

# **Clinical Practice Guideline Number 1**

## **Urinary Tract Infections: Diagnosis and Management**

### **THE PHILIPPINE CLINICAL PRACTICE GUIDELINE ON THE DIAGNOSIS AND MANAGEMENT OF URINARY TRACT INFECTIONS**

**Report of the Task Force on  
Urinary Tract Infections  
1998.**

This guideline is intended for use by a broad range of health care professionals including medical specialists, clinical practitioners, administrators, policy makers and nurses

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## TABLE OF CONTENTS

Background.....	1
Introduction.....	4
I. Acute uncomplicated cystitis in women	
1. Definition .....	5
2. Pre-treatment diagnostic tests .....	5
3. Duration of treatment .....	6
4. Choice of antibiotics .....	6
5. Post-treatment follow-up .....	6
II. Acute uncomplicated pyelonephritis	
1. Definition .....	7
2. Etiologic diagnosis .....	7
3. Treatment .....	7
4. Work-up for urologic abnormalities .....	9
5. Follow-up cultures during and post-therapy .....	9
6. Re-treatment .....	9
III. Asymptomatic bacteriuria	
1. Definition.....	10
2. Screening for asymptomatic bacteriuria.....	10
3. Treatment of asymptomatic bacteriuria .....	10
IV. UTI in pregnancy	
A. Asymptomatic bacteriuria (ASB) .....	11
B. Acute cystitis .....	12
C. Acute pyelonephritis .....	12
V. Recurrent UTI	
1. Definition .....	13
2. Treatment of individual episodes .....	13
3. Prophylaxis .....	13
4. Diagnostic work-up for urologic abnormalities .....	14
5. Prophylaxis in post-menopausal women .....	15
VI. Complicated UTI	
1. Definition .....	15
2. General recommendations for management .....	15
3. Special issues .....	18
VII. Uncomplicated UTI and Prostatitis in males	
A. Uncomplicated UTI in young males .....	19
B. Prostatitis .....	19
VIII. Prevention of catheter-associated UTI	
1. Personnel .....	21
2. The catheter .....	21
3. Methods to prevent endogenous infection.....	21
4. Methods to prevent exogenous infection .....	21
5. Bacteriologic monitoring and treatment.....	22
IX. Algorithms .....	23
References .....	26
Appendices .....	36
Acknowledgments .....	40

## BACKGROUND

Infectious diseases continue to be among the leading causes of morbidity and mortality in the Philippines. Antimicrobial agents are employed in the management of these diseases in a wide variety of patient conditions and clinical situation. The proliferation of newer antibiotics, diagnostic technology and therapeutic, modalities exerts pressure on the physician to keep up with new knowledge. Unfortunately, the demands of clinical practice leave the majority of health professionals little time to critically appraise these developments. Consequently, patients are exposed to wide variations in clinical care even for similar conditions and to potential irrational management. Thus, the impact of irrational medical practice, both in health and economic terms, can be substantial.

One way of addressing the problem is through clinical practice guidelines (CPGs) utilization. This will potentially minimize practice variations and irrationality of management decisions. Unfortunately, for the same clinical condition, there are different CPGs developed by different professional societies and hospitals. These CPGs also employed different techniques and methodologies. Thus, there is potential confusion among the target users in situations where there is divergent recommendation. One of the challenges is to harmonize the CPGs, develop a common standard for all, and collectively advocate for its utilization.

The Philippine Society for Microbiology and Infectious Diseases (PSMID) has been active in CPG development for a number of years. Recently, PSMID focused its efforts in harmonizing its CPGs with other societies, and synergizing activities with them. In addition, of primary concern is to approach these efforts in a more methodical and systematic fashion by following defined and scientifically acceptable processes and standards. The impetus for this is the desire to embrace the evidence-based concept, create effective partnership with appropriate collaborators, broaden the base of stakeholders, enhance education and training, and strengthen effective negotiation skills as strategies for CPG utilization.

### *Philippine Practice Guidelines Group - Infectious Diseases*

Through the initiative of PSMID, a consortium of collaborating societies and agencies organized the Philippine Practice Guidelines Group in Infectious Diseases (PPGG- ID) on 24 August 1997 with a whole-day seminar workshop. Representatives of this consortium signed the Memorandum of Agreement on 21 December 1997.

PPGG-ID is composed of 16 professional societies agencies. The Coordinating Council is the governing arm, with PSMID acting as the Secretariat. Initially, five multidisciplinary Task Forces were created to tackle five common infections, namely community-acquired pneumonia (CAP), urinary tract infections (UTI), bacterial meningitis, pulmonary tuberculosis (PTB), and sexually transmitted disease (STD). Work immediately began earnestly in December 1997.

The processes involved were borrowed heavily from the methodology and experiences of the Multisectoral Task Force on Hypertension Control which in 1995 embarked on CPG development for the detection and management of hypertension. Dr. Antonio Dans, Chair of the Technical Research Committee, was consulted and he offered helpful advice.

### *Objectives*

The objective for PPGG-ID is for the member sectors/societies to develop a common CPG based on the evidence-based approach and consensus-development techniques, and bring the whole effort of CPG development to its full cycle, i.e., including dissemination, implementation and impact assessment.

### *Methods Employed*

The evidence-based approach and formal consensus techniques (nominal group technique, and the modified Delphi technique) were employed in CPG development. Each Task Force membership was multidisciplinary with representatives coming from two or more society partners, including clinical epidemiologist practitioners. Expert panel members were either representative of a society or an acclaimed expert in the discipline. The stakeholders were broad to include representatives from the pharmaceutical industry, educators, administrators, policy makers and key influentials. Each of the following phases had specific outputs in the end. Task Force and Expert Panel members, respectively, had series of meetings or encounters within each phase to achieve their tasks.

#### *Phase I: Preparation of the Evidence-Based Report (EBR)*

The Task Force identified problems and clinical issues. These were prioritized and formulated into agenda for action. They then systematically reviewed and assessed the scientific literature electronically or through ancestry technique. Members tracked, retrieved and appraised current evidence pertaining to the diagnosis, management and prevention of the infectious disease in question. Recommendations were graded according to a scale modified from the Infectious Diseases Society of America (IDSA) Quality Standards for Infectious Diseases (1994) [Appendix 1].

Please refer to Appendix 2 for quality filters in assessing evidence from the scientific literature. The resulting draft was the EBR.

#### *Phase II: Preparation of the Interim Report (IR)*

The Interim Report was the result of review and discussion of the EBR by the same Task Force members. In most instances, Phases I and II were indistinguishable. The nominal group was technique was employed. Consensus was defined as 70% of votes cast, either by written ballots or by raising of hands.

#### *Phase III: Preparation of the Draft Guidelines (DG)*

The Draft Guidelines was the result of Expert Panel review of the IR using the modified Delphi Technique. Expert Panel was composed of Task Force members plus additional experts. All were again requested to vote on the issues until a consensus was reached (70% agreement for each issue; maximum of three circulations). This was done in a meeting, by mail or both.

#### *Phase IV: Preparation of the Final Guidelines (FG)*

The final guidelines considered the comments and feedback of stakeholders (non-panelists). A list of stakeholders was prepared and the DG was sent to them for review. Feedback was either written or verbal during a presentation in a public forum. Due consideration was given if feedback was based on sound clinical evidence. The completion of this Final Guidelines is just one of the milestones. It is the commitment of PPGG-ID to bring the CPG into the utilization phase. After all, "Guidelines do not implement themselves" (Australian National Health and Medical Research Council). Efforts for dissemination, implementation, monitoring and impact assessment are planned (Phases V-VII). Additionally, appropriate research issues and knowledge gaps have been identified and will be acted upon.

## INTRODUCTION

Urinary tract infections (UTI's) are among the most common infections encountered by physicians. In clinics of tertiary centers in Manila, Cavite and Zamboanga, 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. UTI's also constitute over 40% of hospital-acquired infections.

The clinical practice guidelines, (CPGs) on UTI's 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 syndromes, 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.

These recommendations are based on evidence derived from critical review of existing data and utilize modifications of the quality standards of the Infectious Diseases Society of America (IDSA). They are given alphabetical ranking to reflect their strength.

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  $\geq 100$  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 3. Laboratory criteria are based on the requisite that urine specimens are properly collected and handled (see Appendix 4).

Table 1. Risk factors for subacute pyelonephritis or complicated UTI

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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 anti-microbial use (in the past 2 weeks)
Symptoms for $> 7$ days at presentation
Diabetes mellitus
Immunosuppression

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**Summary of evidence:** A diagnostic criterion of  $> 100$  cfu/ml provides the best combined sensitivity and specificity. The threshold of 100 cfu/ml of urine is more sensitive (95% vs. 51%) but less specific (89% vs. 99%) compared to the traditional threshold of 100,000 cfu/ml in the detection of coliform infection in acutely symptomatic women (Stamm 1982, Kunin 1993). The threshold of  $> 1,000$  cfu/ml offers a greater specificity with little loss of sensitivity. It is for this reason that for clinical trials, the Infectious Diseases Society of America (IDSA) has proposed this criterion for the microbiologic diagnosis of acute uncomplicated cystitis in women (Rubin 1992).

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/ $\text{mm}^3$  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.

**Summary of evidence:** There are three techniques used in detecting pyuria: (a) urine microscopy using a hemocytometer and defining pyuria as 8 or more cells/ $\text{mm}^3$  of uncentrifuged urine has a sensitivity of 91%, specificity of 50% (Stamm 1982) (b) standard microscopy using 2 to 5 pus cells/hpf of centrifuged urine, which corresponds to 8 more cells/ $\text{mm}^3$  (Stansfeld 1962) and (c) a positive dipstick (leukocyte esterase test and nitrite test) which has a sensitivity of 83% (95% CI, 73% to 91%) and a specificity of 71% (95% CI, 66% to 77%) (Lachs 1992).

### 2. Pre-treatment diagnostic tests

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

**Summary of evidence:** A decision-analysis model that examined the cost-effectiveness of pre-treatment urine culture vs. urine culture obtained in patients whose symptoms persisted after 2 days of a multiple dose regimen of trimethoprim-sulfamethoxazole (TMP-SMX) showed that the pre-treatment urine culture strategy did not significantly, reduce symptom-days (3.2.4 to 2.97) and it increased the cost, (Carlson 1985). A cost- utility analysis (Barry 1997) showed that empiric therapy (therapy guided by clinical evaluation only without urinalysis and urine culture) with 7 days of antimicrobials is the most cost-effective. If the prior probability of having UTI was less than 30%, therapy guided by the result of a complete urinalysis (dipstick nitrite, leukocyte esterase tests or pyuria) was preferred. The pretest probability of having acute cystitis in a woman described in item 1.1 is 65% (Romanoff 1991). In such instance, it is cost-effective to start treatment without fulfilling the diagnostic criterion of a positive urine culture. The results of the cost-utility analysis and the decision analysis model should be applied with caution to Filipino patients because of differences in costs of physician charges, medications and patient preferences (Barry 1998).

### 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).

**Summary of evidence:** A meta-analysis of 9 randomized controlled trials (RCT) showed that a 3-day therapy had fewer bacterial eradication rates at 3-14 days post-treatment [(OR 0. 71(95% CI, 0.52, 0.95)], 4-6 weeks post-treatment [(OR 0. 69 (95% CI, 0. 54, 0. 89)], and higher relapse rate [(OR 1. 75 (95% CI, 1. 31, 2.33)] compared with the conventional 7-day therapy (Alejandria 1998). Data on the differences in the rates of clinical resolution and adverse events were in conclusive. Another meta-analysis also showed that conventional therapy was more effective than single-dose therapy (Leibovici 1991). A third meta-analysis (de Guzman 1998) comparing single dose with 3-day therapy showed that the latter was more effective (better bacterial eradication). However, the side effects were more frequent in those patients who received a three-day course. The panelists considered clinical resolution as a more important end point and recommended a 3-day course with instructions for the patient to return if symptoms persist or recur.

### 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)

**Summary of evidence.** The antimicrobials used in the RCTs that were included in the 3 meta-analyses can be used (Leibovici 1991, Alejandria 1998, de Guzman 1998). Because of consistently high (40 to 64%) rates of resistance of the most common uropathogen (*E. coli*) to ampicillin and amoxicillin, these drugs should be avoided (Dytan 1998, Raco 1998). There is a need for periodic surveillance to determine antimicrobial resistance patterns of uropathogens causing acute cystitis.

Table 2. Three-day regimen for acute uncomplicated cystitis

TMP/SMX 160/800 mg BID
Nitrofurantoin 100 mg QID
Norfloxacin 400 mg BID
Ciprofloxacin 250 mg BID
Pefloxacin 400 mg BID
Ofloxacin 200 mg BID
Co-amoxiclav 375 mg TID

### 5. Post-treatment follow-up

5.1 Routine post-treatment urine culture and urinalysis in asymptomatic patients are not recommended (Grade C).

**Summary of evidence.** The RCTs that evaluated the effectiveness of different antimicrobials and duration included bacteriologic eradication and/or clinical cure as outcomes. Those patients who had clinical cure but who achieved bacteriologic eradication were not followed up to determine their subsequent course. Since asymptomatic bacteriuria or pyuria in adult non-pregnant

healthy women without risk factors for complicated UTI is not treated, then routine post-treatment urine culture or urinalysis will not be of clinical value. The decision not to treat will not be changed by the presence or absence of bacteriuria or pyuria.

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).

**Summary of evidence.** The cure rate for a three-day antimicrobial therapy for acute uncomplicated cystitis is 81%. Patients whose symptoms worsen or do not improve after a 3-day therapy may harbor a resistant pathogen. This will require a urine culture and the administration of a new antimicrobial pending result of the sensitivity testing (Barry 1997).

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).

**Summary of evidence:** The cure rate for a seven-day therapy for acute uncomplicated cystitis is 94% (Barry 1997). Patients who continue to have symptoms after a 7-day therapy may have a complicated UTI and should be treated as one.

## II. ACUTE UNCOMPLICATED PYELONEPHRITIS

### 1. Definition

The classic syndrome of acute uncomplicated pyelonephritis (AUPN) is characterized by fever ( $>38^{\circ}\text{C}$ ), chills, flank pain, cost vertebral 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 an 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).

**Summary of evidence:** There are no studies that have specifically addressed the diagnostic utility of urine culture and sensitivity test and urine gram stain in AUPN. However, these tests are recommended because treatment options are simplified if a likely or confirmed pathogen is established. The differentiation between gram-positive cocci (staphylococci or enterococci) and gram-negative pathogens can influence empiric antibiotic choice. Results of culture and sensitivity test permit optimal antibiotic selection and may limit the consequences of inappropriate choice in terms of cost, resistance and adverse drug reactions.

2.2 Blood cultures (done twice) are recommended for those who are ill enough to require hospitalization, particularly those with suspected sepsis (Grade C).

