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Urinary Tract Infections During Pregnancy

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► See related patient information handout on urinary tract infections during pregnancy (<http://www.aafp.org/afp/2000/0201/p713.html>), written by the authors of this article.

Urinary tract infections are common during pregnancy, and the most common causative organism is *Escherichia coli*. Asymptomatic bacteriuria can lead to the development of cystitis or pyelonephritis. All pregnant women should be screened for bacteriuria and subsequently treated with antibiotics such as nitrofurantoin, sulfisoxazole or cephalexin. Ampicillin should no longer be used in the treatment of asymptomatic bacteriuria because of high rates of resistance. Pyelonephritis can be a life-threatening illness, with increased risk of perinatal and neonatal morbidity. Recurrent infections are common during pregnancy and require prophylactic treatment. Pregnant women with urinary group B streptococcal infection should be treated and should receive intrapartum prophylactic therapy.

Urinary tract infections (UTIs) are frequently encountered in the family physician's office. UTIs account for approximately 10 percent of office visits by women, and 15 percent of women will have a UTI at some time during their life. In pregnant women, the incidence of UTI can be as high as 8 percent.^{1,2} This article briefly examines the pathogenesis and bacteriology of UTIs during pregnancy, as well as patient-oriented outcomes. We review the diagnosis and treatment of asymptomatic bacteriuria, acute cystitis and pyelonephritis, plus the unique issues of group B streptococcus and recurrent infections.

Pathogenesis

Pregnant women are at increased risk for UTIs. Beginning in week 6 and peaking during weeks 22 to 24, approximately 90 percent of pregnant women develop ureteral dilatation, which will remain until delivery (hydronephrosis of pregnancy). Increased bladder volume and decreased bladder tone, along with decreased ureteral tone, contribute to increased urinary stasis and ureterovesical reflux.¹ Additionally, the physiologic increase in plasma volume during pregnancy decreases urine concentration. Up to 70 percent of pregnant women develop glycosuria, which encourages bacterial growth in the urine. Increases in urinary progestins and estrogens may lead to a decreased ability of the lower urinary tract to resist invading bacteria. This decreased ability may be caused by decreased ureteral tone or possibly by allowing some strains of bacteria to selectively grow.^{1,3} These factors may all contribute to the development of UTIs during pregnancy.

Bacteriology

The organisms that cause UTIs during pregnancy are the same as those found in nonpregnant patients. *Escherichia coli* accounts for 80 to 90 percent of infections. Other gram-negative rods such as *Proteus mirabilis* and *Klebsiella pneumoniae* are also common. Gram-positive organisms such as group B streptococcus and *Staphylococcus saprophyticus* are less common causes of UTI. Group B streptococcus has important implications in the management of pregnancy and will be discussed further. Less common organisms that may cause UTI include enterococci, *Gardnerella vaginalis* and *Ureaplasma ureolyticum*.^{1,4,5}

Diagnosis and Treatment of UTIs

UTIs have three principle presentations: asymptomatic bacteriuria, acute cystitis and pyelonephritis. The diagnosis and treatment of UTI depends on the presentation.

ASYMPTOMATIC BACTERIURIA

[corrected (<http://www.aafp.org/afp/2000/0615/p3567b.html>)] Significant bacteriuria may exist in asymptomatic patients. In the 1960s, Kass⁶ noted the subsequent increased risk of developing pyelonephritis in patients with asymptomatic bacteriuria. Significant bacteriuria has been historically defined as finding more than 10⁵ colony-forming units per mL of urine.⁷ Recent studies of women with acute dysuria have shown the presence of significant bacteriuria with lower colony counts. This has not been studied in pregnant women, and finding more than 10⁵ colony-forming units per mL of urine remains the commonly accepted standard. Asymptomatic bacteriuria is common, with a prevalence of 10 percent during pregnancy.^{6,8} Thus, routine screening for bacteriuria is advocated.

Untreated asymptomatic bacteriuria leads to the development of symptomatic cystitis in approximately 30 percent of patients and can lead to the development of pyelonephritis in up to 50 percent.⁶ Asymptomatic bacteriuria is associated with an increased risk of intra-uterine growth retardation and low-birth-weight infants.⁹ The relatively high prevalence of asymptomatic bacteriuria during pregnancy, the significant consequences for women and for the pregnancy, plus the ability to avoid sequelae with treatment, justify screening pregnant women for bacteriuria.

