ENDOMETRIOSIS AND INFERTILITY

by

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SUMMARY

Among 343 diagnostic laparotomies endometriosis was diagnosed in 73 cases. The diagnosis of endometriosis by laparoscopy was based on visualisation of haemorrhagic areas and was confirmed by laparotomy and by biopsy. Each case was managed individually depending upon the nature of endometrial involvement.

A definite correlation exists between infertility and endometriosis (Kistner, 1979). Persistent infertility is usually the presenting complaint of otherwise healthy, young, married women in whom the diagnosis of endometriosis is made during pelvic examination and subsequent evaluation (Ranney, 1980). The strong association with infertility is proved by 30 to 40 per cent of patients with endometriosis remaining infertile, almost twice the rate of the general population (Kistner, 1979).

The exact cause of infertility in patients with endometriosis is unknown. The oviducts are usually patent, but perisalpingeal and peri-oophoritic adhesions are frequently found with an adherent, retroverted uterus. If other pathologic conditions such as submucous myomas are excluded, it is believed that the most important factor responsible for infertility is an inadequacy of tubo-ovarian motility secondary to fibrosis and scarring. This results in imperfect ovum acceptance by the fimbriae (Kistner, 1979). Extensive destruction of ovarian tissue or replacement by endometrial cysts obviously can interfere with ovulation, while extensive periovarian adhesions can prevent the normal egress of the ovum. (Wharton, 1977). Despite these theories, there is a high incidence of infertility associated with minimal or mild endometriosis, i.e., endometriosis with no peritubal or periovarian adhesions or scarring and no anatomical distortion of pelvic organs (Acosta *et al* 1973, and Buttram 1979). Altered prostaglandin secretion, anovulation, luteal phase defect, luteinised unruptured follicle syndrome, hyperprolactinaemia (galactorrhoeaendometriosis syndrome), autoimmune phenomena, spontaneous abortions, and genetic predisposition are the theories advanced to explain the cause of infertility in mild endometriosis (Muse, and Wilson, 1982). Conversely, the presence of endometriosis does not preclude pregnancy, and many women with endometriosis have had several pregnancies (Kistner, 1979).

Currently endometriosis has been diagnosed more frequently. This is due to increased clinical awareness and better endoscopic diagnostic facilities (Cohen,

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1980). It is also probable that the disease is actually increasing in frequency (Wharton, 1977). The simplicity of laparoscopic visualisation of the internal genital organs, plus biopsy when feasible, has enabled the gynaecologist to make a definitive diagnosis of endometriosis much earlier in the progress of this disease. Endoscopic diagnosis also facilitates proper classification of endometriosis (Acosta *et al* 1973; and Kistner, 1977). It also has a prognostic value in the assessment of results of treatment (Buttram *et al* 1982).

Eventhough there is no consensus as to the optimal form of treatment for endometriosis, conservative surgery has been recommended as the primary treatment of endometriosis in infertile subjects (Buttram, 1979; and Malinak, 1980). Post-operative medical therapy with Danazol has been recommended in patients with severe endometriosis where complete surgical removal of implants is impossible (Wheeler and Malinak, 1981). Earlier, post-operative pseudopregnancy with progestins have been employed wherever all endometrial areas could not be removed (Kistner, 1979). Residual lesions, if diagnosed by repeat laparoscopy, were treated by cauterisation via laparoscopy (Buttram *et al* 1982). Preoperative use of danazol is believed to be beneficial to the patient because it facilitates surgical removal of disease and probably reduces the risk of postoperative adhesions (Buttram *et al* 1982, and Barbieri *et al* 1982).

Still greater controversy exists in the treatment of mild endometriosis. It is held that expectant line of management must be tried initially (Kistner, 1982, and Schenken and Malinak, 1982). Treatment with danazol has been recommended by Wheeler and Malinak (1981), Buttram *et al* (1982 and Barbieri *et al* (1982). While laparoscopic fulguration and release of adhesions have been advocated by European authors (Frangenheim, 1972 and Malinak (1980) prefer open surgical dissection than the endoscopic procedures. According to Cohen (1980) surgical laparoscopy is a very rewarding procedure in releasing the adhesions and resection of endometrioma in patients with moderate endometriosis; and after this minisurgery the patients may show more effective response to medical management.

