

# Diagnosis and Management of Acute Pyelonephritis in Adults

KALYANAKRISHNAN RAMAKRISHNAN, M.D., and DEWEY C. SCHEID, M.D., M.P.H.

University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma

There are approximately 250,000 cases of acute pyelonephritis each year, resulting in more than 100,000 hospitalizations. The most common etiologic cause is infection with *Escherichia coli*. The combination of the leukocyte esterase test and the nitrite test (with either test proving positive) has a sensitivity of 75 to 84 percent and a specificity of 82 to 98 percent for urinary tract infection. Urine cultures are positive in 90 percent of patients with acute pyelonephritis, and cultures should be obtained before antibiotic therapy is initiated. The use of blood cultures should be reserved for patients with an uncertain diagnosis, those who are immunocompromised, and those who are suspected of having hematogenous infections. Outpatient oral antibiotic therapy with a fluoroquinolone is successful in most patients with mild uncomplicated pyelonephritis. Other effective alternatives include extended-spectrum penicillins, amoxicillin-clavulanate potassium, cephalosporins, and trimethoprim-sulfamethoxazole. Indications for inpatient treatment include complicated infections, sepsis, persistent vomiting, failed outpatient treatment, or extremes of age. In hospitalized patients, intravenous treatment is recommended with a fluoroquinolone, aminoglycoside with or without ampicillin, or a third-generation cephalosporin. The standard duration of therapy is seven to 14 days. Urine culture should be repeated one to two weeks after completion of antibiotic therapy. Treatment failure may be caused by resistant organisms, underlying anatomic/functional abnormalities, or immunosuppressed states. Lack of response should prompt repeat blood and urine cultures and, possibly, imaging studies. A change in antibiotics or surgical intervention may be required. (Am Fam Physician 2005;71:933-42. Copyright© 2005 American Academy of Family Physicians.)

See page 835 for strength-of-recommendation labels.

**A**cute pyelonephritis is an infection of the upper urinary tract, specifically the renal parenchyma and renal pelvis (Figure 1). Acute pyelonephritis is considered uncomplicated if the infection is caused by a typical pathogen in an immunocompetent patient who has normal urinary tract anatomy and renal function. Misdiagnosis can lead to sepsis, renal abscesses, and chronic pyelonephritis that may cause secondary hypertension and renal failure. Risk factors for complicated acute pyelonephritis are those that increase susceptibility or reduce host response to infections (Table 1).<sup>1,2</sup>

Approximately 250,000 cases of acute pyelonephritis occur each year, resulting in more than 100,000 hospitalizations.<sup>3</sup>

Women are approximately five times more likely than men to be hospitalized with this condition (11.7 versus 2.4 hospitalizations per 10,000 cases, respectively); however, women have a lower mortality rate

than men (7.3 versus 16.5 deaths per 1,000 cases, respectively).<sup>4</sup> Acute pyelonephritis occurs in 1 to 2 percent of pregnant women, increasing the risk for premature labor and low-birth-weight infants.<sup>5</sup>

## Pathogenesis

Most renal parenchymal infections occur secondary to bacterial ascent through the urethra and urinary bladder. In men, prostatitis and prostatic hypertrophy causing urethral obstruction predispose to bacteriuria.<sup>6</sup> Hematogenous acute pyelonephritis occurs most often in debilitated, chronically ill patients and those receiving immunosuppressive therapy. Metastatic staphylococcal or fungal infections may spread to the kidney from distant foci in the bone or skin.