SCREENING

The American College of Obstetrics and Gynecology recommends that a urine culture be obtained at the first prenatal visit.¹⁰ A repeat urine culture should be obtained during the third trimester, because the urine of treated patients may not remain sterile for the entire pregnancy.¹⁰ The recommendation of the U.S. Preventative Services Task Force is to obtain a urine culture between 12 and 16 weeks of gestation (an "A" recommendation).¹¹

By screening for and aggressively treating pregnant women with asymptomatic bacteriuria, it is possible to significantly decrease the annual incidence of pyelonephritis during pregnancy.^{8,12} In randomized controlled trials, treatment of pregnant women with asymptomatic bacteriuria has been shown to decrease the incidence of preterm birth and low-birth-weight infants.¹³

Rouse and colleagues¹⁴ performed a cost-benefit analysis of screening for bacteriuria in pregnant women versus inpatient treatment of pyelonephritis and found a substantial decrease in overall cost with screening. The cost of screening for bacteriuria to prevent the development of pyelonephritis in one patient was \$1,605, while the cost of treating one patient with pyelonephritis was \$2,485. Wadland and Plante¹⁵ performed a similar analysis in a family practice obstetric population and found screening for asymptomatic bacteriuria to be cost-effective.

The decision about how to screen asymptomatic women for bacteriuria is a balance between the cost of screening versus the sensitivity and specificity of each test. The gold standard for detection of bacteriuria is urine culture, but this test is costly and takes 24 to 48 hours to obtain results. The accuracy of faster screening methods (e.g., leukocyte esterase dipstick, nitrite dipstick, urinalysis and urine Gram staining) has been evaluated (*Table 1*¹⁶). Bachman and associates¹⁶ compared these screening methods with urine culture and found that while it was more cost effective to screen for bacteriuria with the esterase dipstick for leukocytes, only one half of the patients with bacteriuria were identified compared with screening by urine culture. The increased number of false negatives and the relatively poor predictive value of a positive test make the faster methods less useful; therefore, a urine culture should be routinely obtained in pregnant women to screen for bacteriuria at the first prenatal visit and during the third trimester.^{10,11}

TABLE 1.
Accuracy of Screening Tests for Asymptomatic Bacteriuria*

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TREATMENT

Pregnant women should be treated when bacteriuria is identified (*Table 2*^{17,18}). The choice of antibiotic should address the most common infecting organisms (i.e., gram-negative gastrointestinal organisms). The antibiotic should also be safe for the mother and fetus. Historically, ampicillin has been the drug of choice, but in recent years *E. coli* has become increasingly resistant to ampicillin.¹⁹ Ampicillin resistance is found in 20 to 30 percent of *E. coli* cultured from urine in the out-patient setting.²⁰ Nitrofurantoin (Macrochantin) is a good choice because of its high urinary concentration. Alternatively, cephalosporins are well tolerated and adequately treat the important organisms. Fosfomycin (Monurol) is a new antibiotic that is taken as a single dose. Sulfonamides can be taken during the first and second trimesters but, during the third trimester, the use of sulfonamides carries a risk that the infant will develop kernicterus, especially preterm infants. Other common antibiotics (e.g., fluoroquinolones and tetracyclines) should not be prescribed during pregnancy because of possible toxic effects on the fetus.

[View/Print Table](#)

TABLE 2.
Antibiotic Choices for Treatment of UTIs During Pregnancy

ANTIBIOTIC	PREGNANCY CATEGORY	DOSAGE
Cephalexin (Keflex)	B	250 mg two or four times daily
Erythromycin	B	250 to 500 mg four times daily
Nitrofurantoin (Macrochantin)	B	50 to 100 mg four times daily
Sulfisoxazole (Gantrisin)	C*	1 g four times daily
Amoxicillin-clavulanic acid (Augmentin)	B	250 mg four times daily
Fosfomycin (Monurol)	B	One 3-g sachet
Trimethoprim-sulfamethoxazole (Bactrim)	C†	160/180 mg twice daily

*—Contraindicated in pregnant women at term.

†—Avoid during first trimester and at term.

Information from Duff P. Antibiotic selection for infections in obstetric patients. *Semin Perinatol* 1993;17:367–78, and Krieger JN. Complications and treatment of urinary tract infections during pregnancy. *Urol Clin North Am* 1986;13:685–93.

A seven- to 10-day course of antibiotic treatment is usually sufficient to eradicate the infecting organism(s). Some authorities have advocated shorter courses of treatment—even single-day therapy. Conflicting evidence remains as to whether pregnant patients should be treated with shorter courses of antibiotics. Masterton²¹ demonstrated a cure rate of 88 percent with a single 3-g dose of ampicillin in ampicillin-sensitive isolates. Several other studies have found that a single dose of amoxicillin, cephalexin (Keflex) or nitrofurantoin was less successful in eradicating bacteriuria, with cure rates from 50 to 78 percent.^{1,22–24} Fosfomycin is effective when taken as a single, 3-g sachet.

