Human Reproduction Update, Vol.13, No.5 pp. 477–485, 2007 doi:10.1093/humupd/dmm014
Advance Access publication June 11, 2007

The position of diagnostic laparoscopy in current fertility practice

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In everyday clinical practice, it is not always clear if and when exactly in the fertility work-up a diagnostic laparoscopy should be offered. The aim of this review is to analyse the available evidence with respect to alternative diagnostic methods for detecting tuboperitoneal infertility and with respect to the position of diagnostic laparoscopy in women with infertility. A literature search of the National Library of Medicine and the National Institutes of Health (PubMed) was performed using the key words 'diagnostic laparoscopy and infertility'. The study methodology was carefully considered in an effort to present conclusions preferably based on randomized controlled trials (RCTs). The routine use of diagnostic laparoscopy for the evaluation of all cases of female infertility is currently under debate. According to data published in retrospective non-controlled studies, diagnostic laparoscopy after several failed cycles of ovulation induction enables the detection of a significant proportion of pelvic pathology amenable to treatment. A Cochrane review has shown that laparoscopic ovarian diathermy in clomiphene-resistant polycystic ovarian syndrome is at least as effective as gonadotrophin treatment, and results in a lower multiple pregnancy rate. The role of laparoscopy before the start of treatment with intrauterine insemination is controversial, according to one RCT. In women with bilateral ultrasonically visible hydrosalpinges, two RCTs have demonstrated increased implantation and pregnancy rates in IVF cycles after salpingectomy. Although RCTs which have studied the benefit of laparoscopic surgery in moderate or severe endometriosis are still lacking, its value has generally been accepted. In conclusion, some specific clinical settings, solid evidence is available to recommend the use of diagnostic laparoscopy in current fertility practice. There is however a need for more RCTs to answer remaining questions regarding its value in the diagnosis and treatment of some patients with infertility.

Keywords: diagnostic laparoscopy; ovulation induction; endometriosis; intrauterine insemination; *in vitro* fertilization

Introduction

The position of diagnostic laparoscopy in current fertility practice is still under debate. Until recently, laparoscopy was the final diagnostic procedure of the female fertility exploration, as outlined by the American Fertility Society in 1992 and by the World Health Organization guidelines (Rowe *et al.*, 1993). In 1997, Glatstein *et al.* (1997) reported that 89% of all reproductive endocrinologists in the USA routinely performed a laparoscopy in the diagnostic work-up of infertility. However, some investigators showed that the diagnostic laparoscopy did not reveal any pathology or only minimal and mild endometriosis in 40–70% of all cases (Forman *et al.*, 1993).

Already by the mid-1990's, the test 'diagnostic laparoscopy' failed to be an ideal predictor for infertility (Collins *et al.*, 1995). These findings convinced some authors to challenge the need for this procedure in the work-up of infertility (Fatum *et al.*, 2002). Worldwide, diagnostic laparoscopy is increasingly bypassed by IVF clinics in an effort to be cost-effective on the one hand and on the other hand, to protect patients from possible hazards of surgical complications and general anaesthesia.

Disadvantages of diagnostic laparoscopy include the need for general anaesthesia, patient's anxiety and the possibility of adhesion formation. In a large Finnish follow-up study, the complication rate of diagnostic laparoscopy was 0.6 per 1000 procedures (Härkki-Sirén *et al.*, 1999). However, advantages include the possibility to perform both diagnosis and therapy at the same time, and the opportunity to combine the laparoscopy with the hysteroscopic exploration of the uterine cavity with an endometrial biopsy, all as part of day care surgery. In this

review paper, an effort is made to define the position of diagnostic laparoscopy in current fertility practice. A literature search of the National Library of Medicine and the National Institutes of Health was done, using the MeSH terms 'diagnostic laparoscopy and infertility'. The study methodology was carefully considered to present conclusions preferably based on randomized controlled trials (RCTs), if at all available.

We will first address the question whether alternative diagnostic procedures to evaluate tuboperitoneal infertility are reliable enough to replace the laparoscopy. Subsequently, we will discuss the position of diagnostic laparoscopy in the context of treatment for ovulation induction, intrauterine insemination (IUI) and IVF based on two questions: (i) is it necessary to perform a diagnostic laparoscopy before starting these respective infertility treatments to detect significant tuboperitoneal pathology with therapeutic consequences and with impact on the treatment's cumulative ongoing pregnancy rate? and (ii) is it still indicated to perform a laparoscopy after several failed treatment cycles with ovulation induction or IUI/IVF to enhance the couple's success rate? At the end of this paper we will present some conclusions regarding the level of evidence available in the current literature and the strength of recommendations.

Alternative diagnostic procedures for evaluating tubal infertility and endometriosis

The prevalence of peritubal adhesions in infertile patients ranges from 10 to 23% (al Badawi *et al.*, 1999). Thus the first topic to be addressed is the reliability of alternative diagnostic methods for examining the presence of tuboperitoneal infertility, based on medical history, *hysterosalpingography* (HSG) and serum Chlamydiascreening.

Medical history and tuboperitoneal infertility

The positive predictive value of history taking, based on symptoms suggestive for previous pelvic inflammatory disease (PID), a history of abnormal vaginal discharge and a previous diagnosis of a lower genital tract infection was only 56, 59 and 35%, respectively, in predicting tuboperitoneal infertility (Hubacher *et al.*, 2004). With respect to pelvic endometriosis, the predictive value of each symptom or even a combination of symptoms in predicting its presence, remains uncertain. Indeed, these symptoms have a low specificity and a significant proportion of women affected by endometriosis, are without any symptoms (Kennedy *et al.*, 2005).

HSG and HyCoSy

The HSG provides a morphological view of the uterine cavity, the Fallopian tubes and their patency. According to a meta-analysis, HSG has a reasonable specificity (83%) but a low sensitivity (65%) to document patency of the Fallopian tubes (Swart *et al.*, 1995). Fecundability is reduced in the presence of bilateral occlusion and/or hydrosalpinx (odds ratio, OR 0.30; 95% confidence interval, CI 0.13–0.71), but not in the presence of one-sided tubal occlusion or hydrosalpinx (OR 0.81; 95% CI 0.47–1.40) (Mol *et al.*, 1997b). Furthermore, an HSG performed with oil-based contrast media may have therapeutic value in women with infertility. According to a meta-analysis by Watson and co-workers (1994), a higher conception rate has been demonstrated in patients where HSG was performed with oil-based contrast media than those with water-based contrast media (OR 1.89; 95% CI 1.33–2.68), especially in the subgroup of patients with idiopathic infertility (OR 2.71; 95% CI 1.94–3.78). According to a randomized study by Ogata *et al.* (1993), the conception rate was three times higher in infertile women having an HSG performed with oil- soluble contrast medium when compared with a control group without HSG. However, in everyday clinical practice HSG is generally performed with water-based media to prevent allergic reactions despite the fact that no clear additional benefit has been reported with regard to fecundability after HSG with water-based media. The HSG has no value in the diagnosis of endometriosis.

