

# The clinical content of preconception care: infectious diseases in preconception care

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A number of infectious diseases should be considered for inclusion as part of clinical preconception care. Those infections strongly recommended for health promotion messages and risk assessment or for the initiation of interventions include Chlamydia infection, syphilis, and HIV. For selected populations, the inclusion of interventions for tuberculosis, gonorrheal infection, and herpes simplex virus are recommended. No clear evidence exists for the specific inclusion in preconception care of hepatitis C, toxoplasmosis, cytomegalovirus, listeriosis, malaria, periodontal disease, and bacterial vaginosis (in those with a previous preterm birth). Some infections that have important consequences during pregnancy, such as bacterial vaginosis (in those with no history of preterm birth), asymptomatic bacteriuria, parvovirus, and group B streptococcus infection, most likely would not be improved through intervention in the preconception time frame.

**Key words:** infectious disease, preconception, screening

**I**nfectious diseases can impact pregnancy-related outcomes and the reproductive health of women. Some, such as gonorrheal and chlamydial infections, may impact the ability to conceive or the site of implantation. Others, such as group B streptococcus (GBS) infection,

can have important clinical consequences during pregnancy but are not preventable through preconception strategies so are not addressed through preconception care. Others, such as bacterial vaginosis (BV) and periodontal disease, are linked with adverse pregnancy outcomes

in some studies; however, screening and treatment for asymptomatic disease, when initiated during pregnancy, is not associated unequivocally with improved outcomes. Because many prenatal interventions might have more impact when initiated in the preconception period, there is considerable interest in the evaluation of whether screening and treating these 2 conditions in the preconception period proves efficacious. Screening for particular infections as part of the preconception risk assessment can identify a number of potential risks to women's reproductive health and their future pregnancy outcomes and allows for those risks to be addressed before conception. This article discusses those infectious diseases that are important for consideration in preconception care.

## HIV

*Burden of suffering:* Human immunodeficiency virus (HIV) can be transmitted

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from an infected woman to her fetus during pregnancy, labor, and delivery or through breastfeeding.<sup>1</sup> It has been estimated that approximately 280-370 infants in the United States were born with HIV infection in 2000.<sup>2</sup> Worldwide there are > 1900 infant lives lost to HIV daily and > 700,000 lost annually. Perinatal HIV transmission still accounts for > 90% of the cases of pediatric acquired immunodeficiency syndrome in the United States; 40% of these infants are born to mothers who are unaware of their HIV status.

*How detectable is the condition?* Primary prevention includes early education for both men and women about risky sexual behavior, such as unprotected intercourse and multiple partners, intravenous drug use, transfusions before 1985, and the benefit of the identification of HIV status before conception. Evaluation of 2 programs, the opt-in vs the opt-out approach, identifies the effect of 2 different consent designs and the impact on early detection of HIV. The opt-in approach includes informing women of their risk of HIV transmission to their newborn infant and of the ability to test for HIV and offering them the HIV test. The opt-out approach informs women that HIV testing is part of the standard battery of laboratory tests, unless they actively decline testing. Women who are given the opt-out approach tend to test more often, potentially resulting in reduced perinatal transmission.<sup>3</sup> Current recommendations are for a 2-stage approach to laboratory diagnosis of HIV disease in which an initial enzyme-linked immunosorbent assay (ELISA) screen (sensitivity, > 99.5%; specificity, > 99.8%) is followed by a confirmatory Western blot analysis (sensitivity, > 96%; specificity, > 99.9%).<sup>4</sup>

*How effective are the current treatments?* An important turning point occurred in 1994 when the AIDS Clinical Trial Group demonstrated that zidovudine, which was administered to a group of HIV-infected women during pregnancy and labor and to their newborn infants, reduced the risk of perinatal HIV infection by two-thirds, from 25.5-8.3%.<sup>5</sup>

Studies confirm that treating HIV-positive mothers with antiretrovirals can reduce perinatal transmission to  $\leq 2\%$  in those women with a low viral load who do not breastfeed.<sup>6-8</sup>

*Impact of preconception care.* Knowing the HIV status of a woman before pregnancy allows for treatment and reduction of viral load, which decreases the risk of fetal transmission during pregnancy and labor. Women in the United States with HIV are advised not to breastfeed. If HIV infection is identified before conception, antiretroviral treatment can be administered, and women or couples can be given additional information to reduce the risk of mother-to-child transmission. It could also be argued that providing women with information about their HIV status before conception could alter their reproductive plans, with some women choosing not to become pregnant as a result of a positive diagnosis.

*Recommendations by other groups.* Because early identification and treatment initiation is the optimal method for reducing the risk of HIV infection among infants, the American College of Obstetricians and Gynecologists (ACOG), the American Academy of Pediatrics, the US Preventive Services Task Force (USPSTF), and the Centers for Disease Control and Prevention (CDC) recommend universal HIV testing in pregnancy as a routine component of the battery of prenatal blood tests, unless the test is declined. Outside of pregnancy, the CDC recommends screening all men and women from age 13-64 years for HIV.<sup>9</sup> Testing is to be repeated annually for those who are at high risk of acquisition. The USPSTF considers screening adults with risk factors to be an "A" recommendation and those without risk factors to be a "C" recommendation based on an updated systematic review.<sup>10</sup> For HIV-infected women, the USPSTF recommends the following components of preconception care: (1) effective contraception to prevent unintended pregnancy, (2) education about transmission risks and ways of decreasing them, (3) antiretrovirals with low reproductive

toxicity, which can decrease vertical transmission and achieve a low viral load, with care to avoid adverse effects, (4) management of potential opportunistic infections (prophylaxis and immunization), (5) optimal nutritional status, (6) standard preconception care, (7) screening for psychologic and substance use disorders, and (8) possible consultation with a maternal fetal medicine specialist.<sup>11</sup> The British HIV Association makes recommendations for discordant couples who wish to achieve pregnancy: self-insemination for an infected woman with an uninfected male partner, and sperm washing for infected male and uninfected female partners.<sup>12</sup>

*Recommendation.* All men and women should be encouraged to know their HIV status before pregnancy and should be counseled about safe sexual practices. Those women who test positive must be informed of the risks of vertical transmission to the infant and the associated morbidity and mortality rates. These women should be offered contraception. Those women who choose pregnancy should be counseled about the availability of treatment to prevent vertical transmission and that treatment should begin before pregnancy. *Strength of recommendation: A; quality of evidence: I-b.*

## Hepatitis C

*Burden of suffering.* Hepatitis C is becoming the silent epidemic in the United States. Nearly 4 million people in the United States are infected, and many patients are unaware that they are carriers. Hepatitis C is transmitted through contaminated blood and blood products. The most efficient modes of transmission include intravenous drug use and receipt of blood products or an organ transplant before 1992. Of intermediate risk of infection are patients on chronic hemodialysis, patients with undiagnosed liver disorders, and infants who were born to infected mothers. Less efficient modes of transmission occur in health care workers, people with multiple sexual partners, people in monogamous relationships with an infected partner, people who participate in tattooing and body piercing (with the use of common

household products like razors), and people who share straws for intranasal cocaine use. Sporadic transmission has been reported in 5% of cases of acute hepatitis and approximately 30% of cases of chronic hepatitis C. Women who test positive for anti-hepatitis C virus (HCV) antibody in pregnancy range from 0.1-4.5%.<sup>13-15</sup> Of note, there are settings in which the seroprevalence of hepatitis C is much higher, up to 50-90%, which include incarceration, homelessness, intravenous drug use, and migration from endemic areas.

