CLINICAL ASSISTED REPRODUCTION

The Influence of Endometriosis on the Success of Gamete Intrafallopian Transfer (GIFT)

MING-YANG CHANG,^{1,3} CHI-HSIN CHIANG,¹ T'SANG-T'ANG HSIEH,¹ YUNG-KUEI SOONG,¹ and KUANG-HUNG HSU²

Submitted: August 29, 1996
Accepted: October 10, 1996

Purpose: Our purpose was to evaluate the outcomes of gamete intrafallopian transfer (GIFT) therapy in patients with endometriosis.

Methods: One hundred eight GIFT cycles performed under the indication of endometriosis were compared to 156 GIFT cycles with indications of other disease entities. A maximum of seven oocytes was transferred into one or both fimbriate ends with prepared spermatozoa. Clinical pregnancy rates and outcomes were evaluated according to Mantel-Haenszel's chi-square test. Multiple logistic regression analysis was performed to determine factors influencing the success on pregnancy in the total treatment cycles.

Results: The anthropological variables, such as age of patients, duration of infertility, and semen grading, were comparable in both groups. The responses to controlled ovarian hyperstimulation (COH) were progressively decreased while increasing the severity of endometriosis conditions such as nonendometriosis, mild-form endometriosis, and advanced-form endometriosis patients. However, there were no significant differences in the clinical pregnancy rates (40.4, 36.7, and 41.7%, respectively), multiple pregnancy rates (34.9, 27.3, and 45.0%, respectively), and early pregnancy loss rates (27.0, 18.2, and 30.0%, respectively). Multivariate statistics of pregnancy rates that adjusted the effects of patients' age, tubal health, presence of active endometriosis and/or endometriomas, number of

oocytes transferred, and quality of sperm exhibited no statistical significance between endometriosis and nonendometriosis groups.

Conclusions: Our data show that patients with records of endometriosis have both a decreased ovarian response to gonadotropin stimulation and a decreased number of retrieved oocytes. Since the number of oocytes needed for the GIFT procedure is limited, pregnancy results for patients in the study group were comparable with those for patients in the control group.

KEY WORDS: endometriosis; endometrioma; controlled ovarian hyperstimulation; gamete intrafallopian transfer.

INTRODUCTION

Endometriosis is a disease entity characterized by extrauterine endometrial implantation with local inflammatory reaction and manifested by chronic pelvic pain, pelvic mass, and infertility. The exact causes of infertility associated with endometriosis are still a paradox, although possible mechanisms have been hypothesized: (a) disrupted tubal motility and oocyte pickup functions due to mechanical interference only or in association with inappropriate concentration of peritoneal fluid prostaglandins; (b) disordered follicular growth, ovulatory dysfunction, and failed fertilization, as well as embryo development influenced by toxic peritoneal factors; (c) accelerated phagocytosis of sperm by peritoneal macrophages; and probably (d) delaying fecundity due to dyspareunia only (1).

Assisted reproductive techniques have been introduced successfully to improve its subfertile status by endometriosis (2,3). Although previous studies reported that a lower number of preovulatory follicles

¹ Department of Obstetrics and Gynecology, Reproductive Center, Chang Gung Memorial Hospital, 199 Tung-Hua North Road, Taipei, 10591, Taiwan, ROC.

² Department of Public Health, Chang Gung College of Medicine and Technology, 259 Wen-Hua 1st Road, Kwei-Shan, Tao-Yuan, Taiwan, ROC.

³ To whom correspondence should be addressed.

were induced and a subsequently lower number of oocytes obtained in women with stages III or IV endometriosis undergoing in vitro fertilization (IVF-ET) programs (4,5), some recent studies failed to find the differences (6–8). With the exception of one study (9), the in vitro fertilization rates and clinical pregnancy rates after IVF-ET were found unchanged in endometriosis compared with other disease entities (4–8). A decreased potential for embryo implantation among endometriosis patients was reported (6), for which a poor quality of embryos or oocytes among endometriosis patients was postulated. Furthermore, factors influencing pregnancy such as age, severity and extent of endometriosis, and duration of infertility were also reported in patients undergoing IVF-ET (10). In some studies, an ultralong GnRH analogue suppression protocol was used to eliminate the adverse effects of persistent endometriosis before IVF-ET, resulting in an improved success rate (11,12). In addition, one report suggested that a higher autoantibody level may impair the success of IVF-ET therapy in endometriosis patients of some populations (8).