After having reviewed the current concepts in 'endometriosis and infertility' the purpose in this communication is to narrate the experience with endometriosis in infertile women, gained over a period of 6 years. Certain aspects of endometriosis, particularly those releated to diagnosis and surgical management, have already been published in earlier communications (Rajan and Usha, 1980; Rajan and Joseph, 1982; Rajan *et al* 1982 and Rapan *et al* 1983).

Incidence

Beginning in May, 1977, and through January, 1983, in our infertility service, 343 women underwent diagnostic laparoscopy and or infertility laparotomy. Among these 343 subjects pelvic endometriosis was diagnosed in 73 patients. This gives an incidence of 21.28 per cent endometriosis among infertile women undergoing laparoscopy or laparotomy. Of the 73 subjects with endometriosis the condition was diagnosed at laparoscopy in 32 patients among the 181 infertile women undergoing diagnostic laparoscopy (17.67%). The laparoscpic diagnosis of endometriosis was based on the characteristic visual presentation of the

disease: Brownish, haemorrhagic, or purplish to black areas typically found at the uterosacral ligaments, cul-de-sac, utero-vesical fold and ovarian surface, quite frequently associated with ovarian adhesions but not involving the tubes. Ovarian cysts, with or without adhesions, containing chocolate material also evidenced endometriosis. Occassionally the diagnosis was confirmed by endoscopic biopsy.

Diagnosis

Diagnosis was suggested by the history, corroborated by the pelvic examination, suspected by abnormal tubal findings and 'pocheted spill' in HSG., and verified by laparoscopy or laparotomy and if necessary by biopsy. On pelvic examination, in 54 patients, the typical pelvic findings of tender nodularity in the cul-desac and uterosacrals (29 subjects), uterine fixity with unilateral or bilateral adnexal masses (14 subjects) or other types of fixed indurations were located. (Table I). Among the 49 patients with HSG findings, the typical abnormal dye distribution in the pelvic cavity with abnormal tubal shadow suggesting pelvic adhesions was diagnosed in 40 subjects. In 19 patients with unsuspected pelvic findings endometriosis was diagnosed at laparoscopy or laparotomy (Table I). Examination under anaesthesia done prior to laparoscopy, demonstrating retraction of upper posterior vagina and posterior lip of cervix, and cervical stenosis also evidenced endometriosis.

Sites of Endometrial Lesions (Table II)

Except for the involvement of appendix in one patient, endometriosis was chiefly involving the genital organs, the ovary being the organ most frquently involved. In 57 patients (78.08%) either one or both ovaries, independantly or forming adhesions with tubes, uterus or utero-sacral ligaments, were the seat of endometrial growth. Among the 57 patients with ovarian endometriosis, 29 had endometrial cysts with chocolate material, and except 4 all had periovarian and other pelvic adhesions. The remaining 27 patients had endometrial surface implants, either non-invasive or producing scarring and retraction.

Next to ovary the most commonly affected pelvic structures were the utero-sacral ligaments and the cul-de-sac. In

TABLE I
Diagnosis of Endometriosis

Pelvic findings at clinical examination	No.	Percentage
1. Nodularity of cu-de-sac	24	32.87
2. Unilateral adnexal mass	13	17.80
3. Fixity and uterine mass (some with fibroid)	8	10.96
4. Bleeding of uterosacral ligaments	5	6.86
5. Unilateral adnexal	3	4.11
6. Bilateral adnexal	1	1.37
Patients with clinical findings	54	73.97
Patients with no clinical finding but diagnosed at lapa-scopy	19	26.03
Patients having HSG evaluation	49	—
HSG findings indicating pelvic adhesions	40	81.63

TABLE II
Distribution of Endometriosis

Sites of endometrial lesion	No.	Percentage
Bilateral tubo-ovarian adhesions with involvement of uterus and cul-de-sac	27	36.99
Unilateral tubo-ovarian mass with involvement of uterus and cul-de-sac	5	6.86
Bilteral tubo-ovarian mass	3	4.11
One ovary	8	10.96
Both ovaries	8	10.96
Ovary and uterosacral adhesions	6	8.21
Uterosacral ligaments	6	8.21
Cul-de-sac and rectal wall	4	5.47
Surface of uterus	3	4.11
Surface of fallopian tube	3	4.11

addtion to the 6 patients with ovarian adhesions to the uterosacral ligaments, uterosacral involvement alone was found in 6 subjects and cul-de-sac with or without rectal wall involvement in 4 subjets. Endometrial growth of the posterior uterine surface without any other affections was located in 3 subjects. The fallopian tubes per se were rarely affected except secondarily when extensive ovarian endometriosis was present.

