Uterine architecture: building the foundation for a healthy pregnancy

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"The hardest thing to explain is the glaringly evident which everybody has decided not to see."

– Ayn Rand, *The Fountainhead*

The March 1968 issue of *Fertility and Sterility* contains the article, "Protein nutrition and the biochemical composition of the uterus" (1). In this article, Leathem et al. (1) discuss the correlation between undernutrition, decreased fertility, increased menstrual irregularities and reduction in estrogen levels. The etiology was believed to be a reduction in ovarian function with subsequent downstream effect on the uterus. The authors hypothesized that uterine composition could be modified by protein malnutrition. To answer this question, they altered the diet of normal adult rats and fed the experimental group a protein-free diet for 21 days. In doing so they were able to document a decrease in uterine weight as well as a decrease in total protein, RNA and DNA. Interestingly, replacement levels of estrogen and progesterone failed to prevent the nutritional effects on the uterus. They then ovarectomized the mice and compared the impact of estrogen replacement between protein-rich and protein-free diet groups. The protein-rich diet group had a greater increase in uterine weight compared to the protein-free group demonstrating that uterine composition could be altered by protein composition of the diet.

Fifty years later, we have made startling advances in the field of reproductive medicine. The integration of genetics and in vitro fertilization has resulted in exponentially increased implantation rates. Despite this, in 2018, a euploid embryo does not always result in a live birth. Oocyte, sperm and uterine factors are contributory to implantation. Arguably, uterine factors are the most complex, and least understood. Macroscopic attention to the endometrium has focused on thickness and architecture. Increased attention to the microscopic endometrial environment led to the association between hydrosalpinx and reduced implantation (2), endometritis and recurrent pregnancy loss (3), and advances in "omics" have enhanced our understanding of endometrial receptivity (4).

Paying more attention to the macronutrient environment into which embryos are transferred may ultimately influence embryonic competence. One can hope that 50 years from today, implantation rates will approach 100% with better understanding of the microscopic, macroscopic, micronutrient and macronutrient environments in which gametes and embryos develop.

REFERENCES

1. Leathem JH, Oslapas R, Fisher CJ. Protein nutrition and the biochemical composition of the uterus. Fertil Steril 1968;19:206–12.
2. Strandell A, Lindhard A, Waldenstrom U, Thorburn J. Hydrosalpinx and IVF outcome: cumulative results after salpingectomy in a randomized controlled trial. Hum Reprod 2001;16:2403–10.
3. McQueen DB, Bernardi LA, Stephenson MD. Chronic endometritis in women with recurrent early pregnancy loss and/or fetal demise. Fertil Steril 2014;101:1026–30.
4. Diaz-Gimeno P, Horcajadas JA, Martinez-Conejero JA, Esteban FJ, Alama P, Pellicer A, et al. A genomic diagnostic tool for human endometrial receptivity based on the transcriptomic signature. Fertil Steril 2011;95:50–60, 1e-15e.

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