent gestational DM, concurrent nephrolithiasis or urolithiasis, and pre-eclampsia, should be monitored at monthly intervals until delivery to ensure that urine remains sterile during pregnancy (Grade C).

C. Acute Pyelonephritis in Pregnancy

1. When is acute pyelonephritis in pregnancy suspected?

Acute pyelonephritis is characterized by shaking chills, fever (T>38 °C), flank pain, nausea and vomiting, with or without signs and symptoms of lower urinary tract infections and a physical finding 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.

2. What is the appropriate diagnostic test to establish an etiologic diagnosis?

Gram stain of uncentrifuged urine is recommended to differentiate Gram-positive from Gram-negative bacteriuria, which can guide the choice of empiric antibiotic therapy (Grade B).

Table 10. FDA pregnancy risk and Hale's lactation risk categories for commonly prescribed antimicrobials in urinary tract infection

Category B, L1, L2	Category C, L3	Category D, L3
Nitrofurantoin Amoxicillin-clavulanate Cephalosporins	TMP-SMX (Avoid in 1st and 3rd trimester)	Aminoglycosides

Lactation Risk Category

L1	safest, controlled study = fails to demonstrate risk
L2	safer, limited number of women studied without risk
L3	moderately safe, no controlled study or controlled study shows minimal, non life-threatening risk
L4	hazardous, positive evidence of risk, may be used if maternal life-threatening situation
L5	contraindicated, significant, and documented risk

FDA Pregnancy Risk Categories

Category A	well-controlled human study = no fetal risk in first trimester. No evidence of risk in 2nd, 3rd trimesters. Risk to fetus appears remote.
Category B	animal studies do not demonstrate fetal risk, but no controlled study in humans OR animal studies show adverse effect but not demonstrated in human study.
Category C	no controlled study in humans available. Animal studies reveal adverse fetal effects
Category D	positive evidence of human fetal risk. Use in pregnant woman occasionally acceptable despite risk.
Category E	animal or human studies demonstrate fetal abnormality. Evidence of fetal risk based on human study. No indication in pregnancy.

Adapted from: Fitzgerald MA. Urinary Tract Infection: Providing the Best Care. Available at http://www.medscape.com/viewprogram/1920, Accessed Feb 3, 2004.

Urine culture and sensitivity test should be done routinely to guide the choice of antimicrobial agents because of the potential for serious sequelae if an inappropriate antimicrobial is used (Grade B).

Blood cultures are not routinely recommended for pregnant patients with acute pyelonephritis (Grade D).

3. What antimicrobials are recommended for acute pyelonephritis in pregnant women?

All pregnant patients with acute pyelonephritis should be hospitalized and immediate antimicrobial therapy instituted (Grade B). Treatment duration is 10-14 days (Grade B).

Any of the antibiotics for acute uncomplicated pyelonephritis can be used (See Table 6) except for fluoroquinolones and aminoglycosides, which are relatively contraindicated in pregnancy (Grade B). In the absence of urine culture and sensitivity tests, empiric choice of antibiotic should be based on local susceptibility patterns of uropathogens (Grade C).
For pregnant patients with no signs and symptoms of sepsis and are able to take oral medications, outpatient therapy may be considered (Grade B).

4. What is the clinical utility of a post-treatment urine culture in acute pyelonephritis in pregnancy?

Post-treatment urine culture should be obtained to confirm resolution of the infection. Patient should be monitored at intervals until delivery to confirm continued urine sterility during pregnancy (Grade C).

V. RECURRENT URINARY TRACT INFECTION IN WOMEN

A. When is recurrent UTI Diagnosed?

Recurrent UTI is diagnosed when a non-pregnant woman with no known urinary tract abnormalities has episodes of acute uncomplicated cystitis occurring more than twice a year documented by urine culture.

B. When is prophylaxis for recurrent UTI Indicated?

Prophylaxis is recommended in women whose frequency of recurrence is not acceptable to the patient in terms

Table 11. Antibiotics proven effective in reducing the number of recurrences of UTI

Antibiotics	Recommended dose for continued prophylaxis	Recommended dose for post-coital prophylaxis
Nitrofurantoin	100 mg at bedtime	
Trimethoprim	100 mg at bedtime	
TMP/SMX	40 mg/200 mg at bedtime	40 mg/200 mg
Ciprofloxacin	125 mg at bedtime	125 mg
Norfloxacin	200 mg at bedtime	200 mg
Ofloxacin	————	100 mg
Pefloxacin	400 mg weekly	
Cefalexin	125 mg at bedtime	————
Cefaclor	250 mg at bedtime	————

References: Brumfitt 1991, Brumfitt 1995, Melekos 1997, Nicolle 1989, Pfau 1994, Stamey 1977, Stamm 1980

of level of discomfort or interference with activities of daily living. Prophylaxis may be withheld according to patient preference if the frequency of recurrence is tolerable to the patient (Grade C).

