Endometriosis

W. GLENN HURT, M.D.
RAY A. WERTHEIM, M.D.

Department of Obstetrics and Gynecology, Medical College of Virginia, Health Sciences Division of Virginia Commonwealth University, Richmond, Virginia

Endometriosis is diagnosed when tissue which resembles the endometrial lining exists outside the endometrial cavity. Although first described as a pathological entity in the late 1800s, the term "endometriosis" was not introduced until the early 1920s by Sampson.[1] The great volume of literature which has accumulated on this topic is, by and large, a product of the 20th century.

Many theories exist as to the histogenesis of endometriosis. All may be assigned to one of three basic groups in which 1) endometrial tissue is transplanted ectopically as a result of regurgitation, metastasis, or oviduct extension, 2) endometrial tissue develops ectopically in situ from local tissues, or 3) a combination of transplantation and development in situ. Of the three groups, only the first has been documented; the other two are speculative.[2]

Grossly, endometriosis often presents as purplish, dusky red, or brownish spots or elevated nodules surrounded by varying degrees of fibrosis and scarring. Typically it involves the peritoneal surface of the ovary or ovaries, cul-de-sac, or bladder. Less frequently the bowel, appendix, bladder, ureters, cervix, vagina, and vulva are involved. Rarely, it is reported in the umbilicus, pleura, lungs, and extremities. Transplantation into surgical incisions of the abdominal wall and perineum has been documented.

Microscopic evidence of endometriosis is not always clear-cut. One would like to see endometrial-like epithelium, glands or gland-like structures, and stroma accompanied by evidence of hemorrhage. Not infrequently a picture "consistent with endometriosis" will present itself revealing hemosiderin, fibroblasts, and pigment-laden macrophages. However, one cannot be secure in the pathological diagnosis if it is based solely on such evidence.

Malignant degeneration occurring within areas of endometriosis is uncommon—less than 1%. When it does occur, it is seen much more frequently in the glandular component as an adenocarcinoma than in the the stromal component; rarely is the malignancy of a mixed type. Endometroid carcinoma of the ovary does not appear to be directly related in its histogenesis to endometriosis.

Clinically, endometriosis is a disease of the reproductive years. Although it is being seen more frequently in teenagers, it has never been reported to occur before the menarche. The disease may pose a problem for the perimenopausal woman.

The frequency with which endometriosis is reported to occur in a given population is highly variable. Perhaps as many as 20% to 25% of women 24-45 years old have some evidence of endometriosis recognizable at the time of laparoscopy. It is being detected with increasing frequency in blacks, historically a group thought to have a very low incidence of the disease.

The patient with endometriosis usually complains of secondary dysmenorrhea or pelvic pain, menstrual abnormalities, and frequently of infertility.

The pain is highly variable and its severity often cannot be related to the extent of the disease. Pain usually begins some years after

Correspondence and reprint requests to Dr. Glenn Hurt, Box 34, Medical College of Virginia, Richmond, VA 23298.

menarche and may be premenstrual or menstrual in occurrence. Extensive endometriosis may be associated with chronic pain throughout the menstrual cycle. Sometimes the disease causes pelvic pressure or a sense of heaviness and fullness which the patient does not interpret as pain. Low backache and deep dyspareunia are usually the result of uterosacral involvement. Rectal and bladder tenesmus occurs and cyclic sciatica (Head sign) has been reported.

Abormalities of menstruation consisting of hypermenorrhea and an irregular menstrual interval imply ovarian involvement. Ten percent of patients with significant endometriosis have episodes of anovulation. As the disease is commonly associated with an increased incidence of endometrial polyps, leiomyomata, and adenomyosis, these conditions must also be suspect as causes of abnormal menstruation.

Infertility may be the result of a number of factors: ovarian dysfunction, kinking of the oviducts, scarring of the fimbria, uterotubal spasm, and a decrease in coital exposure due to dyspareunia and chronic pelvic discomfort. This problem becomes more perplexing, however, when one is reminded that most patients with endometriosis ovulate, few have blocked tubal lumens, and many have previously borne children.

