Women health and the microbiota

The female urogenital tract is compromised of the vagina, cervix, ovarian system, and the bladder and plays a critical role in reproduction, and sexual and urinary function. Urogenital infections, e.g. vaginal candidiasis, bacterial vaginosis, and urinary tract infections, are very common health problems in women. The unifying feature of all of the above infections is an imbalance or dysbiosis of the natural microbiome(s); thus it follows that the healthy urogenital microbiotas play an important protective role. In fact, women with vaginal microbial dysbiosis are at higher risk of developing symptomatic infections in the vagina and/or bladder. Multiple risk factors have been identified that can cause urogenital microbiota dysbiosis (for instance: antibiotic use, hormonal contraceptive, and vaginal lubricants).
Both vaginal and urinary infections negatively influence patient quality of life, especially affecting self-esteem and sex life. As well, there appears to be further relationships within the urogenital tract, as patients with bacterial vaginosis are at an increased risk of acute urinary tract infections, female infertility and also have an increased risk for complications during pregnancy.

**Urogenital Microbiomes**

**a The vaginal microbiome**

The human vagina is colonised with microorganisms directly after birth. The vagina is inhabited by a range of microbes from a pool of over 50 species. The bacterial communities of healthy vaginas are mainly clustered into one of five groups: four are dominated by lactic acid-producing bacteria like Lactobacillus spp., whereas the fifth has a higher α-diversity with lower proportions of lactic acid bacteria and higher proportions of strictly anaerobic organisms. One of the key functions the vaginal microbiome is to keep the pH low; lactobacilli and other lactic-acid producing bacteria ferment the glycogen released by the epithelial cells, which creates a selective low pH environment that inhibits growth of certain pathogenic species. Pathogens and viruses are further inhibited by additional beneficial compounds produced by vaginal lactobacilli: hydrogen peroxide (H2O2), biosurfactants, and bacteriocins (which are a natural antibiotic of peptide origin). These protective vaginal compounds have even been shown to enhance the antibiotic sensitivity of vaginal pathogens to antibiotics.

The healthy vaginal microbiota is complex and dynamic and changes during the different stages in a woman’s life. Estrogen regulates the thickening of the vaginal epithelium and the production of vaginal glycogen. These changes in the vaginal microbiota seem to be related to estrogen levels, with increasing levels during adolescence and reproductive age. During these life phases that lactobacilli become more dominant, while they follow the declining estrogen levels in menopause. These temporal shifts in the vaginal microbiome are natural, but there are more problematic dysbiosis in the vagina microbiome can be caused by antibiotic use, hormonal (and other) contraconception, sexual intercourse, vaginal lubricants, vaginal douche, menstruation, pregnancy and stress. Women with dysbiosis are likely at higher risk of developing symptomatic infections in the vagina and/or bladder, as well as having an increased risk of sexually transmitted diseases, pregnancy complications, and preterm labor.

**b The urinary microbiome**

In contrary to the long-held paradigm, a healthy bladder is not sterile. New bacterial identification techniques such as 16S rRNA gene analysis and high-throughput DNA sequencing have revealed uncultured in the bladders of both healthy adult female individuals and patients with UTIs. Current research shows that urine samples are dominated by Lactobacillus spp. or Gardnerella spp. or by the family Enterobacteriaceae, which includes Escherichia spp., Klebsiella spp., and Proteus spp. In some women, there is emerging evidence that dysbiosis in the urinary bacterial community may be associated with urgency urinary incontinence, overactive bladder, and UTIs.

The origin of bladder microorganisms has been a point of heated discussion. The urinary tract is a self-contained organ with an impermeable lining, so the current opinion is that retrograde microbial ascent is thought to be the most source of the bladder organisms. Indeed, cultures of urine-isolated
Microorganisms from women have been genetically identified as identical to those cultured from vaginal samples and fecal microorganisms. Furthermore, the same causative UTI pathogen can be isolated for up to three years in adults, hinting at extra-urinary microbial reservoirs. Additional support for the GI tract as one source of bladder microorganisms can also be found in some earlier studies that suggest links between the gastrointestinal microbiota and urinary health.

Shifts in the urinary microbiome causing dysbiosis can be caused by a number of factors including medication, both short term and long-term medication, vaginal infections and sexual intercourse. It is interesting to note that antibiotics are unable to alter the receptivity of urothelial cells to adherence by pathogens, so when complete eradication of the live functioning urinary microbes is not possible, alternatives or adjuncts should be considered.

Probiotics for Urogenital Health

A clear relationship seems to exist between a decrease in the amount of lactobacilli and risk of urogenital infections. It follows that strategies that support recovery of the microbiota can play a role in both vaginal and urinary health. Probiotic bacteria, when administered in amounts over \(1.0 \times 10^8\) CFU for 2 months can normalize the vaginal microbiota and help cure existing infections and prevent recurrence of BV reviewed in Homayouni 2014. The positive use of probiotics has also been demonstrated for the prevention of UTIs. A meta-analysis reported a statistically significant decrease in rUTIs in adult patients given probiotics, denoted by the pooled risk ratio of 0.51 (95% CI:0.26–0.99; \(p = 0.05\)).

An advantage for patients is that urogenital probiotics have no reported adverse side effects, can be used alongside antimicrobial treatment, present minimal discomfort, and can be self-administered. It is clear that urogenital probiotics can improve quality of life and sexual health, and decrease risk of preterm birth. In addition, the evidence from the available studies suggests that probiotics can be used as adjunct treatments to enhance antibiotic treatment and reduce side effects.

One of the main mechanisms of action of probiotics in the prevention and/or treatment of urogenital infections is the restoration of the natural low pH environment. It is thought that colonization is also an important factor in the prevention or treatment of vaginal infections. In addition, probiotics may offer protection through the production of biosurfactants, and co-aggregation with pathogens to block adhesion and/or displace previously adherent pathogens on epithelial cells.
While probiotics may generally have a slightly inferior therapeutic effect than (prophylactic) antibiotics, they present minimal negative disturbances of the microbiota with no risk of antibiotic resistance and systemic side effects. This non-chemotherapeutic role of urogenital probiotics either as an adjuvant to standard treatment or a stand-alone therapy allows a clinician to have an additional option for their patients. To achieve optimal patient care, a clinician should consider to be guided by their clinical logic and experience when weighing the available evidence in the absence of standard guidelines when evaluating probiotic as alternative options such as probiotics.

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