

Management of Pelvic Pain Recurrence: A Quality of Life Issue in Endometriosis

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ABSTRACT

Objective: To outline the appropriate management of patients with endometriosis and pelvic pain recurrence using surgical management with and without hormonal assistance.

Data Sources: Sources include original articles and reviews on etiology and clinical presentation, current classification systems, and surgical techniques ranging from laparoscopic identification to radical resection of endometriosis. All technical sources were written from 1987 to the present.

Methods of Study Selection: Hormonal and surgical management reviews currently used are standard of care in the treatment of endometriosis. Twenty-eight review articles emphasizing clinical presentation, histologic correlation to subtypes of disease, and alleviation of pain and symptoms with surgical intervention were used to compile this management strategy.

Data Extraction and Synthesis: All methods reviewed and outlined constitute appropriate standard of care in the treatment of pelvic pain and endometriosis. In addition, articles addressing the reclassification of endometriosis and its subtypes were utilized.

Conclusions: The multiple presentations of endometriosis and the histologic correlation indicate subtypes of disease. While medical management may be beneficial to some patients with endometriosis, it is at best temporizing for those patients with recurrent pelvic pain. Although there is no cure for endometriosis, carefully selected and appropriate surgical management in the face of recurrent pelvic pain remains the mainstay of treatment.

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ENDOMETRIOSIS IS A COMMON CONDITION in women of reproductive age in which abnormal growths of endometrial tissue are present in locations other than the uterine cavity and should be suspected in any patient of reproductive age complaining of pain and infertility. Endometriosis is present in at least 1% of all women of reproductive age and is found in 20% of women operated on for pelvic pain. Clearly, not every woman who has pain has endometriosis; however, a great number of patients with endometriosis have pain. In

some patients, the recurrence of pelvic pain after expectant and hormonal management requires additional intervention. Often, the severity of pain does not correlate with the amount of disease; a patient's fear of worsened pain or recurrent disease after treatment may in fact increase pain levels. In this chapter, we review the current therapeutic modalities, including both hormonal and surgical, for the alleviation of recurrent pelvic pain in patients with endometriosis.

Spontaneous menstrual cyclicity predisposes women toward endometriosis and as regression occurs during prolonged amenorrhea, such as pregnancy and menopause, retrograde menstruation is viewed as a risk factor (1). Hereditary factors and possible immune system alterations are suggested as women with a first-degree relative with endometriosis have seven times the normal risk of developing the disease, and investigators have linked endometriosis to the presence of particular human lymphocyte antigens (2).

Key Words: pelvic pain; quality of life; endometriosis.

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The diagnosis of endometriosis is suggested from a patient's history. Most describe constant pelvic pain or a low sacral backache that subsides after menses begins. Dyspareunia is often present, particularly with deep penetration. Lesions within the urinary tract or bowel may result in bloody urine or stool in the perimenstrual period. Implantations on or near the external surfaces of the cervix, vagina, rectum, or urethra may cause pain, bleeding with defecation, urination, or intercourse at any time during the menstrual cycle, and a sensation of pelvic pressure may result if large masses are present.

Classically, pelvic examination reveals tender nodules in the posterior vaginal fornix and pain on uterine motion. The uterus may be fixed and retroverted due to cul-de-sac adhesions, and tender adnexal masses may be felt if endometriomas are present. Careful inspection may

reveal implants in healed wounds, especially in episiotomy and cesarean section incisions, in the vaginal fornix or on the cervix. Biopsy may be required to prove that the lesions are due to endometriosis.

The staging system most commonly used for documentation of the progression of endometriosis is the revised American Fertility Society (AFS) staging system shown in Figure 1 (3,4). The point system for the R-AFS is heavily weighted toward ovarian and peritoneal involvement and adhesions as indicators of more severe disease.

Different morphologic types of endometriotic lesions have been shown to have different biosynthetic capabilities and may have varying potential for pelvic pain (5). The "early" papular, atypical lesions exposed to peritoneal fluid might cause functional pain, whereas "older" pigmented, nodular lesions embedded in infiltrating scars



AMERICAN SOCIETY FOR REPRODUCTIVE MEDICINE
REVISED CLASSIFICATION OF ENDOMETRIOSIS

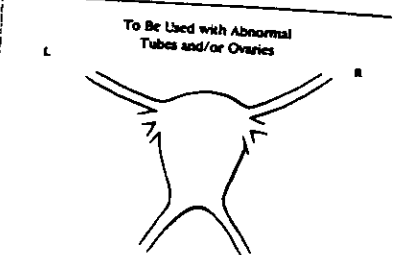
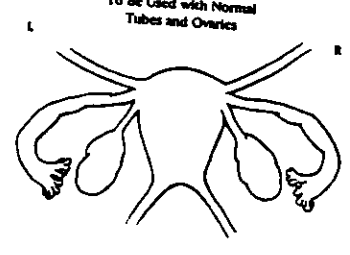
Patient's Name _____ Date _____
 Stage I (Minimal) - 1-5
 Stage II (Mild) - 6-15
 Stage III (Moderate) - 16-40
 Stage IV (Severe) - >40
 Total _____
 Laparoscopy _____ Laparotomy _____ Photography _____
 Recommended Treatment _____
 Prognosis _____