C. How effective are prophylactic regimens in Preventing recurrent UTI?

1. Antibiotic prophylaxis

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

Any of the antibiotics listed in Table 11 given either continuously for 6-12 months or as post-coital prophylaxis have been proven to effectively reduce the number of episodes of UTI (Grade A).

2. Hormonal treatments in post-menopausal women

Consider application of intravaginal estriol cream once each night for two weeks followed by twice-weekly applications for 8 months to prevent recurrent UTI in post-menopausal women (Grade A).

Low dose oral estrogen is not recommended for the prevention of recurrent UTI (Grade D).

3. Vaccines

There is insufficient evidence to recommend immunoactive *E. coli* fractions for the prevention of recurrent UTI (Grade C).

D. How should individual episodes of UTI be treated in women with recurrent UTI?

Any of the antibiotics for acute uncomplicated cystitis (See Table 4) may be used in the treatment of individual episodes of UTI in women with recurrent UTI (Grade B).

Consider intermittent self-administered therapy in highly educated and well-informed patients, wherein the patients are able to recognize the characteristic signs and symptoms of UTI and instructed to take 2 double-strength tablets of TMP/SMX single dose as soon as symptoms first appear (Grade A).

Breakthrough infections during prophylaxis should be treated empirically with any of the antibiotics recommended for uncomplicated cystitis other than the antibiotic being given for prophylaxis. Request for a urine culture and modify the treatment accordingly (Grade B).

E. What diagnostic work-ups are indicated in women with recurrent UTI?

1. Indication for screening for urologic abnormalities

Routine screening for urologic abnormalities is not recommended for women with recurrent UTI (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).

2. Choice of screening procedure

Combined renal ultrasound and a plain abdominal radiograph are recommended (Grade B). Patients with anatomical abnormalities should be referred to a nephrologist and/or urologist for further evaluation (Grade C).

VI. COMPLICATED URINARY TRACT INFECTION

A. When is complicated urinary tract infection suspected or diagnosed

Complicated UTI is significant bacteriuria, which occurs in the setting of functional or anatomic abnormalities of the urinary tract or kidneys. (See Table 12)
The cut-off for significant bacteriuria in complicated UTI has been set at >100,000 cfu/mL. However in certain clinical situations, low-level bacteriuria or counts <100,000 cfu/mL may be significant as in catheterized patients.

B. In patients with suspected complicated UTI, what diagnostic tests should be done to assist the physician in managing the infection effectively?

A urine sample for gram stain, culture and sensitivity testing must always be obtained before the initiation of any treatment (Grade B).

C. Do patients with complicated UTI need to be hospitalized?

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

Table 12. Conditions that define complicated UTI

Presence of an indwelling urinary catheter or intermittent catheterization
Incomplete emptying of the bladder with >100 mL retained urine post-voiding
Obstructive uropathy due to bladder outlet obstruction, calculus and other causes
Vesicoureteral reflux & other urologic abnormalities including surgically created abnormalities
Azotemia due to intrinsic renal disease
Renal transplantation
Diabetes mellitus
Immunosuppressive conditions - e.g. febrile neutropenia; HIV/AIDS
UTI caused by unusual pathogens or drug-resistant pathogens
UTI in males except in young males presenting exclusively with lower UTI symptoms

References: Nickel 1990, Rubin 1992, Ronald 1997, Stamm 1993, Williams 1996

D. What antibiotics are recommended for empiric therapy of complicated UTI?

For mild to moderate illness, oral fluoroquinolones are recommended (Grade A). For severely ill patients, broad-spectrum parenteral antibiotics should be used, choice of which would depend on the expected pathogens, results of the urine Gram stain and current susceptibility patterns of microorganisms in the area (Grade B). See Tables 13 and 14.

E. How long are antibiotics given in complicated UTI?

Antibiotics are modified according to the results of the urine culture and sensitivity test. Patients started with parenteral regimen may be switched to oral therapy upon clinical improvement. At least 7-14 days of therapy is recommended (Grade B).

F. After the completion of antibiotics, what tests or procedures are recommended to reduce the risk of recurrence of complicated UTI?

Repeat the urine culture one to two weeks after completion of therapy (Grade C). If significant bacteriuria persists post-treatment, consider referral to specialties involved with the underlying problem that predisposes to complicated UTI (Grade C).

Further work-up to identify and correct the anatomical, functional or metabolic abnormality is recommended. Referral to the appropriate specialists, such as infectious diseases, nephrology or urology should be made as necessary (Grade C).

