

# BV update: eliminating diagnostic confusion

*In the absence of universally accepted data, 3 leading authorities review the evidence on bacterial vaginosis and discuss their approaches to diagnosing and treating this common vaginal affliction.*

By SEBASTIAN FARO, MD, PhD, WILLIAM LEDGER, MD, and SHARON HILLIER, PhD

**T**he number one reason women visit their gynecologists is for the treatment of vaginal infections. Yet a recent Gallup survey found that only 36% had ever heard of bacterial vaginosis (BV), the most common type of vaginal infection, affecting 1 in 4 American women. BV is a disease caused by an overgrowth of anaerobic bacteria and *Gardnerella*, all of which can be found in low numbers in the healthy vagina. In fact, women who have been diagnosed with BV have up to 1,000 times more anaerobic bacteria than normal women.

Studies have shown that many women confuse the symptoms of BV with a yeast infection and often self-medicate with over-the-counter preparations. Unlike *Candida*, however, BV has been associated with pelvic inflammatory disease (PID), as well as an increased risk of endometritis, cer-

vicitis, and in pregnant women, premature delivery. Therefore, it is imperative that Ob/Gyns properly diagnose and treat BV while creating greater awareness of the signs and symptoms of this widespread disorder among their patients. Here, Sebastian Faro, MD, PhD, William Ledger, MD, and Sharon Hillier, PhD, respond to OBG MANAGEMENT editors' questions on appropriate diagnosis, screening, and management modalities to combat this potentially dangerous yet treatable condition.

**OBG MANAGEMENT:** How does a woman contract BV? What are the predisposing factors?

**Dr. Ledger:** In many cases, it is related to sexual activity, though there are certainly women who are not sexually active who can get it. Basically, there's a change in the bacterial flora of the vagina. Unfortunately, what triggers that change is unknown.

*continued on page 68*

## The panelists



**William Ledger, MD**, is chairman emeritus and professor of OBG at the New York Weill Cornell Medical Center in New York City.



**Sebastian Faro, MD, PhD**, is clinical professor of OBG and reproductive sciences at the University of Texas-Houston Health Science Center in Houston.



**Sharon Hillier, PhD**, is professor of OBG and reproductive sciences at the University of Pittsburgh School of Medicine in Pennsylvania.

## Key points

- Physicians should not diagnose BV with a culture. A standard culture will not identify the number of anaerobic bacteria.
- In diagnosing BV, an Ob/Gyn must perform a microscopic exam, along with a whiff test and pH.
- Metronidazole and clindamycin are only 66% effective in treating BV.
- Topical clindamycin causes a temporary overgrowth of *E. coli* and *Enterococcus* in the vagina.
- Women whose vaginal microflora is colonized with hydrogen peroxide-producing *Lactobacillus* are less likely to acquire BV.
- All women should be screened for BV during an annual exam.

**Dr. Faro:** I think an alteration in pH levels stimulates a change in the vaginal microflora. We don't know what causes that, but this alteration stimulates other bacteria such as *Gardnerella* to grow. Frequency of sexual intercourse does affect the pH and flora.

**Dr. Hillier:** In following a group of women without BV over time, we have found that women who use douching products and those with greater levels of sexual activity are more likely to acquire BV. However, there are many women who are monogamous and who do not douche who acquire BV. In our studies, it turned out that women who had H<sub>2</sub>O<sub>2</sub>-producing *Lactobacillus* vaginally were significantly less likely to acquire BV<sup>1</sup> (Figure 1). There is no way presently for a woman or her physician to tell whether the *Lactobacillus* colonizing the vagina produces H<sub>2</sub>O<sub>2</sub>. Nevertheless, we think that many women who acquire BV simply lack the most protective kind of normal flora.

**OBG MANAGEMENT:** If there is a positive whiff test when examining the patient, is it necessary to do a wet mount or a pH test?

**Dr. Hillier:** A positive whiff test indicates that there are high levels of anaerobic bacteria producing trimethylamine in the vaginal flora. In our experience, nearly every

woman who has a positive whiff test will also have an elevated pH. It is still advisable to do a wet mount on a woman with a positive whiff test in order to evaluate for mixed infections with other agents such as *Trichomonas vaginalis*.

