Screening and Treatment for Sexually Transmitted Infections in Pregnancy

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Many sexually transmitted infections are associated with adverse pregnancy outcomes. The Centers for Disease Control and Prevention recommends screening all pregnant women for human immunodeficiency virus infection as early as possible. Treatment with highly active antiretroviral therapy can reduce transmission to the fetus. Chlamydia screening is recommended for all women at the onset of prenatal care, and again in the third trimester for women who are younger than 25 years or at increased risk. Azithromycin has been shown to be safe in pregnant women and is recommended as the treatment of choice for chlamydia during pregnancy. Screening for gonorrhea is recommended in early pregnancy for those who are at risk or who live in a high-prevalence area, and again in the third trimester for patients who continue to be at risk. The recommended treatment for gonorrhea is ceftriaxone 125 mg intramuscularly or cefixime 400 mg orally. Hepatitis B surface antigen and serology for syphilis should be checked at the first prenatal visit. Benzathine penicillin G remains the treatment for syphilis. Screening for genital herpes simplex virus infection is by history and examination for lesions, with diagnosis of new cases by culture or polymerase chain reaction assay from active lesions. Routine serology is not recommended for screening. The oral antivirals acyclovir and valacyclovir can be used in pregnancy. Suppressive therapy from 36 weeks' gestation reduces viral shedding at the time of delivery in patients at risk of active lesions. Screening for trichomoniasis or bacterial vaginosis is not recommended for asymptomatic women because current evidence indicates that treatment does not improve pregnancy outcomes. (Am Fam Physician 2007;76:265-70, 272. Copyright © 2007 American Academy of Family Physicians.)

▶ **Patient information:** A handout on sexually transmitted infections in pregnancy, written by the authors of this article, is provided on page 272.

Infections during pregnancy affect the mother and often the child, either in utero or at the time of delivery. Many infections have been linked with increased risks of premature delivery and low birth weight, and associated morbidity and mortality. Because of these risks, the Centers for Disease Control and Prevention (CDC) has recommended screening for some sexually transmitted infections (STIs) at the first prenatal visit, then again in the third trimester for mothers at high risk *(Table 1)*.[1] The CDC has also published recommendations for the treatment of STIs during pregnancy.[1]

Screening

All women in the United States should be screened for human immunodeficiency virus (HIV) infection as early as possible during pregnancy. If the patient declines testing, the physician should discuss her objections and continue to strongly encourage testing. Other screening tests that are recommended for all pregnant women include those for hepatitis B, syphilis, and *Chlamydia trachomatis*. Women at risk should be tested for *Neisseria gonorrhea* and hepatitis C. Evidence does not support routine screening for bacterial vaginosis.

Women younger than 25 years and those who are at risk of chlamydia (e.g., those who have multiple sex partners) should be rescreened in the third trimester.[1] Women who continue to be at risk of gonorrhea should also be rescreened in the third trimester.[1]

When infection is detected, the physician must inform the mother, ensure adequate and safe treatment, and advise partner notification and treatment. In many states, cases of STI must be reported to the health department. Physicians should counsel the patient to use condoms and avoid sexual contact until her partner has been treated.

Chlamydia

C. trachomatis is the most common sexually transmitted bacterial pathogen in the United States, and as many as 5 to 15 percent of pregnant women are infected.[2] Mother-to-child transmission of *C. trachomatis* can occur at the time of birth and may result in

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SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*	*Comments*
Azithromycin (Zithromax) is an effective treatment for chlamydia during pregnancy.	B	5	No long-term safety studies have been performed.
Intramuscular ceftriaxone (Rocephin) and oral cefixime (Suprax) are similar in effectiveness for gonorrhea during pregnancy.	B	6, 8	Spectinomycin (Trobicin; not available in the United States) is also effective but is painful to use.
Initiation of acyclovir (Zovirax) or valacyclovir (Valtrex) treatment at 36 weeks' gestation reduces the recurrence of genital herpes lesions and the number of cesarian deliveries performed because of genital herpes.	A	10, 11	In patients with known herpes. Serologic screening is not advocated.
Penicillin is effective in the prevention of congenital syphilis.	A	20	Needs to be found and treated early. Screening should be carried out at the first visit.
Treatment of trichomoniasis does not reduce the incidence of preterm birth.	A	21	Screening in asymptomatic women is not recommended.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 176 or http://www.aafp.org/afpsort.xml.

