

Bacterial Vaginosis

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Bacterial vaginosis (BV) is the most common cause of abnormal vaginal discharge in women of child-bearing age. It is a syndrome of unknown cause characterized by depletion of the normal *Lactobacillus* population and an overgrowth of vaginal anaerobes, accompanied by loss of the usual vaginal acidity. The term 'bacterial vaginosis' was agreed at an international symposium in 1983, replacing the older term 'Gardnerella vaginitis'. This recognized the fact that many anaerobic or facultative anaerobic bacteria are present and that classical signs of inflammation are absent.

Symptomatic women report an offensive, fishy-smelling discharge that is most noticeable after unprotected intercourse or at the time of menstruation. The diagnosis is usually confirmed using the composite (Amsel) criteria. About 50% of women with BV appear to be asymptomatic. Studies in the last decade have established that BV is associated with infective complications in pregnancy and following gynaecological surgery, and may be

a risk factor for the acquisition of HIV.

EPIDEMIOLOGY

In unselected populations, the prevalence of BV is 10 to 20%, but it may be as high as 36% in women attending STI clinics and 28% in those seeking elective termination of pregnancy. A prevalence of more than 50% was reported in rural Uganda. BV is probably more common in women with STIs and in those who have recently changed their sex partner, but has been reported in virgin women. In many studies, it is associated with black race and IUD use. The condition often arises spontaneously around the time of menstruation, and may resolve spontaneously in mid-cycle. It is not known how often BV occurs in postmenopausal women.

AETIOLOGY AND PATHOGENESIS

The aetiology of BV is probably multifactorial, and the condition is

not regarded as an STI, though it is sexually associated. One factor is an increase in vaginal pH from the normal 3.5-4.5 to 7.0, which reduces the inhibitory effect of hydrogen peroxide on anaerobic growth. This is associated with loss of *Lactobacilli* and an up to 1000-fold increase in the concentration of several organisms, most commonly *Gardnerella vaginalis*, *Bacteroides (Prevotella)* spp, *Mobiluncus* spp and *Mycoplasma hominis*. Hormonal changes and inoculation with organisms from a partner might be important.

DIAGNOSIS

BV should be suspected in any woman presenting with an offensive, typically fishy-smelling vaginal discharge. Speculum examination shows a thin, homogeneous white or yellow discharge adherent to the walls of the vagina. *Gardnerella* can be found in low concentrations in more than 50% of women without BV; thus, culture has a poor specificity and should not be used for routine diagnosis.

Amsel Criteria

Amsel criteria (Table 1) remain the mainstay of diagnosis in settings such as genitourinary medicine clinics where microscopy can be performed. They arose from the original description of ‘*Haemophilus vaginitis*’ in 1955 by Gardner and Dukes, who described epithelial cells covered with so many small bacteria that the border was fuzzy. These were termed ‘clue cells’, because their presence was a clue to the diagnosis. A wet-mount examination is used that involves mixing vaginal fluid with a drop of saline and observing it under oil immersion at high power (x 800).

Any of the Amsel criteria may be misleading.

- The appearance of vaginal secretions may be altered by factors such as recent intercourse or douching.

- Both *Candida* and trichomoniasis can give a similar clinical appearance.

- A positive potassium hydroxide test and increased vaginal pH may be found in the presence of semen.

- Vaginal pH may be elevated during menstruation.

- Detection of clue cells is the single most sensitive and specific criterion, but the interpretation of microscopy is subjective. Debris or degenerate cells can be mistaken for clue cells, and lactobacilli sometimes adhere to epithelial cells in low numbers.

Recent studies have concluded that there is a continuum from normal *Lactobacillus*-dominated flora to ‘severe BV’, and the limitations of the Amsel criteria reflect this. Remember that BV can resolve spontaneously. If the history is highly suggestive of BV but the tests are negative, offer further testing if symptoms return.

Other Tests

It is possible to perform three of the Amsel tests in general practice, but simple alternative tests are desirable. Commercially available tests such as *BV blue* and *FemExam* detect biochemical changes in vaginal fluid associated with BV, and an ‘electronic nose’ that identifies volatile metabolites is being investigated. However, the relatively high cost of the currently available

tests compared to use of the Amsel criteria has limited their uptake.

In routine practice, one approach is to measure vaginal pH with pH-sensitive paper. A pH of less than 4.5 almost excludes BV. If the pH is high, send a high vaginal swab to the microbiology laboratory. This should be examined by wet mount or Gram stain.

Gram Stain

Examination of a Gram-stained vaginal smear is a quick and relatively simple means of confirming the diagnosis of BV. Its advantages are that it allows recognition of the intermediate flora, and stored slides can be subsequently evaluated independently in research studies.

