

Editorial

*Corresponding author

Sertaç Esin, MD

Associate Professor
Division of Perinatology
Department of Obstetrics and Gynecology
Baskent University
Şehit Temel Kuşuoğlu Cad. No:34
Bahçelievler, Ankara, Turkey
E-mail: sertacesin@gmail.com

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A Novel Contributor to Endometrial Receptivity: Endometrial Microbiota

Yusuf Aytaç Tohma, MD¹; Sertaç Esin, MD^{2*}

¹Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Baskent University, Ankara, Turkey

²Division of Perinatology, Department of Obstetrics and Gynecology, Baskent University, Ankara, Turkey

In the recent years, our knowledge about human reproductive system has increased with the development of assisted reproductive technologies; however, embryo implantation rate is still around 25-30%.¹ Embryo implantation depends on the quality of the embryo, endometrial receptivity and the embryo/endometrial interface.² The onset of implantation is a successful concurrence of 2 different processes; embryo development and endometrial differentiation. Therefore, synchronization between development of a good quality embryo and receptive endometrium is paramount for the success of embryo implantation and ongoing pregnancy.^{2,3} The association between embryo and receptive endometrium during implantation is not fully understood yet, because *in vivo* studies about implantation are scarce due to ethical and technical problems. So our knowledge about implantation is mostly derived from animal studies.^{4,5}

Microbiota which was fully defined in 2001 is regarded as the second genome, and its importance in reproductive system has newly understood.⁶⁻⁹ Microbiota is a source of genetic diversity and is important for normal immune system, metabolism and behavior of the disease.¹⁰ Microbiota inhabits different systems of the body and there is a synergistic interaction between microbiota and its host.¹⁰ Due to these known synergistic effects, microbiota transplantation has been used as a treatment for recurrent *Clostridium difficile* infection which may be difficult to manage with conventional antibiotic therapies. Fecal microbiota transplantation from a healthy person to the patient restores the gut microbiota to a healthy state.^{11,12}

Endometrial receptivity is regulated by synchronization of different cell types and several factors such as luminal and glandular epithelium, cytokines, growth factors, proteases, glucose, hormones and enzymes.^{2,3} Recent research has also revealed the importance of endometrial microbiota and its possible impact in endometrial receptivity.^{13,14} Until recently, endometrium was classically considered a sterile cavity and when the reproductive system microbiota was considered, vaginal microbiota came to mind.¹⁵ However, new techniques and technologies such as microarrays, DNA fingerprinting, and targeted or whole genome sequencing have empowered the field of metagenomics and have begun to change the way we think of reproductive system microbiota.¹⁶ With help of these innovations, identification of microorganisms in uterine cavity of asymptomatic patients undergoing hysterectomy for benign indications confirmed that the uterine cavity is not sterile and endometrium has an own microbiota such as *Gardnerella vaginalis*, *Lactobacillus* spp., *Enterobacter* spp. and *Mycoplasma hominis* and is independent from hormonal regulation.¹⁴ In the future, endometrial microbiota transplantation may be used for recurrent implantation failure patients.

Recent studies reported that non lactobacillus microbiota domination in endometrial cavities is strongly correlated with failure of implantation as compared to lactobacillus dominated endometrial microbiota.^{14,17} Because balance in inflammatory factors is important for regulation of the adhesion of the blastocyst to the epithelial endometrial wall, non-lactobacillus dominated microbiota may cause inflammation in the uterine cavity and impair endometrial receptivity.¹⁴ We need new studies focusing on the interaction between endometrial microbiota and receptivity.

As a result, a human endometrial microbiota exists and is independent of hormonal regulation. Non-Lactobacillus dominant endometrial microbiota impairs endometrial receptivity and may result in implantation failure and pregnancy loss but lactobacillus dominancy is a supporter of healthy reproductive system. Now, we have to know that endometrial receptivity is not only under control of the morphological and molecular factors but endometrial microbiota has substantial functions for endometrial integrity and successful implantation. It is time to consider microorganisms not only as enemies but also as allies in reproductive medicine.

CONFLICTS OF INTEREST

None of the authors have a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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