**Dr. Ledger:** Unfortunately, many physicians are trying to cut corners on things that are very simple to do. An Ob/Gyn cannot diagnose any vaginitis unless he or she knows how to do a microscopic exam, along with a whiff test and pH (Figure 2). The whole process takes seconds. If they are not doing these tests, they ought to be sending patients to someone who is.

**Dr. Faro:** I think it is critical to perform a microscopic analysis, a whiff test, and a pH. If you only rely on the whiff test, you often will miss BV. Individuals can have an elevated pH of 5, 5.5, or 6, and not have BV. This could signify a dominant flora with *E. coli* or some other bacteria. Furthermore, the *Trichomonas* patient will have a positive whiff test, a pH that's 5 or greater, and not have BV.

**OBG MANAGEMENT:** How important is it to submit a Gram stain to the lab? Should a physician wait for these results to begin treatment?

**Dr. Faro:** Often, we'll get back a diagnosis of BV on a Gram stain. I'll then go back and find that these patients had a normal pH and large bacillary forms, which is in contradistinction to what the cytopathologist is reading. What this means is that Gram stains can be misread.

**Dr. Ledger:** The Gram stain is done when physicians don't have microscopes in their offices. But there is a two-fold problem: the results come back a few days after the patient is seen, and there is a danger of misdiagnosis. I get a diagnosis of BV from a Gram stain at least once a week on patients who had normal pHs and didn't have a positive whiff test. I think it may be identifying patients who have changes in their flora, but who don't clinically have BV. Unfortunately, there are very few physicians who have microscopes or pH paper in their offices. Often, women will be treated for a yeast infection. In that situation, a Gram stain would be more useful. The bottom line is

## Vaginal infections: detecting the difference

	<b>BV</b>	<b>Yeast</b>	<b>Trichomoniasis</b>
<b>Odor</b>	Foul, fishy	None	Foul or fishy
<b>Discharge</b>	Thin, milky-white or gray	Thick, curdy, white	Yellow-green-gray, frothy or sticky
<b>Discomfort</b>	Itching, burning	Itching, burning	Painful urination, itch
<b>Cause</b>	Bacteria	Yeast	Parasite
<b>Health risks</b>	PID, cervicitis, cervical abnormality, endometritis, obstetric complications	None	Obstetric problems

that every Ob/Gyn should have a microscope and pH paper at his or her disposal.

**Dr. Hillier:** I agree. The diagnosis of BV is best made using a microscopic exam of vaginal fluid, evaluation of pH, and the whiff test. However, if a microscope is unavailable or microscopy is not interpretable, a Gram stain of vaginal fluid can be a useful test for BV. Because the test needs to be sent to a central laboratory, it is not as practical as the wet mount, pH, and whiff test, but it does have good correlation with a well-performed clinical examination. If the results are in question following the clinical evaluation, it may be prudent to delay treatment until Gram stain diagnosis is available, which should take no more than 1 working day.

**OBG MANAGEMENT:** Who should be screened and when?

**Dr. Faro:** I think anyone who has any type of abnormality in the lower genital tract, including complaints of discomfort, burning, itching, and odor should be screened. In addition, a patient who is going to have gynecologic surgery or vaginal surgery should be screened. Also, I screen all gravidas, but not to prevent preterm labor. A gravida who has an abnormal flora and has a cesarean is at a greater risk of developing postpartum endometritis than a gravida who has a normal flora.<sup>2</sup>

**Dr. Ledger:** We screen almost everyone. Screening definitely should be done if the patient is complaining of abnormal discharge

or has abnormal vulvar or vaginal findings.

**Dr. Hillier:** Women with symptoms of vaginal discharge or odor should always be evaluated for the presence of BV and other causes of vaginitis. Screening of asymptomatic women should be undertaken for those who are planning termination of pregnancy. Randomized, placebo-controlled trials have demonstrated that treatment of asymptomatic women with BV can reduce the incidence of post-abortion PID.<sup>3</sup> There is a consistent relationship between BV and post-hysterectomy infections, which has led some authorities to recommend routine screening of women before planned hysterectomy.<sup>4</sup>

**OBG MANAGEMENT:** Do you recommend BV screening during an annual exam? A recent study noted that approximately 50% of women with BV are asymptomatic.

