

## Recurrent Endometriosis

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Endometriosis is the common name of a disease with a wide clinical spectrum. The mild form of superficial peritoneal implants is so common, and often asymptomatic, that it may not actually represent disease but a normal variation in pelvic anatomy. The more severe forms of endometriosis are unquestionably pathologic, distorting anatomy with fibrosis and adhesions and usually causing pain and perhaps infertility. To borrow an infectious disease model, mild endometriosis behaves like microbial colonization, living symbiotically with the host tissues, whereas severe endometriosis is akin to infection with its destruction of normal tissue structure and function. Unfortunately, the natural history of endometriosis is yet to be clearly understood, and clinicians cannot yet predict which women will have the mild forms of endometriosis and which will have the destructive forms. Until the natural history of endometriosis is better defined, clinicians must rely on their observations in the treatment of this disease.

### INCIDENCE

One aspect of the natural history of endometriosis is clear: both medical and surgical treatments are associated with all too frequent cases of recurrent disease. Danazol is the drug with the most information available regarding recurrence: following danazol treatment, 5% to 15% of patients per year develop symptomatic recurrence. After 3 years, 40% of women treated with Danazol alone had recurrent endometriosis.<sup>1</sup> Little long-term information as to recurrence following treatment with gonadotropin-releasing hormone (GnRH) agonists is yet available, but one would expect similar recurrence rates as other drugs with similar modes of action.<sup>2</sup>

For several years, we have reported the incidence of recurrence following conservative surgery for endometriosis.<sup>1-3</sup> Of 423 women treated for endometriosis by conservative laparotomy, 20% of women followed for 3 years had recurrent endometriosis diagnosed by repeat surgery (Fig 11-1). One obvious difficulty with the current methods of diagnosing recurrent endometriosis is the reliance on reoperation: only those women with persistent infertility or recurrent symptoms will likely accept the risks and discomforts of repeat operation. Therefore, the incidence of re-

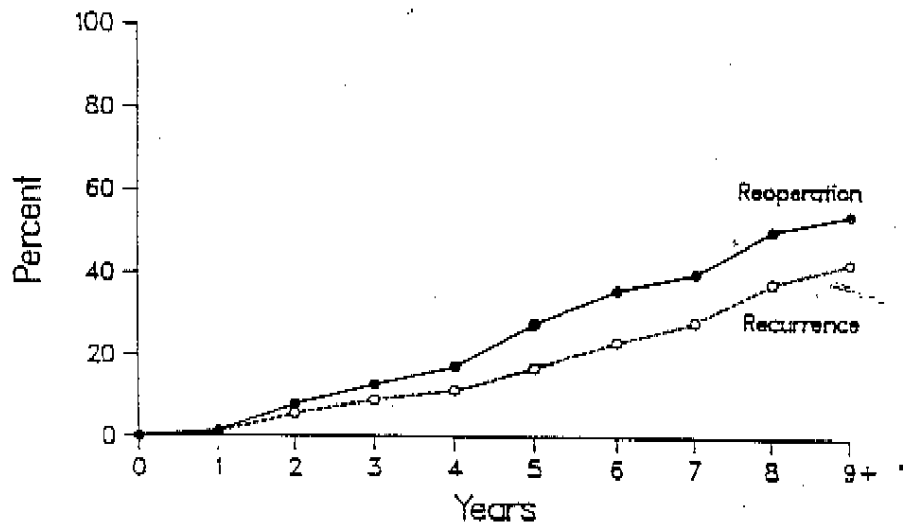


FIG 11-1.

Cumulative rates of reoperation and recurrent endometriosis in 423 infertile women treated by conservative laparotomy. (From Olive D, in Schenken RB [ed]: *Endometriosis. Contemporary Concepts in Clinical Management*. Philadelphia, JB Lippincott Co, 1989, p 235. Used by permission.)

currence after surgery may indeed be higher than that reported from clinical case series. Until noninvasive techniques allow us to diagnose recurrence without resorting to surgery, we will never accurately estimate the incidence of recurrent endometriosis.<sup>6</sup>

### "Recurrence" Versus "Persistence" Following Surgical Treatment

One of the inherent problems with estimating the incidence of recurrent endometriosis after surgery is distinguishing recurrence, the growth of new lesions, from persistence, the growth of lesions inadequately treated at initial surgery. We have previously reported the use of a schematic representation of the pelvis, which allowed recurrent lesions to be distinguished from persistent endometriosis lesions.<sup>7</sup> At short-interval second-look laparoscopy, one half of the patients with implants had persistent disease (i.e., lesions at a site of dissection at primary surgery). Only by adopting this sort of accurate record keeping (Fig 11-2) will we be able to map out the course of endometriosis following surgical treatment.

