JOURNAL OF CLINICAL MICROBIOLOGY, May 2003, p. 1925–1928 Vol. 41, No. 5
0095-1137/03/$08.00+0 DOI: 10.1128/JCM.41.5.1925–1928.2003

BVBlue Test for Diagnosis of Bacterial Vaginosis

Linda Myziuk,[1]* Barbara Romanowski,[1] and Stephen C. Johnson[2]

University of Alberta, Edmonton, Alberta, Canada,[1] Gryphus Diagnostics, L.L.C., Birmingham, Alabama[2]

Received 22 November 2002/Returned for modification 31 December 2002/Accepted 13 February 2003

Bacterial vaginosis (BV) is a disorder of the vaginal ecosystem characterized by a shift in the vaginal flora from the normally predominant *Lactobacillus* to one dominated by sialidase enzyme-producing mixed flora. It is the most common cause of abnormal vaginal discharge in adult women. The BVBlue system (Gryphus Diagnostics, L.L.C.) is a chromogenic diagnostic test based on the presence of elevated sialidase enzyme in vaginal fluid samples. BVBlue was compared to the standard method for diagnosing BV (Amsel criteria and Nugent score). Fifty-seven nonmenstruating women of ≥16 years of age who presented for a pelvic examination were recruited. Demographic features were collected via a self-administered questionnaire. The Amsel criteria were assessed based on three of four of the following characteristics of vaginal discharge: consistency, odor, pH, and presence of clue cells on Gram stain. BVBlue was compared to the Gram stain and Amsel criteria. The sensitivity, specificity, positive predictive value, and negative predictive value for BVBlue versus the Gram stain and Amsel criteria were 91.7, 97.8, 91.7, and 97.8% and 50.0, 100, 100, and 88.2%, respectively. A significantly greater proportion of patients with a vaginal pH of >4.5, a positive amine test, or with clue cells on vaginal Gram smear were found to have a positive BVBlue test ($P < 0.001$). Women previously treated for BV were 2.98 times more likely to have another episode of BV. BVBlue is a useful point-of-care diagnostic tool to provide a presumptive diagnosis of BV, especially in situations where microscopic capabilities are unavailable.

Bacterial vaginosis (BV) is the most common reason for abnormal vaginal discharge in adult women in North America (19). It is a disorder of the vaginal ecosystem characterized by a shift in the vaginal flora from the normally predominant *Lactobacillus* (7, 18) to one dominated by a mixed flora including *Gardnerella vaginalis* (2, 7, 15, 18, 19) and *Mobiluncus* (2, 15, 19), *Prevotella* (2, 3, 15, 18), *Bacteroides* (2, 3, 7, 15), and *Mycoplasma* (2, 7, 15, 18) species. Although the condition is associated with abnormal vaginal discharge, about half of the women with BV, diagnosed by the Amsel criteria, are symptom free (1). Accurate diagnosis of BV is important as it is associated with adverse pregnancy outcome (9, 10, 11, 12, 19), pelvic inflammatory disease (6, 19), chorioamnionitis (8, 10, 19), and endometritis (21). Symptomatic women should be diagnosed and treated to alleviate their discomfort and to decrease these serious sequelae.

The diagnosis of BV is generally made by using the Amsel criteria (1). This encompasses fulfilling three of the following four criteria: (i) presence of abnormal vaginal discharge, (ii) elevated vaginal pH (>4.5), (iii) positive amine odor test, and (iv) presence of clue cells on vaginal Gram smear. Evaluating Gram-stained vaginal smears also aids in the identification of BV (16). The Gram smear is traditionally scored by using the Nugent system (14). The Nugent system uses a scoring system from 0 to 10 based on the number of lactobacilli, gram-negative to gram-variable bacilli, and gram-negative curved bacilli. A score of ≥7 indicates BV infection.

Most women with this condition present to physicians' offices where microscopic capabilities are not available. Hence, it is not possible to completely assess the Amsel criteria without sending a vaginal sample to the lab. Therefore, the diagnosis is usually made on clinical grounds alone, which may be misleading. A point-of-care diagnostic test would refine the diagnosis and result in more appropriate use of antimicrobial agents.