The technique of HSG has several possible adverse effects. Lower abdominal pain and discomfort are commonly experienced by patients undergoing HSG, and can be remembered for years afterwards as one of the most painful outpatient exams in gynaecology. An HSG can induce or exacerbate PID, leading to peritonitis, pelvic abscess and very exceptionally even to death (Chuang *et al.*, 1971). Uterine perforation and post-examination haemorrhage are a possibility. Other complications include granuloma formation and vascular intravasation. Hypersensitivity reactions to iodine exist with any of the HSG media, but allergic reactions are rare. Finally, the ionizing radiation used for HSG can be detrimental to an undiagnozed early pregnancy.

A multicentre RCT comparing cumulative pregnancy rates (CPR) in a group where HSG was followed by diagnostic laparoscopy versus a group where diagnostic laparoscopy alone was performed, showed no significant difference in CPR at 18 months (Perquin *et al.*, 2006).

The authors question the added value of HSG performed at an early stage in the fertility work- up prior to laparoscopy and dye.

The prognostic significance of HSG and laparoscopy for fertility outcome was studied and published in a large prospective cohort study (Mol *et al.*, 1999).Unilateral and bilateral tubal occlusion at HSG and laparoscopy were related to treatment independent pregnancy. The adjusted fecundity rate ratios (FRR) of one-sided tubal occlusion at HSG was 0.80, whereas two-sided tubal occlusion had a FRR of 0.49. In the case of laparoscopy, the adjusted FRRs were 0.51 and 0.15, respectively, for one-sided and two-sided tubal occlusion. A laparoscopy showing two-sided occlusion after a normal or one-sided occluded HSG was found in 5% of the patients and the treatment-independent conception rate in this case was virtually zero. A normal laparoscopic examination after two-sided occluded HSG was found in 42% of all patients; in these cases fertility prospects were only slightly impaired with a three-year cumulative ongoing intrauterine pregnancy rate of 9%. On the other hand, fertility prospects were strongly impaired in cases where laparoscopy showed one-sided and two-sided occlusions after a two-sided occluded HSG; the adjusted FRR were 0.38 and 0.19, respectively. The authors suggest that performing a diagnostic laparoscopy after a two-sided occluded HSG is very useful since it enables a division between two groups with significantly different fertility prospects. Furthermore, laparoscopy can be delayed after normal HSG for at least 10 months because of the very low probability of only 5% that bilateral tubal occlusion may be found.

Hysterosalpingo Contrast Sonography (HyCoSy) is an attractive alternative to HSG because the patient is not exposed to X-rays or iodinated contrast media. Fallopian tubal patency is assessed using transvaginal ultrasonography and a galactose microbubble contrast medium. The concordance rates on the assessment of tubal patency between HyCoSy and HSG are similar, making this ultrasound diagnostic tool an attractive option for the outpatient screening for tubal patency. With reference to the pregnancy rates, a case controlled clinical study has demonstrated that allocation of patients screened as normal with HyCoSy to treatments that rely on an accurate assessment of tubal patency does not change the conception rates (Hamilton *et al.*, 2003).

Serum CAT

The presence of Chlamydia antibodies (by Chlamydia antibody testing or CAT) is indicative of an earlier infection with *Chlamydia trachomatis*, the most important etiologic factor of PID. The accuracy of serum Chlamydial antibodies in the diagnosis of tubal pathology has been scrutinized in a meta-analysis by Mol and co-workers (Mol *et al.*, 1997a). The discriminative capacity of Chlamydia antibody titers by means of ELISA, microimmunofluorescence or immunofluorescence in the diagnosis of any tubal pathology is comparable with that of HSG in the diagnosis of tubal occlusion or hydrosalpinx as indicated by comparable receiver operating characteristics (ROC) curves.

Summary ROC curves of studies using ELISA or (micro) immunofluorescence demonstrated a better discrimination when compared with the summary ROC curve of studies using immunoperoxidase assay (Mol *et al.*, 1997a). The same authors published their results with regard to the cost-effectiveness of HSG, laparoscopy and CAT in >2000 infertile couples enrolled in the Canadian Infertility Treatment Evaluation Study (Mol *et al.*, 2001). The diagnostic work-up to detect tubal pathology in infertile couples should, according to their results, start with CAT in couples with relatively good-fertility prospects and immediate HSG in couples with relatively poor-fertility prospects. Relatively good-fertility prospects were defined by the authors as having a 3-year chance of conception of >14%, whereas relatively poor-fertility prospects were defined by a 3-year chance of conception of <14%.

In summary, both HSG and CAT are reliable diagnostic procedures as a primary screening tool for infertility due to tubal pathology, but not for endometriosis in patients with open Fallopian tubes. With these data in mind, the discussion about if and when a diagnostic laparoscopy should still be performed can now be focused on the following specific clinical infertility situations.

Diagnostic laparoscopy and the treatment of minimal and mild endometriosis

Whether or not minimal and mild endometriosis should be treated in case of infertility still remains a seemingly never-ending discussion. The prevalence of endometriosis in the infertile population (20–68%) is higher than that in the general female population of reproductive age (2.5–3.3%) (Houston *et al.*, 1987; Mahmood and Templeton, 1991). Moderate and severe stage endometriosis leads to disruption of the normal pelvic anatomy, impairing the reproductive function of the internal genital organs. Minimal and mild stage endometriosis may impair fertility by a variety of mechanisms, including toxic factors within the peritoneal fluid, impaired folliculogenesis and luteal function. The monthly fecundity rate is around 7% in stages I–II endometriosis and the cumulative live birth rate with expectant management in endometriosis is low (Collins *et al.*, 1995). Although the association between minimal and mild endometriosis and infertility may be incidental, many sound arguments have been presented to support that the relationship between endometriosis and infertility is causal as previously reviewed (De Hondt *et al.*, 2006).