**Dr. Faro:** Yes. I normally perform a pH test then. If the pH is 4 and she has no symptoms, I stop right there. If the pH is more

**Since there is a consistent relationship between BV and post-hysterectomy infections, some authorities recommend routine pre-hysterectomy screening.**

than 4, I will progress to a whiff test and a microscopic examination of the discharge just to be certain. The dilemma is when you have a lady who may be totally asymptomatic with no complaints, and you find this abnormality in her vaginal flora. Should you treat or not treat? I tend to err on the side of

*continued on page 73*

## Bacterial vaginosis

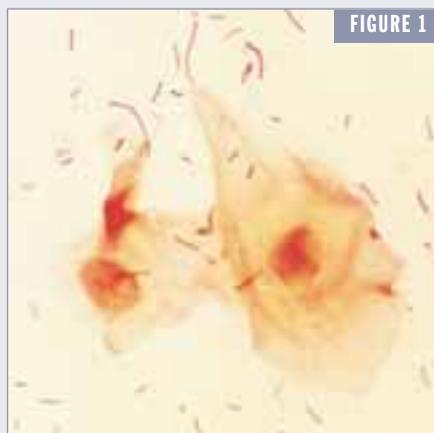


FIGURE 1

*Normal vaginal microflora as seen under a microscope. The flat segments depict the helpful bacteria, lactobacilli.*

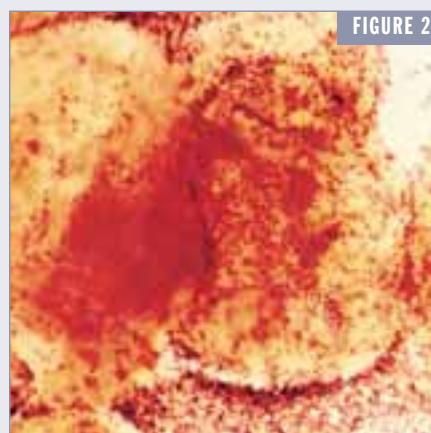


FIGURE 2

*An overgrowth of harmful bacteria called clue cells detected under the microscope confirms a diagnosis of BV.*

not treating because an altered flora does not necessarily mean BV. One of the things we're seeing a lot of lately is group B vaginitis, if such a thing exists.

**Dr. Ledger:** I agree. I also see something called desquamative vaginitis. In 40% of these women, the predominant organism is a group B streptococcus. So I'm not sure whether it's desquamative vaginitis or group B strep. One of the realities is that we see all the patients who are not getting better with their first round of treatment.

**OBG MANAGEMENT:** Gravidas at 23 to 26 weeks' gestation with BV are 40% more likely to deliver a low-birth-weight baby. If you find that gravidas have BV early in their pregnancy, how often do you screen them thereafter?

**Dr. Ledger:** I screen these patients every time I do a vaginal exam. But the problem is I'm not going to diagnose any patients who have asymptomatic BV because I don't do a vaginal exam at every prenatal visit. Hoyme recommends that patients examine themselves twice a week. If they have an alkaline pH, they are to see the doctor right away. If the doctor confirms BV, they are treated.<sup>5</sup> However, I think more studies are needed to determine whether

twice-weekly screening is appropriate in the United States. Guidelines should not be established until we have some good data.

**Dr. Faro:** I also screen my patients every time I do a vaginal exam. As for twice-weekly screening, there has not been any research that has statistically shown a cause and effect between BV and preterm delivery (PTD). To come up with screening guidelines for something we aren't sure is really causing a problem is not in our best interest. Furthermore, we really don't have good treatments for these women. Metronidazole and clindamycin are only 66% effective, and they are a short-term treatment.<sup>6</sup>

**OBG MANAGEMENT:** Can you describe how BV causes preterm delivery?

**Dr. Hillier:** Although we understand that BV leads to an increased incidence of chorioam-

**To normalize pH levels, prescribe Aci-jel and/or boric acid vaginal capsules or suppositories.**

nion infection, placental inflammation, and amniotic fluid infection, the mechanisms by which BV causes preterm delivery are not completely understood. Failure to understand the pathophysiology of infection-related PTD

*continued on page 74*

has complicated these issues. Most women with BV deliver at term without complication. However, a really important question is why some women with BV deliver preterm. When we are better able to target the subset of women at increased risk—and offer them preventive treatment—I believe we will begin to see successes with clinical trials.

