Endometriosis: Surgery Alone Won't Tx Fertility

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NEW YORK – Surgery alone won't completely treat infertility in women with endometriosis, according to one infertility expert.

Instead, physicians need to consider all of their options. In women with significant endometriosis, the best course for improving pregnancy rates may be surgery plus some form of assisted reproductive technology (ART), Dr. Hugh S. Taylor, director of reproductive endocrinology and infertility at Yale University, New Haven, Conn., said at the meeting.

Prospective randomized trials examining surgical interventions in endometriosis do demonstrate improvements in pregnancy rates. In a study by the Canadian Collaborative Group on Endometriosis that included 341 infertile women with mild endometriosis who underwent either a diagnostic laparoscopy or resection or ablation of visible endometriosis, pregnancy rates nearly doubled with removal of endometriotic lesions. Diagnostic laparoscopy resulted in a subsequent pregnancy rate of about 17.7%, while the pregnancy rate was 30.7% in women whose lesions were removed. The pregnancy rates per month rose from about 2.4% in the control group to about 4.7% in the intervention group (N. Engl. J. Med. 1997;337:217-22).

Although the study showed an increase in pregnancy rates, those rates are still very low. Comparatively, without treatment, women with stage I or II endometriosis-associated infertility have a spontaneous monthly fecundity rate between 2% and 3%, Dr. Taylor said, and treatment with in vitro fertilization (IVF) can result in monthly pregnancy rates of 30%-50% in women with endometriosis.

One reason that surgery doesn't provide a meaningful boost in fertility is that surgeons often fail to identify endometriotic lesions and so don't perform a full resection. Adding to this problem, the staging system used for endometriosis isn't very accurate and doesn't correlate well with pain or infertility.

The biggest problem, however, in using surgery to correct fertility problems associated with endometriosis is that the disease creates epigenetic changes in the endometrium that may not be reversible, even if the endometriotic lesions are fully removed. "Once that DNA is modified, it stays that way," Dr. Taylor said. "So we can be removing all of the endometriosis, and yet that change in the uterus won't revert simply by treating the endometriosis."

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DR. TAYLOR

In an effort to get a better handle on this phenomenon, Dr. Taylor has been studying the effect of the HOXA10 gene – which is required for an embryo to attach to the uterus – in mouse and primate models. In mouse models, when the gene is not expressed the uterus will not be receptive to embryos, even normal embryos. In humans, expression of the HOXA10 gene varies with the menstrual cycle. It increases at the time of implantation and is regulated by estrogen and progesterone. "It looks like it's playing an important role in that implantation process." In women with endometriosis, the HOXA10 gene generally fails to increase, suggesting that there is an implantation defect in women with endometriosis. Dr. Taylor has shown that this failure is due to epigenetic reprogramming of the HOXA10 gene (Semin. Reprod. Med. 2010;28:69-74).

But there is some hopeful news for women with endometriosis who want to conceive, Dr. Taylor said. Researchers are looking at ways to use stem cells to replace the damaged cells. The idea is that placing new cells in the endometrium can restore fertility by making the endometrium more receptive to implantation. ■

Disclosures: *Dr. Taylor said he had no conflicts of interest to disclose.*