According to a meta-analysis by Jacobson and co-workers (2004b), the ablation of endometriotic lesions with adhesiolysis to improve fertility in minimal and mild endometriosis is effective compared to diagnostic laparoscopy alone (Table 1). This recommendation is based upon a systematic review of two similar but contradictory RCTs performed in Italy (Parazzini *et al.*, 1999) and in Canada (Marcoux *et al.*, 1997) comparing laparoscopic ablation or excision and adhesiolysis of endometriotic lesions versus diagnostic laparoscopy alone. The fact that these two RCTs have been assembled into one meta-analysis has been criticized (De Hondt *et al.*, 2006) because the Italian study included a low number of patients ($n = 101$), had an unequal number of subjects in both randomized groups, did not include a power analysis or an outcome analysis on the level of monthly fecundity rate or CPR, and was biased by the fact that a large number of patients also took GnRH agonists after surgery (Parazzini *et al.*, 1999; De Hondt *et al.*, 2006).

In the Canadian study in a group of 341 infertile women aged 20–39 years with minimal or mild endometriosis, a higher cumulative probability of ongoing pregnancy after 36 weeks was observed in the surgically treated group (31%) when compared with the control group which had received only diagnostic laparoscopy (18%) (RR = 1.7; 95% CI 1.2–2.6) (Marcoux *et al.*, 1997). However, laparoscopic surgical treatment of endometriosis did not

Table 1: Laparoscopic treatment of minimal/mild endometriosis

	Laparoscopic surgery	Diagnostic laparoscopy	RR
	($n = 172$)	($n = 169$)	
Pregnancies carried beyond 20 weeks	50	29	
36 weeks cumulative probability (Marcoux *et al.* 1997)	30.7	17.7	1.7 (1.2–2.6)
	($n = 54$)	($n = 47$)	
Pregnancy (Parazzini, 1999)	12	13	NS
	($n = 437$)	Peto OR (95% CI)	
Ongoing pregnancy at 20 weeks or live birth (Jacobson *et al.* 2002)		1.64 (1.05–2.57)	

normalize fecundability. Indeed, the monthly fecundity rate among women who underwent laparoscopic surgery (6.1%), albeit double as high as in the diagnostic laparoscopy group, was still much lower than the fecundity rate expected in fertile women (20%). A second criticism concerns the fact that possibly the fertility enhancing effect of the laparoscopic treatment of minimal and mild endometriosis is solely due to the adhesiolysis. However, the authors of the Canadian RCT clearly mention that in the 284 women who did not have adhesions, the destruction of the implants also significantly increased the 36-week cumulative probability of ongoing pregnancy with a cumulative incidence ratio of 1.6 (95% CI 1.1–2.5) (Marcoux *et al.*, 1997). The ESHRE Special Interest Group for Endometriosis who has recently developed guidelines for the diagnosis and treatment of endometriosis recommends surgical treatment for minimal or mild endometriosis in infertile women, but also mentions that some members of the working group questioned the strength of the evidence of the recommendations in the meta-analysis of Jacobson (Kennedy *et al.*, 2005). The number needed to treat from the trials is 12, but one has to adjust for the prevalence of endometriosis in the relevant clinical practice. If endometriosis is diagnosed in 30% of all cases, then the number needed to treat in that particular setting would ultimately be $12/0.3 = 40$, which is less compelling (Practice Committee ASRM, 2006). Clearly, there still is a need for further randomized controlled studies in order to resolve this issue. At the same time, it may be hard to convince ethical committees about the need for such studies, and even harder to recruit patients, in view of the current level of evidence.

Diagnostic laparoscopy and ovulation induction treatment

Should a diagnostic laparoscopy systematically be performed before the onset of any ovulation induction treatment? Can a diagnostic laparoscopy, performed after several failed ovulation induction treatment cycles, reveal significant pathology amenable to surgical treatment with a positive effect on the overall ongoing pregnancy rate?

These seemingly easy questions are difficult to answer because the very few studies available are all retrospective and non-controlled.

Laparoscopy before ovulation induction treatment

The available evidence on the role of laparoscopy before ovulation induction merely focuses on the comparison between HSG and laparoscopy findings for the diagnosis of tubal pathology, the diagnosis and treatment of adhesions and the treatment of minimal and mild endometriosis.

With regard to the routine use of HSG prior to laparoscopy in the fertility work-up, we refer to the multicentre RCT by Perquin *et al.* (2006). With regard to the CPRs at 18 months, no significant differences were found in 344 women randomized to an intervention group with HSG followed by diagnostic laparoscopy (CPR at 18 months 49% CI 42–57) or a control group with diagnostic laparoscopy alone (CPR at 18 months 50% CI 43–58%). Regarding the prospective value of HSG and laparoscopy we refer to the discussion above (Mol *et al.*, 1999).

The relevance of treating minimal and mild endometriosis will, as also has been shown above, depend on the prevalence of this disease in the treated population.

Laparoscopy during ovulation induction treatment

In a retrospective study, Ochoa Capelo *et al.* (2003) performed a diagnostic laparoscopy in 92 patients after four failed cycles of ovulation induction treatment with clomiphene citrate. The patients had at least four ovulatory cycles, confirmed by basal body temperature and midluteal phase serum progesterone, normal HSG findings and male partners with a normal semen analysis. The presence of pelvic pathology in this study (Ochoa Capelo *et al.*, 2003) is summarized in Table 2. Laparoscopic findings were strictly normal in only 36% of cases, whereas endometriosis and/or pelvic adhesions were observed in 50 and 33%, respectively. The authors concluded that laparoscopy continues to be a useful tool in the work-up of an infertile couple but regrettably did not present any pregnancy rates following laparoscopic surgery (Ochoa Capelo *et al.*, 2003).

With regard to the efficacy of laparoscopic treatment for endometriosis, we refer to the evidence presented above. With regard to laparoscopic adhesiolysis, there is only one non-randomized controlled study by Tulandi and co-workers (1990) that documented higher CPRs of 32 and 45% in 12 and 24 months, respectively, after operative laparoscopy when compared with the 11 and 16% CPRs observed in the non-treated control group. To our knowledge, these data have not been confirmed in a randomized controlled study.

Laparoscopic ovarian diathermia in PCOS patients

About 20% of all patients diagnosed with polycystic ovarian disease (PCOS) and infertility, will not ovulate after ovulation induction treatment with clomiphene citrate. Even today, the effective treatment of clomipheneresistant PCOS remains a challenge for the medical profession. More than 20 years ago, Gjonnaess (1994) described that laparoscopic electrocoagulation of the ovarian capsule in 62 clomiphene resistant PCOS patients resulted in an ovulation rate of 92% and a pregnancy rate of 69%.

