

## IVF Treatment in Patients with Endometriosis: A Challenger Approach

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It is estimated that endometriosis affects over 70 million women around the world; more than 30% of those women may also be infertile [1]. Endometriosis can be defined as an endometrium like tissue (glands and stroma) outside the uterine cavity. Among the large spectrum of clinical endometriosis phenotypes, the American Society for Reproductive Medicine (ASRM) resumes endometriosis in four stages (Stage 1: minimal; Stage 2: mild; Stage 3: moderate; Stage 4: severe) [2].

The exact pathophysiology underlying infertility in the presence of endometriosis is poorly understood. Endometriosis may affect fertility via: abnormal folliculogenesis; changes in ovarian steroid enzymes; impaired oocyte maturation leading to poor oocyte quality and consequently reduced fertilization rate or poor embryo quality; high levels of caustic peritoneal fluid components such as oxidative stress and inflammatory interleukins and cytokines; tubal obstruction or other distorted pelvic anatomy particularly with excessive scarring and adhesions present in advanced stages of endometriosis; sperm dysfunction given eutopic endometrial environment; and implantation defects [3-5].

In order to improve the conception and live-birth success among infertile patients with endometriosis, clinical intervention options include pharmaceutical and surgical treatment followed by assisted reproduction therapy. In the presence of severe pain, most clinicians agree that surgical intervention is warranted, particularly given the impact that dyspareunia has upon spontaneous conception. However, in the absence of severe pain, treatment consensus has not yet been reached. As per ASRM and ESHRE guidelines [6,7] disease confirmation is typically the indication for the initial laparoscopy, and often is the point of initial surgical ablation of visualized lesions. However, repeated laparoscopic surgeries can catalyze scarring and adhesion formation and may diminish ovarian reserve [8,9].

Recently, Ziegler et al. [4] proposed an "emergency" in vitro fertilization (IVF) procedure specific to women with endometriosis who were experiencing infertility. In brief, the authors proposed prioritizing measurement of ovarian reserve and hysterosalpingogram evaluation of tubal patency (with inclusion of standard evaluation for indications of male infertility in the partner). If those parameters show alterations, surgical treatment would be avoided with immediate progression to IVF. They stressed this accelerated path to IVF is particularly critical among women older than 38 or those with infertility of long duration. [4]

In addition to consideration of the "emergency" IVF timeline, it is critical for the surgical techniques to minimize ovarian damage when excising endometriomas (enhanced by use of GnRH prior to the surgery in order to reduce the endometrioma size). While no data currently exist regarding lifestyle alteration within endometriosis patients embarking on ART to maximize success, studies of the relation with endometriosis directly suggest that minimizing cigarette smoking and improving diet (increasing healthy fats and vegetables while minimizing unhealthy fats and red meat) may have a beneficial effect on the disease or its symptoms [10,11]. The relation with obesity is complex as thinness has been associated with endometriosis risk [10,12] while obesity may contribute to poor IVF outcomes [13].

Additional randomized controlled trials powered to evaluate differences in success associated with specific endometriosis phenotypes and designed to include long-term follow-up accounting for time-varying covariates such as pregnancy, lactation, anthropometric changes, and lifestyle changes should be conducted [13]. Multidisciplinary teams including endometriosis and ART specialists as well as complementary medicine, epidemiologists, and bench scientists must be formed to elucidate underlying pathophysiology and maximize development of successful clinical and lifestyle interventions [14-16].

### References

1. Giudice LC (2010) Clinical practice. Endometriosis. *N Engl J Med* 362: 2389-2398.
2. (1997) Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril* 67: 817-821.
3. Gupta S, Goldberg JM, Aziz N, Goldberg E, Krajcir N, et al. (2008) Pathogenic mechanisms in endometriosis-associated infertility. *Fertil Steril* 90: 247-257.
4. de Ziegler D, Borghese B, Chapron C (2010) Endometriosis and infertility: pathophysiology and management. *Lancet* 376: 730-738.
5. Carvalho L, Podgaec S, Bellodi-Privato M, Falcone T, Abrão MS (2011) Role of eutopic endometrium in pelvic endometriosis. *J Minim Invasive Gynecol* 18: 419-427.
6. Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, et al. (2005) ESHRE guideline for the diagnosis and treatment of endometriosis. *Hum Reprod* 20: 2698-2704.
7. (2008) Treatment of pelvic pain associated with endometriosis. *Fertil Steril* 90: S260-269.
8. Loh FH, Tan AT, Kumar J, Ng SC (1999) Ovarian response after laparoscopic ovarian cystectomy for endometriotic cysts in 132 monitored cycles. *Fertil Steril* 72: 316-321.
9. Härkki P, Tiitinen A, Ylikorkala O (2010) Endometriosis and assisted reproduction techniques. *Ann N Y Acad Sci* 1205: 207-213.
10. Missmer SA, Hankinson SE, Spiegelman D, Barbieri RL, Marshall LM, et al. (2004) Incidence of laparoscopically confirmed endometriosis by demographic, anthropometric, and lifestyle factors. *Am J Epidemiol* 160: 784-796.
11. Missmer SA, Chavarro JE, Malspeis S, Bertone-Johnson ER, Hornstein MD, et al. (2010) A prospective study of dietary fat consumption and endometriosis risk. *Hum Reprod* 25: 1528-1535.
12. Cooney MA, Buck Louis GM, Hediger ML, Vexler A, Kostyniak PJ (2010) Organochlorine pesticides and endometriosis. *Reprod Toxicol* 30: 365-369.
13. Shah DK, Missmer SA, Berry KF, Racowsky C, Ginsburg ES (2011) Effect of obesity on oocyte and embryo quality in women undergoing in vitro fertilization. *Obstet Gynecol* 118: 63-70.
14. Surrey ES, Silverberg KM, Surrey MW, Schoolcraft WB (2002) Effect of prolonged gonadotropin-releasing hormone agonist therapy on the outcome of in vitro fertilization-embryo transfer in patients with endometriosis. *Fertil Steril* 78: 699-704.

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15. Coccia ME, Rizzello F (2008) Ovarian reserve. Annals of the New York Academy of Sciences 1127: 27-30.
16. Garcia-Velasco JA, Somigliana E (2009) Management of endometriomas in women requiring IVF: to touch or not to touch. Hum Reprod 24: 496-501.