Fertility after laparoscopic management of deep endometriosis infiltrating the uterosacral ligaments

Charles Chapron[1], Xavier Fritel and Jean-Bernard Dubuisson

Service de Chirurgie Gynécologique, Clinique Universitaire Baudelocque, C.H.U.Cochin Port-Royal, 123 Bld Port-Royal, 75014 Paris, France

[1]To whom correspondence should be addressed

The aim of this study was to evaluate fertility outcome after laparoscopic management of deep endometriosis infiltrating the uterosacral ligaments (USL). From January 1993 to December 1996, 30 patients who presented with no other infertility factors were treated using laparoscopic surgery. The overall rate of intrauterine pregnancy (IUP) was 50.0% (15 patients). Only one of these 15 pregnancies was obtained using in-vitro fertilization techniques (IVF). The cumulative IUP rate for the 14 pregnancies which occurred spontaneously was 48.5% at 12 months (95% confidence interval 28.3–68.7). The rate of spontaneous pregnancies was not significantly correlated with the revised American Fertility Society (rAFS) classification. The rate of IUP was 47.0% (eight cases) for patients with stage I or II endometriosis and 46.1% (six cases) for the patients presenting stage III or IV endometriosis (not significant). These encouraging preliminary results show that in a context of infertility it is reasonable to associate classic treatment for endometriosis (e.g. lysis, i.p. cystectomy, bipolar coagulation of superficial peritoneal endometriotic lesions) with resection of deep endometriotic lesions infiltrating the USL. Apart from the benefit with respect to the pain symptoms from which these patients suffer, it is possible to use laparoscopic surgery with substantial retroperitoneal dissection and enable half of the patients to become pregnant. These results also raise the question of the influence of deep endometriotic lesions on infertility.
Key words: endometriosis/infertility/operative laparoscopy/ uterosacral ligaments

Introduction

It has now been definitely demonstrated that it is possible for endometriotic lesions to penetrate the retroperitoneal space (Cornillie *et al*., 1990; Martin *et al*., 1987; Moore *et al*., 1988). Deep endometriosis, defined as existing when the lesions penetrate 5 mm or more (Koninckx *et al*., 1991) is a specific entity (Koninckx *et al*., 1992). Deep endometriosis is responsible for pelvic pain, the intensity of which is correlated with the depth to which the lesions penetrate (Koninckx *et al*., 1991). Operative laparoscopy is an effective treatment for pain

in patients presenting retroperitoneal lesions located on the uterosacral ligaments (USL) (Chapron *et al*., 1998a), on the recto–vaginal septum (Nezhat *et al*., 1992; Donnez *et al*., 1995), in the pouch of Douglas (Martin, 1988; Reich *et al*., 1991, 1992) and on the uterovesical fold (Dubuisson *et al*., 1994; Nezhat *et al*., 1996). In addition to the problems with pain they encounter, some of these patients suffer from associated infertility. It is thus necessary to establish precisely the impact on fertility of this type of operative laparoscopic procedure, using a retroperitoneal approach and often requiring considerable dissection. The aim of this work was to assess the results with respect to fertility for infertile patients who have been given operative laparoscopic treatment for histologically proven deep endometriosis infiltrating the USL.

Materials and methods

From January 1, 1993 to December 31, 1996, 69 patients were treated using operative laparoscopy for histologically proven deep endometriosis infiltrating the USL. All the patients were operated on using a technique described previously (Chapron and Dubuisson, 1996). The essential steps in this technique were as follows. Bowel preparation was systematic for two reasons: it made exposure of the pelvis easier and was essential because, in certain cases, rectal adhesiolysis may be required. Endorectal ultrasonography was used to assess how far the lesions were spread (Ohba *et al*., 1996; Chapron *et al*., 1998b). The principle underlying the operation consists of carrying out the dissection then excision of all deep endometriotic lesions infiltrating the USL. In all cases the dissection was carried out using laparoscopic scissors and haemostasis was always performed with bipolar coagulation. The extent of dissection was correlated with the extent of the lesions. When necessary, due to the spread of the lesions, uterolysis and/or dissection of the lateral rectal fossa was carried out. Associated endometriotic lesions (e.g. ovarian cyst, adhesions, superficial peritoneal and/or ovarian endometriosis etc.) were treated in all cases during the same operative procedure. During the initial diagnostic phase of the laparoscopy, the severity of the endometriotic lesions was categorized using the revised American Fertility Society (AFS) classification (AFS, 1985). Endometriosis was defined histologically by the presence of ectopic glands together with stroma (Jansen and Russel, 1986; Martin *et al*., 1989).