PERITONEUM	ENDOMETRIOSIS		
	< 1cm	1-3cm	> 3cm
Superficial	1	2	4
Deep	2	4	6
OVARY	R Superficial	1	2
	Deep	4	16
L Superficial	1	2	4
	Deep	4	16
POSTERIOR CULDESAC OBLITERATION		Partial 4	Complete 40
OVARY	ADHESIONS		
	R Filmy		
	< 1/3 Enclosure	1/3-2/3 Enclosure	> 2/3 Enclosure
	1	2	4
	Dense	4	8
	16	2	4
L Filmy	1	2	4
	Dense	4	8
R Filmy	1	2	4
	Dense	4	8
L Filmy	1	2	4
	Dense	4	8
TUBE	1	2	4
	Dense	4	8

Fig. 1. Revised American Fertility Society staging for endometriosis. (Reprinted with permission from the American Society for Reproductive Medicine, from the American Fertility Society: Revised American Fertility Society classification of endometriosis. Fertil Steril 1985; 43:351-352 [4].)

*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.
 Denote appearance of superficial implant types as red (R), red, red-pink, flame-like, vesicular blots, clear vesicles, white (W), opacifications, peritoneal defects, yellow-brown, or black (B) black, hemosiderin deposits, blue]. Denote percent of total described as R___%, W___%, and B___%. Total should equal 100%.

Additional Endometriosis: _____
 Associated Pathology: _____



might cause organic pain (6). In addition, although it is now known that peritoneal, ovarian, and retroperitoneal disease are three distinct endometriotic lesions, the current classification system does not incorporate retroperitoneal disease or varying morphologic types into the staging process (7).

Cornillie and associates reported that the cul-de-sac and uterosacral ligaments were frequent sites for deeply infiltrating lesions often associated with pelvic pain. Endometriosis infiltrates through loose connective tissue but stops at the junction of adipose tissue. Because the depth of subperitoneal connective tissue is more substantial in the posterior cul-de-sac and uterosacral ligaments, these areas tend to harbor deeper lesions. There is little retroperitoneal fat in the ovarian fossae, and deep infiltrating lesions are rarely found. Deeply infiltrating lesions (2 to 5 mm) were frequently associated with painful symptoms. Very deep (>10 mm) lesions were found exclusively in patients with pelvic pain. These deep lesions were also more likely to be histologically active and in phase with the endometrium (8). Koninckx found that the degree of pelvic pain was not related to total surface area of endometriosis (9). Ripps and Martin (10) studied the ability to correlate focal tenderness on pelvic examination with the presence of endometriotic lesions. In this study, the presence of focal tenderness was associated with endometriosis at that site in approximately 66% of patients. Of those patients with focal tenderness and endometriotic involvement, 96% of these lesions were fibrotic in nature. The average depth of infiltration was 5.4 mm for these types of lesions.

Koninckx and Martin further described deep endometriotic lesions and subdivided them into three groups. Type I lesions were cone-shaped, with the largest area lining the peritoneal cavity. These lesions were suspected to be formed by local infiltration. Type II lesions represented deeper lesions, which have been covered by dense adhesions. These lesions were believed to be probably formed by retraction. Type III lesions were the most severe and largest lesions and were represented by spherical nodules in the rectovaginal septum. These lesions had their largest area of involvement underneath the peritoneal surface. At laparoscopy, these latter lesions may appear only superficially as small, typical pigmented lesions. In some patients, these lesions can only be identified by digital palpation. Type III lesions were speculated to arise from either closed Allen-Masters defects or from müllerian rests. A poor correlation between the types of deep endometriotic lesions and the revised AFS classification was noted in this report. The most severe type III lesions were actually most frequently associated with patients who had been classified as stage I (39.1%) (11).

To address the limitations of the R-AFS classification with respect to pelvic pain, a panel of international

experts recently recommended a clinical instrument to be in the documentation of the extent of endometriosis and pelvic pain (Fig. 2) (12).

Methods

Expectant

In patients with minimal disease, expectant management is appropriate, with frequent examinations and institution of further therapy if progression of disease is noted. Long-term narcotic use is ineffective in patients with chronic pain. Pain relief from medication diminishes quickly, while euphoric effects may persist. Non-narcotic pain medication, such as nonsteroidal anti-inflammatory agents and prostaglandin synthetase-inhibiting drugs, are appropriate as single-agent therapy for endometriosis if the patient has mild premenstrual pain from minimal endometriosis, no abnormalities on pelvic exam, and no desire for immediate pregnancy, and should be used instead in a continuous fashion. Antidepressants, particularly the tricyclics, may enhance the effectiveness of this regimen. Use of antidepressants in doses lower than those typically prescribed for chronic depression may influence control transmission cells through serotonergic or endogenous opioid mechanisms. Taking medication before bedtime may often improve sleep.

Hormonal

Hormonal regulatory treatment aims to create constant high levels of gonadal steroids and to "burn out" the endometriotic lesions that, historically, were noted to regress during pregnancy. These regimens involve constant daily administration of either estrogen, progestin, or combination oral contraceptives. This regimen relieves pelvic pain in most patients, but the resultant pregnancy rates of 20–40% are less than ideal. Depression and significant breakthrough bleeding are found with these treatments; therefore, patients are often unhappy with the results. Currently, this regimen is best reserved for patients with milder disease who do not require immediate fertility and are unable to take other treatments.

