

UTIs in pregnancy: Managing urethritis, asymptomatic bacteriuria, cystitis, and pyelonephritis

Lower urinary tract infections typically pose minimal risk to mother and fetus with proper treatment; however, acute pyelonephritis may be dangerous. The author outlines diagnostic procedures and antibiotic treatment, particularly which medications should be avoided during pregnancy.

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CASE Pregnant woman with dysuria and suprapubic pain

A 25-year-old primigravid woman at 18 weeks of gestation requests evaluation because of the acute onset of frequent urination, dysuria, urination hesitancy, and suprapubic pain on the morning following intercourse. She has not experienced similar symptoms in the past. On physical examination, her temperature is 38 °C, pulse is 96 beats per minute, respirations are 18 per minute, and blood pressure is 100/76 mm Hg. She has no urethral discharge but is tender to palpation in the suprapubic area.

- What is the most likely diagnosis?
- What tests would be of greatest value in confirming the diagnosis?
- What is the most appropriate treatment for this patient?

Meet our perpetrator

Urinary tract infections (UTIs) are among the most common infections that occur



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during pregnancy. They may take one of 4 forms: acute urethritis, asymptomatic bacteriuria, acute cystitis, and acute pyelonephritis.¹ The first 3 conditions usually are straightforward to diagnose and treat, and they usually do not cause major problems for the mother or fetus. The latter, however, can cause serious complications that pose risk to the mother and fetus.

This article will review the microbiology, clinical manifestations, diagnosis, and treatment of these 4 disorders in pregnancy. Particular emphasis will be placed on measures to avoid adverse effects on the mother and fetus from antimicrobial agents.

Acute urethritis

Acute urethritis can be caused by low concentrations of coliform organisms in the lower urinary tract, but it usually is secondary to infection by *Neisseria gonorrhoea* or *Chlamydia trachomatis*. In most prenatal populations, the prevalence of one or the other of these 2 infections is approximately 5%.¹

The most common clinical manifestations of acute urethritis are a purulent urethral discharge, increased frequency of urination, dysuria, and urination hesitancy. The diagnosis most easily is confirmed by obtaining a specimen of urethral discharge or urine and evaluating the sample by a

nucleic acid amplification test for both gonorrhea and chlamydia.

Antibiotic therapy is preferred. The current recommended treatment for gonococcal urethritis is a single intramuscular injection of ceftriaxone 500 mg. If the patient prefers oral therapy, she can receive cefixime 800 mg in a single dose. For patients with an allergy to beta-lactam antibiotics, the alternative regimen is gentamicin 240 mg in a single intramuscular injection, combined with oral azithromycin in a single 2,000-mg dose. For treatment of chlamydia in pregnancy, the recommended therapy is azithromycin 1,000 mg in a single oral dose.² A test of cure should be performed within 4 weeks of treatment.

Asymptomatic bacteriuria

Asymptomatic bacteriuria (ASB) is the most common UTI in women. Approximately 5% to 8% of all sexually active women have ASB. The condition is not unique to pregnancy; it is associated primarily with the assumption of coital activity. In point of fact, the ASB typically precedes pregnancy by several years.¹

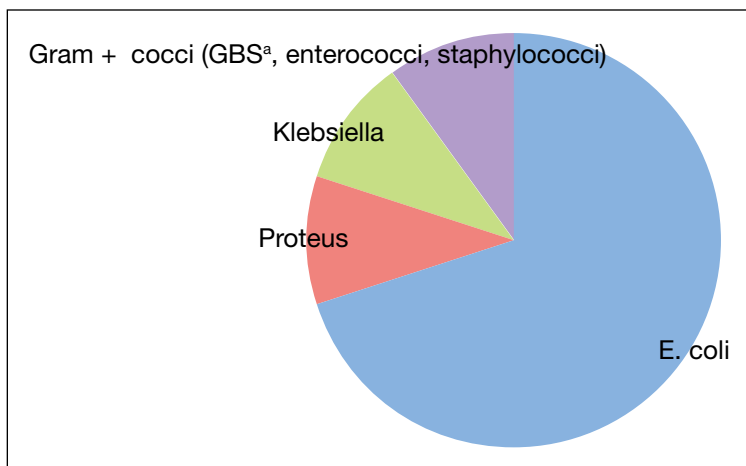
The principal pathogens responsible for ASB are shown in the **FIGURE**. Over 80% of first-time infections are secondary to *Escherichia coli*. As more recurrent episodes occur, the other Gram-negative bacilli (ie, *Klebsiella pneumoniae*, *Proteus* species) become more prevalent. The 3 major Gram-positive cocci that cause UTIs are enterococci, *Staphylococcus saprophyticus*, and group B streptococci.^{1,3,4}