SPECIFIC ISSUES OF CONCERN IN COMPLICATED UTI

A. Catheter-Associated UTI

1. Should all catheterized patients with bacteriuria be treated?

Catheterized patients with significant bacteriuria of ≥100 cfu/mL of urine, who develop signs and symptoms of UTI, fever or other signs of bacteremia should be treated with antibiotics (Grade B).

Consider antibiotic treatment in the following subsets of catheterized patients who have bacteriuria but are asymptomatic: a) those with organisms that cause high incidence of bacteremia in their institution; b) post-solid organ transplant patients; c) neutropenic patients; d) pregnant patients; e) those who will undergo urologic procedures; and f) those who may be part of an infection control plan to manage cluster infections in a unit (Grade C).

Table 13. Pathogens in Complicated UTI

Type of Complicated UTI	Pathogens	Reference
Catheter-associated UTI		
Short-term (<1 week)	*Escherichia coli*	Warren 1997
		Pseudomonas aeruginosa
Long-term (>1 week)	*Escherichia coli, Klebsiella* sp.	Saint 2003
	Enterobacter sp., *Proteus mirabilis*	
	Usually polymicrobial	Ouslander1987
	E coli, Pseudomonas aeruginosa,	
	Proteus mirabilis, Providencia stuartii,	
	Morganella morgagnii, Citrobacter,	
	Enterococcus, *Candida* sp.	
Catheter-associated UTI in Filipino patients	*E. coli,* Klebsiella, *Pseudomonas aeruginosa,* Acinetobacter, *Candida* sp	Billote-Domingo 1999 Alavaren 1993
Anatomic abnormalities	*Escherichia coli*	Childs 1993
	Klebsiella pneumoniae (37%)	
	Pseudomonas aeruginosa	
	Proteus mirabilis	
UTI in diabetics	*Escherichia coli, Klebsiella pneumoniae*	Patterson and Andriole 1997
	Proteus mirabilis	
	Enterobacter	
	Enterococcus	
	Pseudomonas aeruginosa	
	Candida	
Renal transplant recipients	*Escherichia coli* (29-61%)	Schmaldienst and Horl 1997
	Proteus mirabilis and	Mendoza 1997
	Klebsiella pneumoniae (30%)	
	Gram-positive cocci (20%)	
	Enterobacter	
	Enterococci	
	Serratia, Citrobacter	
	Acinetobacter	
	Pseudomonas aeruginosa	
Neutropenic patients	Gram negative bacilli	Korzeniowski 1991
	Pseudomonas aeruginosa	
	Staphylococcus aureus	
	Candida	
UTI in HIV patients	*Escherichia coli,* Enterobacter	Sharifi and Lee 1997
	Klebsiella pneumoniae	
	Pseudomonas	
	Enterococci, *Staphylococcus aureus*	
	Cytomegalovirus, Adenovirus	
	Toxoplasma	
	Pneumocystis carinii	
	Blastomyces dermatidis	
	Mycobacterium tuberculosis	
Complicated UTI in Filipino patients (National Kidney & Transplant Insitute, Philippine General Hospital, Makati Medical Center, Cardinal Santos Medical Center, Davao Medical Center)	*E. coli*	Ninalga 2003
	Klebsiella pneumoniae	Magalit 2003
	Pseudomonas aeruginosa	Dytan 1999
	Proteus mirabilis	Raco 1998
	Enterobacter	

Table 14. Antibiotics that may be used as empiric therapy for complicated UTI

Oral Regimen
Ciprofloxacin *250-500 mg BID x 14 days* Norfloxacin *400 mg BID x 14 days* Ofloxacin *200 mg BID x 14 days* Levofloxacin *250-500 mg OD x 10-14 days*
Parenteral Regimen
Ampicillin *1 g q 6hrs* + gentamicin *3 mg/kg/day q 24h* Ampicillin-sulbactam *1.5-3 g q 6h* Ceftazidime *1-2 g q 8h* Ceftriaxone *1-2 g q 24h* Imipenem-cilastin *250-500 mg q 6-8 h* Piperacillin-Tazobactam *2.25 g q 6* Ciprofloxacin *200-400 mg q 12h* Ofloxacin *200-400 mg q 12h IV* Levofloxacin *500 mg q 24h IV*

Catheterized patients with no risk factors and who do not belong to any of the above-mentioned subsets and are otherwise asymptomatic need not be treated with antibiotics (Grade E).

2. In addition to antibiotic therapy, what other interventions should be done in symptomatic patients with chronic indwelling catheter?

Whenever possible, the indwelling catheter should be removed to help eradicate the bacteriuria (Grade A).

Long-term indwelling catheters should be replaced with new catheters before initiating antimicrobial therapy for symptomatic UTI (Grade A).