In a recent Cochrane review (Farquhar *et al.*, 2005), the efficacy of laparoscopic drilling of the ovarian capsule (laparoscopic ovarian diathermy, LOD) by diathermy or laser in clomipheneresistant PCOS has been compared to gonadotrophin treatment based on a total of 15 RCTs. Only six trials were included for

Table 2: Presence of pelvic pathology on laparoscopy after 4 failed cycles ovulation induction treatment

Findings at laparoscopy	*n*
Normal	33/92
Minimal endometriosis	21/92
Mild endometriosis	6/92
Moderate endometriosis	8/92
Severe endometriosis	2/92
Endometriotic cyst	8/92
Adhesions	30/92
Tubal pathology	1/92

Some patients had concurrent anomalies on diagnostic laparoscopy. Adapted from Ochoa Capelo *et al.* (2003).

further analysis. The primary outcome parameters were the live birth rate, ovulation rate and ongoing pregnancy rate. Secondary outcome parameters included the rate of miscarriage, multiple pregnancy rate, ovarian hyperstimulation syndrome and the total cost of the respective treatments. The results are shown in Table 3: there was no evidence of a difference in the live birth rate or ongoing pregnancy rate between LOD and the gonadotrophins.

However, the multiple pregnancy rates were lower with ovarian drilling than with gonadotrophins. There was no evidence of difference in miscarriage rates between both treatment modalities (OR 0.8; 95% CI 0.36–1.86). Approximately 50% of all treated patients will have a live birth and 16% will have a miscarriage with either treatment. The reviewer's conclusion is that there is no difference in the live birth rate and the miscarriage rate in women with clomipheneresistant PCOS undergoing LOD when compared with gonadotrophin treatment (Farquhar *et al.*, 2005). However, the reduction in multiple pregnancy rate in women undergoing LOD makes this option attractive.

Disadvantages of the LOD procedure include the risks related to laparoscopic surgery, the need for general anaesthesia, the possible risk of thermal damage to adjacent organs and ovarian adhesion formation, and as clearly mentioned in the Cochrane review, the lack of knowledge concerning the possible negative long-term effects of this procedure on the ovarian reproductive function (Farquhar *et al.*, 2005). Moreover it has been pointed out that the effects observed are usually temporary and the signs and symptoms of PCOS may return within months following the LOD (Insler and Lunenfeld, 1993).

Advantages of LOD included the opportunity to treat concomitant pelvic pathology such as peritubal adhesions and endometriosis that can be associated with female infertility. Furthermore, during the same endoscopic procedure, tubal patency can be tested, and a hysteroscopy can be performed as part of the infertility work-up.

In summary, the position of diagnostic laparoscopy in the setting of ovulation induction is at present not clear due to the lack of sound scientific evidence provided by good-quality studies. The routine use of diagnostic laparoscopy to evaluate all cases of female anovulatory infertility cannot be advocated, but laparoscopy can offer the opportunity to assess tuboperitoneal status, to treat pelvic pathology that may limit conception (endometriosis, adhesions), and to perform LOD. Laparoscopic ovarian diathermia is a good option when compared with gonadotrophin treatment in the clomiphene citrate resistant PCOS patient, but counselling should be offered with regard to the unknown long-term effects of this procedure on the ovarian function.

Table 3: Ovarian drilling ± medical ovulation induction versus gonadotrophins only

Study	LOD n/N	Gonadotrophins n/N	OR 95% CI
Outcome: ongoing pregnancy rate (per couple)			
Farquhar *et al.* (2002)	5/29	5/21	0.67 (0.17, 2.68)
Bayram (2004)	56/83	57/85	1.02 (0.53, 1.94)
Lazoviz (1998)	17/29	9/28	2.99 (1.01, 8.84)
Vegetti (1998)	2/16	5/13	0.23 (0.04, 1.46)
Total	80/157	76/147	1.08 (0.67, 1.75)
Outcome: multiple pregnancy rate (per ongoing pregnancy)			
Farquhar *et al.* (2002)	0/5	0/5	Not estimable
Bayram (2004)	1/56	9/57	0.10 (0.01, 0.79)
Lazoviz (1998)	0/14	2/9	0.10 (0.00, 2.44)
Vegetti (1998)	0/3	1/5	0.43 (0.01, 14.08)
Total	1/78	12/76	0.13 (0.03, 0.59)

Adapted from Farquhar *et al.* (2005).

Diagnostic laparoscopy and IUI

IUI is an effective fertility enhancing treatment in cases of cervical factor, unexplained infertility and mild male infertility. Two relevant clinical questions arise in the setting of IUI treatment. First, does a laparoscopy significantly change the intended treatment plan in cases where IUI is clinically indicated? Second, should the laparoscopy be performed before starting IUI or only after several failed IUI cycles?

Laparoscopy before IUI

Whether laparoscopy should be performed after or before IUI was studied in a retrospective study, design by Tanahatoe and co-workers (2003). In a cohort of 495 patients with normal HSG, laparoscopy was performed before proceeding to IUI treatment due to unexplained, cervical or mild male infertility. The diagnostic laparoscopy changed the intended treatment in 124 of 495 patients (25%). Excluding the presence of minimal and mild endometriosis as pelvic pathology without therapeutic implications, the additional value of diagnostic laparoscopy is limited to only 40 of 495 patients (8%). The authors conclude that further prospective studies are needed to determine the real additional value of diagnostic laparoscopy in IUI.

Recently, the same authors published the results of a randomized trial on the role of diagnostic laparoscopy in IUI (Tanahatoe *et al.*, 2005). A group of 154 patients, suitable for IUI treatment due to unexplained, cervical or mild male infertility with normal HSG was randomly allocated to two different treatment strategies. In the first group (diagnostic laparoscopy first, DLSF), 77 patients were randomized to receive a diagnostic laparoscopy before IUI treatment. Further treatment was discontinued in 13 patients, either because of drop out by not giving informed consent ($n = 10$) or because of pregnancy ($n = 3$). A diagnostic laparoscopy was thus performed in the remaining 64 patients. After the laparoscopy, IUI treatment was started. Before and during IUI in the DLSF group, 11 patients dropped out. Of the 31 patients who became pregnant in this group, 9 conceived before or between IUI and 22 conceived due to the IUI treatment. In the second group (IUI first, IUIF), 77 patients were randomized to treatment with IUI during six treatment cycles. The first three IUI cycles were performed without controlled ovarian hyperstimulation (COH). If pregnancy did not occur after three cycles of IUI in