*How detectable is the condition?* Screening for HCV is accomplished with tests to detect HCV antibody (anti-HCV) followed by a confirmatory test, which is usually 1 that detects HCV RNA because a low level of viremia is present in those with HCV.<sup>16</sup> There are no current recommendations for universal screening of women for hepatitis C, and this is not a cost-effective endeavor in low-risk women. However, screening that is based on risk factors seems to be appropriate, although long-term data that show improved outcomes are lacking.

*How effective are the current treatments?* Current recommended treatment for HCV consists of peginterferon and ribavirin for 24-48 weeks, with the dosages and duration dependent on HCV genotype. *Sustained virologic response*, which is defined as the absence of HCV RNA at the end of treatment and 6 months later, occurs in 40-70%, depending on HCV genotype. Currently, it is unclear whether such treatment prevents long-term sequelae of the disease.

*Impact of preconception care.* Women who test positive should be counseled on the risk of transmission to others and possible risk to the newborn infant. The neonatal transmission rate in pregnancy is approximately 5%. Hepatitis C may be transmitted through breastfeeding. The risk of vertical transmission increases in HIV-positive women (15%) and in the presence of maternal viremia, because vertical transmission is not known to occur in absence of detectable viral RNA. Currently, we do not have treatment for mother or infant or means to decrease

perinatal transmission.<sup>17</sup> Because treatment is contraindicated in pregnancy and treatment duration may be up to 48 months, a woman's reproductive plans should be taken into account when considering therapy that includes a discussion of contraception while receiving treatment.

*Recommendations by other groups.* The USPSTF recommends not screening those women without risk factors. It states that there is insufficient evidence to screen in those women with risk factors, citing the lack of long-term data. The American Association for the Study of Liver Disease (AASLD) recommends both screening for those at high risk and treatment with evidence of liver inflammation.<sup>16</sup>

*Recommendation.* There are no data that preconception screening for hepatitis C in low-risk women will improve perinatal outcomes. Screening for high-risk women is recommended. Women who are positive for hepatitis C and desire pregnancy should be counseled regarding the uncertain infectivity, the link between viral load and neonatal transmission, the importance of avoiding hepatotoxic drugs, and the risk of chronic liver disease. Women who are being treated for HCV should have their reproductive plans reviewed and use adequate contraception while receiving therapy. *Strength of recommendation:* C; *quality of evidence:* III.

## **Tuberculosis**

*Burden of suffering.* Worldwide, tuberculosis is the number 1 infectious disease killer. The CDC reported > 15,000 active cases of tuberculosis in 2001 and 10-15 million latent infections. Tuberculosis affects all parts of the body including the pulmonary, skeletal, gastrointestinal, genitourinary, and cutaneous systems. The case fatality rate approaches 50% in untreated patients, multidrug resistant infections, and infants with congenital disease. Tuberculosis during pregnancy is a risk factor for low birthweight and subsequently poor perinatal outcomes' conversion to active disease is more common in the postpartum period.

*How detectable is the condition?* Tuberculosis may be screened with the tuberculin skin test or with QuantiFERON-TB Gold (Cellestis Inc, Valencia, CA), an ELISA test that detects interferon-gamma in blood from sensitized persons. Both have equal sensitivity; however, the QuantiFERON-TB Gold test is believed to have greater specificity. As a result, this latter test has been found to be useful in recent immigrants who have received the bacille Calmette-Guérin vaccine, health care workers, and contact investigations.<sup>18</sup>

*How effective are the current treatments?* Based on clinical trials, treatment of latent tuberculosis infection is effective with isoniazid monotherapy (65% efficacy for 6 months and 75% efficacy for 12 months).<sup>19</sup> More advanced cases, which include multidrug resistant tuberculosis, require more extensive and toxic therapy.

*Impact of preconception care.* Screening for tuberculosis before pregnancy allows for prophylaxis completion, the opportunity to reduce the risk of poor pregnancy outcomes, and the avoidance of conversion to active disease. High-priority groups for treatment for latent tuberculosis infection include persons who converted within the past 2 years; persons with personal contact with someone who has active tuberculosis; illicit drug users; foreign-born persons from high-risk countries who have been in the United States < 5 years; the elderly; children who are < 4 years old and who are exposed to high-risk adults; persons with chronic medical conditions such as HIV, diabetes mellitus, organ transplantation, end-stage renal disease, cancer, chronic steroid use, or underweight; health care workers; persons who are incarcerated; and persons who work in correction institutions.<sup>20</sup> Persons with a positive screening test result and who do not have evidence of active disease usually are treated with a 9-month regimen of isoniazid.<sup>21</sup>

*Recommendations by other groups.* The CDC recommends screening and treatment for latent tuberculosis in those who are at high risk for disease.<sup>21</sup> Pregnant

women may be treated for latent tuberculosis infection while pregnant.

*Recommendation.* All high-risk women should be screened for tuberculosis and treated appropriately before pregnancy. *Strength of recommendation:* B; *quality of evidence:* II-2.

### Toxoplasmosis

*Burden of suffering.* Toxoplasmosis is a disease that is caused by infection with the protozoan *Toxoplasma gondii* that can be transmitted by an infected pregnant woman to her fetus. Raw meat and the feces of newly infected cats are the only other sources for the *Toxoplasma* protozoa infection. Approximately one-third of adult women in the United States have antibodies to toxoplasmosis, and the remainder may be at risk for a primary maternal infection during pregnancy that can result in congenital infection. Prospective studies that have been performed in the United States have established an incidence of congenital toxoplasmosis of 1.1 per 1000 live births. Of children who are born to mothers who had toxoplasmosis during pregnancy, approximately 8% are severely affected at birth. The remainder are affected with mild disease or subclinical infection but are at risk for late sequelae such as chorioretinitis, mental retardation, and sensorineural hearing loss, blindness, and epilepsy. Severe fetal effects are more likely if infection is acquired during the first or second trimester.<sup>22,23</sup>

*How detectable is the condition?* Toxoplasmosis infection is usually asymptomatic. Food and Drug Administration–approved commercial kits are available for the detection of past immunoglobulin G (IgG) and recent immunoglobulin M (IgM) infection. The tests for IgM have been noted to have limited specificity that results in high false-positive rates, especially when the incidence is low.

*How effective are the current treatments?* Treatment of acute toxoplasmosis during pregnancy may reduce but does not eliminate the risk of congenital infection. Should congenital infection be diagnosed, then multiple agent therapy is

recommended. There is some evidence for improved outcomes when the affected infant is treated.

