Journal of in Vitro Fertilization and Embryo Transfer, Vol. 5, No. 5, 1988

In Vitro Fertilization and Embryo Transfer (IVF/ET): An Established and Successful Therapy for Endometriosis

SERGIO OEHNINGER,[1,2] ANIBAL A. ACOSTA,[1] DAVID KREINER,[1] SUHEIL J. MUASHER,[1] HOWARD W. JONES, JR.,[1] and ZEV ROSENWAKS[1]

Submitted: February 17, 1988
Accepted: June 30, 1988 (Central Editorial Office)

The purpose of this report is to present a 6-year experience in the management of endometriosis with in vitro fertilization and embryo transfer (IVF/ET). We divided 136 patients who underwent 280 cycles into three groups: (1) previous history of endometriosis but normal pelvis at the time of oocyte retrieval, (2) stages I–II endometriosis (revised AFS classification), and (3) stages III–IV endometriosis. The stimulation protocols, estradiol (E_2) responses, and distribution of terminal E_2 patterns were similar in all groups. Group 3 had significantly fewer preovulatory and immature oocytes retrieved and fewer embryos transferred. The fertilization rate and the per cycle/per transfer pregnancy rates were similar in all groups. The miscarriage rate was higher in group 3, and the ongoing pregnancy rate per cycle was lower. Luteal phase E_2 and progesterone levels were comparable in all groups. No differences were found when groups 2 and 3 were analyzed for the presence of one or two ovaries or the presence/absence of ovarian endometriosis. The overall fertilization rate, the per cycle/per transfer pregnancy rates, and the miscarriage rate were similar to those of tubal factor patients. We underscore the excellent outcome of patients with minimal or mild endometriosis in IVF/ET. We conclude that patients with moderate or severe endometriosis have a compromised reproductive potential, probably because of a reduced oocyte recovery rate and poor embryo quality.

KEY WORDS: endometriosis; infertility; in vitro fertilization.

INTRODUCTION

Endometriosis is one of the most prevalent gynecologic disorders in our society (1). It appears to be increasing in frequency in the United States, paralleling the increasing use of infertility services in this country (2). The association between endometriosis and infertility has been frequently documented, although the mechanism(s) by which it impairs fertility remain(s) to be fully elucidated (3). With the advent of in vitro fertilization and embryo transfer (IVF/ET), more and more patients failing to conceive with conventional therapy have undergone this procedure. Several IVF groups have reported oocyte recovery, fertilization, and pregnancy rates in women with varying degrees of endometriosis (4–8). However, all studies have been too small to draw definitive conclusions.

In this study we present IVF results in a large series of patients with endometriosis. The main objectives of this study were (a) to evaluate the overall IVF outcome (oocyte quality and quantity at recovery, fertilization rate, and pregnancy outcome) in patients with different stages of the disease and (b) to analyze the influence of the presence or absence of ovarian endometriosis (deep or superficial) and the effect of one ovary or two on the ovarian response to gonadotropin stimulation and, finally, on the pregnancy outcome.

MATERIALS AND METHODS

From March 1981 through March 1987, 1037 patients underwent a total of 2049 IVF attempts (cycles). In 136 patients (13.1%) endometriosis was the established cause of infertility, alone or combined with other factors of infertility. These patients underwent a total of 280 IVF cycles (13.6%).

The diagnosis of endometriosis was made according to medical history and laparoscopic visualiza-

[1] Jones Institute for Reproductive Medicine, Eastern Virginia Medical School, 825 Fairfax Avenue, Norfolk, Virginia 23507.
[2] To whom correspondence should be addressed.

0740-7769/88/1000-0249$06.00/0

tion of endometrial implants and/or endometriomas at the time of oocyte retrieval. Eighty-eight patients presented with endometriosis as the sole condition responsible for infertility, while in 48 patients multiple factors were found: 31 tubal factor, 9 male factor, 2 myomata uteri, and 1 each of tubal factor and myomata uteri, in utero DES exposure, cervical factor, DES exposure and immunologic infertility, tubal factor and luteal-phase defect, and tubal and immunologic factor. Three groups of patients were considered (Table I).