**Summary of evidence:** Published prospective studies of acute uncomplicated pyelonephritis report positive blood cultures, in 6-12 of patients, with bacteremia more commonly reported among hospitalized patients (Johnson 1991, Talan 1998). There is no evidence in the literature that bacteremia portends a worse prognosis or warrants longer therapy in an otherwise healthy individual with AUPN. There are no published studies designed to look into the benefits in terms of cost or outcome of blood cultures in AUPN. However, blood cultures, when positive, provide strong supportive evidence of the causative microorganism and sensitivity tests help guide management.

### 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, case 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).

**Summary of evidence:** *There are no prospective trials that define which patients should be treated as outpatients and which should be hospitalized. Published reports are mainly retrospective studies and case series, which show over 90% cure rates and no excess morbidity in women managed without hospitalization (Ward 1991, Israel 1991, Safrin 1988, Pinson 1994). A retrospective analysis of 94 female outpatients and 100 hospitalized women treated for acute pyelonephritis showed no difference in outcomes but cost analysis demonstrated a 7.5 fold differential favoring the outpatient treatment group (Safrin 1988). The need to minimize cost and de-institutionalize care suggests that outpatient therapy should be explored further to define optimal use of this option.*

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

Characteristic Pathogens	Clinical Situation	Recommended Empiric Treatment
E. coli, P. mirabilis, K. pneumoniae, S. saprophyticus	Mild-to-moderate illness, no nausea or vomiting, - outpatient therapy	Oral* fluoroquinolone, TMP/SMX or co-amoxiclav for 14 days
	Severe illness or possible urosepsis - hospitalization required	Parenteral** aminoglycoside, fluoroquinolone or third generation cephalosporin until fever is gone (usually after 24-48 hrs), then oral fluoroquinolones or TMP/SMX to complete 14 days

\*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 160/800 mg every 12 hours; co-amoxiclav 625 mg. every 8 hours. Ciprofloxacin may be given for seven days (see Section 3.4).

\*\*Parenteral regimens: ceftriaxone 1-2 g once a day; ciprofloxacin 200-400mg 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.

**Summary of evidence:** *There is relative paucity of well-controlled trials comparing the efficacy of various antibiotic regimens in acute uncomplicated pyelonephritis. The recommended regimens in Table 3 have comparable efficacy, provided that the infecting organism is susceptible. The recommendations have taken into consideration the limitations of local reports on sensitivity patterns and are not meant to exclude other effective regimens. For instance, aminoglycosides other than gentamicin may be used. The choice of empiric antimicrobial should largely be based on the epidemiologic information available to the physicians in their locality. As in other countries, resistance to ampicillin of E. coli strains causing UTI in local studies is uniformly high,*

ranging from 43 to 75% (Dytan 1997, Raco 1998). Thus, this agent is no longer the standard of treatment of UTI. Resistance rates to other commonly used agents such as first-generation cephalosporins and TMP/SMX are also high but are expected to vary across patient groups and geographic locations of data sources. Unfortunately, local data on uropathogens causing acute uncomplicated pyelonephritis are not available. Thus, the importance of determining urine culture and sensitivity results for AUPN cannot be over-emphasized.

Treatment with ampicillin resulted in more recurrences compared to treatment with TMP/SMX (12/27 vs. 4/33,  $p < 0.008$ ) among patients with AUPN enrolled in a randomized trial (Stamm 1987). In the same study, recurrences with drug-resistant strains occurred more frequently in the Ampicillin group. In another randomized trial of 14-day ampicillin vs. TMP/SMX (each given IV for the first 3 days, plus gentamicin IV for mean of 6.6 doses in both arms), antimicrobial resistance necessitated modification of therapy in 32% of the ampicillin recipients but in none of the TMP/SMX group ( $p < 0.001$ ) (Johnson 1991). Sandberg (1990) found that 14-day therapy with norfloxacin resulted in more early and late cures than did therapy with cefadroxil ( $P < 0.0001$ ). In this and another comparative trial (Stathakis 1990), cefadroxil therapy resulted in low late cure rates of 44 and 52% respectively. Relatively high recurrence rates with cefadroxil (25-47%) and ampicillin have been reported in the above-mentioned studies in contrast to those for fluoroquinolones and TMP/SMX.

A randomized trial involving more than 100 hospitalized patients compared oral co-amoxiclav (375 mg TID) vs. TMP/SMX (160/800 mg BID) given for 10 days. Patients on co-amoxiclav had comparable early (94% vs. 82%,  $p > 0.05$ ) but higher late cure rates (85% vs. 64%,  $p = 0.02$ ). (Karachalios 1985). There is no evidence to support the use of two combined antibiotics for the treatment of acute pyelonephritis. There is no point in using another drug with an amino glycoside unless one suspects an enterococcal etiology (as when urine gram stain shows gram positive cocci in chains), in which case Ampicillin is added.

**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).

**Summary of evidence:** A systematic review of oral antibiotic regimens for acute pyelonephritis found nine randomized clinical trials comparing oral antibiotics and only one trial comparing oral and IV therapies (Pinson 1992), the latter among pregnant patients. Similar bacteriologic cure rates (~90%) were observed in both IV and oral groups of the last study.

**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 added benefit and is not recommended (Grade E).

**Summary of evidence.** The optimal duration for treatment of pyelonephritis has not been adequately studied and remains undefined. Few studies have specifically addressed this issue. In a randomized controlled trial of women with pyelonephritis, 2-week regimens of ampicillin or TMP/SMX resulted in comparable cure rates as 6-week regimens (79% vs. 64%,  $p > 0.05$ ), but the longer regimen had increased frequency of adverse reactions (Stamm 1987). In a double blind randomized trial, 1 week of therapy using the combination of pivampicillin and pivmecillinan showed recurrences than three weeks of therapy (Jernelius 1988). However, this study did not include

a group treated for two weeks. Data showing high cure rates (83-93%) of 5 days therapy mainly came from case series and randomized studies involving relatively few patients and without appropriate controls (Bailey 1986, 1987, 1992, 1994). The only well designed randomized trial which compared a 14-day vs. 7-day regimen tested oral TMP/SMX + initial ceftriaxone (14 days) and oral Ciprofloxacin + initial Ceftriaxone (7 days) among non-hospitalized patients. Significantly higher bacteriologic (99% vs. 89%) and clinical success rates were seen in the Ciprofloxacin group at 4-11 days post-therapy but no significant difference at 22-48 days post-therapy (Talan 1998). This difference was largely due to higher failure rates among patients on TMP/SMX whose *E. coli* isolates were resistant to the drug. Thus, except for 7-day Ciprofloxacin, routine use of less than 14 days therapy is not supported by currently available comparative clinical trials. Further studies are needed to identify optimal treatment duration for cure of AUPN.

#### 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).

**Summary of evidence.** The only prospective study in which renal ultrasonography was used to evaluate the kidneys during the course of AUPN in adults enrolled 25 women admitted consecutively for treatment of AUPN. The frequency of detecting underlying anatomic abnormalities and focal infectious complications (transient and not requiring intervention) was low at 4% (95% CI, 0-12%) and 8% (9.5% CI, 0-19%), respectively. Given the costs of radiologic work-up and the low diagnostic yield, women presenting with a first episode of AUPN do not require further investigation.

## 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).

**Summary of evidence.** The abovementioned recommendations are mainly based on expert opinion.

## 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 re-treatment 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).

**Summary of evidence:** There are no well-defined randomized controlled studies to identify the optimum duration of treatment for women with recurrent pyelonephritis.

# III. ASYMPTOMATIC BACTERIURIA

## 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.

**Summary of evidence:** In the absence of symptoms, Kass (1956) showed that the quantitative threshold of > 100,000 cfu/ml from midstream urine or catheterized urine was useful to distinguish true bacteriuria from contamination. This threshold has also been validated by other investigators (Platt 1983, Bartlett & Galen 1983). Because these individuals are symptomless, 2 consecutive cultures yielding the same organisms from midstream urine specimens are needed for the diagnosis. There are no population-based studies on asymptomatic bacteriuria among adults in the Philippines. In various surveys of community populations in developed countries, the prevalence of asymptomatic bacteriuria increases with age, and is highest among institutionalized elderly women (25 -53%), institutionalized elderly men (1.5-37%), and ambulatory elderly women (5.8-43%) (Nicole 1997). These studies are variable in terms of the age cut-off for the elderly, the state of wellness of the institutionalized elderly, and the use of antimicrobials for asymptomatic bacteriuria in the study settings. The prevalence of asymptomatic bacteriuria among women undergoing treatment for diabetes mellitus is generally threefold higher than among non-diabetic women (range: 0-29%). The prevalence is lower in diabetic men, ranging from 0.7-11.1%. Many studies have shown that the prevalence rate is not influenced by the type or duration of diabetes, nor by the adequacy of diabetic control (Zhanell 1991), except for a survey among diabetic women in Canada where duration of the diabetes was found to be an independent risk factor (Zhanell 1995). The incidence of significant bacteriuria among catheterized patients with initially absent or low-count bacteriuria

was found to range from 18 - 62% within two days from catheterization (Stark & Maki 1984). In a review of kidney transplant recipients receiving prednisone and azathioprine, the prevalence of infection was 54%, with 91% of these infections being a symptomatic (Ramsey 1979). Since other risk factors such as immunosuppression, presence of diabetes or indwelling catheters are present in these patients, it was not clear from the reviews which of the patient variables were independent risk factors. Among patients with genitourinary abnormalities, the incidence of asymptomatic bacteriuria depends on the primary renal disease: chronic glomerulonephritis, 12%; diabetic nephropathy, 13%; polycystic kidney disease, 41 % and chronic pyelonephritis, 67% (Zhanel 1990)

## 2. Screening for asymptomatic 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.

**Summary of evidence:** *The decision to screen depends on the test characteristics of the screening tool, its cost-effectiveness, and the effectiveness of interventions for treatment, or prevention of transmission once infection is detected (Fletcher & Fletcher, 1996, US. Preventive Services Task Force 1996). Current evidence does not show significant benefit in the treatment of asymptomatic bacteriuria in the elderly population and in those with long-term in dwelling catheters (see Section 3 below); therefore, screening or periodic testing of these populations is not recommended. Asymptomatic bacteriuria among diabetic women has been associated with increased involvement of the upper urinary tract, although the long-term consequences are still poorly documented (Zhanel 1991). Among renal transplant patients, UTIs in the first 3 months post-transplant occur at a high rate of 29 - 95% and are usually asymptomatic. Untreated, UTI's among these immunosuppressed transplant patients are frequently associated with overt pyelonephritis, bacteremia and all graft dysfunction (Korzeniowski 1991). Pyuria has been shown to have a good predictive value in patient populations where the prevalence of asymptomatic bacteriuria is at least 10%. With pyuria of  $> 10$  wbc/hpf, the likelihood ratio (L.R.) for a significant urine culture result among ambulatory, elderly men was 417; for 2-10 wbc/hpf, L.R was 0.03 (Norman 1996).*

## 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).

**Summary of evidence:** *Few RCTs have been done for the treatment of asymptomatic of bacteriuria. However, among asymptomatic women with persistent bacteriuria after catheter removal, it was observed that 26% developed symptoms within 14 days (Harding 1991). In addition, to avoid possible bacteremia and sepsis, asymptomatic bacteriuria should be treated when patients undergo genitourinary manipulation or instrumentation, particularly among patients with compromising medical conditions. Similarly, because of the high risk of complications, several investigators recommend treatment among patients with genitourinary, abnormalities (Zhanel 1990). Randomized controlled trials also need to be done to show that treatment of asymptomatic bacteriuria in diabetic patients provides significant reduction in incidence of symptomatic infection, renal function deterioration, pyelonephritis, perinephric abscess, papillary necrosis or septic complications. However, given the frequency and*

severity of upper UTI among diabetic patients with bacteriuria, many experts recommend treatment (Patterson 1997). There are no well-controlled studies on the treatment of asymptomatic funguria. Retrospective and cohort studies have shown spontaneous clearance of infection for many cases, although resolution could be in a matter of months. Randomized controlled trials are needed to evaluate the effectiveness of amphotericin B or nystatin bladder irrigation vs. systemic anti-fungal drugs such as the imidazoles (Wong-Beringer 1992). A cohort study of ambulatory elderly women showed that asymptomatic bacteriuria was not an independent risk factor for mortality (Abrutyn 1994). Randomized controlled trials in both male and female elderly populations showed no differences between treated and untreated groups (Abrutyn 1994, Nicolle 1983, Nicolle 1987). One randomized clinical trial showed a higher mortality among treated elderly women who had a symptomatic bacteriuria (Nicolle 1987). Two randomized controlled trials among institutionalized elderly women showed increased rates of adverse reactions from antimicrobial therapy, with one showing an increased frequency of re-infection with resistant organisms (Nicolle 1987, Ouslander 1995). Similarly, a randomized controlled trial of routine treatment of asymptomatic long-term catheterized patients showed no benefit, and increased rates of antibiotic-resistant bacteria in the treated group (Warren 1982).

#### 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.

**Summary of evidence:** In the absence of symptoms, Kass (1956) showed that the quantitative threshold of > 100,000 cfu/ml from midstream urine or catheterized urine was useful to distinguish true bacteriuria from contamination. This threshold has also been validated by other investigators (Platt 1983, Bartlett & Galen 198j). Because these individuals are symptomless, 2 consecutive cultures yielding the same organism from midstream urine specimens are needed for the diagnosis.

###### 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).

**Summary of evidence:** The risk of acquiring bacteriuria increases with the duration of pregnancy. The risk of onset of bacteriuria is highest between the ninth and seventeenth weeks of gestation. The sixteenth gestational week appears to be the optimal time to obtain a single screening tests for bacteriuria because treatment given at this time would provide the greatest number of bacteriuria-free gestational weeks (Stenqvist 1989, Andreole 1991). Asymptomatic bacteriuria occurs in 3-10% of all pregnant women and if left untreated can certainly affect both maternal and fetal outcome. This prevalence even increases in high risk pregnant women, such as diabetics (12.5%) and those with a previous history of UTI (18.5%) (Golan 1989). The two most important maternal complications of untreated ASB are acute cystitis and acute pyelonephritis. ASB was studied among normal and high-risk pregnant women (diabetics and those with a previous history of UTI). The proportion of women with prior ASB was higher among those who developed pyelonephritis than among those who had cystitis:

	CYTITIS PYELONEPHRITIS	
NORMAL	33.0%	66.0%
DIABETICS	58.3%	85.7%
PREVIOUS UTI	60.0%	66.6%

Fetal complications such as low birth weight (LBW) and preterm delivery have been associated with asymptomatic bacteriuria. In cohort studies, non-bacteriuric patients had only two-thirds the risk of LBW and half the risk of preterm delivery compared to untreated ASB. A meta-analysis of both cohort and randomized treatment trials indicated a strong association between untreated ASB and low birth weight (LBW) / preterm delivery and that antibiotic treatment is effective in reducing the occurrence of LBW (Romero 1989). Pre-eclampsia has also been reported to increase susceptibility to infection. The association of bacteriuria with pre-eclampsia was first noted in 1936. Kincaid-Smith and Bulba reported that hypertension in pregnancy was more frequent in women with bacteriuria than in those without bacteriuria. The result of a controlled prospective study comparing the frequency of bacteriuria in women who developed pre-eclampsia with that in women with uncomplicated disease was consistent with those previously reported (Hill 1986). The prevalence of ASB in pre-eclampsia is 19%.