ophthalmia neonatorum or pneumonitis in the newborn, or postpartum endometritis in the mother. Some reports have linked chlamydia to low birth weight and preterm birth, but one study found no such association.[2]

The nucleic acid amplification test (NAAT) is the preferred test for chlamydia because of its high sensitivity and specificity and its use on specimens obtained noninvasively.[3] It can be performed using cervical or urine specimens. Nonamplified nonculture tests, such as the DNA probe test, remain an option when the NAAT is not available or is too expensive. Repeat testing three weeks after completion of therapy is recommended for pregnant women.[1]

Tetracyclines are contraindicated in pregnancy because of the risk of bone and tooth abnormalities. Amoxicillin (500 mg orally three times per day for seven days) appears to be effective for microbiologic cure, but there are few data on its long-term effectiveness for neonatal infection.[4] A randomized trial comparing azithromycin (Zithromax) in a single 1-g dose to erythromycin in a dosage of 500 mg every six hours for seven days found enhanced compliance, fewer gastrointestinal side effects, and equivalent effectiveness with azithromycin.[5] No long-term safety studies on azithromycin in pregnancy have been published; however, azithromycin is U.S. Food and Drug Administration pregnancy category B and is recommended as first-line treatment for chlamydia in pregnancy.[1] The single 1-g oral dose can be given in the office when compliance is a concern.

Gonorrhea

N. gonorrhea can be transmitted to the newborn from the mother's genital tract at the time of birth and can cause ophthalmia neonatorum, systemic neonatal infection, maternal endometritis, or pelvic infection. The risk of transmission from an infected mother to her infant is between 30 and 47 percent.[6]

Screening can be performed with a culture on Thayer-Martin media, which is recommended in a population with a low prevalence of infection.[3] Nucleic acid hybridization tests of cervical specimens and NAATs of cervical specimens or urine are also used, with NAATs being the most sensitive and specific.[7] Culture is the most widely available test and has the advantage of providing antimicrobial susceptibility. A repeat test is recommended in the third trimester for those at continued risk.[1]

A Cochrane review of treatment for gonorrhea in pregnancy concluded that ceftriaxone (Rocephin) 125 mg intramuscularly and spectinomycin (Trobicin) 2 g intramuscularly have similar cure rates to oral amoxicillin plus probenecid.[6] One randomized trial found cefixime (Suprax) 400 mg orally to be as effective as ceftriaxone 125 mg

Table 1. CDC Recommendations for STI Screening in Pregnancy

Condition	*Screening recommended?*	*Preferred test*
Bacterial vaginosis*	No	—
Chlamydia	Yes: all pregnant women	NAAT
Gonorrhea	Yes: women who are at risk† or living in a high-prevalence area	NAAT or culture on Thayer-Martin media
Hepatitis B	Yes: all pregnant women	HBsAg serology
Hepatitis C	Yes: women who are at high risk‡	Anti-HCV
Herpes	No (culture lesions if present)	Culture, PCR
HIV	Yes: all pregnant women	EIA, Western blot
HPV	No	—
Syphilis	Yes: all pregnant women	RPR or VDRL
Trichomoniasis	No	—

NOTE: *"Yes" indicates screening is recommended at the first prenatal visit, with repeat screening in the third trimester for those at risk.*

CDC = Centers for Disease Control and Prevention; STI = sexually transmitted infection; NAAT = nucleic acid amplification test; HBsAg = hepatitis B surface antigen; HCV = hepatitis C virus; PCR = polymerase chain reaction; HIV = human immunodeficiency virus; EIA = enzyme immunoassay; HPV = human papillomavirus; RPR = rapid plasma reagin; VDRL = Venereal Disease Research Laboratories.

**—Bacterial vaginosis is not an STI, but it is more common in sexually active women.*
†—Women who have a new or more than one sex partner.
‡—Women with a history of injection drug use, repeated exposure to blood products, or blood transfusion or organ transplant before 1992.

Information from reference 1.

intramuscularly for the treatment of gonorrhea in pregnancy.[8] The CDC recommends either of these as the treatment of choice for gonorrhea.[1] There have been times when cefixime has been in short supply. Spectinomycin is rarely used because of the high volume required for the intramuscular dose.

Hepatitis

The CDC recommends routine screening of all pregnant women for hepatitis B surface antigen (HBsAg) to detect maternal disease and avoid perinatal transmission. HBsAg is present in acute and chronic infections. The presence of immunoglobulin M antibody to hepatitis B core antigen is diagnostic of acute or recently acquired infection. HBsAg is the first detectable virologic marker for hepatitis B infection, often appearing before liver transaminases are elevated, but it may become undetectable after one to two months.

