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# Bacterial vaginosis

## More questions than answers

### Background

Bacterial vaginosis is the commonest cause of abnormal vaginal discharge in women of reproductive age and is associated with serious pregnancy related sequelae and increased transmission of sexually transmissible infections, including HIV. The aetiology, pathology, microbiology and transmission of bacterial vaginosis remain poorly understood.

### Objective

This article discusses the prevalence, clinical features and possible complications of bacterial vaginosis. It summarises what is known about the aetiology, pathophysiology and treatment of the condition and highlights directions for further research.

### Discussion

Bacterial vaginosis is characterised by a complex disturbance of the normal vaginal flora with an overgrowth of anaerobic and other micro-organisms and a corresponding decrease in important lactobacillus species. The cause is not known, but observational evidence suggests the possibility of sexual transmission. Bacterial vaginosis is diagnosed by the Amsel or the Nugent method. Recommended treatment is with 7 days of oral metronidazole or vaginal clindamycin. More than 50% of women will experience recurrence of bacterial vaginosis within 6 months. It is not known whether this represents relapse or re-infection. Further research is needed into the aetiology, pathogenesis and optimal treatment of this condition.

■ **Bacterial vaginosis (BV) is one of the commonest genital conditions occurring in women of reproductive age. In public health terms, it plays a significant role as a risk factor for a wide range of health problems, including preterm birth, spontaneous abortion, and enhanced transmission of sexually transmissible infections (STIs), including human immunodeficiency virus (HIV).**

Previous names for BV include: 'leukorrhoea', 'nonspecific vaginitis', 'haemophilus vaginalis vaginitis', 'gardnerella' and 'anaerobic vaginitis'. Its changing name belies the interesting fact that, despite an increased understanding of its physiology and sequelae, the precise pathogenesis of BV remains controversial and its aetiology, pathology, microbiology and transmission is still poorly understood. Frustratingly for both women and general practitioners, the treatment of BV is also less than satisfactory, and recurrences following recommended therapy remain common.

### Serious sequelae

Bacterial vaginosis is associated with serious pregnancy related sequelae, such as chorio-amnionitis, spontaneous abortion,<sup>1-3</sup> preterm delivery and low birth weight,<sup>1,4,5</sup> postpartum and postabortion endometritis, and posthysterectomy vaginal cuff infection. It is estimated that BV contributes to 30% of preterm delivery in the USA, at a cost of USD1 billion per annum.<sup>6</sup>

Internationally, BV is important as it increases susceptibility to HIV and STIs.<sup>7,8</sup> Bacterial vaginosis increases the risk of HIV transmission 2-4 fold and has been estimated to contribute 23% to antenatal HIV seroconversion in a high prevalence population of pregnant women in Malawi.<sup>7</sup> As BV is most prevalent in populations at risk of HIV, identifying more effective therapies may prove integral to effective HIV control.

The prevalence of BV varies according to the population studied; with a prevalence rate of over 33% in studies of Indigenous Australian women,<sup>9</sup> and in excess of 50% in sub-Saharan African and African American women.<sup>10,11</sup> There are no recent studies of the

prevalence of BV in non-Indigenous Australian women. However, a national Australian study is currently underway which will provide BV prevalence estimates in young women attending general practices.

## Pathophysiology

Much of our knowledge of the microbiology of BV has been established using culture based methods. Bacterial vaginosis is characterised by a complex disturbance of the normal vaginal flora, with a loss of hydrogen peroxide producing *Lactobacilli* bacteria and an increase in Gram variable coccobacilli (*Gardnerella vaginalis* and *Bacteroides* species), anaerobic organisms (*Mobiluncus* spp., *Fusobacterium* spp., *Prevotella* spp. and *Peptostreptococcus* spp.) and genital mycoplasmas (*Mycoplasma hominis* and *Ureaplasma urealyticum*). There is an associated rise in vaginal pH, and increased production of proteolytic enzymes, organic acids and volatile amines.<sup>12</sup>

Recent studies employing DNA based molecular methods have identified novel and fastidious organisms that are highly specific for BV (eg. *Atopobium vaginae* and newly defined *Clostridial* spp. termed 'BVAB1', 'BVAB2' and 'BVAB3').<sup>13</sup> The spectrum of bacteria associated with BV appears to be far more diverse than previously thought.<sup>13</sup>

## Symptoms

Bacterial vaginosis (BV) is the commonest cause of abnormal vaginal discharge in women of reproductive age. Symptoms of BV are characterised by a malodorous and often profuse vaginal discharge, which can cause considerable distress and discomfort. However, some women with a diagnosis of BV may have no symptoms at all.