B. UTI in Diabetic Patients

1. How should UTI in diabetic patients be managed?

Diabetic patients require pre-treatment urine Gram stain, culture, and a post-treatment urine culture. At least 7-14 days of oral antibiotics is recommended with an antimicrobial that achieves high concentrations both in the urine and urinary tract tissues e.g.fluoroquinolones, TMP-SMX (Grade C).

Diabetic patients who present with signs of sepsis should be hospitalized. Urine and blood cultures before starting therapy are indicated. Failure to respond to appropriate therapy within 48 to 72 hours warrants a plain radiograph of the KUB, a renal ultrasound, or a CT-scan (Grade C).

C. UTI in Renal Transplant Patients

1. How should UTI in post-kidney transplant patients be managed?

UTI, which develops on the first three months post-transplant, including UTIs with signs of pyelonephritis or sepsis should 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).

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

2. What is the effective antibiotic prophylaxis for post-kidney transplant patients to reduce the risk for UTI?

For renal transplant patients, prophylaxis with TMP/SMX (160/800 mg) twice daily during the hospitalization period immediately post-transplant, then once daily upon discharge is recommended (Grade A). The dose of TMP/SMX should be adjusted to the renal function. Prophylaxis should be given for at least 6 months (Grade C).

D. UTI in Patients with HIV/AIDS

1. What is the management of UTI in patients with HIV/AIDS?

In addition to the general management of complicated UTI, HIV-AIDS patients with UTI should be evaluated to include other non-bacterial pathogens if clinically suspected and should be referred to an infectious disease specialist (Grade C).

E. Urinary Candidiasis

1. When is candiduria suspected or diagnosed?

Candiduria is defined as the presence of Candida species regardless of colony count in properly collected urine specimens on two separate occasions at least two days apart. The presence of candiduria may represent a whole spectrum of pathologic states from invasive renal parenchymal disease, fungal balls in obstructed ureters, lower UTI to benign conditions such as colonization.

2. When does candiduria require treatment?

Treatment of asymptomatic and minimally symptomatic candiduria is not recommended because it does not provide clear clinical benefits such as long-term (≥2 weeks) eradication (Grade D).

Candiduria should be treated with appropriate antifungal agents in symptomatic patients, critically ill patients in ICUs, patients with neutropenia, post-renal transplant

Table 15. Summary of treatment for Urinary Candidiasis

Condition	First-Line Treatment	Second-Line Treatment
Asymptomatic candiduria	Modify risk factors (rarely requires treatment)	Fluconazole 200 mg daily PO for 7-14 days in patients with indications for treatment
Candida cystitis	Fluconazole 400 mg loading dose then 200 mg per day given orally for 7-14 days	Amphotericin B bladder irrigation (50 mg/L) for 5 days or amphotericin B 0.3 mg/kg IV given in a single dose
Ascending pyelonephritis	Surgical drainage plus prolonged therapy with fluconazole 6 mg/kg/day OR IV amphotericin B 0.6 mg/kg/day for 2-6 weeks to complete a total dose of 1-2 g	____
Renal Candidiasis (hematogenous)	Prolonged therapy (2 to 6 weeks) with fluconazole 6 mg/kg per day OR amphotericin B ≥0.6 mg/kg per day for 4-6 weeks	____

patients and those who will undergo urologic procedures (Grade C).

3. If antimicrobial therapy is deemed necessary for a patient with candiduria, what antifungal agents are effective for treatment?

The first line of treatment is fluconazole 200 mg/day for 7-14 days (Grade A). The route of administration depends on the patient status and oral tolerability.

In clinical situations where resistance to fluconazole is suspected such as patients with *Candida glabrata* or patients suspected to have candidemia from an upper urinary tract obstruction or from other focus, bladder irrigation with amphotericin B at a dose of 0.3-l.0 mg/kg per day for 1-7 days is recommended (Grade B).

Amphotericin B is equally effective in lower urinary tract candidiasis, however because of the cost and difficulty in administration, its use must be limited to patients with indications for amphotericin use as above (Grade D).

4. In adult non-neutropenic patients with asymptomatic candiduria wherein antifungal therapy is not recommended, what other maneuvers can be done to manage the candiduria?

For these patients, modification of risk factors that predisposed to candiduria is the first line approach. These include control of diabetes and discontinuation of antibiotics if possible (Grade C). The removal of indwelling catheters and other urinary tract instruments such as stents is an important first step for the management ofcandiduria, and by itself generally results in spontaneous resolution of the candiduria (Grade B). If removal of these instruments is not possible, at least replacement of the device with new ones is beneficial (Grade A).