Gamete intrafallopian transfer (GIFT) is more a physiological procedure than IVF-ET since it mimics some of the mechanisms involved in a successful fertility cycle. The fertilization and cleavage processes take place in vivo; as a consequence, early development of the very young embryo in the fallopian tube will provide a better chronological suitability for the embryo entering the uterine cavity, yielding a better chance of implantation (13). GIFT also proved to have advantages over IVF-ET in a higher clinical pregnancy rate and take-home baby rate per puncture, with a similar multiple pregnancy rate in multinational cooperative studies (14). In patients with endometriosis, GIFT bypasses the peritoneal endometriosis environment while utilizing the normal site of fertilization in the ampullary region of the fallopian tube. However, it does not avoid possible detrimental effects of endometriosis during fertilization in vivo, embryo transportation, and implantation processes.

Although several investigators reported promising results of conception in their GIFT therapy, one recent study noted that endometriosis impairs the efficacy of GIFT. This study compared the outcomes of GIFT between endometriosis patients and nonendometriosis patients by analyzing confounding factors such as age, number of mature oocytes transferred, and sperm grade (15). In the study, the authors suggested that peritoneal factors might play an important role and proposed either a preparative medical treatment before GIFT or a shift of these patients to IVF-ET treatment. To examine

further possible detrimental effects of endometriosis on GIFT results and the interaction of other anthropologic factors, we have performed a case-control study of endometriosis and nonendometriosis patients using GIFT procedures.

MATERIALS AND METHODS

All consecutive patients undergoing GIFT procedures at our reproductive center between January 1, 1989, and December 31, 1994, were included in this retrospective investigation. All patients had been evaluated with semen analysis and hysterosalpingography before enrolling them into the treatment program. The semen analysis followed the grading methods presented previously (15). Semen was graded based on density and motility. A semen density over $20 \times 10^6/\text{ml}$ and a motility over 50% were regarded as normal, whereas a semen density of $10\text{--}20 \times 10^6/\text{ml}$ and a motility of 30–50% were regarded as subnormal. A semen density of less than $10 \times 10^6/\text{ml}$ and a motility of less than 30% were regarded as severely abnormal. The treatment cycle of severely abnormal patients was shifted to IVF/ET or TET (tubal embryo transfer). One prerequisite for the patients was to have at least one side of the patent tube observed under hysterosalpingography. Any adhesions associated with fallopian tubes were recorded for peritubal adhesion, tubal tortuosity, fimbriate sclerosis, and accessibility. A difficult intubation of the fimbriate orifice or marked tortuosity of the tubal pathway was considered inappropriate for transfer, therefore GIFT was not applicable. Patients with a history or any detectable evidence of endometriosis were recruited for this study. The records of previous surgeries and present GIFT findings were collected and classified according to the revised American Fertility Society (rAFS) classification system (16). The control group was sampled from patients undergoing GIFT procedure in the study period without a history of endometriosis.