*Impact of preconception care.* Preconception testing for immunity to *T gondii* by the measurement of IgG antibody titer might provide physicians with useful information for counseling women. Women who are already immune can be reassured that they cannot become infected during pregnancy. Women who are susceptible should be counseled before pregnancy about cooking meat to a safe temperature, peeling or thoroughly washing fruits and vegetables before consumption, and properly cleansing utensils and cooking surfaces after contact with unwashed fruit or vegetables or raw meat, poultry, or seafood. If they become pregnant, they should be counseled to either avoid changing cat litter or to wear gloves and wash hands thoroughly afterwards, to keep cats inside, and to not feed raw or undercooked meat to cats.<sup>24</sup> Antibody testing during pregnancy that demonstrates *Toxoplasma* infection in a woman who had negative titers before pregnancy indicates that infection has occurred. In the absence of such preconception information, interpretation of titers that are obtained during pregnancy may be difficult. Thus, preconception testing might lead to a prompt diagnosis and timely treatment decisions.<sup>25</sup> There are no studies to suggest such testing is cost-effective or efficacious.

*Recommendations by other groups.* ACOG currently does not advocate testing for *Toxoplasma* infection during pregnancy, citing a low prevalence of the disease. It does advocate counseling women on modes of prevention (level C recommendation).<sup>26</sup> The CDC recommends education and counseling as modes to prevent infection. Testing for immunity is not mentioned.<sup>27</sup>

*Recommendation.* There is no clear evidence that preconception counseling and testing will reduce *T gondii* infection or improve treatment of those women who are infected. However, if preconception testing is done, those women who test positive can be reassured that

they are not at risk of contracting toxoplasmosis during pregnancy; those women who are negative can be counseled about ways to prevent infection during pregnancy. For those women who convert during pregnancy, treatment should be offered. *Strength of recommendation:* C; *quality of evidence:* III.

### Cytomegalovirus

*Burden of suffering.* Human cytomegalovirus is the most common viral infection in pregnancy, with an estimated birth prevalence of 0.6-2.2%. Primary maternal infection occurs in approximately 1% of pregnancies. Congenital cytomegalovirus is the leading cause of hearing loss in children; 15% of infants who are born to mothers who are infected during pregnancy will manifest hearing loss. The severity of fetal infection declines with gestational age, such that 20-30% of fetuses that are infected in the first one-half of pregnancy have serious sequelae that include intrauterine growth restriction, cerebral palsy, mental retardation, hepatosplenomegaly, petechiae, jaundice, chorioretinitis, hearing loss, thrombocytopenia, and anemia. The rate of infection increases with gestational age; therefore, fetal infection is more common later in pregnancy, but most infants are asymptomatic at birth. Cytomegalovirus infection is endemic in the community, with asymptomatic infections common during childhood.

*How detectable is the condition?* Cytomegalovirus is usually asymptomatic. Diagnosis is made by serologic confirmation of cytomegalovirus-specific IgM and a 4-fold rise in cytomegalovirus-IgG in paired sera. False-positive and -negative tests for cytomegalovirus-specific IgM are not rare. Fetal infection is best diagnosed by culture and/or polymerase chain reaction (PCR) of amniotic fluid after 21 weeks of pregnancy. Antenatal ultrasound scanning may identify affected fetuses but cannot exclude significant infection-related morbidity.<sup>28</sup>

*How effective are the current treatments?* There is no effective current treatment for primary cytomegalovirus infection in pregnancy. Ganciclovir crosses the pla-

centa but has not been demonstrated to improve outcomes for congenitally infected fetuses. The administration of cytomegalovirus-specific hyperimmune globulin (passive immunization) was promising in a small preliminary study by decreasing the frequency and severity of primary fetal infection.<sup>29</sup> Good personal hygiene, particularly hand-washing, is the most effective means of preventing infection among pregnant women.<sup>30</sup> There is no evidence that screening and/or treatment programs prevent infection.<sup>31</sup>

**Impact of preconception care.** There is no vaccine at present. Preconception testing of cytomegalovirus is not recommended because there is no evidence that this reduces perinatal infection. However, testing for immunity might be considered to stratify the risk of consequences of cytomegalovirus infection in pregnancy and the need for prevention efforts because primary infection poses a greater risk of sequelae of congenital infection.

**Recommendations by others.** The CDC and the ACOG recommend universal hand-washing precautions for pregnant women and education of reproductive-age women about hand-washing. The CDC recommends the following precautions for prevention: (1) practice good personal hygiene, especially hand-washing with soap and water (for 14-20 seconds) after contact with diapers or saliva (particularly with a child who is in daycare), (2) do not kiss children under the age of 6 years on the mouth or cheek, instead kiss them on the head or give them a hug, (3) do not share food, drinks, or utensils (spoons or forks) with young children, and (4) if pregnant and working in a daycare center, reduce the risk of getting cytomegalovirus by working with children who are > 2½ years of age, especially if you have never been infected with cytomegalovirus or are unsure if you have been infected.<sup>32</sup> Prenatal screening is not recommended.<sup>32</sup>

**Recommendation.** Women who have young children or who work with infants and young children should be counseled about reducing the risk of cytomegalovirus through universal precautions (eg,

the use of latex gloves and rigorous hand-washing after handling diapers or after exposure to respiratory secretions). *Strength of recommendation: C; quality of evidence: II-2.*

### Listeriosis

**Burden of suffering.** Listeriosis is a food-borne infection that is caused by the bacterium *Listeria monocytogenes* and typically affects pregnant women, newborn infants, and individuals with compromised immune systems. Although listeriosis is a rare disease in the United States, the case fatality rate is very high.<sup>33</sup> In the United States, approximately 2500 cases and 500 deaths occur each year.<sup>34</sup> Most cases are caused by ingestion of contaminated foods. Hispanic women in the United States are especially at risk because of ethnic preference for soft fresh cheeses, often made from raw milk. The organism can multiply at 40°F, which is the temperature of many refrigerators. It spreads hematogenously and infects the placenta in pregnancy by producing micro abscesses and fetal infection. *L. monocytogenes* is associated with numerous adverse outcomes that include preterm labor, amnionitis, spontaneous abortion, stillbirth, and early-onset neonatal sepsis syndrome.<sup>35</sup> The common presentation in pregnancy is preterm labor, decreased fetal activity, or fetal death, with an influenza-like illness in the mother. Untreated, the fetal mortality rate approaches 50%.

**How detectable is the condition?** *Listeria* contamination of foods is detectable readily by bacteriologic culture. Listeriosis in humans is detected by culture of the products of conception in the case of spontaneous abortion, by amniocentesis with culture of the amniotic fluid in later pregnancy, or by culture from the placenta after birth.