VII. URINARY TRACT INFECTION IN MEN

A. Uncomplicated Cystitis in Young Men

1. What is the definition of uncomplicated cystitis in young men?

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

2. How is uncomplicated cystitis in males diagnosed?

Significant pyuria in men is defined as ≥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 ≥1,000 colonies of one predominant species/mL of urine and best differentiates sterile from infected bladder urine (Grade C).

3. What is the recommended diagnostic work-up for uncomplicated cystitis in men?

The recommended diagnostic work-up includes a urinalysis and urine culture. A pre-treatment urine culture

should be performed routinely in all men with UTI (Grade C).

Routine urologic evaluation and use of imaging procedures are not recommended (Grade C).

4. What is the recommended treatment?

Seven-day antibiotic regimens are recommended (Grade C). TMP-SMX or fluoroquinolones may be used depending on prevailing susceptibility patterns in the community or institution (Grade C). See Section 1 on acute uncomplicated cystitis in women for antibiotic choices.

B. Prostatitis Syndrome

1. What is the definition of prostatitis?

In recognition of the limitations of the traditional classification of prostatitis syndromes by Drach et al [1978], the National Institutes of Health (NIH) International Prostatitis Collaborative Network, in a consensus conference in 1998, reevaluated the classification of prostatitis syndromes. The revised classification includes four categories and two subcategories as follows: See Table 16

2. What diagnostic tests should be requested for a patient suspected to have prostatitis?

For a presumptive diagnosis of prostatitis, whether acute or chronic, seminal fluid analysis is recommended (Grade C).

a. Acute bacterial prostatitis

Mid-stream urine sample for dipstick test, culture and sensitivity are recommended (Grade C).

Prostatic massage should not be performed on patients with acute bacterial prostatitis since this is extremely painful, could precipitate bacteremia, and is likely to be of little benefit as pathogens are usually isolated from urine.

b. Chronic bacterial prostatitis

The lower urinary tract localization procedure (see Table 17) is recommended in the investigation of chronic bacterial prostatitis (Grade C).

c. Chronic prostatitis/Chronic pelvic pain syndrome

There is no gold-standard diagnostic test for chronic pelvic pain syndrome, and the methodologic quality of available studies of diagnostic tests is weak.

Table 16. The NIH consensus classification of prostatitis syndromes

Category	Characteristic Clinical Features
I. Acute bacterial prostatitis	Acute infection of the prostate gland characterized by fever, chills, low back pain, perineal pain & irritative voiding symptoms. Rectal examination reveals a markedly tender, swollen prostate.
II. Chronic bacterial prostatitis	Recurrent infection of the prostate caused by persistence of the same organism despite treatment. Rectal examination reveals no characteristic finding.
III. Chronic prostatitis / chronic pelvic pain syndrome (CP/CPPS)	No demonstrable infection; primarily pain complaints, plus voiding complaints and sexual dysfunction affecting men of all ages. Usually cause is unknown.
IIA. Inflammatory subtype	Symptomatic patients without bacteriuria but with inflammation (white cells) in semen, expressed prostatic secretions or post-prostatic massage urine
IIIB. Non-inflammatory subtype	No white cells in semen, expressed prostatic secretions or post-prostatic massage urine
IV. Asymptomatic inflammatory prostatitis	No subjective symptoms, inflammation detected either by prostate biopsy or the presence of white cells in expressed prostatic secretions or semen during evaluation of other GU complaints

Source: Krieger 1999

3. What is the recommended treatment?

a. Acute bacterial prostatitis

As acute prostatitis is a serious and severe illness, empiric therapy should be started immediately (Grade C). Adequate hydration should be maintained, rest encouraged, and analgesics such as NSAIDs used (Grade C).

Empiric treatment with TMP/SMX or an oral fluoroquinolone may be started until culture and sensitivity results are known. Duration of treatment should extend to at least 30 days to prevent the development of chronic prostatitis (Grade C). If there is no response within the first week, change the antimicrobial and do culture of EPS (Grade C).

Severely ill patients require hospitalization and parenteral antimicrobials, such as an aminoglycoside-penicillin derivative combination or fluoroquinolones (Grade C). When complications of urinary retention or a prostatic abscess develop, referral to a urologist is recommended (Grade C).

b. Chronic bacterial prostatitis

Treatment should be guided by antimicrobial susceptibility patterns.

For chronic bacterial prostatitis, first line treatment is a quinolone such as:
- Ciprofloxacin 500 mg BID for 28 days (Grade C) OR
- Ofloxacin 200 mg BID for 28 days (Grade C) OR
- Norfloxacin 400 mg BID for 28 days (Grade C)

For those allergic to quinolones, the following are recommended:
- Doxycycline 100 mg BID for 28 days (Grade C)
- Minocycline 100 mg BID for 28 days (Grade C) OR
- Trimethoprim 200 mg BID daily for 28 days (Grade C) OR
- TMP-SMX 160/800 mg BID for 28 days (Grade C)

Men with recalcitrant chronic bacterial prostatitis can be treated with radical transurethral resection of the prostate or total prostatectomy. For symptomatic relief, Sitz baths, anti-inflammatory agents, prostatic massage and other supportive measures can be given (Grade C).