In nonpregnant women, ASB usually remains completely asymptomatic, and ascending infections only rarely occur. In pregnancy, however, urinary stasis is present due to the effects of progesterone on ureteral peristalsis and because of pressure on the ureters (particularly the right) by the expanding gravid uterus. As a result, ascending infection may occur in approximately 20% of patients if the lower tract infection is not identified and treated adequately.¹

Clean-catch specimens and treatment

The standard criterion for the diagnosis of ASB is a urine culture that shows greater

FIGURE Principal uropathogens in pregnant women



^aGBS indicates group B streptococci.

than 100,000 colonies/mL of a recognized uropathogen.¹ The urine usually is obtained as a midstream, clean-catch specimen, and the test should be performed at the time of the first prenatal appointment. Once identified, ASB should be treated promptly with one of the antibiotics listed in the **TABLE**. Nitrofurantoin monohydrate macrocrystals (nitrofurantoin) and trimethoprim-sulfamethoxazole should be avoided in the first trimester unless no other drug is active against the identified microorganism.

TABLE Commonly used oral antibiotics for treatment of asymptomatic bacteriuria and acute cystitis

Drug	Dose
Amoxicillin	500 mg tid or 875 mg bid
Amoxicillin-clavulanate ^a	875 mg/125 mg bid
Cephalexin	500 mg bid or 250 mg four times daily
Nitrofurantoin monohydrate macrocrystals	100 mg bid
Trimethoprim-sulfamethoxazole, double strength	800 mg/160 mg bid

Abbreviations: tid, 3 times daily; bid, twice daily.

^aReserve for resistant organisms and/or refractory infections.

Both have been linked to teratogenic fetal effects.⁵⁻⁸ The defects associated with the former drug include eye abnormalities, heart defects, and facial clefts. The abnormalities associated with the latter include neural tube defects, heart defects, choanal atresia, and diaphragmatic hernia. In the first trimester, amoxicillin and cephalixin are reasonable choices for treatment. As a general rule, a 3-day course of antibiotics will be effective for eradicating the initial episode of ASB. For recurrent infections, a 7- to 10-day course is indicated.^{1,3,4}

Acute cystitis

The microbiology of acute cystitis essentially is identical to that of asymptomatic bacteriuria. The usual clinical manifestations include increased frequency of urination, dysuria, and urination hesitancy in association with suprapubic discomfort and a low-grade fever.

The diagnosis can be quickly confirmed by testing the urine pH and assessing for leukocyte esterase and nitrites. If both the leukocyte esterase and nitrite test are positive, the probability of a positive urine culture is high; however, the nitrite test can be falsely negative if the urine has been incubating in the bladder for only a short period of time or if a Gram-positive organism is responsible for the infection. The urine pH is particularly helpful if it is elevated in the range of 8. This finding strongly is associated with a *Proteus* infection.^{1,9-11}

In-out catheterization is ideal

I recommend that the urine sample be obtained by an in-out catheterization in symptomatic patients. This technique eliminates any concern about contamination of the specimen by vaginal organisms and provides a “pure” sample for culture. When urine is obtained by this method, the criterion for a positive culture result is greater than 100 colonies/mL.³ If the urine is obtained by the midstream clean-catch method, the cutoff for a positive culture remains greater than 100,000 colonies/mL.^{1,3} Unless the clinician

is working in a low resource environment, the culture should always be obtained even though the patient will be empirically treated prior to the culture result being available. The culture can be helpful in guiding changes in antibiotic therapy if the initial response to treatment is poor.

In the first trimester, empiric treatment should be with amoxicillin or cephalixin. Beyond the first trimester, nitrofurantoin should be the drug of choice. This antibiotic is inexpensive and well-tolerated. It has limited effect on the bowel or vaginal flora and is unlikely to cause a secondary yeast infection or diarrhea. If a *Proteus* infection is suspected, however, trimethoprim-sulfamethoxazole double strength (800 mg/160 mg) should be used because this organism is not susceptible to nitrofurantoin. The duration of therapy should be a minimum of 3 days with the first infection and 7 to 10 days with recurrent infections.^{1,3,4}

Acute pyelonephritis

Pyelonephritis may develop de novo or may result from inadequate treatment of lower urinary tract infection. The right kidney is affected in approximately 75% of cases because the right ureter is more subject to compression by the gravid uterus. The principal pathogen is *E coli*, although *Klebsiella pneumoniae* and *Proteus* species also are of importance. Other aerobic Gram-negative bacilli, such as *Pseudomonas* and *Serratia* species, are much less common unless the patient is immunosuppressed or has an indwelling catheter.¹

The characteristic clinical manifestations of acute pyelonephritis are high fever (>39 °C), shaking chills, nausea and vomiting, and flank pain and tenderness. Increased frequency of urination and dysuria also may be present. In addition, pyelonephritis may be accompanied by preterm labor, sepsis, and acute respiratory distress syndrome (ARDS). The diagnosis is established by clinical findings, urinalysis, and urine culture. The urine specimen should be obtained by an in-out catheterization, analyzed initially by dipstick for nitrites and

FAST TRACK

Obtain urine samples for testing with an in-out catheterization technique in symptomatic patients

leukocyte esterase, and submitted for culture and sensitivity. Blood cultures should be obtained, and chest radiography should be performed if ARDS is suspected.

