

Editorial



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Dear Readers,

The endometrium is the only tissue capable of regenerating every month to be functional, or rather, useful, very few times, sometimes none, during the course of life. Its uniqueness has made it a subject of study for decades as it aligns several endocrine organs and coordinates with the development of the embryo to reach its stellar moment in the process of embryonic implantation. As studies using new technologies have been conducted, knowledge about the functioning of the layer that lines the human uterus has increased. Still, implantation of an embryo remains one of the greatest incognitas in the field of human reproduction.

From imaging studies to gene expression analyses or knowledge about the microbiome, data have been provided to understand the physiology and also the changes that occur in the different pathologies that affect the endometrium. Finally, reproductive medicine has assigned its role in the reproductive process, not diminishing its importance in the development of the earliest stages of pregnancy. Understanding its functioning has led to better methods of preparing the luteal phase and understanding and addressing the two main medical problems related to infertility: implantation failure and recurrent miscarriage.

Although there are multifactorial components, not only derived from the endometrial function itself,

knowing the characteristics of a healthy endometrium allows the development of protocols to maintain or improve its functionality and also to establish red lines that mark the clinical limits of its normality, such as its thickness or its microbiological balance. Despite these progresses, the difficulties to study human implantation are huge. Thus the need of developing methods and technologies such as the one shown in our cover of this volume are required.

The endometrium is a dynamic, variable, and extraordinarily sensitive tissue to changes. As a complex tissue, its study, the anamnesis of its pathologies, and its implication in reproductive problems are also complex. Establishing guidelines for its treatment for a successful pregnancy is also complex. Nowadays, there are no clear guidelines for the treatment of a dysfunctional endometrium, with empirical protocols existing for, for example, the treatment of a thin endometrium that range from the use of sildenafil to treatment with growth factor-rich plasma, Granulocyte Macrophage Colony-Stimulating Factor (GM-CSF) therapy, or stem cell transplantation.

One can find in the literature publications both for and against with favorable or null results, leaving the reproductive specialist with the doubt of their true efficiency. William Osler said that "medicine is the science of uncertainty and the art of probability." That phrase takes on even more significance in the

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treatment of a non-functional or refractory endometrium. But that is precisely what makes Medicine an art and not an exact science. In the development of Personalized Medicine, it is necessary to apply knowledge about the endometrium in the most scientific way possible, clearly understanding what we must do, leaving aside subjective criteria. In our world of assisted reproduction, innovation is a constant reality, a continuous challenge. It is our perpetual curiosity that leads us to innovate and seek solutions, that leads us to think we can do more than we do.

From the classic study of the endometrium through pathological anatomy to observe the ancient Noyes criteria, whose first studies date back to 1950, to the development of artificial intelligence for the diagnosis of endometrial receptivity through imaging, the physiopathology of the endometrium has been investigated at the biological level, dissecting at the molecular level the processes that take place in the endometrium throughout the menstrual cycle, especially focusing on the window of implantation that leads to the possibility of an embryonic implantation and a healthy pregnancy. Invasive molecular tools aimed at diagnosing and evaluating endometrial functionality have been developed, highlighting the clinical need to observe the endometrium objectively, trying to improve existing techniques.

The fact that the different tests developed that analyze different genes with different technologies and different algorithms end up obtaining similar results makes us think that, indeed, endometrial gene expression is an objective molecular criterion both for defining endometrial receptivity and for finding factors related to the physiopathology of endometrial tissue. We could say, without fear of being wrong, that in the field of endometrial tests, "all roads lead to Rome" and that the spirit of their conception is to provide the physician with a useful tool. However, it is obvious that although all roads lead to Rome, not all roads are the same, and something even more important than the road is the "way of facing it."

Warm regards,



Ricardo Héctor Asch Schuff



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Every invention or development has its function and usefulness, from scissors to a molecular study, and if used incorrectly or in the wrong place or time, undesirable results are obtained. In recent years, knowledge of the endometrial microbiological ecosystem has resulted in a new unknown facet for clinical study.

The implication of the microbiome in uterine functionality and especially in its alteration has brought to light another variable to consider in certain cases of infertility. The endometrium never ceases to surprise us, and thinking that for decades it was established that the scenario of the beginning of pregnancy was a sterile place. And it is not so. This part of the study of the endometrium may have no end due to its complexity and also to its connections with the intestinal microbiome and gynecological alterations, which in some cases seem to have a dysbiotic origin.

Molecular tools are objective and precise, which allows setting limits, margins, thresholds, and critical levels, but we must not forget the biological variability between individuals and the phenotype associated with lifestyle. Similarly, the latest non-invasive developments for image analysis give the reproductive specialist more data to improve the efficiency in treating the infertile couple. In this monograph, some pathologies related to this unique tissue are also addressed. Pathologies that, likewise, present a varied spectrum of manifestations that affect endometrial functionality at different levels.

This special edition on the endometrium of The Journal of Reproduction only shows some aspects of its complexity but serves to establish the direction in which the efforts of clinicians and researchers are headed in knowing, diagnosing, and above all interpreting the signals that the endometrium shows to treat the patient in a personalized and efficient way for a successful embryonic implantation and a safe pregnancy.