the natural cycle, then the patient could choose between continuing IUI in the natural cycle or starting IUI with COH with recombinant FSH with a maximum of another three cycles. Further treatment in the IUIF group was discontinued in 54 patients because of pregnancy ($n = 38$) or due to drop out ($n = 16$). The remaining 23 patients who did not conceive in the IUIF group all underwent a diagnostic laparoscopy. The main outcome parameters studied were the pregnancy rate per patient and the presence of pelvic pathology with therapeutic implications. The results are presented in Table 4. The pregnancy rate per patient was 40–50% and the presence of pelvic pathology with therapeutic implications was high (48–56%) but both outcome variables were similar in both groups studied (Table 4). Indeed, the at random allocation of patients to one of both study groups did not change significantly the ongoing pregnancy rate per patient nor the presence of pelvic pathology which needed further treatment. The respective ORs were 1.2 (95% CI 0.7–2.3) for the ongoing pregnancy rate per patient and 1.4 (95% CI 0.5–3.6) for the presence of pelvic pathology with therapeutic implications. In the conclusion, the authors stress the need for further randomized studies to verify these conclusions since it was impossible to determine a possible beneficial effect of laparoscopic surgery on the cycle pregnancy rate or on the CPR since only the crude patient pregnancy rate was presented in their study. They calculated that at least 1000 patients should have been included to show a difference of 10% in the cumulative ongoing pregnancy rate (Tanahatoe *et al.*, 2005). They also mention the considerably high natural pregnancy rate in both groups (DLSF $n = 12$; IUIF $n = 16$) in this study.

Scientific evidence suggests that minimal and mild endometriosis, treated surgically before starting COH (COH and IUI may increase the cycle pregnancy rate and reduce the time to pregnancy) (Werbrouck *et al.*, 2006). Indeed, in a retrospective cohort study, D'Hooghe and co-workers (Werbrouck *et al.*, 2006) recently showed data suggesting that it is useful to treat minimal and mild endometriosis before starting COH and IUI. This study included 107 women treated during 259 cycles with COH and IUI, including patients with endometriosis ($n = 58$; 137 cycles) and unexplained infertility ($n = 49$; 122 cycles). All patients with endometriosis had minimal ($n = 41$; 100 cycles) or mild ($n = 17$; 37 cycles) disease that had been laparoscopically removed within 7 months before the onset of treatment with COH and IUI. COH was done by using clomiphene citrate (23 cycles) or gonadotrophins (236 cycles) in combination with IUI. The main outcome measures were the clinical pregnancy rate per cycle and the cumulative live birth rate after four cycles of IUI treatment. COH and IUI shortly after the complete laparoscopic treatment of minimal and mild endometriosis proved to be as effective as COH and IUI in patients with unexplained infertility with respective clinical pregnancy rates per cycle of 21 and 19% in minimal and mild endometriosis and 20% in unexplained infertility. The cumulative live birth rate after four cycles was also similar in patients with minimal endometriosis (70%), mild endometriosis (68%) and unexplained infertility (66%). The authors conclude that surgical treatment prior to IUI restores the clinical pregnancy rate after COH and IUI in women with minimal–mild endometriosis to the same level as that in women with unexplained infertility. This is in contrast with previous studies where the cycle pregnancy rate and CPR seemed to be lower in patients with surgically untreated minimal to mild endometriosis than those with unexplained infertility (Werbrouck *et al.*, 2006). Randomized trials are needed to verify this conclusion, which might have important implications

Table 4: Pregnancy rate per patient and presence of pelvic pathology in patients treated with either diagnostic laparoscopy first (DLSF) or IUI first (IUIF)

	DLSF *n*	IUIF *n*	OR (CI)
No abnormalities	33/64	10/23	
Treated pathology			1.4 (0.5–3.6)
Adhesiolysis	3/64	0/23	
Treatment of endometriosis	28/64	12/23	
Fimbriolysis	0/64	1/23	
Pregnancy rate/patient	34/77	38/77	1.2 (0.7–2.3)

Adapted from Tanahatoe *et al.* (2005).

Laparoscopy after failed IUI cycles

To the best of our knowledge, no studies are available on the additive value of laparoscopy after several failed cycles of COH and IUI. Referring to the above RCT by Tanahatoe and co-workers (2005), one may be expected to find significant pelvic pathology (endometriosis all stages, peritubal adhesions) in at least 50% of cases. Laparoscopic treatment enhances the chance of spontaneous conception. One may, by extrapolation, expect a higher pregnancy rate after laparoscopic treatment after several failed IUI cycles. In conclusion, the position of operative laparoscopy for endometriosis and peritubal adhesions prior to IUI treatment or after several failed IUI cycles seems a matter of debate. Further, randomized controlled studies are needed to define the position of laparoscopy in IUI.

Diagnostic laparoscopy and IVF

Without doubt, the progress in assisted reproductive technology (ART) has limited the field of reproductive surgery and some authors radically advocate immediate treatment with ART after a limited and non-invasive infertility work-up in all infertility patients (Speroff *et al.*, 1999). Two questions of clinical interest can be asked. First, is it always mandatory to complete the diagnostic infertility phase with a laparoscopy to diagnose and treat specific pelvic pathology?

Second, is it still indicated to do a laparoscopy after several failed ART treatment cycles?

Laparoscopy before IVF treatment

Although laparoscopy is still considered to be the gold standard in the diagnosis of tuboperitoneal infertility, alternative diagnostic methods, for example, HSG and CAT screening have proven their clinical value and cost-effectiveness for the diagnosis of tubal infertility in everyday clinical practice (Mol *et al.*, 2001). The value of diagnostic laparoscopy in case of abnormal HSG

findings has been highlighted above (Mol *et al.*, 1999; Perquin *et al.*, 2006). Using these diagnostic procedures and recommendations, it could be argued that diagnostic laparoscopy can be avoided in all cases where the available evidence indicates that IVF is the most appropriate and successful treatment.

However, there is a fair degree of consensus that selected adnexal pathology, such as hydrosalpinx and ovarian endometriotic cysts, still have to be treated by laparoscopic surgery prior to IVF.

