Editorial

Why is metronidazole still the primary antibiotic to treat BV?

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Bacterial vaginosis is a complex polymicrobial vaginal community made up largely of obligate anaerobic bacteria. The presence of a high number or concentration of obligate anaerobes is the likely reason that metronidazole was chosen as the empiric choice for the treatment of BV. The primary bacteria that constitute BV are *Gardnerella vaginalis, Atopobium vaginae, Prevotella bivia, Megasphaera Types I* and *II, BVAB, Mobiluncus curtisii,* and *Sneathia amnii.* Two of the most frequently recovered from the vagina of patients with BV are *Gardnerella vaginalis* and *Atopobium vaginae*. In addition, other bacteria commonly associated with BV are *Corynebacterium amycolatum (facultative anaerobe), Fusobacterium nucleatum* (obligate anaerobe), *Dialister* (obligate anaerobe), *Enterococcus faecalis* (facultative anaerobe), *Eggerthella* (obligate anaerobe), *Leptotrichia* (facultative anaerobe), *Ureaplasma urealyticum* (facultative anaerobe.[1] *Gardnerella vaginalis*, a Gram-variable, facultative anaerobe that has a poor sensitivity to metronidazole, appears to have an essential role in creating an environment that is favorable to the growth obligate anaerobic bacteria in part via its production of succinic acid and sialidase. Resistance to metronidazole has been reported as high as 68%.[2–6] There appears to be four strains that are commonly isolated from women with BV.[5,6] Four species of *Gardnerella; G. vaginalis, G. leopoldii, G. piotii,* and *G. swidsinski*. However, other genomic species have been identified.[6] *Gardnerella vaginalis* has further been categorized into four Clades, 1 (subgroup C), 2 (subgroup B),[7,8] 3 (subgroup D, several unnamed genome species), and 4 (A) [*G. leopolidii* and *G. swidsinski*.[9] Balashov et a. found a positive correlation between BV and clade 1 and clade 3 in vaginal samples from 60 American women. Clade 2 was correlated with intermediate bacterial flora and Clade 4 had no correlation with infection 11).

Since neither metronidazole nor clindamycin provide enough activity against the primary anaerobes found in BV, neither should be used empirically. One alternative is to administer both antibiotics simultaneously. However, this will eventually lead to a microbiome that contains bacteria that are resistant to both antibiotics. There is a need for more intense study employing probiotics as the main treatment for vaginal dysbiosis. Avoiding the empiric use of antibiotics as the primary treatment vaginal dysbiosis should presumably alleviate the pressure that is exerted on the other microbiomes of the human body, as well as reduce the impact of inducing and selecting bacteria carrying genes that prevent these bacterial from acquiring resistant genes.

Research needs to be conducted correlating the species to clades and antibiotic resistance. In addition, the assessment of the vaginal microbiome should include qualitative and quantitative analysis. Perhaps bacterial concentrations determined as low can be treated with probiotics alone. Vaginal concentrations determined to be moderate and high in numbers could be treated with shorter courses of antibiotics or concurrent with non-antibiotic regimens hoping to lower the pathogenic bacterial concentration. Another alternative, not influence other microbiomes of the body (especially the colon) is to administer antibiotics intra-vaginally. Thus, allowing the lactobacilli contained in the probiotic a better opportunity to become established and create a *Lactobacillus* dominant vaginal microbiome.

An additional problem is that there are additional extraneous pressures being placed on the clinician to utilize treatment approaches that do not necessarily support the clinical evidence. Physicians encounter this more and more often when they write for a specific antibiotic, and then they are told that the patient is unable to have that medication filled, and a different class of antibiotic is instead recommended by the patient's health plan. In addition, the patient is often treated with the same antibiotic, repeatedly, with no better outcome, however resistance to allowing a different antibiotic is refused by pharmacy, government, or insurance entities. The directive issued by the health plan is not based on science or the physician's judgement, i.e., what is in the patient's best interest, but by some third-party objective, which focuses more on cost than outcomes. As these restrictions become more and more onerous, one may envision not only specific treatment approaches being directed by third party interests, but also testing options may begin to be more restricted. Already this is being implemented in many states through the MolDX (Molecular Diagnostic Services) program. (MolDX was initiated in 2011 and restricts reimbursement of molecular panels to only 5 targets, or pathogens. This program is currently active in 28 states). MolDX was developed to control coverage, coding, and pricing of molecular pathology services.

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Conflicts of interest

All authors declare any financial interest with respect to this manuscript.

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