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).

**Summary of evidence:** Reagent strip testing of urine specimens for infection has been widely used in clinical practice. This has gained popularity among pregnant patients presenting in emergency rooms for symptoms of acute UTI. It has reduced the number of specimens sent to the laboratory by as much as 75%. Reagent strip testing when compared with the gold standard urine culture and the results were as follows: Sensitivity: 18.8% - 33.3 % (all four tests used. blood, protein, nitrite, leukocyte esterase); Specificity: 91.1% - 99%; Positive predictive value (PPV): 69%; Negative predictive value (NPV): 95% or more (Tincello 1998). Other rapid screening tests were also compared with standard urine culture and the results were as follows:

	SENSITIVITY	SPECIFICITY
Gram's stain	91.7%	89.2%
Urine dipstick	50.0%	96.9%
Urinalysis with leukocytes (Pyuria)	25.0%	99.0%

Urinalysis was never the test of choice in detecting ASB because it detected fewer positive cultures and leukocyte measurement correlated poorly with asymptomatic bacteriuria (Bachman 1993).

### 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).

**Summary of evidence:** A meta-analysis of thirteen studies that compared antibiotic versus no treatment for ASB in pregnancy showed that antibiotic treatment was effective in clearing ASB (OR 0.07, 95% CI, 0.05-0.10), and reduced the incidence of pyelonephritis (OR 0.25, 95% CI 0.19-0.32) and of preterm delivery (OR 0.60, 95% CI 0.45-0.80) (Smaill 1998). The studies included trials that enrolled pregnant women found to have ASB on their initial prenatal visit, compared any antibiotic regimen with no treatment and provided data on the persistence of bacteriuria, development of pyelonephritis or incidence of preterm delivery. While these studies reported a favorable outcome with antibiotic treatment, the studies were not methodologically strong, and that there could be a risk of selection bias since blinding of participant and/or observer was not attempted in all studies. Despite this methodological weakness, the result demonstrated a consistent relationship between asymptomatic bacteriuria and late development of pyelonephritis, with the overall incidence of pyelonephritis in the untreated group to be 19%. The presence of ASB further identifies a population at risk for developing acute pyelonephritis for which treatment is indicated (Smaill 1998). Because of the poor methodology, definitive conclusion with regards to the reduction of preterm delivery should be drawn cautiously. The apparent reduction in preterm delivery is consistent with current theories about the role of infection as a cause of preterm birth (Smaill 1998). A meta-analysis looking at the relationship between ASB and preterm delivery low birth weight showed that non-bacteriuric patients had only about 2/3 the risk (typical relative risk = 0.65; 95% CI, 0.57-0.74) of LBW and half the risk (typical relative risk = 0.50, 95% CI, 0.36-0.70) of preterm delivery of those with untreated ASB. The analysis of randomized clinical trials further showed that antibiotic treatment significantly reduced the risk of LBW (typical relative risk = 0.56, 95% CI, 0.43, 0.73) with a substantial reduction of 6.4 (CI 3.3, 9.5) percentage points in the rate of LEW (Romero 1989).

3.2 It is recommended that antibiotic treatment be initiated upon diagnosis of ASB in pregnancy. 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).

**Summary of evidence:** A meta-analysis of seven randomized or quasi-randomized comparison of antimicrobial regimen differing in duration reported no significant difference between a single-dose therapeutic regimen and a 4-7 day course. However, because of the wide confidence intervals and significant heterogeneity between trials, the conclusion should be interpreted with caution (Netar 1998).

## 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/mm<sup>3</sup> of uncentrifuged urine OR, (b) 5 or more pus cells/hpf of centrifuged urine, and (c) positive leukocyte esterase and nitrate test (Grade C).

*Summary of evidence: See section on acute uncomplicated cystitis.*

### 2. Treatment

Treatment of acute cystitis in pregnancy should be instituted immediately to prevent the spread of the infection ascending 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).

*Summary of evidence: The incidence of acute cystitis during pregnancy is 1.3% (Harris 1981 1984). It often occurs during the second trimester and may not necessarily be preceded by asymptomatic bacteriuria during the previous weeks. Treatment of symptomatic UTI using single (3.5 gm of Ampicillin plus 1 gm probenecid) versus a 10-day course of ampicillin (500 mg 4x/day) showed that multiple-dose cure rate was significantly better than a single-dose regimen (67.3% vs. 57.1%, respectively) (Adelson 1992, abstract only). The effectivity of nitrofurantoin (100 mg 3x/day) and ampicillin (500 mg 3x/day) for 5 days was also compared in a prospective trial involving 103 pregnant patients with acute cystitis. The overall cure rate varied from 87% to 89% with no significant difference between the two regimens (Calderon 1989) (based on abstract, original article in Spanish). There are no studies available on the use of newer antibiotics.*

## C. ACUTE PYELONEPHRITIS IN PREGNANCY

### 1. Definition

Acute pyelonephritis, an inflammation of the renal parenchyma, is characterized by shaking chills, fever (> 38°C), 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 an 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).

*Summary of evidence: See section 2.1 of acute uncomplicated pyelonephritis.*

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

*Summary of evidence: See section on acute uncomplicated pyelonephritis.*

### 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 drug's contraindicated in pregnancy (see Table 4) (Grade C).

Table 4. Antibiotic use in pregnancy

Safe	Use with caution	Contraindicated
Cephalosporins	Aminoglycoside	Tetracycline
Co-amoxiclav	TMP/SMX (1st & 2nd trimester)	Fluoroquinolone
Ampicillin-sulbactam		TMP/SMX (3rd trimester)
Aztreonam (probably)		

(Reese & Betts 1996)

**Summary of evidence:** Acute pyelonephritis is the most frequent complication of the urinary tract during pregnancy and the most common medical reason for hospitalization. The incidence increases as gestation progresses and has been observed in 1-2.5 % of patients (Cunningham 1973, Gilstrap 1980). This illness can potentially lead to maternal sepsis, shock, death and fetal wastage (Harris 1984). In general, patients with acute pyelonephritis are hospitalized and given intravenous antibiotic therapy until the patient is afebrile, after which oral antibiotic therapy can be given to complete 14 days.

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).

**Summary of evidence:** A randomized prospective trial on 90 pregnant patients with acute pyelonephritis was conducted to compare the safety and efficacy of oral (cephalothin 500 mg every 6 hours) versus intravenous (cephalothin 1 gm IV every 6 hours) antibiotic therapy. Bacteremia was noted in 13 (14.4%) of the 90 patients and IV therapy was instituted. Both therapies were successful in eradicating the infection (91.4% oral, 92.9% IV) (Angel 1990).

## 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, cephadrine, ciprofloxacin and lomefloxacin is effective (Grade A). Three-day treatment with any of the antibiotics for simple uncomplicated cystitis (see Section 1) 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).

**Summary of evidence:** The number of trials addressing the issue of treatment of individual episodes in recurrent UTI is limited. Amoxicillin-clavulanate, cephadrine, ciprofloxacin and lomefloxacin have all been found to be effective (Cox 1992, Buffet 1990). There are no published trials on using 3-day therapy for treating individual episodes of UTI in women who have recurrent UTI. However, given the evidence that the microbial flora encountered in patients with recurrent UTI are similar to those observed in women with uncomplicated UTI where 3-day therapy is considered acceptable, it is very likely that 3-day or 7-day therapy with any of the antibiotics recommended for simple uncomplicated UTI will also be effective in this setting. In a trial where 38 patients with recurrent UTI were randomized to receive either continuous prophylaxis with TMP/SMX or intermittent self-administered therapy with TMP/SMX, 92% of symptomatic episodes in the self-therapy group were confirmed microbiologically.

and 86% of the infections responded to the single-dose treatment. Five and 3 patients developed side effects in the prophylaxis and self-therapy groups, respectively (Wong1985). Comparing direct costs the annual cost per person in the prophylaxis group was \$256 versus \$239 in the self-therapy group. The authors cautioned, however, that their population was a select group of women, many of whom had attended a special clinic on UTI and all were sufficiently motivated to enroll in a long-term clinical study.

### 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).

**Summary of Evidence:** There are no reports of long-term sequelae from recurrent UTI. Therefore, the decision to give prophylaxis rests more on weighing the benefit of alleviating the discomfort of UTI and avoiding the inconveniences associated with recurrent episodes versus the potential harm of drug prophylaxis and emergence of resistant strains. The reported incidence of adverse drug effects with prophylaxis ranges from 1.3% to 20% (Melekos 1997, Brumfitt 1995, Brumfitt 1991, Stamm 1980, Nicolle 1989, Stapleton 1990). Studies where vaginal and fecal flora was monitored during prophylaxis showed that the incidence of emergence of resistant strains is very low (Stamey 1977, Pfau 1994). Another relevant issue is cost-effectiveness of prophylaxis versus treating individual episodes of recurrent UTI. A cost-effectiveness study done in the United States in 1981 concluded that continuous prophylaxis with TMP/SMX was more cost-effective than treating individual episodes (Stamm 1981). However, their results do not appear applicable to our setting because of differences in costs of physician charges, medications and extent of laboratory work-up.

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).

**Summary of evidence:** in a double-blind randomized controlled trial of 30 patients comparing norfloxacin given 200 mg daily for 12 months with placebo, no patient developed UTI while on prophylaxis while 67% of patients in the placebo group developed at least one episode of UTI (Nicolle 1989). In another double-blind randomized controlled trial, which compared placebo with nitrofurantoin (100 mg daily for 6 months) and TMP/SWX (40 mg/200 mg daily for 6 months), 77% of patients in the placebo group had at least one episode of UTI compared to 0.08% each in the nitrofurantoin and TMP/SMX groups (Stamm 1980). Post-coital administration of TMP/SWX (40 mg/200 mg as a single dose) given for 6 months was compared with placebo in a randomized controlled trial of 28 women regardless of whether their UTI episodes were temporally related to sexual intercourse or not. The proportion of patients who developed UTI was 75% in the placebo group and 12% in the post-coital prophylaxis group (Stapleton 1990). A comparison of post-coital versus continuous Ciprofloxacin showed that both regimens were equally effective but the rate of discontinuance due to adverse drug reaction was higher in the continuous prophylaxis group (5.35%) compared to the postcoital prophylaxis group (1.3%) (Melekos 1997).

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

	Recommended dose for continuous prophylaxis	Recommended Dose for post-coital prophylaxis
Nitrofurantoin	100 mg at bedtime	
Norfloxacin	200 mg at bedtime	200 mg
TMP/SMX	40 mg/200 mg at bedtime	40 mg/200 mg
Ciprofloxacin	125 mg at bedtime	125 mg
Ofloxacin		100 mg

References: Pfau 1994, Stapleton 1990, Brumfitt 1991, Brumfitt 1995, Stamey 1977, Stamm 1980, Nicolle 1989, Melekos 1997

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

**Summary of evidence:** *In the 6-month period after discontinuation of 6-month prophylaxis, 48% of patients in the treatment groups developed at least one episode of UTI, a rate similar to that of the placebo group (Stamm 1980). One other trial with a 6-month prophylaxis had similar results (Stamey 1977). In one trial of 12-month prophylaxis, the authors report that 69% maintained improvement after discontinuation of prophylaxis but no details were provided (Brumfitt 1991). There is a report of continued suppression of gram-negative introital flora in 36% of women within one) fear of stopping continuous or postcoital ciprofloxacin prophylaxis but this was not accompanied by clinical correlation with actual episodes of urinary tract infection (Melekos 1997).*

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.

**Summary of evidence:** *The reported incidence of infections with organisms resistant to antibiotic being used for prophylaxis ranges from 12% for TMP/SMX (Stapleton 1990), 50% for norfloxacin (Brumfitt 1991), 54% for cefaclor (Brumfitt 1995), and 58% for nitrofurantoin (Brumfitt 1995).*

#### 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).

**Summary of evidence:** *The reported prevalence of urologic abnormalities in women with recurrent UTI significant enough to warrant a change in management ranges from 0% (Fair 1979, Engel 1980, Fowler 1981) to 6% (Fairchild 1982). A systematic review (Mushlin 1989) estimated the overall prevalence at 0.8%. A study of 148 women, which included only those with at least one of the features No. 1 to No. 7 in above list, reported a prevalence of significant urologic abnormalities of 21% (Nickel 1991). Because UTI in childhood is associated with reflux nephropathy, inclusion of this group of women was also recommended although there is no data regarding the predictive value of this feature (Mushlin 1989).*

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).

**Summary of evidence:** *Most studies report urologic abnormalities identified from intravenous pyelography (IVP). However, IVP can cause mild generalized reactions (skin rashes, wheal-type eruptions, itching, periorbital or circumoral edema, nausea and vomiting and syncope) in 5 to 10% of patients (Mushlin 1989). In one study where 120 women underwent both IVP and renal ultrasound (RUS), there was good agreement between the two modalities for diagnosis of hydronephrosis ( $\kappa = 0.91$ ) but less agreement in the diagnosis of major pyelonephritis changes ( $\kappa = 0.79$ ), ureteric calculi and renal calculi  $>5$  mm ( $\kappa = 0.78$ ) and expansile lesions ( $\kappa = 0.38$ ) (Aslaksen 1990). In one study of 94 women with a history of UTI (not limited to recurrent UTI) referred by their physician for IVP or RUS, the findings of a combination of ultrasound and a plain abdominal radiograph was compared with IVP and the only disagreement was in one patient where RUS detected a 1.5cm intrarenal mass not seen on IVP (McNicholas 1991). In another study comparing combined ultrasound and plain abdominal radiograph with IVP performed on 89 women and 69 men with a history of UTI, the two modalities concurred in 152 of the 158 patients. RUS and plain film did not detect 3 cases of duplex kidney, 2 cases of small bladder diverticula and one case each of papillary necrosis and mild bilateral hydronephrosis of unexplained etiology (Spencer 1990).*

## 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).

**Summary of evidence:** *A randomized, double-blind, placebo-controlled trial in 93 post-menopausal women showed that an estriol cream applied intravaginally resulted in an absolute risk reduction in UTI episodes of 39% (Raz 1993).*

## 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 and 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 100,000cfu/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).