Group 1. This group was composed of 23 patients (54 cycles) in whom a normal pelvis without evidence of endometriosis was found at laparoscopy, although all the cases had a history of endometriosis diagnosed at previous laparoscopic procedures. The great majority of these patients had received treatment for their endometriosis, either medical therapy (danazol, methyltestosterone) or laparoscopic fulguration of implants. In all cases, therapy had been completed at least 2 years before entrance into the IVF program.

The fact that no evidence of disease was found at laparoscopic oocyte retrieval may suggest regression of disease (spontaneous or posttherapy) or incorrect diagnosis at the original laparoscopy (5).

Group 2. This group was composed of 91 patients (191 cycles) in whom, according to the revised American Fertility Society classification (9), minimal or mild endometriosis (stage I or II) was found at the time of oocyte retrieval. Stage I was diagnosed in 63 patients; stage II was found in 28 cases. Most patients had received medical or surgical therapy for their endometriosis at least 2 years before the IVF attempt.

Group 3. This group was composed of 22 patients (35 cycles) with moderate or severe endometriosis (stage III or IV) at the time of the IVF attempt. Eighteen patients had stage III, and four patients had stage IV disease. All patients had received medical and/or surgical treatment at least 2 years before the IVF attempt.

Patients from groups 2 and 3 were further analyzed according to (a) the presence or absence of ovarian endometriosis, whether deep or superficial (in group 2, 27 patients, and in group 3, 13 patients with ovarian endometriosis), and (b) the presence of one or two ovaries (in group 2, 8 patients, and in group 3, 4 patients with one ovary—previous oophorectomy).

IVF/ET Procedures

Follicular stimulation was accomplished with human menopausal gonadotropin (hMG) and follicle-stimulating hormone (FSH), alone or in combination, according to previously published protocols (10,11). All patients received an ovulatory triggering dose of 10,000 IU of human chorionic gonadotropin (hCG), and laparoscopic oocyte retrieval was carried out 36 hr thereafter. The techniques and details of oocyte classification, insemination, and culture, and embryo transfer have been previously described (12,13).

Serum values of estradiol (E_2) were obtained daily during the follicular phase; E_2 and progesterone (P) levels were determined every other day during the luteal phase. The techniques of radioimmunoassay have been described in previous reports (14).

After ET all patients received 12.5 mg/day of P in oil intramuscularly as luteal support, starting on the day of transfer and continuing until a β-hCG determination was obtained on luteal days +11 to +13. (This policy was modified in 1986 to 25 mg/day beginning on the day before ET).

Nine hundred seventeen cycles of 447 patients who underwent IVF/ET during the same period and in whom infertility was related to tubal factors were assigned as a control group. The endometriosis and

Table I. Classification of Patients According to the Stage of Endometriosis and Presence of Other Infertility Factors

Group	No. patients	No. cycles	Endometriosis only	Endometriosis plus other factors		
				Male	Tubal	Other
1: Previous history (normal pelvis)	23	54 (19.3%)	37 (68.5%)	1 (1.8%)	11 (20.4%)	5 (9.2%)
2: Stages I–II	91	191 (68.2%)	125 (65.4%)	24 (12.5%)	32 (16.7%)	10 (5.2%)
3: Stages III–IV	22	35 (12.5%)	14 (40.0%)	1 (2.8%)	17 (48.6%)	3 (8.6%)
Total	136	280	176 (62.8%)	26 (9.3%)	60 (21.4%)	18 (6.4%)

tubal groups did not differ in age (35.6 ± 3.9 and 34.2 ± 3.4 years, respectively). The type of ovarian stimulation was likewise similar in the two groups.

Statistical analysis was performed by the two-tailed Student's *t* test with the Bon-Ferroni correction for multiple comparisons and the chi-square test, as appropriate. Values of $P < 0.05$ were considered significant. Results are presented as the mean ± standard deviation.

RESULTS

The mean age of the patients was 36.9 ± 3.8 years for group 1, 35.8 ± 3.9 years for group 2, and 34.1 ± 4.0 years for group 3 (not significantly different).

Type of Stimulation and Stimulation Response

Stimulation protocols, E_2 responses (low, intermediate, or high), and distributions of terminal E_2 patterns (15) were similar in all groups. Nor was the occurrence of a spontaneous endogenous LH surge significantly different among the groups.