Progestational agents are administered in various forms, but oral administration is preferable because of the rapid reversibility of its effects. The most commonly used medication is medroxyprogesterone acetate (MPA) in a dosage of 10 mg two to three times daily for 3 to 6 months. Side effects depend on the specific progestin used and the duration and route of administration. The most common side effect, irregular bleeding, occurs in up to 50% of patients. Other side effects include nausea, breast tenderness, fluid retention, and depression. These side effects are normally well tolerated, and few patients discontinue treatment secondary to undesirable effects (13).

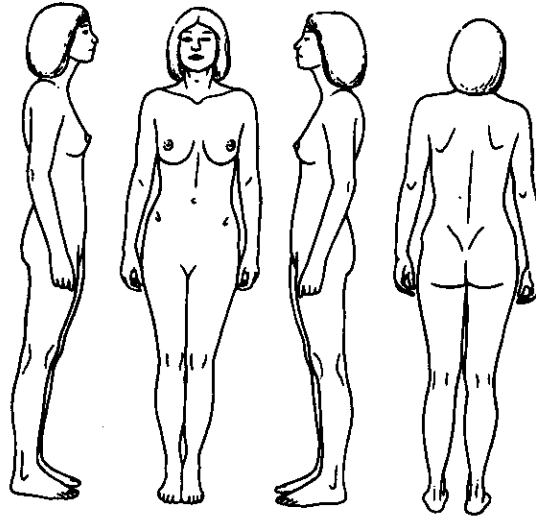
A

**THE AMERICAN FERTILITY SOCIETY
MANAGEMENT OF ENDOMETRIOSIS IN THE PRESENCE OF PELVIC PAIN**
A Clinical Instrument to Document the Extent of Endometriosis and Pelvic Pain*

Patient's Name _____ Age _____ Date _____
PRE-OPERATIVE ASSESSMENT OF PELVIC PAIN

Complaints _____

Describe the patient's symptoms of pain quality and position, and any limitation caused by these symptoms. Abbreviate quality of pain as A = mild, B = discomforting, C = distressing, D = horrible, E = excruciating. On the anatomic drawings below, draw a SOLID LINE around the area(s) of pain described by the patient, and mark the most intense area(s) with an X.



Physical findings _____

Identify the quality and site of tenderness caused by palpation, extent of nodularity, diffuse or focal distribution, and/or fixation of uterus/adnexa. On the anatomic drawings above, draw a BROKEN LINE around the area(s) of tenderness found on examination.
Adjuda: IVP? BE? Sigmoidoscopy? Other? _____

* The association of pelvic pain and endometriosis remains enigmatic because the extent of disease by the previous AFS classifications does not dependably relate to the severity of pelvic pain or tenderness. This form was designed by the AFS Committee on Classification of Endometriosis to carefully document the location and intensity of pelvic pain and tenderness in addition to distribution of endometriosis and pelvic adhesions. Constant recording of this data will permit consistent management of the patient with endometriosis and pelvic pain, and facilitate clinical research.

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Progestins are suspected to have a direct effect on endometrial implants. One controlled human trial showed that high-dose MPA for 6 months resulted in a complete resolution of implants in 50% of patients and partial resolution in 13%. Placebo effects were 12% and 6%, respectively (14).

Danazol is a weak androgen that is the isoxazole derivative of 17 α -ethinyl testosterone (ethisterone) and acts at the hypothalamic level to prevent the rise in gonadotropins that would normally occur when estrogen and progesterone levels are low without affecting basal gonadotropin concentrations. Danazol binds to androgen receptors, stimulating them and thus inhibiting implant growth. In addition, danazol binds strongly to sex hormone-binding globulin and corticosteroid-binding globulin, thus displacing native testosterone and allowing it to

act against the implants as well. Danazol inhibits the steroidogenic enzymes in the ovary that synthesize estrogen. Together, these actions decrease estrogen receptor stimulation within the lesions and inhibit implant growth.

The dose of danazol is 800 mg/d in divided dosages for 6 months. Side effects of danazol include acne, oily skin, deepening of the voice, weight gain, edema, and adverse lipoprotein changes. Danazol is an effective contraceptive at doses of 800 mg/d, thus alleviating the concern of virilization of a female fetus (15).

Gonadotropin-releasing hormone (GnRH) agonists are the newest medical approach to the treatment of endometriosis. These medications have specific amino acid substitutions of the native GnRH peptide, resulting in compounds with longer half-lives and greater receptor binding affinity (Table 1). The net result is downreg-

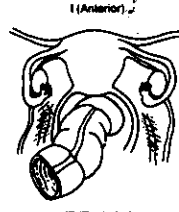
B

Procedure _____

OPERATIVE DESCRIPTION OF PELVIC ADHESIONS
 Describe the location, points of attachment and characteristics of adhesions. Abbreviate characteristics as A = avascular/thin, T = thick/dense, B = band/string-like, S = sheet-like. Draw a picture of these adhesions at the appropriate location in each quadrant.

