Bacterial vaginosis

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Abstract

Bacterial vaginosis is the most common cause of abnormal vaginal discharge in women of childbearing age, with a prevalence as high as 50% in some communities. The symptoms of discharge and offensive smell can cause considerable distress, although 50% of women are asymptomatic when the condition is diagnosed. Microbiologically the usually dominant lactobacillus flora is overwhelmed by an overgrowth of predominantly anaerobic organisms, accompanied by a rise in pH. A biofilm containing predominantly *Gardnerella vaginalis* and *Atopobium vaginae* has been described recently. Metronidazole is the antibiotic of choice for treatment, but relapse within 1 or 2 months is common. Bacterial vaginosis is a risk factor for acquisition of sexually transmitted infections including HIV, and for post-abortion endometritis and adverse pregnancy outcomes such as late miscarriage and preterm birth. Studies of antibiotics in pregnancy have not consistently shown reduced adverse outcomes so better strategies are needed to improve pregnancy outcome.

Keywords *Atopobium*; bacterial vaginosis; biofilm; *Gardnerella*; metronidazole

What's new?

- Molecular techniques have identified several new organisms in bacterial vaginosis, including *Atopobium vaginae*
- The description of a vaginal biofilm containing predominantly *Gardnerella vaginalis* places this organism once more as central in pathogenesis
- The biofilm also offers the opportunity to study potential new treatments for bacterial vaginosis
- Probiotics and lactic acid gels need further study as alternative treatments to antibiotics

Bacterial vaginosis (BV) is the most common cause of abnormal vaginal discharge in women of childbearing 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. In 1983 the term 'bacterial vaginosis' replaced 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.[1]

Women with symptomatic bacterial vaginosis report an offensive, fishy-smelling discharge that is most noticeable after unprotected intercourse or at the time of menstruation. The diagnosis can be confirmed by microscopy with or without additional tests. About 50% of cases are asymptomatic. Bacterial vaginosis is associated with infective complications in pregnancy and following gynaecological surgery, and is a risk factor for the acquisition of sexually transmitted infections (STIs) including HIV.

Epidemiology

In unselected populations in the UK, the prevalence of bacterial vaginosis is 10–20%, but it may be as high as 36% in women attending STI clinics and 28% in those seeking elective termination of pregnancy.[2] A prevalence of more than 50% was reported in rural Uganda.[3] There is continuing debate about whether bacterial vaginosis is an STI or merely sexually associated. A meta-analysis has concluded that bacterial vaginosis has the characteristics of an STI: being associated with partner change and other STIs.[4] The strongest evidence against it being an STI has come from studies reporting similar rates in self-reported virgin and non-virgin women.[5–7] This has been challenged by a detailed study that reported no bacterial vaginosis in women denying any oral or digital genital contact.[8] In many studies, it is associated with black race and intrauterine device (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 bacterial vaginosis occurs in postmenopausal women.

Aetiology and pathogenesis

Lactobacilli dominate the normal vaginal flora, although other organisms may be present in small numbers. When bacterial vaginosis develops the lactobacilli become less numerous and may disappear, while there is an increased concentration of anaerobic and facultative anaerobic organisms. Lactobacilli produce inhibitory mediators including lactic acid, H_2O_2, defensins and bacteriocins. The triggers for bacterial vaginosis are probably multiple. An increase in vaginal pH from the normal 3.5–4.5 to as high as 7.0 is observed, which reduces the inhibitory effect of H_2O_2 on anaerobic growth. Hormonal changes and inoculation with organisms from a partner might also be important.

The organisms classically associated with bacterial vaginosis using culture and those more recently identified using molecular techniques[9,10] are shown in Table 1. The description of the biofilm that develops in BV, by Swidsinski and colleagues places *Gardnerella vaginalis* once again at the centre of pathogenesis of BV.[11] In some women the biofilm covered the entire biopsy; in others it was more patchy. *Gardnerella* accounted for 90% of bacteria seen in the biofilm, with *Atopobium vaginae* the only other numerically important organism. Lactobacilli predominated in women with normal flora, but did not form a biofilm.

Diagnosis

Bacterial vaginosis 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. Amsel's criteria (Table 2) have been the mainstay of diagnosis in settings

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The organisms classically associated with bacterial vaginosis using culture are shown in the first column and those more recently identified through molecular techniques in the second

Gardnerella vaginalis	*Atopobium vaginae*
Bacteroides (*Prevotella*)	BVAB1-3 (*Clostridiales*)
Mycoplasma hominis	*Megasphaera*
Mobiluncus spp.	*Sneathia*
	Leptotrichia

Table 1

such as genitourinary medicine (GUM) clinics where microscopy can be performed. Epithelial cells covered with so many small bacteria that the border is fuzzy are termed 'clue cells', because their presence is a clue to the diagnosis.[12]

However, any of Amsel's criteria can be misleading.