**OBG MANAGEMENT:** The current treatment for BV in gravidas and nonpregnant women is metronidazole and clindamycin. Because clinical studies have shown that these medications are not 100% effective, should physicians consider other agents? If so, what would these be?

**Dr. Ledger:** Certainly. The Europeans have come up with a number of alternate treatments that have lactobacilli in them. These are used to encourage the flora to get back to normal. I know there are researchers in the United States working on this, too. And Secundo Guaschino of Italy recently presented a paper at the seventh annual meeting of the International Infectious Disease Society of Obstetrics and Gynecology in which estrogen therapy for menopausal women resulted in a more normal flora dominated by lactobacilli. Of note, pretreated women with an absence of lactobacilli did not have BV.

**Dr. Faro:** Yes, researchers are working in this area. It is important to note that if *Lactobacillus* is the key organism needed to normalize the vaginal flora, the only way you will be able to correct an altered flora is by creating an environment in the vagina that is conducive to the growth of *Lactobacillus*. But the problem is these patients have such an altered pH that even *Lactobacillus* cannot compete well with other bacteria. To normalize pH levels, I prescribe either 1 applicator of Aci-jel (*Ortho Pharmaceutical Corp, Raritan, NJ*) twice a day for 2 to 3 weeks, and/or 600 mg of boric acid vaginal capsules or suppositories twice a day for 14 days.

**Dr. Ledger:** I think you will find that these agents will not be effective in the long term. But these are things that need to be

confirmed by testing.

**Dr. Hillier:** Current treatment guidelines for BV are based on a substantial body of literature generated over the past 20 years. Both metronidazole and clindamycin have excellent activity against anaerobic bacteria, which are thought to be the primary pathogens among women with BV. Clinical trials have taught us that agents such as sulfa cream or quinolones, which do not have anaerobic activity, yield lower cure rates overall than either metronidazole or clindamycin.<sup>7</sup> It is

important to note that topical clindamycin, because of its broad-spectrum activity against *Lactobacillus* and other organisms, causes a temporary overgrowth of *E. coli* and *Enterococcus* in the vagina.<sup>8</sup> This overgrowth is thought to lead to an increased incidence of early PTD and, perhaps,

neonatal infections in women given intravaginal clindamycin treatment during pregnancy. Therefore, it is important for clinicians to remember that intravaginal clindamycin cream is not a recommended treatment by the Centers for Disease Control and Prevention (CDC) for BV during pregnancy.<sup>9</sup>

**OBG MANAGEMENT:** Does it follow then that metronidazole and clindamycin do not help reestablish normal vaginal flora?

**Dr. Hillier:** In our experience, women who are treated with oral or intravaginal metronidazole have a much more rapid return of normal vaginal flora than women treated with clindamycin. Clindamycin has activity against *Lactobacillus*, so that in the week or two following therapy, women have very low levels of lactobacilli in the vagina.<sup>10</sup>

**Dr. Ledger:** I think these agents help cut down on the numbers of bacteria, which is certainly a better environment for reestablishing normal flora.

**Dr. Faro:** The problem with antibiotics is that they are broad-spectrum agents. They aren't guns with a bullet directed at a certain bacterium or even a certain group of bacteria. They affect all bacteria. This is why we have such poor results.

**Dr. Ledger:** I think we need something more

*continued on page 77*

**Studies have shown that vaginal antifungal cream may markedly reduce the number of good lactobacilli in women who use them.**

specific, but to get it we're going to have to acquire more information on lactobacilli. On the other hand, postmenopausal patients with absent lactobacilli and no BV cast doubt in my mind that the lack of lactobacilli is the sole cause of BV.