In more than 80 percent of cases of acute pyelonephritis, the etiologic agent is *Escherichia coli*.<sup>7</sup> Other etiologic causes include aerobic gram-negative bacteria, *Staphylococcus saprophyticus*, and enterococci. The microbial spectrum associated with different types of urinary tract infections (UTIs) is

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## Strength of Recommendations

Key clinical recommendation	Label	References
Blood cultures should be obtained in patients with acute pyelonephritis only if there is diagnostic uncertainty, the patient is immunosuppressed, or a hematogenous source is suspected.	C	24, 25
Outpatient oral therapy is successful in 90 percent of selected patients with uncomplicated acute pyelonephritis who can tolerate oral intake, will be compliant with the treatment regimen, will return for early follow-up, and have adequate social support.	B	27, 28
Patients hospitalized with acute pyelonephritis should be treated with one of three initial intravenous therapies: a fluoroquinolone; an aminoglycoside with or without ampicillin; or an extended-spectrum cephalosporin with or without an aminoglycoside.	B	29

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, opinion, or case series. See page 835 for more information.

wide (Table 2).<sup>8,9</sup> In elderly patients, *E. coli* is a less common (60 percent) cause of acute pyelonephritis. The increased use of catheters and instruments among these patients predisposes them to infections with other gram-negative organisms such as *Proteus*, *Klebsiella*, *Serratia*, or *Pseudomonas*.

Patients who have diabetes mellitus tend to have infections caused by *Klebsiella*, *Enterobacter*, *Clostridium*, or *Candida*. They also are at an increased risk of developing emphysematous pyelonephritis and papillary necrosis, leading to shock and renal failure.<sup>1,10</sup> Bacteriuria, which frequently is polymicrobial, develops in more than 50 percent of patients who require catheterization for more than five days, and in virtually all patients who have indwelling urinary catheters for more than one month.<sup>1</sup>

Immunosuppression favors the development of subclinical (silent) pyelonephritis and infections caused by nonenteric, aerobic, gram-negative rods and *Candida*. Acute pyelonephritis occurs within two months following renal transplant in 30 to 50 percent of patients because of concomitant immunosuppression and postsurgical vesicoureteric reflux.<sup>2</sup> Acute pyelonephritis is considered complicated in men because they have a higher probability of urinary tract abnormalities, prostatic enlargement causing urethral obstruction with incomplete voiding, or an age-related decrease of antibacterial activity in prostatic secretions.

## Clinical Presentation

The spectrum of acute pyelonephritis is wide, ranging from a mild illness to sepsis syndrome.<sup>1</sup> To diagnose acute pyelonephri-

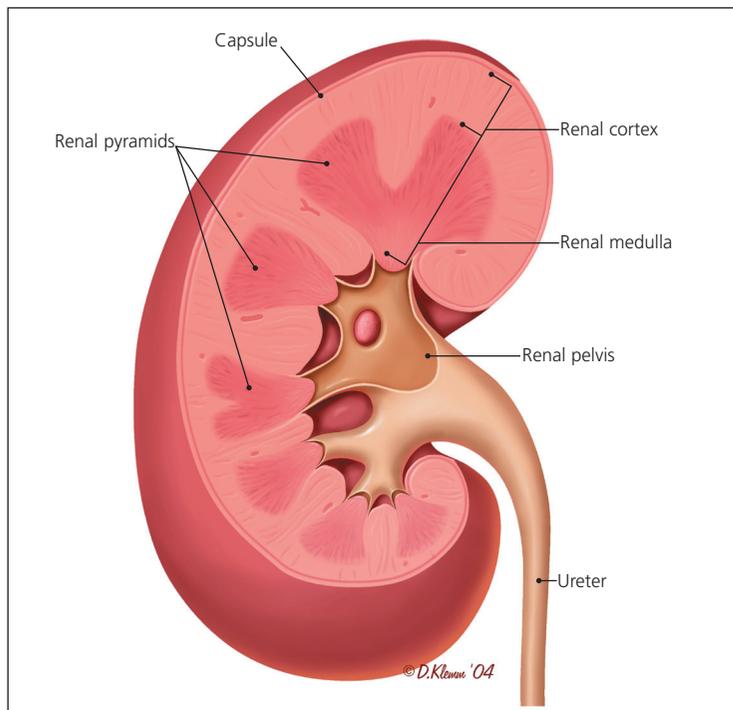


Figure 1. Anatomy of the kidney.

