Bacterial Vaginosis

BV is a polymicrobial clinical syndrome resulting from replacement of the normal hydrogen peroxide producing Lactobacillus sp. in the vagina with high concentrations of anaerobic bacteria (e.g., Prevotella sp. and Mobiluncus sp.), *G. vaginalis*, Ureaplasma, Mycoplasma, and numerous fastidious or uncultivated anaerobes. Some women experience transient vaginal microbial changes, whereas others experience them for longer intervals of time. Among women presenting for care, BV is the most prevalent cause of vaginal discharge or malodor; however, in a nationally representative survey, most women with BV were asymptomatic (*203*).

BV is associated with having multiple male or female partners, a new sex partner, douching, lack of condom use, and lack of vaginal lactobacilli; women who have never been sexually active are rarely affected (*589*). The cause of the microbial alteration that precipitates BV is not fully understood, and whether BV results from acquisition of a single sexually transmitted pathogen is not known. Nonetheless, women with BV are at increased risk for the acquisition of some STDs (e.g., HIV, *N. gonorrhoeae*, *C. trachomatis*, and HSV- 2), complications after gynecologic surgery, complications of pregnancy, and recurrence of BV (*590-593*). BV also increases the risk for HIV transmission to male sex partners (*594*). Although BV-associated bacteria can be found in the male genitalia, treatment of male sex partners has not been beneficial in preventing the recurrence of BV (*595*).

Diagnostic Considerations

BV can be diagnosed by the use of clinical criteria (i.e., Amsel's Diagnostic Criteria) (*596*) or Gram stain. A Gram stain (considered the gold standard laboratory method for diagnosing BV) is used to determine the relative concentration of lactobacilli (i.e., long Gram-positive rods), Gram-negative and Gram-variable rods and cocci (i.e., *G. vaginalis*, *Prevotella*, *Porphyromonas*, and peptostreptococci), and curved Gram-negative rods (i.e., *Mobiluncus*) characteristic of BV. Clinical criteria require three of the following symptoms or signs:

- homogeneous, thin, white discharge that smoothly coats the vaginal walls;
- clue cells (e.g., vaginal epithelial cells studded with adherent coccobacilli) on microscopic examination;

- pH of vaginal fluid >4.5; or
- a fishy odor of vaginal discharge before or after addition of 10% KOH (i.e., the whiff test).

Detection of three of these criteria has been correlated with results by Gram stain (*597*). Other tests, including Affirm VP III (Becton Dickinson, Sparks, MD), a DNA hybridization probe test for high concentrations of *G. vaginalis*, and the OSOM BV Blue test (Sekisui Diagnostics, Framingham, MA), which detects vaginal fluid sialidase activity, have acceptable performance characteristics compared with Gram stain. Although a prolineaminopeptidase card test is available for the detection of elevated pH and trimethylamine, it has low sensitivity and specificity and therefore is not recommended. PCR has been used in research settings for the detection of a variety of organisms associated with BV, but evaluation of its clinical utility is still underway. Detection of specific organisms might be predictive of BV by PCR (*598,599*). Additional validation is needed before these tests can be recommended to diagnose BV. Culture of *G. vaginalis* is not recommended as a diagnostic tool because it is not specific. Cervical Pap tests have no clinical utility for the diagnosis of BV because of their low sensitivity and specificity.

Treatment

Treatment is recommended for women with symptoms. The established benefits of therapy in nonpregnant women are to relieve vaginal symptoms and signs of infection. Other potential benefits to treatment include reduction in the risk for acquiring *C. trachomatis, N. gonorrhoeae*, *T. vaginalis*, HIV, and herpes simplex type 2 (*592,593,600*).