Other antibiotics have not been extensively researched for use in UTIs, and further studies are necessary to determine whether a shorter course of other antibiotics would be as effective as the traditional treatment length.¹ After patients have completed the treatment regimen, a repeat culture should be obtained to document successful eradication of bacteriuria.¹⁰

Acute Cystitis

Acute cystitis is distinguished from asymptomatic bacteriuria by the presence of symptoms such as dysuria, urgency and frequency in afebrile patients with no evidence of systemic illness. Up to 30 percent of patients with untreated asymptomatic bacteriuria later develop symptomatic cystitis.⁶ Over a six-year period, Harris and Gilstrap²⁵ found that 1.3 percent of obstetric patients who delivered at a single hospital developed acute cystitis with no symptoms of pyelonephritis.

TREATMENT

In general, treatment of pregnant patients with acute cystitis is initiated before the results of the culture are available. Antibiotic choice, as in asymptomatic bacteriuria, should focus on coverage of the common pathogens and can be changed after the organism is identified and sensitivities are determined. A three-day treatment course in nonpregnant patients with acute cystitis has a cure rate similar to a treatment course of seven to 10 days, but this finding has not been studied in the obstetric population.¹ Patients treated for a shorter time frame are more likely to have a recurrence of the infection. In the pregnant patient, this higher rate of recurrence with shorter treatment periods may have serious consequences. *Table 2*^{17,18} lists oral antibiotics that are acceptable treatment choices. Group B streptococcus is generally susceptible to penicillin, but *E. coli* and other gram-negative rods typically have a high rate of resistance to this agent.

Pyelonephritis

Acute pyelonephritis during pregnancy is a serious systemic illness that can progress to maternal sepsis, preterm labor and premature delivery. The diagnosis is made when the presence of bacteriuria is accompanied by systemic symptoms or signs such as fever, chills, nausea, vomiting and flank pain. Symptoms of lower tract infection (i.e., frequency and dysuria) may or may not be present. Pyelonephritis occurs in 2 percent of pregnant women; up to 23 percent of these women have a recurrence during the same pregnancy.²⁶

Early, aggressive treatment is important in preventing complications from pyelonephritis. Hospitalization, although often indicated, is not always necessary. However, hospitalization is indicated for patients who are exhibiting signs of sepsis, who are vomiting and unable to stay hydrated, and who are having contractions. A randomized study of 90 obstetric inpatients with pyelonephritis compared treatment with oral cephalexin to treatment with intravenous cephalothin (Keflin) and found no difference between the two groups in the success of therapy, infant birth weight or preterm deliveries.²⁷

Further support for outpatient therapy is provided in a randomized clinical trial that compared standard inpatient, intravenous treatment to outpatient treatment with intramuscular ceftriaxone (Rocephin) plus oral cephalexin.²⁸ Response to antibiotic therapy in each group was similar, with no evident differences in the number of recurrent infections or preterm deliveries.

Antibiotic therapy (and intravenous fluids, if hospitalization is required) may be initiated before obtaining the results of urine culture and sensitivity. Several antibiotic regimens may be used. A clinical trial comparing three parenteral regimens found no differences in length of hospitalization, recurrence of pyelonephritis or preterm delivery.²⁹ Patients in this trial were randomized to receive treatment with intravenous cefazolin (Ancef), intravenous gentamycin plus ampicillin, or intramuscular ceftriaxone.

Parenteral treatment of pyelonephritis should be continued until the patient becomes afebrile. Most patients respond to hydration and prompt antibiotic treatment within 24 to 48 hours. The most common reason for initial treatment failure is resistance of the infecting organism to the antibiotic. If fever continues or other signs of systemic illness remain after appropriate antibiotic therapy, the possibility of a structural or anatomic abnormality should be investigated. Persistent infection may be caused by urolithiasis, which occurs in one of 1,500 pregnancies,³⁰ or less commonly, congenital renal abnormalities or a perinephric abscess.

Diagnostic tests may include renal ultrasonography or an abbreviated intravenous pyelogram. The indication to perform an intravenous pyelogram is persistent infection after appropriate antibiotic therapy when there is the suggestion of a structural abnormality not evident on ultrasonography.³⁰ Even the low-dose radiation involved in an intravenous pyelogram, however, may be dangerous to the fetus and should be avoided if possible.