Oocyte Recovery

There were significantly more oocytes recovered/cycle in groups 1 and 2 than in group 3. There was no difference in the number of preovulatory oocytes recovered in groups 1 and 2; however, both groups had a significantly higher number of preovulatory oocytes retrieved than did group 3 ($P < 0.05$) (Table II).

There were significantly more immature oocytes retrieved in group 1 than in groups 2 and 3, and also, more in group 2 than in group 3 ($P < 0.05$). Group 1 had significantly more degenerated oocytes at retrieval. There was no difference in the incidence of fractured zona oocytes in the three groups. There were no differences in the relative contribution of each category of oocytes (preovulatory, immature, degenerated, and fractured zona) to the total number of oocytes obtained in all groups (Table II).

Fertilization Rate

The fertilization rate of preovulatory oocytes was similar in all groups (83.5, 84.4, and 90.0% for groups 1, 2, and 3, respectively). Nor was the fertilization rate of immature oocytes significantly different in all groups (Table II).

Embryo Transfer

The transfer rate of preovulatory and immature oocytes was similar in all groups (Table III). There was no difference in the number of transferred embryos derived from preovulatory oocytes in groups 1 and 2; however, this figure was significantly higher in group 2 than in group 3 ($P < 0.05$). Group 1 had significantly more transferred embryos derived from immature oocytes matured in vitro than did groups 2 and 3. Groups 1 and 2 had significantly more total oocytes transferred per cycle than did group 3 ($P < 0.05$) (Table II).

Luteal Phase

There was no difference in the serum P levels during luteal days +5, +7, +9, +11, and +13.

Table II. Number and Classification of Oocytes Aspirated, Fertilization Rate, and Number of Concepti Transferred from Preovulatory and Immature Oocytes

	Aspiration				Percentage				No. transferred/cycles with transfer		
Group	Preov.	Imm.	Deg.	Fr. zona	Preov. oocytes/total oocytes	Fertilization rate	Immature oocytes/total oocytes	Fertilization rate	Preov.	Immature	Total
1	3.3 ± 2.7**	2.4 ± 2.4*,**	1.3 ± 1.3**	0.4 ± 0.9	47.0	83.5	34.6	53.4	2.4 ± 1.5	1.1 ± 0.1*,**	3.2 ± 1.5**
2	3.1 ± 2.0**	1.6 ± 1.8**	1.0 ± 1.5	0.3 ± 0.6	53.5	84.4	28.9	43.6	2.5 ± 1.4**	0.6 ± 1.0	3.1 ± 1.6**
3	2.0 ± 1.5	0.6 ± 0.9	0.5 ± 0.8	0.3 ± 0.5	63.4	90.0	20.5	61.9	1.8 ± 1.2	0.3 ± 0.7	2.1 ± 1.3

* $P < 0.05$ compared with group 2.
** $P < 0.05$ compared with group 3.

Table III. Rate of Transfers per Aspirated Oocytes[a]

Group	No. of preovulatory oocytes			No. of immature oocytes		
	Aspirated	Transferred	Transfer rate (%)	Aspirated	Transferred	Transfer rate (%)
1	179	121	67.5	132	40	30.3
2	589	430	73.0	318	101	31.7
3	71	57	80.2	23	11	47.8

[a] No significant difference between the groups.

Mean E_2 levels were lower on luteal days +5 to +9 in group 3, although the differences did not attain statistical significance.

Pregnancy Outcome

The overall per cycle and per transfer pregnancy rates were 22.1 and 24.8%, respectively (62 pregnancies and 24 miscarriages—10 preclinical and 14 clinical abortions) (16). Table IV shows the per cycle, per transfer, and per transfer of preovulatory oocyte pregnancy rates according to the stage of endometriosis. No significant differences were observed among the groups.

However, the abortion rate was significantly higher in group 3 than in groups 1 and 2 ($P < 0.003$) (Table V). Consequently, the per cycle and per transfer ongoing pregnancy rates (≥20 weeks of pregnancy) were lower in group 3 than in groups 1 and 2, although not significantly different.

