

CORRESPONDENCE



Bacteria Associated with Bacterial Vaginosis

TO THE EDITOR: Fredricks and colleagues (Nov. 3 issue)¹ reported complex communities of bacteria and a high level of species diversity in vaginal secretions from women with bacterial vaginosis. However, the study of vaginal fluid alone provides an incomplete picture of disease pathogenesis, since infections also may affect the vaginal epithelium. Fluorescence in situ hybridization of vaginal-biopsy specimens with the use of bacteria-specific probes demonstrates that a clinical diagnosis of bacterial vaginosis is highly associated with the development of a bacterial biofilm on the epithelial surface.² Gardnerella and atropobium species together constitute more than 90 percent of the biofilm mass. The biofilm also contains numerous, less abundant bacterial species, in agreement with the findings of Fredricks and others.^{1,3} Formation of the biofilm allows bacteria to reach higher concentrations than can be achieved in vaginal fluid alone. Desquamation of epithelial cells coated with biofilm in situ results in the clue cells that are

diagnostic of bacterial vaginosis. Given such complex microbiota, it is clear that identification of single pathogens, as was introduced by Koch and Pasteur more than 100 years ago, is inadequate for explaining the pathogenesis of bacterial vaginosis.

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THE AUTHORS REPLY: Dr. Hale and colleagues highlight their study showing that adherent bacterial biofilms commonly were detected in vaginal-biopsy specimens from subjects with bacterial vaginosis, suggesting that biofilms may play a role in the pathophysiology of this syndrome.¹ We agree that it is important to study both the vaginal epithelial surface and free vaginal fluid to determine how bacterial communities may lead to disease. Fluorescence in situ hybridization is an excellent method for studying the spatial relationships and composition of bacteria in these compartments. We also agree that no single bacterium

is likely to be the cause of bacterial vaginosis and that Koch's postulates for disease causation are inadequate for describing potential causal relationships in this syndrome. Bacterial vaginosis probably results from infection with complex communities of bacteria that consist of metabolically interdependent (syntrophic) species. Diseases caused by uncultivated microbes or communities of microbes are not amenable to the application of Koch's postulates in their original formulation²; therefore, we must build a case for causation on the basis of a concordance of scientific evidence.³

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Azithromycin versus Penicillin for Early Syphilis

TO THE EDITOR: In their study on the treatment of early syphilis, Riedner et al. (Sept. 22 issue)¹ concluded that the wider use of oral azithromycin should be encouraged as part of syphilis-control programs in developing countries. Whereas this conclusion would appear to be rational on the basis of the authors' results, we believe that there are other factors that should be considered before opting for such a strategy.

Although the authors acknowledged the potential for the emergence of azithromycin-resistant *Treponema pallidum*, ongoing monitoring for such resistance, as they suggested, requires molecular-sequencing techniques,² which are unavailable in most developing countries. More important, the inability of azithromycin to cross the placenta³ limits its use in the prevention of congenital disease. Treatment of seropositive mothers with oral azithromycin, after routine antenatal screening, could result in declining maternal titers on the rapid plasma reagin test without affecting the potential for fetal infection.

Since the prevention of congenital syphilis remains a major objective of control programs and is a current focus for global elimination activities,⁴ we believe that azithromycin has only a limited role in the management of syphilis in resource-constrained settings.

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TO THE EDITOR: Riedner and colleagues report that azithromycin is equivalent to penicillin G benzathine in treating early syphilis and may be useful in developing countries in which use of penicillin G benzathine is problematic, and they alert us about the cases of azithromycin-resistant *T. pallidum*. In Brazil, we struggle even with inexpensive drugs, such as penicillin G benzathine; azithromycin is not widely available and can be 10 times as expensive as penicillin G benzathine. We believe that it is not wise to change from a known, inexpensive drug with few cases of resistance after a half century of use¹ to a more expensive, unfamiliar drug that has already shown resistance after a few years of use.² Thus, the implementation of azithromycin in developing countries remains prohibitive because of the cost and because of the possibility of resistance, and this drug should not be used as a first choice yet.

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