The fertility study was carried out for those patients who complied with the following inclusion criteria: aged >20 years and <40 years; infertility was defined as at least 12 months of unprotected intercourse without resulting in pregnancy (Marcoux *et al*., 1997); positive histological result; no associated infertility factors (tubal patency at preoperative hysterosalpingography); no associated male infertility. The spermogram was considered to be normal if the following three parameters were satisfactory: sperm count >20×10^6/ml; >30% motility and >50% normal morphology (Adamson *et al*., 1993).

The patients were seen in consultation every 4 months for the first year after operation and then every 6 months. Fertility was studied

globally and also as a function of each of the following parameters: woman's age, parity, body mass index (BMI), duration of infertility, a past history of endometriosis, the rAFS score (AFS, 1985), the duration of the operation, the necessity or not of associated pelvic adhesiolysis and/or intraperitoneal cystectomy with resection of the deep endometriotic lesions infiltrating the USL, and the existence or not of pre- or post-operative medical treatment.

Data are presented as mean ± SD. The crude probabilities of pregnancies were calculated by using Kaplan–Meier survival analysis (Kaplan and Meier, 1958). The starting point for life-table calculations was the date of the operative laparoscopy. The end point was the date pregnancy began (worked out by early ultrasound examination at 10 weeks of amenorrhoea) or last contact if not pregnant (contact by mail in January 1997). Differences between groups were analysed for significance by the Fisher exact test and the Mann–Whitney U-test. $P < 0.05$ was considered to be significant.

Results

Of the 69 patients operated upon, 44 patients (63.7%) presented with infertility. Among these infertile patients ($n = 44$), 30 (68.2%) complied with the inclusion criteria. The 14 other patients (31.8%) were excluded for or more of the following reasons: associated male infertility (five cases); associated tubal infertility (one case); negative histology (10 cases). For the 30 patients for whom the fertility results could be analysed, 13 (43.3%) had already been given ovarian stimulation.

The mean age of the 30 patients complying with the inclusion criteria was 31 ± 4.7 years (range 20–40). The infertility was primary in 14 cases (46.7%) and secondary in 16 cases (53.3%). The mean duration of infertility was 35 ± 18.6 months (range 13–85). Mean parity for the patients was 0.3 ± 0.65 (range 0–3). A total of 24 patients (80%) were nulliparous. In all, 24 patients (80%) were nulliparous. The average weight of patients was 58 ± 10.5 kg (range 49–96). Their average height was 165 ± 7.2 cm (range 150–170). Their BMI was 21 ± 3 kg/m^2 (range 17–31). Of these patients, 25 (83.3%) presented with painful pelvic symptoms associated with their infertility. The types of pain, sometimes more than one in the same patient, were the following: dysmenorrhoea (22 cases); deep dyspareunia (18 cases); chronic pelvic pain (eight cases). A total of 11 patients (36.7%) had already undergone one or more surgical procedures (range 1–6) for endometriosis in another establishment. The clinical examination data were the following: in eight cases (26.7%) there was a palpable nodule on the USL; in 12 cases (40.0%) the USL were tense and/or infiltrated but had no palpable nodule; in 10 cases (33.3%) the USL appeared clinically normal. For these 10 patients the indication for laparoscopy was chronic pelvic pain associated with infertility. For these 10 patients who presented with functional pain symptoms, laparoscopic resection of the USL was carried out due to finding at laparoscopy of peritoneal retraction, induration and/or asymmetry of the USL amongst other indications (Chapron *et al.*, in press).

The mean duration of the operation was 119 ± 57.7 min (range 45–290). The mean rAFS score was 22 ± 20.6 (range 4–80). Distribution of the patients according to the rAFS classification (AFS, 1985) was the following: stage I: three
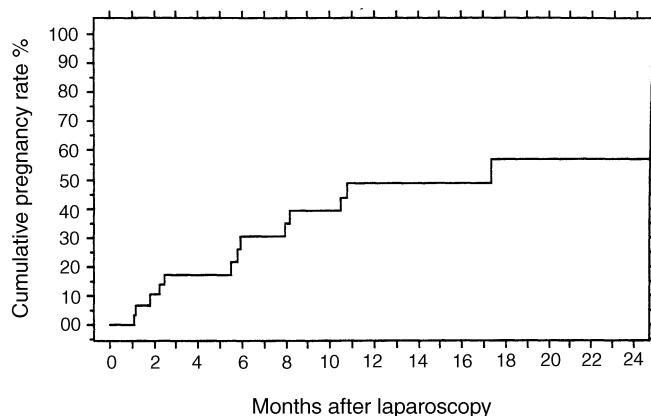

