



Editorial

Lactobacillus and health

Evidence shows that *Lactobacillus* species are the dominant vaginal bacteria in a majority of women, contributing to an acidic environment (pH 3.5–4.5) in the vaginal area. *Lactobacillus* also contributes to the production of hydrogen peroxide to inhibit overgrowth of other pathogens, including group B streptococci, *Escherichia coli*, *Staphylococcus aureus*, *Gardnerella vaginalis*, or other fastidious or uncultivated anaerobes.¹ Lactic acid, through the production of *Lactobacillus* species, is a potent and broad-spectrum bactericide and virucide. Therefore, many interventional efforts have been and are being made to restore vaginal health through the application of oral or vaginal probiotic formulations of *Lactobacillus* species.² In addition, the benefits of restoring vaginal microbiomes in women are not only related to the health status of women themselves but also to obstetric outcomes when these women get pregnant.^{3,4} Therefore, management, manipulation, and restoration of a robust vaginal microbiota might be advantageous in vastly improving women's health and disease prevention.² This is because historically, the presence of *Lactobacillus* species has been thought to be the *sine qua non* of healthy vaginal microbial communities in women during the reproductive age,⁴ and it might also be useful in the prevention of the benign or malignant lower genital tract diseases, such as bacterial vaginosis, sexually transmitted disease, and possible neoplasms, such as cervical intraepithelial neoplasm or cervical cancers.^{5,6} However, a scientific level understanding of how the vaginal microbiota is associated with obstetric, gynecological, and reproductive health remains problematic and deficient. Furthermore, a big gap in the development of effective preventive approaches to improved women's health is that the normal distribution of *Lactobacillus* species within the healthy vagina of women, especially in the different geographic areas, is still uncertain. Actually, the detailed information about the *Lactobacillus* species in the vagina of healthy women in different geographic areas might be one of the critical steps. Therefore, it is acknowledged that all new information addressing this topic should be thoroughly reviewed.⁷

The study by Mousavi et al⁸ in this issue of the *Journal of the Chinese Medical Association* focused on this issue to isolate and identify the *Lactobacillus* species in the vagina of healthy Iranian women who live in the Ahvaz area. The

authors evaluated the 50 healthy women, and found that only 66% of those women were identified to have *Lactobacillus* species, which included the most common form as *Lactobacillus crispatus* (42.4%, $n = 14$). The second-most common form of *Lactobacillus* species was *Lactobacillus rhamnosus* (27%, $n = 9$), followed in order by *Lactobacillus gasseri* (18.2%, $n = 6$), and *Lactobacillus salivarius* and *Lactobacillus plantarum* (both 6%, $n = 2$).⁸ Furthermore, *L. rhamnosus* has the most powerful capacity to attach two epithelia cell lines, including Vero cells (African Green monkey kidney epithelium) and HeLa cells (human squamous cell carcinoma epithelium).⁸ This study is interesting and worthy of further discussion.

First, it is not surprising to see the most frequently identified *Lactobacillus* species from the vagina of Iranian healthy women as *L. crispatus* and *L. gasseri*,⁸ because it has been reported that both species and another two unidentified species by the authors—*Lactobacillus iners* and *Lactobacillus jensenii*, seem to be specific to the human vagina, where they leverage a unique anaerobic nutritional environment to produce copious amounts of lactic acid as a fermentation product,² suggesting that the probiotic formulations of *Lactobacillus* species marketing in Iran should include *L. crispatus* and *L. gasseri*. A recent publication also supported the positive role of *L. crispatus* in women's health.⁹ *L. crispatus*-dominated cervicovaginal microbiota is considered more beneficial than *L. iners*-dominated cervicovaginal microbiota, because it is less likely to shift to dysbiosis and is associated with lower prevalence of sexually transmitted infections.⁹

Second, Mousavi et al's⁸ study was consistent with our understanding that not all healthy reproductive-age women have the presence of *Lactobacillus* species in their vagina (only two-thirds of the women in the current study). It has been reported that a large proportion of women lack appreciable numbers of *Lactobacillus* species (10–42% of women).² In fact, these women who lack appreciable numbers of *Lactobacillus* species are at risk for urogenital infection, and can remain asymptomatic for bacterial vaginosis.

Third, it is important to find that *L. rhamnosus* attached more readily to the epithelial cells, including cervical cancer cell line (HeLa cells) than did the other *Lactobacillus* species.⁸ Audirac-Chalifour et al⁵ tried to investigate the relationship

between high-risk human papillomavirus persistence in cervical cancer and the immunosuppressive tumor micro-environment mediated by cytokines, which is indirectly determined by vaginal microbeta. Audirac-Chalifour et al's⁵ study showed that human papillomavirus-negative women had an elevated proportion of *L. crispatus* (46%) and a lesser proportion of *L. iners* (14.9%), whereas human papillomavirus-positive women had proportions of 13.3% and 2.1%, respectively. In addition, these proportions seemed to switch with the presence of human papillomavirus, and *L. crispatus* was found in smaller proportions in squamous intraepithelial lesions (14.4%) and cervical cancers (1.3%), whereas *L. iners* dropped to 2.1% in squamous intraepithelial lesions and was totally absent in cervical cancers. It is also noted that other species of *Lactobacillus*, *L. jensenii* and *Lactobacillus vaginalis*, were found only in samples from women with normal cytology from Papanicolaou smear.⁵ In an early UK study, Mitra et al¹⁰ also found that increasing disease severity of cervical intraepithelial neoplasia was associated with a decreasing relative abundance of *Lactobacillus* species, supporting the importance of *Lactobacillus*-dominated vaginal microbiota for regulating human papillomavirus persistence and progression of cervical intraepithelial neoplasia. Furthermore, one study showed that *L. crispatus* and *L. rhamnosus* culture supernatants can decrease expression of ATG14 (autophagy related 14) and BECN1 (beclin 1) as well as the human papillomavirus early 6 (HPV E6) oncogene, suggesting that downregulation of HPV E6 by *Lactobacillus* species may have therapeutic potential for cervical cancer.¹¹

In conclusion, the publication⁸ of the *Journal of the Chinese Medical Association* brings to mind the reconsideration of the important interaction between microorganisms and human beings. Besides use of the human papillomavirus vaccine to prevent the cervical intraepithelial neoplasm,¹² restoration of good and healthy microbiota environments in human beings (probiotics)¹³ might reveal promising prospects for the future.

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Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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