Pregnant women seeking STI treatment who have not previously been vaccinated should be vaccinated against hepatitis B. Infants of HBsAg-positive mothers should receive hepatitis B immune globulin as well as hepatitis B vaccine at birth. Further information on treating women with hepatitis B and their infants can be found at http://www.cdc.gov/mmwr/PDF/rr/rr5416.pdf.

Routine screening for hepatitis C in pregnancy is not recommended.[1] Women with known risk factors (e.g., history of injection drug use, blood transfusion or organ transplant before 1992) should be offered counseling and testing for hepatitis C antibodies.[1] Approximately 5 percent of infants whose mothers are infected with hepatitis C become infected.[1] Breastfeeding does not appear to transmit hepatitis C.[1]

Herpes Simplex Virus

Herpes simplex virus (HSV) is an extremely common STI that has potentially devastating effects on perinatally infected neonates. The risk of transmission is 30 to 50 percent higher among women who acquire genital HSV near the time of delivery. The clinical diagnosis of genital herpes during pregnancy in HIV-infected women may be a risk factor for perinatal HIV infection.[9]

Screening is performed clinically by visualization of lesions or by patient history. Diagnosis is by culture or polymerase chain reaction assay of an active lesion. Routine serologic testing is not recommended.[1]

Administration of acyclovir (Zovirax) or valacyclovir (Valtrex) starting at 36 weeks' gestation has been shown to significantly reduce the recurrence of herpes simplex lesions and viral shedding at the time of delivery in patients at risk of active lesions, and to reduce the number of cesarean deliveries performed because of genital herpes.[10-12] Acyclovir therapy has been shown to be cost-effective and is the CDC's recommended treatment for HSV infection during pregnancy.[1,13] The CDC also recommends using acyclovir during pregnancy for women who have recurrent genital herpes near term.[1]

Human Immunodeficiency Virus

The U.S. Public Health Service and the U.S. Preventive Services Task Force recommend that all pregnant women in the United States be tested for HIV infection, ideally at the first prenatal visit.[14,15] Testing should be voluntary and free of coercion. Women who are at high risk (e.g., those who have a history of sexually transmitted diseases, who exchange sex for money or drugs, who have multiple sex partners during pregnancy, who use illicit drugs, or who have sex partners who are HIV positive or at high risk) should be retested in the third trimester. Testing is done with an enzyme immunoassay for antibodies against HIV. Positive test results are confirmed with a Western blot or an immunofluorescence assay to rule out false-positive results.

Goals of therapy are to control maternal infection and reduce transmission to the fetus. Highly active antiretroviral therapy (HAART) is used during pregnancy to suppress viral load,[14,16] with the exception of efavirenz (Sustiva), which is pregnancy category D because of teratogenicity in animal studies. Elective cesarean delivery at 38 weeks reduces the risk of transmission in women not taking antiretrovirals or taking only zidovudine (Retrovir).[17] HIV treatment guidelines are available on the AIDSinfo Web site at http://www.aidsinfo.nih.gov/guidelines/default.aspx. Because concepts relevant to HIV management evolve rapidly, the recommendations are regularly updated.

Human Papillomavirus

Human papillomavirus (HPV) infection is extremely common and often resolves spontaneously. Testing for HPV is considered useful in triage of women with atypical squamous cells of undetermined significance on Papanicolaou smear. Treatment is not recommended in women with no cervical squamous intraepithelial lesions or genital warts.[1]

Diagnosis of genital warts is made by visual inspection. Biopsy may be needed if the diagnosis is uncertain, if the warts do not respond to standard treatment, or if they are pigmented, ulcerated, fixed, or bleeding. Because genital warts can proliferate and become friable during pregnancy, many specialists recommend their removal.[1] Podofilox (Condylox), imiquimod (Aldara), and podophyllin are not recommended during pregnancy. Trichloroacetic acid 80-90% applied by a health care professional weekly has been used safely in pregnancy.

Syphilis

Treponema pallidum, the cause of syphilis, is highly transmissible, even in the absence of any specific symptoms or clinical findings.[18] Maternal syphilis has been associated with complications such as hydramnios, spontaneous abortion, and preterm delivery. Fetal complications such as fetal syphilis, fetal hydrops, prematurity, fetal distress, and stillbirth also occur. Neonatal complications can include congenital syphilis, neonatal death, and late sequelae.[19]

Screening is performed with a blood test—the rapid plasma reagin or Venereal Disease Research Laboratories test—and confirmed with a fluorescent treponemal antibody serology and *T. pallidum* particle agglutination. A single serologic test is insufficient because false-positives occur with other illnesses.

