The Role of Lactobacilli in Vaginal Health

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The role of lactobacilli in the maintenance of vaginal health was first recognized by Doderlein in the late 1800's. One of the first strategies used to treat gonorrhea in commercial sex workers was the application of exogenous *Lactobacillus* obtained from health women. Thus, the concept of providing exogenous *Lactobacillus* for maintenance of an optimal vaginal microflora is over a century old.

Pregnant women with a *Lactobacillus*-predominant flora have a decreased incidence of preterm delivery, chorioamnionitis, and postpartum infections. In addition women without a *Lactobacillus*-predominant vaginal flora appear to be at increased susceptibility for sexually transmitted infections including gonorrhea, chlamydia, herpes simplex virus 2 and human immunodeficiency virus. As treatment of bacterial vaginosis does not inevitably lead to re-establishment of a *Lactobacillus*-predominant flora, use of exogenous strains of lactobacilli have been suggested by several different research groups for enhancing the normal microbial defense of the vagina.

The attributes of an optimal strain for use in colonization of the vagina is unknown, but several properties have been proposed as being important in establishing a colonization with an exogenously supplied strain of *Lactobacillus*. These properties include ability to bind to vaginal epithelial cells, production of lactic acid, production of H_2O_2, and resistance to phage lysis. Recent studies published from Italy, the United States, Japan and other countries have established that *Lactobacillus crispatus* and *Lactobacillus jensenii* are two of the most commonly recovered vaginal species in women with a *Lactobacillus*-predominant flora. These species are nearly universal in their ability to produce peroxide and their ability to bind to vaginal epithelial cells. Unfortunately, most of the over-the-counter products containing *Lactobacillus* in the United States do not contain these types of lactobacilli.

Studies utilizing *Lactobacillus*-containing products such as yogurt have largely been unsuccessful in demonstrating successful colonization with the exogenous strain and influencing clinical outcomes related to bacterial vaginosis. Studies funded by the US National Institutes of Health have lead to the development of a *Lactobacillus crispatus* vaginal capsule which has been evaluated for use in combination with oral metronidazole for treatment of bacterial vaginosis and to re-establish a *Lactobacillus*-predominant flora. A safety study of *Lactobacillus crispatus* capsule was performed in 90 women aged 14-21 in Pittsburgh, Pennsylvania and showed that use of the capsules by women without bacterial vaginosis was safe and led to colonization by the exogenous strain in approximately 65% of the women. A second study was conducted in Pittsburgh and Seattle, Washington among 424 women with both clinical signs and Gram stain evidence of bacterial vaginosis. All women were provided with a single 2 gram dose of oral metronidazole, and capsules containing 10^8 colony forming units of *Lactobacillus crispatus* were instilled intravaginally twice daily for 3 days. Women were re-evaluated at one month, two months and three months following enrollment. At each

monthly visit, women were provided with additional vaginal capsules for use and bacterial vaginosis was re-treated with oral metronidazole if women were found to be persistently infected. In this study, most (90%) of the women had bacterial vaginosis in the previous year. Thus, the population represented predominately women with recurrent bacterial vaginosis. This study demonstrated that 88% of the women who reported using the intravaginal capsules containing *Lactobacillus* were colonized by the exogenous strain of *Lactobacillus* sometime during the three month period of follow-up. The identity of the exogenous strain of *Lactobacillus crispatus* was verified using a Rep PCR fingerprinting method which could distinguish endogenous *Lactobacillus* from those present in the capsule. These data suggest that women with recurrent bacterial vaginosis can be recolonized by exogenous strains of lactobacilli. Among women who were successfully colonized by the *Lactobacillus crispatus* strain, there was a significant improvement in clinical resolution of bacterial vaginosis compared to women given the placebo capsules. However, women who were given exogenous capsules which contained *Lactobacillus* but who were not colonized by this strain had increased rate of BV treatment failure compared to the placebo-treated women. These studies demonstrate that it is feasible to establish vaginal colonization with an exogenous strain of *Lactobacillus crispatus* and that women who become colonized have better clinical outcomes than women who are not colonized by this strain. In summary, use of exogenous lactobacilli for normalization of the flora is a concept which is widely accepted as being of great potential benefit. Preliminary studies using *Lactobacillus* provided exogenously in capsule form are promising, and future studies will be needed to verify whether use of exogenously provided *Lactobacillus crispatus* can effectively decrease the risk of recurrent bacterial vaginosis and enhance resistance to sexually transmitted infections.