Long-term, low-dose suppressive therapy may be required for patients who do not respond to full dose treatment. TMP-SMX 80/400 mg once daily is recommended for 4 to 6 weeks (Grade C).

c. Chronic prostatitis / Chronic pelvic pain syndrome

Antibiotics and alpha-adrenergic blockers are not recommended for long-standing, refractory CP/CPPS (Grade D).
Heat treatment may be useful to relieve chronic pelvic pain syndrome (Grade C).

Allopurinol for nonbacterial prostatitis is not recommended at this time (Grade C).

VIII. PREVENTION OF CATHETER-ASSOCIATED URINARY TRACT INFECTION

A. How effective are the different catheter care and management policies in preventing catheter-associated UTI?

1. Personnel

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

1.2 Hand washing should be done immediately before and after catheter insertion or care (Grade B).

Table 17. Lower urinary tract localization procedure

Specimen	Procedure
Voided bladder 1 (VB1)	Initial 5-10 mL of urinary stream
Voided bladder 2 (VB2)	Midstream specimen
Expressed prostatic secretions (EPS)	Secretions expressed from prostate by digital massage after midstream specimen
Voided bladder 3 (VB3)	First 5-10 mL of urinary stream immediately after prostate massage

Unequivocal diagnosis of chronic bacterial prostatitis requires a 10-fold higher concentration of a uropathogen in the VB3 of EPS specimen when compared to the VB1 specimen. The organism is identical to organisms causing repeated episodes of bacteriuria.

Source: *Krieger 2003*

2. Catheter insertion procedure-related interventions

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

2.2 Catheters should be inserted using aseptic technique and sterile equipment (Grade A). Handwashing and cleaning of the periurethral area with water before insertion of a sterile catheter with gloved hands may be acceptable alternatives (Grade B).

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

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

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

2.6 Remove the urinary catheter as soon as possible (Grade A). Consider instituting automatic stop orders or chart reminders to decrease prolonged unnecessary catheterization (Grade B).

2.7 Do not change catheters and drainage bags at arbitrary fixed intervals (Grade D).

3. Methods to avoid endogenous infection

3.1 Daily meatal care is not recommended (Grade E).

4. Methods to avoid exogenous infection

4.1 Irrigation of the bladder with antimicrobial agents is not recommended (Grade D).

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

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

5. Bacteriologic monitoring and prophylactic systemic antibiotics

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

5.2 Systemic antibiotic prophylaxis in catheterized patients is not recommended (Grade D).

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).

B. How effective are the different types of indwelling urethral catheters in reducing the risk of catheter-associated UTI?

1. Antiseptic-impregnated catheters vs standard catheters

1.1 Consider using silver alloy catheters, if available, to reduce the risk of catheter-associated UTI (Grade B).

2. Antimicrobial-impregnated catheters vs standard catheters

2.1 The use of antimicrobial-impregnated catheters in reducing the risk of catheter-associated UTI is not recommended (Grade D).

3. Other types of indwelling urethral catheters

3.1 Consider using hydrophilic-coated catheters, if available, for patients who require intermittent self-catheterization to reduce the degree of urethral trauma (Grade C).

3.2 Consider using siliconised catheters, if available, to decrease urethral side effects in men requiring short-term catheterization (Grade B).

IX. NON-PHARMACOLOGIC INTERVENTIONS FOR UTI

1. How effective are non-pharmacologic interventions in preventing or treating urinary tract infections?

1.1 Cranberry juice and cranberry products are not recommended for the prevention and treatment of urinary tract infections in populations at risk (Grade D).

1.2 Lactobacilli both in oral form and vaginal suppositories are not recommended in the prevention of UTI (Grade C).

1.3 There is insufficient evidence to recommend oral water hydration in the prevention or treatment of UTI (Grade C).

1.4 There is insufficient evidence to recommend coconut juice in the prevention or treatment of urinary tract infection (Grade C).

1.5 There is insufficient evidence to recommend drinking more water and voiding soon after intercourse to prevent urinary tract infection (Grade C).