**How effective are the current treatments?** If the diagnosis is made antenatally and the mother is treated with ampicillin, the maternal and neonatal outcomes are generally good.<sup>36</sup>

**Impact of preconception care.** Primary prevention efforts include improvements in food processing and consumer

education.<sup>37</sup> The disease is not a grave problem before pregnancy in normal women; however, because exposure in early pregnancy can lead to pregnancy loss and severe maternal illness, preconceptional education is important to avoid exposure.

**Recommendations by other groups.** The CDC has investigated epidemics of listeriosis. Individual states have recommended education to avoid consumption of products that are implicated in such outbreaks.<sup>38</sup> An ACOG patient education pamphlet warns pregnant women of the disease and describes measures for food preparation to avoid it.<sup>39</sup>

**Recommendation.** Because it is not clear at what point in pregnancy women who are exposed to *Listeria* will become ill, preconception care should include teaching women to avoid pâté and fresh soft cheeses that are made from unpasteurized milk and to cook ready-to-eat foods such as hotdogs, deli meats, and left-over foods when trying to conceive or pregnant. *Strength of recommendation: C; quality of evidence: III.*

### Parvovirus or fifth disease

**Burden of suffering.** Fifth disease is caused by infection with human parvovirus B-19. Infections are most common in school-aged children. The typical infection is characterized by malaise, low-grade fevers, and a facial rash (the slapped-cheek appearance of childhood).<sup>40</sup> Although 60% of adults have immunity,<sup>26</sup> in healthy adults, it can cause arthritis, arthralgias, and rarely, anemia.<sup>41</sup> Transmission occurs through close association, such as respiratory secretions and hand-mouth contact. Most women who are infected during pregnancy have healthy babies; however, infection during the first 20 weeks of pregnancy is associated with severe anemia, miscarriage, and fetal hydrops. Seroconversion is more likely through household than classroom exposure. The overall risk of fetal loss after maternal exposure is 6.5%. In an observational study of > 1000 women with acute parvovirus B-19 exposure, the risk of hydrops was 3.9%,<sup>42</sup> and fetal death occurred only with exposure at < 20 weeks of gestation.

Parvovirus has not been associated with congenital malformations.

*How detectable is the condition?* Both IgG and IgM antibodies can be detected with ELISA techniques as evidence of parvovirus infection. IgM can be detected after symptoms approximately 10 days after exposure; IgM antibody persists for approximately 3 months. IgG positivity provides evidence of past infection. Both are 80-90% sensitive for clinical infection. Parvovirus B-19 DNA can be detected with PCR in the amniotic fluid of affected fetuses.

*How effective are the current treatments?* In adults, parvovirus infection is usually mild, and there is no specific treatment for the condition unless anemia develops. There is concern for fetal effects. Frequent ultrasound surveillance is justified because parvovirus infection can lead to fetal anemia and hydrops. Cordocentesis and transfusion have proved effective in treating severe hydrops.<sup>43,44</sup> In fact, a survey of > 500 perinatologists with 539 cases of hydrops suggests that 89% used ultrasonography in initial management of parvovirus infection. Thirty-four percent of these cases of hydrops spontaneously resolved; 30% resulted in a fetal death, and 29% of the time there was a resolution with transfusion. Because of the possibility of spontaneous resolution, transfusion is reserved for cases of severe anemia and fetal compromise.<sup>45</sup> In utero exposure to parvovirus B-19 has not been associated with neurodevelopmental delay in the absence of fetal hydrops; however, a retrospective study showed that 32% of children who required in utero fetal transfusion demonstrated mild-to-severe neurodevelopmental delay.<sup>46,47</sup>

*Impact of preconception care.* No data have emerged to suggest preconception screening for immunity to parvovirus infection would prove beneficial.

*Recommendations by other groups.* ACOG has no preconception recommendations.

*Recommendation.* There is not yet evidence that screening for antibody status against parvovirus or counseling about ways to avoid infection in pregnancy will

improve perinatal outcomes. Good hygiene practices should be encouraged for all pregnant women. *Strength of recommendation:* E; *quality of evidence:* III.

### Malaria

*Burden of suffering.* Globally, malaria is 1 of the most common infections during pregnancy. Malaria is endemic in > 100 countries where > 24 million pregnant women are affected each year.<sup>48,49</sup> Malaria infection during pregnancy can have adverse effects on both mother and fetus and includes maternal anemia, fetal loss, premature delivery, intrauterine growth restriction, and delivery of low birthweight infants. In sub-Saharan Africa, which is the region of the world that is hardest hit by malaria, malaria infection is estimated to cause 400,000 cases of severe maternal anemia and 75,000-200,000 infant deaths annually. Maternal anemia contributes significantly to maternal death and causes an estimated 10,000 maternal deaths per year.<sup>50</sup> In the United States, 1324 cases of malaria were reported in 2004; all but 4 of those cases were imported. A total of 30 cases of malaria were reported among pregnant women in the United States in 2004.<sup>51</sup>

*How detectable is the condition?* In the United States, screening is not used because malaria is not endemic. Diagnosis rests on clinical criteria and confirmation of malaria through microscopy<sup>52</sup> or recently approved rapid diagnostic tests for malaria antigens.<sup>53</sup>

*How effective are the current treatments?* Guidelines exist for malaria infection that is diagnosed in the United States<sup>54</sup> that should be consulted. It is recommended that treatment be initiated only when confirmed with laboratory testing. Treatment regimens vary based on the disease severity, the species of malaria that was identified, and the region in which the disease was acquired (chloroquine resistant/sensitive). Specific regimens are recommended for pregnant women.<sup>55</sup>

*Impact of preconception care.* The traveler can reduce her risk of acquiring malaria by following several preventive approaches that include personal pro-

tection to avoid infective mosquito bites and the use of antimalarial chemoprophylaxis.<sup>56</sup> Women who are planning a pregnancy should be advised to (1) remain indoors between dusk and dawn, if mosquitoes are active outdoors during this time, (2) if outdoors at night, wear light-colored clothing, long sleeves, long pants, shoes, and socks, (3) stay in well-constructed housing with air-conditioning and/or screens, (4) use permethrin-impregnated bed nets, and (5) use insect repellents that contain N,N-diethyl-3-methylbenzamide (DEET) as needed. Permethrin and DEET have been shown to reduce the risk of malaria infection and are considered safe in pregnancy.<sup>57-59</sup>

Antimalarial chemoprophylaxis should be provided to women who are planning a pregnancy and traveling to malaria-endemic areas. For pregnant women who travel to areas with chloroquine-sensitive *Plasmodium falciparum* malaria, chloroquine has been used for malaria chemoprophylaxis for decades with no documented increase in birth defects. For pregnant women who travel to areas with chloroquine-resistant *P falciparum*, mefloquine can be used for chemoprophylaxis during the second and third trimesters. For women in their first trimester, most evidence suggests that mefloquine prophylaxis causes no significant increase in spontaneous abortions or congenital malformations, if taken during this period. Because there is no evidence that chloroquine and mefloquine are associated with congenital defects when used for prophylaxis, the CDC does not recommend that women who are planning pregnancy need to wait a specific period of time after their use before becoming pregnant.<sup>60,61</sup> The safety of atovaquone/proguanil use in early pregnancy has not been established, and doxycycline should be avoided in women who are planning a pregnancy. Primaquine should also be avoided because the drug may be passed transplacentally to a glucose-6-phosphate dehydrogenase-deficient fetus and cause hemolytic anemia in utero. Despite recent encouraging results, a vaccine against malaria infection in pregnancy is currently unavailable.<sup>62</sup>

*Recommendations by other groups.* The CDC publishes up-to-date information on malaria prevention for travelers for providers for adults and pregnant women.<sup>63,64</sup> In addition their online “Yellow Book” can be consulted.