With respect to hydrosalpinx, two RCTs have demonstrated increased implantation and pregnancy rates in IVF cycles after salpingectomy for ultrasonically visible hydrosalpinges (Dechaud *et al.*, 1998; Strandell *et al.*, 1999). Both these trials have been included in a recent Cochrane review (Johnson *et al.*, 2004). The Scandinavian trial (Strandell *et al.*, 1999) reports a delivery rate per started cycle of 27% in IVF patients undergoing salpingectomy prior to IVF treatment versus 17% in the control group without salpingectomy in the intention-to-treat analysis ($P = 0.13$; RR = 1.57; 95% CI 0.9–1.57, not significant). A further subgroup analysis showed a marked improvement of the delivery rate in patients with hydrosalpinx visible by ultrasound (40 versus 17%, $P = 0.038$; RR = 2.40; 95% CI 1.09–5.28, on treatment analysis). The highest improvement in delivery rate occurred in the patients with bilateral ultrasound demonstrable hydrosalpinx (55 versus 16%, $P = 0.019$; RR = 3.48; 95% CI 1.15–10.59, on treatment analysis). According to the meta-analysis (Johnson *et al.*, 2004), eight women would have to undergo salpingectomy prior to IVF to gain one additional live birth. The adverse effect of hydrosalpinx on ART success rates can be explained by several mechanisms: the direct toxic effect of tubal fluid on the embryos, the negative effect of tubal fluid on the endometrium by flushing out embryos, dilution of implantation factors and prevention of normal embryonic-endometrial apposition (Erel and Senturk, 2005). Some authors have warned against the indiscriminate and blind victimization of the Fallopian tube and have advocated selective salpingostomy in selected cases (Puttemans *et al.*, 1996). A RCT of reconstructive tubal surgery versus salpingectomy and IVF in women with hydrosalpinx is needed to define the position of both treatment strategies in everyday clinical practice, but can only be done in countries with a high prevalence of PID (Sabatini and Davis, 2005).

With respect to endometriosis, unfortunately there are no RCTs or meta-analyses available to answer the question of whether surgical treatment of moderate and severe endometriosis enhances the pregnancy rates after spontaneous conception or after IVF (Kennedy *et al.*, 2005). It is however generally accepted that in case of infertility, moderate and severe stage endometriosis should be treated by surgery. There seems to be a negative correlation between the stage of endometriosis and the spontaneous cumulative pregnancy rate after surgical removal of endometriosis based upon the evidence of three studies (Adamson *et al.*, 1993; Guzick et al., 1997; Osuga *et al.*, 2002), but statistical significance for this statement was only reached in one study (Osuga *et al.*, 2002). With respect to endometriosis and ART, the recent ESHRE guidelines state that IVF is appropriate treatment especially if tubal function is compromised, if there is also male factor infertility and if other treatments have failed (Kennedy *et al.*, 2005).

The IVF pregnancy rates are lower in patients with endometriosis than in those with tubal infertility according to a systematic review of 22 non-randomized studies by Barnhart and co-workers (2002). These authors conclude that there is an overall 54% reduction in pregnancy rate after IVF in patients with endometriosis and that the success is poorer with advancing severity of the disease according to the r-AFS classification system. In some large databases e.g. SART and HFEA, however, endometriosis does not seem to adversely affect the reported pregnancy rates (Templeton *et al.*, 1996). There are no available randomized trials that have tested the hypothesis that surgical treatment of endometriosis prior to IVF results in higher pregnancy rates when compared to expectant management of endometriosis.

Ovarian endometriotic cysts need extra attention in the context of ART since they can be disadvantageous for IVF treatment: they may interfere with COH, create difficulties in aspirating the ovarian follicles during oocyte retrieval, and be held responsible for producing detrimental substances that are toxic to maturing oocytes, thus impeding embryo cleavage and implantation. Laparoscopic surgery for advanced stage endometriosis can be technically very demanding, time-consuming and high risk with significant postoperative morbidity and long revalidation. The removal of ovarian endometriomas prior to COH may be associated with significant bleeding and destruction of normal adjacent ovarian tissue, thus diminishing the reproductive ovarian function. There are no randomized studies comparing the live birth rates after IVF treatment in women who were surgically treated for endometriotic cysts prior to IVF versus women who were not. In a retrospective case-controlled study, Garcia-Velasco *et al.* (2004) demonstrated that the removal of endometriotic cysts prior to IVF did not improve fertility outcome. Especially in the case of asymptomatic small endometriotic cysts (<3 cm), immediate proceeding to IVF may reduce the time to pregnancy, treatment costs and the possible detrimental effects of inappropriate surgery on the ovarian function. However, laparoscopic cystectomy of larger symptomatic endometriotic cysts (>4 cm) improves fertility and reduces recurrence of these cysts when compared to cyst drainage and coagulation (Beretta *et al.*, 1998; Chapron *et al.*, 2002; Vercellini *et al.*, 2003b).

Laparoscopic treatment of endometriosis after failed IVF treatment

Finally, is it worth doing laparoscopic surgery in patients with endometriosis after several failed IVF cycles? Although no randomized trials are available, a retrospective cohort study by Littman *et al.* (2005) deserves a closer look. In a series of 29 patients with several failed IVF cycles and endometriosis, a radical treatment of all endometriotic lesions was performed by one very experienced laparoscopic surgeon. After surgery, 22 pregnancies were obtained, including 15 spontaneous pregnancies and 7 pregnancies after repeated IVF treatment. The non-controlled retrospective evidence in this study stresses the importance of referring patients with severe endometriosis to a centre with the necessary expertise (Kennedy *et al.*, 2005), in which case even after several failed IVF cycles, radical and appropriate surgery may still be beneficial to their reproductive outcome. It is clear that further randomized controlled studies are needed to support this view on laparoscopic treatment of severe endometriosis after failed IVF cycles.

Conclusion

The routine use of diagnostic laparoscopy for the evaluation of all cases of female infertility is currently under debate.

Current evidence indicates that the surgical treatment of minimal or mild endometriosis increases the spontaneous pregnancy rate in infertile women. The position of operative laparoscopy for endometriosis and adhesions prior to IUI treatment or after failed IUI treatment is a matter of debate, and further prospective randomized studies are needed to test the hypothesis that this surgical approach can improve the pregnancy rates during IUI treatment. Randomized trials confirming the role of the surgical treatment of moderate and severe endometriosis in infertility are lacking, but its value has generally been accepted.

The position and timing of diagnostic laparoscopy in ovulation induction treatment is difficult to establish due to a lack of randomized controlled studies. Diagnostic laparoscopy is indicated in all cases of bilateral anomalies on HSG. Exclusion of bilateral anatomical tubal pathology by diagnostic laparoscopy could avoid IVF treatment in these cases. LOD in the treatment of the clompihene resistant PCOS patient is at least as effective as gonadotrophin treatment, and has a significantly lower risk of multiple pregnancy. There is however a lack of knowledge regarding the long-term outcome of this procedure on the reproductive function of the ovary. It is unknown if surgical treatment of minimal to mild endometriosis coexisting with PCOS can improve the success of ovulation induction.