Figure 1. Cumulative intrauterine pregnancy rates after laparoscopic management of deep endometriosis infiltrating the uterosacral ligaments.

cases (10.0%); stage II: 14 cases (46.7%); stage III: eight cases (26.6%); stage IV: five cases (16.7%). Half the patients had a rAFS score of less than 13. Resection of the USL was bilateral in nine cases (30.0%). When resection was unilateral (21 cases; 70.0%) the lesions were more often located on the left ($n = 14$) than the right ($n = 7$) ($P = 0.007$). The following laparoscopic surgery procedures, sometimes more than one in the same patient, were associated with resection of the USL: adnexal adhesiolysis (18 cases; 60.0%); intraperitoneal cystectomy (five cases; 16.7%); bipolar coagulation of superficial peritoneal endometriotic lesions (23 cases; 76.7%); ureterolysis (22 cases; 73.3%) and dissection of the lateral rectal fossa (10 cases; 33.3%).

The overall intrauterine pregnancy (IUP) rate, including births and miscarriages, was 50.0% (15 patients). A total of 11 IUP occurred spontaneously. Three patients were pregnant with the use of ovulation induction, following dysovulation associated with endometriosis. One pregnancy was achieved after in-vitro fertilization (IVF). Of these 15 IUP, 12 patients gave birth normally at term, and three had an early miscarriage. None of the patients had an ectopic pregnancy. We recommend that patients who do not become pregnant after 1 year following intervention should undergo IVF.

The cumulative pregnancy rate for the 14 IUPs obtained without IVF was 48.5% at 12 months (95% confidence interval 28.3–68.7) (Figure 1). The average time before these IUP occurred was 7 ± 5.8 months (range 1–20). Half the patients were pregnant within 6 months after the operation. The IUP rate obtained without IVF was not correlated in statistically significant fashion with the rAFS classification (AFS, 1985). Whereas the IUP rate obtained without IVF was 47.0% (eight cases) for patients presenting stage I or II endometriosis, it was 46.1% (six cases) for patients with stage III or IV endometriosis (not significant) (Table I).

The results given in Table II show that the IUP rate was not significantly correlated with the following parameters: woman's age, parity, BMI, duration of infertility, a past history of endometriosis, the rAFS score (AFS, 1985), duration of the operation, the need or not to associate pelvic adhesiolysis and/or i.p. cystectomy with resection of the deep endometriotic

Table I. Intrauterine pregnancy rates obtained without using in-vitro fertilization (IVF) after laparoscopic management of deep endometriosis infiltrating the uterosacral ligaments according to the revised American Fertility Society (AFS, 1985) classification

rAFS classification		IUP rate	
Stage	Patients	n	%
I	3	0	0.0
II	14	8	57.1
I + II	17	8[a]	47.0
III	8	3	37.5
IV	5	3	60.0
III + IV	13	6[a]	46.1
Total	30	14	46.7

[a]Not significantly different.

Table II. Spontaneous intrauterine pregnancy rate according to patient characteristics (with the exception of one pregnancy obtained by in-vitro fertilization)

Patient characteristics	Pregnant patients (n = 14)	Non-pregnant patients (n = 16)
Age (years)	31.3 (23.3–37.8)	30.4 (20.0–39.8)
Parity	0.36 (0–3)	0.25 (0–1)
Weight (kg)	61.2 (46–96)	55.4 (47–70)
BMI (kg/m^2)	22.4 (17.5–31.3)	20.1 (16.8–23.4)
Duration of infertility (months)	29.2 (13.3–72.1)	40.9 (12.7–85.3)
Previous endometriosis	4 (28.6%)	7 (43.7%)
rAFS score	21.6 (5–60)	21.5 (4–80)
Duration of operation (mins)	135 (45–290)	105 (55–210)
Associated adhesiolysis and/or IPC	8 (57.1%)	10 (62.5%)
Pre-operative treatment	5 (35.7%)	4 (25.0%)
Post-operative treatment	3 (21.4%)	1 (6.25%)

BMI = body mass index; IPC = i.p. cystectomy.
Comparison of the pregnant and non-pregnant patients showed no statistically significant differences in the patients' characteristics.

lesions infiltrating the USL, and the existence or not of pre- or post-operative medical treatment.