*Recommendation.* Women who are planning a pregnancy should be advised to avoid travel to malaria-endemic areas. If travel cannot be deferred, the traveler should be advised to defer pregnancy and use effective contraception until travel is completed and to follow preventive approaches. Antimalarial chemoprophylaxis should be provided to women who are planning a pregnancy and traveling to malaria-endemic areas. *Strength of recommendation: C; quality of evidence: III.*

### Gonorrhea

*Burden of suffering.* According to the CDC in 2005, gonorrhea occurs in about 116 per 100,000 persons;<sup>65</sup> infection with *Neisseria gonorrhoea* is the second most common reportable disease in the United States. Some women with gonorrhea can be asymptomatic; however, gonorrhea is a major cause of cervicitis and pelvic inflammatory disease. Women with pelvic inflammatory disease are at risk for internal infections, chronic pelvic pain, and damage to fallopian tubes, which can cause infertility and increased risk of ectopic pregnancy.<sup>66</sup> Gonorrhea in pregnancy is associated with chorioamnionitis, premature rupture of membranes, and preterm labor. Perinatal transmission to the infant can result in severe conjunctivitis that leads to blindness if untreated and, rarely, meningitis and endocarditis.<sup>66</sup>

*How detectable is the condition?* A variety of tests are available for the detection of gonorrhea that include culture, amplified nucleic acid assays, direct immunofluorescence, and direct hybridization techniques. Sensitivity for amplification tests ranges from 66.7-100%, and specificity ranges from 96.8-100%.<sup>66</sup> Screening can be done in both men (from swabs of the urethra) and women (from swabs of the endocervix) or noninvasively in urine samples with amplified nucleic acid assays.<sup>67</sup>

*How effective are the current treatments?* Effective treatment for uncomplicated gonorrhea is available, is updated regularly, and can be accessed online.<sup>68</sup> Recently, because of resistance to quinolones, these agents are no longer recommended for treatment of gonorrhea infection.<sup>69</sup>

*Impact of preconception care.* Men and women who are being treated for sexually transmitted infections should be counseled about the risk of infertility that is imposed by having sexually transmitted diseases. Neonatal infection may result in blindness, joint infections, or blood infections. Currently, there are no data to support the greater effectiveness of screening before pregnancy over screening during pregnancy in preventing pregnancy-related complications.

*Recommendations by other groups.* The USPSTF recommends screening women (pregnant or not) for gonorrhea infection if risk factors exist.<sup>70</sup> The CDC makes similar recommendations.

*Recommendation.* High-risk women should be screened for gonorrhea during a preconception visit, and women who are infected should be treated. Screening should also occur early during pregnancy and be repeated in high-risk women. *Strength of recommendation: B; quality of evidence: II-2.*

### Chlamydia

*Burden of suffering.* *Chlamydia trachomatis* is the most common bacterial sexually transmitted infection in the United States. Approximately 3 million new cases occur annually. Reported rates are higher in women than men, probably because women are more likely to receive routine health care encounters, which include testing of asymptomatic individuals.<sup>71</sup> Seventy to 90% of women are asymptomatic.<sup>71</sup> If untreated, *Chlamydia* infection can lead to pelvic inflammatory disease, infertility, and an increased risk of HIV infection. With relation to pregnancy, *Chlamydia* infection is associated with ectopic pregnancies, neonatal eye infections, and pneumonia.

*How detectable is the condition?* Numerous testing options exist for *Chlamydia* infection. The newer antigen detection tests may provide improved sensitivity, lower expense, and timeliness of results over culture; a sensitivity of 70-80% and a specificity of 96-100% have been reported for antigen detection tests.<sup>67</sup> Testing through urine specimens may improve access to and convenience of testing.

*How effective are the current treatments?* A well-designed randomized trial demonstrated that screening women who are at risk reduced the incidence of pelvic inflammatory disease from 28 per 1000 woman-years to 13 per 1000 woman-years and that the prevalence of chlamydial infection has declined in populations such as family planning clinics, which have been targeted by screening programs.<sup>67</sup> Reinfection is common; therefore, identification and treatment of all sexual partners is warranted. Effective treatments for *Chlamydia* infection are available from the CDC and are updated regularly.

*Impact of preconception care.* Identification and treatment before pregnancy has the potential to reduce infertility and ectopic conceptions; identification and treatment during pregnancy would be necessary to prevent neonatal eye infections and pneumonia. However, because of the risk of infertility from *Chlamydia* or gonorrhea infection, sexually active persons should be counseled to prevent transmission of sexually transmitted diseases and screened regularly for asymptomatic infections.

*Recommendations by other groups.* The USPSTF recommends screening non-pregnant women aged < 25 years and older women who are at high risk for *Chlamydia* infection as a strategy to prevent pelvic inflammatory disease as an “A” level recommendation.<sup>71</sup> Early treatment leads to decreased risk of infertility and ectopic pregnancy. They state that there is no evidence to support screening of men.<sup>72</sup> The CDC recommends annual screening for *Chlamydia* infection for women who are at high risk and for all pregnant women.<sup>68</sup> ACOG

recommends routine screening for chlamydial infection for all sexually active adolescents and other asymptomatic women who are at high risk for infection.

*Recommendation.* All sexually active women aged  $\leq 25$  and all women who are at increased risk for infection with *Chlamydia* (including women with a history of sexually transmitted infection, new or multiple sexual partners, inconsistent condom use, sex work, and drug use) should be screened annually at encounters before pregnancy. *Strength of recommendation:* A; *quality of evidence:* I-a, II-2.

### Syphilis

*Burden of suffering.* The World Health Organization estimates that 12 million new cases of syphilis occur annually. In 2002, the CDC reported 32,000 cases of syphilis. Syphilis has declined in both women and neonates. In adults, the clinical presentation of syphilis ranges from being asymptomatic (latent syphilis) to local symptoms as in primary syphilis (genital ulcers) to more widespread symptoms such as skin rash, lymphadenopathy and mucocutaneous lesions (secondary syphilis) and finally to complications that are associated with tertiary syphilis (gummatous lesions and those that involve the neurologic, visual, and auditory systems). Congenital syphilis can come with devastating complications that include stillbirth, premature birth, neonatal death, developmental delay, blindness, deafness, bone and teeth abnormalities, and seizures.