Glossary of Terms

Terms used to assess accuracy or clinical utility of diagnostic tests/signs/symptoms

Likelihood ratio (LR) - ratio of the probability of a test result/symptom (e.g. positive or negative) in patients with the disease to the probability in people who do not have the disease. It summarizes how many times more (or less) likely that patients with the disease are to have the test result/symptom compared to those without the disease. It expresses the likelihood that a given test result would be expected in a patient with the disease of interest as opposed to one without. A likelihood ratio >1 indicates that the test result is associated with the presence of the disease, while a likelihood ratio <1 indicates that the test result is associated with the absence of the disease. The further likelihood ratios are from 1 the stronger the evidence for the presence or absence of the disease. In general, likelihood ratios above 10 and below 0.1 are considered to provide strong evidence to rule in or rule out diagnoses respectively in most circumstances. When the diagnostic test reports results as being either positive or negative, the two likelihood ratios are called the positive likelihood ratio and the negative likelihood ratio. For tests with only two outcomes, the likelihood ratios can be computed directly from the sensitivities and specificities.

Negative predictive value (NPV) - proportion of patients with negative tests who do not have the disease/condition

Positive predictive value (PPV) - proportion of patients with positive tests who do have the disease/condition

Pre-test probability - the probability of the target condition being present before the results of a diagnostic test are available

Sensitivity - proportion of patients with the disease/condition correctly identified by the diagnostic test

Specificity - proportion of patients without the disease/condition correctly identified by the diagnostic test

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

Quality filters in assessing the evidence from 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 trial without randomization, from cohort or case-control 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 based on clinical experience, descriptive studies, or reports of expert committees

2. Studies on prognosis or causation

Criteria for assessing quality of evidence
1. An inception cohort was chosen.
2. Reproducible and inclusion and exclusion criteria were used
3. Follow-up was complete for at least 80% of subjects.
4. Statistical adjustment was carried out for confounders or extraneous factors.
5. 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. None of the 5 criteria was met.

3. Systematic reviews/ meta-analysis

Criteria for assessing quality of evidence
1. Comprehensive search of evidence
2. Focused criteria for selection of articles
3. Independent assessment of the validity of the articles

cited
4. Conclusions supported by data and analysis presented

Level of Quality of Evidence

I. All 4 criteria must be met.
II. 3 of 4 criteria are met
III. 2 of 4 criteria are met
IV. 1 or 4 criteria is met
V. None of the 4 criteria was met.

Appendix 2

Key Points on Proper 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. Urethral catheterization may be needed in adults who are suspected to have infection and cannot provide a clean-voided specimen. In such case, inform the laboratory that the specimen is catheterized urine.
5. First void morning specimen 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 specimen should be delivered to the laboratory immediately and should be cultured within one hour after voiding or refrigerated.

Appendix 3

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
Hypercalcemic nephropathy
Lithium toxicity
Hyperoxalosis
Heavy metal toxicity
Carcinoma of the bladder
Renal calculi
Allergic interstitial pyuria
Sickle cell disease
Sarcoidosis
Idiopathic interstitial cystitis
Glomerulonephritis

Infectious disease conditions
Tuberculosis
Chlamydial and gonococcal urethritis
Leptospirosis
Viral cystitis

Infections adjacent to the urinary tract
Appendicitis
Diverticulosis

RESERVED FOR FLOXEL (MEDICHEM)

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 PPD reference systems.

Aminoglycosides
Amikacin
Amikacide
Amikin
Kormakin
Nica
Gentamicin
Adelanin
Garamycin Injectable
Servigenta
Netilmicin
Netromycin

Carbapenems
Ertapenem
Invanz
Imipenem/Cilastatin
Tienam
Meropenem
Meronem

Cephalosporins
1st Generation
Cefadroxil monohydrate
Drozid
Drugmaker's Biotech Cefadroxyl
Duracef
Lexipad
Cefalexin
Am-europharma Cefalexin
Bloflex
Cefalin Capsule
Cefalin Drops/Suspensin
Ceporex
Cidoxine
Cromlex
Drugmaker's Biotech Cefalexin
Eliphorin
Exel
Forexine
Gesenal
Harvexyl
Keflex
Lefex
Lexibase
Lexum
Lonarel
Lyceplix
Medoxine
Nerfalex
Oneflex
Oranil
Pectril
Pharex Cefalexin
Ritemed Cefalexin
Selzef
Servispor
Vamsler Cefalexin
Xinflex
Zeporin
Cefazolin sodium
Faxilen
Lupex
Stancef
Cephradine
Drugmaker's Biotech Cephradine
Sedinef
Tolzep
Velodyne
Velosef
2nd Generation
Cefaclor
Aczebri
Ceclobid
Ceclor/Ceclor BID/Ceclor CD
Clorotir
Drugmaker's Biotech Cefaclor
Pharex Cefaclor
RiteMED Cefaclor
Xelent
Xeztron
Zunecar
Cefatrizine
Zanitrin
Cefprozil
Procef
Cefotiam
Ceradolan
Cefoxitin
Mefoxin
Monowel
Cefuroxime
Drugmaker's Biotech Cefuroxime
Infekor
Kefox
Lifurox
Profurex
RiteMed Cefuroxime
Romicef
Shincef
Zegen
Zinacef
Zinnat
3rd Generation
Cefixime
Tergecef
Ultraxime
Zefral
Cefotaxime
Cladex
Claforan
Cefoperazone
Sulperazone
Cefpodoxime
Banan
Ceftazidime
Fortum
Ritemed Ceftazidime
Tazidem
Zeptrigen
Zydime
Ceftibuten
Cedax
Ceftizoxime
Tergecin
Unizox
Ceftriaxone
Forgram
Keptrix
Megion
Retrocor
Ritemed Ceftriaxone
Rocephin
Xefatrex
Xtenda
4th Generation
Cefepime
Cepimax
Cefpirome
Cefrom