Recommended Regimens

- **Metronidazole** 500 mg orally twice a day for 7 days
  OR
- **Metronidazole** gel 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days
  OR
- **Clindamycin** cream 2%, one full applicator (5 g) intravaginally at bedtime for 7 days

Alcohol consumption should be avoided during treatment with nitroimidazoles. To reduce the possibility of a disulfiram-like reaction, abstinence from alcohol use should continue for 24 hours after completion of metronidazole. Clindamycin cream is oil-based and might weaken latex

condoms and diaphragms for 5 days after use (refer to clindamycin product labeling for additional information).

Women should be advised to refrain from sexual activity or use condoms consistently and correctly during the treatment regimen. Douching might increase the risk for relapse, and no data support the use of douching for treatment or relief of symptoms.

Alternative Regimens

- **Tinidazole** 2 g orally once daily for 2 days
  OR
- **Tinidazole** 1 g orally once daily for 5 days
  OR
- **Clindamycin** 300 mg orally twice daily for 7 days
  OR
- **Clindamycin** ovules 100 mg intravaginally once at bedtime for 3 days*

*Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g., condoms and vaginal contraceptive diaphragms). Use of such products within 72 hours following treatment with clindamycin ovules is not recommended.

Alcohol consumption should be avoided during treatment with nitroimidazoles. To reduce the possibility of a disulfiram-like reaction, abstinence from alcohol use should continue for 72 hours after completion of tinidazole.

Alternative regimens include several tinidazole regimens (*601*) or clindamycin (oral or intravaginal) (*602*). An additional regimen includes metronidazole (750-mg extended release tablets orally once daily for 7 days); however, data on the performance of this alternative regimen are limited.

Certain studies have evaluated the clinical and microbiologic efficacy of using intravaginal lactobacillus formulations to treat BV and restore normal flora (*603-607*). Overall, no studies support the addition of any available lactobacillus formulations or probiotic as an adjunctive or replacement therapy in women with BV. Further research efforts to determine the role of these regimens in BV treatment and prevention are ongoing.

Other Management Considerations

All women with BV should be tested for HIV and other STDs.

Follow-Up

Follow-up visits are unnecessary if symptoms resolve. Because persistent or recurrent BV is common, women should be advised to return for evaluation if symptoms recur. Detection of certain BV-associated organisms has been associated with antimicrobial resistance and might be predictive of risk for subsequent treatment failure (*608-613*). Limited data are available regarding optimal management strategies for women with persistent or recurrent BV. Using a different recommended treatment regimen can be considered in women who have a recurrence; however, retreatment with the same recommended regimen is an acceptable approach for treating persistent or recurrent BV after the first occurrence (*614*). For women with multiple recurrences after completion of a recommended regimen, 0.75% metronidazole gel twice weekly for 4–6 months has been shown to reduce recurrences, although this benefit might not persist when suppressive therapy is discontinued (*615*). Limited data suggest that an oral nitroimidazole (metronidazole or tinidazole 500 mg twice daily for 7 days) followed by intravaginal boric acid 600 mg daily for 21 days and then suppressive 0.75% metronidazole gel twice weekly for 4–6 months for those women in remission might be an option for women with recurrent BV (*616*). Monthly oral metronidazole 2g administered with fluconazole 150 mg has also been evaluated as suppressive therapy; this regimen reduced the incidence of BV and promoted colonization with normal vaginal flora (*617*).

Management of Sex Partners

Data from clinical trials indicate that a woman's response to therapy and the likelihood of relapse or recurrence are not affected by treatment of her sex partner(s) (*595*). Therefore, routine treatment of sex partners is not recommended.

Special Considerations

Allergy, Intolerance, or Adverse Reactions

Intravaginal clindamycin cream is preferred in case of allergy or intolerance to metronidazole or tinidazole. Intravaginal metronidazole gel can be considered for women who are not allergic to metronidazole but do not tolerate oral metronidazole. It is advised to avoid consuming alcohol during treatment with nitroimidazoles. To reduce the possibility of a disulfiram-like reaction, abstinence from alcohol use should continue for 24 hours after completion of metronidazole or 72 hours after completion of tinidazole.