### MORPHOLOGY OF ENDOMETRIOSIS IMPLANTS

The many visual appearances of endometriosis presents another problem for surgical treatment and estimating recurrence. In addition to the classic blue or blue-black blebs, endometriosis was histologically confirmed in lesions that were flat, red to pink, subperitoneal, or even clear and vesicular.<sup>8</sup> As described by Stripling and colleagues<sup>7</sup> and then Batt and Smith,<sup>9</sup> peritoneal pockets as those depicted in Figure 11-3 may often contain endometriosis implants; these pockets may be everted and excised either laparoscopically or at laparotomy. The surgeon must be alert to the many visual appearances of endometriosis at the time of surgery; aware-

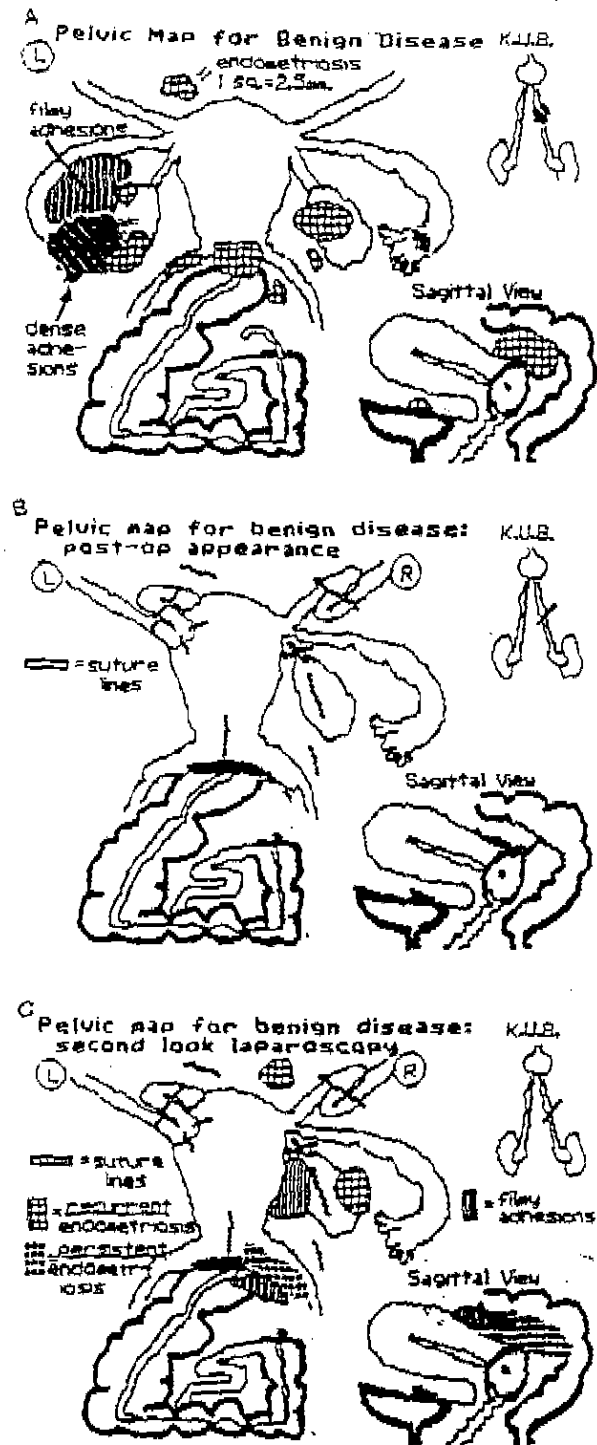


FIG 11-2.

Pelvic mapping to distinguish recurrent from persistent endometriosis after conservative laparotomy. **A**, extent and size (each square = 0.25 cm) of endometriosis and adhesions found at laparotomy. **B**, postoperative appearance of the pelvis, including suture lines. **C**, appearance at second-look laparoscopy 4 weeks after laparotomy. Recurrent lesions are de novo implants, whereas persistent lesions are at sites of previous dissection and represent incomplete excision.