**Dr. Faro:** I've seen patients whose counts run around 10 to 4 or 10 to 5, yet they have healthy floras. I think the reason is that the *Lactobacillus* species they have are very potent producers of bacteriocin and hydrogen peroxide. In addition, we have found some ladies with strains or biotypes of *Gardnerella* who get recurrent BV and some who never have had the infection. So we end up dealing with a dual problem. We have a shift in the environment and we're nurturing an organism that's unaffected by the biodefense mechanisms that *Lactobacillus* produces. It's very complex because we're trying to change the environment of an ecological system to make it more conducive to the growth of *Lactobacillus*.

**OBG MANAGEMENT:** Since we know that lactobacilli excrete the natural disinfectant hydrogen peroxide to help maintain a healthy and normal balance of microorganisms in the vagina, is there an agent or a way to recolonize the vagina with it?

**Dr. Hillier:** In order for *Lactobacillus* to colonize the vagina it is necessary for the organism to attach to the vaginal epithelial cells. We are currently conducting trials to evaluate the value of recolonization therapy using a human-derived strain of a peroxide-producing *Lactobacillus*. In our study, women with BV were treated with metronidazole and randomized to receive capsules containing either 10<sup>8</sup> *Lactobacillus crispatus* or placebo. The results are promising.

**Dr. Ledger:** There are other factors to consider since some women do not have a vaginal environment conducive to the health of lactobacilli. In fact, Guaschino showed that postmenopausal women not receiving HRT achieved a lactobacilli-dominated vaginal flora with exogenous estrogen therapy.

**OBG MANAGEMENT:** A recent survey noted that 30%

of women thought it was acceptable to self-medicate symptoms of vaginal infections with home remedies. What are your thoughts?

**Dr. Faro:** Patients who self-diagnose and self-medicate often misdiagnose and medicate with the wrong agent.

**Dr. Ledger:** That's right. In fact, Onderdonk, a premier clinical microbiologist at Harvard Medical School, looked at the impact of 1 vaginal antifungal cream and demonstrated that it markedly reduced the number of good lactobacilli in women who used it.<sup>11</sup> It could be that some of these women who are self-

**The male ejaculate may alter the vaginal microflora because it is usually very alkaline and has some immunologic-suppressing activities.**

---

medicating with over-the-counter antifungals may be altering their vaginal flora and doing more harm than good by creating an abnormal bacterial environment.

**Dr. Faro:** Absolutely. There are agents such as clotrimazole and tioconazole that have antibacterial activity that may alter their flora.<sup>12,13</sup>

**OBG MANAGEMENT:** How do you manage a patient with recurrent BV?

**Dr. Hillier:** There are no clear guidelines at present based on large, randomized, placebo-controlled trials showing that any specific regimen is effective for management of women with recurrent BV. Based on a small, randomized treatment trial presented by Sobel at the second international BV meeting, it was suggested that use of intravaginal metronidazole therapy for 10 days followed by twice-weekly intravaginal metronidazole for 3 months effectively suppressed the recurrence of BV in most women.<sup>14</sup> Since this is a well-tolerated regimen that presents a practical approach, we currently employ this strategy. Larger randomized trials evaluating this strategy are ongoing.

**Dr. Ledger:** I have never been a big fan of giving antibiotics to the male partner in women with recurrent BV. One of the things that I do with recurrent BV patients is have the male use a condom. While there is no scientific evidence, I find that these women do not

*continued on page 78*

experience as many recurrences. The male ejaculate can alter the vaginal microflora because it is usually very alkaline. Also, the male ejaculate does have some immunological-suppressing activities. Sperm are foreign antigens that may inhibit the mechanisms that help control the growth of bacteria in the vagina. This may be what is affecting the overgrowth in some women

**Dr. Faro:** When we see a woman with recurrent BV, we base our treatment on the premise that this is an ecological situation and not an infection. We then try to change the pH

using Aci-jel and boric acid suppositories. Currently, we're looking at some buffering agents in clinical studies. In addition, we also ask the patient not to have sexual intercourse because, as Dr. Ledger suggested, the male ejaculate can

have a tremendous impact on the vaginal ecosystem. If we're fortunate to get the pH down below 4.5, we usually see a correction. In instances where we're having difficulty getting the pH down, we will go to an antibiotic, such as oral metronidazole.