**Summary of evidence:** *In contrast to the other forms of UTI, complicated UTI usually needs more supervised medical attention, closer follow-up and more sophisticated management strategies (Ronald & Harding 1997). Structural and anatomic abnormalities of the urinary tract interfere with the normal storage and flow of urine, which makes infection more likely, with a tendency to be more chronic unless abnormalities are corrected. Patients with hormonal, metabolic and immunologic deficiencies are more prone to infection by various pathways. Usually, all these patients have pathogens, which are more difficult to eradicate (Nickel 1988). Until this time there is little evidence clarifying the epidemiology of complicated UTI. Population-based studies are lacking to describe the burden of illness of complicated UTI (Ronald & Harding 1997). Some groups however are better studied like UTI associated with an indwelling Foley catheter. In a large series of a ten-year surveillance database in a US university hospital (Bronsema 1993), catheter-associated UTI comprised 88% of the 6,824 hospital-acquired UTI identified. In two other studies, catheter-associated UTI presented with significant excess in morbidity (Givens and Wenzel 1980), higher cost and a three-fold underlying mortality (Platt 1982). Infection with the indwelling catheter occurs at a rate of 5-10% per day of catheterization and at 30 days, almost 100% of catheterized patients still demonstrate bacteriuria (Warren 1981). Other causes of complicated UTI, particularly those which cause obstructive uropathy, would require a more definitive treatment to remove the cause of obstruction in addition to the, antimicrobial treatment. For instance, in the management of renal stones, removal of the stones by lithotripsy combined with effective antibiotics has achieved up to 90% cure rate of the UTI. On the other hand, conservative management with antibiotics alone has been cited to approach a mortality rate of 30%. Diabetes mellitus has been identified as an independent risk factor for the occurrence of nosocomial UTI (Platt 1986). Morbidity that occurs with diabetics who develop UTI explains it, why these patients are included in the complicated UTI category. Complications of UTI in diabetics include: bacteremia, renal and perinephric abscess, emphysematous pyelonephritis, xanthogranulomatous pyelonephritis, renal papillary necrosis and fungal urinary tract infections (Patterson & Andriole 1997). Infections, which occur in recipients of renal transplants, comprise a population, which have received much interest in research. It is known that UTI is the most common infection that occurs post-surgery. Retrospective studies have shown UTI to have an incidence rate ranging from 30-95% (Waller 1975, Ramsey 1979, Belitsky 1982, Stuby 1989, Rubin 1993, Renoult 1994). There is a trend towards a gradual decline in the incidence through the years attributed to the developed refinements in the post-operative care of transplant patients (Rubin 1993). UTI in this group is associated with severe morbidity in terms of sepsis. The highest rates of UTI occurred during the first seven days following transplant and consisted mainly of UTI associated with the indwelling Foley catheter. In the Philippines, experience in renal transplant has been limited to highly specialized centers like the National Kidney and Transplant Institute*

where in a ten-year period from 1983-1994, a total of 1,019 kidney transplants were performed in 1,008 patients. A one-year prospective study by Mendoza et al (1997) followed the course of 513 patients post-transplant. UTI and pneumonia were the most frequently encountered bacterial infections in these patients. Neutropenic patients ( $PMNs < 100/mm^3$ ) require special attention because they may not manifest with the usual symptoms of UTI like dysuria, frequency and urgency. Pyuria may also be absent. In an early series by Sickles (1975) and cited by Korzeniowski (1991), the incidence of UTI was associated with the severity of neutropenia, increasing from 13% with  $PMNs > 100/mm^3$  to 56% when the  $PMNs < 100/mm^3$ . Finally, UTI in patients with Acquired Immune Deficiency Syndrome (AIDS) are included in the category, of complicated UTI because of the complexity of pathogens that are encountered (see Table 6). The data on UTI in AIDS patients is engrossing but still limited. The incidence of UTI in this group ranges from 8-50% from various reports cited by Sharifi and Lee (1997).

## 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).

**Summary of evidence:** Because of the wide range of organisms, which can cause complicated UTI and the possibility of antibiotic resistance, urine culture and sensitivity should be ordered before any treatment is started (Williams 1996, Farland 1993, Neu 1992, Powers 1991). Table 6 lists the diverse spectrum of microbiology cited from different studies. A urine gram stain will provide a clue to the organisms.

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).

**Summary of evidence:** Controlled clinical trials with stratification of patients according to degree of illness and outcome with or without hospitalization is not available.

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).

**Summary of evidence:** Because of the variety of conditions under complicated UTI and the limited clinical trials in these populations, generalizations on specific antibiotic regimens remain difficult. Drugs of choice for empiric therapy of complicated UTI has not been well established. There have been a lot of published comparative drug trials in complicated UTI. Many, however, were poorly designed or the definition of bacteriologic cure is not eradication of initial pathogen.

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).

**Summary of evidence:** No data providing evidence over the advantage of 7, 10 or 14 days of antibiotic treatment in terms of likelihood of cure versus the incidence of adverse effects of prolonged antibiotic use. Most experts would recommend at least 14 days of antimicrobials.

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

**Summary of evidence:** In many cases of complicated UTI, further intervention is necessary to eradicate the infection in addition to the administration of antibiotics. For instance, in the management of UTI with struvite stones, more definitive treatment like extracorporeal shock wave lithotripsy and/or percutaneous nephrolithotomy or lithotripsy may be required in most patients. Bacteria live within the stone and persist contributing to stone growth. Patients who fail to undergo stone removal almost always have progressive renal deterioration (Rose 1997). Further work-up to identify anatomic abnormalities may include the following

when appropriate: radiologic tests like abdominal films, kidney-ureter-bladder films, renal ultrasound, intravenous pyelogram, CT scans and MRI. Work-up for immunodeficient states may be undertaken when considered.

Table 6: Pathogens identified in complicated UTI

Type of Complicated UTI	Pathogens	Reference
Catheter-associated UTI		
Short-term (<1 week)	E. coli, Pseudomonas aeruginosa	Warren 1997
Long-term (>1 week)	Proteus mirabilis, Enterobacter Usually polymicrobial E. Coli, P. aeruginosa, P.mirabilis, Providencia stuartii, Morganella morgagnii, Citrobacter, Enterococcus, Candida sp. E. coli, Klebsiella pneumonia (37%), P. aeruginosa,	Ouslander 1987
Anatomic abnormalities UTI in Diabetics	Proteus mirabilis E. coli, Klebsiella pneumoniae, Proteus mirabilis, Enterobacter, Enterococcus, P. Aeruginosa, Candida sp.	Childs 1993 Patterson and Andriole 1997
Renal Transplant Recipients	E. coil (29-61%), Proteus mirabilis and Klebsiella pneumoniae (30%), Gram positive cocci (20%), Enterobacter, Enterococci, Serratia, Acinetobacter, Citrobacter, Pseudomonas aeruginosa	Schmaldienst and Horl 1997
Neutropenic Patients	Gram negative bacilli spec. Pseudomonas aeruginosa, Staphylococcus aureus, Candida	Korzeniowski 1991
UTI in AIDS	E. coli Enterobacter, Klebsiella pneumoniae, Pseudomonas, Enterococci, Staphylococcus aureus, Cytomegalovirus, Adenovirus, Toxoplasma, Pneumocystis carinii, Blastomyces dermatidis, Mycobacterium tuberculosis	Sharifi and Lee 1997

Table 7. Antimicrobial regimens that may be used as empiric therapy for complicated UTI

Antibiotic Regimen
Oral Regimen
Ciprofloxacin 250 mg po q 12hrs x 14 days
Norfloxacin 400 mg BID po x 14 days
Ofloxacin 200 mg q 12hrs po x 14 days
Trimethoprim-sulfamethoxazole 160/800 q 12hrs po x 10 days
Parenteral Regimen
Ampicillin 1 gm q 6hrs IV + gentamicin 3 mg/kg/day OD IV
Ceftazidime 1-2 gm q 8hrs IV
Ceftriaxone 1-2 gm OD IV
Ciprofloxacin 200-400 mg q 12hrs IV
Imipenem-cilastatin 250-500 mg q 6-8 hrs IV
Ofloxacin 200-400 mg q 12hrs IV.

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).

**Summary of evidence:** Without correction of the underlying abnormalities, which predisposed to the development of complicated UTI, the infection is likely to recur thus necessitating to check urine cultures one to two weeks after completion of antibiotics (Stamm and Houston 1993). This will also document bacteriologic cure.

### 3. Special issues

3.1 Catheter-associated UTI. Catheterized patients with significant bacteriuria of > 100 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).

**Summary of evidence:** *A one year prospective study of Ouslander (1987) of 54 male nursing home patients with chronic indwelling urinary catheters documented 106 episodes of symptomatic UTI, 80% of patients had at least one symptomatic UTI and 48% had two or more. Despite institution of parenteral antibiotics in the nursing home in the moderately ill patients, 7% had to be hospitalized because of complications related to the UTI. At least 2 deaths were temporally related to the UTI despite ongoing treatment. UTI in asymptomatic catheterized patients occupy a gray zone in recommendations regarding therapy. In a prospective trial of Warren (1982) comparing cephalexin vs. control in afebrile, long-term (>1week) catheterized patients with susceptible bacteriuria, results trended towards no difference in prevalence of bacteriuria, incidence of bacteriuric episodes, duration of bacteriuric episodes, number of bacterial strains per week, febrile days or catheter obstruction between cephalexin vs. control. Instead a difference was noted in the development of cephalexin-resistant bacteria. However, many patients in the control group received non-protocol antibiotics. Warren, in his review article (1997) cited many experts recommending that asymptomatic bacteriuria need not be treated as long as the catheter remains in place except in the following exceptions: (1) for particular bacterial strains in a given institution noted to cause a high incidence of bacteremia from catheter-associated bacteriuria; (2) of antibiotic therapy is part of a hospital infection-control plan to manage a cluster of infections by a particular organism in a medical unit; (3) patients at risk like those with neutropenia, received solid organ transplants and pregnant ones; (4) patients who will undergo urologic procedures. Removal of catheter resulting in the spontaneous resolution of bacteriuria within 14 days was documented by a prospective randomized controlled study of Harding (1991). This was seen more frequently in women who were 65 years old and younger.*

3.2 Patients with diabetes. Acute uncomplicated cystitis in diabetic patients requires 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).

**Summary of evidence:** *Strong evidence is lacking but experts agree that because of the concern for upper tract involvement, longer duration of antibiotic therapy is advocated in diabetic patients even with just lower UTI (Patterson & Andriole 1997 Stamm & Hooton 1983). It is for this same reason and the predilection for upper tract complications and recurrent tract disease that UTIs and its treatment be documented by urine culture*

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).

**Summary of evidence:** *Failure to respond to therapy within 48 to 72 hours requires serious consideration for any of the severe complications of upper urinary tract infection peculiar to diabetics. This includes any of emphysematous pyelonephritis, emphysematous cystitis, renal papillary necrosis, acute focal or multifocal bacterial nephritis, renal cortical abscess, renal corticomedullary abscess and xanthogranulomatous. Emphysematous pyelonephritis, although rare, carries a poor prognosis if not detected early and treated with medical management alone. Mortality is up to 60% without surgical intervention (Evanoff 1987). A plain abdominal radiograph can detect up to 85% of cases. A screening ultrasound should be considered early to rule out obstructive uropathy and detect parenchymal lesions. If there is a high degree of clinical suspicion despite a negative ultrasound, CT scanning should be pursued.*

3.3. Renal transplant patients. UTI, which develop in the first three months post-operatively, as well as other UTI's which develop later 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 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).

**Summary of evidence:** *The timing of the UTI is the most important factor that determines morbidity from the infection. Early in-hospital UTI has been reported to lead to bacteremia in 12% of cases and graft infection in 90% of post-transplant UTI. UTI in the first three months post-transplant is frequently associated with overt pyelonephritis (Rubin 1979), bacteremia, all graft dysfunction and a high rate of relapse when treated with the conventional two-week course of antibiotics. On the other hand, UTI's, which develop after the first three months, usually have a benign course and responds well with the routine antibiotic*

duration of 14 days. These UTI's are rarely associated with bacteriuria, rarely requires hospitalization and have an excellent prognosis (Rubin 1981).

For renal transplant patients, prophylaxis with 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).

**Summary of evidence:** A large, prospective, randomized, double blind, placebo-controlled study was done with 66 renal transplant patients per group using TMP/SMX initially 760/800 mg per day vs. placebo (Fox 7990). At the 7<sup>th</sup> month of the study the TMP/SMX dose was increased to twice daily based on serum levels that were consistently low. With an average of 8.5 months on the study drug (minimum of 3 weeks), there was an overall reduction in the incidence of bacterial infection during the entire post-transplant period including out patient follow-up. In particular, a significant reduction was observed in the frequency of UTI (24 UTI's in the TMP/SMX group vs. 54 in the placebo group;  $p < 0.005$ ) and bloodstream infections (one in the TMP/SMX group vs. 9 in the placebo group  $P < 0.01$ ). Prophylaxis did not prevent UTI associated with the urethral catheter during the early post-transplant period. Of the infections, which occurred on prophylaxis, 18 of 24 (75%) were due to resistant organisms in the TMP/SMX group vs. 13/54 (24%) in the placebo group ( $p < 0.01$ ). TMP/SMX was well tolerated. The dose was decreased to once daily after hospital discharge. At the time of discharge, surveillance cultures did not show significant differences in colonization by Gram-negative bacilli resistant to TMP/SMX between patients on prophylaxis vs. placebo. However there was increase in colonization with methicillin-resistant *Staphylococcus aureus* with those on prophylaxis.

3.4. Patients with acquired immunodeficiency syndrome (AIDS). 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).

**Summary of evidence:** Table 6 summarizes documented etiologic agents of UTI among AIDS patients.

## 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 years old) otherwise healthy sexually active male with no clinical or historical evidence of a structural or functional urologic abnormality is considered as uncomplicated UTI.

**Summary of evidence:** This definition was adapted from Kim and Schaeffer, 1994 and is currently being used as a working definition in most textbooks and clinical studies. Krieger (1993) reported on the occurrence of uncomplicated lower UTI in healthy university men aged 15 to 40 years old with acute dysuria. The mean incidence was 5 infections per 10,000 men per year. In this population, factors implicated for male UTI such as anatomical abnormalities, urinary tract instrumentation, bacterial prostatitis and lack of circumcision were seldom identified. A similar incidence of acute uncomplicated UTI in men was also recognized by Lipsky (1989), and further stated that a - urologic evaluation is often unrewarding in these patients.

#### 2. Diagnosis

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

**Summary of evidence:** The presence of  $> 10 \text{ wbc/mm}^3$  of urine had a PPV of 0.77 and a NPV of 0.69 and sensitivity of 71 % and specificity of 76% in the prediction of bladder bacteriuria. Growth of 1000 cfu had a sensitivity of 97% and a specificity of 97% (Lipsky 1987). Norman likewise estimated good correlation of up to 88% between pyuria of  $> 10/\text{mm}^3$  and significant bacteriuria (Norman 1996).

### 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).

**Summary of evidence:** In a review article on UTI in young men, Stamm and Hooton (1993) recommended a urinalysis to screen for pyuria and a pre-treatment urine culture for patients with significant pyuria. Independent studies of Krieger (1993) and Lipsky (1989) both of which documented uncomplicated UTI in males showed that patients who do not have clinical or historical evidence of a functional or anatomic abnormality; neurological disorders, genitourinary tract instrumentation and prostatitis respond well to a single course of antimicrobial therapy. Comprehensive urological evaluation seems to be unwarranted in these men.