If syphilis is diagnosed after 20 weeks' gestation, ultrasonography should be performed to evaluate for fetal syphilis. Although fetal infection can be cured by treating the mother, treatment failure is much higher in the presence of fetal hepatomegaly, ascites, hydrops, polyhydramnios, and placental thickening, which are signs of fetal syphilis detected on ultrasonography.

Treatment has been with benzathine penicillin G. A Cochrane review concluded that although penicillin is effective for the treatment of syphilis in pregnancy and the prevention of congenital syphilis, the optimal treatment regimen is uncertain.[20] The CDC recommends benzathine penicillin G, 2.4 million units intramuscularly, with desensitization in patients who are allergic to penicillin.[1]

Vaginal Infections

Trichomonas vaginalis, a sexually transmitted vaginal infection, has been associated with preterm delivery and low birth weight.[21] *Trichomonas* infection can have unpleasant symptoms such as itching, heavy discharge, vaginal irritation, and odor. It also causes a chronic inflammatory condition and may facilitate HIV transmission.[22] Women with symptoms of trichomoniasis should be evaluated with a saline wet mount or culture for the presence of trichomonads. Screening for *Trichomonas* in asymptomatic women is not recommended.[1]

Metronidazole (Flagyl) 2 g orally in a single dose or 500 mg twice per day for seven days is the treatment for trichomoniasis in pregnancy,[1] although many physicians wait until after the first trimester to initiate it. It is pregnancy category B, but the manufacturer recommends caution in using it in the first trimester. One meta-analysis found no relationship between exposure to metronidazole in the first trimester and birth defects; however, it included only five studies.[23] Tinidazole (Tindamax) is the only other drug available in the United States that is effective against *Trichomonas* and it is not recommended in pregnancy (category C). The outcome of treating trichomoniasis during pregnancy is uncertain.[24] Treatment has not been shown to reduce the incidence of preterm birth.[21]

Bacterial vaginosis is not an STI, but it is more common in sexually active women. Although many studies have shown an association between bacterial vaginosis and preterm birth, premature rupture of membranes, and low birth weight, it is not known whether the bacterial overgrowth causes these complications, or if it is a marker for intrauterine colonization. Screening for and treating bacterial vaginosis in asymptomatic pregnant women does not appear to reduce the risk of pregnancy complications.[21,25] A summary of treatments for the infections discussed is provided in *Table 2*.[1,4-6,8,14,16,19,20,25]

Table 2. Treatment of STIs in Pregnancy

Condition	*Treatment options*
Bacterial vaginosis*	Metronidazole (Flagyl) 500 mg orally two times per day for seven days[1]
Chlamydia	Azithromycin (Zithromax) 1 g orally in a single dose[1,4,5] Amoxicillin 500 mg orally three times per day for seven days[1]
Gonorrhea	Ceftriaxone (Rocephin) 125 mg intramuscularly in a single dose[1,6,8] Cefixime (Suprax) 400 mg orally in a single dose[1,8]
HIV	Highly active antiretroviral therapy (individualized)[1,14,16]
HSV type 2	
First episode	Acyclovir (Zovirax) 400 mg orally three times per day or 200 mg orally five times per day for seven to 10 days[1] Valacyclovir (Valtrex) 1 g orally two times per day for seven to 10 days[1]
Recurrent	Acyclovir 400 mg orally three times per day for five days[1] Valacyclovir 1 g orally once per day for five days[1]
Suppressive therapy	Acyclovir 400 mg orally two times per day[1] Valacyclovir 500 mg orally once per day[1]
Syphilis	Benzathine penicillin G 2.4 million units intramuscularly[1,19,20] Primary: single dose Positive serology, no symptoms: three doses one week apart Desensitization recommended in patients who are allergic to penicillin[1]
Trichomoniasis	Metronidazole 2 g orally in a single dose[1,25]

STI = sexually transmitted infection; HIV = human immunodeficiency virus; HSV = herpes simplex virus.

**—Bacterial vaginosis is not an STI, but it is more common in sexually active women.*

Information from references 1, 4 through 6, 8, 14, 16, 19, 20, and 25.

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