For superovulation, routine pituitary suppression with luteal-phase administration of gonadotropin releasing hormone agonists (GnRHa) followed by gonadotropin stimulation (long protocol) was used for most patients. Leuprolide acetate, 1 mg per day s.c. (LA; Lupron; Abbot Australia Pty., Ltd., Kurnell, NSW, Australia), was administered on day 21 of the menstrual cycle for 10 consecutive days. A serum estradiol level of less than 35 pg/ml and a nonpalpable ovarian cystic lesion noted by vaginal ultrasound were recognized as adequate ovarian suppression and

defined as day 1 of the treatment cycle. Two ampoules of FSH (Metrodin; Serono Laboratories, Randolph, MA) and 2 ampoules of hMG (Pergonal; Serono Laboratories) were administered daily for the first 3 days. A serum estradiol assay followed on day 4, with a value of 100 pg/ml or higher suggesting a reduction of the daily dose of gonadotropin to 2 ampoules of hMG for the next 3 days. Vaginal ultrasonography and serum estradiol estimation were performed intermittently thereafter until at least two follicles reached 18 mm or larger and the E₂ level exceeded 500 pg/ml. Ten thousand international units of hCG (Pregnyl; Organon, Oss, The Netherlands) was administered, followed by transvaginal oocyte retrieval after 36 hr.

Oocytes were classified by their morphology into mature, immature, and postmature stages (17). A maximum of six mature oocytes was transferred into the fimbriate ends via laparoscope, while the rest of the oocytes were inseminated in vitro and the embryos cryopreserved for later use. The luteal phase was supplemented with oral progesterone (Utrogestan; Laboratories Piette International, Belgium). A urine pregnancy test was performed 17 days after the GIFT procedure. Clinical pregnancy was defined when intrauterine gestational sacs were detected by vaginal ultrasound or where there was any pathological confirmation of gestational tissue in surgical specimens from ectopic pregnancy or therapeutic D & C. Early pregnancy loss was defined as those spontaneous abortions before 12 weeks of gestation after the last menstrual period and those with ectopic pregnancies.

To compare continuous variables among the nonendometriosis group, stage I/II endometriosis group, and stage III/IV endometriosis group, we utilized ANOVA tests for statistical analysis. A Mantel-Haenszel monotonic trend test was used to analyze tendencies from nonendometriosis to severe-form endometriosis groups. As pregnancy results were binomial variables in this study, we used the Mantel-Haenszel chi-square test to perform univariate analyses between demographic parameters and pregnancy. To adjust further the effects of multiple variables, a multiple logistic regression analysis was applied in the study.

RESULTS

A total of 264 individual GIFT cycles was reviewed during the study. The number of endometriosis patients in each GIFT cycle was 25, 35, 25, and 23 for stage I, stage II, stage III, and stage IV, respectively. In the case group, we further classified the first two stages

as a mild form of endometriosis and the last two stages (III/IV) as an advanced form of endometriosis. The 156 patients in the control group included 55 patients of mild pelvic abnormalities due to either pelvic adhesion, previous tubal surgery, or uterine leiomyomas; 30 cycles of mild male subnormality; and 71 cycles of unexplained infertility. No significant difference was detected in female age, infertility duration, and seminal parameters among the three groups (data not shown).

After controlled ovarian hyperstimulation, patients with higher stages of endometriosis were found to have a lower estradiol concentration on the day of hCG administration (Table I). Subsequently, the variables number of follicles with a diameter ≥ 14 mm, number of retrieved oocytes, number of oocytes transferred, and number of spare embryos for cryopreservation were decreased relative to increasing stages of endometriosis. The in vitro fertilization rates of the spared oocytes were not affected by the stages of endometriosis (nonsignificant for trend test), however, a significant difference was detected when comparing fertilization rates between the control and the stage III/IV group (71.2 vs 61.6%; $\chi^2 = 4.51$, $P < 0.05$).

In Table II, no significant difference was observed for pregnancy rate, pregnancy loss rate, and multiple pregnancy rate among study groups. The implantation rate of patients with stage III/IV diseases was significantly higher than that of the other two groups, but not significant by Mantel-Haenszel's monotonic trend test from control to stage III/IV groups.