In IVF treatment, laparoscopic salpingectomy of ultrasound visible hydrosalpinx is indicated because of the beneficial effect on IVF pregnancy rates. Small asymptomatic endometriotic cysts probably need no treatment prior to IVF according to non-randomized evidence.

Generally, there is a need for further RCTs defining the position and timing of diagnostic/operative laparoscopy in current fertility practice.

Acknowledgements

The authors acknowledge the help and critical remarks of the following colleagues: Drs De Bruyn, Van Boxelaer, Delattin, De Rop, Dufraimont, Lannoey, Caluwaerts, Werbrouck, Despierre (Department of Obstetrics and Gynaecology, Imeldahospitaal Bonheiden), Professor Gerris (Department of Obstetrics and Gynaecology, University Hospital Gent), The members of the Board of the VVOG (Vlaamse Vereniging Obstetrie en Gynaecologie) and Professor Mathieu (Department of Endocrinology, University Hospital Gasthuisberg, Leuven).

References

Adamson GD, Hurd SJ, Pasta DJ, Rodriguez BD. Laparoscopic endometriosis treatment: is it better? *Fertil Steril* 1993;**59**:35–44.

al Badawi IA, Fluker MR, Bebbington MW. Diagnostic laparoscopy in infertile women with normal hysterosalpingograms. *J Reprod Med* 1999;**44**:953–957.

Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. *Fertil Steril* 2002;**77**:1148–1155.

Bayram N, van Wely M, Kaaijk EM, Bossuyt PMM, van der Veen F. Using an electrocautery strategy or recombinant follicle stimulating hormone to induce ovulation in polycystic ovary syndrome: randomized controlled trial. *BMJ* 2004;**328**:192.

Beretta P, Franchi M, Ghezzi F, Busacca M, Zupi E, Bolis P. Randomized clinical trial of two laparoscopic treatments of endometriomas: cystectomy versus drainage and coagulation. *Fertil Steril* 1998;**70**:1176–1180.

Chapron C, Vercellini P, Barakat H, Vieira M, Dubuisson JB. Management of ovarian endometriomas. *Hum Reprod Update* 2002;**8**:6–7.

Chuang JT, Hewett WJ, Hreshchyshyn M. Death after hysterosalpingography in choriocarcinoma with pelvic abscess. Report of a patient. *Obstet Gynecol* 1971;**37**:543–545.

Collins A, Burrows EA, Willan AR. The prognosis for live birth among untreated infertile couples. *Fertil Steril* 1995;**64**:22–28.

Dechaud H, Daures JP, Arnal F, Humeau C, Hedon B. Does previous salpingectomy improve implantation and pregnancy rates in patients with severe tubal factor infertility who are undergoing in vitro fertilization? A pilot prospective randomized study. *Fertil Steril* 1998; **69**:1020–1025.

De Hondt A, Meuleman C, Tomassetti C, Peeraer K, D'Hooghe TM. Endometriosis and assisted reproduction: the role for reproductive surgery? *Curr Opin Obstet Gynecol* 2006;**18**:374–379.

Erel CT, Senturk LM. Is laparoscopy necessary before assisted reproductive technology? *Curr Opin Obstet Gynecol* 2005;**17**:243–248.

Farquhar C, Lilford RJ, Marjoribanks J, Vandekerckhove P. Laparoscopic drilling by diathermy or laser for ovulation induction in anovulatory polycystic ovary syndrome. *Cochrane Database Syst Rev* 2005;**3**:CD001122.

Fatum M, Laufer N, Simon A. Investigation of the infertile couple: should diagnostic laparoscopy be performed after normal hysterosalpingography in treating infertility suspected to be of unknown origin? *Hum Reprod* 2002;**17**:1–3.

Forman RG, Robinson JN, Mehta Z, Barlow DH. Patient history as a simple predictor of pelvic pathology in subfertile women. *Hum Reprod* 1993;**8**:53–55.

Garcia-Velasco JA, Mahutte NG, Corona J, Zuniga V, Giles J, Arici A, Pellicer A. Removal of endometriomas before in vitro fertilization does not improve fertility outcomes: a matched case-control study. *Fertil Steril* 2004;**81**:1194–1197.

Gjonnaess H. Polycystic ovarian syndrome treated by ovarian electrocautery through the laparoscope. *Fertil Steril* 1994;**41**:20–25.

Glatstein IZ, Harlow BL, Hornstein MD. Practice patterns among reproductive endocrinologists: the infertility evaluation. *Fertil Steril* 1997;**67**:443–451.

Guzick DS, Silliman NP, Adamson GD, Buttram VC, Canis M, Malinak LR, Schenken RS. Prediction of pregnancy in infertile women based on the American Society for Reproductive Medicine's revised classification of endometriosis. *Fertil Steril* 1997;**67**:822–829.

Hamilton J, Latarche E, Gillott C, Lower A, Grudzinskas JG. Intrauterine insemination results are not affected if Hysterosalpingo Contrast Sonography is used as the sole test of tubal patency. *Fertil Steril* 2003;**80**:165–171.

Härkki-Sirén P, Sjöberg J, Kurki T. Major complications of laparoscopy: a follow-up Finnish study. *Obstet Gynecol* 1999;**94**:94–98.

Houston DE, Noller KL, Melton LJ, Selwyn BJ, Hardy RJ. Incidence of pelvic endometriosis in Rochester, Minnesota, 1970–1979. *Epidemiol* 1987;**125**:959–969.

Hubacher D, Grimes D, Lara-Ricalde R, de la Jara J, Garcia-Luna A. The limited clinical usefulness of taking a history in the evaluation of women with tubal factor infertility. *Fertil Steril* 2004;**81**:6–10.

Insler V, Lunenfeld B. Polycystic ovarian disease, pp. 661–678. In: *Infertility, Male and Female*, 2nd edn. Edinburgh, New York: Churchill Livingstone, 1993.

Jacobson TZ, Barlow DH, Koninckx PR, Olive D, Farquhar C. Laparoscopic surgery for subfertility associated with endometriosis (cochrane review). In: *The Cochrane Library*, Issue 3. Chichester, UK: John Wiley & Sons LtdChichester, UK, 2004b.

Johnson NP, Mak W, Sowter MC. Surgical treatment for tubal disease in women due to undergo in vitro fertilization. *Cochrane Database Syst Rev* 2004;**3**:CD002125.

Kennedy S, Bergqvist A, Chapron C, D'Hooghe T, Dunselman G, Greb R, Hummelshoj L, Prentice A, Saridogan E. ESHRE guidelines for the diagnosis and treatment of endometriosis. *Hum Reprod* 2005;**20**:2698–2704.