- The appearance of vaginal secretions may be altered by factors such as recent intercourse and douching.
- Both candidiasis and trichomoniasis can give a similar clinical appearance.
- A positive potassium hydroxide test may be found in the presence of semen.
- Vaginal pH may be elevated during menstruation, or by the presence of semen.
- 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 bacterial vaginosis'. This is recognized in Gram-stain scoring systems but not with Amsel's criteria. When the history is highly suggestive of the condition but the tests are negative, further testing should be offered if symptoms return.

Gram-staining

Examination of a Gram-stained vaginal smear is a quick and relatively simple means of diagnosis. It enables recognition of intermediate flora, and stored slides can be evaluated independently in research studies at a later date.

Composite (Amsel's) criteria for the diagnosis of bacterial vaginosis

- Vaginal pH >4.5
- Release of a fishy smell on addition of alkali (10% potassium hydroxide)
- Characteristic discharge on examination
- Presence of 'clue cells' on microscopy of vaginal fluid mixed with normal saline

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

Table 2

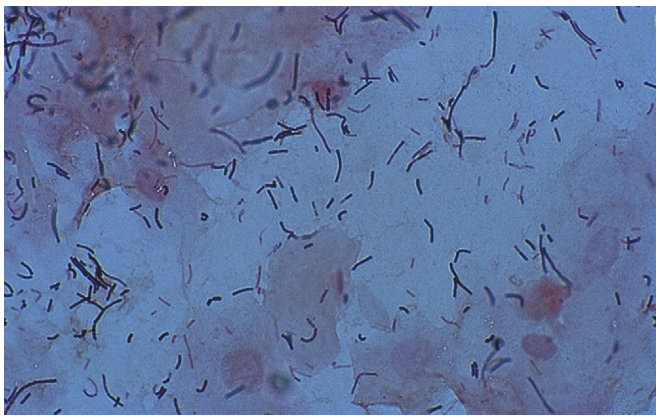

Figure 1 Gram-stained vaginal smear from a woman with normal flora. Epithelial cells and their nuclei can be seen clearly. Gram-positive rods are typical of lactobacilli.

Typical lactobacilli are large, Gram-positive rods with blunt ends. *G. vaginalis* is usually a Gram-negative coccus. The normal flora includes plentiful lactobacilli (Figure 1), whereas in bacterial vaginosis there are large numbers of Gram-negative cocci and small rods (Figure 2). Curved rods (*Mobiluncus* spp.) may be present. Recognition of intermediate categories can be more difficult and entails subjective assessment of the morphotypes. Scoring systems (e.g. Nugent) have attempted to reduce inter-observer variability.[13] A simplified scoring system (Hay—Ison criteria) has been recommended for use in GUM clinics in preference to Amsel's criteria.[14]

Other tests

Commercially available tests such as BV Blue and *FemExam* detect biochemical changes in vaginal fluid associated with bacterial vaginosis. However, the relatively high cost of the currently available tests compared with use of the Gram-stain or Amsel's criteria has limited their uptake. In routine practice, vaginal pH can be measured using pH-sensitive paper. A pH of less than 4.5 almost excludes bacterial vaginosis. If the pH is

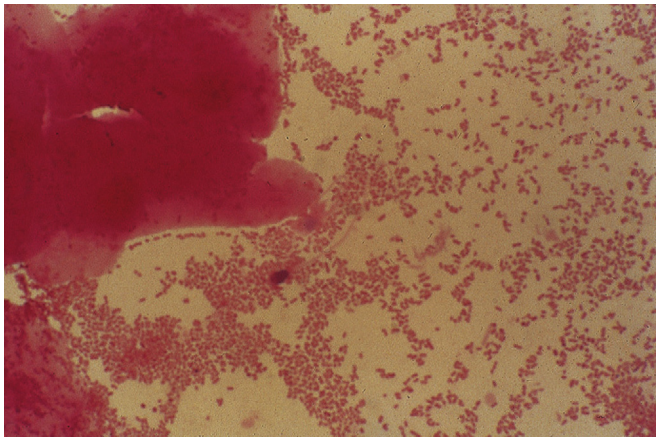

Figure 2 Gram-stained vaginal smear from a woman with bacterial vaginosis. There are many small bacteria present, some Gram-positive and some Gram-negative. Large, curved rods, typical of *Mobiluncus mulieris*, are present. Clue cells are not part of most scoring systems for bacterial vaginosis, and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