Discussion

The prevalence of endometriosis is estimated to be ~3% in women of reproductive age (Houston *et al.*, 1987) and it is observed in 20 to 70% of patients presenting with infertility (Counseller, 1938; Hull *et al.*, 1985; Mahmood and Templeton, 1991; Koninckx, *et al.*, 1991; Matorras *et al.*, 1995). At present it is generally agreed that surgical treatment is the treatment of choice for infertile patients presenting with endometriosis. Hughes *et al.* (1993) showed that ovulation suppression is an ineffective treatment for endometriosis-associated infertility. For patients presenting with moderate or severe endometriosis, the fertility results were better with surgical treatment than with no treatment or with medical treatment (Adamson and Pasta, 1994). Analysis of the fertility results according to the means of surgical treatment of endometriosis-associated infertility showed no significant difference between laparoscopy and laparotomy (Adamson and Pasta, 1994). Finally, Marcoux *et al.* (1997) recently showed in a randomized, controlled, multicentre trial that operative laparoscopic treatment for patients presenting with minimal or mild endomet-

riosis enhances fecundity in infertile patients. All these findings indicate the choice of operative laparoscopic treatment for endometriosis-associated infertility (Adamson *et al.*, 1993).

The USL are one of the most frequent locations for deep endometriosis (Cornillie *et al.*, 1990). Medical treatments are more often purely palliative (Wingfield and Healy, 1993) and the treatment of choice for patients with deep endometriosis is surgery (Koninckx and Martin, 1995). In order to be effective with regard to pain it is necessary during the laparoscopic procedure to resect all of the deep endometriotic lesions infiltrating the USL. This treatment requires extensive dissection and ureterolysis for some patients (73.3% of cases in this series) and/or dissection of the lateral rectal fossa (33.3% of cases in this series).

The fertility results found in this study after operative laparoscopic treatment of deep endometriosis infiltrating the USL are encouraging (Figure 1). These results are interesting when deciding on the strategy to use for infertile patients presenting with deep endometriotic lesions. For the patients in this series, none of whom had other infertility factors apart from the deep endometriosis infiltrating the USL, the laparoscopic surgery treatment enabled 47.6% of them (14/30) to become pregnant without having to use IVF. These results match those of Reich *et al.* (1991) who, in a series of 100 women with cul-de-sac obliteration secondary to retrocervical deep endometriosis treated by operative laparoscopy, had a 70% (32/46) viable intrauterine pregnancy rate among patients with infertility. Although these results are satisfactory, this does not mean that it can be stated that the deep endometriotic lesions were the only lesions responsible for the infertility these patients suffered from. During the operation, in addition to resecting the deep lesions, all the other associated endometriotic lesions were treated. However these results do show that it is logical in this context to associate the standard treatment for endometriosis (e.g. lysis, i.p. cystectomy, bipolar coagulation of superficial peritoneal endometriotic lesions) with resection of deep endometriotic lesions infiltrating the USL. There are two arguments in favour of this attitude. Firstly, apart from the benefit in terms of pregnancy, which is comparable to that reported in other publications (Adamson *et al.*, 1993; Marcoux *et al.*, 1997), resection of the deep endometriotic lesions means that the patients, who in most cases present with pelvic pain, find that the pain symptoms are significantly reduced in 75% of cases (Chapron *et al.*, 1998a). Secondly, one third of the patients in this study had already undergone one or more surgical procedures in connection with this infertility, during which exeresis of the deep endometriotic lesions had not been carried out.

The fertility results were not correlated with the rAFS Classification (AFS, 1985) (Table I). The fertility results observed for patients with stage I and II endometriosis fit in with the conclusions drawn by Marcoux *et al.* (1997) who, in a controlled multicentre trial, demonstrated that laparoscopic resection or ablation of minimal and mild endometriosis enhances fecundity in infertile women. The fact that the rAFS classification (AFS, 1985) is not a sensitive predictor of pregnancy following treatment has been reported by other authors (Adamson and Pasta, 1994; Guzick *et al.*, 1997).

C.Chapron, X.Fritel and J.-B.Dubuisson

Although this classification at least enables gynaecologists to adopt a common staging system, it is not perfect. Changes following a period of careful consideration would seem to be essential (Dubuisson and Chapron, 1994). The fact that the fertility results for patients who present little if any anatomical alterations (stages I and II according to the rAFS classification) are not significantly different from those of patients who had stage III or IV endometriosis confirms that factors other than purely anatomical impairment must be involved in order to explain the influence of endometriosis on fertility. Certain authors have suggested that the morphological appearance of implants and certain biomarkers (e.g. CA-125) may affect infertility (Vernon *et al.*, 1986; Lessey *et al.*, 1994; Pittaway *et al.*, 1995).