I (Anterior) IIa (Right lateral)

IIa (Left lateral) IIb (Right lateral)

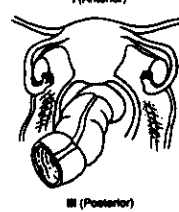


IV (Other sites) III (Posterior)

OPERATIVE APPEARANCE OF THE DISTRIBUTION OF ENDOMETRIOSIS
 After mobilizing the pelvic viscera, measure the size (mean diameter in millimeters) and depth of each visible lesion. Use a calibrated endoscopic probe, if necessary. Record the location, dimension, visual appearance and histologic confirmation of these lesions. Abbreviate the visual appearance as C = clear, V = vesicles/blisters, P = pink, R = red/fusco-blue, B = black/blue, Y = yellow/brown, W = white, F = peritoneal fibrinosa. Document the site of each lesion by positioning the index number (No. on the table below) at the appropriate location in each quadrant.

I (Anterior) IIa (Right lateral)

IIa (Left lateral) IIb (Right lateral)



IVa (Other intra-abdominal sites) III (Posterior)

IVb (Outside peritoneal cavity)

No.	Size in mm	Depth	Appearance	Histology	Location	No.	Size in mm	Depth	Appearance	Histology	Location
i.e.	8 m	2 mm	F	Glands & stroma	II						
1						11					
2						12					
3						13					
4						14					
5						15					
6						16					
7						17					
8						18					
9						19					
10						20					

Histology _____

Results _____

Fig. 2. Pain instrument to document pelvic pain and endometriosis. (Reprinted with permission from the American Society for Reproductive Medicine, from the American Fertility Society, Management of endometriosis in the presence of pelvic pain. *Fertil Steril* 1993;60: 952-955 [12].)



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ulation of pituitary GnRH receptors and resultant "medical oophorectomy" from the hypogonadotropic state.

Three agonists—goserelin, nafarelin acetate, and leuprolide acetate—are approved for treatment of pelvic pain associated with endometriosis in the United States. Nafarelin is administered as a nasal spray in a dosage of 200 or 400 mg twice daily. Leuprolide acetate is usually administered in a depot form in a dose of 3.75 mg monthly. Goserelin is administered as a subcutaneous injection of 3.6 mg monthly. Six months of therapy is the standard regimen for all compounds. Numerous side effects are associated with GnRH agonist treatments, mainly transvaginal bleeding, hot flashes, vaginal dryness, decreased libido, breast tenderness, insomnia, depression, irritability and fatigue, headache, joint stiffness, and

skin changes. Hypoestrogenic side effects such as hot flashes are more common with GnRH agonists than with danazol. Two significant concerns are the effect of GnRH agonists on lipoprotein levels and bone loss. Studies indicate that GnRH agonists do not have the same adverse effect on lipoproteins as danazol or progestins. A 6% loss of trabecular bone density, however, has been shown after 6 months of GnRH agonist use. There does not appear to be any significant decrease in cortical bone density. Most studies indicate that the trabecular bone density decrease is reversible after discontinuation of therapy (13).

Several GnRH agonists have been shown to be effective in inducing atrophy of the ectopic endometriotic tissue and stroma. Reductions in the AFS classification score have been reported with the use of GnRH agonist therapy. The

Table 1. GnRH Agonists

Name	Structure	Route
Leuprolide (Lupron)	pGlu-His-Trp-Ser-Tyr-DLeu-Leu-Arg-Pro-NHEt	Subcutaneous (SC), depot, 2 months rod implant
Buserelin (Superfact)	pGlu-His-Trp-Ser-Tyr-DSer(O ^t Bu)-Leu-Arg-Pro-NHEt	SC, nasal, depot, 3 months depot
Nafarelin (Synarel)	pGlu-His-Trp-Ser-Tyr-D2Nal-Leu-Arg-Pro-GlyNH ₂	SC, nasal
Goserelin (Zoladex)	pGlu-His-Trp-Ser-Tyr-DSer(O ^t Bu)-Leu-Arg-Pro-AzaglyNH ₂	SC, depot
Histrelin (Supprelin)	pGlu-His-Trp-Ser-Tyr-DHis(Bzl)-Leu-Arg-Pro-AzaglyNH ₂	SC
Decapeptyl	pGlu-His-Trp-Ser-Tyr-DTrp-Leu-Arg-Pro-GlyNH ₂	SC, depot

(Reprinted with permission from Lunenfeld B, Haviv F, Insler V. Gonadotropin-releasing hormone analogs in perspective: A promise fulfilled, in Adashi E, Rock JA, Rosenwacks Z (eds.): Reproductive Endocrinology, Surgery and Technology. Philadelphia, PA, Lipincott-Raven, 1996, 1651.)

degree of regression and relief of pain is similar to that caused by danazol, but implants rendered inactive by GnRH agonists are later capable of growth (16). In addition, the time to recurrence of endometriosis-associated pain after treatment was slightly longer for those treated with danazol than after GnRH-agonist treatment (17).

Miller et al. (17) examined the recurrence of pain after medical treatment in 327 patients given either danazol or leuprolide. These patients had their pain assessed at pre-treatment, post-treatment, and first menstruation post-treatment and the time of treatment-requiring pain recurrence was recorded. The median time until pain recurred was 6.1 months for danazol-treated patients versus 5.2 months for those given leuprolide. Those patients who received add-back therapy in addition to leuprolide had a 2.6-month interval before recurrence. Not surprisingly, the time to recurrence differed with the stage of endometriosis as well. Those with stage I or II treated with danazol had a recurrence at 6.0 months, and those with stage III or IV at 6.3 months. Those treated with leuprolide in stage I or II had a pain recurrence at 5.3 months compared to those with stage III or IV, with recurrence at 5.9 months. Those patients experiencing dysmenorrhea with the first menstruation post-treatment had a shorter interval to recurrence between both treatment groups. No significant findings could be observed among four GnRH agonists (leuprolide, goserelin, buserelin, and nafarelin), although variations in time to recurrences were noted.