## Making the diagnosis

Bacterial vaginosis is commonly diagnosed using one of two methods:

- the Amsel, or
- the Nugent method.

### The Amsel method

The Amsel method combines clinical and laboratory findings and is the most widely used method in clinical practice. Bacterial vaginosis is diagnosed if three or more of the following four criteria are present:

- a characteristic homogenous, white, adherent vaginal discharge (Figure 1)
- vaginal pH over 4.5
- clue cells present on microscopy (Figure 2), and
- a positive amine test (the presence of a fishy odour upon addition of potassium hydroxide to vaginal secretions).

The clue cell is considered to be the most specific microscopic sign associated with BV and represents exfoliated vaginal epithelial cells studded with Gram variable and Gram negative coccobacilli (Figure 2). The presence of clue cells is routinely reported by most laboratories. Practitioners can measure vaginal pH by applying pH paper to vaginal secretions (not cervical mucous which has an elevated pH), and can perform a bedside amine test by placing a drop of potassium hydroxide into the removed speculum and smelling the odour.

Figure 1. Characteristic white homogenous discharge associated with bacterial vaginosis



Photo courtesy: Melbourne Sexual Health Centre

Figure 2. The clue cell: exfoliated vaginal epithelial cells studded in Gram variable and Gram negative coccobacilli

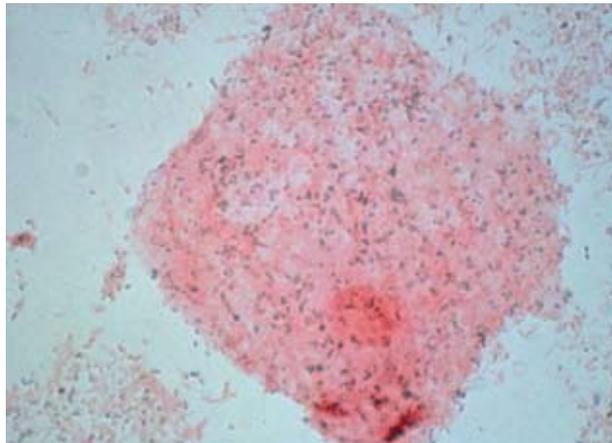


Photo courtesy: Melbourne Sexual Health Centre

### The Nugent method

The Nugent method is the current 'gold standard' to diagnose BV. It is widely used in clinical trials and consists of a microscopic score of vaginal bacteria. This method scores:

- the loss of lactobacilli
- increasing numbers of Gram variable and Gram negative coccobacilli, and
- increasing numbers of *Mobiluncus* spp.

A score of 0–3 is considered normal flora, 4–6 as intermediate flora and 7–10 as BV. Despite the widespread recognition of the Nugent method as one of the most objective methods for the diagnosis of BV, few commercial laboratories report a Nugent score if BV is queried by the practitioner.

Importantly, laboratories do routinely report the culture of *G. vaginalis*. As this organism also commonly occurs in women without BV, treatment for BV on the basis of culture of *G. vaginalis*



is inappropriate. Practitioners should apply the Amsel method where possible, and document the presence of the characteristic discharge, elevated vaginal pH and fishy odour, and insert the clue cell result when the laboratory report is available.

Point of care tests and DNA probe tests are currently in development and these may offer sensitive and specific methods to detect BV (and may even be possible at the bedside).

### Is bacterial vaginosis a STI?

Several factors indicate that BV is an infective process rather than just a 'derangement of vaginal flora'. Observational evidence increasingly supports sexual transmission of BV.<sup>14–16</sup> A recent meta-analysis found that BV is associated with recognised STI risk factors, such as multiple sexual partners, and that condoms were protective against BV.<sup>15</sup> However, there is evidence against the sexual transmission of BV. Studies testing the impact of male partner treatment have failed to reduce BV recurrence in women,<sup>17–19</sup> and some studies have identified BV in women who have not engaged in penile-vaginal sex.<sup>20,21</sup>

Research actively continues into the cause of this disease and whether or not it is a STI. The message for patients and their partners is confusing while aetiology and transmissibility remain unknown. However, evidence for the prevention of BV does support the promotion of safe sexual practices, with advice to reduce the number of sexual partners and to use condoms.

Interestingly, there are more data to support transmission of BV between women. Women who have sex with women (WSW) have consistently demonstrated higher BV prevalence rates than exclusive heterosexually active women.<sup>10,14,15</sup> The first evidence of female-to-female transmission of BV emerged in the 1950s when asymptomatic volunteers were directly inoculated with the vaginal secretions of women with BV, and BV was established in the recipients.<sup>22</sup> Consistent with this concept, studies of female-female monogamous couples demonstrate extremely high concordance for BV (73–95%).<sup>23</sup> Given these findings, partner testing and treatment for WSW with BV is often recommended.