Table VI depicts the number of pregnancies according to the number of concepti derived from transferred preovulatory oocytes. No significant differences were observed in a comparison of the different categories of endometriosis patients.

Presence or Absence of Ovarian Endometriosis

No significant differences were observed in the number of mature oocytes retrieved, the per cycle and per transfer pregnancy rates, or the miscarriage rate when results in groups 2 and 3 were compared (Table VII).

One Ovary Versus Two Ovaries

There was no significant difference in the number of preovulatory oocytes retrieved when the results in groups 2 and 3 were compared. There were no pregnancies in group 3 patients with one ovary (stage III or IV), although the small number involved (four patients, eight cycles) does not permit meaningful conclusions (Table VIII).

Control Group (Tubal Infertility)

The mean number of preovulatory oocytes retrieved per cycle was 2.7 ± 2.1, and the mean number of embryos transferred per transfer was 2.2 ± 1.5 in the tubal factor population. The overall fertilization rate for preovulatory oocytes was 88.4%. The pregnancy rate per cycle was 22.3%, the preg-

Table IV. Pregnancy Rate by Patient, Cycle, Transfer, and Transfer of Preovulatory Oocytes According to the Stage of Endometriosis[a]

Group	No. cycles	No. transfers	No. pregnancies	Pregnancy rate (%) per			
				Patient	Cycle	Transfer	Transfer of preov. oocytes
1	54	50 (92.6%)	9	39.1	16.7	18.0	20.0
2	191	168 (87.9%)	46	50.5	24.1	27.4	28.4
3	35	31 (88.6%)	7	31.8	20.0	22.6	23.3

[a] No significant differences between the groups.

Table V. Miscarriage and Ongoing Pregnancy Rates

Group	No. pregnancies	Preclinical miscarriages	Clinical miscarriages	Miscarriage rate (%)	Ongoing preg. rate (%) per Cycle	Ongoing preg. rate (%) per Transfer
1	9	—	2	22.0	12.9	14.0
2	46	7	10	36.9	15.1	17.2
3	7	3	2	71.4*	5.7[a]	6.4[a]

[a] No significant differences between the groups.
* $P < 0.003$ compared with groups 1 and 2.

nancy rate per transfer was 25.1%, and the ongoing pregnancy rate per transfer was 16.4%. The miscarriage rate was 28.2%. None of these values differed significantly from the overall results of the endometriosis patients taken as a whole.

DISCUSSION

We present a 6-year experience in the management of endometriosis infertility with IVF/ET as an extension of a previous publication (5). The responses to the stimulation protocols (gonadotropin hormone combination) as evidenced by the follicular-phase E_2 response, periovulatory hormone profiles (distribution of terminal E_2 patterns and frequency of spontaneous LH surge), and luteal-phase E_2 and P levels were similar in all groups, suggesting an endocrinologically homogeneous group of patients.

The fertilization rate of preovulatory oocytes was comparable in all groups (overall fertilization rate of 85.3% for mature oocytes), similar to that of tubal factor patients (88.4%), and higher (although not significantly different) than in patients with unexplained infertility (67.4%) (17) studied during the same period. These results confirm the first report from the Norfolk group (5) as well as others (7,8) and documents that the fertilization rate of preovulatory and immature oocytes is not reduced in patients with endometriosis, contrary to the report of Wardle *et al.* (6) and the first results published by Yovich *et al.* (18). Furthermore, the presence or degree of endometriosis does not affect the cleavage rate, since the rate of concepti transferred per oocytes aspirated was similar in the groups (5). The overall per cycle and per transfer pregnancy rates (22.1 and 24.8%) were similar to those of patients with tubal disease (22.3 and 25.1%) and patients with unexplained infertility (29.2 and 35.9%) (17) studied during the same period. The per cycle, per transfer, and per patient pregnancy rates did not differ significantly in the varying categories of endometriosis.

However, the miscarriage rate (preclinical and clinical abortions) was significantly higher in patients with moderate or severe endometriosis; consequently, the per cycle and per transfer ongoing pregnancy rates were lower than in the other two groups, although the differences did not attain statistical significance. These figures represent the "take-home baby rate" and are what the patient and the clinician are really interested in.