Surgical Management

Endometriosis is diagnosed by visualizing lesions at the time of operation or after finding the characteristic histologic appearance in resected or biopsied tissue. The gross appearance of endometriosis at operation is quite characteristic and, to an experienced surgeon, is sufficient for diagnosis. The smallest and earliest implants are red, petechial lesions on the peritoneal surface. With further growth, menstrual-like debris accumulates within the

lesion, giving it a cystic, dark brown, dark blue, or black appearance. The surrounding peritoneal surface becomes thickened and scarred. These "powder burn" implants typically attain a size of 5 to 10 mm in diameter. With progression of disease, the number and size of lesions increase and extensive adhesions may develop. Ovarian cysts may enlarge to several centimeters in size, called "endometriomas" or "chocolate cysts." Severe disease can erode into underlying tissues and distort the remaining organs with extensive adhesions. Surgery is useful not only for diagnosis, but is an ideal therapeutic means to remove endometriosis and restore normal pelvic anatomy as well.

Laparoscopic Therapy

Operative laparoscopy gives immediate diagnosis, and therapy should begin at the time of laparoscopy. Initiation of treatment during laparoscopy optimizes patient recovery and medical resources and decreases the patient's overall expense.

Laparoscopy is optimally performed during the follicular phase of the menstrual cycle, because tissues are less hyperemic and recognition of endometriotic lesions is easier. Additionally, during the luteal phase, there is risk of damage to the corpus luteum, which may bleed, and there is decreased risk of operating during an unrecognized pregnancy and interrupting it. While short-term suppression of ovarian function by agents like danazol or GnRH agonists is acceptable, long-term use of agents that suppress ovarian steroidogenesis agonists should be avoided before surgery, because they make endometriotic lesions much more difficult to identify and staging will be inaccurate (18).

Treatment of endometriotic implants through the laparoscope can be accomplished through a variety of techniques. Small implants may be electrosurgically ablated with unipolar or bipolar cautery. Bipolar cautery is usually safer. With this method, the implant is picked up between the two paddles, and current is applied. Tissue

necrosis is much more controlled, but implants deeper than 1 to 2 mm are difficult to remove. Unipolar cautery may be more beneficial in deeper lesions because of deeper penetration, but this carries a greater risk of damaging adjacent structures such as the ureter, bladder, bowel, or vessels by causing a greater area of thermal destruction.

Carbon dioxide (CO₂) laser ablation is a method of endometriosis ablation that allows great precision in removal of disease, with minimal bleeding and minimal damage to surrounding tissue. One of the most appealing features of the CO₂ laser is that the energy does not penetrate much beyond the surface of the tissue being removed. Thermal damage is usually limited to 0.2 mm beyond visible damage. Therefore, ablation by the CO₂ laser may be safer because of greater accuracy. The zone of thermal necrosis for CO₂ laser vaporization is minimal, especially when in superpulse mode. For implant ablation, the standard CO₂ laser laparoscope utilizes a focal point approximately 2 cm from the end of the delivery port. Depending on the area to be coagulated or vaporized, spot sizes vary from 0.5 to 2.5 mm. In the continuous firing mode, power densities of 2,500 to 5,000 W/cm² are used. Lesions that are close to vital structures may be ablated using single-pulse or superpulse modes of 0.05 to 0.1 second in order to limit the extent of tissue vaporization (19).

Endometrial implants should be vaporized completely, with copious irrigation to remove carbon debris and to expose the base of the lesion. Repeated vaporization may be necessary to eradicate the implant completely. Argon, potassium-titanyl-phosphate (KTP) and neodymium:yttrium-aluminum-garnet (Nd:YAG) fiber lasers are also used for ablating endometriosis.

Laparoscopic treatment of endometriomas can be performed safely and effectively at laparoscopy but should be reserved for endometriomas less than 5 cm. Initially, the ovary should be mobilized, with lysis of adhesions. It is important to note that a small-appearing lesion may represent the superficial portion of a much larger endometrioma. First, the cyst is punctured, aspirated, opened, and lavaged. The cyst lining is examined to confirm the diagnosis of endometrioma; the lining will be smooth and without papillary excrescences. If the cyst is confirmed as an endometrioma, the wall can be ablated with electrocauterization or laser vaporization. Second, the wall can be removed by grasping the cyst lining and stripping it from the ovary in a corkscrew manner. Any portions of the cyst wall remaining can then be ablated. The defect is closed with laparoscopic suturing or may be left to heal with secondary intention.

Recently, Danielle (20) reported laparoscopic enterolysis for chronic abdominal pain. Among 42 patients, 28 (67%) were improved with extensive lysis of adhesions through the laparoscope. Of special significance is the

observation of Kligman et al. (21), who used immunohistochemical techniques to show nerve fibers in pelvic adhesions. The authors showed that fibers were present in specimens in 10 of 17 patients. It has also been shown that endometriosis-related adhesions contain more inflammatory cells and tissue edema than postsurgical or postinfectious adhesions (22). Interestingly for both studies, although the authors were able to show the presence of nerve fibers in pelvic adhesions, their presence was not more prevalent among patients with pelvic pain. The findings support the concept that the formation of adhesions has different stages, the final formation of mature connective tissue with its own vascularization and innervation.