### Treatment

As the cause of BV is unclear, current treatment is directed toward alleviation of symptoms and restoration of normal flora, rather than eradication of a specific aetiological agent. First line internationally recommended therapies include:

- 7 days of oral metronidazole (400 mg twice daily) or,
- vaginal clindamycin (1 g at night).<sup>24</sup>

These antibiotics have equivalent 1 month efficacy with cure rates of 70–90%,<sup>25</sup> but recurrence rates in excess of 50% within 6 months of treatment have been described.<sup>26</sup> Single dose therapies such as 2 g metronidazole have been shown to be less effective than 7 day regimens and are considered second line therapies.<sup>25</sup>

Until recently, longer term data about rates of recurrence were lacking. However, a recent large prospective Australian study of BV over 12 months after 7 days of oral metronidazole found recurrence

rates for BV of 58%.<sup>26</sup> This finding confirms what most clinicians and their patients already know – that current therapies provide often only short term symptom relief and are associated with high rates of long term recurrence. Frustratingly, it is not known if recurrence is due to relapse of disease or re-infection, although some treatment trials report that re-exposure to a regular partner and lack of condom use after treatment increased recurrence rates of BV.<sup>26,27</sup>

Serious infectious complications of BV include pelvic inflammatory disease following invasive procedures such as termination of pregnancy (TOP) and vaginal cuff infection following hysterectomy. Several studies have investigated the benefits of treating women with BV before a TOP and, although inconsistent, results have supported routine screening and treatment of BV for women being referred for invasive upper genital tract procedures, such as TOP,<sup>25,28–30</sup> and before hysterectomy. Studies are currently underway to determine whether women should be screened for BV before intrauterine device insertion. Screening should also include other lower genital tract infections such as *C. trachomatis* and *N. gonorrhoea*.

Treatment of symptomatic BV in pregnancy is indicated, although at present there is no international consensus on the best antibiotic, ideal route of administration, or the appropriate duration and optimal timing of therapy. Australian national guidelines recommend either clindamycin 300 mg orally 12 hourly for 7 days (category A) or metronidazole 400 mg orally 12 hourly for 7 days (category B2).<sup>31</sup> Oral therapy is currently recommended over vaginal therapy by national guidelines as there is some concern that topical therapy may not be effective against BV organisms in the endometrial cavity, although this has not been supported by recent clinical trials.

The latest Cochrane review found that antibiotic therapy, whether given orally or vaginally, is highly effective in eradicating BV; however, there was no overall reduction in preterm delivery or low birth weight.<sup>32</sup> Much of this could be explained by heterogeneity in trials in terms of the timing, duration and types of treatments used, the diagnostic criteria applied and differing risk profiles of women enrolled in studies. Importantly few trials had treated women early in pregnancy. A meta-analysis of four recent trials that used clindamycin (either oral or vaginal) early in pregnancy found there was a significant reduction in preterm delivery before 37 weeks and late miscarriage compared to placebo.<sup>33</sup> Much interest now surrounds the suggestion that early initiation of antibiotic therapy could prevent the adverse obstetric sequelae associated with BV.

A recent review of BV treatments concluded that '...no sound scientific basis exists for recommending any particular treatment',<sup>34</sup> however despite this, 7 day regimens with either oral metronidazole or vaginal clindamycin are currently recommended first line therapy for BV.

Improved regimens for the treatment of BV are clearly needed, in particular given the public health significance of BV in preterm delivery and HIV transmission. It is understandable, in the absence of a clear aetiology or causative agent(s) for BV, and the lack of knowledge as to whether re-infection is occurring, that our management of this common condition is less than ideal.



Hopefully the question of optimal treatment of BV in nonpregnant women will be addressed by a National Health and Medical Research Council funded randomised controlled trial currently underway in Australia. This study is comparing currently recommended therapy with 7 days of metronidazole to combination antibiotic therapy (metronidazole plus vaginal clindamycin), to metronidazole and a vaginal *Lactobacillus* spp. This trial will determine the efficacy of these therapies over a 6 month period.

## Conclusion

Further research is clearly needed into the aetiology, pathogenesis and optimal treatment for this intriguing and common condition currently known as 'bacterial vaginosis'. Better understanding and treatment will clearly have significant international public health implications for women, pregnant women, and the transmission of STIs, including HIV.

Conflict of interest: none declared.

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