Classification of Endometriosis

We have employed the classification modified after that of Acosta *et al* (1973). *Mild endometriosis,* with small superficial brownish, purplish, or haemorrhagic popular lesions (not producing scarring or retraction or adhesions) of pelvic peritoneum, uterine ligaments, cul-de-sac, or surface of one or both ovaries, was diagnosed in 7 patients. *Moderate endometriosis* included lesions cited for mild endometriosis plus scarring and retraction, and minimal periovarian, peritubal or peritoneal adhesions; in this series 23 patients had moderate endometriosis. *Severe endometriosis*: was diagnosed in 43 patients having endometrioma of ovaries (5 cms or more) or moderate or severe adhesions of tubes, ovaries or peritoneal reflections, or adhesions to bowel or urinary tract (Table III).

TABLE III
Classification of Endometriosis

Classification	Particulars	No.	Percentage
Mild endometriosis	Surface lesions with no scarring, retraction or adhesions	7	9.59
Moderate endometriosis	Surface implants with scarring retraction and minimal tubo-ovarian adhesions	23	31.50
Severe endometriosis	Enlarged ovaries with endometrial cysts, moderate or severe pelvic adhesions	43	58.91

Treatment

We do not rigidly follow any particular treatment schedule, since it is felt that each case must be managed individually depending upon the nature of endometrial involvement. Conservative surgery as the primary treatment of endometriosis currently enjoys the greatest popularity and reamins the best therapeutic modality for patients desiring to enhance their fertility. It also benefits by offering treatment for co-existing disorders such as pelvic adhesions and uterine fibroids. Pregnancy rates are higher with primary surgical treatment and most conceptions following surgical therapy occur within the first 6 months after surgery (Acosta *et al* 1973).

We prefer to undertake lapartomy for all cases of severe endometriosis and most cases of moderate endometriosis. If laparotomy is performed following diagnostic laparoscopy, either both operations are completed under the same anaesthesia or laparotomy is planned for a later date. Conservative operation is routinely accomplished through a lower abdominal transverse incision (P fannensiel incision). Careful lysis of adhesions by sharp or sometimes blunt dissection is the initial step. Maintaining the opened peritoneal sites the path of ureter is followed to prevent any harm to the ureter at the time of resection of adherent ovarian tissue. Resection of most endometriosis implants in the peritoneal cavity comprises the next operative step. Large implants with active disease are sharply resected. Ovaries and tubes are released from adhesions. Endometrial cysts of the ovaries are enucleated and the capsule reformed by subcapsular stitches, taking care to avoid dissection deep in the hilus of the ovary. Surface implants on the ovary are resected and ovarian structure reformed. Wherever possible tubal patency is tested by transfundal chromotubation. Usually a pre-operative HSG will be available evidencing tubal function. When a significant disparity in degree of involvement exists between the ovaries and tubes, we elect to perform a unilateral salpingo-oophorectomy than to risk leaving a compromised ovary or tube. While we are quite aggressive in our approach to unilateral adnexal removal our approach to dense cul-de-sac adhesion is very conservative. When there are dense adhesions in the cul-de-sac involving the uterosacrals, posterior lower uterus and the anterior rectal wall we leave the diseased areas undisturbed lest we may produce more severe post-operative adhesions by attempting an extensive lysis. It is unsafe to dissect and of no benefit to the patient to attempt a dissection wherever a complete separation of adhesion and thorough reperitonisation is not possible. However, an earnest attempt is made to resect the implants on the uterosacrals, cul-de-sac, surface of uterus and other peritoneal reflections; adhesions are prevented either by careful reperitonisation or by placing peritoneal grafts. Occasionally peritoneal surface implants and ovarian surface implants have been fulgurated.