The detection and measurement of microbial enzymes, in particular sialidase, has potential to be used to rapidly diagnose BV (22, 23). Sialidases are enzymes that play a role in bacterial nutrition, cellular interactions, and immune response evasion (4, 5). Sialidases also improve the ability of bacteria to adhere, invade, and destroy mucosal tissue (3, 23). They are present extensively among bacteria (5, 21), viruses, mycoplasmas, fungi, and protozoa (20, 21). Sialidases are secreted from anaerobic gram-negative bacterial rods such as *Bacteroides*, *Gardnerella*, and *Prevotella* species (3, 4, 13, 17, 21).

In a 1992 study, 84% of women diagnosed with BV (defined by the presence of a vaginal pH of >4.5, homogeneous vaginal discharge, odor in the presence of 10% KOH, and the presence of clue cells) demonstrated elevated levels of sialidase activity in their vaginal fluid (3). Further, 96% of women with BV and positive sialidase activity had sialidase-positive bacteria recovered from vaginal fluid. Increased levels of sialidase were not found in women without BV. Briselden et al. found that *Prevotella* and *Bacteroides* spp. are the probable sources of sialidase in patients with BV (3). They could not correlate the presence of *Gardnerella vaginalis*, *Mobiluncus* spp., *Peptostreptococcus* spp., or *Mycoplasma hominis* with increased sialidase activities of greater than 7 U (micromoles of 4-methylumbelliferone formed per milligram of protein per minute at 37°C).

McGregor et al. conducted a study to examine the association of BV with preterm birth and the presence of vaginal fluid mucinase and sialidase (11). They reported that 45% of women with BV (according to the Amsel criteria) demonstrated siali-

* Corresponding author. Mailing address: University of Alberta, #1000, 8215-112 St., Edmonton, Alberta T6G 2C8, Canada. Phone and fax: (780) 436-4900. E-mail: lmyziuk@docromanowski.com.

TABLE 1. Relationship of women with and without vaginal sialidase activity and previous diagnosis of STD[a]

STD	No. (%) of women with vaginal fluid sialidase activity ($n = 12$)	No. (%) of women without vaginal fluid sialidase activity ($n = 45$)	*P*
Chlamydia	2 (18.2)	7 (15.6)	NS
Genital HSV	0	7 (15.9)	NS
Genital HPV	6 (54.5)	12 (26.7)	NS
Gonorrhea	1 (8.3)	3 (6.7)	NS
HIV	0	2 (4.5)	NS
PID	0	1 (2.2)	NS
Syphilis	1 (8.3)	0	NS

[a] HSV, herpes simplex virus; HPV, human papillomavirus; HIV, human immunodeficiency virus; PID, pelvic inflammatory disease; NS, not significant.

dase activity versus 12.4% of women without BV ($P < 0.001$). The isolation of *G. vaginalis*, *Mobiluncus* spp., *M. hominis*, *Chlamydia trachomatis*, and yeast correlated with sialidase activity. This study did not specifically identify *Prevotella* spp. or other anaerobic bacteria associated with BV. McGregor et al.'s findings differ from those of Briselden et al. and may be due to differing microbiologic techniques used. At an 8-week follow-up visit, women with persistent vaginal fluid sialidase activity were at greater risk of preterm birth and premature rupture of membranes.

In another study, Smayevsky et al. used a filter paper spot test to indicate sialidase activity in 109 nonpregnant women (18). They found very good sensitivity (81%) and specificity (94%) of sialidase activity in vaginal secretions of women with BV (as defined by the presence of a vaginal pH of >4.5, amines, and clue cells). The prevalence of *Peptostreptococcus* spp., *Prevotella bivia*, *Porphyromonas* spp., *G. vaginalis*, and *M. hominis* demonstrated a strong association with BV ($P < 0.001$).

A rapid detection system to detect sialidase activity has been developed. The BVBlue system (Gryphus Diagnostics, L.L.C.) is a chromogenic diagnostic test for the detection of sialidase activity in vaginal fluid specimens. BVBlue detects vaginal fluid sialidase activity at levels of ≥7.8 U. One unit of sialidase activity is defined as the amount of enzyme required to liberate 1 nmol of substrate/ml/min at 37°C.

The purpose of this study was to compare the sensitivity and specificity of BVBlue to pH, amine odor, clinical characteristics of vaginal discharge, and vaginal Gram stain (Nugent scoring) in sexually active women. We also sought to correlate patient demographics with the diagnosis of BV.