A number of potential factors influencing GIFT pregnancy rates were analyzed in the endometriosis and nonendometriosis cycles. The overall odds ratio of pregnancy between the endometriosis group and the control group was 0.96. Further stratified analyses of these potential factors influencing GIFT pregnancy rates revealed no significant difference (Table III). Among these potential factors, the number of oocytes transferred, which was less than four, was found to have a higher pregnancy rate (odds ratio = 4) in the endometriosis group than in the control group, but with no statistically significant difference. A multiple logistic regression analysis of all these potential factors revealed no statistical difference on pregnancy between endometriosis and control groups, a multivariate-adjusted odds ratio of 0.95 (Table IV). The most effective factor on pregnancy was "number of oocytes transferred," since the odds ratio of pregnancy between "greater or equal to 4" and "less than 4" was statistically significant, 3.07.

Table I. Stimulation Response and Laboratory Performance in GIFT Cycles

	Control (n = 156)	Endometriosis		p ^a
		Stage I/II (n = 60)	Stage III/IV (n = 48)	
Total FSH/hMG ampoules	26.7 ± 13.7	27.5 ± 10.7	30.0 ± 14.6	N.S.
E ₂ on hCG administration	1861 ± 971	1649 ± 807	1547 ± 791	0.0161
No. follicles ≥ 14 mm	7.2 ± 3.8	7.5 ± 3.5	5.3 ± 2.3	0.0057
No. oocytes retrieved	11.1 ± 6.6	8.6 ± 4.5	7.3 ± 3.1	<0.0001
No. oocytes replaced	5.2 ± 1.5	5.1 ± 1.7	4.5 ± 1.5	0.0006
Spare oocytes for IVF	5.6 ± 6.1	3.5 ± 4.0	2.8 ± 2.5	0.0002
Fertilization rate	538/873 (61.6) ^b	131/208 (63.0)	94/132 (71.2)	N.S. ^c
No. embryos for cryopreservation	2.6 ± 3.2	1.7 ± 2.3	1.6 ± 1.9	0.0127

^aANOVA F test.^bNumbers in parentheses are percentages.^cMantel-Haenszel's monotonic trend test; $\chi^2 = 4.51$, $P < 0.05$, between control and stage III/IV group.

DISCUSSION

The effect of endometriosis on patients undergoing assisted reproductive therapies is still under debate. Contradictory data have been reported in the results of controlled ovarian hyperstimulation, quality of retrieved oocytes, in vitro fertilization rate, embryo quality, implantation capability, and pregnancy outcomes (4-9). The GIFT procedure has been considered a more physiologic therapy than the IVF-ET technique since the only bypassed step of reproduction is oocyte pickup by fallopian tubes. Therefore, a higher pregnancy rate had been established by several multicenter studies with this procedure (13,14). The role of endometriosis is not clear when utilizing the GIFT procedure for assisted reproductive therapies. We anticipated that it could exert detrimental effects within the tubal lumen, therefore we compared the above variables in patients with different stages of endometriosis.

In our retrospective analysis, we detected a trend of decreasing gonadotropin response in patients with

increasing stages of endometriosis (Table II). In this study, a significant trend of decreasing estradiol concentrations, numbers of dominant follicles, and numbers of oocytes retrieved was detected. The results were consistent with some previous investigations (4,5), while contradictory results were reported by two other studies (7,8). They observed an increasing trend but not statistical significance of the variables mentioned when endometriosis progressed. The numbers of endometriosis patients in these studies were apparently small for mild endometriosis, such as 30 versus 89 and 29 versus 100 cycles. Small-sample size studies are effective for further examining their statistical power. On the other hand, comparing groups of two close spectra of disease conditions such as non- versus mild-endometriosis patients is one explanation for these nonsignificant outcomes. The distribution of disease stages in our study population is more consistent with that in other studies. It is worthwhile to mention that our patients who received GIFT therapy generally had less severe endometriosis than those who received