### 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).

**Summary of evidence:** Krieger (1993) studied 38 previously healthy university men who presented with 40 symptomatic urinary tract infections over a 6-year period. Thirty-seven of the 40 infections (93%) were caused by *E. coli*, with 8 of the isolates resistant to ampicillin, cephalothin, sulfonamides and tetracyclines. Three symptomatic infections were caused by other bacteria including *S. aureus* (resistant to ampicillin), *P. aeruginosa* (resistant to ampicillin, tetracycline, cephalothin, sulfamethizole, cotrimoxazole and nitrofurantoin), and *Enterobacter cloacae* (resistant to ampicillin and cephalothin). None of the isolates exhibited resistance to fluoroquinolones. Stamm and Hooton (1993) reviewed several articles on UTI in young men and recommended a 7-day regimen of TMP/SMX or a fluoroquinolone.

## 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 prostate 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 swollen, firm and warm.

1.2. Chronic bacterial prostatitis. Chronic bacterial prostatitis is a more subtle illness than acute prostatitis typified by relapsing or 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.

**Summary of evidence:** These definitions adapted from Pewitt and Schaeffer (1997) are actually based on the original classification proposed by Drach (1978) and Meares (1980) and is currently being used in most textbooks and clinical studies. In 1995, the National Institutes of Health Consensus Conference on Prostatitis proposed the following classification of prostatitis syndromes:

- Category 1 Acute Bacterial Prostatitis
- Category 2 Chronic Bacterial Prostatitis
- Category 3 Chronic Pelvic Pain Syndromes
  - a. Inflammatory
  - b. Non-inflammatory
- Category 4 Asymptomatic Prostatitis

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 specimen is free or WBC. The diagnosis of prostatic infection is confirmed when the quantitative bacterial colony counts of EPS and the next 5 to 10 ml of urine (VB3) significantly exceed those of the urethral (VBI) and bladder (VB2) specimens. The colony count of the EPS and VB3 should exceed the VBI by at least 1 logarithm (Grade C).

**Summary of evidence:** *These procedures have been recommended by Pewitt (1997). The cut off of > 10 WBC in the EPS has also been recommended by several authors in different studies (Drach 1978, Meares 1980, Blacklock 1969, Anderson & Weller 1979 and Schaeffer 1981). Anderson & Weller (1979) compared the quantitative content of leukocytes in a counting chamber among 43 patients with bacterial and non-bacterial prostatitis and 20 normal controls. Statistically significant difference between the two groups was noted at 10 wbc/hpf. This pre-and post-massage test of prostatic fluid has been calculated to have 91% sensitivity and 91% specificity (Vickel 1997). The finding of fat-laden macrophages further localizes the site of inflammation to the prostate since these could not be seen from urethral exudates (Meares 1980).*

## 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).

**Summary of evidence:** *In a review article, Meares (1980) recommended the use of TMP/SMX or a fluoroquinolone as empiric treatment. Most isolated organisms are sensitive to these drugs. The same regimen and duration of treatment were likewise recommended by Pewitt (1997). In separate review articles Leigh (1993), Weidner (1992) and Meares (1980) showed that in acute and chronic bacterial prostatitis, E. coli still predominate, although other causative agents include Enterobacter, Klebsiella, Pseudomonas spp. and Serratia.*

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).

**Summary of evidence:** *Pewitt and Schaeffer (1997), Roberts (1997) and Meares (1980) in separate review articles have recommended the use of an amino glycoside-penicillin derivative combination or a fluoroquinolone for initial parenteral therapy for acutely ill patients until a suitable antibiotic based on culture and sensitivity studies is substituted.*

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

**Summary of evidence:** *Several review articles have evaluated the efficacy of TMP/SMX and fluoroquinolones in chronic bacterial prostatitis. Britton and Carson (1998) have noted 33-50% cure rates with TMP/SMX while the same study together with Roberts (1997) and Pewitt have reported 60-90% cure rates with fluoroquinolones.*

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 80mg/400mg once daily is recommended (Grade C).

**Summary of evidence:** *Several review articles (Pewitt 1997, Meares 1980, Roberts 1997) have advocated radical transurethral resection of the prostate with projected 30-100% cure rates in selected patients. Combination of prostatic massage with antibiotics (Hennenfent and Feliciano 1998) for treatment of refractory cases also showed favorable results. Low-dose, chronic*

suppressive therapy does not cure the infection but usually prevents bacteriuria and controls symptoms. Discontinuation of therapy however, results in recurrence of bacteriuria and symptoms (Meares 1980).

## VII. 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).

**Summary of evidence:** Within 48 hours of catheterization, female patients catheterized by licensed practical nurses and registered nurses were observed to have more than thrice (34%) and twice (21%) the rate of acquired bacteriuria, respectively than patients catheterized by the more trained physicians (10%) (Garibaldi 1974). In addition, use of aseptic technique and sterile equipment by trained personnel was shown to be a cost-effective application of the Centers for Disease Control guideline for the prevention of catheter-associated urinary tract infections (Wong 1983, Epstein 1985).

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

**Summary of evidence:** Carriage of exogenous organisms on the hands of hospital personnel causing infections in patients (cross-infections) have been implicated, in reports of case clusters (Maki 1973, Kaslow 1976) and epidemics (Schaberg 1976) of nosocomial urinary tract infections. The role of cross-infection was demonstrated in a prospective study of case clustering in 15.5% of non-epidemic nosocomial bacteriuria of which 90% of clustered cases and 71 % of non clustered cases were associated with indwelling urinary catheters (Schaberg 1980). Handwashing before and after catheter care have been emphasized to minimize the risk of personnel hand contamination and to prevent cross infection (Steere 1975, -Wong 1983, Garner 1985). Renewed emphasis of this measure together with spatial separation of infected catheterized patients, controlled the outbreak of catheter-associated urinary tract infections (Maki 1973, Kaslow 1976).

### 2. The catheter

2.1. Avoid unnecessary catheter use (Grade C).

**Summary of evidence.** Two prospective studies have demonstrated that the presence of pathogenic bacteria in the periurethral area and an indwelling urethral catheter are two major risk factors that predispose to catheter-associated UTI (Daifuku 1984, Garibaldi 1980). In both studies, majority (67-85%) of patients with positive meatal cultures who acquired catheter-associated UTI's had the same species of bacteria recovered from the meatal culture. 110 of the 612 patients (18%) with positive meatal culture acquired bacteriuria more significantly ( $p < 0.0001$ ) than patients with negative ones (28 of 601 or 5%) (Garibaldi 1980). In the female patients, approximately 70% of episodes of catheter-associated bacteriuria occur when bacteria ascend into the bladder urine by way of the catheter (Garibaldi 1980). Antecedent rectal colonization with the same infecting organism preceded 78% of infections in women (14 of 18) and 29% (5 of 17) of infections in men (Daifuku 1984). In addition, the indwelling catheter, by itself is an important site for bacterial attachment and persistence in catheterized patients (Stamm 1991). Thus, true prevention begins by avoiding unnecessary catheter use.

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).

**Summary of evidence:** There are no studies that have evaluated the indication for catheterization as an alterable predisposing factor to catheter-associated urinary tract infection. For the past decades, urethral catheterization has been generally indicated for the following: (1) to obtain accurate measurements of urine output in critically ill patients, (2) to aid in urologic surgery or other surgery of contiguous structures. (3) to relieve urinary tract obstruction, and (4) to allow urinary drainage in patients with neurogenic bladder dysfunction and urinary retention (Kunin 1966. Wong 1983. Warren 1997).

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

**Summary of evidence:** As previously mentioned, use of sterile equipment and correct aseptic technique by trained personnel proved to be cost-effective measures in preventing catheter-associated UTI (Epstein 1985), as prescribed by the 1983 CDC

guideline. More specifically, these include the use of sterile gloves, sterile catheter, antiseptic solution for perineal cleansing, and water-soluble lubricating jelly for catheter insertion. (Wong 1983, Kunin 1979, Desatels 1962, Kass 1957).

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

**Summary of evidence:** A greater frequency of catheter-associated bacteriuria 48 hours after errors in catheter care by hospital personnel was observed than when there were no lapses in sterile technique or care of the closed drainage system (Garibaldi 1974). In this study, bacteriuria occurred in 13.3% when the catheter-tubing junction had been disconnected at least once and in 9.5% with closed catheter-tubing junction; 17.9% of cases acquired bacteriuria when improper technique was observed against 11.8% when improper technique was not observed. However, the differences were not statistically different. In another study, disconnection of the catheter junction was associated with high rate of infection that was twice the number of days than when there was no disconnection (Warren 1978). More importantly, adherence to the sterile continuously closed system of urinary drainage reduced the rate of infection to 16-23% (Garibaldi 1974, Kunin 1966) from an inevitable 100% 4 days after insertion when open drainage as used (Kass 1959). However, infection becomes almost 100% by 30 days with closed drainage (Garibaldi 1974, Burke 1986). Thus, the principal benefit of closed drainage is to delay, if not prevent, the onset of infection.

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

**Summary of evidence:** Urine for examination should be aspirated at the distal end of the catheter with sterile needle and syringe after disinfecting the area (Wong 1983). It has been emphasized that the junction of the catheter and drainage tube should not be disconnected for this purpose (Garibaldi 1974, Warren 1978, Platt 1983, Huth 1992). As previously discussed, disconnection of the catheter junctions, whether to collect urine specimens or to irrigate the bladder, was associated with high rates of infection (Garibaldi 1974, Warren 1978).

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

**Summary of evidence:** High bacterial colony counts can develop in the collection bag and ascend against the flow of urine to infect the urinary bladder within two days (Kunin 1966, Thorton 1970, Garibaldi 1974). To achieve free flow of urine: (1) the collection bag should be lower than the level of the bladder at all times, (2) the catheter and collecting tube should be kept from kicking, (3) the catheter should not be clamped except when a culture specimen is collected or when the patient must be separated from the drainage bag, and (4) the bag should be emptied regularly (Wong 1983, Reese 1997).

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

**Summary of evidence:** Experts agree that a catheter should not be changed on a routine schedule (Stamm 1975/1995, Wong 1983). Indications for catheter change include: (1) malfunction or leakage, (2) catheter obstruction, (3) contamination (e.g. disconnection between catheter and drainage tube), (4) bacteriuria that require antibiotics, (5) concretions in catheter lumen that may precede to its obstruction, and (6) candiduria (Stamm 1995).

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

**Summary of evidence:** One of the most important risk factors for the development of catheter-associated bacteriuria is the duration of catheterization (Garibaldi 1974, Harstein 1981). The daily incidence of developing bacteriuria approximates 3% to as high as 16% per day (Garibaldi 1974, Haley 1981, Kunin 1966, Burke 1986). Two prospective Studies (Harstein 1981, Jain 1995) have demonstrated that a substantial proportion of catheter days were unnecessary and prompt removal would have theoretically prevented 40% of all infections. Thus, if the catheter can be removed before bacteriuria develops, postponement of bacteriuria becomes prevention (Warren 1997).

### 3. Methods to prevent endogenous infection

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

**Summary of evidence:** Five randomized controlled trials of either once or twice daily, meatal cleansing, whether using soap and water or polyantibiotic cream, did not have any significant reduction in catheter-associated UTI (Burke 1981, Britt 1976, Classen 1991, Huth 1992).

## 4. Methods to prevent exogenous infection

### 4.1 Irrigation of the bladder with antimicrobial agents is not useful (Grade D)

**Summary of evidence:** Most randomized controlled trials have proven that bladder irrigation, using antimicrobial agents did not prevent most catheter-associated bacteriuria (Bastable 1977, Warren 1978, Gillespie 1983, Davies 1987), even if given continuously (Maki 1972, Warren 1978, Bastable 1977).

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

**Summary of evidence:** Instillation of disinfectants in the drainage bag (Thomson 1984, Sweet 1984, Willie 1993) or the use of antireflux vents and valves (Garibaldi 1974, Keys 1979) did not demonstrate lowered incidence of bacteriuria in most randomized controlled trials.

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

**Summary of evidence:** Risks of cross-contamination can be minimized if a patient with catheter-associated UTI is not placed in the same room as another patient with an indwelling catheter (Maki 1972, Wong 1983). Spatial separation of infected catheterized patients, in conjunction with emphasis on hand washing, controlled the outbreak of catheter-associated UTI's (Maki 1973, Kaslow 1976).

## 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).

**Summary of evidence:** Garibaldi (1982) studied the value of daily bacteriologic monitoring in catheterized patients and found that symptomatic catheter-associated UTI's in hospitalized patients tended to occur on the first day of bacteriuria. Thus, in most patients, there is no asymptomatic bacteriuria to treat in order to prevent symptomatic UTI. Furthermore, this study showed that it would require 250 urine cultures to prevent one symptomatic UTI.

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

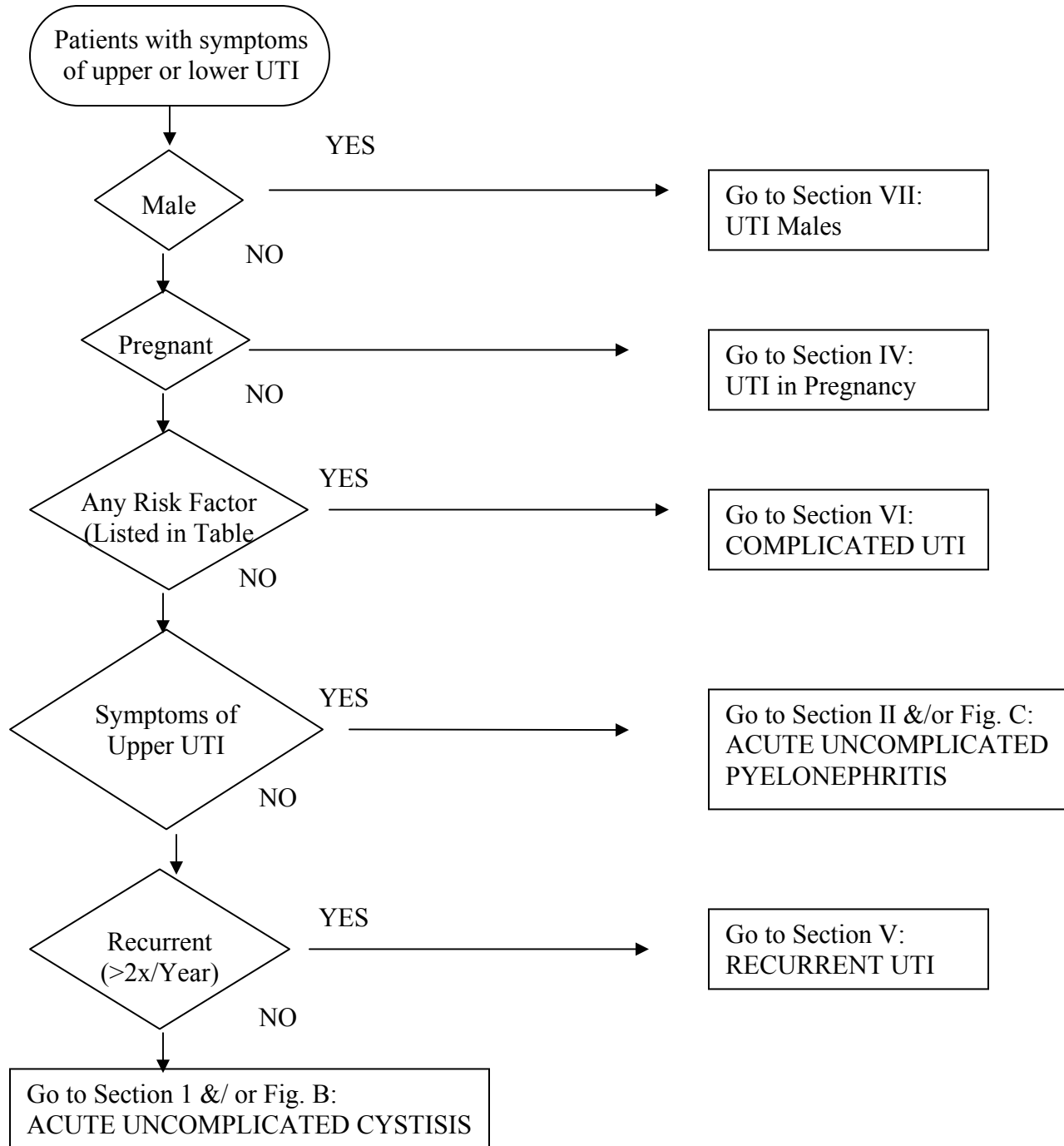
**Summary of evidence:** Most of the randomized clinical trials of antibiotic prophylaxis had positive outcomes, however, these studies were confined to certain groups of patients, such as males undergoing prostatectomy or other surgical operations. In addition, long-term follow-up showed that antibiotics were effective for the first few days (up to a week) but then resistant organisms appeared in the urine. Because of side effects, additional costs, and emergence of resistant bacteria, antibiotics to postpone bacteriuria or treat asymptomatic bacteriuria is discouraged (Warren 1997, Mountokalakis 1985, Slade 1985, Schaberg 1986, Kunin 1987).