**TABLE 1**  
**Risk Factors for Complicated Acute Pyelonephritis**

Age	Immunosuppressed state	Obstruction
Infants	Diabetes mellitus	Foreign body
Elderly (> 60 years of age)	Sickle cell disease	Calculi
Anatomic/functional abnormality	Transplantation	Bladder neck obstruction
Polycystic kidney disease	Malignancy	Posterior urethral valve
Horseshoe kidney	Chemoradiation	Benign prostatic hypertrophy
Double ureter	HIV infections	Neurogenic bladder
Ureterocele	Corticosteroid use	Pregnancy
Vesicoureteric reflux	Male sex	Miscellaneous
Foreign body	Anatomic abnormalities	Inappropriate antibiotics
Urinary, ureteric, or nephrostomy catheters	Prostatic obstruction	Resistant organisms
Calculus		Instrumentation

HIV = human immunodeficiency virus.  
Information from references 1 and 2.

tis, physicians must rely on evidence of UTI from urinalysis or culture, along with signs and symptoms suggesting upper UTI (fever, chills, flank pain, nausea, vomiting, costovertebral angle tenderness). Symptoms that

are suggestive of cystitis (dysuria, urinary bladder frequency and urgency, and suprapubic pain) also may be present.

In a study<sup>11</sup> of young and middle-aged women presenting to an emergency depart-

**TABLE 2**  
**Microbial Organisms Causing Specific Types of Urinary Tract Infections**

Microbial organism	Acute uncomplicated cystitis (%) <sup>*</sup>	Acute uncomplicated pyelonephritis (%)	Complicated UTI (%)	Catheter-associated UTI (%)
<i>Escherichia coli</i>	68	89	32	24
<i>Staphylococcus saprophyticus</i>	8	0	1	0
Proteus	6	4	4	6
Klebsiella	4	4	5	8
Enterococci	3	0	22	7
Pseudomonas	0	0	20	9
Mixed	3	5	10	11
Yeast	0	0	15	8

UTI = urinary tract infection.

<sup>\*</sup>—One study<sup>9</sup> showed that 25 percent of *E. coli* isolates were resistant to ampicillin, 24 percent to tetracyclines, and 11 percent to trimethoprim-sulfamethoxazole (TMP-SMX; Bactrim, Septra).

Adapted with permission from *The Johns Hopkins Ambulatory Clerkship in Medicine. Dysuria*. Accessed online December 5, 2004, at: <http://deptmed.med.som.jhmi.edu/ambclerk/dysuria.html>, with additional information from reference 9.

ment with fever, pyuria, and other features of upper UTI, 98 percent had acute pyelonephritis. In the absence of fever, 16 percent were given alternative diagnoses.<sup>11</sup> However, up to one third of elderly patients with acute pyelonephritis have no fever; in 20 percent of elderly patients, the predominant symptoms are gastrointestinal or pulmonary.<sup>1</sup> Fever and leukocytosis are of little value in diagnosing acute pyelonephritis in patients who have indwelling bladder catheters, especially when infections are caused by gram-positive cocci or *Candida*.<sup>12</sup> The differential diagnosis of acute pyelonephritis includes pelvic inflammatory disease, cholecystitis, appendicitis, lower lobe pneumonia, perforated viscus, and the prodrome of herpes zoster.

Up to 30 percent of women presenting with cystitis-like symptoms have upper urinary tract involvement (subclinical pyelonephritis), but these infections rarely cause any cortical damage. This situation is more common in pregnant women and patients with recurrent UTI, diabetes, immunosuppression, renal tract pathology, or previous UTI occurring before 12 years of age.<sup>2</sup> In the presence of obstruction (stone, tumor, bladder neck obstruction, enlarged prostate), acute pyelonephritis can be extremely severe and recalcitrant to treatment, and may progress to renal abscess.

**Fever and leukocytosis are of little value in diagnosing acute pyelonephritis in patients who have indwelling bladder catheters.**

## Diagnostic Testing

Urinalysis and urine culture confirm the diagnosis of acute pyelonephritis. The consensus definition of pyelonephritis established by the Infectious Diseases Society of America (IDSA) is a urine culture showing at least 10,000 colony-forming units (CFU) per mm<sup>3</sup> and symptoms compatible with the diagnosis.<sup>13</sup> Lower counts (1,000 to 9,999 CFU per mm<sup>3</sup>) are of concern in men and pregnant women. Urine specimens generally are obtained by a midstream clean-catch technique, and one study<sup>14</sup> showed that cleansing does not decrease contamination rates in adults.