MATERIALS AND METHODS

Study design. Women were recruited from a sexually transmitted disease clinic and an infectious disease referral practice. Nonmenstruating women of ≥16 years of age who presented for a pelvic examination, regardless of the reason, were eligible for entry into the study. Participants completed a self-administered questionnaire. The following information was collected: age of sexual debut, sexual orientation, number of lifetime sexual partners, number of partners in the last 6 months, date of last sexual contact, contraception utilized, use of condoms with last sexual partner, history of sexually transmitted diseases (STD), last menstrual period, date of last Pap smear, and Pap smear results. The patient's chief complaint as well as clinical findings of abnormal vaginal and/or cervical discharge, vaginal pH, and an amine odor test were recorded. A diagnosis of BV was based on both the Amsel criteria and the Gram stain results, which were immediately available.

A vaginal speculum, lubricated with water only, was inserted, and vaginal fluid was collected from the posterior fornix with two cotton swabs. One swab was used for pH determination and preparation of a slide for Gram staining. The second swab was utilized to undertake the BVBlue test. Amine odor was tested after removal of the speculum by adding 10% potassium hydroxide to the posterior lip of the speculum. The vaginal fluid was not cultured. The patient samples and study-related documents were identified by using a unique identifier.

The study was approved by the Health Ethics Review Board, Faculty of Medicine, University of Alberta.

Laboratory. The Gram-stained smear of vaginal discharge was assessed for normal vaginal flora and the presence or absence of hyphae, buds, polymorphonuclear cells, clue cells, and trichomonads by a medical laboratory technologist. The Gram-stained slide was assessed by using the Nugent scoring system (14).

The second swab was inserted in the BVBlue testing vessel and incubated for 10 min at 37°C. Two drops of BVBlue developer solution was added, and the color reaction was immediately read. A blue or green color indicated the sample contained elevated levels of sialidase and was therefore positive. A yellow color indicated a negative result and no increased sialidase activity.

Statistical analysis. Data were entered in the statistical analysis system (SAS). Probability values (*P*) were calculated by using the two-tailed Fisher exact test for each risk factor to compare the proportion of patients with or without sialidase activity. The relative risk of sialidase activity was calculated for each risk factor, including 95% confidence intervals (CI). Continuous variables, such as age, were compared relative to sialidase activity by using a two-sample *t* test. Probability values of <0.05 were considered significant. The kappa coefficient was used as a measure of intertest reliability. McNemar's chi-square test for paired designs was used to compare the two methods.

RESULTS

Demographics. Fifty-seven women consented to participate in the study. Their mean age was 30.7 years, and the mean age of sexual debut was similar for women with and without vaginal fluid sialidase activity, 17.2 and 17.5 years, respectively. There was no significant difference in the mean number of lifetime sexual partners or the mean number of partners within the past 6 months between women who had a positive or negative BVBlue test. Approximately 72% of the women with sialidase activity had their last sexual contact ≤7 days ago versus 45% of those women without sialidase activity ($P = 0.2$). There was no significant difference in the proportion of women utilizing any form of contraception and BVBlue results ($P = 0.3$).

Women with a history of STD were not more likely to have an elevated sialidase activity (Table 1). Although statistically insignificant, 54.5% of women with vaginal fluid sialidase activity had a previous diagnosis of genital warts versus 26.7% of women without sialidase activity ($P = 0.1$).

Some of the women (33.9%) had been previously treated for BV, and 72.7% of those had a recurrence of BV according to the presence of sialidase activity ($P = 0.004$) (Table 2). Women were not asked when they had received previous treatment. Women with a previous history of BV were 2.98 times more likely to have a positive BVBlue test. No significant correlation

TABLE 2. Relationship of women with and without vaginal sialidase activity and previous treatment of BV, *T. vaginalis*, or vaginal candidiasis infection

Condition previously treated	No. (%) of women with vaginal fluid sialidase activity ($n = 12$)	No. (%) of women without vaginal fluid sialidase activity ($n = 45$)	*P*
BV	8 (72.7)	11 (24.4)	0.004
T. vaginalis	0	2 (4.4)	NS[a]
Vaginal candidiasis	9 (90.0)	34 (75.6)	NS

[a] NS, not significant.

TABLE 3. Sensitivity, specificity, PPV, and NPV of investigated methods compared to Gram stain score[a]

Method	*n*	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
BVBlue	57	91.7	97.8	91.7	97.8
Amsel criteria[b]	57	50.0	100	100	88.2
Abnormal vaginal discharge	31	58.3	46.7	22.6	80.8
Vaginal fluid pH >4.5	12	66.7	91.1	66.7	91.1
Vaginal fluid amines	7	50.0	97.8	85.7	88.0
Clue cells	11	91.7	100	100	97.8

[a] Gram stains were scored by using the Nugent method; intermediate scores were considered negative.