These preliminary results are interesting. For infertile patients presenting with deep endometriosis infiltrating the USL without any other cause of infertility, complete operative laparoscopic treatment of endometriosis enables a spontaneous IUP rate of 46.7% to be obtained. These results mean that these patients can be offered operative laparoscopic treatment, during which extensive retroperitoneal dissection may be carried out, enabling half of the patients to become pregnant. In other words, extensive laparoscopic surgery procedures in this context would not seem to adversely affect fertility. Further studies are essential in order to confirm these preliminary results, and also achieve a better understanding of the physiopathology of endometriosis with respect to infertility.

References

Adamson, G.D. and Pasta, D.J. (1994) Surgical treatment of endometriosis-associated infertility: Meta-analysis compared with survival analysis. *Am. J. Obstet. Gynecol.*, **171**, 1488–1505.

Adamson, G.D., Hurd, S.J., Pasta, D.J. and Rodriguez, B.D. (1993) Laparoscopic endometriosis treatment: is it better? *Fertil. Steril.*, **59**, 35–44.

American Fertility Society (1985) Revised American Fertility Society classification for endometriosis. *Fertil. Steril.*, **43**, 351–352.

Chapron, C. and Dubuisson, J.-B. (1996) Laparoscopic treatment of deep endometriosis located to the uterosacral ligaments. *Hum. Reprod.*, **11**, 868–873.

Chapron, C., Dubuisson, J.-B., Tardif, D. *et al.* (1998a) Retroperitoneal endometriosis and pelvic pain. Results of laparoscopic uterosacral ligament resection according to the rAFS Classification and histological results. *J. Gynecol. Surg.*, **14**, 51–58.

Chapron, C., Dumontier, I., Dousset, B. *et al.* (1998b) Results and place of endorectal endoscopic ultrasonography for patients with deep pelvic endometriosis. *Hum. Reprod.*, **13**, 2266–2270.

Chapron, C., Dubuisson, J.-B., Fritel, X. *et al.* (1998c) Deep endometriosis infiltrating the uterosacral ligaments: Technique and results of operative laparoscopic management. *J. Am. Assoc. Gynecol. Laparosc.*, in press.

Counseller, V.S. (1938) Endometriosis. A clinical and surgical review. *Am. J. Obstet. Gynecol.*, **36**, 877–890.

Cornillie, FJ, Oosterlynck, D., Lauwereyns, J.M. and Koninckx, P.R. (1990) Deeply infiltrating endometriosis: histological and clinical significance. *Fertil. Steril.*, **53**, 978–983.

Donnez, J., Nisolle, M., Casanas-Roux, F. *et al.* (1995) Rectovaginal septum, endometriosis or adenomyosis: laparoscopic management in a series of 231 patients. *Hum. Reprod.*, **12**, 2214–2216.

Dubuisson, J.-B. and Chapron, C. (1994) Classification of endometriosis. The need for modification. *Hum. Reprod.*, **12**, 2214–2216.

Dubuisson, J.-B., Chapron, C., Aubriot, F.X. *et al.* (1994) Pregnancy after laparoscopic partial cystectomy for bladder endometriosis. *Hum. Reprod.*, **9**, 730–732.

Guzick, D.S., Silliman, N.P., Adamson, G.D. *et al.* (1997) Prediction of pregnancy in infertile women based on the American Society for Reproductive Medicines' revised classification of endometriosis. *Fertil. Steril.*, **57**, 822–829.

Houston, D.E., Noller, K.L., Melton,L.J. III *et al.* (1987) Incidence of pelvic endometriosis in Rochester, Minnesota, 1970–1979. *Am. J. Epidemiol.*, **125**, 959–969.

Hughes, E.G., Fedorkow, D.M. and Collins, J.A. (1993) A quantitative overview of controlled trials in endometriosis-associated infertility. *Fertil. Steril.*, **59**, 963–970.

Hull, M.G.R., Glazener, C.M.A., Kelly, N.J. *et al.* (1985) Population study of causes, treatment and outcome of infertility. *Br. Med. J.*, **291**, 1693–1697.

Jansen, R.P.S. and Russel, P. (1986) Non-pigmented endometriosis: clinical, laparoscopic and pathologic definition. *Am. J. Obstet. Gynecol.*, **155**, 1154–1158.