**OBG MANAGEMENT:** Once a patient has been treated, what is the best way to determine normal vaginal microflora? When is she in the clear, so to speak?

**Dr. Faro:** We go back and do a pH and microscopic analysis. If a physician relies solely on a whiff test, he or she is going to be in error because many ladies will have a pH that is 5 or greater and not have BV. This is because the flora has shifted and is now dominated by other bacteria. The pH is key for us because if it has not gone below 4.5, we know there's still a problem.

**Dr. Hillier:** The most underutilized test in women's health today is the vaginal pH. The easiest way to determine whether there has been reestablishment of *Lactobacillus*-predominant flora is to measure vaginal pH. A vaginal pH of less than 4.7 indicates a predominance of vaginal lactobacilli.

**Dr. Ledger:** I'd like to stress here that, despite

dozens of articles and hundreds of chapters in medical textbooks, physicians should not diagnose BV with a culture. They often will get a report showing the presence of *Gardnerella*. The problem is that *Gardnerella* can be present in the vagina of normal people and in women who have been successfully treated. A standard culture will not identify the number of anaerobic bacteria.

**OBG MANAGEMENT:** Women often experience a certain amount of discharge. What would you consider normal?

**Dr. Faro:** Normal discharge is white to slightly gray in color, odorless, and has a pH of 3.8 to 4.2. When you look at it microscopically, the squamous cells are well-estrogenized and white blood cells are rare. Also, you see only 1 dominant form of bacteria: large rods. When you culture this, it will be *Lactobacillus*. If you do the microbiology, you'll find other bacteria, but their counts are 10 to 3 or lower per milliliter of fluid. Lastly, the amount of discharge a woman has is also related to her hormonal status.

**OBG MANAGEMENT:** A recent study conducted by the CDC found that many women still douche despite the fact that clinicians do not support the practice. In fact, douching has been linked to the development of BV. What should physicians recommend to their patients?

**Dr. Ledger:** I would not advise a patient to douche. However, I don't believe that douching is a risk factor for BV. Rather, sexual intercourse and exposure to the male ejaculate are such culprits. Retrospective epidemiological studies have linked douching to BV. But these same analyses overstated the risk of infection with regard to intrauterine devices, as indicated in a recent study from Mexico City.<sup>15</sup> While it is said that douching lowers the number of good lactobacilli in the vagina, over-the-counter antifungal agents have the same impact on vaginal lactobacilli. Further, the absence of lactobacilli in postmenopausal women is not uniformly associated with BV. The danger of douching is when women who have been exposed to bacterial agents delay medical care because of this primary intervention method.

**Dr. Hillier:** There is definitely a link between

**When examined  
microscopically, normal  
discharge contains only 1  
dominant form of bacteria—  
*Lactobacillus*.**

douching and acquiring BV. We think that douching can deplete the beneficial *Lactobacillus* from the vagina, especially those with unstable flora. We routinely counsel the women who come to our clinic to avoid douching.

**Dr. Faro:** Many of my patients have been douching for years—more than 10 to 20 years—and have experienced problems with vaginitis. This practice has been going on for several generations. Patients who have never douched are discouraged from beginning such a practice because it presents no benefits and there is the possibility of an adverse reaction. However, it would be difficult to get women who have not had an adverse effect to douching to discontinue a practice that has been an integral part of their hygienic practices.

**OBG MANAGEMENT:** Many women mistake BV for a yeast infection and seek over-the-counter medication. How can physicians manage and educate this population?

**Dr. Hillier:** Most women who mistake BV for a yeast infection have never heard of BV. In fact, most women have been “educated” by reading articles in women’s magazines and watching television ads. Although it is important for physicians to review the symptoms of BV and other common infections with their patients, they also should advise them that symptoms are not necessarily predictive of specific diagnoses. Among women seeking care at our hospital, we find that only 1 in 4 who think they have yeast infections actually do have yeast vaginitis. When we followed women who had absolutely no evidence of yeast by culture, assessing them at 4-month intervals over a year, 25% of them reported using vaginal yeast medication. The overuse of topical medications and the inaccuracy of self-diagnosis is a huge problem in women’s health today. Personally, I would like to see much less diagnosis over the telephone and better testing for vaginal infections so that women are given the correct diagnosis.