Group B Streptococcal Infection

Group B streptococcal (GBS) vaginal colonization is known to be a cause of neonatal sepsis and is associated with preterm rupture of membranes, and preterm labor and delivery. GBS is found to be the causative organism in UTIs in approximately 5 percent of patients.^{31,32} Evidence that GBS bacteriuria increases patient risk of preterm rupture of membranes and premature delivery is mixed.^{33,34} A randomized, controlled trial³⁵ compared the treatment of GBS bacteriuria with penicillin to treatment with placebo. Results indicated a significant reduction in rates of premature rupture of membranes and preterm delivery in the women who received antibiotics. It is unclear if GBS bacteriuria is equivalent to GBS vaginal colonization, but pregnant women with GBS bacteriuria should be treated as GBS carriers and should receive a prophylactic antibiotic during labor.³⁶

Recurrence and Prophylaxis

The majority of UTIs are caused by gastrointestinal organisms. Even with appropriate treatment, the patient may experience a reinfection of the urinary tract from the rectal reservoir. UTIs recur in approximately 4 to 5 percent of pregnancies, and the risk of developing pyelonephritis is the same as the risk with primary UTIs. A single, postcoital dose or daily suppression with cephalexin or nitrofurantoin in patients with recurrent UTIs is effective preventive therapy.³⁷ A postpartum urologic evaluation may be necessary in patients with recurrent infections because they are more likely to have structural abnormalities of the renal system.^{26,30,38} Patients who are found to have urinary stones, who have more than one recurrent UTI or who have a recurrent UTI while on suppressive antibiotic therapy should undergo a postpartum evaluation.^{30,38}

Outcomes

The maternal and neonatal complications of a UTI during pregnancy can be devastating. Thirty percent of patients with untreated asymptomatic bacteriuria develop symptomatic cystitis and up to 50 percent develop pyelonephritis.⁶ Asymptomatic bacteriuria is also associated with intrauterine growth retardation and low-birth-weight infants.⁹ Schieve and associates³⁹ conducted a study involving 25,746 pregnant women and found that the presence of UTI was associated with premature labor (labor onset before 37 weeks of gestation), hypertensive disorders of pregnancy (such as pregnancy-induced hypertension and preeclampsia), anemia (hematocrit

level less than 30 percent) and amnionitis (*Table 3*³⁷). While this does not prove a cause and effect relationship, randomized trials have demonstrated that antibiotic treatment decreases the incidence of preterm birth and low-birth-weight infants.¹³ A risk of urosepsis and chronic pyelonephritis was also found.⁴⁰ In addition, acute pyelonephritis has been associated with anemia.⁴¹

[View/Print Table](#)

TABLE 3.

Comparison of Adverse Outcomes in Pregnant Patients Who Developed UTI During Pregnancy and Those Who Did Not

OUTCOME	ODDS RATIO	95% CONFIDENCE INTERVAL
Perinatal		
Low birth weight (weight less than 2,500 g [5 lb, 8 oz])	1.4	1.2 to 1.6
Prematurity (less than 37 weeks of gestation at delivery)	1.3	1.1 to 1.4
Preterm low birth weight (weight less than 2,500 g and less than 37 weeks of gestation at delivery)	1.5	1.2 to 1.7
Maternal		
Premature labor (less than 37 weeks of gestation at delivery)	1.6	1.4 to 1.8
Hypertension/preeclampsia	1.4	1.2 to 1.7
Anemia (hematocrit level less than 30%)	1.6	1.3 to 2.0
Amnionitis (chorioamnionitis, amnionitis)	1.4	1.1 to 1.9

UTI = urinary tract infection.

Information from Pfau A, Sacks TG. Effective prophylaxis for recurrent urinary tract infections during pregnancy. *Clin Infect Dis* 1992;14:810–4.

Neonatal outcomes that are associated with UTI include sepsis and pneumonia (specifically, group B streptococcus infection).^{31,42} UTI increases the risk of low-birth-weight infants (weight less than 2,500 g [5 lb, 8 oz]), prematurity (less than 37 weeks of gestation at delivery) and preterm, low-birth-weight infants (weight less than 2,500 g and less than 37 weeks of gestation at delivery)³⁹ (*Table 3*³⁷).

Final Comment

UTIs during pregnancy are a common cause of serious maternal and perinatal morbidity; with appropriate screening and treatment, this morbidity can be limited. A UTI may manifest as asymptomatic bacteriuria, acute cystitis or pyelonephritis. All pregnant women should be screened for bacteriuria and subsequently treated with appropriate antibiotic therapy. Acute cystitis and pyelonephritis should be aggressively treated during pregnancy. Oral nitrofurantoin and cephalexin are good antibiotic choices for treatment in pregnant women with asymptomatic bacteriuria and acute cystitis, but parenteral antibiotic therapy may be required in women with pyelonephritis.

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