Pregnancy

Treatment is recommended for all symptomatic pregnant women. Studies have been undertaken to determine the efficacy of BV treatment among this population, including two trials demonstrating that metronidazole was efficacious during pregnancy using the 250-mg regimen (*618,619*); however, metronidazole administered at 500 mg twice daily can be used. One trial involving a limited number of participants revealed treatment with oral metronidazole 500 mg twice daily to be equally effective as metronidazole gel, with cure rates of 70% using Amsel criteria to define cure (*620*). Another trial demonstrated a cure rate of 85% using Gram-stain criteria after treatment with oral clindamycin (*621*). Multiple studies and meta-analyses have failed to demonstrate an association between metronidazole use during pregnancy and teratogenic or mutagenic effects in newborns (*622,623*). Although older studies indicated a possible link between use of vaginal clindamycin during pregnancy and adverse outcomes for the newborn, newer data demonstrate that this treatment approach is safe for pregnant women (*624*). Because oral therapy has not been shown to be superior to topical therapy for treating symptomatic BV in effecting cure or preventing adverse outcomes of pregnancy, symptomatic pregnant women can be treated with either of the oral or vaginal regimens recommended for nonpregnant women. Although adverse pregnancy outcomes, including premature rupture of membranes, preterm labor, preterm birth, intra-amniotic infection, and postpartum endometritis have been associated with symptomatic BV in some observational studies, treatment of BV in pregnant women can reduce the signs and symptoms of vaginal infection. A meta-analysis has concluded that no antibiotic regimen prevented preterm birth (early or late) in women with BV (symptomatic or asymptomatic). However, in one study, oral BV therapy reduced the risk for late miscarriage, and in two additional studies, such therapy decreased adverse outcomes in the neonate (*625*).

Treatment of asymptomatic BV among pregnant women who are at high risk for preterm delivery (i.e., those with a previous preterm birth) has been evaluated by several studies, which have yielded mixed results. Seven trials have evaluated treatment of pregnant women with asymptomatic BV at high risk for preterm delivery: one showed harm (*626*), two showed no benefit (*627,628*), and four demonstrated benefit (*618,619,629,630*).

Similarly, data are inconsistent regarding whether treatment of asymptomatic BV among pregnant women who are at low risk for preterm delivery reduces adverse outcomes of pregnancy. One trial demonstrated a 40% reduction in

spontaneous preterm birth among women using oral clindamycin during weeks 13–22 of gestation (*630*). Several additional trials have shown that intravaginal clindamycin given at an average gestation of >20 weeks did not reduce likelihood of preterm birth (*628*,*631-633*). Therefore, evidence is insufficient to recommend routine screening for BV in asymptomatic pregnant women at high or low risk for preterm delivery for the prevention of preterm birth (*111*).

Although metronidazole crosses the placenta, no evidence of teratogenicity or mutagenic effects in infants has been found in multiple cross-sectional and cohort studies of pregnant women (*634*). Data suggest that metronidazole therapy poses low risk in pregnancy (*317*).

Metronidazole is secreted in breast milk. With maternal oral therapy, breastfed infants receive metronidazole in doses that are less than those used to treat infections in infants, although the active metabolite adds to the total infant exposure. Plasma levels of the drug and metabolite are measurable, but remain less than maternal plasma levels (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACTExternal). Although several reported case series found no evidence of metronidazole-associated adverse effects in breastfed infants, some clinicians advise deferring breastfeeding for 12–24 hours following maternal treatment with a single 2-g dose of metronidazole (*635*). Lower doses produce a lower concentration in breast milk and are considered compatible with breastfeeding (*636*,*637*). Data from studies of human subjects are limited regarding the use of tinidazole in pregnancy; however, animal data suggest that such therapy poses moderate risk. Thus tinidazole should be avoided during pregnancy (*317*).