Typical *Lactobacilli* are large Gram-positive rods with blunt ends. *Gardnerella* is usually a Gram-negative coccus. Normal flora shows plentiful *Lactobacilli* (Figure 1), whereas in BV there is a large number of Gram-negative cocci and small rods. (Figure 2)

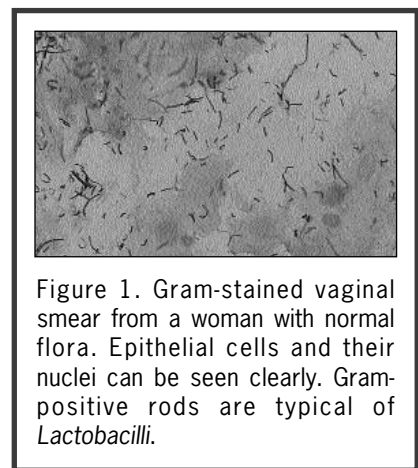


Figure 1. Gram-stained vaginal smear from a woman with normal flora. Epithelial cells and their nuclei can be seen clearly. Gram-positive rods are typical of *Lactobacilli*.

Table 1. Composite (Amsel) Criteria for the Diagnosis of Bacterial Vaginosis

1. Vaginal pH >4.5
2. Release of a fishy smell on addition of alkali (10% potassium hydroxide)
3. Characteristic discharge on examination
4. Presence of ‘clue cells’ on microscopy

At least three of the four criteria must be fulfilled to make a diagnosis of bacterial vaginosis.

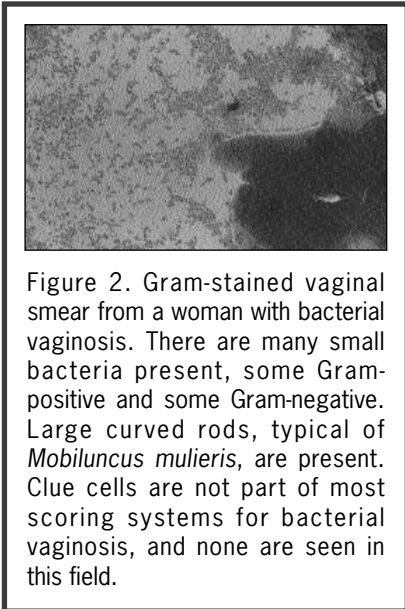


Figure 2. Gram-stained vaginal smear from a woman with bacterial vaginosis. There are many small bacteria present, some Gram-positive and some Gram-negative. Large curved rods, typical of *Mobiluncus mulieris*, are present. Clue cells are not part of most scoring systems for bacterial vaginosis, and none are seen in this field.

Curved rods (*Mobiluncus* spp) may be present. Recognition of intermediate categories can be more difficult and entails subjective assessment of the morphotypes. Scoring systems (eg. the Nugent) have attempted to reduce interobserver variability.

Differential Diagnosis

Other common causes of vaginal discharge are cervicitis caused by *Chlamydia* or gonorrhoea, candidosis and trichomoniasis, all of which can also coexist with BV. (Table 2) In cervicitis, there may be contact bleeding and purulent discharge may be visible in the external os. *Candida* typically causes a curdy discharge and is associated with itching. *Trichomonas* causes a more purulent discharge, and is associated with soreness and erythema. These organisms can be sought on specific diagnostic tests.

MANAGEMENT

BV is sometimes distressing, and must be managed with sensitivity. Because it has a relapsing-remitting course in many women, the value of treating asymptomatic BV has not been established. There is also no evidence that treatment reduces the prevalence in the community. Treatment should therefore be prescribed for control of symptoms, and in situations in which it might prevent complications of a procedure or in pregnancy.

Antibiotics

Antibiotics with good anti-anaerobic activity should be an effective treatment for BV, and metronidazole and clindamycin are obvious choices. Theoretically, an antibiotic that is not active against *Lactobacilli* (eg. metronidazole) might facilitate more rapid restoration of the vaginal flora than one that is active against *Lactobacilli* (eg. clindamycin). However, clindamycin has better activity against *M. hominis*, *Mobiluncus* spp and *G. vaginalis* than does metronidazole.

The standard treatment for BV is metronidazole 400 mg po bd for 5 days. An alternative is a 2 g single dose. The cure rate immediately after treatment with metronidazole is up to 95%, but after 4 weeks this falls to 80% in open-label studies and less than 70% in blinded studies.

Topical treatments with intravaginal 2% clindamycin cream or 0.75%

metronidazole gels are licensed for the treatment of BV. They are more expensive than oral metronidazole, but have similar efficacy and can be useful when systemic treatment is not desirable.

Adverse Effects of Treatment

Oral metronidazole is associated with well-recognized side effects of nausea, a metallic taste and alcohol intolerance. Allergic rashes occur occasionally. Initial concerns about potential teratogenicity have not been substantiated and metronidazole can be used in pregnancy. Oral clindamycin can induce rashes and occasionally pseudomembranous colitis. About 10% of women develop symptomatic candidosis following treatment for BV.