Pyuria is present in almost all patients with acute pyelonephritis and can be detected rapidly with the leukocyte esterase test or the nitrite test. The combination of the leukocyte esterase and nitrite tests (with a positive result on either) for UTI is more specific but less sensitive than either test alone<sup>15</sup> (Table 3).<sup>3,15-21</sup> Although white cell casts may be observed in other conditions, they are, along with other features of UTI, specific for acute pyelonephritis. Hematuria may be present in patients with cystitis and pyelonephritis.<sup>3</sup>

In some complicated cases, Gram stain analysis of urine can aid in the choice of initial antibiotic therapy.<sup>22</sup> Another option is the use of the antibody-coated bacteria assay, which may be helpful in localizing subclinical upper UTIs.<sup>23</sup>

Urine cultures are positive in 90 percent of patients with acute pyelonephritis, and culture specimens should be obtained before initiation of antibiotic therapy. Blood cultures have been recommended for hospitalized patients; up to 20 percent of these patients have positive cultures.<sup>1</sup> In two studies,<sup>24,25</sup> however, completion of blood cultures did not result in changes in management strategies in patients with acute pyelonephritis. There is no evidence that positive blood cultures indicate a more complicated course in otherwise healthy persons with pyelonephritis.<sup>26</sup> Therefore, blood cultures are indicated only if there is diagnostic uncertainty, the patient is immunosuppressed, or a hematogenous source is suspected.<sup>24,25</sup>

## The Authors

KALYANAKRISHNAN RAMAKRISHNAN, M.D., is associate professor in the Department of Family and Preventive Medicine at the University of Oklahoma Health Sciences Center, Oklahoma City. Dr. Ramakrishnan received his medical degree from the Jawaharlal Institute, Pondicherry, India. He completed a family practice residency at the University of Oklahoma Health Sciences Center.

DEWEY C. SCHEID, M.D., M.P.H., is associate professor in the Department of Family and Preventive Medicine at the University of Oklahoma Health Sciences Center. Dr. Scheid received his medical degree from the University of Cincinnati (Ohio) College of Medicine. He completed a family practice residency at Memorial Medical Center in Corpus Christi, Tex., and a master of public health degree at the Johns Hopkins Bloomberg School of Public Health.

*Address correspondence to Kalyanakrishnan Ramakrishnan, M.D., University of Oklahoma Health Sciences Center, Dept. of Family and Preventive Medicine, Residency Division, 900 N.E. 10th St., Room 2614, Oklahoma City, OK 73104 (e-mail: kalyanakrishnan-ramakrishnan@ouhsc.edu). Reprints are not available from the authors.*

**TABLE 3**  
**Laboratory Diagnosis of Urinary Tract Infection**

Test	Finding	Sensitivity (%)*	Specificity (%)*
Urinalysis <sup>16,17</sup>	> 5 WBCs/HPF	72 to 95	48 to 82
	> 10 WBCs/HPF	58 to 82	65 to 86
Leukocyte esterase test <sup>3</sup>	Positive	74 to 96	94 to 98
Nitrite test <sup>18</sup>	Positive	35 to 85	92 to 100
Leukocyte esterase and nitrite tests <sup>15,19</sup>	Either test positive	75 to 84	82 to 98
Dipstick hematuria <sup>20</sup>	Positive	44	88
Gram stain of uncentrifuged urine <sup>21</sup>	> 1 bacterium per HPF	93	95

WBCs/HPF = white blood cells per high-power field.

\*—For identification of > 100,000 colony-forming units per mm<sup>3</sup>.

Information from references 3 and 15 through 21.

