A new way lactic acid can reduce a woman's risk of getting an STI

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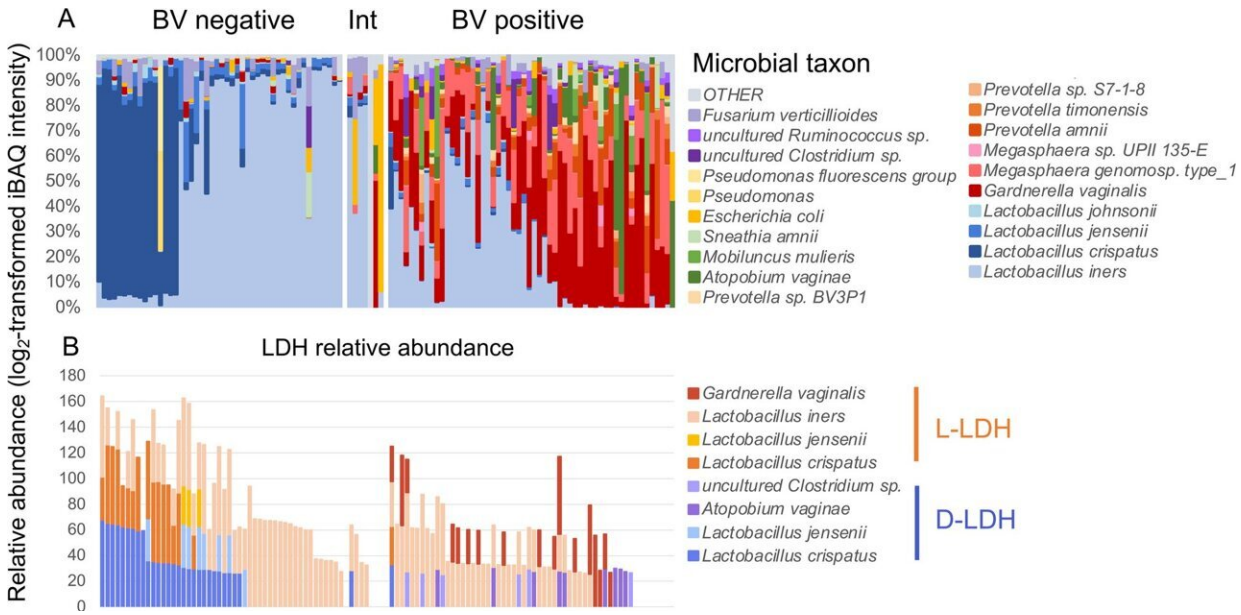

Higher relative abundance of bacterial LDH in women with a Lactobacillus-dominated microbiome. The vaginal microbiome composition of 113 young women from Cape Town, South Africa, was determined using liquid chromatography-tandem mass spectrometry, and participants were classified as being bacterial vaginosis (BV) negative, positive, or intermediate (Int) using Nugent-BV criteria. Proteins were identified using MaxQuant, and a custom database was generated using de novo sequencing to filter the UniProt database. Taxonomy was assigned using UniProt, and relative abundance of each taxon was determined by aggregating the intensity-based absolute quantification (iBAQ) values of all proteins identified for each taxon. The relative abundance of the 20 most abundant bacterial species is indicated for each participant in (A). The relative abundance of L- and D-lactate dehydrogenase (LDH) protein derived from various bacterial sources was measured in vaginal secretions using

metaproteomic analyses for each participant (B). Credit: *Microbiome* (2022). DOI: 10.1186/s40168-022-01337-5

Lactic acid strengthens the junctions between cells in the female genital tract that form a physical barrier to harmful bacteria and viruses.

New Burnet Institute-led research, published in the journal *Microbiome*, shows another way the metabolite reduces a woman's risk of getting a sexually transmitted infection (STI).

Like the gut—but perhaps not as well-known—the vagina also has a microbiome, said Burnet Ph.D. student Brianna Jesaveluk, who was the equal first author on the study. But unlike the gut where a diverse microbiome is ideal, the optimal situation in the vagina is to have a particular type of bacteria dominating—Lactobacillus. "These species have been shown to promote really good outcomes for a lot of different health benefits," Jesaveluk said.

In particular, scientists have long known that women with vaginal microbiomes dominated by Lactobacillus species have a reduced risk of getting STIs, including HIV, although they don't yet know exactly why. Previous Burnet research has shown that lactic acid—which is made by the Lactobacillus species—reduces inflammation. Inflammation in the genital tract is bad because it increases HIV risk. Lactic acid can also directly kill bacteria and viruses like HIV.

This latest discovery shows that lactic acid strengthens the female genital tract's ability to act as a physical barrier to harmful microbes. Imagine the cells lining the female genital tract are like a paling fence, said Burnet Deputy Program Director Disease Elimination, Dr. Anna Hearps, who was a senior author on the study.

"Lactic acid keeps the palings of the fence close together, and stops things from sneaking through," Dr. Hearps said. The researchers are now looking at how these discoveries can be used therapeutically. "We're planning a trial of an intravaginal gel containing lactic acid," Dr. Hearps said.

The aim of the trial is to confirm that the benefits the scientists are seeing in the lab are also what's happening in women, and to determine what the optimal lactic acid concentration and composition of the gel would be.

"One of the potential applications of our work would be an intravaginal ring that women could insert that would slowly secrete lactic acid," Dr. Hearps said. While there are already gels on the market containing lactic acid, they are marketed as cosmetics not therapeutics, and hence haven't been subject to this kind of rigorous study. "So, some of these gels on the market could actually be doing harms that we don't really know about," Dr. Hearps said.

In the long term, the researchers are working towards women having their own effective mechanisms for protecting themselves against HIV.

"Women in Sub-Saharan Africa at risk of HIV for example, are not always in a position to necessarily negotiate other mechanisms of protection like condom use," Jesaveluk said. "If we can develop a therapeutic intervention that's women-led, women-controlled, then they can protect themselves."

It's about acknowledging that women want and need multiple different options in different populations, in different cultural settings, and in different environments, Dr. Hearps said.

This work was led by Burnet Head of Life Sciences, Professor Gilda

Tachedjian, and underpins the EVE-M initiative.

EVE-M stands for Enhancing the Vaginal Environment and Microbiome and aims to transform women's sexual and reproductive health by advancing knowledge on the genital microbiome to translate into novel strategies to prevent STIs including HIV and adverse obstetric outcomes.

The study was an international multidisciplinary collaboration between researchers in Australia, South Africa, Morocco, and the United States, and analyzed samples collected from young women in the Women's Initiative in Sexual Health study conducted in South Africa.

More information: David Jose Delgado-Diaz et al, Lactic acid from vaginal microbiota enhances cervicovaginal epithelial barrier integrity by promoting tight junction protein expression, *Microbiome* (2022). DOI: 10.1186/s40168-022-01337-5

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