Conservative Surgery at Laparotomy

Laparotomy is required for any patient with persistent pain after a trial of expectant management, medical management, or laparoscopic treatment and when severe disease has invaded the bowels, ureters, or other surrounding structures. It is also necessary when the extent of disease exceeds the operative skill of the surgeon or the availability of laparoscopic instrumentation.

Conservative surgery is best accomplished with the use of a microsurgical technique. The pelvis is copiously irrigated throughout the operation to maintain moist tissues. Ringer's lactate, with 5,000 IU heparin and 1 g hydrocortisone added to each liter, is recommended. Adhesions are removed without damage to underlying tissues and sent for pathologic documentation of endometriosis. If hemostasis cannot be maintained by bipolar cautery, a bioabsorbable suture should be used.

Palpation is often necessary for deeper lesions, and these should be excised rather than ablated to avoid surrounding healthy tissue damage and to enable complete resection. Deep nodules of endometriosis are not uncommon; in one study, 25% of patients with clinical disease had lesions that penetrated deeper than 5 mm. The pouch of Douglas and the uterosacral ligaments are two areas that need careful inspection and palpation for deeper implants of endometriosis (8,10).

Ovarian Endometriosis. Removal of ovarian endometriosis during laparotomy is similar to that used during laparoscopy. First, careful inspection of the ovary is performed in order to identify all endometriotic lesions. Next, ovarian adhesiolysis is performed. Filmy adhesions of the ovary can be lifted and excised without cutting into the ovary. It is curious to note that 40–50% of subovarian adhesions contain endometriosis (23). If the ovary is adherent to the ovarian fossae, great care should be used in the dissection so as to avoid damage to the ureter. Superficial lesions of the ovary can be ablated with bipolar or laser electrocautery with copious irriga-

tion. If an endometrioma is observed, removal of the capsule should be complete. Ideally, the cyst wall is removed without rupture. It is also useful to place lint-free lap packs around the ovary with the endometrioma to contain any spillage that may occur. Once the endometrioma is removed, bipolar cautery is used to achieve hemostasis prior to ovarian reconstruction. Laparotomy has the advantage of palpation to detect smaller deep lesions that may be undetected laparoscopically. Previously, if disease appeared unilateral, the diseased adnexa was removed. Now, with assisted reproductive technology, surgery has become much more conservative, and oocyte retrieval from small ovarian remnants has been successful.

Retroperitoneal Endometriosis. Retroperitoneal endometriosis usually causes severe pain, dysmenorrhea, and dyspareunia in patients. A typical examination will reveal tender nodules in the cul-de-sac, uterosacral ligaments, rectosigmoid junction, and rectovaginal septum. Often, the uterus is retroverted and fixed posteriorly. The histologic origin of this type of endometriosis arises from coelomic metaplasia, not from retrotubal flow (24). Hormonal management is not effective in the treatment of pain from this type of endometriosis, and complete surgical resection is necessary.

Extensive retroperitoneal disease often is not easily accessible by the laparoscope. Removal of disease requires retroperitoneal dissection, which may be facilitated by placing a bougie in the rectum, sponge forceps in the vagina, and a Foley catheter in the bladder. The pararectal and paravaginal spaces may be exposed by applying traction in the appropriate direction. Once the ureters and the rectum are dissected free of retroperitoneal fibrosis, the uterosacral ligaments are removed by sharp dissection or bovie electrocautery; care should be taken to reperitonealize after the ligaments and fibrosis are resected to decrease postoperative adhesion formation.

Endometriosis of the Bowel. Endometriosis of the bowel is rare, but it occurs in up to 25% of women with endometriosis (25). Location of disease (rectosigmoid, large bowel, small bowel, or appendix) will determine the type of surgery necessary. Endometriosis of the gastrointestinal tract commonly involves segments that are close in proximity to the uterus, fallopian tubes, and ovaries. One study showed the resulting distribution: 72.4% sigmoid, rectosigmoid, or rectal cases; 13.5% rectovaginal septum; 7% small bowel; 3.6% cecum; 3% appendix.

Before a treatment modality is chosen, the patient's symptoms must be evaluated. These symptoms include rectal pain (74%), dyspareunia (46%), constipation (49%), and rectal bleeding (31%) (26). Complete intestinal obstruction is rare but mandates a laparotomy and

resection when it occurs (27). If clinical symptoms are present before surgery, it is prudent to assess the bowel for evidence of involvement. A barium enema is most useful and will reveal a smooth (nonmalignant) crater if disease involves the mucosa. Endovaginal ultrasonography has been helpful in diagnosing disease of the anterior rectal wall (28). Colonoscopy with biopsies will confirm endometriosis if there is mucosal involvement and will help plan the appropriate procedure (29).

Any patient with suspected bowel involvement should have a complete mechanical and antibiotic bowel preparation before surgery. At laparotomy, superficial lesions of the bowel may be excised, fulgurated, or laser vaporized. Lesions that are deeper are best treated with segmental bowel resection. If childbearing is complete, a total abdominal hysterectomy with bilateral salpingo-oophorectomy should be considered. Alternatively, ovarian preservation may be possible if the lesion can be resected completely.