## Treatment

Although patients with acute pyelonephritis traditionally have been hospitalized and treated with intravenous antibiotics, outpatient oral therapy is successful in 90 percent of selected patients with uncomplicated acute pyelonephritis who can tolerate oral intake, will be compliant with the treatment regimen,

will return for early follow-up, and have adequate social support<sup>27,28</sup> (Figure 2). Patients with complicated acute pyelonephritis who are more ill or have not responded to outpatient therapy should be hospitalized. Using specific hospitalization criteria (Table 4),<sup>1</sup> up to 70 percent of patients can be selected for outpatient management. Another option is initial therapy with parenteral antibiotics in an inpatient observation unit, followed by oral therapy as an outpatient.<sup>26,29</sup>

Of the common uropathogens, resistance to fluoroquinolones remains very low (1 to 3 percent).<sup>30</sup> Fluoroquinolones are absorbed well from the gastrointestinal tract and have excellent kidney penetration. In selected patients with moderate or severe acute pyelonephritis, clinical outcomes are equivalent with intravenous and oral ciprofloxacin (Cipro) therapy.<sup>31</sup> Therefore, for empiric therapy in uncomplicated acute pyelonephritis, the IDSA recommends the use of an oral fluoroquinolone<sup>29</sup> (Table 5). Oral amoxicillin-clavulanate potassium (Augmentin), a cephalosporin, and trimethoprim-sulfamethoxazole (TMP-SMX; Bactrim, Septra) provide acceptable alternatives for susceptible organisms.<sup>29</sup>

The U.S. Food and Drug Administration has classified fluoroquinolones as pregnancy

**Urine cultures should be obtained before initiation of antibiotic therapy.**

**TABLE 4**  
**Indications for Hospitalization in Patients with Acute Pyelonephritis**

### Absolute indications

- Persistent vomiting
- Progression of uncomplicated UTI
- Suspected sepsis
- Uncertain diagnosis
- Urinary tract obstruction