FIG 11-3. Posterior cul-de-sac peritoneal pocket under left uterosacral ligament; excision demonstrated endometriosis foci. (From Batt RE, Smith RA: *Obstet Gynecol Clin North Am* 1989; 16:15-28. Used by permission.)

ness combined with magnification will likely improve the completeness of removing subtle forms of the disease. Unfortunately, microscopic endometriosis cannot be identified by the surgeon's eye: 20% of biopsy specimens of grossly normal peritoneum were found to harbor endometriosis using electron microscopy.<sup>10</sup> Again, our failure to understand the natural history of endometriosis prevents us from determining whether "microscopic endometriosis," whether defined by light or electron microscopic criteria, is at all clinically relevant to the treatment of women with endometriosis.<sup>11</sup>

The problem of persistent microscopic endometriosis prompted several investigators to study combination medical and surgical therapy.<sup>12</sup> The concept inspiring combination therapy was adapted from the treatment of epithelial tumors of the ovary: initial surgery should be debulking, removing as much disease as possible, with postoperative chemotherapy used to treat residual implants. In women with moderate and severe endometriosis, 3 to 6 months of postoperative Danazol produced lower long-term recurrence rates than those patients treated by surgery alone.<sup>13</sup> This study still needs to be confirmed with the experience of other authors

and, preferably, a longitudinal prospective comparative trial. Until then, many clinicians use adjunctive postoperative medical treatment in more severe cases of endometriosis.

### WHY DOES RECURRENCE OCCUR AFTER "COMPLETE" OPERATIONS?

The most obvious answer to this question is the multifocal nature of endometriosis and the likely possibility of missing a lesion or two during surgery. More than 20 years ago, Rogers and Jacobs at our institution emphasized the importance of en bloc dissection of juxtaposed endometriosis implants.<sup>14</sup> As shown in Figure 11-4, the many implants in the posterior cul de sac were considered a "field," and the entire field was completely removed. In those days, 2-0 chromic sutures were used to close the peritoneum. Many of us have wondered if those days of sharp dissection of multiple implants were associated with lower recurrence rates. One could safely assume that complete removal of the involved peritoneum, including the entire depth of the lesions, would certainly not increase the risk of recurrence.

Because the depth of infiltration of endometriosis implants is so variable, more superficial treatments might well fail to treat deeper depths of disease. Martin and co-workers found that one fourth of patients had lesions that penetrated the peritoneum greater than 5 mm.<sup>15</sup> Because one pass of the CO<sub>2</sub> laser will vaporize tissue to a depth of 0.1 to 0.5 mm, even several passes of the laser could leave disease behind. Endometriosis has been histologically confirmed immediately juxtaposed to carbon particles from previous laser surgery, suggesting incomplete treatment.<sup>16</sup> Whenever possible, fields of endometriosis should be excised, whether the surgeon is using knife, scissors, or laser, to incise peritoneum. Figure 11-5 depicts this principle using laser as the instrument for peritoneal incision; note the peritoneum is removed completely to the depth of retroperitoneal fat. Whether surgery is performed by laparoscopy or laparotomy, the ureter must be clearly identified throughout the case to avoid injury.

### REPEAT CONSERVATIVE SURGERY

When persistent infertility or recurrent somatic symptoms warrant evaluation for recurrent endometriosis, laparoscopy is performed. The pelvis is systematically inspected for implants of endometriosis; care must be taken not to confuse suture materials previously used for uterine suspension, presacral neurectomy, or peritoneal closure with implants of endometriosis. Many cases can be performed laparoscopically, adapting the same microsurgical principles used during laparotomy. Tissues are manipulated bluntly to provide traction and countertraction for lysis of adhesions. If grasping instruments are used, the adnexa are manipulated only by the utero-ovarian ligament; the tube and ovarian cortex are not grasped. Adhesions are excised rather than incised; all visible endometriosis is excised or completely vaporized. Ample irrigation and meticulous hemostasis complete the laparoscopic procedure. In most cases, 100 mL of dextran 70 (Hyskon) is instilled as an attempt to inhibit adhesion formation.

If the disease is not amenable to laparoscopic treatment, the patient is prepared