The information obtained after IVF/ET may provide insight into the true mechanisms of infertility caused by endometriosis. Several pathophysiological conditions have been associated with mild or moderate endometriosis [luteal-phase defects (19,20), hyperprolactinemia (21), anovulation (22), luteinized unruptured follicle syndrome (23), autoimmunity (24,25), increased levels of prostaglandins (26,27), and/or macrophages (28), interleukin-1

Table VI. Number of Pregnancies According to Number of Concepti Transferred Originating from Preovulatory Oocytes[a]

Group	One embryo (preovulatory) No.	Preg.	%	Two embryos (preovulatory) No.	Preg.	%	Three embryos (preovulatory) No.	Preg.	%
1	9	2	22.2	16	2	12.5	20	5	25
2	42	9	21.4	40	13	32.5	80	24	30
3	15	1	6.7	7	3	42.9	8	3	37.5

[a] No significant differences between the groups.

Table VII. IVF Results According to the Presence or Absence of Ovarian Endometriosis[a]

	Percentage			
	No. preov. retrieved/ total oocytes	No. pregnancies/ No. transfers	No. pregnancies/ No. cycles	No. miscarriages/ No. pregnancies
Group 2				
Ovarian endometriosis (27 patients, 59 cycles)	57.8	34.0	30.5	33.3
Absence (64 patients, 192 cycles)	52.0	24.3	21.2	39.3
Group 3				
Ovarian endometriosis (13 patients, 21 cycles)	58.7	22.2	19.0	50.0
Absence (9 patients, 14 cycles)	73.0	23.1	21.4	100.0

[a] No significant differences between the groups.

(29,30), peritoneal fluid embryo toxicity (31), and abnormal sperm/oocyte interaction (32)], as well as with severe and extensive endometriosis (distortion of the normal architecture of the pelvis usually with concomitant tubal obstruction, deficient oocyte pickup or transport through the fallopian tube, and/or endometriomas) (33,34). Our results show that patients with minimal or mild disease do not differ from other major infertile groups (tubal and unexplained infertility) in overall IVF/ET outcome. Nor does the presence of ovarian endometriosis (superficial implants or endometriomas) or the absence of one ovary affect preovulatory oocyte recovery, pregnancy, or miscarriage rates in the initial stages.

On the other hand, patients with moderate or severe disease (stages III and IV) have a compromised IVF/ET outcome. In these patients the total number of oocytes—but more important, the number of preovulatory oocytes recovered—is significantly reduced. Also reduced in these patients is the number of transferred embryos derived from preovulatory oocytes, the total number of embryos transferred per cycle, and the number of patients who received a single embryo transfer derived froma preovulatory oocyte. The presence of pelvic adhesions and ovarian availability or a decreased gonadotropin-sensitive follicular apparatus—but not the occurrence of ovarian endometriosis (endometriomas)—might be responsible for these findings. Transvaginal ultrasound-guided oocyte retrieval may help some of these patients. However, even though the number of oocytes retrieved is lower, the fertilization, cleavage, and pregnancy rates do not differ from those of the groups with less extensive or minimal disease. Consequently, this does not represent the limiting, crucial factor in the adverse overall results. Nor does the hormonal milieu of the patient seem to represent a problem. The incidence of a significantly higher miscarriage rate suggests a poor embryo quality, perhaps derived from poor-quality oocytes in the more severe stages of the disease. Whether additional uterine factors (35) are involved, affecting implantation and postimplantation events, remains to be elucidated. Recently Kreiner *et al.* (36) reported the presence of endometrial antibodies in patients with endometri-

Table VIII. IVF Results According to the Presence of One vs Two Ovaries[a]

	Percentage			
	No. preov. retrieved/ total oocytes	No. pregnancies/ No. transfers	No. pregnancies/ No. cycles	No. miscarriages/ No. pregnancies
Group 2				
One ovary (8 patients, 14 cycles)	64.4	16.7	14.3	50.0
Two ovaries (83 patients, 177 cycles)	53.0	28.2	24.9	36.4
Group 3				
One ovary (4 patients, 8 cycles)	50.0	—	—	—
Two ovaries (18 patients, 27 cycles)	65.3	29.2	25.9	71.4

[a] No significant differences between the groups.

osis and suggested that an endometrial immune response may create an environment unfavorable for nidation and continued growth of the embryo.