It is still unclear whether to perform an appendectomy in patients who are undergoing bowel resection for endometriosis. In a 1988 study, of 926 patients who underwent laparotomy with bowel resection for endometriosis, 126 patients (13.6%) underwent incidental appendectomy. Only two patients were shown to have microscopic involvement. It is felt that unless involvement of the appendix is evident, appendectomy is optional (30).

Endometriosis of the Urinary Tract. Urinary tract endometriosis is rare, affecting only 1.2% of women with endometriosis. Diagnosis begins with clinical suspicion; symptoms include frequency, dysuria, and hematuria. Cystoscopy is most useful for diagnosing vesicle endometriosis. Radiographic studies are useful to determine any ureteral involvement. An intravenous pyelogram is probably indicated for all patients undergoing surgery for extensive endometriosis.

Treatment of urinary tract endometriosis should begin with medical management with danazol or a GnRH agonist, but close surveillance of renal function is necessary (31). Endometriosis of the bladder may be ablated during surgery if it is superficial. More extensive disease may need partial cystectomy. Endometriosis of the ureter requires ureterolysis or resection of the involved segment with accompanying ureteroneocystostomy or uretero-ureterostomy. Nephrostomy urinary diversion is considered when severe hydronephrosis is present and ureterolysis is not possible (32).

Extrapelvic Endometriosis. Extrapelvic endometriosis is rare but can cause significant disease. Diagnosis needs biopsy confirmation. If complete excision is not possible, hormonal suppression may be necessary. Table 2 represents a staging system for extrapelvic endometriosis (33).

Table 2. Staging System for Extrapelvic Endometriosis

Classification	
Class I:	Endometriosis involving the intestinal tract
Class U:	Endometriosis involving the urinary tract
Class L:	Endometriosis involving the lung and thoracic cage
Class O:	Endometriosis involving other sites outside the abdominal cavity
Staging of extrapelvic endometriosis	
Stage I No organ defect	
1.	Extrinsic: surface of organ (serosa, pleura)
a.	<1-cm lesion
b.	1- to 4-cm lesion
c.	>4-cm lesion
2.	Intrinsic: mucosal, muscle, parenchyma
a.	<1-cm lesion
b.	1- to 4-cm lesion
c.	>4-cm lesion
Stage II Organ defect*	
1.	Extrinsic: surface of organ (serosa, pleura)
a.	<1-cm lesion
b.	1- to 4-cm lesion
c.	>4-cm lesion
2.	Intrinsic: mucosal, muscle, parenchyma
a.	<1-cm lesion
b.	1- to 4-cm lesion
c.	>4-cm lesion

*Organ defect includes but is not limited to obstruction and partial obstruction of the urinary tract and the intestinal tract and hemothorax, hemoptysis, and pneumothorax.
 (Reprinted with permission from W.B. Saunders from Markham SM, Carpenter SE, Rock JA. Extrapelvic endometriosis. *Obstet Gynecol Clin North Am* 1989;16:193-219 [33].)

Adjunctive Procedures

Laparoscopic Uterosacral Nerve Ablation

Laparoscopic uterosacral nerve ablation (LUNA) interrupts the uterosacral ligament at the insertion into the cervix and destroys a large amount of sensory nerve fibers that innervate the cervix and lower uterine segment. LUNA can be accomplished with laser or electrocoagulation, but this procedure is controversial because the uterosacral ligament is rarely completely incised. Exposure of the uterosacral ligament is, of course, the key. This is achieved by flexing the uterus forward by a uterine manipulator. The ureters should be fully identified before ablation to prevent damage. The area of the posterior cervix between the uterosacral insertion points may also be ablated superficially to destroy fibers that cross to innervate contralateral sides. Once the segment has been coagulated, laparoscopic scissors are used to transect the ligament. The efficacy of the LUNA procedure has yet to be confirmed and is difficult to study because, although the uterosacral ligament is transected, endometriosis may recur deep in the ligament.

Presacral Neurectomy

The sensory pathways from pelvic viscera involve the lumbar and lower thoracic sympathetic ganglia, as well as

the superior, middle, and hypogastric plexus. Pain impulses from the cervix, uterine corpus, and proximal portions of the fallopian tubes are transmitted through afferent fibers that accompany the sympathetic nerves into the spinal cord at T10, T12, and L1. These afferent sensory fibers course through the uterosacral ligaments and the posteriolateral portions of the pelvis to mesh together in the midline as the presacral nerve before turning cephalad to enter into the spinal cord at the lower thoracic and upper lumbar nerve roots. It is the ovarian plexus, however, that receives afferent sensory fibers from the ovary, broad ligament, and distal fallopian tube. This plexus follows the blood supply, trailing up the ovarian artery to blend with the meshwork of nerves arising from the aortic and renal plexus.

Presacral neurectomy is an adjunctive procedure at laparotomy for treatment of central dysmenorrhea owing to endometriosis. Patient selection is important for effectiveness of the procedure. One study showed that patients with midline pain had excellent results after presacral neurectomy, but patients with adnexal pain symptoms had a quite variable relief of pain (34). Interestingly, Chen and Soong (35) have reported laparoscopic presacral neurectomy as an effective alternative for patients wishing to avoid laparotomy.

The immediate but rare complications of presacral neurectomy include damage to ureter and blood vessels, but the risk is greatly diminished with proper surgical technique. Side effects include constipation, vaginal dryness and bladder dysfunction. As a rule, these symptoms will resolve over several months.