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).

**Summary of evidence:** One prospective, randomized, double-blind study using TMP/SMX at a daily dose of 160/800 mg demonstrated the cost-benefit of TMP/SMX as prophylaxis against infections, including catheter-associated UTI's, and in renal transplant patients (Fox 1990).

## VIII. ALGORITHMS

FIGURE A. Algorithm for UTI



<sup>1</sup>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.

FIGURE B: Algorithm for Acute Uncomplicated Cystitis

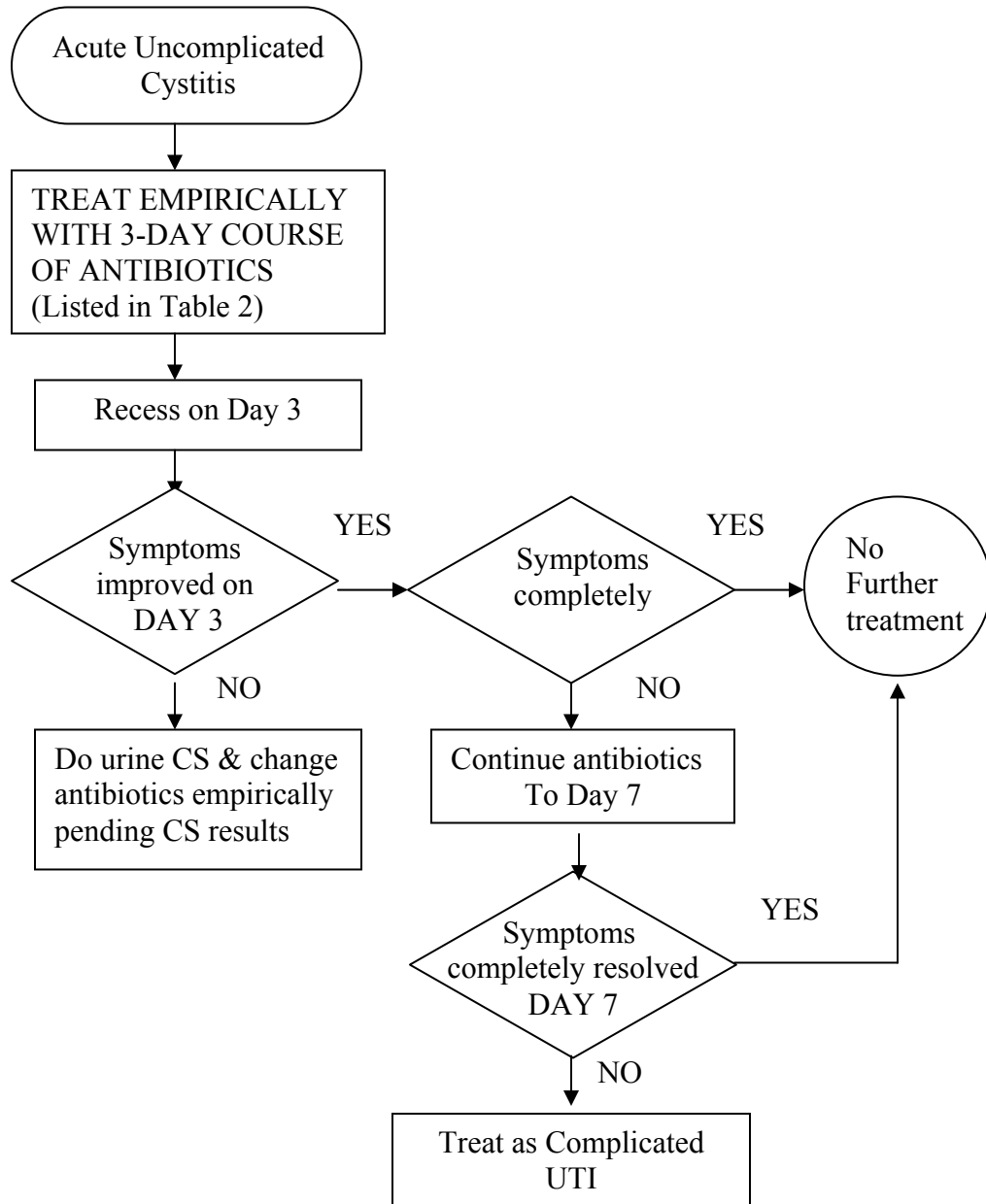
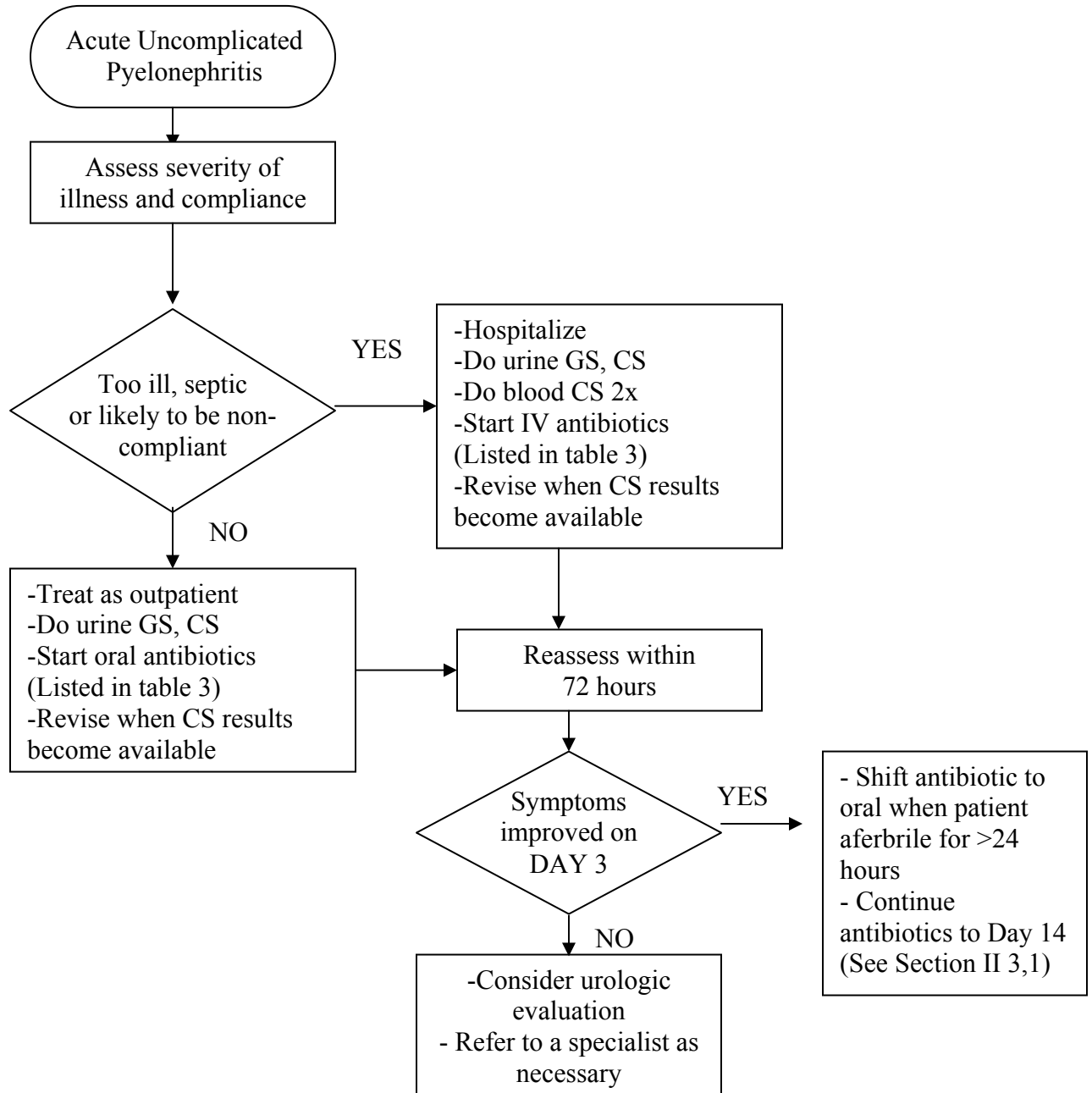


FIGURE C. Algorithm for Acute Uncomplicated Pyelonephritis



## References:

- Abrutyn E, Mossey J, Berlin JA, Boscia J, Levison M, Pitsakis P, Kaye D. 1994. Does asymptomatic bacteriuria predict mortality and does antimicrobial treatment mortality and does antimicrobial treatment reduce mortality in elderly ambulatory women. *Ann Intern Med* 120:827-833.
- Abyad A. 1991. Screening for asymptomatic bacteriuria in pregnancy: urinalysis vs. urine culture. *J Family Practice* 33:471-474.
- Adelson MD, Graves WL, Osborne NG. 1992. Treatment of urinary infections in pregnancy using single versus 10-day dosing [abstract]. *J Natl Med Assoc* 84:73-75.
- Alejandria MM, Manapat BD. 1998. Three-day versus conventional antibiotic regimen for uncomplicated urinary tract infections in women: a meta-analysis of randomized trials. *PJMID* 27:41-48.
- Andriole VT, Patterson TF. 1991. Epidemiology, natural history and management of urinary tract infections in pregnancy. *Med Clin North Am* 75:359-373.
- Andriole VT. 1975. Hospital acquired urinary tract infection and the indwelling catheter. 1975. *Urol Clin North Am* 2:451-469.
- Angel JL, O'Brien WF, Finas MA, Morales WJ, Lake M, Knuppel RA. 1990. Acute pyelonephritis in pregnancy: a prospective study on oral versus intravenous antibiotic therapy. *Obstet Gynecol* 76:28-32.
- Aslaksen A. 1990. Intravenous urography vs. ultrasonography in the evaluation of women with recurrent urinary tract infection. *Scand J of Primary Health Care* 8:85-9.
- Bachman JW, Heise RH, Naessons JM, Timmerman MG. 1993. A study of various tests to detect asymptomatic urinary tract infections in an obstetric population. *JAMA* 270:1971-1974.
- Bailey RR. 1994. Duration of antimicrobial treatment and the use of drug combinations for the treatment of uncomplicated acute pyelonephritis. *Infection* 22 Suppl 1:S50-52.
- Bailey RR. 1992. Quinolones in the treatment of uncomplicated urinary tract infections. *Int J Antimicrobial Agents* 2:19-28.
- Bailey RR, Lynn KL, Robson RA, Peddie BA, Smith A. 1986. Comparison of netilmicin with ceftriaxone for the treatment of severe or complicated urinary tract infections. *NZ Med J* 99:459-461.
- Bailey RR, Lynn KL, Robson RA, Peddie BA, Smith A. 1992. Comparison of ciprofloxacin with netilmicin for the treatment of acute pyelonephritis. *NZ Med J* 105:102-103.
- Bailey RR, Peddie BA. 1987. Treatment of acute urinary tract infection in women. *Ann Intern Med* 107:430.
- Barlett RC, Galen RS. 1983. Predictive value of urine culture. *Am J Clin Pathol* 79:756-757.
- Bastable JR, Peel RN, Birch DM, Richards B. 1977. Continuous irrigation of the bladder after prostatectomy: Its effect on post-prostatectomy infection [abstract]. *Br J Urol* 49:689-693.
- Belitsky P, Lannon SG, McDonald AS, Cohen AD, Marie TJ, Houlihan P, Whalen A. 1982. Urinary tract infections after kidney transplantation. *Transplant Proc* 14:696-699.
- Bergeron MG. 1979. Treatment of pyelonephritis in adults. *Med Clin North Am* 79:619-649.
- Boerama JBJ, Domen WBM, Branolte JH. 1985. Comparative efficacy and safety of ciprofloxacin and co-trimoxazole in the treatment of patients with complicated urinary tract infections [abstract]. *Proceeding of the 14 th International Congress of Chemotherapy*. Kyoto, Japan. S50-7.
- Bronsema DA, Adams JR, Pallares R, Wenzel RP. 1993. Secular trends in rates and etiology of nosocomial urinary tract infections in women. *QJ Med*. 81:811-20.
- Brumfitt W. 1991 Comparative trial of norfloxacin and macrocrystalline nitrofurantion in the prophylaxis of recurrent urinary tract infections in women. *QJ Med* 81:811-20.
- Brumfitt W. 1990 Comparative study of cephadrine and amoxicillin-clavulanate in the treatment of recurrent urinary tract infections. *Antimicrob Agents Chemother* 34:1803-1805.
- Brumfitt W. 1995. A comparative trial of low dose cefaclor and macroxystalline nitrofurantion in the prevention of recurrent urinary tract infection. *Infection* 23:98-102.
- Burke JP, Garibaldi RA, Britt MR, Jacobson JA, Conti M, Alling DW. 1981. Prevention of catheter associated urinary tract infections. Efficacy of daily meatal care regimens. *Am J Med* 70:655-658
- Burke JP, Jacobson JA, Garibaldi RA, Conti MT, Alling DW. 1983. Evaluation of daily meatal care with poly-antibiotic ointment in prevention of urinary catheter-associated bacteriuria [abstract]. *J Urol* 129:331-334.
- Calderon JE, Arredondo GJL, Olvera SJ, Echaniz AG, Conde GC, Hernandez NP. 1989. Acute urethritis during pregnancy [abstract]. *Gynecol Obstet Max* 57:57-63
- Carlos CC. 1997. Antimicrobial resistance surveillance program progress report.
- Carlson KJ, Mulley AG. 1985. Management of acute dysuria. A decision-analysis model of alternative strategies. *Ann Intern Med* 102:244-249.
- Classen DC, Larsen RA, Burke JP, Allin DW, Stevens LE. 1991. Daily meatal care for prevention of catheter-associated bacteriuria: Results using frequent applications of polyantibiotic cream [abstract]. *Infect Control Hosp Epidemiol* 12:57-162
- Cox CE. 1992. A comparison of the safety and efficacy of lomefloxacin and ciprofloxacin in the treatment of complicated or recurrent urinary tract infections. *Am J Med* 92 Suppl n4A:835-86S.
- Cox CE. 1980. Ofloxacin in the management of complicated UTI including prostatitis. *Am J Med Suppl* 6C:61
- Cunningham FG, Morris GE, et al. 1975. Acute pyelonephritis of pregnancy: A clinical review. *Obstet Gynecol* 12:112.
- Cuvelier R, Pirson Y, Alexandre GRJ, van Ypersele de Strihou C. 1985. Late urinary tract infection after transplantation: Prevalence, predisposition and morbidity. *Nephron* 40:76-78.