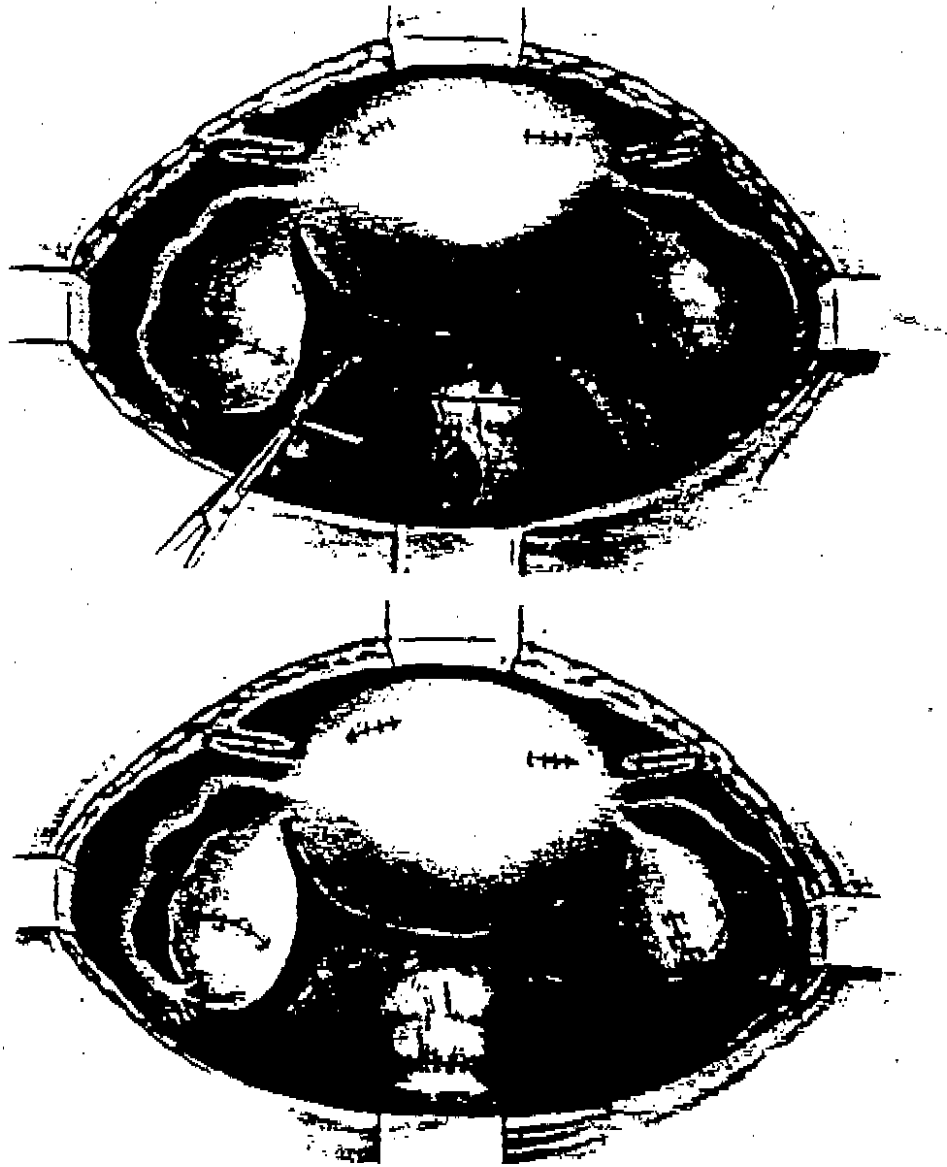


FIG 11-4.

Management of posterior cul-de-sac with numerous endometriosis implants after closure of ovarian and uterine lesions. The entire field is excised en bloc and the peritoneum closed with continuous absorbable suture. (From Rogers SF, Jacobs WM: *Fertil Steril* 1968; 19:529-536. Used by permission.)

for repeat laparotomy. The previous scar is usually excised in elliptiform fashion, wedging the subcutaneous fat down to the anterior rectus fascia. Care is taken on incising the peritoneum because omentum or bowel may adhere to the previous anterior abdominal wall incision. Once moistened laparotomy sponges are placed around the wound edges and self-retaining retractor is positioned, the procedure is performed very much like primary conservative surgery for endometriosis.<sup>17</sup> However, repeat presacral neurectomy is usually not attempted due to difficulty in dissection and bleeding caused by retroperitoneal scarring.<sup>18</sup> Magnification in the form