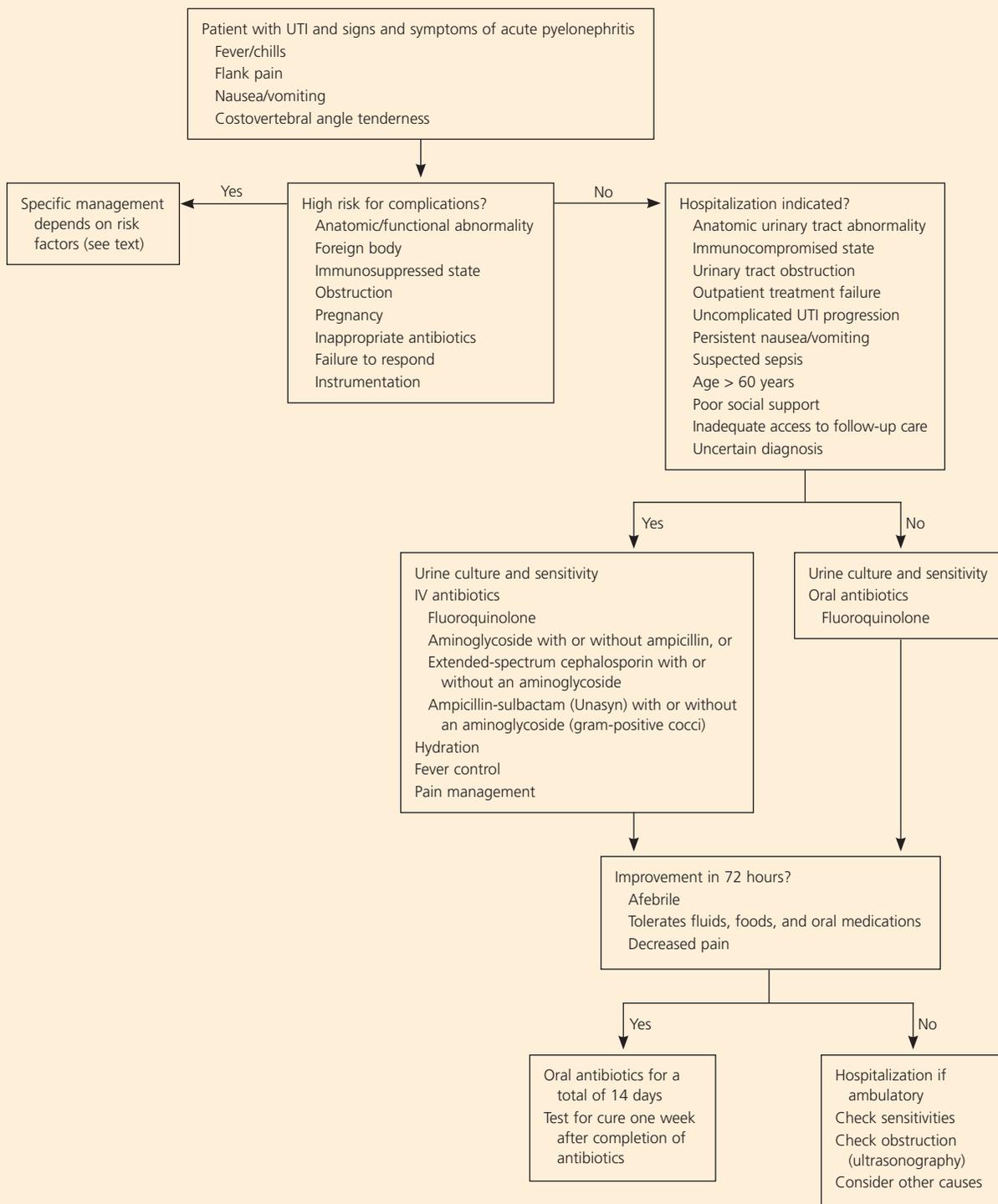
### Relative indications

- Age > 60 years
- Anatomic urinary tract abnormality
- Immunocompromised (diabetes mellitus, cancer, sickle cell disease, organ transplant)
- Inadequate access to follow-up
- Frailty, poor social support

UTI = urinary tract infection.

Information from reference 1.

## Evaluation and Management of Acute Pyelonephritis



**Figure 2.** Algorithm for the evaluation and management of acute pyelonephritis (UTI = urinary tract infection; IV = intravenous).

category C drugs, and their use should be avoided in pregnant women. Amoxicillin or amoxicillin-clavulanate potassium is preferred during pregnancy and in the treat-

ment of infections caused by gram-positive organisms. Some physicians administer a single parenteral dose of an antibiotic (ceftriaxone [Rocephin], gentamicin [Garamy-

cin], or a fluoroquinolone) before initiating oral therapy,<sup>29</sup> but there is little evidence that this step improves outcomes.<sup>1</sup> Table 5 reviews antimicrobial agents used in the treatment of acute pyelonephritis.

If the patient requires hospitalization, the IDSA guidelines<sup>29</sup> recommend one of three initial intravenous therapies: (1) a fluoroquinolone; (2) an aminoglycoside with or without ampicillin; or (3) an extended-spectrum