- Daifuku R, Stamm WE. 1984. Association of rectal and urethral colonization with urinary tract infection in patients with indwelling catheters. *JAMA* 252:2028-2030.
- Davies AJ, Desai HN, Turton S, Dyas A. 1987. Does instillation of chlorhexidine into the bladder of catheterized geriatric patients help reduce bacteriuria. *J Hosp Infect* 9:72-75.
- De Guzman V, Nicolas C, Naidas O. 1998. Efficacy of single dose versus three days of antibiotics for uncomplicated urinary tract infection: A meta-analysis of randomized trials. In press.
- Dytan AT, Chua JA. 1998. Study of uncomplicated urinary tract infection [abstract] *PJMID* 27:S15.
- Epstein SE. 1985. Cost-effective application of the Centers for Disease Control Guideline for Prevention of catheter-associated urinary tract infections [abstract]. *Am Infect Control* 13:272-275.
- Fairchild TN. 1982. Radiographic studies for women with recurrent urinary tract infections. *J Urol* 128:344-345.
- Fletcher RH, Fletcher SW, Wagner EH. 1996 *Clinical Epidemiology: The Essentials*. Baltimore: Williams & Wilkins.
- Forland M. 1993. Urinary tract infection: How has its management changed? *Post Grad Med* 93:71-86.
- Forland M, Thomas V, Shelokov A. 1997. Urinary tract infections in patients with diabetes mellitus: Studies on antibody coating of bacteria. *JAMA* 238:1924-1926.
- Fox BC, Sollinger HW, Belzer FO, Maki DG. 1990. Prospective randomized double-blind study of trimethoprim-sulfamethoxazole for prophylaxis of infection in renal transplantation: Clinical efficacy, absorption of trimethoprim-sulfamethoxazole, effects on the microflora and the cost-benefit of prophylaxis. *Am J Med* 89:255-274.
- Fox CE, Tack KJ. 1988. Safety and efficacy of ofloxacin vs. trimethoprim-sulfamethoxazole for complicated urinary tract infections. *Rev Infect Dis* 10 Suppl 1:S175.
- Garibaldi RA, Burke JP, Dickman ML, Smith CB. 1974. Factors predisposing to bacteriuria during indwelling urethral catheterization. *N Engl J Med* 291:215-219.
- Garibaldi RA, Burke JP, Britt MR, Miller WA, Smith CB. 1980. Meatal colonization and catheter associated bacteriuria. *N Engl J Med* 303:316-318.
- Gillespie WA, Simpson RA, Jones JE, Nashef L, Teasdale C, Speller DC. 1983. Does the addition of disinfectant to urine drainage bags prevent infection in catheterized patients? *Lancet* 1:1037-1039.
- Gilstrap LC III, Cunningham FG, Whalley PJ. 1981. Acute pyelonephritis in pregnancy: An anterospective study. *Obstet Gynecol* 57:409-413.
- Golan A, Wexler S, Amit A, Gordon D, David M. 1989. Asymptomatic bacteriuria in normal and high risk pregnancy. *Eur J Obstet Gyne Reproductive Biol* 33:101-108.
- Guerra JG, Falconi E, Palomino JC, et al. 1983. Clinical evaluation of norfloxacin vs. cotrimoxazole in urinary tract infections. *Eur J Clin Microbiol* 2:260-265.
- Harding GKM, Nicolle LE, Ronald AR, Preiksaitis, JK Forward KR, Low DE, Cheang M. 1991. How long should catheter-acquired urinary tract infection in women be treated? A randomized controlled study. *Ann Intern Med* 114:713-719.
- Harris RE. 1979. The significance of eradication of bacteriuria during pregnancy. *Obstet Gyne* 53.
- Harris RE. 1984. Acute urinary tract infections and subsequent problems. *Clin Obstet Gyne* 27:8974-890.
- Harris RE, Gilstrap LG III. 1981. Cystitis during pregnancy: A distant clinical entity. *Obstet Gyne* 57:578.
- Harstein AI, Garber SB, Ward TT, Jones SR, Morthland VH. 1981. Nosocomial urinary tract infection: A prospective evaluation of 108 catheterized patients [abstract]. *Infect Control* 2:380-386.
- Hill JA, Devoe LD, Bryans IC. 1986. Frequency of asymptomatic bacteriuria in pre-eclampsia. *Obstet Gyne* 67:529-532.
- Hooton TM, Stamm WE. 1997. Diagnosis and treatment of uncomplicated urinary tract infection. *Infect Dis Clin North Am* 11:551-581.
- Hooton TM, Winter C, Tiu F, Stamm WE. 1995. Randomized comparative trial and cost analysis of 3-day antimicrobial regimens for treatment of acute cystitis in women *JAMA* 273:1:41-5.
- Huth TS, Burke JP, Larsen RA, Classen DC, Stevens LE. 1992. Randomized trial of meatal care with silver sulfadiazine cream for the prevention of catheter-associated bacteriuria. *J Infect Dis* 165:148.
- Israel RS, Lowenstein SR, Marx JA, et al. 1991. Management of acute pyelonephritis in an emergency department observation unit. *Ann Emerg Med* 20:253-257.
- Jernelius H., Zbornik J, Bauer CA. 1988. One or three weeks treatment of acute pyelonephritis? A double-blind comparison, using a fixed combination of pivampicillin plus pivmecillinam. *Acta Medica Scand* 223:469-477.
- Johnson JR, Lyons MF, Pearce W, et al 1991. Therapy for women hospitalized with acute pyelonephritis: a randomized trial of ampicillin vs trimethoprim-sulfamethoxazole for 14 days. *J Infect Dis* 163:325-330.
- Johnson JR, Vincent LM, Wang K, Roberts PL, Stamm WE. 1992. Renal ultrasonographic correlates of acute pyelonephritis. *Clin Infect Dis* 14:15-22.
- Kanel KT, Kroboth FJ, Schwentker FN, Lecky JW. 1983. The intravenous pyelogram in acute pyelonephritis. *Arch Intern Med* 148:2144-2148.
- Kass EH. 1956. Asymptomatic infections of the urinary tract. *Trans Assoc Am Phys* 69:56-64.
- Keys TF, Maker MD, Segura JW. 1979. Bacteriuria during closed urinary drainage: an evaluation of top-vented versus bag-vented systems *J Urol* 122:49-51.
- Kim ED, Schaeffer AJ. 1994. Antimicrobial therapy for urinary tract infections. *Seminars in Nephrology*. 14:551-69.
- Komaroff AL. 1991. Acute dysuria in adult women. In: Panzer RJ, Black ER, Griner PF, editors *Diagnostic strategies for common medical problems*. Philadelphia: Am College of Physicians p 239.
- Korzeniowski OM. 1991. Urinary tract infection in the impaired host. *Med Clin North Am* 75:391-404.

- Kraft JK. 1977. The natural history of symptomatic recurrent bacteriuria in women. *Medicine* 56:55-60.
- Kunin CM, Mc Cormack RC. 1966. Prevention of catheter-induced urinary tract infection by sterile closed drainage. *N Engl J Med* 274:1155-1162.
- Kunin CM. 1992. Editorial guidelines for the evaluation of new anti-infective drugs for the treatment of urinary tract infections. *Clin Infect Dis* 15:1041-1044.
- Kunin CM. 1997. Detection, prevention and management of urinary tract infections. 5th ed. Philadelphia: Lea and Febiger.
- Kunin C, White L, Hua Hua T. 1993. A re-assessment of the importance of 'low count' bacteriuria in young women with acute urinary symptoms. *Ann Intern Med* 119:454-59.
- Lacks MS, Nacharin I, Edelstein P. 1992. Spectrum bias in the evaluation of diagnostic test. Lessons from rapid dipstick test for urinary tract infection. *Ann Intern Med* 117:135-40.
- Leibovici L, Wysenbeck. 1991. Single-dose antibiotic treatment for symptomatic urinary tract infection in women: A meta-analysis of randomized trials. *J Med* 285:43-57.
- Lenke RR, Van Dorsten JP, Schifrin BS. 1983. Pyelonephritis in pregnancy: a prospective randomized trial to prevent recurrent disease evaluating suppressive therapy with nitrofurantion and close surveillance [abstract]. *J Obstet Gynecol* 146:953-957.
- Lipsky BA, Ireton R, et al 1987. The diagnosis of bacteriuria in men: Specimen collection and culture interpretation *J. Infect Dis* 155:847-54
- Malinverni R, Glauser MP. 1988. Comparative studies of fluoroquinolones in the treatment of urinary tract infections. *Rev Infect Dis* 10 suppl 1:S153-163.
- McHenry MC, Braun WE., Popowniak KL, Banowsky H, Deodhar SD. 1976. Septicemia in renal transplant recipients. *Urol Clin North Am* 3:647-666.
- McNicholas MM. 1991. Ultrasound of the pelvis and renal tract combined with a plain film of abdomen in young women with urinary tract infection: can it replace intravenous urography? *Br J Radiol* 64:221-4.
- Meares EM Jr. 1980. Prostatitis syndromes. New perspectives about old woes. *J Urol* 123:141-147.
- Melekos MD. 1997. Post-intercourse versus daily ciprofloxacin prophylaxis for recurrent urinary tract infections in premenopausal women. *J Urol* 157:935-939.
- Mendoza MT, Liquete RR, Ona ET, Alano FA. 1997. Infections in renal allograft recipients: a review of the Philippine experience. *Int J Infect Dis* 1:222-225.
- Mittendorf R, Williams MA, Kass EH. 1992 Prevention of preterm delivery and low birth weight associated with asymptomatic bacteriuria. *Clin Infect Dis* 14:927-32.
- Mountokalakis T, Shounakis M, Tselentis J. 1985. Short-term versus prolonged systemic antibiotic prophylaxis in patients treated with indwelling catheters. *J Urol* 134:506-508.
- Mouton J, Ajana F, Chidiac C. et al. 1992. A multicenter study of lomefloxacin and trimethoprim-sulfamethoxazole in the treatment of uncomplicated acute pyelonephritis. *Am J Med* 92 suppl 4A:S87.
- Mushlin AI, Thorbury JR. 1989. Intravenous pyelography: the case against its routine use. *Ann Intern Med* 111:58-70.
- Myerowitz RL, Medeiros AA, O'Brien TF. 1972. Bacterial infection in renal homotransplant recipients: A study of fifty-three bacteremic episodes. *Am J Med* 53:308-314.
- Neu HG. 1992. Urinary tract infections. *Am J Med* 92 Suppl 4A:63S-70S
- Nickel JC. 1990. Special considerations in the management of complicated urinary tract infections. *International Congress and Symposium Series: Management of Urinary tract Infections*. 85-95.
- Nicolle LE. 1997. Asymptomatic bacteriuria in the elderly. *Infect Dis Clin North Am* 11:647-662
- Nicolle LE, Mayhew JW, Bryan L. 1987 Prospective randomized comparison of therapy and no therapy for asymptomatic bacteriuria in institutionalized women. *Am J Med* 83:27-33.
- Nicolle LE, Bjornson J, Harding GKM MacDonell JA. 1983. Bacteriuria in elderly institutionalized men. *N Engl J Med* 309:1420-1425.
- Nicolle LE. 1989. Prospective, randomized, placebo-controlled trial of norfloxacin for the prophylaxis of recurrent urinary tract infection in women. *Antimicrob agents Chemother* 33:1032-5.
- Norman DC, Yamamura R Yoshikawa TT. 1966. Pyuria: Its predictive value of asymptomatic bacteriuria in ambulatory elderly men *J Urol* 135:520-522.
- Norby SR 1994. Useful agents in the management of urinary tract infections. *Int. J antimicrob agents* 4:129-134
- North DH, Speed JE, Weiner WB, Morrison JC. 1980. Correlation of urinary tract infection with urinary screening at the first antepartum visit. *J MSMA*: 331-333.
- Ouslander JG, Schapira M, Schnelle JF, et al. 1995. Does eradicating bacteriuria affect the severity of chronic urinary incontinence in nursing home residents? *Ann Intern Med* 122:749-754.
- Ouslander JG, Greengold B, Chen S. 1987. Complications of chronic indwelling urinary catheters among male nursing home patients: a prospective study *J of Urol* 138:1191-1195.
- Patterson JE, Andriole VT. 1997. Bacterial urinary tract infections in diabetes. *Infect Dis North Am* 7325:750.
- Pena AC, Mendoza MT, Go-Yap J. 1996. A randomized open-label tolerance and efficacy study of oral tosufloxacin vs. oral trimethoprim-sulfamethoxazole forte in the treatment of patients with complicated and uncomplicated urinary tract infections in the Philippines. *PJ IM* 34:123-128.
- Peters HJ. 1986. Comparison of intravenous ciprofloxacin and mezlocillin in treatment of complicated urinary tract infection. *Eur J Clin Microbiol* 5:253-255.