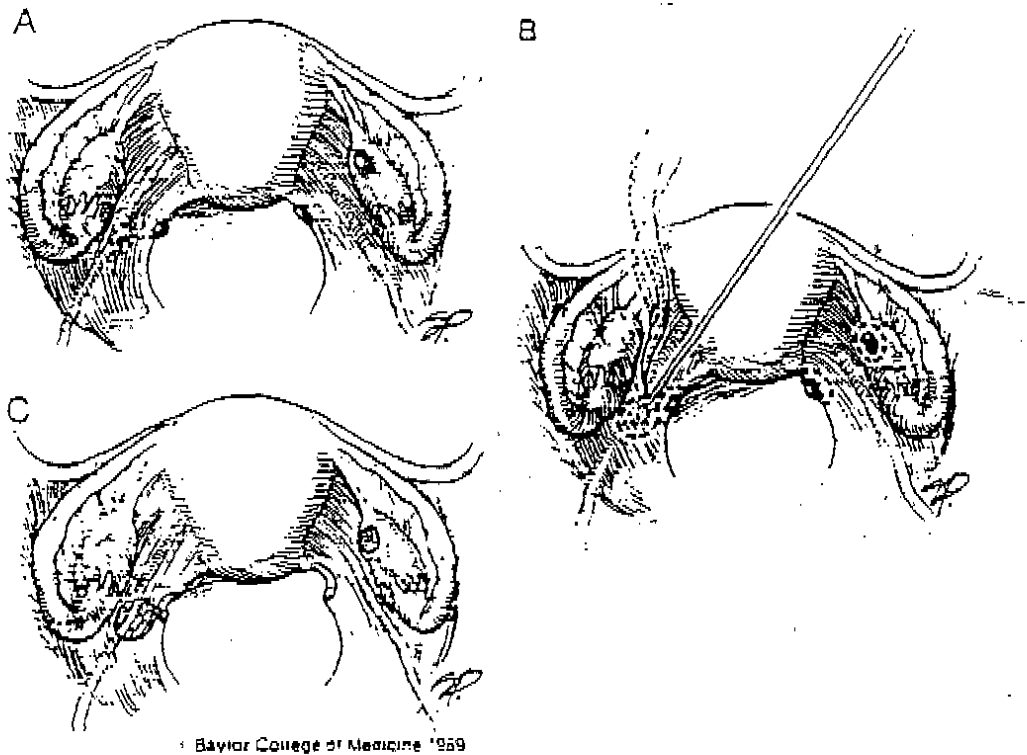


FIG 11-5.

Management of diffuse endometriosis lesions with laser. **A**, group of lesions, removed with 2- to 4-mm margins of normal tissue, through the full thickness of the peritoneum. **B**, lesions are circumscribed with CO<sub>2</sub> laser highly focused with 10 to 20 W of power, preferably with superpulse mode. Once the lesion is circumscribed, the edge is lifted, and the laser is passed to and fro under the peritoneum to separate it from underlying adventitia and fat. Carbonization is minimized. **C**, retroperitoneal fat as it appears after excision of the lesion; the same effect is possible with sharp dissection. The position of the ureter must be known to the surgeon operating via laparoscopy or laparotomy. (Copyright © Baylor College of Medicine.)

of 2.5 or 4 × loupes, or microscope, is useful in removing as much disease as possible. Tissues are handled minimally and kept continually moistened with a solution of warmed lactated Ringer's with 20 mg of dexamethasone and 5,000 units of heparin/L. The procedure is anatomically orchestrated to effect complete removal of disease. Special attention is paid to the gastrointestinal (GI) tract, including the appendix, which may have been previously incompletely treated.<sup>19</sup>

Once all areas of endometriosis and adhesions are excised, there are several options in the management of the peritoneal defects. If the peritoneum can be reapproximated with 4-0 or 5-0 absorbable suture without tension, primary closure is our usual first choice. Peritoneal defects may be left open if underlying tissue is vital and clean. Free peritoneal grafts have been useful in some of our cases with large, raw areas; these areas have been remarkably free of adhesions at short-interval, second-look laparoscopy. Free omental grafts have been abandoned, whereas fashioning a large omental carpet may be used on huge peritoneal defects. Also, new barriers such as Interceed (TC7) will help prevent adhesions of deperitonealized areas.<sup>20</sup> If Interceed is not available, many surgeons use 100 to 200 mL of intraperitoneal dextran 70 following conservative laparotomy for endometriosis.

The role of second-look laparoscopy 2 to 12 weeks after conservative laparotomy is useful in lysing new adhesions but has unknown effect on recurrence of endometriosis.

## "COMPLETE" OPERATIONS

All treatises on surgical management of endometriosis include a section on so-called complete, or definitively curative, operations.<sup>17</sup> Unfortunately, endometriosis may recur following hysterectomy and oophorectomy if special care is not taken to completely remove all areas involved with disease.<sup>21</sup>