The patient with complaints suggestive of endometriosis may or may not have the classic physical findings of pelvic tenderness, cul-de-sac nodularity, organ fixation, or abnormal adnexal masses. Many, with minimal endometriosis, appear to offer the most complaints, whereas others, with extensive involvement, may appear relatively asymptomatic. There is yet another group in which endometriosis is only an incidental finding at the time of laparoscopy or laparotomy.

Although the pelvic findings may confirm the suspicion of endometriosis, the diagnosis cannot be made unless the disease process is visualized or biopsied. Laparoscopy has proved invaluable in the diagnosis and management of patients suspected of having endometriosis. Indications for laparoscopy are given in Table 1. When endometriosis is encountered, diagrams of the extent of involvement should be entered in the patient's medical record. The Baylor classification of pelvic endometriosis is helpful in documenting findings and serving as a guide to medical and/or surgical therapy (Table 2).[3]

TABLE 1
Indications for Laparoscopy

Severe unexplained pelvic pain
Progressively severe dysmenorrhea
Dyspareunia, especially with deep penetration
Metrorrhagia uncontrolled by dilatation and curettage and/or hormones
Pelvic findings suggestive of endometriosis
Unexplained infertility

Medical management of endometriosis is aimed at the relief of pelvic discomfort and the preservation of the patient's childbearing potential. Initially, analgesics and heat may provide relief. The patient should be advised to avoid the continued use of narcotics and alcoholic beverages. It is best not to undertake the medical suppression of endometriosis using hormonal therapy unless the disease has been documented visually or by biopsy, and the extent of involvement determined. Hormonal therapy is associated with many undesirable side effects and is expensive. Patients thought to have the disease but who in fact do not have it should be spared prolonged courses of hormonal therapy.

Current hormonal regimens employ the

TABLE 2
Classification and Treatment

MILD:	Fresh implants, minimal scarring, no adhesions, minimal or no ovarian involvement
	Rx: Medical suppression—
	Gestogens (pseudopregnancy)
	Danazol (pseudomenopause)
	Supportive therapy—
	Analgesics, heat
	No therapy
MODERATE:	Implants with scarring and retraction, adhesions, endometrioma <2 cm, minimal peritubular and periovarian adhesions
	Rx: Laparoscopic minisurgery
	Conservative surgery
	Medical suppression
SEVERE:	Endometrioma >2 cm, tube(s) and ovary or ovaries bound down by adhesions, cul-de-sac obliteration, bowel or urinary tract involvement
	Rx: Conservative surgery
	Hysterectomy with salpingo-oophorectomy
	Medical suppression, postoperative, if indicated

gestogens to achieve pseudopregnancy or danazol to achieve pseudomenopause. Hormones appear to give the best results in the treatment of mild degrees of endometriotic involvement. They are capable of relieving pain and of reducing the extent of the disease to some degree; however, they are not likely to eliminate all foci of disease and thereby effect a cure.

The gestogens, combinations of estrogen and progesterone, interrupt the negative feedback within the hypothalamic-pituitary-ovarian axis at the pituitary level. Follicle stimulating hormone (FSH) and luteinizing hormone (LH) secretions are suppressed, ovarian follicular development and ovulation are inhibited, and the secretion of ovarian estrogen and progesterone is reduced. The inherent estrogenic and progestational properties of the gestogens initially stimulate endometrial growth and induce decidual change within the endometrial tissue. Subsequently, amenorrhea and gradual atrophy of the uterine and ectopic endometrial tissue results in symptomatic relief. Pseudopregnancy regimens have been reported to provide symptomatic relief in up to 94% of patients and a corrected pregnancy rate after treatment as high as 50%.[4] The return of symptoms and the recurrence of endometriosis after therapy appear to increase progressively with the length of follow-up unless menopause ensues. The side effects of gestogen therapy include nausea, mastodynia, vaginal discharge, fluid retention, breakthrough bleeding, and on occasion, thromboembolism. Pseudopregnancy regimens should be avoided in patients with a history of thromboembolic disease and breast or endometrial carcinoma.