Lazovic G, Milacic D, Terzic M, Spremovic S, Mitijasevic S. Medicaments or surgical therapy of PCOS. *Fertil Steril* 1998;**70**;S472.

Littman E, Giudice L, Lathi R, Berker B, Milki A, Nezhat C. Role of laparoscopic treatment of endometriosis in patients with failed in vitro fertilization cycles. *Fertil Steril* 2005;**84**;1574–1578.

Mahmood TA, Templeton A. Prevalence and genesis of endometriosis. *Hum Reprod* 1991;**6**:544–549.

Marcoux S, Maheux R, Bérubé S, The Canadian Collaborative Group on Endometriosis. Laparoscopic surgery in infertile women with minimal or mild endometriosis. *N Engl J Med* 1997;**337**:217–222.

Mol BWJ, Collins JA, Burrows EA, van der Veen F, Bossuyt PM. Comparison of hysterosalpingography and laparoscopy in predicting fertility outcome. *Hum Reprod* 1999;**14**:1237–1242.

Mol BWJ, Collins JA, van der Veen F, Bossuyt PMM. Cost-effectiveness of hysterosalpingography, laparoscopy and Chlamydia antibody testing in subfertile couples. *Fertil Steril* 2001;**75**:571–580.

Mol BWJ, Dijkman B, Wertheim P, Lijmer J, van der Veen F, Bossuyt PMM. The accuracy of serum chlamydial antibodies in the diagnosis of tubal pathology: a meta-analysis. *Fertil Steril* 1997a;**67**:1031–1037.

Mol BWJ, Swart P, Bossuyt PMM, van der Veen F. Is hysterosalpingography an important tool in predicting fertility outcome? *Fertil Steril* 1997b;**67**:663–669.

Ochoa Capelo F, Kumar A, Steinkampf MP, Azziz R. Laparoscopic evaluation following failure to achieve pregnancy after ovulation induction with clomiphene citrate. *Fertil Steril* 2003;**80**:1450–1453.

Ogata R, Nakamura G, Uchiumi Y, Yokoyama M. Therapeutic efficacy of hysterosalpingography (HSG) in a prospective, randomized, clinical study. *Jpn J Fertil Steril* 1993;**38**:91–94.

Osuga Y, Koga K, Tsutsumi O, Yano T, Maruyama M, Kugu K, Momoeda M, Taketani Y. Role of laparoscopy in the treatment of endometriosis-associated infertility. *Gynecol Obstet Invest* 2002;**53**(Suppl):33–39.

Parazzini F. Ablation of lesions or no treatment in minimal-mild endometriosis in infertile women: a randomized trial. Gruppo Italiano per lo Studio dell'Endometriosi. *Hum Reprod* 1999;**14**:1332–1334.

Perquin DAM, Dörr PJ, de Craen AJM, Helmerhorst FM. Routine use of hysterosalpingography prior to laparoscopy in the fertility workup: a multicentre randomized controlled trial. *Hum Reprod* 2006;**21**:1127–1231.

Practice Committee of ASRM. Interpretation of clinical trial results. *Fertil Steril* 2006;**86**(Suppl 5):S161–167.

Puttemans PJ, Brosens IA. Salpingectomy improves in-vitro fertilization outcome in patients with a hydrosalpinx: blind victimization of the fallopian tube? *Hum Reprod* 1996;**11**:2079–2081.

Rowe PJ, Comhaire FH, Hargreave TB, Mahmoud AMA. WHO manual for the standardized investigation of the infertile couple. Cambridge, UK: Cambridge University PressCambridge, UK, 1993.

Sabatini L, Davis C. The management of hydrosalpinges: tubal surgery or salpingectomy? *Curr Opin Obstet Gynecol* 2005;**17**:323–328.

Speroff L, Glass RH, Kase NG. Female infertility. In: Speroff L, Glass RH, Kase NG (eds). *Clinical Gynaecologic Endocrinology and Infertility*, 6th edn. Philadelphia, PA: Lippincott Williams & WilkinsPhiladelphia, PA, 1999.

Strandell A, Lindhard A, Waldenstrom U, Thorburn J, Janson PO, Hamberger L. Hydrosalpinx and IVF outcome: a prospective, randomized multicentre trial in Scandinavia on salpingectomy prior to IVF. *Hum Reprod* 1999;**14**:2762–2769.

Swart P, Mol BWJ, van der Veen F, van Beurden M, Redekop WK, Bossuyt PMM. The value of hysterosalpingography in the diagnosis of tubal pathology, a meta-analysis. *Fertil Steril* 1995;**64**:486–491.

Tanahatoe SJ, Hompes PGA, Lambalk CB. Accuracy of diagnostic laparoscopy in the infertility work-up before intrauterine insemination. *Fertil Steril* 2003;**79**:361–366.

Tanahatoe SJ, Lambalk CB, Hompes PGA. The role of laparoscopy in intrauterine insemination: a prospective randomized reallocation study. *Hum Reprod* 2005;**20**:3225–3230.

Templeton A, Morris JK, Parslow W. Factors that affect outcome of in-vitro fertilization treatment. *Lancet* 1996;**348**:1402–1406.

Tulandi T, Collins JA, Burrows E, Jarrell JF, McInnes RA, Wrixon W. Treatment-dependent and treatment-independent pregnancy among women with periadnexal adhesions. *Am J Obstet Gynecol* 1990;**162**:354–357.

Vegetti W, Ragni G, Baroni E, Testa G, Marsico S, Riccaboni A *et al*. Laparoscopic ovarian drilling versus low-dose pure FSH in anovulatory clomiphene-resistant patients with polycystic ovary syndrome: randomized prospective study. *Hum Reprod* 1998;**13**:S120.

Vercellini P, Chapron C, De Giorgi O, Consonni D, Frontino G, Crosignani PG. Coagulation or excision of ovarian endometriomas? *Am J Obstet Gynecol* 2003b;**188**:606–610.

Watson A, Vandekerckhove P, Lilford R, Vail A, Brosens I, Hughes E. A meta-analysis of the therapeutic role of oil soluble contrast media at hysterosalpingography: a surprising result? *Fertil Steril* 1994;**61**:470–477.

Werbrouck E, Spiessens C, Meuleman C, D'Hooghe T. No difference in cycle pregnancy rate and in cumulative live birth rate between women with surgically treated minimal to mild endometriosis and women with unexplained infertility after controlled ovarian hyperstimulation and intrauterine insemination (IUI). *Fertil Steril* 2006;**86**:566–571.

Submitted on February 13, 2007; resubmitted on April 14, 2007; accepted on April 25, 2007