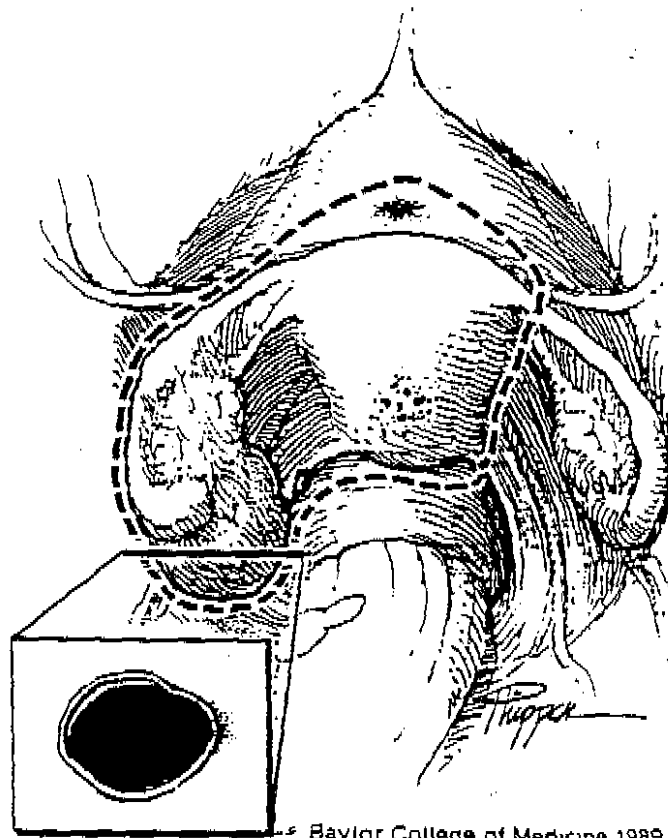
If a woman has completed her childbearing, and recurrent endometriosis is suspected of causing pelvic pain, laparoscopic examination may demonstrate only mild to moderate extent of disease. If the woman is otherwise a good candidate anatomically for vaginal hysterectomy, operative laparoscopic techniques may be used to vaporize or coagulate adhesions or endometriosis inaccessible to the vaginal surgeon. Certainly, vaginal hysterectomy should be undertaken only if the goal of complete removal of disease, including ovarian endometriosis, is attainable. Thus, most hysterectomies for endometriosis, especially more severe forms of the disease, are better treated by total abdominal hysterectomy.

Abdominal hysterectomy is usually performed via the previous incision, unless a separate indication warrants a midline incision. We maintain careful tissue handling at hysterectomy quite similar to that of conservative laparotomy; the only tissues clamped or grasped are those that will be ultimately removed. Remaining tissues are kept moist and not abraded with sponges. As depicted in Figure 11-6, an en bloc incision is made, and all contiguously involved peritoneal surfaces are removed. All lesions of endometriosis are removed with 2- to 4-mm circumferential margins and to the depth of retroperitoneal fat. In more cases than not, the ureter has to be identified high on the pelvic brim and dissected free of diseased peritoneum, especially if a severely diseased adnexa is being removed. If the posterior cul-de-sac is obliterated, the rectum must be dissected free, leaving as much disease on the uterus and as little residual on the colon as possible. If dissection is not possible, segmental resection and anastomosis of prepared bowel probably decrease the likelihood of future long-term recurrence of endometriosis. Dissection of the pararectal spaces in cases of endometriosis, leaving only healthy uninvolved tissues behind, is likely to lessen recurrence.<sup>22</sup> Following definition of these margins for hysterectomy, a standard *extrafascial* hysterectomy is performed.<sup>23</sup> If cervical or vaginal endometriosis is suspected from preoperative speculum examination, the involved portion of the posterior vagina is included with the hysterectomy specimen. Otherwise, the cervix is completely removed, and the vaginal length is maximized.

In the most severe cases of endometriosis, the margins for dissection between the uterus, rectum, and bladder can be obliterated by active disease and fibrosis. Intrafascial hysterectomy is appropriate in these circumstances to avoid ureteric injury if they cannot be dissected free of disease. If fibrosis prevents safe intrafascial hysterectomy, we will still occasionally perform supracerical hysterectomy in particularly severe cases.

Ovarian preservation at the time of hysterectomy for endometriosis is controversial. Each ovary should be removed if it is seriously involved with endometriosis