**Dr. Faro:** Unfortunately, even we clinicians can look at a wet mount and miss a field that has yeast in it. We’ll look at 10 fields on each patient. Yet, when we culture that patient, it

comes back positive. That raises an interesting question. Is it the yeast that’s causing their symptoms or not?

**Dr. Ledger:** Most studies suggest that only 30% to 40% of women who think they have yeast, actually do. If there were a good over-the-counter test that was sensitive and specific, that would be terrific. But I don’t see that on the horizon quite yet. ■

**The overuse of topical medications and the inaccuracy of self-diagnosis is a huge problem.**

#### REFERENCES

1. Hawes SE, Hillier SL, Benedetti J, et al. Hydrogen peroxide-producing lactobacilli and acquisition of vaginal infections. *JID*. 1996;174:1058-1063.
2. Watts DH, Krohn MA, Hillier SL, et al. Bacterial vaginosis as a risk factor for post-cesarean endometritis. *Obstet Gynecol*. 1990;75:52-58.
3. Larsson PG, Bergman B, Forsum U, et al. Mobiluncus and clue cells as predictors of PID after first-trimester abortion. *Acta Obstet Gynecol Scand*. 1989;68:217-220.
4. Larsson PG, Platz-Christensen J, Thejls H, et al. Incidence of pelvic inflammatory disease after first-trimester legal abortion in women with bacterial vaginosis after treatment with metronidazole: a double-blind, randomized study. *Am J Obstet Gynecol*. 1992;166:100-103.
5. Hoyme U, et al. Results and potential consequences of the Thuringa prematurity prevention campaign 2000. *Geburtsch Frauenbeilk*. 2002;62:257-263.
6. Paavonen J, Mangioni C, Martin MA, et al. Vaginal clindamycin and oral metronidazole for bacterial vaginosis: a randomized trial. *Obstet Gynecol*. 2000;96:256-260.
7. Sobel JD, Chaim W, Thomason J, Livengood C, et al. Comparative study of intravaginal metronidazole and triple-sulfa therapy for bacterial vaginosis. *Infect Dis Obstet Gynecol*. 1996;4:66-70.
8. Hill GB, Livengood CH. Bacterial vaginosis-associated microflora and effects of topical intravaginal clindamycin. *Am J Obstet Gynecol*. 1994;171:1198-1204.
9. Centers for Disease Control and Prevention. 1998 guidelines for treatment of sexually transmitted diseases. *MMWR*. 1998;47(No. RR-1).
10. Hillier SL, Krohn MA, Watts DH, et al. Microbiologic efficacy of intravaginal clindamycin cream for the treatment of bacterial vaginosis. *Obstet Gynecol*. 1990;76:407.
11. Ross RA, et al. Effect of *Candida albicans* infection and clotrimazole treatment on vaginal microflora in vitro. *Obstet Gynecol*. 1995;86:925-930.
12. Clissold SP, Heel RC. Tioconazole: a review of its antimicrobial and therapeutic use in superficial mycoses. *Drugs*. 1986;31:29-51.
13. Jones RN, Cali MJ, Hoban D, et al. In vitro antimicrobial activity of tioconazole and its concentration in vaginal fluids following topical (vagi-stat-1 6.5%) application. *Diag Microbiol Infect Dis*. 1993;17:45-51.
14. Sobel JD, Leaman D. Suppressive maintenance therapy of recurrent bacterial vaginosis utilizing 0.75% metronidazole vaginal gel. *Int J Gynecol Obstet*. 1999;67:S41, abstract #010.
15. Hubacher D, et al. Use of copper intrauterine devices and the risk of tubal infertility among nulligravid women. *N Engl J Med*. 2001;345:561-567.

Dr. Faro reports no financial relationship with any companies whose products are mentioned in this article. Dr. Ledger reports receiving research grants from 3M. Dr. Hillier reports that she has received research grants on vaginitis treatments from 3M and Pfizer, and is a consultant for Johnson & Johnson.