In general, no post-operative medical treatment is advised, and instead the patient is encouraged to attempt pregnancy at earliest. Pseudo-pregnancy with progestins (Proluton Depot 500 mg every week plus Premarin 1.30 mg for 10 days a month—for 3 months) or pseudo-menopause by danazol (400 to 800 mg per day for 3 to 6 months) were employed post-operatively, only to eradicate microscopic evidence of this disease that could have been overlooked or incompletely removed during major surgery. While it is well

conceived that conservative surgery should be the treatment of choice in severe endometriosis and it would be hard to believe that medical therapy would have any effect upon adhesions. Barbieri *et al* (1982) advise the use of danazol preoperatively to reduce the overall extent of the endometriosis and thereby probably reduce the extent of the surgery and postoperative adhesions. These authors prefer to avoid postoperative danazol therapy because majority of the conceptions occur within 6 months of surgery. However, Wheeler and Malinak (1981) have enough reasons to believe that postoperative danazol therapy in severe endometriosis substantially improves the pregnancy rate.

During diagnostic laparoscopy when mild endometriosis or moderate disease affecting the ovary are diagnosed, minisurgery through the laparoscope is preferred. Laparoscopic lysis of ovarian adhesion, aspiration of endometrial cysts and fulguration of endometrial implants are the routine procedures undertaken in our service. However, in situations where the implants cannot be coagulated properly for fear of intestinal, tubal or ureteric harm we have preferred medical treatment. However, many authors (Kistner, 1979, and Malinak, 1980) do not advocate surgical laparoscopy for endometriosis and suggest either medical treatment with danazol or major surgical correction. They argue that endoscopic surgery is incomplete, carries a risk of ureteric or bowel injury and proper peritonisation is not possible. Cohen (1980) has advised to combine surgical laparoscopy and danazol, so that adhesions could be lysed by laparoscopy and implants could be taken care of by danazol.

Since disorders of ovulation is a well recognised cause for infertility in patients with endometriosis we have employed wedge resection or ovulation induction with clomiphene citrate postoperatively in subjects with proved anovulation. Because hyperprolactinaemia is incriminated (Muse and Wilson, 1982) we treated one patient with marginal hyperprolatinaemia and galactorrhoea with bromocriptine after one year of conservative surgery. She had severe endometriosis for which surgery was performed in a different clinic (hence not included in this statistics). Since she failed to conceive after one year of surgery, HSG was performed to ensure tubal function. Since she was galactorrheic endocrine profile was obtained which suggested marginal hyperprolactinaemia. She conceived by the first cycle of bromocriptine treatment, (5 mg/day) and presently she is 4 months pregnant.

Results of Treatment

Fifteen pregnanices were recorded in 14 patients (excluding the hyperprolactinaemic subject) over this period of study. When the recently operated patients were not included, for 40 subjects operated 14 achieved a conception, a pregnancy rate of 35 per cent. Pregnancy wastage in the form of abortion was recorded in 3 patients, of whom one had a full term normal delivery after the abortion. Nine patients had full term live births either by caesarean section or vaginal delivery. Two subjects are currently pregnant, and one patient who reported pregnancy was lost to follow-up. (Table IV).

The pregnancy rate for mild endometriois (among total 40 subjects followed) was 20%, moderate 30.76% and severe 40.90%. Of the 14 subjects who had conceived, 6 had undergone unilateral adnexal removal, 5 had release of ovarian adhesions and or enucleation of endometrial cyst and none had tubal adhesions,

TABLE IV

Treatment of Endometriosis

Conservative surgery	No. of patients operated	No. of patients followed	No becoming pregnant	%
Conservative surgery	73	40	14	35.00
Mild endometriosis	7	5	1	20.00
Moderate endometriosis	23	13	4	30.76
Severe endometriosis	43	22	9	40.90

Full term live birth—9, abortions—3, currently preg.—2, lost to follow-up—1. (Total 15 pregnancies in 14 patients).

Unilateral adnexal removal: 6 pregnancies
Release of ovarian adhesions or enucleation of ovarian endometriosis: 5 preg.
Ovariolysis and salpingolysis: 2 pregnancies
Resection of uterosacral implants (no tubal or ovarian involvement: 1 preg.

2 had unilateral or bilateral ovariolysis and salpingolysis, and 1 had resection of uteriosacral endometriosis. In general, it was found that patients with minimal or no tubal adhesions and undergoing surgery for ovarian endometriosis and those undergoing unilateral adnexal removal of the relatively more damaged tube and ovary had better chances for conception.

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