

The search for the ideal microbiota in human reproduction

Joshua Lederberg (1925-2008) 1958 Nobel Prize in Physiology and Medicine was the first to use the term microbiota to describe the ecological environment of microorganisms that inhabit the human body. The study of the diversity of the human microbiota started with Antonie van Leeuwenhoek (1632-1723), who, as early as the 1680s, had compared his oral and fecal microbiota using his handcrafted microscopes. He noted the striking differences in microbes between these two habitats and also between samples from individuals in states of health and disease in both of these sites.

The development of molecular techniques has increased the detection of different microorganisms, the number of known species, and the understanding of bacterial communities. *Homo sapiens* could be described as an ecosystem, with a constant interaction between the trillions of cells that are the products of our genes (the 'host') and 10-100 trillions of microorganisms that colonize the body (the 'microbiota') mainly our skin, mucosa and gastrointestinal tract (Odent M and Jauniaux E. Caesarean delivery and human evolution. In Textbook of caesarean section. Oxford University Press. 175-190, 2016).

The physiological variations in the vaginal microbiota (Figure) were first described by Cruickshank and Sharman (J Obstet Gynaecol Br Emp 1934;41:369-84). Its imbalances and their possible clinical consequences have now been studied for more than 60 years. In 1948, Nancy Laughon, a lecturer in Virology and Bacteriology at the University of Birmingham studied the vaginal swabs a group of 39 "married" women attending the local fertility clinic (J Obstet Gynaecol Br Emp 1948;55:608-13). These women's main complaint was infertility and they were "free of organic pelvic disease" at the time of the study. She found that the absence of *Lactobacillus acidophilus* or Döderlein's bacillus (discovered by the German gynaecologist Albert Döderlein in 1892) in vaginal samples and the presence of coliforms, enterococci and vibrios were associated with higher numbers of leucocytes and elevated vaginal pH. She suggested that deposition of vaginal glycogen is "deranged" and "indicative of ovarian dysfunction". These findings led a decade later to the concept of "bacterial vaginitis" and Laughon's findings are still valid today.

It is now well established that lactobacilli are essential to a balanced vaginal microbiota and control the development and growth of other bacteria by producing lactic acid (Witkin SS and Linhares IM (BJOG 2017, this issue). Ilya Iyich Mechnikoff (1845-1916) a Russian zoologist who shared the 1908 Nobel Prize in Physiology and Medicine with Paul Ehrlich (1854-1915), a German physician, for their work on immunity, is credited for having

suggested that aging could be delayed by manipulating the intestinal microbiota with host-friendly bacteria found in yogurt (Mackowiak PA. *Front Public Health*. 2013;1:52), opening the world of pre- and probiotics. As suggested by Witkin and Linhares, prebiotics that promote the growth of lactic acid-producing bacteria may improve fertility and pregnancy outcome in women with sub-optimal vaginal microbiota without requiring antibiotics. An essential strategy in a new area of antimicrobial resistance which requires the development of new pre- and probiotics products and their prospective rigorous evaluation.

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Disclosure of interests

The authors declare no conflicts of interest.

Figure 1: Infant vaginal epithelial cells and Döderlein's vaginal bacilli. Gram. (x 1000). From Cruickshank and Sharman (*J Obstet Gynaecol Br Emp* 1934;41:369-84

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