[b] An Amsel criteria positive result requires a positive result for three of the following four criteria: abnormal vaginal discharge, vaginal fluid pH of >4.5, presence of vaginal fluid amines, and the presence of clue cells.

of past infections of *Trichomonas vaginalis* or vaginal candidiasis was seen between women with or without increased sialidase activity.

There was no significant correlation between the date of the last menstrual period and evidence of sialidase activity. No women who reported having abnormal Pap smears in the last 12 months showed evidence of sialidase activity in their vaginal fluid.

Clinical findings. Of all the women, 54% presented with abnormal vaginal discharge. Of these women, 8 had BV and 7 had yeast infections, and the remaining women with abnormal vaginal discharge had nonspecific vaginitis, cervicitis, or herpes simplex virus or were previously inadequately treated for BV.

BVBlue. Twelve (21%) of the participants had a positive BVBlue test. Ninety-two percent of women with sialidase activity and 2% of women without sialidase activity exhibited a decrease in *Lactobacillus* spp. All 12 women exhibiting elevated sialidase activity had an increase of gram-negative to gram-variable morphotypes compared to those without sialidase activity ($P \leq 0.001$). Clue cells were absent in all sialidase-negative samples and were present in 92% of sialidase-positive samples. Sialidase activity did not influence the number of polymorphonuclear cells present on the Gram smear. One subject was coinfected with *T. vaginalis*.

In comparing the agreement between BVBlue and the Nugent score, the kappa coefficient was 0.894 (95% CI, 0.75 to 1.04). This indicates excellent agreement between the two test methods, with only 2 of 57 tests (3.5%) failing to agree. McNemar's chi-square test for paired designs was used to compare the disagreements between BVBlue and the Nugent score. There was no significant difference at the alpha = 0.05 level between the two methods ($P = 1.000$).

The Gram-stained smears of vaginal discharge (assessed by Nugent score) were compared to BVBlue, Amsel criteria, abnormal vaginal discharge, vaginal fluid pH, vaginal fluid amines, and clue cells. Table 3 summarizes the sensitivity, specificity, and positive and negative predictive values (PPV and NPV, respectively). BVBlue was much more sensitive than Amsel criteria, 91.7 versus 50.0% when compared to Nugent scores. The specificity was similar at 97.8 and 100%, respectively. The individual criteria for Amsel were also compared with the Nugent score. The reliability of abnormal vaginal discharge alone was unreliable when compared to Gram stain, with a sensitivity, specificity, PPV, and NPV of 58.3, 46.7, 22.6, and 80.8%, respectively. When a pH of >4.5 was used alone, the specificity and NPV were high but the sensitivity and PPV were low (91.1, 91.1, 66.7, and 66.7%, respectively). The presence of clue cells alone was very sensitive and specific (91.7 and 100%, respectively). The presence of vaginal fluid amines alone was specific but not sensitive (97.8 and 50.0%, respectively). A significantly greater proportion of patients with vaginal fluid with a pH of >4.5, vaginal fluid amines, or clue cells present were found to have a positive BVBlue test in the study ($P < 0.001$).

DISCUSSION

In our study, BVBlue was used to detect sialidase activity in sexually active women. The sensitivity and specificity of BVBlue was compared to pH, amine odor, and vaginal Gram stain. We demonstrated a statistically significant correlation between a positive BVBlue test and elevated pH, presence of vaginal fluid amines, and clue cells. There was excellent agreement between the sensitivity and specificity of BVBlue and Gram stain (Nugent score). A limitation of this study is that it was carried out under ideal conditions with on-site expertise. We speculate that if BVBlue was compared to Amsel criteria and Gram stain performed in the average physician's office, the difference would be much more marked in favor of BVBlue.