Danazol, a weak synthetic testosterone, has antigonadotrophic properties similar to the gestogens. It is capable of inducing a pseudomenopausal state with its associated amenorrhea and endometrial atrophy but is unassociated with many of the undesirable side effects of gestogen therapy. Danazol suppresses FSH and LH secretion and therefore inhibits follicular development, ovulation, and corpus luteum formation. Ovarian estrogen and progesterone secretion is reduced to a minimum, causing endometrial atrophy and amenorrhea. This inactivity and atrophy of ectopic endometrial tissue allows reabsorption and healing. Side effects of danazol therapy include the vasomotor symptoms of menopause, weight gain, edema, vaginal spotting, and acne. Fortunately, significant androgenic effects are rare as the usual antigonadotrophic dose required for the treatment of endometriosis is approximately one third that capable of causing masculinization in the woman. Symptomatic improvement with the danazol-pseudomenopausal regimen is reported in up to 92% of patients. Clinical improvement is noted in approximately 60% and a corrected pregnancy rate of 50% is said to exist. Unfortunately, the recurrence of symptoms is relatively high after discontinuance of therapy. As with the pseudopregnancy regimen, conception after therapy prolongs the asymptomatic interval.

Moderate involvement with endometriosis is best treated with laparoscopic minisurgery for the lysis of adhesions, freeing of the ovaries, and cauterization of implants; a more extensive laparotomy may be required. Conservative surgery, in cases of moderate and severe involvement with endometriosis, is undertaken in an effort to correct reflux menstruation, relieve pelvic pain, and improve fertility. It consists primarily of lysis of adhesions, the excision or destruction of all discernable endometriotic implants and cysts, and is often accompanied by uterine suspension and presacral neurectomy in an effort to prevent subsequent retrofixation of the uterus and provide relief of pelvic pain. Conservative surgical approaches have been shown markedly to improve symptoms and childbearing potential. The addition of a pseudopregnancy regimen to surgery, although recommended by some, has in most cases not significantly added to the success of the operation as measured by subsequent pregnancy or reducing the need for future surgery. Approximately one quarter of patients undergoing conservative surgical therapy for endometriosis will require future operative procedures because of endometriotic involvement.[5]

In severe cases of endometriotic involvement, "radical" surgery, such as total abdominal hysterectomy and bilateral salpingo-oophorectomy, may offer the only hope of a cure. If this is not an acceptable alternative for the particular patient, the physician should realistically think in terms of palliation rather than cure. The growth of ectopic endometrial tissue cannot be permanently eradicated as long as functioning ovarian tissue remains within the body. Castration causes the involution and

death of active foci of endometriosis; however, the patient may still be left with fibrotic adhesions and other residua which continue as a source of chronic pain. In selected cases, it may be advisable to follow a surgical approach to the treatment of endometriosis with a pseudopregnancy or pseudomenopausal regimen for the continued suppression of residual disease.

Hormonal therapy for the surgically-induced menopause may be required. If this can be anticipated, it is best to be sure that all foci of disease are removed at the time of surgery and not to depend upon castration alone to inactivate residual disease. If all endometriosis has been removed, the patient may be started on conjugated equine estrogen. If it is thought that some endometriosis remains, it is best to delay hormonal therapy for six months or treat the patient for that period of time with medroxyprogesterone acetate; subsequently conjugated equine estrogen therapy may be instituted on a cyclic basis.

Table 2 is adapted from *Obstetrics and Gynecology* (42:19–25, 1973).

REFERENCES

1. SAMPSON JA: Perforating hemorrhagic (chocolate) cysts of the ovary. *Arch Surg* 3:245–323, 1921.

2. RIDLEY JH: The histogenesis of endometriosis. *Obstet Gynecol Surv* 23:1–35, 1968.

3. ACOSTA AA, BUTTRAM VC, BESCH PK, ET AL: A proposed classification of pelvic endometriosis. *Obstet Gynecol* 42:19–25, 1973.

4. SOTREL G, DMOWSKI WP: Endometriosis and its management. *Obstet Gynecol Digest*, June 1976.

5. ANDREWS WC, LARSEN GD: Endometriosis: Treatment with hormonal pseudopregnancy and/or operation. *Am J Obstet Gynecol* 118:643–651, 1974.