Penicillins
Amoxicillin
Aldemox
Amoxil
Amusa
Athenalyn
Axmel
Bacihexal
Bactigent
Cartrimox
Cilfam
Clearamox
Daisamox
DLI Amoxicillin
Drugmaker's Biotech Amoxicillin
Eleomox
Emilex
Glamox
Globamox
Globapen

Harvimox
Himox
IHC-Amoxicillin
Littmox
Macropage
Medimoxil
Megamox
Moxillin
Multicare Amoxcillin
Novamox
Oramox/Oramox Forte
Pediamox
Pharex Amoxicillin
Pharmamox
Polymox
Promox
Ritemed Amoxicillin
Servimox
Shinamox
Sumoxil
Teramoxyl
Vaxman
Zymoxyl

Ampicillin
Ampicin
Ampin
Amplivacil
Bactimed
DLI Ampicillin
Drugmaker's Biotech Ampicillin
Eurocin
Excillin
Pensyn
Pentrexyl
Polypen
Saloxin
Shinapen

Co-Amoxiclav
Amoclav
Augmentin
Augmex
Bactoclav
Bioclavid
Drugmaker's Biotech Amoxicillin + Clavulanic acid
Natravox
Prostaphlin-A

Pen G Benzathine
Penadur L-A

Sulbactam/Ampicillin
Unasyn IM/IV

Sultamicillin
Unasyn Oral

Tazobactam/Piperacillin
Tazocin

Ticarcillin/Clavulanate
Timentin

Quinolones

Ciprofloxacin
Ciprobay/Ciprobay XR
Cipromet
Cirok
Drugmaker's Biotech Ciprofloxacin
Floroc
Iprolan
Pharex Ciprofloxacin
Xipro
Zalvos
Zunexan
Zyflox

Gatifloxacin
Tequin

Levofloxacin
Floxel
Levox

Moxifloxacin
Avelox

Norfloxacin
Drugmaker's Biotech Norfloxacin
Ellatracid
Euroflox
Lexinor
Nortram
Pharex Norfloxacin
Uritracin Reformulated
Urobacid
Winaflox

Ofloxacin
Drugmaker's Biotech Ofloxacin
Gyros
Inoflox
Pharex Ofloxacin
Qiflon
Qinolon

Perfloxacin
Floxin
Peflacine

Sulfonamide Combinations

Cotrimoxazole
Am-Europharma Cotrimoxazole
Bacidal
Bactille Forte
Bactille-TS
Bactrim
Bacxal
Colimox
Cotrexel
Cotribase
Cotrimoxazole-Vamsler
DLI-Cotrimoxazole
Doctrimox
Drugmaker's Biotech Cotrimoxazole
Fedimed
Globaxol
Intrafort
Kathrex
Lagatrim Forte
Lictora
Macromed
Microbid/Microbid DS
Onetrim
Pharex Cotrimoxazole
Procor
RiteMED Cotrimoxazole
Septrin
Synerzole
Thoprim
Trihexal
Trim-S
Trimephar
Trizole Suspension

Trimethoprim/Sulfadiazine
Globec/Globec Forte
Triglobe
Trizine

Tetracyclines

Doxycycline
Atrax
Doryx
Doxin
Drugmaker's Biotech Doxycycline
Harvellin
Servidoxyne
Vibramycin

Lymecycline
Tetralysal

Oxytetracycline
Noxebron
Terramycin

Tetracycline
Moncycline
Ritemed Tetracycline
Tetracycline-B
Unimycin

Antifungals

Amphotericin
Fungizone

Fluconazole
Diflucan
Funzela

Urinary Antiseptics

E. Coli Lyophilized bacterial lysate
Uro-Vaxom

Methenamine hippurate
Hiprex

Nalidixic acid
Hanadex
Wintomylon

Nitrofurantoin
Harfurin
Macrodantin

Pinene/Camphene/Borneol Anethol/Fenchone/Cineole
Rowatinex

Intravaginal Estriol cream
Ovestin