*How detectable is the condition?* Identification of syphilis usually begins with a nonspecific nontreponemal test (Venereal Disease Research Laboratory or rapid plasma reagin) with sensitivity that ranges from 80-85% for primary syphilis to 90-95% for latent infection. These tests, when positive, are usually followed by a confirmatory treponemal test (fluorescent treponemal antibody-adsorption treponema pallidum particle agglutination assay). This combination of tests has been used successfully in screening programs.

*How effective are the current treatments?* Antibiotics (usually penicillin G) can be used successfully to treat all stages of syphilis. Importantly, congenital syphilis can be treated and prevented with treatment early in pregnancy.<sup>68</sup>

*Impact of preconception care.* Preconception screening for syphilis in high-risk populations is an important step in the reduction of neonatal syphilis. Persons who are at risk for syphilis include men who have sex with men, persons in correctional facilities, commercial sex workers, persons who have sex with high-risk individuals, and persons who are diagnosed with other sexually transmitted infections. Syphilis can be cured if treated in its early stages. However, treatment does not prevent reinfection. Even if adequate treatment is established, repeat testing should occur during pregnancy in the first and third trimesters. Studies show that most stillbirths occur at about 30 weeks of gestation. Therefore, even in unplanned pregnancies, prompt and immediate treatment of syphilis might decrease the risk of stillbirth and other perinatal morbidities. Perinatal morbidity and mortality rates can be as high as 40% in women who are untreated. Preconception screening and treatment may have the additional advantage of avoiding costly and complicated penicillin desensitization in patients with penicillin allergies.

*Recommendations by other groups.* The US Preventive Services Task Force (USPSTF) recommends screening all pregnant women for syphilis in the first trimester ("A" level recommendation). They also recommend screening women at high risk for infection ("A" level recommendation). Many states require syphilis screening as a requirement to obtain a marriage license.<sup>73,74</sup> The CDC also recommends screening pregnant women, with repeat screening in the early third trimester for those at high risk (including those with a positive test earlier in pregnancy), or in areas with high morbidity from syphilis.

*Recommendation.* High-risk women should be screened for syphilis during a preconception visit, and women who are

infected should be treated. Because the USPSTF and CDC recommend screening all women during pregnancy for syphilis, screening for syphilis immediately before conception is recommended. *Strength of recommendation:* A; *quality of evidence:* II-1.

### Herpes simplex virus

*Burden of suffering.* At least 50 million persons in the United States have genital herpes infection. Neonatal transmission occurs in approximately 1 in 3000 deliveries. Forty percent of neonatal herpes cases result in localized skin infections. Encephalitis develops in 25% of cases, with the poorest prognosis for 25% of infected neonates who go on to have disseminated disease that can affect multiple organ systems.

*How detectable is the condition?* When a patient has clinical symptoms and characteristic lesions, the diagnosis is straightforward; however, clinical diagnoses should be confirmed with a culture. Although cultures have good specificity, sensitivity may be limited, as low as 50% in some cases. PCR-based tests have higher sensitivity. Evidence of past infection may be detected through serologic testing.

*How effective are the current treatments?* Treatment for HSV infection consists of antiviral therapy, which cannot eradicate infection. Instead, treatment is aimed at reducing symptoms, the duration of lesions, or the recurrence of lesions.

*Impact of preconception care.* The risk of HSV-2 sexual transmission can be reduced by the daily use of acyclovir or valacyclovir by an infected person.<sup>75,76</sup> Couples with an infected male partner should be encouraged to consider suppressive antiviral therapy as part of a strategy to prevent transmission, in addition to consistent condom use and avoidance of sexual activity during recurrences. Most individuals with genital herpes infection are asymptomatic, so it is important to teach couples about the signs and symptoms of genital herpes infections.<sup>77</sup> Women with a history of genital herpes should be counseled about the risk of vertical transmission to the fetus



and newborn child. Women who have active lesions or prodromal symptoms at the time of delivery are offered cesarean delivery to reduce perinatal transmission. To reduce the risk of recurrence at delivery and of cesarean delivery for women with a history of genital herpes, prophylactic antiviral agents may be used from 36 weeks until delivery.<sup>78</sup> Both HSV-1 and -2 can cause perinatal infection. Couples with a history of orolabial herpes should be counseled about good hygiene practices, because orolabial disease can also be transmitted to the newborn infant.

*Recommendation by other groups.* ACOG recommends cesarean delivery for women with active lesions during labor and possible suppressive therapy late in gestation. The USPSTF recommends against routine serologic screening of pregnant women or asymptomatic adults. The CDC recommends against routine serologic screening for HSV in pregnant women and states that there is not sufficient evidence to support routine suppression for women with a history of recurrent HSV.

*Recommendation.* During a preconception visit, women with a history of genital herpes should be counseled about the risk of vertical transmission to the fetus and newborn child; those women with no history should be counseled about asymptomatic disease and acquisition of infection. Although universal serologic screening is not recommended in the general population, type-specific serologic testing of asymptomatic partners of persons with genital herpes is recommended. *Strength of recommendation:* B; *quality of evidence:* II-1.

### Asymptomatic bacteriuria

*Burden of suffering.* Asymptomatic bacteriuria occurs in 3-8% of pregnant women and is a risk factor for low birthweight. Between 20% and 40% of pregnant women with asymptomatic bacteriuria without adequate treatment or follow-up experience acute pyelonephritis with an attendant increased risk of fetal death and morbidity.

*How detectable is the condition?* Most urine tests with immediate results (urine

dipstick or direct microscopy) have poor predictive values, which limits their use in screening for asymptomatic bacteriuria. Urine culture, although more expensive and time-consuming, is the test of choice for screening.

*How effective are the current treatments?* Appropriate antibiotic treatment of bacteriuria is 90-95% effective in the prevention of progression to pyelonephritis.

*Impact of preconception care.* Data are not consistent as to whether treatment has a significant positive effect on birthweight or on gestational age at birth in women with asymptomatic bacteriuria who do not go on to have acute pyelonephritis. A review of 17 studies that investigated the relationship between asymptomatic bacteriuria and low birthweight/prematurity concluded that women with asymptomatic bacteriuria have an increased rate of low birthweight/prematurity when compared with women with sterile urine. They also concluded from the 8 randomized clinical studies that were available that women with asymptomatic bacteriuria who are treated have a lower rate of low birthweight than untreated women. There are no data to suggest that screening before pregnancy is more beneficial than screening and treating during pregnancy.

*Recommendations by other groups.* The USPSTF concluded that early detection of asymptomatic bacteriuria is of value for pregnant women, but that screening of asymptomatic adults is not justified because of concerns that serious urinary tract disorders are relatively uncommon, the positive predictive value of screening urinalysis is low, and the effectiveness of early detection and treatment is unproved.<sup>79</sup>

*Recommendation.* There have been no studies to show that women with asymptomatic bacteriuria who are identified and treated in the preconception period have lower rates of low birthweight births. Further, women often have persistent or recurrent bacteriuria despite repeated courses of antibiotics; such reinfection frequently occurs within a few months of treatment. Thus, a woman

who is identified and treated for asymptomatic bacteriuria before conception must be screened again during pregnancy. For these reasons, screening for this condition as part of routine preconception care is not recommended. *Strength of recommendation:* E; *quality of evidence:* II-1.