Male Partners

Four double-blind placebo-controlled trials have failed to show any difference in relapse rates of BV following treatment of male partners with metronidazole, tinidazole or clindamycin, 150 mg qds. Many physicians advocate screening for STIs in the partners of women with recurrent BV, but this is not based on prospective studies.

Relapses

In some women, BV recurs frequently following treatment. Management of such cases is difficult. It is reasonable to screen the sex partner for infections. The author usually prescribes

Table 2. Differential Diagnosis of Vaginal Discharge

Symptoms and Signs	Candidosis	Bacterial Vaginosis	Trichomoniasis	Cervicitis
Itching or Soreness	++	–	+++	–
Smell	May be 'yeasty'	Offensive, fishy	May be offensive	–
Colour	White	White or yellow	Yellow or green	Clear or coloured
Consistency	Curdy	Thin, homogeneous	Thin, homogeneous	Mucoid
Other Signs				Purulent mucus at cervical os
Potassium Hydroxide Test	–	++	±	–
pH	<4.5	4.5-7.0	4.5-7.0	<4.5
Confirmation	Microscopy and culture	Microscopy	Microscopy and culture	Microscopy, tests for <i>Chlamydia</i> and gonorrhoea

metronidazole 400 mg bd for 3 days starting 2 days before menstruation and again on the fifth day of menstruation for 3 months, in the hope that suppressing BV will allow the return of a more normal vaginal environment. Even when BV recurs frequently over several months, it usually regresses following repeated treatment. A test of cure is not needed. The concept of recolonizing the vagina with healthy strains of *Lactobacilli* that produce large amounts of H₂O₂ to prevent relapse after treatment is being investigated.

Patient Advice and Self-Help

Vaginal douching and the use of shower gel and bubble bath should be avoided. If the woman washes her hair in the shower, she should avoid contact between the shampoo and the vulval area. It is sensible to use condoms with new sex

partners to protect against infections, possibly including BV.

COMPLICATIONS

Pregnancy

BV is associated with second-trimester miscarriage and preterm birth. The reported odds ratio is 1.4 to 7.0. It is thought that women with BV are at increased risk of chorioamnionitis, which can stimulate preterm birth through the release of pro-inflammatory cytokines. Several studies have evaluated the value of screening for and treating BV to prevent an adverse outcome in pregnancy. The results have been variable; some studies show a benefit with treatment in terms of reducing preterm birth rates, but the largest study to date showed no benefit from treatment with short courses of metronidazole.¹

On the basis of these studies, it cannot be concluded that antibiotic treatment of BV in pregnancy will universally reduce the incidence of preterm births. The results of further studies are awaited.

Termination of Pregnancy

Women infected with *Chlamydia trachomatis* who undergo elective termination of pregnancy are at high risk of endometritis and pelvic inflammatory disease. BV also confers an increased risk, and may be present in almost 30% of such women. A double-blind placebo-controlled trial in Sweden demonstrated that the risk of endometritis in women without *Chlamydia* was 12.2% in placebo-treated women and 3.8% in women prescribed oral metronidazole before termination.² A more recent randomized controlled trial in Sweden found a fourfold reduction in infective

complications with clindamycin cream compared to placebo.³

Other Gynaecological Surgery

BV has been associated with vaginal cuff cellulitis, wound infection and abscess formation after hysterectomy. No randomized trials have been performed to investigate the value of screening and treatment before such surgery. The potential role of BV in infections following IUD insertion, hysteroscopy, and dilatation and curettage has not been systematically studied.

HIV and STIs

HIV has spread rapidly through sub-Saharan Africa and Southeast Asia in the last two decades. Initial reports identified genital ulcer STIs as co-factors for transmission. BV emerged as a co-factor for HIV acquisition in the Rakai study in rural Uganda.⁴ A study of pregnant women in Malawi reported BV to be associated with HIV acquisition during pregnancy and the postnatal period.⁵ Potential mechanisms by which BV might enhance HIV transmission include effects on local immune mediators. Additionally, H₂O₂ produced by *Lactobacilli* can inhibit HIV *in vitro*, and is absent in most women with BV. If

BV is established as an important risk factor for HIV spread, its control will become an important public health issue in many countries.

BV has also been associated with an increased incidence of non-gonococcal urethritis in male partners.

PREVENTION

Because the aetiology of BV is not fully understood, it is not known how to prevent it. Antibiotics inhibit the growth of the anaerobes, but do not necessarily eliminate the factors that led to the development of BV; thus, relapse is relatively common. In the Rakai study, intermittent 'mass treatment', which included a course of metronidazole, did not reduce the prevalence of BV.

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