Table II. Pregnancy Outcome After GIFT Procedures

	Control (n = 156)	Endometriosis		p ^a
		Stage I/II (n = 60)	Stage III/IV (n = 48)	
No. clinical pregnancies/GIFT cycle	63 (40.4) ^b	22 (36.7)	20 (41.7)	N.S.
No. early pregnancy losses	17 (27.0)	4 (18.2)	6 (30.0)	N.S.
No. multiple pregnancies	22 (34.9)	6 (27.3)	9 (45.0)	N.S.
No. triplet pregnancies	8 (12.7)	1 (4.5)	5 (25.0)	N.S.
No. deliveries/pregnancies	46 (73.0)	18 (81.8)	14 (70.0)	N.S.
Mean sac number per pregnancy	1.5 ± 1.0	1.2 ± 0.7	1.9 ± 1.3	N.S.
Implantation rate	93/813 (11.4)	27/306 (8.8)	38/216 (17.6)	N.S. ^c

^aMantel-Haenszel's monotonic trend test.^bNumbers in parentheses are percentages.^c $\chi^2 = 8.93$, $P < 0.025$, between control and stage III/IV group; $\chi^2 = 5.82$, $P < 0.005$, between stage I/II and stage III/IV.

Table III. Univariate Statistics and Odds Ratios for Pregnancy^a

	Control (n = 156)		Endometriosis (n = 108)		Odds ratio	χ^2
	Pregnancy	PR (%)	Pregnancy	PR (%)		
Age						
≥ 40	3/9	33.3	0/5	0	0.00	0.160
< 40	60/147	40.8	42/103	40.8	1.00	0.000
Tubal health						
Diseased	15/41	36.6	19/40	47.5	1.57	0.980
Normal	48/115	41.7	23/68	33.8	0.71	1.120
Endometriosis						
Active	—	—	18/49	36.7	—	—
Inactive	63/156	40.4	24/59	40.7	1.01	0.002
Endometrioma						
Present	—	—	6/12	50	—	—
Absent	63/156	40.4	36/96	37.5	0.89	0.206
No. mature oocytes						
< 5	6/22	27.3	6/24	25	0.89	0.030
≥ 5	57/134	42.5	36/84	42.9	1.01	0.002
No. oocytes transferred						
< 4	1/12	8.3	4/15	26.7	4.00	1.430
≥ 4	62/144	43.1	38/93	40.9	0.91	0.111
Quality of sperm						
Subnormal	25/66	37.9	11/35	31.4	0.77	0.345
Normal	38/90	42.2	31/73	42.5	0.99	0.001
Total	63/156	40.4	42/108	38.9	0.96	—

^a Mantel-Haenszel's χ^2 test.^b Pregnancy rate.

IVF/ET therapy. The significant results in less severe cases in our study suggest further studies of this trend among IVF/ET cases.

Surgery has been considered an efficient treatment for endometriosis, by either laparotomy or laparoscopy. The benefit of the surgical approach is eradicating all endometrial lesions within the pelvic cavity, including enucleation of endometriosis and electrocauterization of ovarian endometriosis. Although com-

plete removal of endometriosis lesions may decrease the possibility of recurrence, the removal cannot ameliorate the patient's fecundity (1). The drawback of such an operation is to decrease the ovarian reserve if ovarian endometriosis is treated by electrocauterization. The ovarian reserve of patients after endometriosis surgery has not been reported. Our data implied that ovarian responsiveness to gonadotropin stimulation was decreased by previous endometriosis. This

Table IV. Multivariate-Adjusted Odds Ratios for Pregnancy

Variable	Pregnancy (%)	Not pregnant (%)	Odds ratio	χ^2
Age				
≥ 40	3 (21.4)	11 (78.6)	0.47	1.21
< 40	102 (40.8)	148 (59.2)	1.00	
Tubal health				
Diseased	34 (42.0)	47 (58.0)	1.10	0.10
Normal	71 (38.8)	112 (61.2)	1.00	
No. of oocytes transferred				
≥ 4	100 (42.2)	137 (57.8)	3.07	4.67*
< 4	5 (18.5)	22 (81.5)	1.00	
Quality of sperm				
Subnormal	36 (26.3)	101 (73.7)	0.74	1.19
Normal	69 (42.3)	94 (57.7)	1.00	
Endometriosis				
Yes	42 (38.9)	66 (61.1)	0.95	0.03
No	63 (40.4)	93 (59.6)	1.00	

* $P < 0.05$.

phenomenon can be explained by ovarian electrocauterization performed during previous surgery.