**TABLE 5**  
**Antimicrobial Agents Used in the Treatment of Acute Pyelonephritis**

Agent	Dosing schedule	Oral dose (mg)	IV dose	Comments
<b>Penicillins</b>				
Amoxicillin	Every 8 to 12 hours	500	—	None
Amoxicillin- clavulanate potassium (Augmentin)	Every 8 to 12 hours	500/125	—	GI side effects*
Ampicillin-sulbactam (Unasyn)	Every 4 to 6 hours	—	150 to 200 mg per kg per day	GI side effects*
Aztreonam (Azactam)	Every 6 to 8 hours	—	1 to 2 g	Phlebitis; GI side effects*
Imipenem (Primaxin I.V.)	Every 6 hours	—	0.5 g	None
Piperacillin (Pipracil)	Every 6 hours	—	3 g	GI side effects*; phlebitis
Piperacillin-tazobactam (Zosyn)	Every 6 to 8 hours	—	3.375 g/4.5 g	GI side effects*; rash; headaches; insomnia
Ticarcillin-clavulanate (Timentin)	Every 4 to 6 hours	—	3.1 g	GI side effects*; rash; phlebitis
<b>Cephalosporins</b>				
Cefotaxime (Claforan)	Every 8 to 12 hours	—	1 to 2 g	Thrombophlebitis
Ceftriaxone (Rocephin)	Once in 24 hours	—	1 to 2 g	Leukopenia; elevated BUN and liver enzyme levels
Cephalexin (Keflex)	Every 6 hours	500	—	GI side effects*
<b>Fluoroquinolones</b>				
Ciprofloxacin (Cipro)	Every 12 hours	500	400 mg	Nausea; headache; photosensitivity; pregnancy category C
Enoxacin (Penetrex)	Every 24 hours	400	—	Pregnancy category C
Gatifloxacin (Tequin)	Every 24 hours	—	400 mg	Pregnancy category C
Levofloxacin (Levaquin)	Every 24 hours	250 to 750	250 to 750 mg	ECG QT prolongation; pregnancy category C
Lomefloxacin (Maxaquin)	Every 24 hours	400	—	Pregnancy category C
Norfloxacin (Noroxin)	Every 12 hours	400	—	Pregnancy category C
Ofloxacin (Floxin)	Every 12 hours	200 to 400	400 mg	Pregnancy category C
<b>Aminoglycosides</b>				
Amikacin (Amikin)	Every 12 hours	—	7.5 mg per kg	Ototoxicity; nephrotoxicity
Gentamicin (Garamycin)	Every 24 hours	—	5 to 7 mg per kg	Ototoxicity; nephrotoxicity
Tobramycin (Nebcin)	Every 24 hours	—	5 to 7 mg per kg	Ototoxicity; nephrotoxicity
<b>Other antibiotics</b>				
TMP-SMX (Bactrim; Septra)	Every 12 hours	160/800	8 to 10 mg per kg (TMP)	G6PD deficiency; sulfa allergy; do not use in third trimester

IV = intravenous; GI = gastrointestinal; BUN = blood urea nitrogen; ECG = electrocardiogram; TMP-SMX = trimethoprim-sulfamethoxazole; G6PD = glucose-6-phosphate dehydrogenase.

\*—GI side effects include nausea, vomiting, and diarrhea.

cephalosporin with or without an aminoglycoside. With gram-positive cocci, ampicillin-sulbactam (Unasyn) with or without an aminoglycoside is recommended. Aminoglycosides should be avoided in patients with pre-existing renal disease. Oral treatment is feasible as soon as the patient becomes afebrile, has improved clinically, and can tolerate oral hydration and medications. It is not necessary to use the same agent for both parenteral and oral therapy.<sup>26</sup> There is no benefit from additional hospital observation to determine the success of switching to an oral antibiotic.<sup>32</sup>

A seven- to 14-day course of antibiotics is effective in women who are immunocompetent and do not have underlying illness.<sup>1,27,30</sup> Studies<sup>29,33,34</sup> suggest that therapy lasting only

five to seven days is comparable to seven to 14 days in terms of clinical and bacteriologic outcome in patients with mild pyelonephritis and in those having a dramatic initial response to therapy. Acute pyelonephritis associated with immunosuppressive states responds well to a 14- to 21-day course of a fluoroquinolone or TMP-SMX.<sup>2</sup>

Post-treatment urine cultures are recommended in all patients at the follow-up visit, one to two weeks after completion of antibiotic therapy.<sup>35</sup>

Fever generally resolves within 72 hours of starting antibiotic therapy. In a study<sup>36</sup> of hospitalized patients who had no complications, however, 26 percent remained febrile at 48 hours, and 13 percent were febrile at 72 hours. Thus, persistence of fever after 72 hours in an otherwise stable and improving patient may not necessarily warrant a change in therapy or further investigation.

The two most common causes of initial treatment failure are resistant organisms and nephrolithiasis. In the absence of clinical response, many physicians obtain a blood count, urinalysis, and blood and urine cultures, seeking an indication of persisting infection and antibiotic resistance; however, there is little evidence to support the routine use of these tests. A rectal or vaginal examination should be performed.