### Periodontal disease

*Burden of suffering.* Periodontal disease affects up to 40% of pregnant women, with a disproportionate burden among low income women. It has been proposed that chronic infection and inflammation around the teeth might stimulate maternal or fetal responses that lead to preterm birth. Two large prospective studies have shown that maternal periodontal disease was associated with a 2- to 7-fold increase in odds for preterm delivery, with increasing risk for decreasing gestational age.<sup>80,81</sup> Another similar prospective study linked maternal periodontal disease to preeclampsia.<sup>82</sup>

*How detectable is the condition?* Periodontal disease is detectable by a detailed oral health examination that is performed by trained dental professionals.

*How effective are the current treatments?* Treatment of periodontal disease is highly effective in reducing the burden of oral disease, but treatment during pregnancy has not yet been proved clearly to improve perinatal outcomes.

*Impact of preconception care.* Interventional trials during pregnancy have demonstrated consistently improved maternal oral health, but findings regarding preterm birth risk reduction are conflicting. A randomized study found some reduction in premature birth for women who had scaling and root planning during pregnancy, compared with women who were treated with tooth cleaning and polishing, but the results were not statistically significant.<sup>81</sup> A subsequent Chilean study did find benefit in a group of women who were treated for periodontal disease compared with women who were chosen randomly for treatment after delivery.<sup>83</sup> However, a recent large US multicenter trial that compared 407 women who were treated at < 21

weeks of gestation to 405 women who were assigned randomly to treatment after delivery found no reduction in preterm birth at < 37 weeks of gestation, although there was a trend for reduced preterm birth at < 32 weeks of gestation.<sup>84</sup> The current data cannot allow for a definitive conclusion regarding cause and effect between maternal periodontal disease and preterm birth. Different studies have used different definitions of periodontal disease, and all the intervention trials have initiated treatment after the first trimester, which may be too late to reduce the risk that is associated with preterm birth. A randomized study of preconception screening and treatment of periodontal disease is needed.

*Recommendations by other groups.* The American Academy of Periodontology recommends that women who are pregnant or planning to become pregnant undergo a periodontal examination.<sup>85</sup> The Canadian Task Force of Periodic Health Examination found fair (B level) evidence for tooth brushing, good (A level) evidence for flossing to prevent gingivitis, and fair (B level) evidence to support prophylaxis and scaling, depending on periodontal status.<sup>86</sup>

*Recommendation.* There are no studies that have evaluated the role of preconception or interconception screening and treatment of periodontal disease and its effect on reproductive outcomes. Routine screening and treatment of periodontal disease during preconception care is of considerable benefit to the mother but cannot yet be recommended as having benefit for the fetus. *Strength of recommendation:* C; *quality of evidence:* I-b.

## BV

*Burden of suffering.* BV results from a shift in the normal vaginal bacterial flora to 1 that is characterized by an increase in *Gardnerella*, *Mycoplasma* and anaerobic bacteria, and a decrease in *Lactobacilli*.<sup>87</sup> BV is a common cause of abnormal vaginal discharge. The true prevalence of BV in the community is not known, but studies in academic medical centers and public hospitals found that 9-23% of pregnant women had BV, with infection

being more common among African American women than white women.<sup>88</sup> A data synthesis supports the idea that BV organisms are found in the upper reproductive tract and contribute to the risk for pelvic inflammatory disease.<sup>89</sup> Observational studies consistently have shown an association between BV and adverse pregnancy outcomes that include preterm delivery (relative risk, 1.4-6.9), preterm premature rupture of membranes (relative risk, 2.0-7.3), spontaneous abortion (relative risk, 1.3-2.0), and preterm labor (relative risk, 2.0-2.6).<sup>90-93</sup> Studies that find a higher relative risk of preterm delivery for BV are those with the earliest gestational age for BV screening. The risk of preterm delivery is > 7-fold higher for women with BV at < 16 weeks of gestation and greater than 4-fold higher for women with BV at < 20 weeks of gestation.<sup>94</sup>

*How detectable is the condition?* The most common manner in which a diagnosis of BV is made clinically is with the Amsel criteria, which were developed to evaluate symptomatic women. The Amsel criteria are (1) presence of a homogeneous white discharge, (2) presence of an amine or "fishy" odor (which may be accentuated with the addition of KOH to the specimen), (3) the presence of "clue cells" on microscopy, and (4) a vaginal fluid of pH > 4.5. Three of the 4 criteria must be present to make a diagnosis of BV.<sup>95</sup> Gram's stain of vaginal discharge can also be used to diagnose BV and offers improved reproducibility and quality assurance, compared with the Amsel criteria. The Gram's stain method uses the Nugent criteria and scores vaginal flora from 1-10 on the basis of bacterial types and quantities: 0-3, normal flora; 4-6, intermediate abnormal flora; 7-10, BV.<sup>96</sup> Although these criteria are used commonly in research settings, they are not practical for clinical settings, given the need to prepare and critically read Gram's stains.

*How effective are the current treatments?* A short course of antibiotic therapy can alter the microflora imbalance that is associated with BV, but cure rates are variable and recurrences are common.<sup>97</sup> A

review of the evidence has established that the benefits of therapy for BV among nonpregnant women are the relief of vaginal symptoms and signs of infection and the reduction in the risk of infectious complications after induced abortion or hysterectomy.<sup>89</sup> Many randomized controlled trials have investigated whether treating BV during pregnancy improves pregnancy outcomes, with conflicting results.<sup>98-106</sup> Results of 15 good-quality trials that involved 5888 women are summarized in a recent Cochrane review.<sup>107</sup> The Cochrane review concluded that there is little evidence that screening and treating all pregnant women with asymptomatic BV prevents preterm delivery, but there is some suggestion that early screening and treatment at < 20 weeks of gestation may reduce the risk of preterm delivery. The review also concluded that, among women with a previous preterm delivery, treatment does not affect the risk of a subsequent preterm delivery but is associated with a decrease in the risk of preterm premature rupture of membranes. Further support for the potential effectiveness of early screening and treatment of BV among asymptomatic pregnant women comes from a recently presented abstract from the Syracuse Healthy Start Project.<sup>108</sup> This project encouraged providers for pregnant women who reside in high-risk zip codes of Syracuse to screen for and treat BV at the first prenatal care visit. They report that premature delivery (11.4% vs 13.2%;  $P = .2$ ), low birthweight (8.6% vs 11.5%;  $P = .02$ ), delivery at < 32 weeks of gestation (2.1% vs 4.4%;  $P = .001$ ), and very low birth rate (1.9% vs 3.8%;  $P = .006$ ) were lower in the screened/treated group, compared with the unscreened group. First screening and treatment were at a median of 11 and 14 weeks of gestation, respectively.