The quality of oocytes from endometriosis patients has been studied with regard to their fertilization rates, embryo qualities, implantation rates, and spontaneous abortion rates. Although the number of oocytes retrieved was negatively associated with endometriosis stages, the rate of mature oocytes was not altered (data not shown). Furthermore, although optimal oocytes had been chosen for primary transfer, the remaining oocytes revealed no difference in vitro fertilization rate, embryo quality, and cryopreservation rate (Table I). These findings were generally comparable to others in the literature (4–8) except for one report (9). This implied that the fertilization and development of oocytes arising from hyperstimulated ovaries are not altered by an endometriosis environment. The mechanism of this observation warrants further studies.

The pregnancy outcomes were basically not significantly different among our study groups, including pregnancy rate, early pregnancy loss rate, and multiple pregnancy rate (Table II). Although the data revealed some variability among groups, we believe that the diversity was due to the small number of pregnancies in each group. Although this was in agreement with some recent reports (7,8), it was not supported by others (4,5), which suggested a decreased pregnancy rate in patients with increasing severity of endometriosis. The implantation rate for the GIFT procedure may be different from that for the IVF-ET procedure, because the exact in vivo fertilization rate in GIFT is not clear. Geber *et al.* reported a comparable implantation rate for endometriosis patients between stage III/IV and stage I/II (7). Our results are plausible according to these findings. Furthermore, we detected a higher implantation rate in the severe group (17.6%) than in the mild-form group and control group (8.8 and 11.4%, respectively). However, Simon *et al.* reported a lower implantation rate for IVF-ET patients in the endometriosis group than in the tubal-factor group. This study further addressed that the implantation rate was not different between groups when oocytes were donated from nonendometriosis to endometriosis patients. They also implied that the implantation rate was significantly decreased, particularly when oocytes were donated from those by IVF-ET (6). Our data suggested that implantation efficiency was not impaired by conditions of endometriosis.

Several factors affecting the success rate of pregnancy had been reported previously, such as the age of patients, duration of infertility, severity and activity of the endometriosis, number of oocytes replaced, tubal

health, and semen grading (4–12). One report found that the pregnancy rate of GIFT was impaired by endometriosis (15). Our results failed to support their findings (Table IV). By analyzing various factors described previously, we found no difference between patients with and patients without endometriosis. Furthermore, multivariate-adjusted odds ratios for the pregnancy rate of our total GIFT cycles revealed that a significant difference existed in the number of oocytes transferred. There was no statistical significance in the variable of endometriosis by multiple logistic regression analysis (Table IV).

The pregnancy rate by GIFT procedures is reportedly higher than that by IVF-ET procedures (13,14). This might be because of the different characteristics of patients, since patients who had the GIFT procedure would have a better pelvic condition than those who did not. The selection of GIFT patients in our department was based on a consistent standard which required patients' tubal condition and semen grading on a minimum level. Under these conditions, the pregnancy rate was generally consistent regardless of the condition of endometriosis while controlling confounding factors. Only the number of oocytes transferred in GIFT significantly affected the pregnancy rates. Although higher-staged endometriosis decreased the ovarian response to gonadotropin stimulation, most of the patients obtained more oocytes than were actually needed. This could be a reason for the absence of a pregnancy difference in univariate analysis. However, multivariate analysis revealed a low possibility of this explanation.

In conclusion, from our retrospective analysis of patients undergoing GIFT therapy, we found a tendency for a decreased ovarian response in patients with an increased severity of endometriosis. However, pregnancy rates were not impaired by conditions of endometriosis.