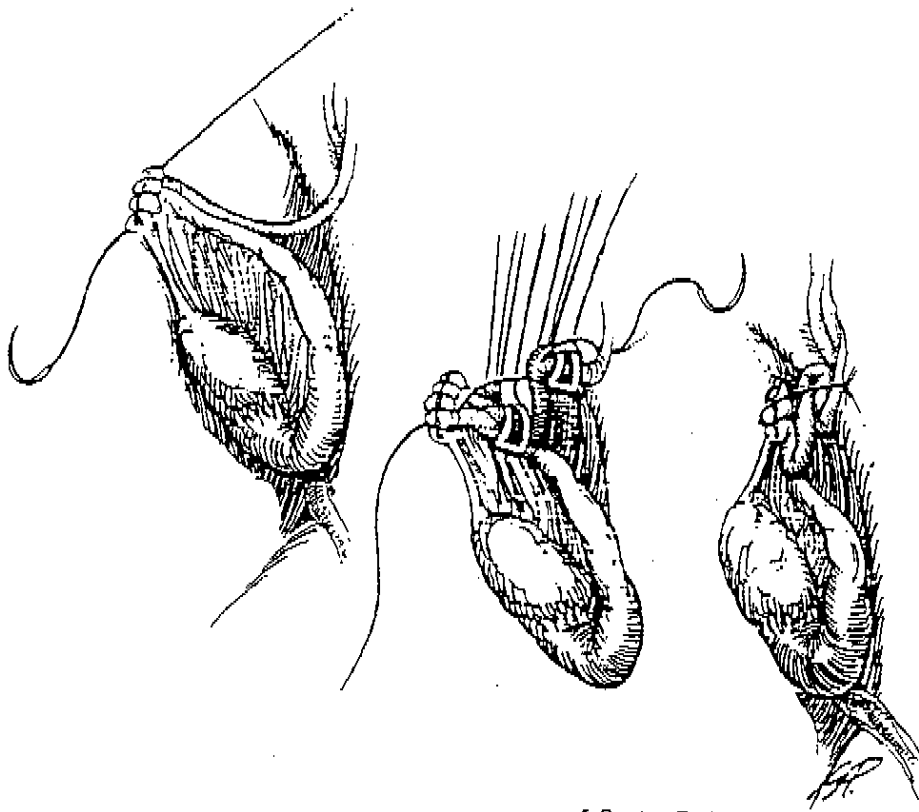
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FIG 11-6.

Hysterectomy for endometriosis. All endometriosis lesions are removed, preferably as an en bloc dissection (dashed line). Any residual implants are removed or destroyed with laser or cautery. The left ovary containing a large endometrioma (inset) is removed. The normal right ovary can be preserved if the patient has no symptoms referable to that adnexa. (Copyright © Baylor College of Medicine.)

or compromised by adhesions. An ovary with only a superficial implant or two may be preserved. Also, if the woman gives a history more of adnexal pain rather than the more classic central pain, removal of the ovaries is more likely to give complete pain relief. In our experience, if the ovaries are suitable for preservation at the time of hysterectomy and are suspended away from the vaginal cuff, the chances of subsequent need for reoperation is 5% or less. One technique of ovarian suspension after hysterectomy is depicted in Figure 11-7. The interrupted round and utero-ovarian ligaments are sutured to the high lateral abdominal wall, without kinking the infundibulopelvic ligament and without the ovaries resting on the vaginal cuff.

Following hysterectomy, all areas are carefully checked for hemostasis; the cuff can be safely closed if hemostasis is complete. The abdomen and pelvis are copiously irrigated. Reperitonealization is performed only with fine sutures and only if it can be done without tension. If a large raw bed of deperitonealized tissue remains, and if hemostasis was complete enough to permit closure of the cuff, several techniques may lessen adhesion formation: a vascularized omental carpet or a particularly redundant rectosigmoid colon can cover most of the pelvis, and Interceed can be applied to the suture lines, or intraperitoneal dextran 70 can be instilled. If



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FIG 11-7.

Management of the uninvolved adnexa at hysterectomy. The ovary is suspended from the proximal round ligament/utero-ovarian ligament stump high on the lateral abdominal wall. Care is taken not to distort the infundibulopelvic ligament with the suspension. (Copyright © Baylor College of Medicine.)

the adnexa are preserved, they must not be near any raw areas because they adhere and cause pain.

The appendix is removed if it is involved with endometriosis or if the cecum is redundant enough to allow the appendix to reach the pelvis and possibly adhere postoperatively. Cecopexy may be used to prevent descent of the cecum into the true pelvis.

### Recurrence After Hysterectomy and Bilateral Oophorectomy...

Occasionally, a patient who has had hysterectomy and bilateral salpingo-oophorectomy will present with symptoms and signs suggestive of ovarian remnant syndrome (see Chapter 23). Laboratory findings of high-normal levels of follicle-stimulating hormone, or nearly normal estradiol levels suggest the presence of ovaries. However, ovarian remnants can cause pain and masses even without biochemical evidence of ovarian function. These cases are managed surgically by careful dissection of the ureters and pararectal spaces, followed by removal of large areas of

peritoneum containing the residual ovarian tissue.<sup>21</sup> In these cases, postoperative treatment with Danazol or GnRH agonist may be warranted due to the possibility of residual disease.