- Pewitt EB, Schaeffer AJ. 1997. Urinary tract infection in urology, including acute and chronic prostatitis, *Infect Dis Clin North Am* 11.
- Pfau A. 1994. Effective postcoital quinolone prophylaxis of recurrent urinary tract infections in women. *J Urol* 152:136-138.
- Pinson AG, Philbrick JT, Lindbeck GH, Schorling JB. 1992. *J Gen Intern Med* 7:544-553.
- Pinson AG, Philbrick JT, Lindbeck GH, Schorling JB. 1994 ED management of acute pyelonephritis in women: a cohort study. *Am J Emerg Med* 12:271-278.
- Pittmann W, Moon JO, Hamrick LC, Cox CE, Clark J, Childs Pizzutti D, Fredericks J, St. Clair P. 1993. randomized double-blind trial of high and low dose fleroxacin versus norfloxacin for complicated urinary tract infection. *Am J Med* 94 suppl 3A:101S-107S.
- Platt R. 1983. Quantitative definition of bacteriuria. *Am J Med* 75:44-52.
- Platt R, Murdock B, Polk BF, Rosner B. 1983 Reduction of mortality associated with nosocomial urinary tract infection. *Lancet* 1:893-897.
- Power RD. 1991. New directions in the diagnosis and therapy of urinary tract infections. *Am J Obstet Gynecol* 164:1387-1389
- Raco MO, Barez MYC. 1998. Profile of community acquired urinary tract infections in Davao City *PJMID* 27:2:62-66
- Ramsey DE, Finch WT, Birtch AG. 1979 Urinary tract infection in kidney transplant recipients. *Arch Surg* 114:1022-1026.
- Raz R, Stamm WE. 1993. A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. *N Engl J Med* 329:753-756.
- Reddy J, Campbell A. 1985. Bacteriuria in pregnancy. *Aust & NZJ Obstet Gynecol* 25:176-178.
- Reese RE, Betts RF, editors. 1997. Catheter-associated UTI. A Practical approach to infectious disease 4th ed. 12:506-511
- Renoult E, Aouragh F, Mayeuz D, Hestin D, Lataste A, Hubert J, L'Hermite J, Kessler M. 1994. Factors influencing early urinary tract infections in kidney transplant recipients. *Transplant Proc* 26:2056-2058.
- Roberts FJ. 1986 Quantitative urine culture in patients with urinary tract infection and bacteremia. *Am J Clin Pathol* 85:616-618.
- Romero R, Oyarzun E, Mazor M, Sirtori M, Hobbins JC, Bracken M. 1989. Meta-analysis of the relationship between asymptomatic bacteriuria and preterm delivery/low-birth weight. *Obstet gynecol* 73:576-582
- Ronald AR, Harding GK. 1997 complicated urinary tract infections. *Infect Dis Clin North Am* 11:583-592.
- Ronald AR, Pattullo ALS. 1991. The Natural History of Urinary infection in Adults. 75:299-312.
- Rose BD. 1997. Struvite stones. UptoDate Inc.
- Rubin RH, Bean TR, Stamm WE. 1992. An approach to evaluating antibacterial agents in the treatment of urinary tract infection. *Clin Infect Dis* 14 suppl 2:S246:251.
- Rubin RH, Fang LST, Cosimi AB, Herrin JT, Varga PA, Russell PS, Tolkoff-Rubin NE. 1979. Usefulness of the antibody-coated bacteria assay in the management of urinary tract infection in the renal transplant patient. *Transplantation* 27:18-20.
- Rubin RH, Shapiro ED, Andriole VT, Davis RJ, Stamm WE. 1992. General guidelines for the evaluation of new anti-infective drugs for the treatment of urinary infections. *Clin Infect Dis* 15 suppl 1:S216-27.
- Rubin RH, Beam TR Jr, Stamm WE. 1992. An approach to evaluating antibacterial agents in the treatment of urinary tract infection. *Clin Infect Dis* 14 Suppl 2:S246-251.
- Rubin RH Shapiro ED andriole VT et al 1992 evaluation of new anti-infective drugs for the treatment of urinary tract infection. *Clin Infect Dis* 15 Suppl 1:S216-27.
- Rubin RH, Wolfson JS, Cosimi AB, Tolkoff- Rubin NE. 1981. Infection in the renal transplant recipient. *Am J Med* 70:405-411.
- Sabbaj J, Hoagland VL, Shih WJ. 1985. Multiclinic comparative study of norfloxacin and trimethoprim-sulfamethoxazole for treatment of urinary infections. *Antimicrob Agents Chemother* 27:297-301.
- Safrin S, Siegel D, Black D. 1988. Pyelonephritis in adult women: inpatient vs outpatient therapy. *Am J Med* 85:793-798.
- Sandberg T, Englund G, Lincoln, et al. 1990. Randomized double-blind study of norfloxacin and cefadroxil in the treatment of acute pyelonephritis. *Eur J Clin Microbiol Infect Dis* 9:317-323.
- Sanford J. 1964. Hospital acquired urinary tract infection. *Ann Int Med* 60:903-913.
- Schaberg DR, Haley RW, Highsmith AK, Anderson RL, McGowan JE. 1980. Nosocomial bacteriuria. A prospective study of case clustering and antimicrobial resistance. *Ann Intern Med* 93:420-424.
- Schmaldienst S, Horl WH. 1997. Bacterial infections after renal transplantation. *Nephron* 75: 140-153.
- Sharifi R, Lee M. 1997. Urinary tract infections in HIV infected men *Infect. Urol* 10:24-25.
- Small F. 1998 Antibiotic vs no treatment for symptomatic bacteriuria in pregnancy. *Cochrane Review. The Cochrane Library* (2):1-10
- Spencer J, Lindsell D, Mastorakou L. 1990. Ultrasonography compared with intravenous urography in investigation of urinary tract infection in adults. *BMJ* 301:221-224.
- Stamey TA. 1977. Prophylactic efficacy of nitrofurantoin macrocrystals and trimethoprim-sulfamethoxazole in urinary infections: Biologic effects on the vaginal and rectal flora. *N Engl J Med* 296:780-783.
- Stamm WE, Hooton TM. 1993. Management of urinary tract infection in adults. *N Engl J Med* 319:1328-1334.
- Stamm WE, Counts GW, Running KR, et al. 1982. Diagnosis of coliform infection in acutely dysuric women. *N Engl J Med* 307:463.
- Stamm WE. 1980. Antimicrobial prophylaxis of recurrent urinary tract infections: a double-blind, placebo-controlled trial. *Ann Intern Med* 92:770-5.
- Stamm WE, Mckevitt M, Counts GW. 1987. Acute renal infection in women: treatment with trimethoprim-sulfamethoxazole or ampicillin for two or six weeks; a randomized trial. *Ann Intern Med* 106:341-345.
- Stansfeld JM. 1962. The measurement and meaning of pyuria. *Arch Dis Child* 37:257-6.

- Stapleton A. 1990. Postcoital antimicrobial prophylaxis for recurrent urinary tract infection: a randomized double-blind, placebo-controlled trial. *JAMA* 264:703-6.
- Stark RP, Maki DG. 1984. Bacteriuria in the catheterized patient: What quantitative level of bacteriuria is relevant? *N Engl J Med* 311:560-564.
- Steele AC, Mallison GF. 1975. Handwashing practices for the prevention of nosocomial infections. *Ann Intern Med* 83:683-90.
- Stenqvist K, Dahlen-Nilsson I, Lichin-Janson G. 1989. Bacteriuria in pregnancy. *Am J Epidemiol* 129:372.
- Stuby U, Kaise W, Grafinger P, Beisenbach, Zazgornik J. 1989. Urinary tract infection after renal transplantation under conventional therapy and cyclosporine. *Transplant Proc* 21:2110-2111.
- Sweet DE, Goodpasture HC, Holl K, Smart S, Alexander H, Hedari A. 1985. Evaluation of H2O2 prophylaxis of bacteriuria in patients with long-term indwelling foley catheters: a randomized controlled study [abstract]. *Infect Control* 6:263-266.
- Talan DA, Stamm WE, Reuning-Scherer J, Church D, and the Pyelonephritis Investigators Group. 1998. Ciprofloxacin 7 day vs TMP-SMX 14 day + ceftriaxone for acute uncomplicated pyelonephritis: A randomized, double-blind trial [abstract] 8th International Congress on Infectious Disease. Boston, Mass.
- Thompson RL, Haley CE, Seacy MA, Guenther SM, Kaise DL, Groschel DH, et al. 1984. Failure to reduce attack rates using periodic instillations of a disinfectant into urinary drainage systems. *JAMA* 251:747-751.
- Tincello D, Richmond DH. 1998. Evaluation of reagent strips in detecting asymptomatic bacteriuria in early pregnancy: Prospective case series. *BMJ* 316:435-437.
- Tulkoff-Rubin NE, Rubin RH. 1997. Urinary tract infection in the immunocompromised host: Lessons from kidney transplantation and the AIDS epidemic. *Infect Dis Clin North Am* 11:707-717.
- US Preventive Services Task Force. 1996. Guide to Clinical Preventive Services. Baltimore: William & Wilkins.
- Van Dorsten P, Lenke RR, Schifrin GS. 1987. Pyelonephritis in pregnancy. The role of in-hospital management and nitrofurantion suppression. *J Rep Med* 32:895-900.
- Van Dorsten PJ, Bannister ER. 1986. Office diagnosis of asymptomatic bacteriuria in pregnant women. *Am J Obstet Gynecol* 155:777-780.
- Villar J, Lyndon-Rochelle MT, Gulmezoglo AM. 1998. Duration of treatment of asymptomatic bacteriuria during pregnancy. *Cochrane Review. The Cochrane Library.* (2).
- Wadland, William C, Plante, Dennis A. 1989. Screening for asymptomatic bacteriuria in pregnancy: A decision and cost-analysis. *J Family Practice* 29:372-376.
- Walter S, Pedersen FB, Vejlsgeaer R. 1975. Urinary tract infection and wound infection in kidney transplant patients. *Brit J Urol* 47:513-517.
- Ward G, Jordan RC, Severance HW. 1991. Treatment of pyelonephritis in an observation unit. *Ann Emerg Med* 20:258-261.
- Warren JW. 1997. Catheter-associated urinary tract infections. *Infect Dis Clin North Am* 11:609-622.
- Warren JW, Anthony WC, Hoopes JM, Muncie HL. 1982. Cephalexin for susceptible bacteriuria in afebrile, long-term catheterized patients. *JAMA* 248:454-458.
- Warren JW, Platt R, Thomas RJ, Rosner B, Kass EJ. 1978. Antibiotic irrigation and catheter-associated urinary tract infections. *N Engl J Med* 299:570-573.
- Warren JW. 1997 Catheter-associated urinary tract infections. *Infect Dis Clinics North Am* 11:609-622.
- Warren JW, Anthony WC, Hoopes JM, Muncie HL. 1982 Cephalexin for susceptible bacteriuria in afebrile long term catheterized patients. *JAMA* 248:454-458.
- Wilkie ME, Almond MK, Marsh FP. 1992. Diagnosis and management urinary tract infection in adults *BMJ* 305:1137-1141.
- Willinam DN. 1996. Urinary tract infection: emerging insights into appropriate management. *PostGrad Med* 99:189-201.
- Willie JC, Blusse van Oud Alblas A, Thewessen EA. 1993. Nosocomial catheter-associated bacteriuria: a clinical trial comparing two closed urinary drainage systems [abstract]. *J Hosp Infect* 25:191-198.
- Winston DJ, Gale RP, Meyer DV, Young LS. 1979. Infectious complications of human bone marrow transplantation. *Medicine* 58:1-31.
- Wong ES. 1983. Guidelines for prevention of catheter-associated urinary tract infections. *Am J Infect Control* 11:28-36.
- Wong ES. 1985. Management of recurrent urinary tract infections with patients-administered single-dose therapy. *Ann Intern Med* 102:302-7.
- Wong-Beringer A, Jacobs RA, Guglielmo J. 1992. Treatment of funguria. *JAMA* 267:2780-2785.
- Zhanel GG, Harding GKM, Guay DRP. 1990. Asymptomatic bacteriuria: which patients should be treated? *Arch Intern Med* 150:1389-1397.
- Zhanel GG Harding GK Nicolle LE 1991. Asymptomatic bacteriuria in patients with diabetes mellitus. *Rev Infect Dis* 13:150-154
- Zhanel GG, Harding GK, Nicolle LE. 1995. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes mellitus. *Clin Infect Dis* 21:316-322.

## 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 (preferable 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 and 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. None of the 5 criteria was met.

### Appendix 3

#### Laboratory criteria for significant pyuria and bacteriuria

Syndrome	Cut-off for pyuria*	Strength of recommendation	Cut-off for bacteriuria	Strength of recommendation
1. Acute uncomplicated cystitis	a. $\geq 8$ pus cells/ mm <sup>3</sup>	C	$\geq 100$ cfu/ml	A
	b. $\geq 5$ pus cells/ hpf	C	$\geq 1000$ cfu/ml (clinical trials)	C
2. Acute uncomplicated pyelonephritis	$\geq 5$ pus cells/hpf	C	$\geq 10,000$ cfu/ml	B
3. Asymptomatic bacteriuria	$> 10$ pus cells/ hpf	C	$\geq 100,000$ cfu/ml	A
4. Complicated UTI			$\geq 100,000$ cfu/ml (with exceptions)	C
5. UTI in males	a. $\geq 10$ pus cells/mm <sup>3</sup>	C	$\geq 1000$ cfu/ml	C
	b. $\geq 5$ pus cells/ hpf	C		

\*Pus cell per mm<sup>3</sup> and per hpf refer to number found in uncentrifuged and centrifuged urine respectively.

### 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. Urethral 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 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 a screw-top lid.

Adapted from Kunin CM 1997. Detection, Prevention And Management of Urinary Tract Infections

### Appendix 5

#### 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 bladder
- Renal calculi

- Allergic interstitial nephritis
- Sickle cell disease
- Sarcoidosis
- Idiopathic interstitial cystitis
- Glomerulonephritis

Infectious diseases  
 Tuberculosis  
 Chlamydial and gonococcal urethritis  
 Leptospirosis  
 Viral cystitis  
 Infections adjacent to the urinary tract  
 Appendicitis  
 Diverticulitis

## Appendix 6

### Cost of oral drugs commonly used for UTI

Drug/Regimen	3-day	7-day	14-day
Co-trimoxazole (Generic) 160/800 mg q 12h	PhP 66.00	PhP 154.00	PhP 308.00
Nitrofurantoin 100 mg q 6h	178.20	415.80	831.60
Amoxicillin/Clavulanate 375 mg q8h	546.48	1,575.12	3,150.24
Ciprofloxacin 250 mg q 12h	180.00	420.00	840.00
500 mg q 12h	245.70	573.30	1,146.60
Ofloxacin 200 mg q 12h	204.78	477.82	955.64
400 mg q 12 h	256.02	597.38	1,194.76
Norfloxacin 400 mg q 12h	120.00	280.00	560.00
200 mg q 12h	87.00	203.00	406.00

### Cost of antimicrobial prophylaxis regimens for recurrent UTI

Daily Regimen	Cost (pesos)/day
Nitrofurantoin 50 mg	PhP 7.50
Co-trimoxazole (Generic) 40/200 mg (1/2 tab)	6.40
Norfloxacin 200 mg	14.50
Cephalexin 250 mg	12.01
500 mg	21.88

### Cost of parenteral regimens for UTI

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

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