Kaplan, E.L. and Meier, P. (1958) Nonparametric estimation from incomplete observation. *Am. J. Stat. Assoc.*, **53**, 457–481.

Koninckx, P.R. and Martin, D.C. (1995) Surgical treatment of deeply infiltrating endometriosis. In Shaw, R. (ed.), *Endometriosis. Current Understanding and Management.* Blackwell Scientific, Oxford, UK, pp. 264–281.

Koninckx, P.R., Meuleman, C., Demeyere, S. *et al.* (1991) Suggestive evidence that pelvic endometriosis is a progressive disease, whereas deeply infiltrating endometriosis is associated with pelvic pain. *Fertil. Steril.*, **55**, 759–765.

Koninckx, P.R., Rittinen, L., Seppala, M. and Cornillie, F.J. (1992) Ca-125 and placental protein 14 concentrations in plasma and peritoneal fluid of women with deeply infiltrating pelvic endometriosis. *Fertil. Steril.*, **57**, 523–530.

Lessey, B., A., Castelbaum, A.I., Sawin, S.J. *et al.* (1994) Aberrant integrin expression in the endometrium of women with endometriosis. *J. Clin. Endocrinol. Metab.*, **79**, 643–649.

Mahmood, T.A. and Templeton, A. (1991) Prevalence and genesis of endometriosis. *Hum. Reprod.*, **6**, 544–549.

Marcoux, S., Maheux, R., Berubé, S. and the Canadian Collaborative Group on Endometriosis (1997) Laparoscopic surgery in infertile women with minimal or mild endometriosis. *N. Engl. J. Med.*, **337**, 217–222.

Martin, D.C. (1988) Laparoscopic and vaginal colpotomy for excision of infiltrating cul-de-sac endometriosis. *J. Reprod. Med.*, **33**, 806–808.

Martin, D.C., Hubert, G.D. and Levy, B.S. (1987) Depth infiltration of endometriosis. *J. Gynecol. Surg.*, **5**, 55–60.

Martin, D.C., Hubert, G.D., Vandre Zwaag, R. and El-Zeky, F. (1989) Laparoscopic appearances of peritoneal endometriosis. *Fertil. Steril.*, **51**, 63–67.

Matorras, R., Rodriqez, F., Pijoan, J.I. *et al.* (1995) Epidemiology of endometriosis in infertile women. *Fertil. Steril.*, **63**, 34–38.

Moore, J.G., Binstcok, M.A. and Crowdon, W.A. (1988) The clinical implications of retroperitoneal endometriosis. *Am. J. Obstet. Gynecol.*, **158**, 1291–1298.

Nezhat, C., Nezhat, F. and Pennington, E. (1992) Laparoscopic treatment of lower colorectal and infiltrative rectovaginal septum endometriosis by the technique of the video laparoscopy. *Br. J. Obstet. Gynaecol.*, **99**, 664–667.

Nezhat, C., Nezhat, F., Nezhat, C.H. *et al.* (1996) Urinary tract endometriosis treated by laparoscopy. *Fertil. Steril.*, **66**, 920–924.

Ohba, T., Mizutani, H., Maeda, T. *et al.* (1996) Evaluation of endometriosis in utero sacral ligaments by transrectal ultrasonography. *Hum. Reprod.*, **11**, 2014–2017.

Pittaway, D.E., Rondinone, D., Miller, K. and Barnes, K. (1995) Clinical evaluation of CA-125 concentrations as a prognostic factor for pregnancy in infertile women with surgically treated endometriosis. *Fertil. Steril.*, **64**, 321–324.

Redwine, D.B. (1992) Laparoscopic en bloc resection for the treatment of obliterated cul-de-sac in endometriosis. *J. Reprod. Med.*, **37**, 695–698.

Reich, H., McGlynn, F. and Salvat, J. (1991) Laparoscopic treatment of cul-de-sac obliteration secondary to retrocervical deep fibrotic endometriosis. *J. Reprod. Med.*, **36**, 516–522.

Vernon, M.S., Beard, J.S., Graves, K. and Wilson, E.A. (1986) Classification of endometriotic implants by morphologic appearance and capacity to synthesize prostaglandin F. *Fertil. Steril.*, **46**, 801–806.

Wingfield, M. and Healy, D.L. (1993) Endometriosis: medical therapy. *Baillière's Clin. Obstet. Gynecol.*, **7**, 813–8338.