Empiric treatment should be started as soon as these initial diagnostic tests are completed. Many women in the first 20 weeks of pregnancy will not be seriously ill and may be treated as outpatients. I recommend an initial dose of intramuscular ceftriaxone 2 g followed by oral amoxicillin-clavulanate (875 mg twice daily) for a total of 10 days. If the patient is allergic to beta-lactam antibiotics, oral trimethoprim-sulfamethoxazole double strength (800 mg/160 mg) twice daily would be an excellent alternative.^{1,12}

Treating seriously ill patients

Patients who are more seriously ill, particularly in the second half of pregnancy when preterm labor is more likely, should be hospitalized for supportive care (intravenous [IV] fluids, antipyretics, anti-emetics) and treatment with parenteral antibiotics.^{1,12} At our medical center, IV ceftriaxone (2 g every 24 hours), is the agent of choice. It has a convenient dosing schedule and covers almost all of the potential uropathogens. If an unusually drug-resistant organism is suspected, gentamicin or aztreonam can be combined with ceftriaxone to ensure complete coverage (see dosage recommendations below).

If the patient is allergic to beta-lactam antibiotics, alternative IV agents include:

- trimethoprim-sulfamethoxazole (8–10 mg/kg/d in 2 divided doses)
- gentamicin (5 mg/kg of ideal body weight every 24 hours)
- aztreonam (2 g every 8 hours)

Parenteral antibiotics should be administered until the patient has been afebrile and asymptomatic for 24 hours. At this point, oral antibiotics, based on sensitivity testing, can be started, and the patient can be discharged to complete a 10-day course of therapy.

Treatment failure

Obstetric patients with pyelonephritis usually respond promptly to antibiotics. More than 75% will be afebrile within 48 hours,

Take-home points

- Chlamydia and gonorrhea are the most common causes of acute urethritis.
 - *Escherichia coli* is the dominant cause of asymptomatic bacteriuria, acute cystitis, and acute pyelonephritis.
 - Once the patient is beyond the first trimester, nitrofurantoin is the preferred antibiotic for treatment of lower urinary tract infections.
 - *Proteus* is the one organism that is not susceptible to nitrofurantoin.
 - Pyelonephritis may lead to preterm labor and severe sepsis. Most patients should be hospitalized and treated with intravenous ceftriaxone.
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and more than 90% will be afebrile within 72 hours. When patients fail to respond promptly, 2 major causes should be considered. The first is antibiotic resistance, and this problem can be corrected on the basis of the sensitivity studies. The second is ureteral obstruction, secondary either to the effect of the gravid uterus or a urinary stone. If obstruction is suspected, renal ultrasonography should be performed. Depending upon the cause of the obstruction, a procedure such as a percutaneous nephrostomy or cystoscopic removal of the stone may be necessary.

Recurrence is possible. Following an initial episode of pyelonephritis, approximately 20% of patients will experience a recurrent lower or upper tract infection.¹ Because of this recurrence rate, I recommend that these patients receive suppressive doses of antibiotics for the remainder of pregnancy. An ideal agent for suppression is nitrofurantoin (100 mg at bedtime). An alternative agent is trimethoprim-sulfamethoxazole double strength (800 mg/160 mg) once daily. Amoxicillin and cephalexin are less desirable for prophylaxis because of their adverse effects on vaginal and bowel flora and their propensity for precipitating yeast infection and/or diarrhea.

CASE Resolved

The most likely diagnosis in this patient is acute cystitis. An in-out catheterization should be performed to obtain an uncontaminated urine specimen. A portion of the specimen should be

FAST TRACK

Patients with recurrent pyelonephritis should receive suppressive doses of antibiotics for the remainder of their pregnancy

forwarded to the laboratory for urine culture and sensitivity. Another portion should be used for assessment by dipstick. If the nitrite and leukocyte tests are positive, the diagnosis of acute cystitis is confirmed. Since this infection is the

patient's first episode, a reasonable antibiotic regimen would be oral nitrofurantoin (100 mg twice daily) for 3 days. The course should be extended to 7 days if symptoms persist at the end of 3 days. ●

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