Imaging studies may identify complicating factors such as anatomic abnormalities, obstruction, acute bacterial nephritis (localized, nonliquified interstitial inflammation), or subjacent infections such as appendicitis, cholecystitis, or perinephric abscess (*Figure 2*). Options include plain radiography of the kidneys, ureter, and bladder; renal ultrasonography; computed tomographic (CT) scan; magnetic resonance imaging; and intravenous pyelography. In most patients, ultrasound examination identifies acute bacterial nephritis, abscesses, ureteral obstruction, and hydronephrosis.<sup>37</sup> Acute bacterial nephritis may progress to frank abscess and requires a protracted course of antibiotics. If renal ultrasonography fails to define a lesion but shows marked renal enlargement, or if invasive intervention is being considered, a CT scan can exclude renal and perinephric abscesses.

Differences between UTI in men and women support the classification of male acute pyelonephritis as complicated. Men younger than 60 years without obstruction, renal abnormalities, or prostatitis respond well to 14 days of antibiotic therapy.<sup>2</sup> Men who have recurrent UTIs require a six-week regimen. Men with acute prostatitis require four weeks of treatment with an antibiotic that has high penetration into prostatic tissue, such as doxycycline (Vibramycin), TMP-SMX, or a fluoroquinolone; men with chronic prostatitis require six to 12 weeks of such therapy.<sup>2,38</sup> The optimal duration of treatment for hospitalized patients is 14 days.

Short-term antibiotic therapy (three days), which is appropriate in the treatment of cystitis, results in a 50 percent relapse rate in patients with subclinical acute pyelonephritis. The most reliable indicator of treatment failure is a positive follow-up culture in patients with presumed cystitis.<sup>2</sup> If relapse is noted after a two-week course of antibiotics, and no urologic abnormality is found on imaging, the uropathogen and sensitivities should be confirmed and treatment extended to six weeks.

If the pathogen causing reinfection is different from the original pathogen, two weeks of treatment are sufficient. Immedi-

**Short-term antibiotic therapy (three days), which is appropriate in the treatment of cystitis, results in a 50 percent relapse rate in patients who have subclinical acute pyelonephritis.**

ate release of any existing obstruction combined with a 14-day course of appropriate antibiotics minimizes failure and recurrence.<sup>2</sup> Relief of obstruction and antibiotic therapy may be successful in emphysematous pyelonephritis, but nephrectomy must be strongly considered in patients with unresponsive infections.<sup>1</sup> If parenchymal involvement including abscesses is observed, longer courses of antibiotics (intravenous or oral) or sequential therapy may be necessary.

Pregnant women with pyelonephritis require hospitalization (for at least a short observation period) for aggressive hydration and parenteral antibiotics. Antibiotic treatment is similar to the treatments of other adult regimens. During pregnancy, 86 percent of women have uterine contractions in the first hour after initiation of antimicrobial therapy, and 50 percent continue to have contractions after five hours of therapy.<sup>39</sup> One study<sup>40</sup> found no difference in clinical responses among pregnant women treated with ampicillin and gentamicin, cefazolin (Ancef), or ceftriaxone. Fluoroquinolones should be avoided because of concerns about their teratogenic effects on the fetus.<sup>1</sup>

Most patients with mild acute pyelonephritis who are pregnant (90 percent) can be treated successfully with parenteral antibiotics under brief (two to 24 hours) observation, followed by outpatient oral therapy.<sup>41,42</sup> Although some experts state that selected patients may be treated safely with oral antibiotics, there have been no outpatient trials in which oral therapy alone was used.<sup>43</sup> Because 25 percent of patients with mild acute pyelonephritis who are pregnant have a recurrence, these patients should have monthly urine cultures or antimicrobial suppression with oral nitrofurantoin (Macrochantin), 100 mg daily, until four to six weeks postpartum.<sup>43</sup> All pregnant women, especially those who have diabetes and had a previous UTI, should be screened for asymptomatic bacteriuria during the first prenatal visit.

No antibiotic prophylaxis is effective in reducing complications associated with indwelling catheters. Sterile insertion and

care of the catheter, minimizing the duration of catheterization, intermittent catheterization, closed drainage systems, and silver-alloy-coated catheters may reduce the risk of symptomatic infection.<sup>1,44</sup>

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