*Impact of preconception care.* To date, no studies have evaluated the role of preconception or interconception screening and treatment of BV on subsequent pregnancy outcomes; this has been identified as an important area for future research, given its established association with preterm delivery. BV is a particularly appealing risk factor to target, be-

cause it is potentially preventable and treatable. Furthermore, because of its higher prevalence among black women, the prevention and treatment of BV may help reduce at least part of the racial disparity in preterm delivery.<sup>89</sup> However, the frequency of recurrence of BV and the variable cure rate may be factors that limit the value of preconception detection and treatment in terms of the eradication of BV before a subsequent pregnancy. Because BV is common, screening and treatment could subject a substantial number of women to the inconvenience and minor side-effects of antibiotics. Although the regimens that are used to treat BV generally are considered safe in pregnancy, several studies do raise the possibility of harm to some women or their infants. In 2 studies, a subgroup of women who did not have BV, but who received treatment with metronidazole or clindamycin, experienced trends toward higher incidence of preterm delivery at < 34 weeks of gestation (12-13% vs 4-5%).<sup>109</sup> In addition, neonatal sepsis was increased significantly among women who received vaginal clindamycin therapy.<sup>110</sup>

**Recommendations by other groups.** Presently, the USPSTF,<sup>111</sup> the CDC,<sup>68</sup> and the ACOG<sup>112</sup> do not recommend screening and treatment for BV among pregnant women of any risk category. The USPSTF states that “there is good evidence that screening and treatment of BV in asymptomatic women of average risk does not improve outcomes such as preterm labor or preterm birth” and recommends against routinely screening average-risk asymptomatic pregnant women for BV. The USPSTF goes on to state that there are “good-quality studies with conflicting results that screening and treatment of asymptomatic BV in high-risk pregnant women reduces the incidence of preterm delivery.” The magnitude of benefit exceeded the risk in several studies,<sup>113,114</sup> but the single largest study reported no benefit among high-risk pregnant women.<sup>115</sup> Thus, the USPSTF concludes that the evidence is insufficient to recommend for or against routinely screening high-risk pregnant women for BV. The USPSTF does pro-

vide clinical considerations when making decisions to screen and treat or not and states that, for women with a history of preterm delivery, screening for BV is an option, noting that the optimal screening test for BV is not certain nor is the optimal time to screen and the optimal treatment regimen. The 3 trials that demonstrated a reduction in preterm delivery screened in the second trimester (13-24 weeks of gestation) and used oral metronidazole or oral metronidazole and erythromycin. Reasons for the conflicting results are not clear but may involve differences in other risk factors for preterm delivery among enrolled women, which include variations in immunologic response to BV, or differences in drug regimens or timing of therapy.<sup>116</sup>

**Recommendation.** There are no studies that evaluate the role of preconception or interconception screening and treatment for asymptomatic BV and its effect on reproductive outcomes; such studies are a high priority. Routine screening and treatment of BV among asymptomatic pregnant women of average risk should not be performed because of the lack of demonstrated benefit and the possibility of adverse effects of treatment for women without BV. For pregnant women with previous preterm delivery, the inconsistent results of well-done studies prevent a clear recommendation for or against screening; however, some studies support early screening and treatment with a regimen containing oral metronidazole. For women with symptomatic BV infection, treatment is appropriate for pregnant women and for women planning pregnancy. *Strength of recommendation:* D (for women without previous preterm delivery), C (for women with previous preterm delivery); *quality of evidence:* I-b.

### GBS

**Burden of suffering.** The gastrointestinal tract serves as the natural reservoir for GBS and is the likely source of vaginal colonization. Genital tract colonization is found in approximately 10-30% of women and can be transient, chronic, or intermittent. GBS is a common cause of

early-onset neonatal sepsis (1700 cases in the United States in 2001<sup>117</sup>) and meningitis and can be transmitted to the newborn infant by passage through a colonized genital tract (0.4 cases per 1000 live births in 2006).<sup>118</sup>

**How detectable is the condition?** Culture of the lower vagina/rectum is done with traditional laboratory methods and detects lower tract colonization. Rapid tests have been produced but may not detect light colonization such that they have not been incorporated into screening programs.<sup>119</sup> PCR techniques appear to have adequate sensitivity, but questions arise regarding availability on a 24/7 basis.

**How effective are the current treatments?** Intrapartum antibiotics are 90% effective at the prevention of early-onset neonatal sepsis.<sup>119</sup>

**Impact of preconception care.** Pregnant women should be screened for vaginal/rectal GBS colonization at 35-37 weeks of gestation. Women who are colonized should receive antibiotics in labor to reduce the risk of vertical transmission to the newborn infant. There is no evidence that identification of genital tract colonization in the nonpregnant patient provides clinical benefit. In fact, even genital tract colonization in early pregnancy is not predictive of neonatal GBS sepsis.<sup>120</sup>

**Recommendations by other groups.** The CDC has recommended a strategy of universal screening for genital colonization by GBS at 35-37 weeks of gestation, with antibiotics in labor for those with positive cultures. This strategy has been endorsed by ACOG and other groups. There are no recommendations for screening nonpregnant adults.

**Recommendation.** Screening for GBS colonization at a preconception visit is not indicated and should not be performed. *Strength of recommendation:* E; *quality of evidence:* II-2.

### Comment

As discussed in this article, there is ample evidence that clinicians should address many infectious conditions in their preconception care activities. Risk assessment,

screening, and treatment for specific infections should be a component of preconception care (strength of recommendation of "A") because there is convincing evidence that treatment of these infections before pregnancy prevents infertility, ectopic implantation, and neonatal infections (*Chlamydia*); consequences to the developing fetus (syphilis); or transmission of an infectious agent with potential for chronic infection of the offspring (HIV). Infections with less strong recommendation ("B") for consideration in preconception care include the detection and treatment of tuberculosis, gonorrheal infection, and HSV in selected individuals. Those infections that lack clear evidence for inclusion in preconception care (strength of recommendation of "C") include hepatitis C, toxoplasmosis, cytomegalovirus, listeriosis, malaria, BV in women with previous preterm birth, and periodontal disease. In some cases, such as for toxoplasmosis, the interventions are primarily patient education; it is unclear whether the recommendation by a provider (to avoid certain foods and changing cat litter boxes) impacts patient behavior or, ultimately, the pregnancy outcome. In the case of periodontal disease and BV, randomized trials that have been conducted during pregnancy have had mixed results for the prevention of preterm birth, although data that have evaluated the potential impact of intervention in the preconception period are altogether lacking. Given the association of periodontal disease and BV with preterm birth in observational studies, trials to evaluate specifically the effect of preconception treatment interventions for these conditions are warranted. A number of infections have important consequences during pregnancy yet should be excluded from preconception care, for example with a "D" level recommendation for BV in those with no history of preterm birth and "E" level recommendations that include parvovirus, asymptomatic bacteriuria, and GBS infection. ■

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