Several studies have suggested an increased spontaneous clinical abortion rate in women with untreated endometriosis which improved after therapy (37,38). Our data provide further evidence for a higher incidence of miscarriages in the more advanced stages of the disease.

We conclude that IVF/ET is an established and successful therapy for infertile patients with stages I and II endometriosis and that patients with moderate or severe disease have an impaired reproductive potential, mainly as a result of the poor embryo quality, reflected in a lower "take-home baby rate." Other probable adverse factors are limited ovarian availability, low ovarian reserve (secondary to severe disease or previous therapy?), and perhaps endometrial factors which impact upon implantation and embryo development.

ACKNOWLEDGMENTS

The authors wish to thank Ms. Debbie Jones for statistical analysis and Dr. Charlotte Schrader for editorial assistance.

REFERENCES

1. Olive DL, Haney AF: Endometriosis-associated infertility: A critical review of therapeutic approaches. Obstet Gynecol Surv 1986;47:538–555
2. Aral SO, Cates W Jr: The increasing concern with infertility: Why now? Science 1983;250:2327
3. Schmidt CL: Endometriosis: A reappraisal of pathogenesis and treatment. Fertil Steril 1985;44:157–173
4. Mahadevan MM, Trounson AD, Leetou JF: The relationship of tubal blockage, infertility of unknown cause, suspected male infertility, and endometriosis to success of in vitro fertilization and embryo transfer. Fertil Steril 1983;40:755–762
5. Chillik C, Acosta A, Garcia JE, Perera S, Van Uem JF, Rosenwaks Z, Jones HW Jr: The role of in vitro fertilization in infertile patients with endometriosis. Fertil Steril 1985; 44:56–61
6. Wardle PG, Mitchell JD, McLaughlin EA, Ray BD, McDermott A, Hull MG: Endometriosis and ovulatory disorder: Reduced fertilization in vitro compared with tubal and unexplained infertility. Lancet 1985;2:236–239
7. O'Shea RT, Chen C, Weiss T, Jones WR: Endometriosis and in vitro fertilization. Lancet 1985;2:723
8. Matson PL, Yovich JL: The treatment of infertility associated with endometriosis by in vitro fertilization. Fertil Steril 1986;46:432–434
9. American Fertility Society: Revised classification of endometriosis: 1985. Fertil Steril 1985;43:351–352
10. Jones HW Jr, Acosta AA, Andrews MC, Garcia JE, Jones GS, Mayer J, Rosenwaks Z, Sandow B, Veeck L, Wilkes C: Three years of in vitro fertilization at Norfolk. Fertil Steril 1984;42:826–834
11. Rosenwaks Z, Muasher S, Acosta A: Use of hMG and/or FSH for multiple follicular development. Clin Obstet Gynecol 1986;29:148–157
12. Veeck L, Maloney M: Insemination and fertilization. *In* In Vitro Fertilization—Norfolk, HW Jones, Jr, GS Jones, GD Hodgen, Z Rosenwaks (eds). Baltimore, Williams and Wilkins, 1986, pp 168–200
13. Veeck LL: Extracorporeal maturation: Norfolk. Ann NY Acad Sci 1985;774:357–367
14. Jones GS, Garcia JE, Rosenwaks Z: The role of pituitary gonadotropins in follicular stimulation and oocyte maturation in the human. JCEM 1984;59:178–180
15. Jones HW Jr, Acosta A, Andrews MC, Garcia JE, Jones GS, Mantzavinos T, McDowell J, Sandow B, Veeck L, Whibley T, Wilkes C, Wright G: The importance of the follicular phase to success and failure in IVF. Fertil Steril 1983; 40:317–321
16. Jones HW Jr, Acosta A, Andrews MC, Garcia JE, Jones GS, Mantzavinos T, McDowell J, Sandow B, Veeck L, Whibley T, Wilkes C, Wright C: What is a pregnancy? A question for programs of in vitro fertilization. Fertil Steril 1983;40:728–733
17. Navot D, Muasher S, Oehninger S, Liu HC, Veeck L, Kreiner D, Rosenwaks Z: The value of in vitro fertilization for the treatment of unexplained infertility. Fertil Steril 1988;49:854–857
18. Yovich JL, Yovich JM, Tuvik AI, Matson PL, Wilcox DL: In vitro fertilization for endometriosis. Lancet 1985;2:552
19. Hargrove JT, Abraham CK: Abnormal luteal function in endometriosis. Fertil Steril 1980;34:302
20. Pittaway DE, Maxson W, Daniell J, Herbert C, Wentz AC: Luteal phase defect in infertility patients with endometriosis. Fertil Steril 1983;39:712–713
21. Muse K, Wilson EA, Jawad MJ: Prolactin hyperstimulation in response to thyrotropin-releasing hormone in patients with endometriosis. Fertil Steril 1982;38:419–422
22. Ronnberg L, Kaupilla A, Rajaniemi H: Luteinizing hormone receptor disorder in endometriosis. Fertil Steril 1984;64–68
23. Brosens IA, Koninckx PR, Corveleyn PA: A study of plasma progesterone, estradiol 17-β, prolactin and LH levels, and of the appearance of the ovaries in patients with endometriosis and infertility. Br J Obstet Gynecol 1978; 85:246–250
24. Weed JC, Arquembourg PC: Endometriosis: Can it produce an autoimmune response resulting in infertility? Clin Obstet Gynecol 1980;23:885–893
25. Dmowski WL, Steele RW, Baker GF: Deficient cellular immunity in endometriosis. Am J Obstet Gynecol 1981; 141:377–383
26. Rock JA, Dubin NH, Ghodgaonbar RB, Bergquist CA, Erozan YS, Kimball AW Jr: Cul-de-sac fluid in women with endometriosis: Fluid volume and prostanoid concentration during the proliferative phase of the cycle—days 8 to 12. Fertil Steril 1982;37:747–750
27. Drake TS, O'Brien WF, Ramwell PN, Metz SA: Peritoneal fluid thromboxane B_2 and 6-keto-prostaglandin F_1 alpha in endometriosis. Am J Obstet Gynecol 1981;140:401–404