The BVBlue system was evaluated in a study comparing and measuring bacterial sialidase activity in 118 women (J. A. McGregor, J. I. French, G. Morrison, and S. C. Johnson, Abstr. Annu. Sci. Meet. Infect. Dis. Soc. Obstet. Gynecol., poster no. 9, 2002). The sensitivity and specificity of BVBlue compared to Gram stain results by Nugent score were found to be 90.3 and 96.6%, respectively, with a PPV of 90.3% and an NPV of 96.6%. Our research supports this data. McGregor et al. also presented data demonstrating superior performance of BVBlue in comparison to Amsel criteria when both were compared to Gram stain. The sensitivity and specificity of Amsel criteria were 58.1 and 95.4%, respectively (J. A. McGregor, J. I. French, G. Morrison, and S. C. Johnson, Abstr. Annu. Sci. Meet. Infect. Dis. Soc. Obstet. Gynecol., poster no. 8, 2002). We found similar values for the sensitivity and specificity. McGregor et al. quantitatively evaluated sialidase activity and demonstrated that women with BV exhibit 4.6-fold-higher levels of sialidase activity than do healthy controls. The mean vaginal fluid sialidase activity was 12.3 U (95% CI, 8.1 to 16.6 U) for women with BV and 2.7 U (95% CI, 2.23 to 3.17 U) for the healthy controls. Women with vaginal candidiasis and trichomoniasis had mean sialidase activities of 3.7 U (95% CI, 2.6 to 4.8 U) and 1.99 U (95% CI, 0.6 to 3.4 U), respectively. The quantitation of sialidase activity was beyond the scope of our study.

BVBlue is a simple and rapid diagnostic test for detecting BV. A test detecting sialidase activity would prove to be beneficial in the clinic setting where microscopic capabilities are unavailable. The nature of the test could benefit physicians, patients, and the laboratory. Evaluating Amsel criteria or Gram-stained smears is time consuming and requires skilled personnel. The physician can perform BVBlue at the clinic, avoiding the time delay of sending a sample to the lab. Results for BVBlue are available in 10 min versus a possible delay of days for specimen transport, analysis of the Gram stain or wet mount, and generation and receipt of results. The patient may

then need to be recalled for further management. With the use of BVBlue, the patient will benefit from the quick diagnosis and prompt treatment will help prevent women from developing sequelae that can arise from a missed diagnosis. BVBlue could be adapted for the lab setting and could possibly be more economical than conventional evaluation.

As with most diagnostic tests, BVBlue has limitations. Since mixed vaginal infections may occur, the presence of sialidase activity does not rule out the presence of yeast, *T. vaginalis*, or other organisms. To prevent adverse performance of BVBlue, it should not be used in women who have recently douched, engaged in vaginal sexual intercourse, or used spermicides, vaginal lubricants, or feminine deodorant sprays within 72 h prior to testing.

BVBlue is a quick and easy test that detects the presence of sialidase activity by utilizing a chromogenic substrate of bacterial sialidase to produce a color reaction when a color developer solution is added to the reaction vessel. BVBlue appears to be a useful point-of-care tool to provide presumptive diagnostic information for women with BV when used in conjunction with clinical and patient information.

ACKNOWLEDGMENTS

We thank the staff of the STD Clinic, Edmonton, Alberta for recruitment efforts.

Gryphus Diagnostics, L.L.C., provided financial support for this study.