Postoperative Adhesion Prevention

The mainstays for preventing postoperative adhesion formation are meticulous hemostasis, minimal tissue trauma, proper suture selection, and peritoneal irrigation, which avoid tissue trauma, anoxia, and ischemia. Some adhesions will always form, however, and can undo the reconstructive work performed after resection of endometriosis and cause pain.

Multiple agents have been used intraperitoneally and intravenously after resection of endometriosis to prevent adhesions, including dextran, nonsteroidal anti-inflammatory agents, corticosteroids, promethazine, and heparin. Briefly, three mechanical barrier agents will be discussed here: modified hyaluronic acid with carboxymethylcellulose (Seprafilm; Genzyme, Cambridge, MA), oxidized regenerated cellulose (Interceed; Johnson & Johnson Medical, Arlington, TX), and expanded polytetrafluoroethylene (PTFE) (Gore-Tex; W.L. Gore & Associates, Phoenix, AZ). These products may be placed between the ovary and the pelvic sidewall to prevent adhesion formation.

Oxidized regenerated cellulose designed in a knitted weave is known as TC-7. It is applied to a hemostatic peritoneal surface and will form a continuous gel covering within approximately 8 hours. This forms a mechanical barrier to prevent opposing raw surfaces from adhering to each other and is resorbed in 3 to 4 days (36).

PTFE (Gore-Tex) has been evaluated on the development of post-surgical adhesions in patients who served as their own controls and was found to have greatly decreased adhesions and was superior to oxidized regenerated cellulose. One disadvantage of this surgical membrane is that it is nonabsorbable and requires a second-look laparoscopy for removal (37).

Several major academic centers have been involved in the study of a chemically modified hyaluronic acid and carboxymethylcellulose (Seprafilm). It has been found safe and effective in human trials but did not completely eliminate adhesions in all patients. Efficacy relies on the area in question to be fully covered. Randomized myomectomy patients were assessed recently, and Seprafilm significantly reduced the incidence, severity, extent, and area of postoperative uterine adhesions at second-look laparoscopy (38).

Uterine Suspension

Uterine suspension has been proposed as a method to reduce adhesion formation, especially over the posterior uterus or in the cul-de-sac. Also, there is a theoretical

decreased risk for tubes and ovaries to adhere to sites of resection when they are elevated. This procedure may also benefit those patients with a retroflexed or retroverted uterus. The authors recommend a modified method of Gilliam suspension in which the round ligament is shortened by pulling it through the internal ring and suturing it to the rectus sheath.

Semiconservative and Radical Surgery

Some cases are refractory to conservative management, and when childbearing is no longer an issue, the last resort is to proceed with total abdominal hysterectomy with or without bilateral salpingo-oophorectomy. The surgical premise is to remove all visible endometriosis, or complete cytoreduction.

Radical surgery requires careful counseling of the patient and significant preoperative preparation by the surgeon. Initial evaluation involves pelvic imaging studies to rule out the presence of other entities with similar clinical presentations. A large endometrioma may present as a pelvic mass consistent with an ovarian malignancy. In these situations, the mass should be treated as a malignancy until proven otherwise. Pelvic washings are obtained for opening cytology. An intravenous pyelogram may be helpful if prior surgery or pelvic adhesions are suspected to have modified the course of the ureters and also to rule out the presence of a duplicated collecting system. Bowel preparation is necessary in cases in which any bowel involvement is suspected. Bowel preparation will allow for primary repair rather than the need for colostomy placement.

Once the decision has been made to proceed with hysterectomy, the patient and the surgeon must decide between semiconservative surgery (preservation of the ovaries) and radical surgery (removing all ovarian tissue). This decision involves consideration of the patient's age, severity of disease, and prior surgical history. Namnoum et al. (39) showed that women with endometriosis who underwent hysterectomy with ovarian conservation had a 6.1 times greater risk of developing recurrent pain and 8.1 times greater risk of reoperation.

Although bilateral oophorectomy has the advantage of decreasing the risk of recurrent symptoms of endometriosis, there are several significant side effects, including severe menopausal symptoms and future risk of cardiovascular disease and osteoporosis. Whereas estrogen replacement should address these risks, there is a high level of patient noncompliance with long-term users, and the patient requires careful and extensive counseling before surgery.

Most investigators support starting estrogen replacement therapy immediately after surgery for endometriosis. Hickman et al. (40) showed that there was no greater risk for pain recurrence in patients who started estrogen replacement therapy immediately as opposed to those

who waited 6 months. Successful use of estrogen add-back therapy with GnRH agonists in the medical management of endometriosis also supports the contention that the amount of estrogen in replacement therapy is not enough to stimulate endometriosis.

Discussion

Endometriosis remains a challenging disease after years of study toward medical and surgical management. Its elusive nature supports subtypes of disease that are yet unclassified and encompass infertility and pain. Surgery, combined with adjunctive measures such as presacral neurectomy, has been effective in those patients with recurrent painful symptoms from endometriosis when medical management has failed. There are current efforts under way to reclassify the disease and its various presentations along with its relationship to the severity of pain. Also necessary are further animal models to simulate the various presentations of disease. Although we have been able to slow the disease process with hormonal suppression and ablate and resect visible lesions, absolute curative treatment is not yet available.

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