## COMPLICATIONS

If the endometriosis is amenable to laparoscopic surgery, care must be taken to avoid injury to the ureters and GI tract. The largest blood vessels encountered by the careful operative laparoscopist are usually branches of the uterine artery during uterosacral ligament dissection, which can bleed severely unless grasped and coagulated or ligated. Reports of laser laparoscopic injury to the ureters are only now starting to be publicly discussed but are likely to occur in 1% or 2% of cases. Although the GI tract may be treated laparoscopically, the same precautions are taken as at laparotomy: prepared bowel, intrarectal finger to assess mural depth of dissection, and endosuturing of large areas of excision.

Repeat conservative laparotomy is associated with rare complications. Ureteric injuries may be largely prevented if the ureter is identified high on the pelvic brim and the overlying peritoneum is dissected free. The ureter itself should never be stripped of its adventitial tissue, because vascular compromise may occur, promoting fistula formation. If the ureter is denuded due to direct invasion of endometriosis, a cystoscopically placed diversionary stent should be used until healing can be assured.

If endometriosis is mild enough to permit vaginal hysterectomy, no additional complications over the ordinary are likely. However, severe endometriosis treated by abdominal hysterectomy can be as difficult as cases of severe tubo-ovarian abscess or ovarian carcinoma. Again, the ureters must be identified and dissected free under direct vision. The integrity of the bowel must also be protected; a preoperative mechanical and antibiotic prep is sorely missed should the colon be inadvertently entered.

If the blood supply to the adnexa (even if visually normal) is compromised by the surgery, oophorectomy is indicated. Otherwise, the adnexa are surgically suspended to the high lateral abdominal wall above the iliac vessels and far above the ureters and vaginal cuff.

## RESULTS

Virtually no data are available on recurrence of endometriosis after a second procedure. We have reported a 47% (7/15) pregnancy rate in infertile women treated with a second conservative laparotomy and followed at least 18 months.<sup>1</sup> We have performed a third conservative operation only rarely; this is usually in the form of an operative laparoscopy. If, on the third operation, the endometriosis is severe beyond laparoscopic surgical bounds, hysterectomy is advocated. In consultation, we have seen a single woman with endometriosis and pelvic pain operated on six times in 18 months (three laparoscopies, three conservative laparotomies); she had never had a trial of any medical treatment. The conscientious pelvic surgeon should be well versed in medical treatment of endometriosis, including peri-

operative adjunctive use. We use postoperative medical treatment for 3 months in women with severe endometriosis and those with known residua that could not be dissected free at surgery.

## HORMONAL REPLACEMENT IN THE WOMAN WITH RECURRENT ENDOMETRIOSIS

Women undergoing hysterectomy with bilateral salpingo-oophorectomy for endometriosis are often young and would benefit from estrogen replacement therapy. However, there is some concern that exogenous estrogens might stimulate endometriosis regrowth. If macroscopic disease is left behind, 3 to 6 months of postoperative Danazol or GnRH agonist treatment may decrease further recurrence. Medroxyprogesterone acetate in doses of 20 to 30 mg daily may treat both residual endometriosis and some symptoms of surgical menopause.

If there is no macroscopic residual disease, many clinicians wait 6 weeks or so before starting hormone replacement. Then, the lowest dose possible that will control symptoms is prescribed, typically beginning with 0.625 mg of conjugated estrogens daily. Due to the concern of unopposed estrogens encouraging recurrence of endometriosis, 2.5 to 5 mg of medroxyprogesterone daily is usually added.

## SUMMARY

Many of the principles for treating endometriosis at initial operation hold true for treating recurrent disease. Surgical success is dependent on excision or vaporization of all gross disease; postoperative medical treatment may then help with microscopic lesions or lesions incompletely removed at initial surgery. The infertile woman with endometriosis may be counseled that a second conservative laparotomy (and probably operative laparoscopy) has a reasonable chance of success; alternatives are *in vitro* fertilization or hysterectomy. For the woman with pelvic pain, preferably having completed her family, hysterectomy offers the greatest chance of long-term freedom from the pain of her disease. At hysterectomy, the ovaries may be preserved if normal, and oophoropexy away from the cuff will lessen the chance for deep dyspareunia that otherwise would be attributed to recurrent disease.

The frequent recurrence of endometriosis, like its ability to invade contiguous structures and metastasize to distant sites, is another example of the malignant nature of this histologically benign disease. To the woman with endometriosis, risk of recurrence is a concern second only to likelihood of relief of pain or success of conception. More research is needed as to what factors and surgical techniques promote recurrence, as well as improved noninvasive methods of screening for recurrence, such as the antibody CA 125.<sup>23</sup> Until then, the most complete operation that is also the least damaging to remaining tissues is the method of choice, requiring case-by-case individualization by the gynecologic surgeon.

## Acknowledgment

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