28. Haney AF, Muscato JI, Weinberg JF: Peritoneal cell populations in infertility patients. Fertil Steril 1981;35:696–698
29. Fabih H, Bagget B, Holtz G, Tsang KY, Lee JC, Williamson HD: Interleukin-1: A possible role in the infertility associated with endometriosis. Fertil Steril 1987;47:213–217
30. Hill JK, Haimovici F, Politch J, Anderson DJH: The effects of soluble products of activated lymphocytes and macrophages (lymphokines and monokines) on human sperm motion parameters. Fertil Steril 1987;47:460–465
31. Morcos RN, Gibbons WE, Findley WE: Effect of peritoneal fluid on in vitro cleavage of 2-cell mouse embryos: Possible role in infertility associated with endometriosis. Fertil Steril 1985;44:678–683
32. Sueldo C, Lambert H, Steinleitner A, Rathwick G, Swanson J: The effect of peritoneal fluid from patients with endometriosis on murine sperm-oocyte interaction. Fertil Steril 1987;48:697–699
33. Chillik C, Rosenwaks C: Endometriosis and in vitro fertilization. Semin Reprod Endocrinol 1985;3:377–380
34. Oak MF, Vaughan CA, Elstein: The current status of infertility associated with pelvic endometriosis. Clin Reprod Fertil 1983;2:97
35. Saifuddin A, Buckley CH, Fox H: Immunoglobulin content of the endometrium in women with endometriosis. Int J Gynecol Pathol 1983;2:255
36. Kreiner D, Fromowitz F, Richardson D, Kenigsberg D: Endometrial immunofluorescence associated with endometriosis and pelvic inflammatory disease. Fertil Steril 1986; 46:243–246
37. Groll M: Endometriosis and spontaneous abortion. Fertil Steril 1984;41:933–935
38. Wheeler JM, Johnston BM, Malinak LR: The relationship of endometriosis to spontaneous abortion. Fertil Steril 1983;39:656–659