REFERENCES

1. Speroff L, Glass RH, Kase NG: Endometriosis. In Clinical Gynecologic Endocrinology and Infertility, L. Speroff (ed). Baltimore, Williams and Wilkins, 1994, pp 853–871
2. Wessels PH, Trumpelmann MD, Cronje HS, Grobler S, Oosthuizen AP, Hamlett DK: Cost-effectiveness of gamete intrafallopian transfer in comparison with induction of ovulation with gonadotropins in the treatment of female infertility: A clinical trial. *Fertil Steril* 1992;57:163–167
3. Mills MS, Eddowes HA, Cahill DJ, Fahy UM, Abuzeid MIM, McDermott A, Hull MGR: A prospective controlled study of in-vitro fertilization, gamete intra-fallopian transfer and intra-

- uterine insemination combined with superovulation. *Hum Reprod* 1992;7:490-494
4. Chillick CF, Acosta AA, Garcia JE, Perera S, Van Uem JFHM, Rosenwaks Z, Jones HW Jr: The role of in vitro fertilization in infertile patients with endometriosis. *Fertil Steril* 1985;44:56-61
 5. Matson PL, Yovich JL: The treatment of infertility associated with endometriosis by in vitro fertilization. *Fertil Steril* 1986;46:432-434
 6. Simon C, Gutierrez A, Vidal A, de los Santos MJ, Tarin JJ, Remohi J, Pellicer A: Outcome of patients with endometriosis in assisted reproduction: results from in-vitro fertilization and oocyte donation. *Hum Reprod* 1994;9:725-729
 7. Geber S, Paraschos T, Atkinson G, Margara R, Winston RML: Results of IVF in patients with endometriosis: The severity of the disease does not affect outcome, or the incidence of miscarriage. *Hum Reprod* 1995;10:1507-1511
 8. Dmowski WP, Friberg J, Rana N, Papierniak C, Michalowska J, El-Roeiy A: The effect of endometriosis, its stage and activity, and of autoantibodies on in vitro fertilization and embryo transfer success rates. *Fertil Steril* 1995;63:555-562
 9. Wardle PG, Mitchell JD, McLaughlin EA, Ray BD, McDermott A, Hull MGR: Endometriosis and ovulatory disorder: Reduced fertilization in vitro compared with tubal and unexplained infertility. *Lancet* 1985;2:236-239
 10. Schmidt CL: Endometriosis: A reappraisal of pathogenesis and treatment. *Fertil Steril* 1985;44:157-173
 11. Nakamura K, Oosawa M, Kondou I, Inagaki S, Shibata H, Narita O, Suganuma N, Tomoda Y: Menotropin stimulation after prolonged gonadotropin releasing hormone agonist pretreatment for in vitro fertilization in patients with endometriosis. *J Assist Reprod Genet* 1992;9:113-117
 12. Dicker D, Feldberg D, Goldman JA, Ashkenazi J, Levy T: The impact of long-term gonadotropin-releasing hormone analogue treatment on preclinical abortions in patients with severe endometriosis undergoing in vitro fertilization-embryo transfer. *Fertil Steril* 1992;57:597-600
 13. Abramovici H, Dirnfeld M, Bornstein J, Lissak A, Gonen Y: Gamete intrafallopian transfer. An overview. *J Reprod Med* 1993;38:698-702
 14. Asch RH: GIFT: Indications, results, problems, and perspectives. In Capitanio GL et al, editors: *GIFT: From Basics to Clinics*, Sero Symposia, Vol 63, EL Capitanio *et al.* (eds). New York, Raven Press, 1989
 15. Guzick DS, Stovall DW, Yao YAS, Kubik CJ, Berga SL, Zeleznik AJ, Krasnow JS: Endometriosis impairs the efficacy of gamete intrafallopian transfer: Results of a case-control study. *Fertil Steril* 1994;62:1186-1191
 16. American Fertility Society: Revised American Fertility Society classification of endometriosis. *Fertil Steril* 1985;43:351-354
 17. Veeck LL: *Atlas of the Human Oocyte and Early Conceptus*. Baltimore, Williams & Wilkins, 1986