REFERENCES

1. **Amsel, R., P. A. Totten, C. A. Spiegel, K. C. Chen, D. Eschenbach, and K. K. Holmes.** 1983. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. Am. J. Med. **74:**14–22.
2. **Blackwell, A. L., A. R. Fox, I. Phillips, and D. Barlow.** 1983. Anaerobic vaginosis (non-specific vaginitis): clinical, microbiological, and therapeutic findings. Lancet **ii:**1379–1382.
3. **Briselden, A., B. J. Moncla, C. E. Stevens, and S. Hillier.** 1992. Sialidases (neuramidases) in bacterial vaginosis and bacterial vaginosis-associated microflora. J. Clin. Microbiol. **30:**663–666.
4. **Cauci, S., S. Driussi, R. Monte, P. Lanzafame, E. Pitzus, and F. Quadrifoglio.** 1998. Immunoglobulin A response against *Gardnerella vaginalis* hemoysin and sialidase activity in bacterial vaginosis. Am. J. Obstet. Gynecol. **178:**511–515.
5. **Corfield, T.** 1992. Bacterial sialidases-roles in pathogenicity and nutrition. Glycobiology **2:**509–521.
6. **Eschenbach, D. A., S. Hillier, C. Critchlow, C. Stevens, T. DeRouen, and K. K. Holmes.** 1988. Diagnosis and clinical manifestations of bacterial vaginosis. Am. J. Obstet. Gynecol. **158:**819–828.
7. **Eschenbach, D. A., P. R. Davick, B. L. Williams, S. J. Klebanoff, K. Young-Smith, C. M. Critchlow, and K. K. Holmes.** 1989. Prevalence of hydrogen peroxide-producing *Lactobacillus* species in normal women and women with bacterial vaginosis. J. Clin. Microbiol. **27:**251–256.
8. **Gibbs, R. S.** 1993. Chorioamnionitis and bacterial vaginosis. Am. J. Obstet. Gynecol. **169:**460–462.
9. **Hillier, S. L., R. P. Nugent, D. A. Eschenbach, M. A. Krohn, R. S. Gibbs, D. H. Martin, M. F. Cotch, R. Edelman, J. G. Pastorek, Jr., A. V. Rao, D. McNellis, J. A. Regan, J. C. Carey, and M. A. Klebanoff.** 1995. Association between bacterial vaginosis and preterm delivery of a low-birth-weight infant. N. Engl. J. Med. **333:**1737–1742.
10. **Howe, L., R. Wiggins, P. W. Soothill, M. R. Millar, P. J. Horner, and A. P. Corfield.** 1999. Mucinase and sialidase activity of the vaginal microflora: implications for the pathogenesis of preterm labour. Int. J. STD AIDS **10:**442–447.
11. **McGregor, J. A., J. I. French, W. Jones, K. Milligan, P. J. McKinney, E. Patterson, and R. Parker.** 1994. Bacterial vaginosis is associated with prematurity and vaginal fluid mucinase and sialidase: results of a controlled trial of topical clindamycin cream. Am. J. Obstet. Gynecol. **170:**1048–1060.
12. **McGregor, J. A., J. I. French, R. Parker, D. Draper, E. Patterson, W. Jones, K. Thorsgard, and J. McFee.** 1995. Prevention of premature birth by screening and treatment for common genital tract infections: results of a prospective controlled evaluation. Am. J. Obstet. Gynecol. **173:**157–167.
13. **Moncla, B. J., P. Braham, and S. L. Hillier.** 1990. Sialidase (neuraminidase) activity among gram-negative anaerobic and capnophilic bacteria. J. Clin. Microbiol. **28:**422–425.
14. **Nugent, R. P., M. A. Krohn, and S. L. Hillier.** 1991. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of Gram stain interpretation. J. Clin. Microbiol. **29:**297–301.
15. **Puapermpoonsiri, S., N. Kato, K. Watanabe, K. Ueno, C. Chongsomchai, and P. Lumbiganon.** 1996. Vaginal microflora associated with bacterial vaginosis in Japanese and Thai pregnant women. Clin. Infect. Dis. **23:**748–752.
16. **Schwebke, J. R., S. L. Hillier, J. D. Sobel, J. A. McGregor, and R. L. Sweet.** 1996. Validity of the vaginal Gram stain for the diagnosis of bacterial vaginosis. Obstet. Gynecol. **88:**573–576.
17. **Shah, H. N., and D. M. Collins.** 1990. *Prevotella*, a new genus to include *Bacteroides melaninogenicus* and related species formerly classified in the genus *Bacteroides*. Int. J. Syst. Bacteriol. **40:**205–208.
18. **Smayevsky, J., L. F. Canigia, A. Lanza, and H. Bianchini.** 2001. Vaginal microflora associated with bacterial vaginosis in nonpregnant women: reliability of sialidase detection. Infect. Dis. Obstet. Gynecol. **9:**17–22.
19. **Spiegel, C. A.** 1991. Bacterial vaginosis. Clin. Microbiol. Rev. **4:**485–502.
20. **Taylor, G.** 1996. Sialidases: structures, biological significance and therapeutic potential. Curr. Opin. Struct. Biol. **6:**830–837
21. **Von Nicolai, H., R. Hammann, S. Salehnia, and F. Zilliken.** 1984. A newly discovered sialidase from *Gardnerella vaginalis*. Zentbl. Bakteriol. Hyg. **258:** 20–26.
22. **Wiggins, R., T. Crowley, P. J. Horner, P. W. Soothill, M. R. Millar, and A. P. Corfield.** 2000. Use of 5-bromo-4-chloro-3-indolyl-α-D-*N*-acetylneuraminic acid in a novel spot test to identify sialidase activity in vaginal swabs from women with bacterial vaginosis. J. Clin. Microbiol. **38:**3096–3097.
23. **Wiggins, R., S. J. Hicks, P. W. Soothill, M. R. Millar, and A. P. Corfield.** 2001. Mucinases and sialidases: their role in the pathogenesis of sexually transmitted infections in the female genital tract. Sex. Transm. Infect. **77:** 402–408.